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会長講演 (Presidential Lecture)

ともに歩む、広がる産婦人科の未来へ

Walk hand-in-hand into the expansive future of obstetrics and gynecology

東京大学 大須賀 穰

The University of Tokyo

OSUGA Yutaka

世界的にみても規模の大きい日本産科婦人科学会の会長を担当いたしますことは身に余る光栄です。科学に国境はないと言いますが、医療には明確に国境があります。若いころは普遍性のある医学に興味を持って仕事をしていましたが、年長になるにつれ多様な社会的要因を総合的に勘案してベストの医療を実践する産婦人科学に魅力を感じて仕事をするようになりました。私個人としての業績は残念ながらほとんどありませんが、我が国の産婦人科に少しでも貢献するため長年にわたり多くの仲間と行ってきた仕事と考えてきたことをご紹介させていただければと存じます。私は1985年に卒業しました。解像度の悪い経腹超音波しかなく、開腹手術しかない時代でした。体外受精は始まっていましたが、妊娠率は悪く、極めて限られた治療と考えられていました。肺サーファクタントの実用化前で新生児治療は今よりはるかに厳しく、24週未満は胎児が母体外において生命を保持することのできない時期とされていました。また、子宮頸がんにおいてはその原因はHPVであることがやっとわかってきた時代でした。私が初期の臨床研修を終えるころ大学で体外受精が開始されたこともあり、生殖医療に興味をもちました。不妊症診療と腹腔鏡の進歩により、それまであまり注目されなかった子宮内膜症が注目され始めた時代でもあります。学位の仕事と留学先での仕事は生殖生理に関するものでしたが、2000年ころより子宮内膜症の診療と研究に注力するようになりました。子宮内膜症の病因はいまだ謎に包まれており、抜本的な治療法は見つかっていません。し

かしながら、時代とともに疾患の問題点の解明と対策の進歩が着実に進んでいます。子宮内膜症は生殖医学、女性医学、婦人科腫瘍学、周産期医学のすべてに関わっており、産婦人科全体の理解なくして対応できない疾患と言えます。また、子宮内膜症診療の進歩は関連する領域の進歩と密接にかかわっています。例えば、不妊症との関係では生殖補助医療の発展とともに子宮内膜症への対応が変化しています。腹膜病変、癒着病変が重視された時代について、チョコレート嚢胞への対応について検討が進み、昨今は卵子凍結の併用が検討されるようになってきました。また、女性医学の観点から見ると、女性活躍における疼痛コントロールが重要視されてきたため長期間の薬物療法の開発が進みました。晩産化にともない子宮内膜症の類縁である子宮腺筋症の治療も重要な問題となっており、本疾患の手術療法は日本が中心になって進んでいます。私が取り組んできた子宮内膜症の研究と診療を軸にダイナミックに変化する産婦人科診療の姿と、日本の産婦人科の将来に向けて皆でどのように取り組み、発展させていくことができるかを考えてみたいと思います。

My work for my PhD degree and the work I did abroad as a post-doc was mainly for reproductive physiology. From around 2000 I began to focus on the treatment and research of endometriosis. Endometriosis is related to reproductive medicine, general gynecology, gynecological oncology, and perinatal medicine, and it is not exaggerated to say that it is a disease that cannot be treated without the understanding of all fields in obstetrics and gynecology. That's the attractiveness of "endometriosis". Advances in endometriosis treatment are closely related to advances in the related fields. For example, in re-

lation to infertility, the treatment of endometriosis has been changed along with the development of ART. Historically, following the era when emphasis was placed on peritoneal lesions and adhesions, consideration has been given to the treatment of chocolate cysts, and in recent years, to the combined use of egg freezing. From the perspective of general gynecology, the development of long-term drug therapy has progressed as pain control has become more important for working women. In my talk, I would like to extrapolate the concept and philosophy I found in endometriosis to the whole OBGYN.

特別講演 1

不妊症克服のためにさらなる原因の究明と新たな治療法を目指して

手稲溪仁会病院 山田 秀人

卒業した後の1984年、大学病院で研修中に妊娠24週頃に死産を繰り返すオホーツク地方の赤い顔をした妊婦の3回目の妊娠の担当になった。梅毒反応偽陽性で、妊娠が進むにつれて血小板数が減るので病名ITPをつけてPSL 60mg/日を投与していた。保険適用となっていなかったが、Imbach (1981) と Wenske (1983) の論文があったので、大学校費により免疫グロブリン大量療法を初めて実施した。重症妊娠中毒症をヒドララジン、メチルドパで何とかしのぎ、妊娠30週にたどり着いて生児を得ることができたので、新人ながら大変嬉しかった。症例は、私の最初の論文業績となった。Harris (1983) と Hughes (1986) によって提唱された抗リン脂質抗体症候群は、札幌で開催された国際カンファレンスの Sapporo Criteria によって世界に広まった。一方、夫リンパ球免疫は、Taylor (1981) と Beer (1981) から始まり、Mowbray (1985) がRCTで有効であると報告した。直後から全国の大学教室ラボで、実験助手が Ficoll で夫リンパ球を分離し照射して、看護師が皮下注射をし始めた。倫理委員会が存在しない時代である。Muller-Eckhardt が、免疫グロブリンが習慣流産に有効であると論文発表した1991年に、教授から大学の習慣流産外来を担当するように言われ、口が悪い講師からは習慣流産は重箱の隅をつつく学問だと言われた。しかし、習慣流産は、光り輝いていた。多くは Lancet である。大学には、難治性疾患をもつ多くの患者がたえず紹介されてくる。産科は予知と予防である。遺伝病、膠原病、胎児異常、習慣流産、好むと好まざるによらず、だれかが主治医となって、次の妊娠は今回より上手いかせなくてはならない、それが不妊症だと思う。これを機に私の不妊症研究が始まった。

<免疫学的異常の解明>

絨毛抗原に対する細胞性免疫活性化、高い HLA-DR4 allele 頻度、子宮内膜 Th 細胞減少、血液 NK 細胞の抑制型レセプター減少、染色体正常流産リスクの NK 細胞高活性と MIF 低レベル、慢性子宮内膜炎、子宮内膜フローラ異常など免疫学的異常が関与する新知見を発表した。

<ゲノム疫学解析>

遺伝子多型解析により、GSTMI null, IL-6 634 G, PAPP-A C, CYP17 A2 が不妊症の、CYP17 A1 と COMT L は胎児発育不全の疾患感受性遺伝子であることを発見した。特に、CYP17 A2*1 F (C731A) 保因者はカフェイン摂取量の増加にともない、不妊症リスクが高くなることを初めて報告した。

<免疫グロブリン大量療法の開発と有効性の証明>

4回以上流産歴のある原因不明難治性の不妊症に対する妊娠初期免疫グロブリン大量療法 (IVIg) を世界で初めて発表した (1998)。流産マウスモデルで、IVIg の脾細胞を介した流産抑制効果を証明した。多施設共同研究として6年以上にわたる二重盲検ランダム化比較試験を完了し、IVIg はプラセボに比べて妊娠継続率と生産率が有意に高いことを証明した (2022)。本治療の保険収載が待ち望まれる。

<新たな抗リン脂質抗体の発見と応用>

私たちが2015年に発見したネオセルフ抗体 (anti- β 2GPI/HLA-DR antibody) は、不妊症、不妊症、子宮内膜症性不妊、反復着床不全、妊娠高血圧症候群、胎児発育不全の15~29%に高頻度で陽性となる。妊娠前に抗体検査を受け、陽性では低用量アスピリン、ヘパリン、HCQなどの抗炎症、抗凝固治療によって安心安全な妊娠と出産、健康な出生児に繋ぐ、不妊、不育、周産期にわたるプ

レコンセプションケアを確立させたい。

Special Lecture 1

A perspective of new therapeutic approaches and future investigation of the cause in re

YAMADA Hideto

Teine Keijinkai Hospital

From 1984, I have long been engaged in the practice, basic and clinical researches, and the development of new therapeutic modality for recurrent pregnancy loss (RPL) and antiphospholipid syndrome (APS). As an historical background of those days, Imbach (1981) and Wenske (1983) found intravenous immunoglobulin treatment (IVIG) was effective for immune thrombocytopenia through Fc receptor. Harris (1983) and Hughes (1986) first proposed APS as a new clinical entity, and thereafter Sapporo Criteria was established in 1998. Taylor (1981) and Beer (1981) started lymphocyte immunization, and then Mowbray (1985) propagated it by a randomized placebo-controlled trial. In 1991, Muller-Eckhardt first reported intravenous immunoglobulin treatment (IVIG) was effective against habitual abortion. In a such circumstance, my research on RPL and APS began to progress.

<Immunological abnormality and inflammation >

We demonstrated that immunological abnormalities including the presence of embryo-toxic factor, high HLA-DR4 allele frequency, decreases in NK cell inhibitory receptor in the blood, decreases in Th cells in the uterine endometrium, and the presence of chronic endometritis are causally associated with unexplained RPL. High NK cell activity and low levels of macrophage migration inhibitory factor in the blood during early pregnancy increase a risk of subsequent

miscarriage with normal chromosome karyotype.

<Genetic polymorphism >

GSTM1null, IL-6 634G, PAPP-A C and CYP17 A2 are risk alleles for RPL, while CYP17 A1 and COMT L are for fetal growth restriction. Women with CYP17 A2*1F (C731A) carry a higher risk of developing RPL as caffeine intake increases.

<A high dose of IVIG >

In 1998, we for the first time reported 11 cases of RPL women who received a high dose of IVIG (400 mg/kg, 5 days) during early pregnancy. Immunoglobulin administration restored fecundity in poly (I : C) induced mouse model of miscarriages. A 6-year multicenter study in Japan, a double-blind, randomized, placebo-controlled trial on women with primary RPL, revealed a high dose of IVIG during early gestation, especially treated at 4-5 weeks of gestation, was highly effective in increasing live birth rates in women with ≥ 4 RPLs of unexplained etiology in 2022. As IVIG increased Treg percentages and suppressed NK cell activity in the blood, these could be mechanisms of the efficacy.

<Neo-self antibody >

In 2015, we discovered a neo-self antibody (anti- β 2GPI/HLA-DR antibody) is involved in obstetric APS. Women with RPL, infertility, endometriosis, recurrent implantation failure, hypertensive disorders of pregnancy, and fetal growth restriction have been found to test posi-

tive for the antibody with a high incidence of 15-29%. A new preconception care, where high-risk women undergo neo-self antibody screening prior to pregnancy and those with a positive test receive anticoagulation and/or antiinflammation

therapy before and during pregnancy, could lead to improved fertility, favorable pregnancy outcomes and healthy newborns throughout fields of reproduction, obstetrics and neonatology.

特別講演 2

妊産婦死亡登録事業から母体安全への提言と J-CIMELS へ

三重大学 池田 智明

2006年に起こった、奈良県大淀町立病院における分娩中の脳出血による妊産婦死亡と、前年に発生した福島県立大野病院の癒着胎盤による妊産婦死亡は、わが国の周産期医療の弱点をついた、産婦人科のみでなく社会的な事件であった。これらの事件に直接、間接的に関与してきた私は、一人でも妊産婦死亡例を減らすために努力すべきと強く思った。偶然にも2006年から厚生科学研究の研究代表者として、わが国の妊産婦死亡に関する研究班を主催してきたことから、専門性、中立性、公平性を担保した、英国で行われているような死亡事例検討評価組織がわが国でも必要であると考えていた。

日本産婦人科医会にお願いし、2010年から従来あった偶発事例報告事業から、妊産婦死亡を切り離し、妊産婦死亡報告事業が開始された。わが国で発生した妊産婦死亡を日本産婦人科医会で登録し、死因、行われた医療との関連、予防策などを、一つ一つ検討していくシステムである。妊産婦死亡症例検討委員会は、産婦人科医師のみでなく、麻酔科医、法医、救急医、病理医、精神科医、内科医、脳神経外科医および弁護士などの多職種で構成されている。毎月開かれる小委員会での報告案を、3か月毎に開催の本委員会で承認する形をとっている。2023年6月までの13年半の間に、587例が登録され、558例を解析した。毎年、「母

体安全への提言」を発刊し、産婦人科のみでなく麻酔科、病理などの多職種にも配布している。この提言の一部は、産婦人科診療ガイドラインにも採用されている。13年前は、産科危機的出血が死因の約30%とトップであったが、最近では、産科危機的出血、頭蓋内出血・梗塞、心肺虚脱型羊水塞栓症、心・大血管疾患、感染症および肺血栓塞栓症の6つの疾患が、代わる代わるのトップとなっている状態である。2019年をボトムに全体死因の7%と減少していた産科危機的出血は、2020年から再度上昇し20%前後である。出血死の原因も、「子宮羊水塞栓症」が以前は半数を占めていたが、最近の増加は、癒着胎盤と子宮破裂が増加し、生殖医療との関連が疑われる。2021年からは、「ニアミス症例」として周産期心筋症など6疾患の生存例を登録する妊産婦重篤合併症報告事業も開始した。また、2015年からは、救急医との協働により、日本母体救命システム普及協議会(J-CIMELS)を設立した。これは、日本産科婦人科学会など6団体からなる、周産期医療関係者に標準的な母体救命法を普及させることを目的とした、講習会の運営などを行う事業である。これまで、全都道府県で行われ、ベーシックコースは約20,000人が受講した。これらの事業を通して、妊産婦死亡を一人でも減少するように、活動している。

Special Lecture 2

Maternal death registration projects, Recommendations for Maternal Safety and the J-CIMELS

IKEDA Tomoaki

Mie University Hospital

The maternal deaths in 2006 at Oyodo Town Hospital in Nara Prefecture due to cerebral hemorrhage during delivery, and the death at Fukushima Ohno Hospital due to placenta accreta in the previous year, highlighted significant flaws in Japan's perinatal care. These incidents, which transcended medical issues and became social concerns. The author, as the Principal Investigator of Health and Welfare Science Research since 2006, led a research group on maternal deaths in Japan. Recognizing the necessity for a professional, neutral, and impartial evaluation organization for death case reviews in Japan, similar to the system in the UK, the author advocated for such an initiative to improve care standards.

In 2010, the Japan Society of Obstetricians and Gynecologists (JSOG) initiated a separate maternal death reporting project from the existing accidental case reporting system. This project involves the Japan Obstetrician-Gynecologist Association registering maternal deaths in Japan, examining each case for cause of death, medical

treatment relationships, and preventive measures. The committee includes diverse professionals like obstetricians, anesthesiologists, forensic physicians, and more. From its start until June 2023, 587 cases were enrolled and 558 analyzed. Annually, the "Recommendations for Maternal Safety" are published and distributed widely across medical fields. Previously, obstetric hemorrhage was the leading cause of maternal death (about 30%), but recently it has been replaced by six diseases including intracranial hemorrhage and amniotic fluid embolism. There's been a recent rise in obstetric hemorrhage deaths, possibly linked to reproductive medicine complications. From 2021, a project to report serious maternal complications, including "near miss cases", began. Additionally, in 2015, the Japan Council for the Dissemination of Maternal Life Support Systems (J-CIMELS) was established to disseminate standard lifesaving methods in perinatal care, with about 20,000 participants in its courses across Japan. These efforts aim to significantly reduce maternal deaths.

特別講演 3

産婦人科と感染症診療 特に母子感染と胎盤関門

日本大学病態病理学系微生物学分野 早川 智

19世紀末から20世紀にかけての微生物学・免疫学の進歩は感染症診療の革命をもたらした。産婦人科領域でも、ゼンメルワイスによる無菌法の開発に始まり、抗微生物薬やワクチンの開発は多くの手術や分娩、周産期管理を安全なものとした。1967年には米国の公衆衛生の責を負う高官が議会で「いまや感染症の教科書を閉じる時がきた」と喝破した。しかしながら、現実にはそうでないことを AIDS, SARS, MARSそして今回の COVID-19 などの新興感染症、そして結核や梅毒などの再興感染症の世界的流行が物語っている。

私は卒後40年、米国留学中を除き常に産婦人科診療と同時に母子感染と生殖免疫の研究に従事してきた。脱落膜における母体免疫応答の解析中に、まず妊婦が感染症に罹患しても必ずしも子宮内感染が成立しないことから、免疫系以外に未知の胎盤関門の存在するのではないかという疑問を持った。ベトナムと共同研究により世界に先駆けて垂直感染しやすい HIV サブタイプと、絨毛細胞における細胞内ウイルス核酸認識機構を発見した。次に、長く謎であった風疹の経胎盤感染には絨毛の低血糖・高血糖による酸化ストレスが重要であること、ジカ熱では炎症により誘導される TGF- β がレセプターの増強を介して関与することを明らかにした。一方、消化管や生殖器における細菌叢と粘膜免疫の研究では、子宮内腔に存在するごく少量の *Lactobacillus crispatus* が絨毛の浸潤を促進する一方、口腔から迷入する歯周病菌 *Polyphyllomonas gingivalis* はこれを抑制し FGR や HDP 発症に関与する可能性を示唆した。2007年以降、第一線の産婦人科診療から基礎医学であ

る微生物学・免疫学の教室に移籍したが、引き続き産婦人科の Physician Scientist を目指し続けた。我が国では広域性抗菌薬の不適切な長期投与が日常的に行われており、有名な MRSA に加えて ESBL 産生菌やカルバペネマーゼ産生菌の分離率が上昇しているため他科の医師とともに抗菌薬適正使用の呼びかけや LAMP 法、multiplex PCR による耐性診断と耐性菌分離率の解析を続けた。ここに降ってわいたのが COVID-19 である。日本産科婦人科学会、日本産婦人科医会、日本産婦人科感染症学会のご協力で2020年春という早い時期から COVID-19 感染妊婦に関する全国規模の臨床統計を開始、併せて国のガイドラインである「診療の手引き」の策定、胎盤病理と胎盤関門の解析、ワクチンの副反応の全国調査、新規ワクチン候補の開発と今までの経験を全て傾注した。当初危惧された母子感染は極めて稀であったが、未接種者では母体の重症化に加えて、胎盤炎による胎児機能不全や死産が多いことから、積極的なワクチン接種を呼びかけた。興味深いことに COVID-19 感染妊婦の多くでは胎盤にウイルスが検出されるが、児には感染せず強力な胎盤バリアが存在することが示唆された。この分子機構も現在いくつかの候補遺伝子を同定するに至った。幸いなことに我国では妊婦の接種率が高いこともあって母体死亡はなく、死産も諸外国に比較して少ない。「人間生まれてきたからには一事を成せ」司馬遼太郎が「坂の上の雲」で主人公秋山好古に託した言葉である。コロナウイルスとの戦いで産婦人科と感染・免疫を専攻する一医学徒が何かできればこれほど嬉しいことはない。

Special Lecture 3

Infection disease control in Obstetrics and Gynecology Especially focus on placental barriers and maternal-fetal transmission

HAYAKAWA Satoshi

Nihon University

Advances in microbiology and immunology from the 19th century revolutionised the treatment of infectious diseases. In obstetrics and gynaecology, developing antimicrobial agents and vaccines, beginning with the aseptic technique discovered by Semmelweiss, has made surgeries, deliveries, and perinatal care safer.

In 1967, a senior official responsible for public health in the United States exclaimed to Congress, "It is time to close the textbook on infectious diseases." However, this is not the case, as evidenced by the global epidemics of emerging and re-emerging infectious diseases.

As a post-doctoral fellow in the United States, I began researching unknown placental barriers in placental tissue. In collaboration with Vietnam, we were the first to discover the HIV subtypes susceptible to vertical transmission and the intracellular viral recognition mechanism in trophoblastic cells. Next, we found that oxidative stress in the trophoblasts is essential for transplacental transmission of rubella and that TGF- β induced by inflammation is involved in Zika fever. We also studied bacterial flora and mucosal immunity in the gastrointestinal tract and reproductive organs. We discovered enhanced trophoblastic invasion by *Lactobacillus crispatus* and suppression by *Polyphyomonas gingivalis*, a periodontal bacteria which might cause FGR and

HDP. In Japan, inappropriate long-term administration of broad-spectrum antimicrobial agents is joint, and the isolation rates of ESBL or carbapenemase-producing bacteria are increasing. Thus, we also continued to analyse the diagnosis of antimicrobial resistance by molecular techniques.

Then COVID-19 appeared in late 2019. We started a nationwide clinical survey on COVID-19-infected pregnant women in the early spring of 2020. We also devoted all of our experience to formulating the "Shinryo no Tebiki" national guideline based on the analysis of clinical courses. We also examined placental pathology, the placental barrier, and the development of new vaccine candidates. Interestingly, in many COVID-19-infected pregnant women, the virus was detected in the placenta, but the fetus was not infected, suggesting the existence of a robust placental barrier. We have now identified several candidate genes for this molecular mechanism. Fortunately, in Japan, there have been no maternal deaths and fewer stillbirths than in other countries due in part to the high vaccination rate among pregnant women.

Nothing would make me happier than to do something in the fight against COVID-19 as a physician-scientist in obstetrics, gynaecology, infection, and immunology.

特別講演 4

新しい胚着床機構の解明とその臨床応用を目指して

金沢大学 藤原 浩

哺乳類はその生殖機構として子宮内での胎児発育を選択したため、子宮内膜への胚侵入から胎盤形成に至る一連の着床過程で、胚-母体間の相互応答や母体組織の再構築を行うことが必要となった。着床に必要な子宮内膜分化の誘導には卵巣から分泌される性ステロイドホルモンのみならず、胚からの因子も重要と推察され、胚-母体間のクロストークの存在が想定されているがその詳細な分子機構は解明されていない。演者らは体外受精・胚移植法でスキップしている受精および胚発生に伴う生体内で一連の胚-母体間の相互応答の過程を免疫学的な機構に焦点をあてて解析し、この機

構を応用して着床不全患者に対する自己免疫細胞を用いた治療法を開発してきた。一方で着床後の胎盤形成について子宮内膜に浸潤する絨毛外栄養膜細胞の機能に焦点をあて、絨毛外栄養膜細胞に特異的に発現するリーベリン分子を発見し、新規の胚シグナル分子としてその機能を解明してきた。その結果リーベリン分子の免疫系に対する作用やがん細胞における役割が明らかにされ、産婦人科から他科に発信する新たながん治療法の開発へと繋がってきた。本講演では生殖医学から他領域の学問への橋渡しの研究例としてこれまでの成果を紹介する。

Special Lecture 4

Embryo implantation mechanisms and clinical application

FUJIWARA Hiroshi

Kanazawa University

Since mammals have chosen to develop the fetus in the uterus as their reproductive mechanism, the embryo-maternal interaction and the remodeling of maternal tissues became necessary during the series of implantation processes, from embryo invasion into the endometrium to placenta formation. In order to induce endometrial differentiation sufficient for embryo implantation, not only sex steroid hormones secreted by the ovary but also factors from the embryo are thought to be essential. However, the detailed molecular mechanism of embryo-maternal crosstalk has not been elucidated. We focused on immunological mechanisms and analyzed the series of in-vivo embryo-maternal interactions accompanying fertilization and embryonic development, which are skipped in in vitro fertilization and embryo transfer treatment.

Applying this mechanism, we have developed a new treatment method using autoimmune cells for patients with implantation failure. On the other hand, regarding placenta formation after implantation, we focused on the function of extravillous trophoblast cells that invade the maternal endometrium, and discovered a new embryonic signal molecule called “laeverin” that is specifically expressed on extravillous trophoblast cells. The subsequent functional analysis revealed that laeverin regulates the immune system. It has also been shown that cancer cells use this molecule, leading to the development of new cancer treatments. In this lecture, we will introduce our results as an example of translational research from reproductive medicine to other medical fields.

特別講演 5

とことんやろう—婦人科がんの予後向上を目指して（二つの視点）—

東海大学 三 上 幹 男

医師になってから約40年、私はその大部分を婦人科腫瘍の臨床・研究に費やしてきた。体調を崩すまでは眼前の患者のために根治を目指し長時間にわたる手術を実践し、特に“Super-Radical Hysterectomy”および“Para-Aortic Lymphadenectomy”については、国内はもとより世界、欧州、米国、アジアでの婦人科腫瘍学会でその動画を披露する機会を得、術式・適応について多くの議論をすることができた。過去24年間（2017年まで）に行った手術件数は4000例に及ぶ。

また日本婦人科腫瘍学会（JSGO）が策定している婦人科がん治療ガイドライン作成に12年間かわり、その導入により日本全国でのがん治療の均霑化を行うことが可能となり、眼前の患者でなく全国の患者の予後改善を可能とすることも実感した。日本産科婦人科学会（JSOG）婦人科腫瘍委員会にも参加し、検証が必要ではあるが、婦人科癌の中で最も治療に難渋し予後が不良である卵巣がんの発症予防としての良性疾患における卵管切除を本邦で普及させた。

さらにJSOG倫理委員会（2022.6臨床倫理監理委員会に改称）にて着床前遺伝学的検査に関わる立場となり、遺伝性乳がん卵巣がん患者本人および血縁者への着床前遺伝学的検査の応用の可否についての議論を開始する素地を整えることができた。今後、社会を巻き込んだ話し合いを期待したい。

またJSGOにおいてJESGO（婦人科悪性腫瘍総合入力システム）の立ち上げを行った。これは

JSOG, JSGO, 日本産婦人科内視鏡学会（JSGOE）の会員が共同で悪性腫瘍データを入力することが出来る施設サマリノートのようなシステムである。まだいくつかの段階を踏む必要があるが、将来的には日本全国の悪性腫瘍患者データを常時収集できる米国のSEERデータベースのようなものを構築することが可能となる。

さて私がライフワークとしてきた研究テーマは「血清糖蛋白を用いた卵巣がん早期発見」である。既存血清がん関連糖蛋白（CA125, HE4など）と血清総糖蛋白を分解して得られた全糖ペプチドピークデータ、つまり卵巣がんが分泌する腫瘍マーカーと被験者の健康状態を反映していると予想される糖ペプチドすべてを、人口知能に学習させ卵巣がんの有無の診断を行うモデルを開発し、現在そのモデルの精度向上と社会実装を目指して検診センターと複数の共同研究施設とで臨床研究に取り組んでいる。

長年に渡る婦人科腫瘍医としての歩みから私が学んだことは、臨床腫瘍学を実践するには眼前の患者を診る視線と日本あるいは世界全体を俯瞰してみる視線を持ち、両者の重要性を理解することであった。本講演では、この二つの視点を婦人科腫瘍学を学ぶ医師に伝え、豊かな人間性を備え患者に寄り添いかつ常に最新の医学知識・技術を備えた医師、日本国内に留まらず世界レベルで婦人科腫瘍で悩む患者をトータルで考え何をすべきかを考えていける医師、が育っていくことを期待したい。

Special Lecture 5

Let's go all the way-Toward improving the prognosis of gynecological cancer (two perspective)

MIKAMI Mikio

Tokai University Hospital

For the past 40 years, since I became a physician, I have dedicated most of my time to clinical and research endeavors in gynecologic oncology. I spent countless hours performing surgeries to cure patients before me, particularly procedures like “Super-Radical Hysterectomy” and “Para-Aortic Lymphadenectomy.” I had the opportunity to showcase videos of these techniques in Japan, Europe, the United States, and Asia.

I also played a crucial role in the development of gynecological cancer treatment guidelines by JSGO for 12 years. Recognizing that these guidelines could standardize cancer treatment across Japan, improving the prognosis of patients nationwide, was profoundly gratifying. Additionally, I contributed to the Gynecologic Oncology Committee of JSOG. While further verification is necessary, I advocated for the use of tubal excision in benign diseases as a preventive measure against ovarian cancer.

Furthermore, my involvement in preimplantation genetic testing (PGT) at the JSOG Ethics Committee paved the way for discussions about applying PGT to patients with hereditary breast cancer, ovarian cancer, and their blood relatives. We eagerly anticipate more societal discussions in the future.

I also helped launch JESGO (Japan Entry System of Gynecologic Oncology), a system akin to an institutional summary note. It enables members of JSOG, JSGO, and JSGOE to input malig-

nant tumor data collaboratively. Though several steps are still needed, our goal is to create a database resembling the SEER database in the U.S., collecting malignant tumor patient data from all over Japan continuously.

My research theme has been “Early detection of ovarian cancer using serum glycoproteins”. I have developed a model that uses total glycopeptide peak data obtained from the degradation of serum total glycoprotein (which is expected to reflect the health status of the subject) and tumor markers (CA125, HE4, etc.) secreted by ovarian cancer to train artificial intelligence to diagnose whether ovarian cancer is present. Clinical research is currently underway to improve the accuracy of the model and to implement it in society.

What I have learned over the years as a gynecologic oncologist is that in order to practice clinical oncology, one must have the perspective of seeing the patient in front of one's eyes and the perspective of looking at Japan or the world as a whole, and one must understand the importance of both. In this lecture, I would like to share these two perspectives with physicians studying gynecologic oncology, and hope that they will become physicians with rich humanity, who are close to their patients and always equipped with the latest medical knowledge and techniques, and who can consider patients suffering from gynecologic oncology on a global level

as well as in Japan, and what they should do in their total care.

招請講演 1

ハイパフォーマンスからライフパフォーマンスへ～国民のライフパフォーマンス向上を目指した取組

スポーツ庁 室 伏 広 治

招請講演

スポーツ活動を通し国民が生涯にわたり、心身の健康の保持増進及び安全の確保が図られることは重要である。そのためには、自主的かつ自律的に個人の適性及び健康状態に応じたスポーツが実施される仕組みが必須である。

このため、スポーツ庁では、第3期スポーツ基本計画に基づき、多くの人々が「楽しさ」や「喜び」、スポーツを通じた心身の健康増進等といったスポーツの価値を享受できる社会の構築を目指し、スポーツの実施に関し、広く一般に向けた普及啓発や環境整備を行うなど、国民のスポーツ実施率を向上させるための施策を推進している。一方、これまでの取組に加え、運動・スポーツの効果をより高めるべく、質的な視点を持った取組を更に推進することが重要である。

運動・スポーツを実施することで得られる効果は、体力向上から不安・抑うつ等の軽減まで多岐にわたる。これらの効果を高めるためには、スポーツを支える土台としてのコンディショニングや、その方法としての多様な目的を持った運動（エクササイズ等）の実施により、心身に多様な変化を与えることが重要となる。これまでスポーツ医・科学分野では、コンディショニングを含めた運動・スポーツの効果に関する知見が数多く報告されている一方、そのような知見を国民一般に活用するまでには十分に至っていない。こうしたハイパフォーマンススポーツのサポートで得られたスポーツ医・科学分野の知見等を国民一般の運動・スポーツの実施に活用することが必要であり、それは、運動・スポーツの質を高め、その後の継続や定着が図られることに加え、運動・スポーツを通じてライフパフォーマンスの向上（それぞれの

ライフステージにおいて最高の能力が発揮できる状態）が図られることにより、健康増進、QOLを高められるなど、生きがいのある人生を送ることに寄与することができる。

女性アスリートの場合、スポーツ医科学に係る研究や様々な取組によって、多くの知見が報告されている。競技成績を求めた過度な練習や食事の制限は、貧血や無月経、疲労骨折などの障害の発症リスクの増大といった健康被害につながる場合もあるため、アスリート本人や指導者を含め、全ての関係者が、それぞれに正しい知識を身に付けることが重要となる。

スポーツ庁でも、これまで、「女性アスリートの育成・支援プロジェクト」、「大学等における調査研究」、「研究で得られた知見を競技現場に還元する取組」、「女性アスリート支援プログラム」、「中高部活動における女子生徒の課題解決型実践プログラム」等の様々な取組を行ってきた。

これらの取組によって、トップレベルのアスリートには、過度な練習や食事制限による危険性がかなり認知されてきた。他方、ジュニア世代や中学生、高校生世代の選手は正しい知識がないまま激しいトレーニングをしているような指摘もあり、知見の普及は十分に至っていない。

こうしたことを踏まえ、スポーツ医科学で得られた知見をトップアスリートに加えて、ジュニア世代や、さらにその指導者、保護者の方々を含めて、全ての女性の運動・スポーツの実施やその指導に活用することが必要である。このような取組は、運動・スポーツの質を高め、その後の継続や定着が図られ、女性アスリートのパフォーマンスの向上や怪我の予防から女性の運動実施率向上や

ライフパフォーマンスの向上にも寄与することが できる。

Invited Lecture 1

From High Performance to Life Performance-Initiatives Aimed at Improving the Life Performance of the Nation

MUROFUSHI Koji

Japan Sports Agency

Promoting lifelong physical and mental health through sports is crucial. The Japan Sports Agency has developed its third-term basic sports plan and strives to create a society where people embrace the values of sports and enhance their well-being. Initiatives involve widespread promotion, environmental enhancements, and efforts to elevate the quality of sports participation.

To amplify the benefits of sports, such as enhanced fitness and mental well-being, a focus on conditioning and diverse exercises is imperative. Importantly, applying insights from top athletes' (high-performance) conditioning knowledge to the general population (life-performance) is critical for optimal health promotion.

Within the context of female athletes, acquiring proper knowledge is essential to mitigate health risks tied to intense training and dietary restrictions. The Japan Sports Agency has initiated projects to foster the development and support of female athletes. While risks have been identified among top athletes, disseminating this knowledge to junior athletes is crucial. The application of sports medicine insights, not only to elite athletes but also to the wider population, including coaches and parents, is necessary. These initiatives contribute to advancing sports quality, ensuring continuity, enhancing female athlete performance, and promoting increased overall female sports participation and life performance.

招請講演 2

Medical Abortion

Karolinska Institutet, Sweden Gemzell Danielsson Kristina

Safe, effective and acceptable comprehensive abortion care includes access to safe abortion, postabortion care, postabortion contraception provision and reproductive health counseling. This is a prerequisite for reproductive health and thus forms fundamental human rights. There is a global need to increase knowledge among abortion providers to provide the most effective evidence-based methods and to stop using outdated methods. Medical abortion holds the potential to improve reproductive health and autonomy.

Medical abortion with mifepristone and a prostaglandin analogue was innovated at the WHO collaborating centre at Karolinska Institutet and developed into a safe and effective method for induced abortion in the 1980ies. Today the prostaglandin analogue of choice is misoprostol and medical abortion is a safe option for termination of pregnancy at all gestational lengths. Medical abortion is as effective as surgical abortion and can increase access to safe and acceptable abortion care. However, several barriers remain that limit global access to safe abortion services. Simplifying medical abortion can contribute to increased access and acceptability. Possible approaches include the option to self-administer misoprostol at home. Another possibility is task sharing with midlevel providers to allow these health care professionals to be more

involved with the care of healthy women undergoing medical abortion. Today Internet is a major source of information for people all over the world. Another and more recently described alternative is the telemedicine service provided by providers such as “Women on Web” (WoW). A simplified treatment regimen may also include other models of telemedicine, and selfcare including home self-evaluation of complete abortion.

Medical abortion is a safe option for termination of pregnancy at all gestational lengths. Very early medical abortion (VEMA) initiated at the time of a missed menstruation and before any intrauterine gestation can be confirmed by ultrasound is safe and reduces waiting time for women. A simplified treatment regimen also includes the possibility of quickstarting post abortion contraception. Today medical abortion including post abortion contraception can be self-managed or offered as a “one stop clinic” in the first trimester.

Adequate information, having a method choice, correct dosage and adequate pain management are keys to treatment success. Those who which for it should also be allowed to have a partner/friend present during the abortion if possible as this increases acceptability of the procedure.

シンポジウム 1 **P** 革新的技術の統合がもたらす婦人科がん治療の未来

1) 多角的研究基盤を統合した探索的研究に基づく卵巣明細胞癌の新規個別化医療開発

東北大学 重田昌吾

【目的】

上皮性卵巣癌は発生起源から分子生物学的特徴に至るまで組織亜型毎に多様を極めるが標準治療は高異型度漿液性癌中心のエビデンスに基づいている。卵巣明細胞癌(OCCC)はアジアを中心に比較的高頻度に発生する組織亜型であり本邦では上皮性卵巣癌の約1/4を占める。進行再発OCCCは標準治療に抵抗性を示す難治性癌であり、個別化医療の開発は喫緊の課題である。

腫瘍遺伝学的特徴としてOCCCではPIK3CA, ARID1A 変異がそれぞれ50%以上で認められる。腫瘍増殖シグナルを活性化するPIK3CA 変異に対して選択的PI3K 阻害剤の有効性が臨床試験で検証される段階に至っている。一方クロマチンリモデリングに関わるARID1A 変異を有するOCCCではヒストンメチル化酵素EZH2やヒストン脱アセチル化酵素HDACなどエピジェネティクス制御分子の機能阻害により合成致死が誘導される。演者らも卵巣癌細胞や癌オルガノイドを用いた先行研究でヒストン修飾分子BETがOCCCに対する治療標的であることを示しており、ARID1A 変異がもたらすエピジェネティクス制御機構の変化はOCCCの治療開発において重要な研究課題であると考えられる。

エピジェネティクスはタンパク質発現や癌代謝に直接的影響を及ぼす。癌個別化医療開発には次世代シーケンシング技術に基づくオミックス解析が大きく貢献してきたが、本研究では質量解析技術を応用したプロテオーム解析、メタボローム解析を用いてARID1A 変異がタンパク質発現や癌代謝に及ぼす影響を解析し、ARID1A 変異陽性OCCCに対する新規個別化医療の可能性を検証

した。

【方法】

クリニカルバイオバンクに治療開始前血漿及び初回手術検体が保管されたOCCC 21例を研究対象とした。腫瘍組織からDNAを抽出し全エクソーム解析を行った。ClinVer及びsnpEffを参照して病的変異を決定した。治療開始前血漿からタンパク質、代謝産物をそれぞれ抽出し、超高速液体クロマトグラフィーを用いて絶対定量によるプロテオーム解析及びメタボローム解析を行った。ARID1A 変異の有無で層別化し血漿タンパク質濃度及び血漿代謝産物プロファイルについて比較検証した。ARID1A 野生型OCCC細胞RMG1にCRISPR-Cas9によるゲノム編集でARID1A ノックアウトを導入し、検証結果から得られた知見について実験的に検証した。

【成績】

①血漿プロテオーム解析

全エクソーム解析の結果、21症例中12症例でARID1A の病的変異が検出された。検出された変異はいずれもframeshift 変異もしくはnonsense 変異であった。ARID1A 野生型9症例と変異陽性12症例で群分けしプロテオーム解析データを判別解析した結果、2群間の血漿タンパク質濃度の特徴は明確に異なっていた。各タンパク質について2群間で濃度を比較し統計学的に有意差のあったタンパク質を決定した。Enrichment 解析の結果、有意差の観察されたタンパク質には免疫グロブリンや補体など液性免疫に関与するタンパク質が集積していることが明らかとなった。このうち免疫グロブリンG(IgG)に関してはすべてのサブタイプにおいてARID1A 変異陽性群で血漿中の

濃度が低値であった。腫瘍表面抗原を標的とする抗体薬は標的抗原が持つ腫瘍増殖シグナルを抑制する他にエフェクター細胞による機能を介した抗体依存性細胞障害(ADCC)による抗腫瘍腫瘍効果を示すが、血漿中IgGはADCCを抑制する作用があることが明らかとなっている。本研究結果からARIDIA変異陽性OCCCでは血漿表面抗原を標的とした抗体薬の応用で高い抗腫瘍効果が得られる可能性が示唆された。また免疫グロブリンはB細胞のみが分泌する抗体であると考えられてきたが、癌細胞が分泌する腫瘍特異的IgGが存在する事が明らかとなっている。現在ARIDIAノックアウトモデルや腫瘍組織の免疫化学染色を用いて血中IgG濃度と腫瘍特異的IgGの関連、腫瘍微小環境におけるエフェクター細胞やB細胞の集簇について検証を行っている。

②血漿メタボローム解析

血漿中の代謝産物は食事や嗜好、生活習慣などの影響を受けることが想定されたため、予備的検証として一般住民コホートと卵巣癌患者の間での血漿代謝産物プロファイルの比較、および再発卵巣癌患者の血漿代謝産物濃度の経時変化と病勢との相関を検証し血漿代謝産物が癌固有の代謝活動を反映していることを確認した。プロテオーム解析と同様にARIDIA変異の有無で2群に分け判別解析を行った結果2群間で血漿代謝産物プロファイルは明らかに異なっていることが確認され、さらにEnrichment解析ではスフィンゴ脂質代謝に相違が存在することが示唆された。より詳細な検証によりARIDIA変異陽性OCCCではスフィンゴ脂質代謝の中心であるセラミドの血中濃度がほぼ全ての分子種で低下し、セラミドを基質として合成されるスフィンゴミエリンの血中濃度が上昇していることが明らかとなった。セラミドはスフィンゴ脂質として皮膚保護作用などに関わる他、細胞内シグナル伝達を担うメディエーター脂質でもあり癌においてはアポトーシスを誘導することが知られている。加えて演者らは卵巣癌においてセラミドによるネクロプトーシスの誘導、播種転移能の抑制効果を報告しており、セラミド

は腫瘍増殖抑制的に働くと考えられる。ARIDIA変異陽性OCCCに対するセラミドを応用した治療開発の可能性を検証するためRMG1及びARIDIAノックアウトRMG1を用いてセラミド製剤及びセラミド分解酵素阻害剤による抗腫増殖抑制効果を検証した。ARIDIAノックアウトRMG1はRMG1と比較してセラミド分解酵素阻害剤に対し高感受性であること、さらにセラミド製剤とセラミド分解酵素阻害剤の併用で相乗的な抗腫瘍効果が得られる可能性があることが明らかとなった。

【結論】

質量解析技術を用いた血漿プロテオーム解析、メタボローム解析からARIDIA変異陽性OCCCに対して細胞表面抗原を標的とする抗体薬による治療応用の可能性、セラミドを中心としたスフィンゴ脂質代謝経路を標的とした新規治療の可能性を示した。現在卵巣癌で使用可能なベバシズマブはADCCを誘導しないが、OCCCでも一定の頻度で高発現することが報告されているHER2やPD-L1に対する抗HER2抗体薬、抗PD-L1抗体薬などの応用が検討される。またセラミドについては既にナノリボソーム化セラミドの第I相臨床試験が固形癌で開始されており、今後ARIDIA変異陽性OCCCでの臨床応用を視野に入れた研究を進めていく予定である。

本研究ではメタボローム解析やプロテオーム解析が卵巣癌の個別化医療開発に有用な研究基盤であることを示した。血漿を試料とすることで腫瘍内不均一性や腫瘍含有率の相違、試料保存までの影響を最小限に留めた解析を実現し、将来的には癌の経時変化に対応したリキッドバイオプシーへの応用も視野に入れることが可能である。一方で本研究結果はタンパク質、代謝産物共に1000未満の分子の同時定量解析結果に基づいており、より網羅的な質量解析技術の応用やトランスクリプトーム解析なども含めた多層オミックス解析の展開によりさらに包括的な視点から卵巣癌の治療開発が可能になると考えられた。

Symposium 1 **P** :

The future of gynecologic cancer treatment through the integration of innovative technologies

1) A Multifaced approach for the development of novel therapeutic strategies for clear cell carcinoma of the ovary

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[Objective]

Ovarian clear cell carcinoma (OCCC) is a chemo-resistant subtype constituting approximately one-fourth of epithelial ovarian cancers in Japan. Despite advancements of precision medicine, patients with advanced or recurrent OCCC have not fully benefited from it. There exists an unmet need for the development of innovative therapeutic strategies tailored to OCCC.

ARIDIA mutation is one of the characteristic genomic alterations observed in over half of OCCC cases. The reported synthetic lethal interaction between *ARIDIA* mutation and the inhibition of histone modification molecules, such as *EZH2* and *HDAC*, underscores the importance of investigating the involvement of *ARIDIA* mutation in the epigenetic regulatory mechanism.

Given that epigenetics can directly impact protein expression or cancer metabolism, this study investigated the novel therapeutic strategies for OCCC by employing proteomic and metabolomic methodologies with plasma from patients with OCCC.

[Methods]

Plasma and corresponding tumor samples from 21 patients with OCCC underwent analysis. DNA extracted from tumor tissue were subjected to whole exome sequences. After the extraction of proteins and metabolites from plasma,

samples were subjected to proteomic and metabolomic analyses using liquid chromatography, respectively. *ARIDIA* knockout was induced in the *ARIDIA* wild type OCCC cell line RMG1 to validate insights gained from the proteomic and metabolomic analyses.

[Results]

Whole exome sequencing identified *ARIDIA* frameshift or nonsense mutation in 12 out of 21 patients with OCCC. Discriminant analysis revealed distinct profiles in both plasma protein and metabolites between patients with *ARIDIA* wild-type and mutated-type OCCC. In the proteome analysis, the concentration of humoral immunity-related proteins significantly differed between the two groups. Notably, the plasma from patients with *ARIDIA*-mutated OCCC exhibited a significantly lower concentration of immunoglobulin gamma. Regarding metabolomic analysis, disparities in sphingolipid metabolism were evident between *ARIDIA* wild-type and *ARIDIA* mutated OCCC. More importantly, patients with *ARIDIA*-mutated OCCC showed significantly lower plasma ceramide concentration, which is proven to act as a tumor-suppressive lipid chemical mediator. Experimental studies with cell models revealed that *ARIDIA* knockout confers sensitivity to ceramidase inhibitors treatment. Synergistic interaction was also ob-

served in the combination therapy with ceramide nanoliposome and ceramidase inhibitors in *ARIDIA* knockout RMG1.

[Conclusion]

The Proteomic approach identified lower plasma IgG level in patients with *ARIDIA*-mutated OCCC. Given IgG's proven inhibitory effect on antibody dependent cellular cytotoxicity, one of the essential anti-cancer mechanisms facilitated by antibody drugs, this study suggests

the potential benefits of antibody drugs targeting cancer cell membrane antigens such as anti HER2 antibodies and anti PD-L1 antibodies for patients with *ARIDIA*-mutated OCCC. Additionally, the metabolomic approach identified ceramide metabolism pathway as a therapeutic target for *ARIDIA*-mutated OCCC. This study highlighted the potential of proteomic and metabolomic approaches in advancing precision medicine for OCCC.

シンポジウム 1 **P** 革新的技術の統合がもたらす婦人科がん治療の未来

2) 革新的技術を統合した HPV 関連子宮頸癌の発癌リスクの層別化

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【目的】

多くの子宮頸癌はヒトパピローマウイルス (HPV) 感染が原因となる。90% 以上の HPV 感染はヒト免疫により自然に排除されるが、一部では HPV 持続感染が成立し、さらにごく一部の患者では子宮頸部異形成 (CIN) を経て子宮頸癌に至る。HPV 感染子宮頸部病変の予後を考えるにあたり、ヒト免疫によるウイルス感染細胞の排除と感染 HPV ジェノタイプの特徴を考慮する必要がある。特に、ウイルスの排除や CIN の退縮にはヒト免疫応答が強く関わっており、CIN 進展や発癌には感染 HPV の種類が重要である。

ウイルス感染細胞に対する免疫応答が働くためにはヒト白血球抗原クラス I (HLA-I) を介したウイルス抗原の提示が不可欠である。HLA-I の発現低下や機能障害が感染症や腫瘍の増悪に関わることが知られている。CIN においても HLA-I の多型と CIN の罹患率の関係が報告されており、HLA-I の機能低下が CIN の進展や退縮不全と関連する可能性がある。

また、感染 HPV ジェノタイプについては、13 種類の HPV ジェノタイプが発癌と関連する高リスク HPV とされているが、その振る舞いは HPV タイプ毎に異なり、感染 HPV タイプの特徴を考慮した CIN 管理方法の確立が重要視されてきている。高リスク HPV の中で、HPV18 型は他の HPV にはない特徴を有する。HPV18 型由来の子宮頸癌は前がん病変が見つかりにくく、悪性度の高い腺癌や小細胞癌の発生率が高いことから、特に臨床的に管理が難しい。HPV18 型の多様な組織像に注目した組織型分化の解明や HPV18 型の起源細胞の同定は、臨床管理が難しい HPV18 型の予防法や治療法に結び付く可能性がある。本研

究では、ヒト免疫応答と HPV ジェノタイプの双方からアプローチすることで、HPV 関連子宮頸癌の発癌リスクの層別化を目指す。

【方法】

1. CIN における HLA-I の特徴解析

CIN 138 例 (CIN1 以下: 69 例, CIN2/3: 69 例) について、HLA-I 遺伝子座 (HLA-A, HLA-B, HLA-C) 全長についてロングリードシーケンサーを用いた変異解析を行い、各アレルにおける感染 HPV 由来の抗原提示能を推定した。

2. 高リスク HPV タイプ別の子宮頸癌発癌リスクの検討

2-1. Markov モデルを用いた HPV タイプ別の予後解析

過去 10 年間に当院でフォローした CIN 患者のうち、初診時に HPV タイピングを行った 1417 例を後向きコホートと設定した。CIN は進展と退縮の双方向性に変化するという自然史がある。本研究では、双方向性変化に対して予後予測を行える機械学習法 (マルコフモデル) を用い、HPV タイプ別に、2 年後に CIN3/AIS/頸癌を発症する確率をシミュレーションした。

2-2. HPV18 型の発癌形式と標的細胞の検討

HPV18 型の多様な組織像に注目して、過去 5 年間に手術を行い HPV タイプが同定できている 42 例を対象に子宮頸部混合がん症例 4 例を抽出した。混合がんの各組織型をマイクロダイセクションで打ち抜き、全エクソン解析と RNA-seq 解析を行った。ゲノム解析から系統樹解析を行い、RNA-seq 解析から HPV インテグレーション部位を同定して、異なる組織型ごとに細胞起源が共通するかどうかを検討した。また、混合がんの起源細胞の特徴を検討するためヒト遺伝子発現解析を

行った。

さらに、HPV18型の標的細胞を同定するため、オルガノイド培養技術を用いて検討した。まず、子宮頸部扁平上皮接合部(SCJ)オルガノイド培養を樹立し、SCJオルガノイドにHPV18型転写調整領域(HPV18-LCR-GFP)を導入し、HPV18型が複製可能な細胞を単離し、単一細胞解析を用いてHPV18型ゲノム維持に必要な遺伝子を同定した。

【結果】

1. CINにおけるHLA-Iの特徴解析

CINにおけるHLA-I解析の結果、いずれのHLA-Iも、CIN2/3でCIN1以下の症例に比べて有意にloss of heterozygosity (LOH)の頻度が高かった。また、喪失したアレルは対立アレルに比べて感染HPV由来の抗原提示能が高かった。

2. 高リスクHPVタイプ別の子宮頸癌発癌リスクの検討

2-1. Markovモデルを用いたHPVタイプ別の予後解析

CIN患者の予後を、マルコフモデルを用いて解析した。HPV16型患者は、CIN3以上への2年後進展率が最も高く、CIN1、CIN2からはそれぞれ17.7%と27.8%であった。一方、HPV52、58型患者では同じ病態が継続する傾向にあり、55-70%の患者で2年後もCIN1からCIN2の状態を維持した。

2-2. HPV18型の発癌形式と標的細胞の検討

混合がん4例中3例でHPV18型陽性、1例でHPV16型陽性であった。ゲノム解析に基づく系統樹解析の結果、混合がんは共通の細胞起源を有することが分かった。またRNA-seq解析からHPVインテグレーション部位は症例ごとに共通しており、HPVインテグレーションは組織型分化前に起

こっていることが示唆された。RNA-seqデータに基づくヒト遺伝子解析の結果、HPV18陽性混合がんは幹細胞成分を保持しておりさらにその成分では抗原提示能が低下し免疫応答が減弱していることが分かった。

HPV18型がSCJのどの細胞に感染するかを特定するために、SCJオルガノイドを樹立し、HPV18-LCR-GFPレンチウイルスを導入した。その結果、SCJ細胞中にGFP陽性細胞を確認できた。GFP陽性細胞を単離し、単一細胞遺伝子発現解析を行った結果、GFP陽性細胞では、89個の遺伝子で発現上昇していることがわかった。さらに、siRNAによるノックダウン法により、89個の遺伝子の中から、ヒストンシャペロン蛋白であるNPM3はHPV18型の複製を阻害することを確認した。また、NPM3のノックダウンは細胞の多分化能に関連する遺伝子発現を低下させた。

【結語】

HPV感染子宮頸部病変の予後を層別化するため、免疫応答と感染HPVジェノタイプの観点から、革新的技術を用いて検討した。免疫応答に関する検討では、HLA-IのLOHを介した抗原提示能の低下がCIN進展と関連することが示唆された。HPVジェノタイプに関する検討では、マルコフモデルを応用することでHPV16型は段階的なCIN進展を特徴とし、HPV52、58型はCIN病変の持続を特徴とすることが解明できた。また、HPV18型については、幹細胞様細胞への感染の成立と幹細胞成分を維持した発癌が関連していると考えられた。HLA-IのLOHや感染HPVジェノタイプを考慮することで、HPV感染子宮頸部病変の予後の層別化を通して個別化管理に繋がることが期待できる。

Symposium 1 **P** :

The future of gynecologic cancer treatment through the integration of innovative technologies

2) Stratification of carcinogenic risk of HPV-associated cervical cancer by intergrating innovative technologies

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[Objective]

The prognosis for HPV-infected cervical lesions varies by individual. In particular, the human immune response is strongly involved in viral elimination, whereas the infecting HPV genotypes are associated with cervical intraepithelial neoplasia (CIN) progression. Among immune-related molecules, human leukocyte antigen class I (HLA-I) responsible for antigen presentation is essential for the immune response to virus-infected cells. In addition, the prognosis of CIN depends on the infected high-risk HPV genotype, among which HPV18-associated cervical cancer is particularly challenging to manage because of the difficulty in detecting precancerous lesions and the high incidence of adenocarcinomas. Elucidation of histological differentiation and cellular origin of HPV18 may lead to preventive and therapeutic methods for HPV18-associated cervical cancer. This study aimed to stratify the risk of developing HPV-associated cervical cancer

[Methods]

1. HLA-I in CIN

HLA-I analysis was performed on 138 CIN cases using a long-read sequencer.

2. HPV-genotype-based approaches

2-1. Prognostic analysis using the Markov model

CIN has a natural history of bidirectional

change between progression and regression. Using a machine learning method (Markov model) that can predict prognosis for bidirectional change, we simulated the probability of developing CIN3/AIS/cervical cancer in 2 years by HPV genotype.

2-2. HPV18-associated carcinogenesis

Focusing on the intratumor heterogeneity of HPV18, we performed a multi-omics analysis of HPV18-positive mixed cancers.

To further identify target cells for HPV18, we established cervical squamocolumnar junction (SCJ) organoid cultures and introduced the HPV 18 transcriptional regulatory region (HPV18-LCR-GFP) into SCJ organoids followed by single-cell analysis.

[Results]

1. HLA-I in CIN

CIN2/3 had a significantly higher frequency of HLA-I loss of heterozygosity (LOH) than CIN1 did; alleles with a higher ability to present HPV antigens tended to be deficient.

2. HPV genotype-based approaches

2-1. Prognostic analysis using the Markov model

HPV16-positive CIN had the highest rate of 2-year progression to CIN3 or higher, whereas HPV52- and 58-positive cases maintained CIN1/2 status.

2-2. HPV18-associated carcinogenesis

Genomic and RNA-Seq analysis revealed that mixed cancers share a common cellular origin and HPV integration occurred prior to histological differentiation. In addition, HPV18-positive mixed carcinomas retain a stem cell component, reducing antigen-presenting capacity and attenuating immune response.

Single-cell analysis revealed that NPM3, a histone chaperone protein, is involved in HPV18 replication. NPM3 knockdown also reduced the expression of genes associated with cellular multipotency.

[Conclusion]

Decreased antigen-presenting capacity of HLA-I via LOH is associated with CIN progression.

By applying the Markov model, we were able to elucidate that HPV16 is characterized by step-wise CIN progression, whereas HPV52 and 58 are characterized by the persistence of CIN lesions. In addition, stem-cell carcinogenesis might be related to HPV18-associated carcinogenesis.

Consideration of HLA-I LOH and infected HPV genotypes will lead to individualized management through stratification of HPV-infected cervical lesion prognosis.

シンポジウム 1 **P** 革新的技術の統合がもたらす婦人科がん治療の未来

3) マルチオミックス統合解析に基づいた難治性卵巣がんの新規治療戦略

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【目的】

卵巣がんは組織型毎に異なる発生母地や分子生物学的特徴を有しているため、組織型毎の分子生物学的特性の解明とその特性にあった治療法の選択が重要になる。本研究では、化学療法に抵抗性で、進行すると予後不良な、2つの難治性卵巣がん(卵巣成熟奇形腫の悪性転化, 卵巣明細胞癌)に焦点をあて、トランスクリプトームとゲノムを統合したマルチオミックス解析を行うことで、新規治療戦略を構築することを目的とした。

【方法】

1. 大規模データを用いた卵巣成熟奇形腫悪性転化症例に対するマルチオミックス解析

多施設共同研究(新潟大学, 大阪大学, 自治医科大学, 県立がんセンター新潟病院)を行い, 卵巣成熟奇形腫悪性転化 29 例を収集した。6 例に対し RNA シーケンスを行い, 遺伝子発現プロファイルについて, Pan-Cancer Atlas に登録されていて扁平上皮癌が発生する 4 つの臓器(頭頸部, 食道, 肺, 子宮頸部)に, 皮膚, 卵巣を加えた計 6 種類の臓器に発生する癌腫(2,316 例)と比較した。得られた結果に対し, 卵巣成熟奇形腫悪性転化 24 例で免疫染色による検証を行った。また, 10 例に対して全エクソンまたはターゲットシーケンスを施行し, 遺伝子異常を評価した。そのうち, 2 例で腫瘍内の複数箇所からサンプリングを行い, 腫瘍内不均一性について評価した。

2. 層別化治療を目的とした卵巣明細胞癌のマルチオミックス解析

新潟大学で収集した卵巣明細胞癌 112 例に対し, RNA シーケンスを行った。癌関連遺伝子経路の発現について, クラスタリング解析を行い, 遺伝子発現サブタイプを同定した。同定したサブタイプと臨床情報や遺伝子変異の相関を評価した。

同定したサブタイプについて, 細胞種毎の発現評価を行うために, 12 例にシングルセル RNA シーケンスを施行した。また, 蛋白質発現の空間的評価を行うために, 各サブタイプの症例に対し, CODEX 多重免疫蛍光染色を施行した。

【成績】

1. 卵巣成熟奇形腫悪性転化症例の遺伝子発現プロファイルは, 組織型毎に異なっていた。卵巣成熟奇形腫由来の扁平上皮癌は, 肺扁平上皮癌と類似した遺伝子発現プロファイルをもち, サイトケチンの蛋白質発現パターンでもその類似性が確認された。また, 卵巣成熟奇形腫由来の扁平上皮癌に高発現している遺伝子として, CD8 陽性 T 細胞の活性化に重要なケモカインである *XCL1* を同定した。免疫染色で腫瘍 *XCL1* 発現例を 13/24 (56%) で認めたが, 卵巣成熟奇形腫では認めなかった。*XCL1* の機能を考慮し, 腫瘍内 CD8 陽性 T 細胞の腫瘍内浸潤と腫瘍細胞の PD-L1 発現を評価したところ, 16/24 (67%) で CD8 陽性 T 細胞の高度浸潤を認め, 15/24 (63%) で腫瘍 PD-L1 発現を認めた。CD8 陽性 T 細胞高度浸潤例は予後良好であり, 腫瘍免疫微小環境が重要であることが示唆された。*XCL1* 発現は, CD8 陽性 T 浸潤の程度と腫瘍 PD-L1 発現とそれぞれ有意に相関していた。一方, ゲノム解析では *TP53*, *PIK3CA* 変異を高頻度に認めること, 免疫療法の効果を予測するバイオマーカーの候補である, APOBEC 型変異が多くを占めることが明らかとなった。また, マルチサンプリング例で, 採取部位により遺伝子変異プロファイルが大きく異なり, 強い腫瘍内不均一性を有することが確認された。以上より, 遺伝子異常を治療標的にすることは注意を要するが, 本疾患の多くに抗 PD-1 抗体が有効である可能性と, *XCL1* がそのバイオマー

カーとなる可能性が示唆された。

2. 卵巣明細胞癌のトランスクリプトーム解析により、T細胞浸潤、炎症、上皮間葉移行関連遺伝子の高発現を特徴とする Hot (49/112, 44%)、細胞周期関連遺伝子・MYCの高発現を特徴とする Cold (63/112, 56%) に大別された。Hot はさらに、T細胞浸潤や炎症が優位の Hot immune-high (23/112, 21%) と、上皮間葉移行が優位の Hot mesenchymal-high (26/112, 23%) に細分され、3つのサブタイプ (Cold, Hot immune-high, Hot mesenchymal-high) を同定した。サブタイプ毎に進行期や遺伝子変異の頻度に有意な違いを認めなかったが、Hot immune-high は予後良好で Hot mesenchymal-high は予後不良であった。シングルセル解析で、細胞種毎の割合が各サブタイプで異なり、Cold は癌細胞が大部分を占めるのに対し、Hot immune-high は免疫細胞、Hot mesenchymal-high は Cancer-associated fibroblast (CAF) が占める割合がそれぞれ高かった。細胞種毎に癌関連経路の発現を評価すると、Cold の特徴であった遺伝子経路は癌細胞が高発現しており、Hot immune-high や Hot mesenchymal-high の特徴であった遺伝子経路は、微小環境の細胞が高発現していた。これらから、卵巣明細胞癌では、癌細胞と微小環境の細胞の割合の違いが、サブタイプに強く影響していると考えられた。多重免疫蛍光染色でも同様に、各サブタイプで癌細胞、微小環境の細胞の割合に違いを認めた。さら

に、各サブタイプで免疫細胞の局在に顕著な違いを認め、Hot immune-high で免疫細胞の多くが腫瘍内に浸潤しているのに対し、Hot mesenchymal-high では、免疫細胞の多くが CAF 内に浸潤していた。Hot mesenchymal-high では腫瘍免疫微小環境の不均一性を認め、CAF の部分が増大するにつれ、免疫細胞の浸潤が腫瘍内から CAF 内に変化していた。以上から、3つの遺伝子発現サブタイプは、腫瘍免疫微小環境の細胞の割合やその局在に、顕著な違いを有することが明らかとなった。

【結論】

2つの難治性卵巣がんで、いずれも腫瘍免疫微小環境が予後やサブタイプを規定する重要な因子であった。卵巣奇形腫由来の扁平上皮癌に対しては、抗 PD-1 抗体が有効な可能性が高いと考えられた。本研究結果から、卵巣扁平上皮癌に対する抗 PD-1 抗体の有効性を評価する、JGOG3029 試験が進行中である。一方、卵巣明細胞癌に対しては、腫瘍免疫微小環境による治療層別化が有効と考えられた。免疫療法は Hot immune-high でより有効な可能性が高い。Hot mesenchymal-high では免疫賦活化につながる治療と免疫療法との併用が有効な可能性が高く、CAF を標的とした治療がその候補に挙げられる。大部分が癌細胞で構成される Cold の治療について、我々は本疾患の特徴である血液凝固能亢進と、癌細胞による組織因子の高発現に着目しており、組織因子を標的とした新しい治療法を検討中である。

Symposium 1 P :**The future of gynecologic cancer treatment through the integration of innovative technologies****3) Novel treatment strategies for refractory ovarian cancer based on integrated multi-omics analysis**

TAMURA Ryo

*Niigata University***【Objective】**

We aimed to develop novel therapeutic strategies for two refractory ovarian cancers [malignant transformation of mature cystic teratoma (MCT) and clear cell carcinoma (CCC)] by integrating transcriptomic and genomic analyses.

【Methods】

1. We collected 29 cases of malignant transformation of MCT. We performed RNA sequencing for six samples and compared gene expression patterns between our data and publicly available pan-cancer data. To validate our findings, we performed an immunohistochemistry analysis. To evaluate genetic abnormalities, we also performed whole-exome or targeted gene sequencing for ten samples.

2. We performed RNA sequencing for 112 CCCs to identify gene expression subtypes. We evaluated the correlation of the identified subtypes with clinicopathological findings and genetic alterations. We performed single-cell RNA sequencing in 12 cases to further assess the subtypes. We also evaluated multiplex immunofluorescence staining for each subtype to assess spatial expression.

【Results】

1. The gene expression profiles of patients with malignant transformation of MCT were different for

each histological type. In particular, squamous cell carcinoma arising from MCT (MCT-SCC) had a gene expression profile similar to lung SCC. We identified XCL1 as a specifically expressed gene in MCT-SCC. XCL1 expression was also significantly associated with the number of tumor-infiltrating CD8-positive T cells and PD-L1 expression on tumor cells. Genomic analysis revealed APOBEC signature, a biomarker candidate for predicting efficacies of anti-PD1 antibody, predominated in most cases.

2. By performing transcriptomic analysis, CCC was divided into Hot (49/112, 44%), characterized

by high expression of T-cell infiltration, inflammation, and epithelial-mesenchymal transition, and Cold (63/112, 56%), characterized by high expression of cell cycle-related genes and MYC. Hot was further divided into immune-high (23/112, 21%) with high expression of T-cell infiltration and mesenchymal high (26/112, 23%) with high expression of epithelial-mesenchymal transition. Hot immune-high had a good prognosis, and Hot mesenchymal-high had a poor prognosis. In single-cell analysis, Cold was dominated mainly by cancer cells, while Hot immune-high and Hot mesenchymal-high had higher percentages of immune cells and cancer-associated fibroblasts, respectively. Most immune cells in Hot

immune-high were infiltrated within the tumor, whereas most immune cells in Hot mesenchymal-high were infiltrated within the cancer-associated fibroblasts.

【Conclusion】

Our studies demonstrated that the tumor immune microenvironment was significant in the

biology of both cancers. Anti-PD-1 antibodies may be effective against MCT-SCC. The three gene expression subtypes in CCC have markedly different tumor immune microenvironments, suggesting that stratified therapy tailored to these differences may be effective.

シンポジウム 1 **P** 革新的技術の統合がもたらす婦人科がん治療の未来4) 複合的シーケンス解析による婦人科がんの新規治療開発を目指した病態
解明

名古屋大学 吉 田 康 将

次世代シーケンス解析は、近年急速に発展しており、核酸を「高速に・大量に・安価に」解析できる時代となった。そして、様々な解析アプリケーションも発展により、現在の分子生物学的研究に必要な不可欠な解析ツールとなっている。生物学の基本として、我々の細胞はゲノム情報を DNA に有し、その情報を RNA へ転写し、機能的なタンパク質へ翻訳することにより生命現象を営んでいる。そのため、DNA 修復機構を越える DNA 損傷が生じた場合、ゲノム変異が生じ、変異の種類によっては異常タンパク質が生じることとなる。そして、がん遺伝子の機能亢進をもたらす変異や、がん抑制遺伝子の機能低下をもたらす変異が生じた場合は、発がんの原因となる。従って、次世代シーケンス技術に基づくがんゲノム検査が、広く臨床応用されてきている。しかし、生命現象は単純ではなく、ゲノム変異を伴わない異常、すなわちエピゲノム変化の重要性もまた指摘されている。例えば、DNA のメチル化やマイクロ RNA 等により、がん遺伝子もしくはがん抑制遺伝子の発現が変化することもがんの発生および進展に寄与する重要な生命現象である。我々の研究室では、希少婦人科がんに対して、次世代シーケンスを使用した RNA レベルの網羅的解析を進めてきており、その研究成果を報告する。

<RNA シーケンスに基づくアプローチ>

子宮平滑筋肉腫を対象疾患とし、RNA シーケンスを用いた新規治療薬開発を行った。子宮平滑筋肉腫は、極めて悪性度の高い婦人科腫瘍であり、有効な治療方法は確立されていない。また、希少がんであり、研究開発も進んでいない状況であった。そこで、国立がん研究センターと共同研究を

企画した。2011 年から 2020 年に、国立がん研究センターバイオバンクに保管されていた新鮮凍結組織（子宮平滑筋肉腫 6 例および子宮筋腫 3 例）を解析に用いた。RNA シーケンスの結果、子宮平滑筋肉腫と子宮筋腫は異なる遺伝子発現プロファイルを示し、ボルケーノプロットの結果、512 個の発現変動遺伝子（子宮平滑筋肉腫において発現上昇 387 個、発現低下 125 個）が同定された。次に、この 512 個の発現変動遺伝子に対して、IPA ソフトウェアを用いてパスウェイ解析を行ったところ、細胞周期関連パスウェイの有意な変調が示唆された。また、IPA ソフトウェアにより、これらの発現変動遺伝子をもたらす上流制御因子について解析を行ったところ、子宮平滑筋肉腫において PLK1, CHEK1, CDK1 等の細胞周期関連キナーゼの有意な活性化が示唆された。そこで、細胞株を用いて、これらのキナーゼに対する阻害剤の効果を検討したところ、PLK1 阻害剤と CHEK1 阻害剤は極めて高い抗腫瘍効果を示した。さらに、これらの阻害剤はマウスモデルにおいても有効性を示しており、子宮平滑筋肉腫に対する新規治療薬候補として期待される。

<マイクロ RNA シーケンスに基づくアプローチ>

マイクロ RNA は、22 塩基程度の短鎖の RNA であり、相補配列を有する標的遺伝子の発現を制御する機能を有する。また、分子としての安定性も高く、リキッドバイオプシーとして期待されている。第一に、卵巣明細胞がんを対象疾患とし、初発時と再発時のマイクロ RNA 発現について網羅的に解析した。名古屋大学で手術が行われた卵巣明細胞癌患者の病理検体の FFPE 組織を解析

に用いた。FIGO ステージI期の初発がん組織(20例)、再発がん組織(5例、いずれも対応する初発がん検体あり)、正常卵巣組織(10例)よりRNAを抽出し、マイクロRNA分画を切り出し、マイクロRNAシーケンスを施行した。その結果、初発がん組織と再発がん組織では異なるマイクロRNAプロファイルを示しており、再発がん組織において、著明に発現低下するマイクロRNA(miR-508-3p, miR-509-3p, miR-509-3-5p, miR-514a-3pなど)を同定した。そして、それらのマイクロRNAのゲノム領域に着目すると、X染色体上の特定の領域に密集して存在していることが明らかになった。このようなマイクロRNAは、マイクロRNAクラスターと称されるため、今回我々が同定したマイクロRNAをchrXq27.3マイクロRNAクラスターと称する。そして、in vitroの機能解析の結果、miR-509-3pとmiR-509-3-5pを強制発現させると、シスプラチン感受性が亢進することが明らかになった。すなわち、再発明細胞がんは、これらのマイクロRNAの発現低下によって、シスプラチン抵抗性を獲得していることが示唆される。従って、chrXq27.3マイクロRNAクラスターは、卵巣明細胞がんの治療抵抗性のバイオマーカーとなり、新規治療標的となる可能性がある。加えて、成熟奇形腫の悪性転化に対してもマイクロRNAシーケンスによる研究を施行した。成熟奇形腫の悪性転化は、成熟奇形腫より二次性に発がんする希少がんであり、その病態はほとんど明らかにされていない。名古屋大学において手術が行われた7例の症例から扁平上皮がん組織と対側正常卵巣組織を解析に用いた。その結果、扁平上皮がん組織において、miR-151a-3pとmiR-378a-3pの

発現上昇、miR-26a-5pとmiR-99a-5pの発現低下を認めた。さらにマウスモデルの血中において、miR-151a-3pとmiR-378a-3pは、腫瘍の増大に伴い発現増加することも示された。従って、成熟奇形腫の悪性転化の病態にもマイクロRNAは関与し、非侵襲的なバイオマーカーとなりうると考えられる。

<空間的トランスクリプトームに基づくアプローチ>

次世代シーケンス解析技術はさらに進歩し、組織切片上の位置情報を保持したままRNAシーケンスを行う空間的トランスクリプトーム解析が微小環境研究において注目を集めている。我々は、名古屋大学と国立がん研究センターより計5例の成熟奇形腫の悪性転化症例の新鮮凍結組織を収集し、空間的トランスクリプトーム解析を実施し、がん組織の中でも特にがん細胞において*KLF5*の発現が亢進していることを見出した。そして、我々の研究室で樹立された成熟奇形腫の悪性転化由来の細胞株(NOSCC-1)を用いて機能解析を行ったところ、*KLF5*の発現を低下により細胞増殖が有意に抑制される結果となった。現在、*KLF5*の制御機構を解析中であるが、*KLF5*は成熟奇形腫の悪性転化において重要な因子と考えられる。

総じて、次世代シーケンスを用いた解析は、希少婦人科がんの病態解明を飛躍的に進歩することが期待される。特に、メッセンジャーRNAやマイクロRNAなどの機能的なRNAが、新たな治療薬やバイオマーカーの創出に繋がる有望な分子であると考えており、更なる研究が求められる。

Symposium 1 **P** :

The future of gynecologic cancer treatment through the integration of innovative technologies

4) Elucidation of the molecular background of gynecological malignancies through multi-omics analysis

YOSHIDA Kosuke

Nagoya University

In recent years, next-generation sequencing (NGS) technologies have advanced dramatically, and NGS has become an essential analysis in DNA and RNA research. Human cells contain genomic information in their DNA, and proteins are synthesized through the processes of transcription and translation. Mutations in genomic DNA can result in abnormal protein production, hence, genetic mutations are associated with carcinogenesis and cancer progression. Therefore, gene panel testing is frequently performed in clinical settings for a variety of cancers. However, the importance of epigenomic regulation, such as DNA methylation and microRNAs (miRNAs), is also emphasized. In our laboratory, we conducted research on RNA expression in rare gynecological malignancies using NGS.

First, we performed RNA sequencing to identify novel therapeutic targets for uterine leiomyosarcoma (ULMS). ULMS is one of the most aggressive gynecologic malignancies, and no standard treatment has been established. Fresh-frozen samples of six ULMS and three myoma samples were collected from the National Cancer Center Biobank. RNA-seq revealed that the gene expression profile was different between ULMS and myoma, and 512 differentially expressed genes were identified. Moreover, pathway analysis showed that cell cycle-related pathways were

significantly activated in ULMS than in myoma. Then, PLK1 or CHEK1 inhibitors exerted strong anti-cancer effects in both *in vitro* and *in vivo*. Therefore, cell cycle-related factors would be novel therapeutic targets for ULMS.

Second, we investigated miRNA, which regulates the expression of target genes. We compared the miRNA profiles of recurrent and primary ovarian clear cell carcinoma (OCCC). The miRNA sequencing revealed that the expression of miRNAs belonging to the chrXq27.3 miRNA cluster (miR-508-3p, miR-509-3p, miR-509-3-5p, and miR-514a-3p) were downregulated in recurrent OCCC. Moreover, *in vitro* analysis showed that miR-509-3p and miR-509-3-5p were associated with the sensitivity of cisplatin. Therefore, the chrXq27.3 miRNA cluster might contribute to the development of OCCC. In addition, we also investigated the miRNA profiles of squamous cell carcinoma arising from mature teratoma (SCC-MT). The miRNA-seq revealed that miR-151a-3p and miR-378a-3p were upregulated while miR-26a-5p and miR-99a-5p were downregulated in cancer tissues compared with contralateral normal ovarian tissues. Moreover, the two upregulated miRNAs were elevated in the peripheral blood of patient-derived xenograft models of SCC-MT. Therefore, miRNAs might contribute to the development of SCC-MT and be po-

tential non-invasive biomarkers.

Finally, we performed spatial transcriptome analysis for SCC-MT. As a result, spatial transcriptome showed that the expression of *KLF5* was upregulated in the cancer tissue than in normal tissue. Functional analysis using an SCC-MT-derived cell line, NOSCC-1, showed that the downregulation of *KLF5* significantly impaired

cell proliferation.

In conclusion, NGS has contributed to the elucidation of the molecular background of rare gynecologic malignancies. In particular, mRNAs and miRNAs would be promising molecules for the development of novel therapeutic agents and biomarkers.

シンポジウム 2 **P** 難治性不妊症の新規診断・治療法の開発に向けた病態解明

1) 早発卵巣不全 (POI) の妊娠アウトカム向上をめざした総合戦略

名古屋大学 大須賀 智 子

【目的】

早発卵巣不全 (POI) は、早期の原始卵胞数減少により、40 歳未満で卵巣性無月経を呈し難治性不妊症の原因となる。提供卵子を用いた生殖補助医療が選択肢となるが、本邦ではアクセスが困難であるとともに、自身の卵子を用いた妊娠を望む例も多い。通常ホルモン補充療法 (HRT) 中の卵胞刺激ホルモン (FSH) 値低下を指標に卵巣刺激を開始し卵胞発育を期待するが、結果が得られないことも多く治療に難渋する。従って、卵胞発育の制御機構の解明や、より正確な卵胞発育の予測法が求められてきた。また、POI が成立する前にリスクを予測できれば、卵子凍結保存等の対策を講じたりライフプラン形成に役立つことから、早期診断法の開発や若年者への介入も望まれる。POI 患者の妊娠アウトカムを向上させるためには、これらに対し多角的な取り組みが必要である。本研究では、POI 患者の自身の卵による妊娠への寄与ならびに、ハイリスク例の抽出、若年者への介入による将来の難治性不妊症減少を目標とし、以下の検討を行った。

【方法】

人を対象とする研究は当該倫理委員会の承認と対象の同意を得て行った。

1. 高感度 Anti-Müllerian hormone (AMH) 値測定による卵胞発育予測

AMH は通常 ng/mL 単位で測定され、POI 患者では低値～測定感度以下を示す。POI 患者において小胞状卵胞の存在による僅かな血清 AMH 値の変化を捉えることで、卵胞発育を予測できるかを検討するため、微量の血清 AMH を測定する ELISA キット (MenoCheck picoAMH, Ansh Labs) を使い、周期毎に pg/mL 単位での血清 AMH 値測定 (測定下限値: 1.3 pg/mL) し、卵胞

発育との関連を検討した。

2. 卵巣局所エストラジオール (E2) の卵胞発育制御における作用

POI 患者は低 E2 状態であり、HRT による治療が行われる。E2 は卵巣局所における初期卵胞発育への関与も指摘されている。マウスを用いた検討において、原始卵胞活性化に寄与する Stefin A に対し E2 が抑制的に作用するという知見を得ており、性成熟期マウスへのエストロゲンレセプター (ER) アンタゴニストの投与による原始卵胞活性化への影響を forkhead boxO3a (FOXO3a) の局在により検討した。

3. 卵巣自己抗体による POI 新規診断マーカーの検討と抗原分子の機能解析

POI 患者は甲状腺自己抗体等の自己抗体を保有する例が多いが、既存自己抗体陽性でも POI を呈しない例もある。そこで POI 患者は卵巣に対する抗体も有するという仮説の下、POI 患者血清を抗体として用いたヒト卵巣に対する免疫染色やヒト非黄体化顆粒膜細胞株 (HGrC1) 由来タンパクとの免疫沈降により、POI 患者血清中の卵巣に対する抗体の存在を検討した。さらに抗原候補分子を免疫沈降検体のプロテオーム解析により同定、同分子の強制発現細胞株から精製した抗原タンパクを用い ELISA を作成、患者血清中の自己抗体の定量化を行った。免疫染色によりヒト卵巣での局在を確認、同分子を発現増強した HGrC1 を作成し、機能解析を行った。

4. 卵胞液中 Extracellular vesicles (EVs) を用いた妊娠予測

不妊症患者の採卵時に得られた卵胞液について、EVs に内包される small non-coding RNAs (ncRNAs) を解析、胚移植後、妊娠に至った卵の卵胞 (妊娠検体: n=8) と至らなかった卵胞 (非妊

娠検体：n=12)での比較を行い、妊娠予測マーカーとなる small ncRNAs を抽出した。

5. 若年者における潜在的な卵巣予備能低下例の抽出と意識調査

若年者に対する妊娠能についての意識調査や意識づけのため、20歳代前半の大学生に対し、妊娠能に関する講義ならびに、講義の前後でアンケートを行い理解度の変化を測定した。また、同意が得られた女子大学生529名に対し月経異常調査とAMH値測定を行い、潜在的な卵巣予備能低下例を抽出した。

【成績】

1. POI患者(40歳未満かつ、3か月以上の続発性無月経かつ、2回以上の血清FSH値 > 40mIU/mL)19名91周期の検討を行った。91周期のうち、14周期で高感度AMH陽性であり、陽性周期中9周期で卵胞発育を認めた。AMH陽性周期の中央値は7.7pg/mLであり、通常法の測定下限値より低値であった。AMH陽性周期の卵胞発育に対する陽性的中率と陰性的中率はそれぞれ、0.643と0.935、血清FSH値 < 10mIU/mL周期の陽性的中率と陰性的中率は0.250と0.873であり、AMH陽性周期のほうがいずれも高値であった。

2. 性成熟期マウスにおいて性周期のいずれの段階においても胞状卵胞周囲(50 μ m以内)の原始卵胞の活性化率はそれ以外に比し低かった。さらにERアンタゴニスト投与により、胞状卵胞周囲以外の原始卵胞の活性化率は増加したが、胞状卵胞周囲の原始卵胞の活性化率は変化しなかった。以上より、卵巣局所のE2が、原始卵胞の維持に重要であることが示された。

3. 免疫染色ならびに免疫沈降より、POI患者血清中の抗卵巣抗体の存在が示唆された。プロテオーム解析から抗卵巣抗体に対する抗原の候補として、霊長類の性腺・胎盤・前立腺特異的に発現するとされるProstate, ovary, testis, ankyrin domain family member F (POTEF)タンパクが検出された。ELISA測定によりPOI患者血清におい

て抗POTEF抗体価が高値であることが確認された。また免疫染色よりPOTEFタンパクの原始卵胞～一次卵胞の初期の卵胞の顆粒膜細胞における局在が示された。HGrC1に薬剤誘導性遺伝子発現システムを用いた検討で、POTEF発現は顆粒膜細胞の増殖を抑制することが確認された。

4. 妊娠検体では非妊娠検体に比し、3種類のマイクロRNA(miRNA)の発現上昇、10種類のmiRNAの発現低下が同定された。このうち、3種類のmiRNA(miR-16-2-3p, miR-378a-3p, miR-483-5p)の組み合わせにより、高精度に妊娠を予測(AUC 0.96)できること、また同一患者でもこの3種類のmiRNAは妊娠検体と非妊娠検体で発現が異なっていることを確認した。

5. アンケート調査において、講義前では89%が卵巣予備能について「全く聞いたことがない」という結果であったが、講義後には、60%が「知っている」と回答した。血清AMH値を測定した女子大学生529名のうち、血清AMH値1.0ng/mL以下は18名(3%)、2.0ng/mL以下は66名(12%)であり、うち月経不順を認めたのはそれぞれ、5名、15名であった。AMH低下症例ならびに月経不順の自覚がある例で、通院による加療をうけていたのは1例のみであった。

【結論】

POI成立後は周期的なHRT施行下の高感度AMH値測定により、卵胞発育周期を逃さず予測することで自身の卵による妊娠に寄与すると考えられる。妊娠成立の有無で異なる発現を示す卵胞液中EVs内small ncRNAの知見は、妊娠成立予測に役立つとともに、発現制御等による治療応用への展開も期待される。若年者において、既存マーカーであるAMH測定や、新規自己抗体マーカー測定によりハイリスク例を早期に抽出することができれば、卵子凍結等の具体的な対策の提案やライフプランマネジメントにつながり、将来の難治性不妊症の減少に貢献し得る。

Symposium 2 **P** :

Elucidation of pathophysiology for the development of new diagnostic and therapeutic methods for intractable infertility

1) A comprehensive strategy for improving outcomes in Premature Ovarian Insufficiency (POI)

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[Objective]

Primary ovarian insufficiency (POI) is defined as the development of hypogonadotropic hypogonadism in women aged < 40 years. Patients with POI should maximize the use of their remaining follicles to conceive with their own oocytes. This study aimed to maximize pregnancy outcomes in patients with POI by maintaining residual follicles, predicting follicular development and pregnancy, identifying high-risk cases, and intervening in younger women.

[Methods]

1. To predict follicle development cycles in patients with POI, we measured very low serum Anti-Müllerian Hormone (AMH) levels using an ultrasensitive enzyme-linked immunosorbent assay kit. We further evaluated follicle growth in each patient during each cycle in patients with POI who received hormone replacement therapy.

2. Based on our findings that E2 has an inhibitory effect on Stefin A, which contributes to primordial follicle activation (PFA), we investigated the effect of estrogen receptor (ER) antagonist treatment on PFA in adult female mice by evaluating the localization of forkhead boxO3a (FOXO3a).

3. To identify a novel marker for POI, we evaluated the immunoprecipitation products of

proteins from the granulosa cell line (HGrC1) and patients with POI.

4. To predict the oocyte to achieve pregnancy, we isolated extracellular vesicles from the follicle fluid of pregnant and non-pregnant cases of infertility patients and performed small RNA sequencing to investigate the profiles of small non-coding RNAs.

5. To assess the fertility of women in their early twenties, we conducted lectures and analyzed their serum AMH levels.

[Results]

1. We investigated 19 patients with POI in whom we analyzed 91 cycles ; 14 cycles were AMH positive, and 9 of those cycles showed follicular development. The positive predictive value of positive serum AMH for follicle growth was higher than that of low follicle-stimulating hormone levels (< 10 mIU/mL).

2. In the mouse ovaries, the rate of PFA around antral follicles (within 50 μ m) was lower than that of other areas, and ER antagonist administration promoted PFA. This result supports that local ovarian E2 contributes to preservation of follicles.

3. POTE (prostate, ovary, testis, and placenta) F protein was identified as a candidate antigen by mass spectrometry of the immunoprecipitation products. The levels of serum anti-

POTEF autoantibodies were higher in POI patients than in control patients with normal menstrual cycles.

4. We found that a specific combination of small non-coding RNAs (miR-16-2-3p, miR-378a-3p, and miR-483-5p) could predict pregnancy.

5. Eighteen of the 529 young women had serum AMH levels of 1.0 ng/mL or less, indicating

that some women had potentially low ovarian reserve.

[Conclusion]

These multidirectional approaches can help patients with POI conceive with their own eggs and reduce the number of patients who develop POI and interactive infertility in the future.

シンポジウム 2 **P** 難治性不妊症の新規診断・治療法の開発に向けた病態解明

2) ヒト配偶子・胚を用いた ART の細胞生物学的な解析：add-ons 医療の本質の究明

秋田大学 白澤 弘 光

【背景】

マテリアルとしてヒト配偶子・胚を用いた研究は、倫理的ハードルから、その機会は限られる。生殖補助医療においては、各 add-ons が先進医療の枠組みでその有用性が検討されており、基礎的な研究の必要性が更に増している。近年は未受精卵子凍結も本邦で拡がり (Shirasawa H, Terada Y. et al. Heliyon 2023), ヒト配偶子の時点から細胞生物学的な知見を積み重ねていく意義は大きい。我々は、これまでヒト配偶子・胚を用い、未成熟卵子、成熟卵、初期胚、着床前期胚、長期培養までの一連の過程を研究対象とし、体外成熟培養 (in vitro maturation, IVM), タイムラプステクノロジー (time-lapse technology, TLT), 着床前胚染色体異数性検査 (preimplantation genetic testing for aneuploidy, PGT-A) などを用い解析・検討を行ってきた。本シンポジウムでは、add-ons を用いた研究成果から今後の研究課題を整理したい。

【目的】

良好胚獲得及び良好胚選別手法について、add-ons 医療の観点を踏まえ、「ヒト配偶子・ヒト胚を用いて難治性不妊症の新規診断・治療法の開発に向けた病態解明」につながる基礎的知見を得る事を目的とした。

【方法】

当院の倫理委員会の承認を得て下記研究を実施した。

1. ヒト未成熟卵子を用いた IVM に関する研究

ヒト未成熟卵子回収に非刺激下ヒト摘出卵巣を用いた。子宮体癌 8 症例 (87 個) (Shirasawa H, Terada Y. et al. JARG 2013), 子宮体癌 14 症例 (79

個) (Shirasawa H, Terada Y. et al. RMB 2019), 子宮体癌 8 症例 (63 個) (Shirasawa H, Terada Y. et al. F&S Sci 2020), 卵巣組織凍結時摘出卵巣 4 症例 (20 個) (Shirasawa H, Terada Y. et al. ASRM 2021) のほか、卵巣手術時における未成熟卵子 (Shirasawa H, Terada Y. et al. Gynecol Onco Rep 2016) をマテリアルとし検討を行った。IVM により第 1 極体 (fPB) を放出し、meiosis II (MII) 期に至った割合 (maturation rate), IVM から fPB 放出までの時間、施設間回収卵液輸送が maturation rate に与える影響、IVM 由来 MII 卵の単為発生能と前核挙動解析、蛍光免疫染色等を施行し、ヒト個体加齢, in vitro aging との関連を解析した。

2. ヒト卵子・ヒト胚における TLT に関する研究

当院 ART のヒト廃棄胚を用いた。18 症例 (38 個) の胚を融解後 TLT により観察し、拡張面積、虚脱 (contraction) 回数、hatching などの動的挙動と、蛍光免疫染色を用いた栄養外胚葉 (TE 細胞) と内部細胞塊 (ICM) に対する 3 次元細胞カウント結果の関連を検討した (Iwasawa T, Shirasawa H, Terada Y. et al. PLoS One 2019)。また 11 症例 (20 個) の胚を用いて、Na⁺/K⁺ ATPase について、 $\alpha 1$, $\beta 1$, $\beta 3$ アイソフォームの胚における局在を蛍光免疫染色、RT-qPCR を用い、拡張、hatching との関連を解析した (Hirakawa T, Shirasawa H, Terada Y. et al. Hum Reprod 2022)。

3. ヒト胚に対する PGT-A に関する研究

ART ヒト廃棄胚を用いた。12 症例 (20 個) の胚を用い、5, 6 日齢の胚盤胞を融解後、10 日齢まで長期培養し、胚培養液中の cell-free DNA を用

いた非侵襲的 PGT-A (niPGT-A) と PGT-A の一致率について検討を行った (Shitara A, Shirasawa H, Terada Y. et al. PLoS One 2021). また, 11 症例 (29 個) の胚盤胞を用い, TE 細胞生検による PGT-A と, TE 細胞生検後の胚盤胞全体を解析した PGT-A の結果について, モザイクを含めた一致率を検討した (Takahashi H, Shirasawa H, Terada Y. et al. RMB 2021).

【成績】

1. Maturation rate は 12.6%, 50.9%, 55.2%, 71.4%, 33.3% と各検討で差を認めた. commercial base の IVM キットを用いた maturation rate は 54.5% であり, 2013 年の報告における 12.6% に比し有意な改善を認めた. また IVM 開始から fPB 放出までは 53.1% が 24 時間以内であったが, TLT を用い詳細な観察を行うと 4.7-57.0 時間と幅広い range を認める事が明らかになった. また, 卵胞液を施設間 250km 輸送後に IVM を施行すると maturation rate が 38.6% と有意に低下した. 単為発生刺激では, 2cell 以上の卵割が 46.9%, morula 以上は 6.3% であり, 単為発生胚発育と, fPB 放出タイミングおよび前核出現から消失までの間隔, それぞれの関連性が示唆された. また卵巣組織凍結では fPB 放出から卵子凍結や ICSI までのタイムラグが 2.0-24.3 時間生じていた.

2. 胚拡張において, 非拡張の胚に比し ICM, TE の各細胞数が有意に多く, 融解後の胚の拡張割合および hatching 有無が, TE 細胞数と有意に関連することが明らかになった. contraction 回数と TE 細胞数には有意に負の相関を認めたが, ICM 細胞数との相関は認めなかった. また, Na⁺/K⁺ ATPase の $\alpha 1$, $\beta 3$ アイソフォームが TE 細胞側底側 (basolateral) に, $\beta 1$ アイソフォームが TE 細胞間に局在していることが, ヒト胚で初めて明らかになった. また $\beta 3$ mRNA の発現は有意に hatching 後に増加しており, ヒト胚における Na⁺/K⁺ ATPase と TLM による動的挙動の関連が認められた.

3. IVC1, IVC2 medium を用い最長 10 日目まで

長期培養を施行し, 胚全体に対する PGT-A を施行した. Day6 における PGT-A, niPGT-A と長期培養後 PGT-A の一致率は, PGT-A 43.8%, niPGT-A 56.3% であった. niPGT-A は感度 100%, 特異度 87.5%, PGT-A は感度 87.5%, 特異度 77.8% であった. また TE 細胞生検と胚全体の PGT-A の結果として 37.9% (11/29) に不一致が認められた. また TE 生検でモザイクや部分的な染色体異常を認めた 10 症例全てにおいて, 胚全体の PGT-A との不一致が認められ, PGT-A の有用性を考慮する際の重要な知見が得られた.

【今後の展開】

我々は最近, マウス胚を用い, mRNA などの injection 操作を要さない, 蛍光化学プローブを用いた初期胚分裂過程のライブセルイメージング手法を報告した (Okabe M, Shirasawa H, Terada Y. et al. RMB 2023). 現在は, 研究協力施設から得たヒト凍結前核期胚を用い, 蛍光化学プローブにより DNA, チュープリンを染色し, 前核消失から 2 細胞期, 4 細胞期の分裂過程をライブセルイメージングにて観察を行っている (Ono Y, Shirasawa H, Terada Y. et al.). この観察により 2 細胞期の多核率, 多極染色体分離, 紡錘体形態に関連があることが明らかになった. また, 2 細胞期に多核であった場合も, 引き続き第二分裂過程において, 多くが単核に修正される事も明らかになった. これら初期有糸分裂過程の知見を, add-ons 関連の研究成果と融合し多角的に検討していく.

【結論】

未成熟卵子, 成熟卵, 初期胚, 着床前期胚, 長期培養までの各ステージにおいて, add-ons を用いた検討を行った. 実用的な良好胚獲得及び良好胚選別手法を確立する為, 各ステージの細胞生物学的な事象を連続的に評価していく取り組みは不可欠である. 将来的には未受精卵子の IVM から, 受精から初期胚分裂過程および, その後の胚発育まで連続的かつ非侵襲的に観察する事で, 良好胚選別を可能とするアルゴリズム, 機器の実装が理想であり, 基礎的知見の集積を進めていきたい.

Symposium 2 **P** :

Elucidation of pathophysiology for the development of new diagnostic and therapeutic methods for intractable infertility

2) Cellular and biological analysis of human gametas and embryos in assisted reproductive technology : investigating the essence of add-ons
medicine

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[Background]

Our research has continuously focused on human oocytes and embryos, studying the entire process, employing in vitro maturation (IVM), time-lapse technology (TLT), and preimplantation genetic testing for aneuploidy (PGT-A).

[Objective]

To obtain fundamental insights into developing novel diagnostic and treatment methods for refractory infertility, leveraging human oocytes and embryos, focusing on obtaining and selecting quality embryos in light of add-on medical treatments.

[Methods]

1. Research on in vitro maturation (IVM)

We focused on the first polar body (fPB) release, maturation rate, and the effects of follicular fluid transport on maturation. Additionally, we analyzed the parthenogenetic potential and pronuclear behavior of MII oocytes.

2. Research on time-lapse technology (TLT)

We studied 18 cases with TLT, focusing on expansion, contraction, and hatching behaviors, plus trophoctoderm (TE) and inner cell mass (ICM) cell counts. We analyzed Na⁺/K⁺ ATPase isoforms $\alpha 1$, $\beta 1$, and $\beta 3$ in embryos using fluorescent immunostaining and RT-qPCR, assessing their links to expansion and hatching.

3. Research on preimplantation genetic testing for aneuploidy (PGT-A)

We extended the embryo culture to day ten to compare non-invasive PGT-A (niPGT-A) using cell-free DNA with traditional PGT-A. We compared PGT-A results from TE cell biopsy and whole blastocyst analysis, considering concordance rates and mosaicism.

[Results]

1. Maturation rates across studies varied (12.6% to 71.4%), significantly increasing to 54.5% using a commercial IVM kit. Over half of the cases released the fPB within 24 hours, though TLT revealed a broader range of 4.7-57.0 hours. Transporting follicular fluid lowered the maturation rate to 38.6%. Parthenogenetic stimulation led to 46.9% of oocytes undergoing 2-cell division and 6.3% reaching the morula stage, indicating a link with fPB release timing and pronucleus dynamics.

2. In embryo expansion studies, non-expanding embryos had fewer ICM and TE cells, with TE cell count significantly influencing expansion and hatching. A negative correlation was noted between contraction frequency and TE cell count but not with ICM cells. Na⁺/K⁺ ATPase $\alpha 1$ and $\beta 3$ isoforms were basolaterally located in TE cells, while $\beta 1$ was between them. Post-

hatching, $\beta 3$ mRNA expression significantly increased, linking Na^+/K^+ ATPase activity in embryos.

3. Concordance rates for PGT-A and niPGT-A were 43.8% and 56.3%, respectively. NiPGT-A showed 100% sensitivity and 87.5% specificity, compared to PGT-A's 87.5% and 77.8%. Notably, 37.9% of cases showed discrepancies between TE cell biopsy and whole blastocyst PGT-A.

[Conclusion]

Our study has recently focused on human em-

bryos in the pre-nuclear stage. We employ fluorescent chemical probes to stain DNA and tubulin, allowing us to observe cell division from the pronucleus to the 4-cell stages through live cell imaging. This observation has revealed a correlation between the multinucleation rate, multipolar chromosome segregation, and spindle morphology. Our future goals include developing algorithms and devices that non-invasively select high-quality embryos.

シンポジウム 2 P 難治性不妊症の新規診断・治療法の開発に向けた病態解明

3) 脱落膜化不全の病態解明にむけて：C/EBP β による脱落膜化制御機構の解明

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【目的】

子宮内膜間質細胞 (endometrial stromal cell ; ESC) の脱落膜化はプロゲステロンの影響により誘導される細胞の形態的・機能的変化であり、着床や妊娠の維持に寄与すると考えられている。脱落膜化の異常は着床不全や習慣流産の原因となり得ることが報告されているが、実際にどのくらいの頻度で脱落膜化不全患者が存在するのか、なぜ脱落膜化の異常が着床不全の原因となるのかについては未だ不明な点が多いままである。我々は、その病態解明を目指して研究を進めてきた。この脱落膜化という現象は、多くの遺伝子の発現変化によって誘導される。脱落膜化における遺伝子発現調節は、これまで主に転写因子による制御のみに着目され研究が行われてきた。しかし我々は、脱落膜化における遺伝子発現調節を「転写因子による調節」だけでなく「epigeneticsによる調節」の視点から解明に取り組んだ。さらに、包括的な遺伝子発現の調節機構を理解するため、次世代シーケンサーを用いて、遺伝子発現変化およびヒストン修飾変化をゲノムワイドな視点から統合的に解析した。

【方法】

1. 不妊症患者における子宮内膜脱落膜化不全について

32名の不妊患者に対し、分泌期後期(排卵後11日~13日)に子宮内膜を採取し、子宮内膜日付診を行なった。間質の形態から、正常群(排卵後日数と日付診のずれが1日以内)と脱落膜化遅延群(ずれが2日以上)に分け、脱落膜化不全症例の存在割合を検討し、脱落膜化に重要とされる転写因子C/EBP β (後述)の発現の状況を評価した。脱

落膜化遅延が20例(62.5%)と高率に認められ、これらの症例のESCにおけるC/EBP β の発現は、脱落膜化遅延群で有意に低かった。すなわち、不妊症患者において脱落膜化不全症例が高頻度に存在することがわかり、脱落膜化不全は看過できない病態であることが明らかとなった。さらに、脱落膜化不全とC/EBP β の発現低下との関連性が示された。

2. 新たなin vitro着床モデルの開発と脱落膜化不全の病態解明

これまで報告されているin vitro着床モデルでは、胚モデル細胞として絨毛癌細胞株が用いられ、それを二次元培養のESCの上で共培養するというものであり、生体内の着床現象を反映しているものとは言い難い。近年樹立されたヒト栄養膜幹細胞(trophoblast stem cell ; TS細胞)は、組織に浸潤することで絨毛細胞に分化する特徴を持つ。よって、この細胞を胚モデル細胞として用いることで脱落膜化細胞層内での絨毛細胞の分化過程を再現できると考えた。そこで、TS細胞を脱落膜化ESCと3次元共培養することで、オルガノイド構造を作製し、より生体内に近い着床モデルの作製を試みた。TS細胞を脱落膜化ESCと共培養した時は、非脱落膜化ESCと共培養したときに比べ、TS細胞の合胞体性栄養膜細胞(syncytiotrophoblast cell ; SyT細胞)への分化が促進された。C/EBP β をノックダウンしたESCとの共培養では、SyT細胞への分化は抑制された。新たなin vitro着床モデルを用いることで、脱落膜化はTS細胞のSyT細胞への分化に重要な役割を果たしていること、脱落膜化不全ではこの過程に障害が起きるため着床不全となっていることが示唆され

た。

3. 転写因子 C/EBP β によるゲノムワイド遺伝子発現制御とヒストン修飾制御の検討

増殖期後期の子宮内膜から ESC を分離・培養した。siRNA による C/EBP β ノックダウン下、非ノックダウン下で脱落膜化刺激を加え、ゲノムワイド発現解析を RNA-sequence で、ヒストンアセチル化 (H3K27ac) 修飾変化を ChIP-sequence で解析した。C/EBP β は、脱落膜化で発現が上昇する 4190 遺伝子のうち半分以上の 2498 遺伝子の発現を調節していた。これらの遺伝子は脱落膜化で誘導される様々な細胞機能変に関連しており、C/EBP β は脱落膜化を調節する重要な上流転写因子であることがわかった。さらに興味深いことに、脱落膜化で誘導される H3K27ac 上昇領域の 88.8% は C/EBP β により制御されていた。またこれらの多くの領域には、histone acetyltransferase (HAT) 活性をもつ転写共役因子である p300 の結合領域が存在することが分かった。一般的に H3K27ac は、凝集したクロマチン構造領域に pioneer factor と呼ばれる転写因子が結合し、そこに HAT 活性をもった転写共役因子がリクルートされることで誘導される。すなわち、C/EBP β がヒストン修飾を誘導する pioneer factor として働き、そこに p300 がリクルートされるという機序が、脱落膜化におけるゲノムワイドな H3K27ac 誘導とそれに伴うゲノムワイドな遺伝子発現調節の主なメカニズムであることが明らかとなった。また、C/EBP β -p300 複合体により誘導される H3K27ac 修飾変化は、転写調節研究において着目されてきた転写開始点付近だけでなく、多くの遠位領域にも起こっていることが明らかとなった。これらは、これまで着目されてない未知の enhancer 領域であると考えられ、さらにこの

領域が enhancer 活性を実際に持つことをゲノム編集法により内在性の enhancer 領域を欠失した細胞を作製することで証明することに成功した。

【結論】

不妊症患者の中には高頻度に脱落膜化不全症例が存在し、これらの症例では転写因子 C/EBP β の発現が低下していることが明らかとなった。また、我々が独自に開発した TS 細胞と ESC のオルガノイドを用いた in vitro 着床モデルを活用することで、脱落膜化という現象は、着床時における TS 細胞の SyT 細胞への分化に貢献しているという新たな脱落膜化の役割が明らかとなった。さらに、脱落膜化不全においては、この分化誘導が阻害されているために着床障害が引き起こされていることが示唆された。我々はこれまで、脱落膜化ではゲノムワイドなヒストン修飾変化が起き、これにより多くの遺伝子発現が調節されていることを世界に先駆けて報告してきた。この結果に基づき、さらに、C/EBP β が脱落膜化におけるヒストン修飾変化や遺伝子発現変化を制御している重要な転写因子であることをゲノムワイドな視点から明らかにした。これまでも脱落膜化を制御する分子は報告されているが、遺伝子発現のみならずゲノムワイドなエピゲノムを調節する因子を同定した報告はない。さらに、これらのゲノムワイドデータとゲノム編集法を応用することで、C/EBP β によって活性化される新規 enhancer 領域を同定することにも成功した。すなわち、C/EBP β により誘導されるべきこれらのゲノムワイドなヒストン修飾変化や遺伝子発現、細胞機能変化の欠如が脱落膜化不全を引き起こし、TS 細胞の SyT 細胞への分化障害が起こり、着床不全の一因となっていると考えられた。C/EBP β を指標とした新たな診断法や治療法に結びつくものである。

Symposium 2 **P** :

Elucidation of pathophysiology for the development of new diagnostic and therapeutic methods for intractable infertility

3) Pathogenesis of decidualization failure : regulatory mechanism of decidualization by C/EBP β

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[Objective]

Decidualization failure of endometrial stromal cells (ESCs) has been thought to induce implantation failure and miscarriage. However, it remains unclear how frequently decidualization failure is observed among infertile patients, and why decidualization failure may cause implantation failure. In this study, we examined the prevalence of decidualization failure and the role of decidualization by developing a novel in vitro implantation model. We also investigated the regulation mechanisms of decidualization by performing genome-wide epigenetic analysis.

[Methods]

1. Endometrial samples were obtained from 32 infertile patients in the late secretory phase for endometrial dating. If the endometrial dating was more than 2 days earlier than the actual day after ovulation, they were diagnosed with decidualization failure. Expression of C/EBP β , an important factor for decidualization, was examined by immunohistochemistry.

2. To investigate how decidualization contributes to implantation, we developed a novel in vitro implantation model. Recently established human trophoblast stem cells (TS cells) have the potential to differentiate into syncytiotrophoblasts (SyT cells). We co-cultured ESCs with TS cells under 3D culture condition.

3. We previously reported that decidualization stimulus up-regulates genome-wide histone H3K27acetylation (H3K27ac ; an active marker of histone modification) and gene expression. To investigate the involvement of C/EBP β , the transcriptome and H3K27ac status of three types of cells (control cells, cAMP-treated cells, and cAMP-treated + C/EBP β -knockdown cells) were examined by RNA-sequence and ChIP-sequence, respectively.

[Results]

20 cases (62.5%) showed the morphological delay of decidualization. C/EBP β expression was impaired in ESCs with decidualization failure. Co-culture with decidualized ESCs promoted TS cell differentiation into SyT cells compared to co-culture with non-differentiated ESCs or C/EBP β -knockdown ESCs. Of 4190 genes upregulated by cAMP, 2239 genes (53.4%) were under the regulation of C/EBP β and were associated with various key cellular functions for decidualization, indicating that C/EBP β is a critical transcription factor. 88.8% of the H3K27ac-increased regions was under the regulation of C/EBP β . Many of these regions contain binding regions for p300, a transcription cofactor with histone acetyltransferase (HAT) activity, indicating that C/EBP β works as a pioneer factor by recruiting p300 to alter the genome-wide H3K27ac

and gene expression during decidualization.

[Conclusion]

A high rate of decidualization failure exists among infertile patients, suggesting that decidualization failure is one of the reasons for infertility that should not be overlooked. We found a novel role of decidualization, in which decidualization contributes to the differentiation of TS cells into SyT cells, indicating that decidualiza-

tion failure leads to implantation failure through the suppression of TS cell differentiation. Regarding the regulation of decidualization, *C/EBP β* works as a key regulator because it alters the genome-wide H3K27ac and gene expression. In fact, *C/EBP β* expression in ESCs with decidualization failure was impaired. Taken together, *C/EBP β* may be one of the target molecules to treat decidualization failure.

シンポジウム 2 P 難治性不妊症の新規診断・治療法の開発に向けた病態解明

4) 遺伝子改変マウスモデルを駆使した子宮内膜機能解析に基づく反復着床不全の予測法の確立

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【目的】

難治性不妊症の中で着床不全は診断・治療法が十分でなく病態も不明である。着床は単に胚が着床の場である子宮内膜に結合するだけの現象でなく、胚が子宮内膜管腔上皮へ接着する時期（胚接着期）や、胚が子宮内膜間質へ浸潤する時期（胚浸潤期）という段階を経ると考えられ、また子宮内膜の各種細胞間・分子間の絶妙な協調により成立するとされているがその詳細は不明である。本研究の目的は、着床不全のうち子宮因子に着目し、マウス・ヒトの着床期子宮内膜を用いて、着床不全の新規予測法確立のための科学的基盤を構築することである。着床不全の病態を明らかにする基礎研究が将来的に着床不全の診療の質向上に繋がるものと考えた。

【方法】

(1) マウスモデルを用いた胚接着・胚浸潤機構の解析

子宮内膜腺上皮から分泌され着床に必須のサイトカイン LIF (Leukemia Inhibitory Factor) による着床調節機構には不明な点が多い。LIF の下流である LIF 受容体 (LIFR), STAT3 シグナルの経路を介した子宮内膜上皮・間質の相互作用や、LIF 分泌を調節する転写因子 FOXA2 について子宮全体・間質・上皮特異的な遺伝子欠損マウスを作成し解析した。また、マウス子宮内膜と子宮頸部上皮の LIF 発現の同期性と着床との関連について着床不全マウスモデルを用いて解析した。

プロスタグランジン (PG) 産生を調節する COX (Cyclooxygenase) は着床調節因子と考えられているものの、その作用の詳細は不明である。COX の2つのアイソザイム COX-1 と COX-2 に着目

し、子宮内膜全体の COX-2 欠損マウスと全身性の COX-1 欠損マウスを用いて胚接着、胚浸潤を解析した。リピドミクスを用いてマウス子宮の PG 定量を行った。

胚浸潤の過程に関わる分子機構は未解明であるため、胚浸潤期に機能的な役割を果たす分子として、COX のほかに、細胞増殖抑制因子である網膜芽細胞腫遺伝子 RB と低酸素誘導因子 HIF に着目し、子宮内膜全体・上皮・間質の遺伝子欠損マウスを作成し解析した。

(2) ヒト検体を用いた解析

ホルモン補充周期で採取したヒト着床期子宮内膜 (P+7) を用いて、細胞増殖能評価、RNA シーケンス、PG 定量を行い、着床不全群と対照群（子宮内膜生検直後の胚移植で妊娠した不妊患者の群）で比較した。

婦人科子宮摘出検体を用いて、増殖期と着床期（分泌期中期）の子宮頸部の LIF 発現を *in situ hybridization* で調べた。

【成績】

・LIF は子宮内膜管腔構造と胚接着を調節する因子である

LIFR・STAT3 の子宮内膜上皮/間質特異的遺伝子欠損マウスの解析により、LIF は子宮内膜上皮の LIFR に作用し STAT3 活性化を介して子宮内膜管腔構造を調節し、子宮内膜間質では LIF 以外のリガンドによる STAT3 活性化を介して胚接着直前の上皮細胞増殖抑制に作用し、これらが協調し胚接着することが判明した。

・LIF は FOXA2 と性ホルモンにより発現調節を受け着床の窓を規定する

野生型マウスに対する排卵直後から着床直前ま

での高用量のプロゲステロン (P4) 投与の実験により、高用量 P4 による LIF 抑制を介した着床阻害作用が示された。内因性のエストラジオール (E2) を除去・抑制することで胚接着開始を一時的に保留する Delayed Implantation マウスモデルと FOXA2 欠損マウスとを比較して行った解析により、LIF 分泌不全が胚接着を保留に作用すること、卵巣からの内因性 E2 が LIF 分泌を誘導していること、LIF が着床の窓 (Implantation Window) を規定していることが示された。

・着床期の子宮頸部上皮の LIF 発現が着床能の指標となる可能性がある

LIF は、ヒトおよびマウス共に子宮内膜だけでなく子宮頸部上皮でも着床期に発現が増加していること、P4 受容体阻害剤および酸化ストレス誘導剤を用いた着床不全マウスモデルでは子宮頸部上皮の LIF 発現が低下することが判明した。子宮頸部細胞の LIF 発現が着床能の指標になる可能性が示唆され、子宮頸部細胞診同様の非侵襲的手法で採取できる子宮頸部細胞を用いた検査により、着床能が評価できる可能性が考えられた。

・子宮腺筋症合併症例における子宮内膜の PG 増加は着床不全予測マーカーになる可能性がある

COX-2 欠損マウスでは子宮の PG 減少により胚浸潤が障害され、COX-1/COX-2 の 2 遺伝子の欠損マウスではさらに顕著な子宮の PG 低下により胚浸潤より前の過程である胚接着が障害された。PG 補充で着床不全の表現型の改善が認められ、PG 依存的な着床の表現型が示された。ヒト着床期子宮内膜において、妊娠群に比べて着床不全群の COX-2 mRNA 発現に低下傾向を認めたが ($P=0.08$)、妊娠群と着床不全群のリピドミクスの比較では予想に反して各 PG 量に差を認めなかった。一方で子宮筋腫、子宮腺筋症、子宮内膜症合併症例についてサブ解析を行ったところ、子宮腺筋症合併症例では妊娠群に比較し着床不全群で PG 産生が有意に増加していた。子宮腺筋症で着床不全を生じる機序に子宮内膜の過剰な PG の関与が推測され、着床期子宮内膜の PG 増加が子宮腺筋症患者の着床不全予測マーカーになる可能性

が示された。

・着床期子宮内膜上皮の細胞増殖抑制は上皮の細胞死を誘導し胚浸潤を調節する

マウスでは胚接着の直前に子宮内膜上皮細胞増殖抑制と子宮内膜間質細胞増殖亢進 (Proliferation-differentiation switching ; PDS) が起こるが、それが着床に機能的な役割を果たすかを調べた。RB は細胞周期抑制作用を有し、子宮内膜全体の RB 欠損マウスは上皮細胞増殖抑制と胚浸潤が障害され、P4 補充によりいずれも救済された。この P4 投与による胚浸潤誘導には子宮内膜上皮消失が関わっており、上皮の細胞死 (ネクロトーシス) と死細胞の栄養膜細胞による貪食を介するという新たな胚浸潤機序が明らかになった。子宮内膜上皮の細胞増殖亢進を伴う着床不全に対して P4 補充が有効である可能性が考えられた。また子宮内膜間質の HIF2 α 欠損マウスでは子宮内膜上皮消失が起こらず胚浸潤障害をきたすことが示され、子宮内膜間質の HIF2 α 欠損マウスも RB 欠損マウスと同じ機序で着床不全をきたしていることが示唆された。

・子宮内膜上皮の細胞増殖能評価は反復着床不全の予測法となりうる

マウスモデルから得られた子宮内膜上皮の増殖能の知見をヒトで検証するため、ヒト着床期子宮内膜の管腔上皮の細胞増殖能を評価したところ、着床不全群では上皮の細胞増殖能が有意に亢進していた。ヒト着床期子宮内膜上皮の細胞増殖能評価により着床能が予測できる可能性が示された。

【結論】

本研究により、着床過程のうち胚接着および胚浸潤というステップごとの子宮内膜の機能調節分子とその作用機序、細胞間の作用連携の詳細を明らかにした。着床不全マウスモデルを用いた基礎研究により、着床のステップを調節する子宮内膜の分子機構や細胞間の情報伝達機構の存在が明らかとなり、また、ヒト着床不全の病態の理解や類似の機序の存在を新たに見出すことができ、今後は着床能や着床不全予測検査としての臨床応用が期待される。

Symposium 2 **P** :

Elucidation of pathophysiology for the development of new diagnostic and therapeutic methods for intractable infertility

4) Novel Methods for Predicting Repeated Implantation Failure : Innovations Through Analysis of Gene-Modified Mice Models

MATSUO Mitsunori

The University of Tokyo Hospital

[Objective] Recurrent Implantation Failure (RIF) is a major problem in artificial reproductive treatment (ART). Evaluation methods and therapeutic strategies for RIF are required ; however, the pathophysiology of RIF is not fully understood. This study aimed to create a scientific basis for establishing a novel way to predict implantation failure.

[Methods] To analyze the mechanism of embryo implantation regulation by LIF (Leukemia Inhibitory Factor), which is secreted by the endometrial gland epithelium and essential for implantation, we focused on LIFR (LIF-receptor) and STAT3 (Signal transducer and activator of transcription3), acting as downstream factors of LIF, and the transcription factor FOXA2 (Forkhead box protein A2), which regulates LIF secretion. We analyzed the roles of COX (Cyclooxygenase), which regulates prostaglandin (PG) synthesis and is crucial for embryo implantation, and Rb (Retinoblastoma protein). We generated and analyzed conditional KO mice using Cre/loxP System. Based on the findings from the mouse study, human uterine endometrium samples in the implantation phase were analyzed.

[Results] LIF contributes to implantation chamber formation and embryo attachment via LIFR-STAT3 signaling in uterine epithelium. LIF expression is regulated by FOXA2, and LIF signaling controls implantation window. Furthermore, we showed that cervical LIF is a possible

biomarker that detected uterine receptivity without invasive endometrial damage since LIF expression is increased not only in the uterine endometrium but also in the cervical epithelium during the implantation period in both humans and mice. Cox1 KO mice and COX2 cKO mice analysis shows that PG decline impairs embryo invasion and adhesion. Analysis using human uterine endometrium in implantation phase showed that changes in PG levels in the uterine endometrium may be a predictive marker of implantation failure in patients with uterine adenomyosis. Analysis using RB cKO mice revealed novel mechanisms in which RB regulates endometrial epithelial cell cycle arrest and necrosis precisely and leads to successful embryo invasion. Cell proliferation evaluation of endometrial epithelium can be a predictive method for RIF.

[Conclusion] Using the implantation failure mouse model, we have clarified the role of key molecules in each step of embryo implantation, such as adhesion and invasion. These studies have revealed coordinated molecular networks and signaling pathways that precisely regulate the uterine endometrium. These findings in basic research have led to the understanding of the pathophysiology of human implantation failure. In the future, new methods for assessing receptivity or predicting implantation failure are expected for RIF patients.

教育講演 1

卵巣癌におけるゲノム医療の up to date

琉球大学 関 根 正 幸

進行卵巣癌の初回治療においては、BRCA 遺伝学的検査や相同組換え修復不全 (HRD) の有無に基づいた維持療法の薬剤選択が行われている。オラパリブ単剤維持療法では BRCAAnalysis による生殖細胞系列の遺伝学的検査が、オラパリブとベバシズマブの併用療法では myChoice 診断システムによる腫瘍組織の HRD スコアリングが、コンパニオン診断として用いられている。どちらの検査を優先して行うのか、その結果と患者の状態により一体どの薬剤を選択するのがベストなのか、その方針は主治医や施設によって意見が異なるのが現状である。

また、BRCA 遺伝学的検査の普及により BRCA 遺伝子に病的バリエントを有する家系が多数見いだされ、家系内健常者のサーベイランスやリスク

低減手術に関するカウンセリングが急増している。その状況において、発癌リスクに関する日本人のデータが強く求められている。特に卵巣癌においては、日本人は欧米に比べて罹患率が低く、罹患年齢も遅いなどの違いがみられ、BRCA 遺伝子病的バリエント型も日本人特有の型が存在する。日本人を対象に個別化した癌発症リスクのカウンセリングが可能となれば、リスク低減卵管卵巣摘出術 (RRSO) を実施する年齢を遅らせることが可能になるなど、BRCA 遺伝子病的バリエント保持者に対するメリットは非常に大きい。

現状における進行卵巣癌に対するゲノム医療の問題点を浮き彫りにし、最新データを踏まえて薬剤選択と遺伝学的フォローについて再考してみたい。

教育講演 2

今だから知っておきたい子宮体がん診療 Up to date

慶應義塾大学 山 上 亘

子宮体がんは本邦で最多の婦人科腫瘍であるが、比較的前後良好な疾患である。経膈超音波検査や子宮内膜細胞診によるスクリーニングの後、子宮内膜生検や子宮内膜全面搔爬による確定診断を行い、MRIやCT、PET-CTなどの画像診断で病変の広がりや進行度を推定し、治療方針を決定する。初回治療はIA期相当であれば鏡視下手術の適応となり、IB期以上は開腹手術を行う。術後病理診断にて進行期決定と再発リスク分類を行い術後療法を決定するが、本邦ではplatinum doubletを用いた化学療法が施行されることが多い。再発腫瘍に対してもtreatment free intervalに応じた化学療法が選択されてきた。

上記の診断・治療戦略には長らく大きな変化がなかったが、近年パラダイムシフトが生じている。診断においてはWHO組織分類(第5版)が2020年に発刊されたことに伴い、本邦においては子宮体癌取扱い規約病理編第5版が2022年に刊行された。組織分類の一部変更と、分子遺伝学的分類(TCGA分類, ProMisE分類)が紹介されたことが主な改訂項目である。さらに、The International Federation of Gynecology and Obstetrics (FIGO)によりFIGO2023進行期分類が公表された。従来の病変進行に加えて、脈管侵襲の程度、組織型、そして分子遺伝学的分といった複数の評価軸により、進行期が決定することになる。加えて、従来よりも重分類が細分化されることになったことで、より正確に再発リスクが進行期に反映されると想定される一方で、進行期決定の手順がより複雑化するため、その普及には産婦人科医のより深い理解が必要となる。現在、子宮体癌取扱い規約臨床編の改訂作業中であり完成が待たれる。

一方、治療については、特に進行再発がんに対する薬物療法において、近年多くのエビデンスが明

らかになってきている。いずれも免疫チェックポイント阻害薬(ICI)を軸とした併用療法であり、化学療法既往のある進行再発がんに対しマルチキナーゼ阻害薬であるLenvatinibと抗PD-1抗体のPembrolizumabとの併用療法(LP療法)の、化学療法単剤への優越性を検証する第III相試験(KEYNOTE-775試験)の結果から、LP療法が2021年に保険収載され広く普及している。また、TC療法へPembrolizumabの上乗せ効果を検証したNRG-GY018試験、抗PD-1抗体であるDostarlimabの上乗せ効果を検証したRUBY試験、抗PD-L1抗体であるAtezolizumabの上乗せ効果を検証したAtTEnd試験、抗PD-L1抗体のDurvalumabとPARP阻害薬のOlaparibの上乗せ効果を検証したDUO-E試験などの結果が明らかになり、dMMR、pMMR症例に対する効果が示された。これらの結果から、進行再発がんに対する薬物療法の選択肢が、より複雑化することが推測される。さらに、術後療法としてのTC療法にPembrolizumabを上乗せ(KEYNOTE-B21試験)や、dMMR症例に対しTC療法に比してPembrolizumabの有効性(KEYNOTE-C93試験)を検証する試験なども進行中であり、結果によっては早いラインでのICI投与が標準治療となる可能性がある。

また、早期高分化がんや子宮内膜異型増殖症に対する妊孕性温存療法も、現状では酢酸メドロキシプロゲステロン(MPA)のみ本邦の保険適応を有するが、国内で実施されたFELICIA試験でメトホルミンの上乗せ効果が示されれば、新たな治療戦略が加わる可能性がある。また、子宮鏡手術の併用で治療成績が向上する可能性が海外のメタアナリシスで示されており、今後子宮鏡手術の適応症の拡大が望まれる。

教育講演 3

HPV の発癌機序と宿主免疫制御から見た子宮頸癌に対する免疫療法の新展開

日本大学 川 名 敬

ヒトパピローマウイルス (HPV) はありふれたウイルスであり、ほぼすべての成人の男女が感染したことがある。HPV には 200 種以上の遺伝子型があり、性行為によって生殖器に感染する粘膜型 HPV の中で癌と関連の深いハイリスク HPV には 13-14 種の遺伝子型がある。ハイリスク HPV の中でも HPV16, 18 型は特に悪性度が高いことが知られている。例を挙げれば、子宮頸癌以外の HPV 関連癌 (咽頭癌, 肛門癌, 陰茎癌, 外陰癌, 陰癌) は約 90% が HPV16, 18 型に起因している。また若年の子宮頸癌では HPV16, 18 型が約 90% を占める。HPV16 型と 18 型も違いがある。子宮頸癌のうち 18 型は腺癌が多く、16 型と比べ 18 型子宮頸癌は予後不良である。HPV による発癌機序には遺伝子型による差異があることを理解しておくべきである。

一方で、HPV16 型に感染しても約 90% の女性は宿主の免疫応答によってウイルス増殖を制御し HPV 検査も陰転化する。つまり、HPV に対する感染免疫が誘導されるかどうかは HPV 関連疾患、HPV 関連癌の病態を考えるうえで外せない因子となる。つまり HPV には誰でも感染するが、HPV に対する免疫 (細胞性免疫) が誘導された女性と誘導されなかった女性で、臨床的な結果が大きく異なる。免疫が誘導されない女性に対して HPV に対する免疫を誘導するワクチン (治療ワクチン) があれば CIN や子宮頸癌の新しい治療法になりうる。HPV ワクチンによる感染予防が一次予防として確実であるが、世界の HPV ワクチン接種率は 40% 程度であり、日本の接種率も 10% 程度と推定されている。HPV ワクチンは注射薬であり医

療資源がない低中所得国では注射ができない現実もある。Global health の観点から世界保健機関 (WHO) は、HPV 予防ワクチンの次の一手として “HPV 治療ワクチン” の開発をめざしている。

子宮頸癌と CIN2-3 には、HPV の癌蛋白質 E6, E7 が恒常的に高発現していることが知られている。特に E7 蛋白質はヒトでの抗原性も高く免疫療法の最適な標的となる。現在世界で開発中の 20 以上ある HPV 治療ワクチンは、ほぼすべて E7 蛋白質をワクチン抗原としたワクチンである。我々が開発している経口 HPV 治療ワクチン IGMKK16E7 は HPV16 型の E7 蛋白質を乳酸菌表面に表出させた内服薬である。HPV16 型陽性 CIN2-3 を対象疾患として第 I/II 相医師主導治験 (プラセボ対照二重盲検ランダム化比較試験) が終了している。HPV16 型単独陽性 CIN2-3 では 40% (プラセボ群は 11%) が半年以内に正常化した。CIN2-3 に対する免疫療法として非侵襲的治療であり、かつ医療資源が不要な治療になりうる。

HPV は免疫サーベイランスから逃れて持続感染するために免疫逃避機構を持っている。その代表は免疫チェックポイント PD-L1 発現である。HPV 感染細胞、CIN、子宮頸癌のいずれの病変でも PD-L1 発現が高くなっている。子宮頸癌に対する免疫療法として抗 PD-1 抗体薬、抗 PD-L1 抗体薬が PD-L1/PD-1 による免疫抑制状態を阻害することが期待される。

このように子宮頸癌の HPV による発癌機序とそれに対する宿主免疫応答を紐解くことによって子宮頸癌 (HPV 発癌) に特化した免疫療法が新たに展開される時代になってきたと言える。

教育講演 4

子宮頸癌の予防と治療：課題と将来の展望

帝京大学 長 阪 一 憲

世界全体で、新規がん症例全体の約5% (690,000例) が、高リスク型のヒトパピローマウイルス (HPV) 持続的感染が原因とされており、これは感染症に起因するがん全体の29.5%に相当する。女性の半数が25歳までにはHPV感染をするとされており、子宮頸がんは紛れもなく感染症の一種である。一方で、男性においても約3人に1人が生涯に一度はHPV感染をする。子宮頸癌の予防には、HPVワクチン接種が有効である。HPVワクチンは、L1タンパク質を自己増殖させたウイルス粒子のVLP (Virus-like particle) を構造とし、筋肉注射で接種されることで、B細胞とT細胞を強力に誘導する。本邦では、2013年に政府がHPVワクチン定期接種の積極的勧奨中止を決定してから再開するまで約8年間、接種率が1%未満に低下する事態となっていた。そのため2000年以降に出生した「ワクチン停止世代」と呼ばれる女兒が、これから子宮頸がん検診を受ける時期となっている。有効な子宮頸がん検診についても早急に議論を進める必要がある。令和4年4月よりHPVワクチン定期接種の積極的勧奨の再開が始まり、同時にキャッチアップ接種も始まった。さらに令和5年4月からは、9価HPVワクチンの定期接種、そして有効性が非劣性とされる15歳未満の2回接種も導入された。一方、海外のデータでは、男子への接種推奨、また1回接種の有効性まで示されている。他ワクチンにはないVLP構造自体の特質が示されており、1回接種の有効性は科学的にも裏付けている。今後、本邦でも検討すべき課題である。子宮頸がんの予防戦略は刻々と変化しており、正しい知識を身につける必要がある。

また進行・再発子宮頸癌に対する化学療法による治療戦略は、ここ数年で新たな選択肢が増えて

おり、標準治療が様変わりしている。KEYNOTE-826試験では、放射線同時化学療法の場合を除いた化学療法による治療歴のない再発・残存・転移子宮頸癌に対して、ペバシズマブ併用の有無を問わないパクリタキセルとプラチナ製剤併用療法へのベムプロリズマブ上乗せ効果を検討しており、PD-L1発現に関わらず、全生存期間、無増悪生存期間の改善を認めた。そしてEMPOWER-Cervical 1/GOG-3016/ENGOT-cx9試験においては、対象比較が主治医の選択した単剤化学療法ではあるが、抗PD-1抗体薬であるセミプリマブが、パクリタキセルとシスプラチン併用化学療法後に増悪した再発・転移性子宮頸癌 (全組織型) に対して、PD-L1陽性率と関係なく、死亡リスクを31%減少させた (OS中央値：セミプリマブ単剤12か月 vs 単剤化学療法群8.5か月；HR=0.69； $p<0.001$)。さらには、本邦未導入であるが、第II相試験 inno-vaTV 204/GOG-3023/ENGOT-cx6試験において、治療歴のある再発・転移性子宮頸癌に対し、組織因子指向性抗体-微小管阻害剤複合体であるチソツマブ ベドチン単剤療法が、24%の奏効率 (完全奏効7%、部分奏効17%) を示した。現在第III相試験に加えて、チソツマブ ベドチンを既存治療に上乗せしたマルチコホート第Ib/II相試験が登録中である。注目すべきは、第II相DESTINY-PanTumor02試験である。トラスツマブ デルクステカン (T-DXd) 療法 (5.4mg/kg 3週間間隔) が、HER2変異陽性の固形腫瘍全患者において奏効期間中央値 (DOR) で未到達となり、強力な抗腫瘍効果を示した。子宮頸癌でHER2が過剰発現している症例はあり、新たな選択肢となる可能性がある。子宮頸癌の撲滅に向け、予防と治療についての最新データを概説する。

教育講演 5

婦人科腫瘍におけるリキッドバイオプシーの現状と展望

金沢医科大学 高倉 正博

近年の個別化医療の進歩に伴い腫瘍組織の生体情報を得ることは、病理診断のみならずコンパニオン診断の目的の遺伝変異や遺伝子発現解析のため、あるいは予後予想のために重要性が増してきている。しかしながら腫瘍の生検はときに侵襲が大きかったり、そもそも不可能である場合もあり、臨床上的問題となっている。

リキッドバイオプシーとは患者より血液などの検体を採取し、そこに含まれるがん細胞やがん細胞由来成分を解析する技術である。対象となる検体は血液が主であるが、尿、唾液、便、脳脊髄液などを用いたものも報告されている。解析対象としてはがん細胞（末梢循環腫瘍細胞）(circulating tumor cells, CTCs)、DNA (circulating tumor DNA, ctDNA あるいは cell-free DNA, cfDNA)、RNA (cell-free RNA, cfRNA)、マイクロRNA (circulating miRNA)、エクソソームなどの細胞外小胞があげられる。これらの手法は低侵襲に繰り返し検査を行えることが最大のメリットと言えるであろう。

体液中に腫瘍由来物を検出する試みの嚆矢は1840年の多発性骨髄腫患者の尿中の異常タンパク質（Bence Jones protein）検出や、1869年のがん死患者の血中に腫瘍細胞を認めたとする報告に遡る。その後、1999年の血清中RNAのRT-PCRによるメラノーマ特異的なチロシナーゼの発現検出をはじめとしてRT-PCRベースの検討が2000年代にさかに行われた。また2007年には上皮特異的抗原EpiCAMベースのCTCs検出システムがFDAに認可され、CTCsの定量が各種のがん

で予後予想や治療効果判定マーカーとなることが報告された。これらはいずれもその感度や臨床的意義の低さから、現在では下火になっている。殊にCTCsは解析対象として大変興味深いものであるが、その測定系の煩雑さと再現性の低さがネックとなってブレイクスルーが起っていない。

一方で2010年頃以降、次世代シークエンサーやデジタルPCRを応用した血中核酸の解析が急速に発展してきた。様々ながん種での検討が行われているが、特に大腸癌の領域では大規模な前向き検討が展開されており、術後のctDNAの有無が予後と非常によく相関するというデータが示されている（Kotani D et al. Nature Med 2023）。2021年には血液検体のctDNAを用いたがん遺伝子パネル検査であるFoundationOne Liquid CDxが保険収載されている。これは産婦人科領域では唯一保険適応可能な検査であるが、通常のがんパネル検査と同様に実施は1回に限られており、リキッドバイオプシーの利点を最大限に活かしているとは言い難い。

婦人科領域では腫瘍生検が困難な卵巣癌において比較的知見が蓄積されているが、前向きの大規模な臨床試験は未だ行われていない。リキッドバイオプシーはポテンシャルとして早期診断（スクリーニング）、治療選択（コンパニオン診断）、再発検出などすべてのステップで有効になりうるが、解決すべき課題も多い。そのために現状を確認するとともに、今後に向けての展望を考えたい。

教育講演 6

子宮筋腫に対する子宮動脈塞栓術

久留米大学 津 田 尚 武

子宮筋腫は性成熟期の女性の約2~3割に認められる良性子宮腫瘍であり、筋腫径の増大に伴って様々な自覚症状を呈する。症状としては、子宮内膜の圧排による過多月経からの貧血症、骨盤内臓器（膀胱や直腸）の圧排による頻尿や便秘、骨盤内血管や下大静脈の圧排による深部静脈血栓症などが挙げられる。そして子宮筋腫に対する治療は、患者の生活の質を左右するような自覚症状を有している場合に考慮される。

子宮筋腫に対する治療の選択肢は薬物療法（ホルモン療法、漢方療法など）、手術療法（開腹手術、腹腔鏡手術、手術支援ロボット支援下手術、子宮鏡下手術、子宮内膜焼灼術）、そしてUAEが挙げられる。治療選択にあたっては患者の年齢、妊娠出産歴、合併症、子宮筋腫のサイズや部位（筋層内、粘膜下、漿膜下）、悪性腫瘍との鑑別、患者のライフスタイルなどをもって総合的に検討する。

子宮筋腫に対するUAEの初めての治療は1995年のフランスのRavinaらにより報告された。2013年6月に多血性腫瘍に対しての血管塞栓用マイクロスフィアが製造販売承認、子宮筋腫に対するUAE手技が2014年4月に保険収載され、UAEが保険診療として施行可能になり、全国の

IVR可能な施設での急速な拡がりをみせている。UAEの選択にあたっては、患者状況に応じて薬物療法、手術療法と並列で判定する必要がある、またUAE施行後も有害事象のモニタリング含め治療前後わたるIVR施行の放射線科医と産婦人科医の緊密な連携が必須である。

本講演では子宮筋腫のUAEにおける治療適応の検討の流れと、放射線科と産婦人科の連携に関して報告する。

【目的】

子宮筋腫に対する子宮動脈塞栓術（子宮動脈塞栓術：Uterine Artery Embolization）の適応を検討する。

【方法】

久留米大学病院の産婦人科と放射線科においてのUAEに対する診療連携、治療成績を後視的に検討する。

【成績】

UAE治療における治療成績、有害事象、UAE不適格例、治療の実際（動画）を報告する。

【結論】

産婦人科と放射線科の緊密な連携体制の構築が子宮筋腫の治療管理において重要である。

教育講演 7

婦人科悪性疾患に対する低侵襲医療のこれまでとこれから

大分大学 小林 栄 仁

婦人科悪性疾患に対する低侵襲手術は、この20年で目まぐるしく変遷してきた。かつては良性疾患にのみ適用されてきた腹腔鏡手術が、開腹手術で難度が高いとされる子宮悪性疾患などの手術手技へと適応拡大がなされ爆発的に普及した。私自身は子宮悪性疾患に対する低侵襲手術の導入のため、新規医療技術の先進医療や臨床研究などを通して、2018年子宮頸癌に対する腹腔鏡手術の保険収載に主たる医療機関として承認を得ることに関わってきた。しかし子宮頸癌に対する腹腔鏡手術が保険収載された2018年と年を同じくして、MDアンダーソン癌センターのRamirezらにより、ARHとMinimally invasive surgery (laparoscopic or robot-assisted radical hysterectomy)の予後に関する大規模第三相比較試験(LACC (Laparoscopic Approach to Cervical Cancer) trial)の結果が報告された。今までの低侵襲手術と開腹手術で予後が変わらないとする多数の後方視的な研究結果を覆す報告に世界中で衝撃が起こった。このことは出版バイアス(Publication Bias)すなわち、研究結果の内容や方向性に依りて、研究が出版される確率が異なる現象を指し、過去に報告されているエビデンスが全て正しいわけではないことに加え、その後の報告により手術適応、手

術手技や術者の経験も重要である可能性を再認識させてくれた。現在は上記経験を踏まえた上で卵巣がんに対する低侵襲手術の保険診療への導入に取り組み、婦人科悪性疾患に対する低侵襲手術の発展に貢献したいと考えている。

一方内視鏡外科手術の技術的困難性を克服すべく手術支援ロボットが開発され我が国でも急速に広がりを見せ、働き方改革に伴うソロサージェリー化の動きが加速すると考えられる。近年の手術動画を用いたAI技術の目覚ましい発展に伴い、手術動画情報やロボットログを教育や研究に加え、医工連携に基づく産業利用へのニーズが高まっている。私は、今まで開腹で行われていた手術手技を低侵襲手術に置換する時代から、これら新たなテクノロジーを積極的に活用する時代に変わってきていると感じている。今回赴任した大分大学は、外科を中心に大学全体として低侵襲手術の導入及び発展に積極的に取り組まれており、かつ医療資源の乏しい国への国際貢献を積極的に行われております。私自身、これまで行ってきた経験に加え積極的に大学と共に、新規医療に取り組み国内のみならず近隣諸国での医療に積極的に貢献したいと考えており上記内容についての講演を行う。

教育講演 8

病因・病態にもとづいて考える理想的な子宮内膜症の管理

千葉大学 甲 賀 かをり

Sampson が“Endometriosis”という疾患名を American Journal of Obstetrics and Gynecology 中で初めて提唱した 1925 年から 99 年経った。当時稀とされていた本症は、昨今の少産・晩産化と初経年齢の低下により、一人の女性が生涯に経験する月経回数が増え、(Sampson の唱えた月経血逆流説にもとづけば、腹腔内での月経血曝露の機会が増えたためと解釈出来るが)、罹患率が上昇しつづけている。さらに、将来の挙児希望はあるものの現時点ではまだ挙児は希望しない、という状況で本症に罹患する女性が非常に増え、我々はその扱いに苦慮することが多い。また、子宮内膜症は不妊の原因となることはもちろん、昨今では妊娠中に増悪すること、さらに妊娠合併症を増加させることも知られるようになった。またひとたび閉経を迎えても、本症はがん化のリスクもあり、さらに本症既往女性は心脈管系疾患の罹患率が上昇することも知られてきている。さらに興味深いことに、本症は卵巣・腹膜といった好発部位だけでなく、腸管・尿路系・胸腔内・臍部といった稀少部位にも発生し、その罹患部位に依存してさまざまな症状を呈する。このようなことから、本症の取り扱いにおいては、様々な治療法のリスクとベネフィット、さらに症状の強さや、年齢や社会的背景、ご本人の根治性と機能温存に関する希望を勘案し、薬物療法・手術療法・不妊治療を組み

合わせた、長期的な管理が必要である。

私達はこれまでに、子宮内膜症患者より採取した、病巣組織や腹腔内貯留液中のサイトカイン等の生化学的因子、好中球・M1M2 マクロファージ・Myeloid-derived suppresser cells・樹状細胞等の免疫担当細胞の解析から、本症は Sampson のいう「逆流月経血」の存在だけが原因でなく、それが腹膜等に生着・増殖する機序として、免疫寛容・慢性炎症や血管新生促進等が関与していることを明らかにしてきた。一方、本症が卵巣機能不全や周産期合併症の原因となる機序とその予防については、ヒト同様の所見を呈するマウスモデルを確立し、解明を試みてきた。

本講演では、これらの基礎的研究から得られた子宮内膜症の病因・病態に関する知見をもとに、薬物療法・手術療法・不妊治療の最適な使い分けについてディスカッションしたい。さらに、現存のエストロゲンをターゲットとした薬物療法、病巣切除に依存する手術療法に替わる新規の治療法として、レスベラトロール、メラトニン、漢方薬、プロスタグランジン受容体拮抗薬といった、抗炎症・抗酸化物質の効果の可能性につき、マウスを用いた in vivo の研究や、子宮内膜症初代培養細胞を用いた in vitro の研究にもとづき紹介し、さらにビタミン D サプリメントや、磁気を用いた新規医療機器の臨床試験についても解説したい。

教育講演 9

患者中心の医療 (patient centered medicine) の実践～これからの診療の在り方を予見して～

山梨大学 吉野 修

会員の皆様は患者中心の医療 (Patient Centered Medicine) を展開するために、患者報告アウトカム (Patient Reported Outcome ; PRO) を利用されておられますでしょうか? PRO のうち、痛みのスケール法 (Visual Analogue Scale : VAS) による評価はご存知の方も多いかと思われませんが、近年、健康に関連する Quality of Life (QOL) を PRO で評価する報告が多くなってきています。具体的には short form-36 (SF-36) や Eur-Qol 5 dimension (EQ-5D) などがあり、患者が疾患をどのように捉えているかを身体的、社会的、精神的側面から、多面的に評価を行っていきます。私が診療の中心としている子宮内膜症治療においても、前述した患者さんの訴えを PRO として診療に取り込むことで、問題志向型、患者中心の医療にシフトすることが提唱されています (Vercellini P, Fertil and Steril 2015)。たしかに PRO などを活用することで患者さんの声を聴く、所謂 Narrative Based Medicine (NBM) は今の時代に重要なのでしょうか、その際、科学的な視点、統計学

的有意差を重要視する Evidence Based Medicine (EBM) を診療の拠り所としている我々、医療者はどのような立場をとるべきなのでしょう? 本講演では子宮内膜症診療における PRO による QOL 評価の意義についてお話させていただくと共に、Narrative Based Medicine (NBM) と Evidence Based Medicine (EBM) の調和にまで言及させていただきます。本講演のキーワードを以下に記載いたします。Patient Centered Medicine (PCM), Patient Reported Outcome (PRO), Narrative Based Medicine (NBM), Evidence Based Medicine (EBM), そして、Shared Decision Making (SDM)。

略語が多いですが、意味に関しては既にご理解をいただいている言葉は多いかと思います。これからキーワードを用いて、これから医療の進むであろう方向性について、患者さん、職場の同僚、論文などから教わったことを共有させていただき、皆様の考えるきっかけになれば幸いです。

教育講演 10

子宮腺筋症へのアプローチ～妊孕能維持・改善を目指して～

東京大学 廣 田 泰

30代後半～40代前半が好発年齢とされる子宮腺筋症は、月経痛・月経過多・不正性器出血などAUBの症状により、罹患女性のQOL低下を引き起こす。加えて、子宮腺筋症が不妊症、不育症、周産期合併症の原因となり妊孕能低下をきたす可能性が示されている。子宮腺筋症の存在が子宮の血流障害・炎症・線維化による筋層の機能不全を介して、妊娠に関連する各種病態を引き起こし、妊孕能を低下させている可能性が推測される。一方で、挙児希望を有する子宮腺筋症患者に対しては標準的な治療が示されておらず、妊娠に向けて対応に苦慮することも多い。子宮腺筋症合併不妊症に対する生殖補助医療においては低い妊娠率・高い流産率・低い出生率を示すこと、子宮腺筋症合併妊娠においてはpPROMやHDPなどの周産期合併症を併発すること、が最近の報告で示されている。挙児希望を有する子宮腺筋症の薬物療法としては、生殖補助医療の場合にはGnRHアゴニスト前投与のうえ凍結融解胚移植が行うことがで

きるが、出生率の改善が得られるかは判明していない。そのため、子宮摘出が基本とされる子宮腺筋症の手術療法において、子宮腺筋症病変を取り除き子宮を修復する子宮腺筋症病巣除去術が実施されている。これは妊孕能温存を希望する患者のための手術と考えられ、妊孕能維持・改善が期待されている。また最近の研究では、子宮腺筋症病巣除去術の有効性として、月経随伴症状の改善に加えて流産やHDPを予防する効果がある可能性が示唆されている。本講演では、子宮腺筋症合併不妊症の妊娠成績や生殖補助医療の治療成績、子宮腺筋症合併妊娠の周産期予後、子宮腺筋症病巣除去術の治療成績に焦点を当てて、挙児希望を有する子宮腺筋症に対する治療の現況と課題について述べる。さらに、子宮腺筋症病巣除去術の課題克服に向けて、日本産科婦人科学会の生殖・内分泌委員会小委員会や先進医療の取り組みについても紹介する。

教育講演 11

国内の分娩管理における新たな潮流と課題

国際医療福祉大学成田病院 永松 健

少子化に伴い、本邦の分娩件数は80万件を下回り減少を続けている。その一方で妊婦の高年齢化および妊娠・出産に求められるニーズの多様化が進んでおり現代の周産期診療は限られたリソースの活用が大きな課題となっている。特に、妊婦の高年齢化は様々な周産期転帰の悪化に関わる問題であり、分娩管理の面では帝王切開率の上昇に直接影響する因子となっている。そのため、高年齢の特に初産婦に対していかに対応するのかが重要な課題である。そして、妊婦のニーズの高まりに呼応して大都市圏を中心に硬膜外麻酔分娩（いわゆる無痛分娩）の導入を行う施設が増加しているが、安全性を確保しながら妊婦の満足度を高めてゆくことは決して容易ではない。無痛分娩の安全管理では、麻酔合併症の対策が注目されやすいが、実際には分娩第2期の遷延、器械分娩率増加、弛緩出血への対応などの産科的管理の難易度が増加することにも十分意識を向けるべきであろう。また、無痛分娩に際しては麻酔管理の可能な時間帯に合わせた分娩時間の調整が必要となることから計画誘発分娩と合わせた実施が進められる場合も多い。そうした中で分娩誘発の分野では、頸管熟化促進の新たなアプローチとしてジノプロストン腔内留置用製剤の国内での臨床使用が開始されたことで、分娩誘発のアプローチの多様性が広がった。そして、従来使用されてきた器械的熟化法と

の組み合わせも含めて、各施設の診療体制に応じた誘発プロトコルの工夫が求められている。分娩誘発の時期について、low-riskの初産婦において妊娠39週での分娩誘発の方が待機的な管理よりも母児の転帰が向上したとする米国ALLIVE trialの報告は、従来の予定日超過の段階で初めて介入を行うという分娩誘発開始の概念を覆すものであり、後続する研究では、高血圧や肥満などのリスク因子を有する妊婦集団での効果についても検討が進められている。ただし、大規模施設で集約された分娩管理が行われる諸外国の状況と本法の周産期医療体制は大きく異なっていることを念頭に置いて結果を解釈することが必要である。分娩進行の評価において、内診技術は分娩進行評価の要であり、産婦人科医はその技術を高める努力をしてきた。それに対して、経会陰超音波法を用いた分娩進行評価技術が発展してきており、内診を補完してより精度の高い分娩進行管理に寄与することが示されている。特に、児頭下降度や第2回旋の評価に有用であるとされており、経時的な分娩進行を可視化、数値化することができる。そして、確実に短時間での娩出が求められる器械分娩において、娩出失敗のリスク低減に役立つことが期待されている。本講演では、そうした近年の分娩管理の変化に伴う課題を踏まえて国内外のエビデンスを紐解きながら議論を進める。

教育講演 12

人工知能 (AI) の産婦人科領域への応用～研究から臨床まで AI 分析を生かす～

福岡大学 四 元 房 典

Artificial Intelligence (AI) の技術発展は目覚ましく、医療分野でも診断や治療で活用されている。産婦人科領域でも胎児エコーや CTG、婦人科悪性腫瘍の早期診断、卵子や精子の質の評価など、AI 技術を取り入れることで精度の高い診療が実現可能になってきている。また、医学研究においても様々な解析機器からデータがハイスループットに排出される時代になり、とくにゲノム解析で用いる次世代シーケンサーから得られる膨大なデータ量の保存や解析には、設備だけでなく高度な情報解析のための知識が必要であり、その解析ツールとして、AI 技術を活用した分析が大量のデータを高速で処理し、精度の高い分析結果を出すことを可能にしている。

本講演では、当講座で行っている産婦人科領域における AI 分析を用いた研究についてご紹介する。これまでの多くの報告では一つのモダリティ (一種類の画像データ等) を用いて特定の疾患の診断を行うユニモーダル AI が採用されているが、当講座の研究では複数のモダリティ (問診や血液検査、画像などの異なる形式の臨床情報やゲノム解析データ) を統合して同時に学習させるマルチモーダル AI を導入している。このマルチモーダル AI は、複数の情報源を統合して同時にデータ処理することで、異なるモダリティ間の相互作用を考慮しながら、AI モデルの予測精度を向上させることができる。そのためデータの多重共線性を考慮せずに予測モデルの構築が可能であり、利用可能なデータを全て使用することができ、さらに使用するデータを増やすこともできるメリットがある。まず、テキストデータとしては、紙による

問診表、化学療法の副作用チェック表、臨床研究に用いるアンケート調査などを QR コードで電子化して電子カルテに直接入力を行い、外来受診時だけでなくメールを用いて在宅時の状態についてもデータを回収することで、医師の労力を効率化すると同時にリアルタイムでのデータ管理・解析を可能にしている。腫瘍領域では、遺伝子情報に基づくがんゲノム医療で活用されている新規治療薬に抵抗性を示す内膜症性関連卵巣癌に対して、空間トランスクリプトーム遺伝子発現解析を行うことで、遺伝的背景の影響を受けない真のがん化プロセスの実態を把握し、臨床情報と MRI 画像データを組み合わせた AI 分析による早期診断システムと治療薬の開発を行っている。次に周産期領域において、子宮内感染を伴った早産例でマルチオミクス解析 (メタボローム・細菌組成・臨床情報の統合解析) に AI 分析を取り入れて、早産や破水との関連や早産児の神経発達障害を来たす新生児疾患との関連を解明し、新規治療法のターゲットを探索している。最後に不妊・内分泌領域では、これまで当講座が行ってきた難治性の着床不全症例や子宮内膜症に対する脂肪幹細胞を用いた再生医療での成果に AI 分析を取り入れて、加齢による卵質低下や受精卵分化機能の低下を改善する研究や子宮内膜再生の研究へ展開している。

この講演では、単一施設での取り組みを紹介する内容となっているが、これまで解決できなかった医療現場の課題にどのように AI を取り入れて、産婦人科医療のどのような近未来像を目指すのかを考える契機となれば幸いである。

教育講演 13

HPV をターゲットにした子宮頸がん予防戦略

昭和大学 松本光司

HPV 検査を用いた検診は、2003年に米国で細胞診との併用検診の形で初めて導入された。HPV 単独検診は2017年にオランダと豪州、2019年に英国、2020年にフランスに導入され、欧州を中心に導入が進んでいる。HPV 単独検診ではHPV 陽性者のみが細胞診でトリージングされ、HPV 陰性者では次回検診は5年後となる。発癌性 HPV を感度良く客観的に検出する HPV 検査は CIN2 以上の病変をほぼ見逃さなく検出する。HPV 陰性者では5年以内に新たに病変を生じるリスクも格段に低い。検診間隔を延長できる。しかし、感染しているだけの女性も偽陽性者としてひっかけてしまう。一方、細胞診では偽陽性は少ないが、細胞形態による診断であるため感度・再現性が乏しく、時に見落としが見られる。細胞診は特異度重視、HPV 検査は感度重視の検診ツールと言えるが、「5年以内に子宮頸がんと診断されるリスクは HPV 陰性者では細胞診陰性者よりも約70%も低く、検診ツールを細胞診から HPV 検査に替えるだけで子宮頸がん発症率が約半分に抑えられる」という海外データを考えると、HPV 検査を検診に取り入れるのは当然に思える。併用検診は HPV 単独検診と比較して、併用にしたことによって新たに検出できる癌はごくわずかであるにもかかわらず、費用がかかり偽陽性が増えること、アルゴリズムが複雑になり精度管理の点から実施可能性が低いことを理由に、海外諸国は併用検診ではなく、HPV 単独検診に舵を切った。

海外諸国が HPV 検診を導入したもう一つの理由は HPV ワクチンである。HPV ワクチンは性交開始前に接種すれば非常に強力な感染予防効果を得られることが、臨床試験だけでなく各国の接種プログラムによるリアルワールドデータで示されたからである。すでにスウェーデン、デンマーク、

英国、米国から子宮頸がんに対するワクチン効果が報告されている。我々の MINT スタディグループは、がん登録データの解析から日本でも2011年以降は20代の子宮頸がん罹患が減少に転じていることを報告した。しかし、これは検診効果や性行動の変化を反映したものかもしれない。そこで我々は、ワクチン特異的な効果を検証するため2012年以降新規に診断された40歳未満の若い子宮頸がんおよび CIN/AIS 患者において2価/4価ワクチンによって感染を予防できる HPV16/18 の陽性率をモニターしてきた。HPV16/18 陽性率は20代でのみ、2017年までに CIN/AIS において低下し、続いて2017年以降は子宮頸がんでも低下していることから、日本でも子宮頸がんに対して一定のワクチン効果が見られると我が国で初めて報告した。CIN2-3/AIS 患者における HPV16/18 陽性率のデータ解析から、HPV ワクチンを初交前に接種した場合にワクチン効果は100%であったこと、ワクチン接種率の高い世代では未接種者にも集団免疫効果が見られることを明らかにし、HPV 型分布の解析から今後9価ワクチンが普及すれば子宮頸がんや CIN2-3/AIS に対する予防効果は約90%に達すると試算した。すなわち、子宮頸がんや CIN/AIS 患者が激減する HPV ワクチンの時代には細胞診による目視でのスクリーニングには限界がある一方で、HPV 陽性者も減少することで HPV 検診で問題となる偽陽性は著しく減少することが予想される。

このように子宮頸がん予防戦略を考える上で、すでに検診とワクチンは切り離せない。我が国は HPV ワクチンの接種率を取り戻し、HPV 単独検診に踏み切れるのか？ 今こそ日本が世界に追いつくべきときである。

教育講演 14

一絨毛膜双胎における内分泌環境の変化と病態形成メカニズムの解明

東邦大学 中 田 雅 彦

一絨毛膜双胎では双胎間輸血症候群 (TTTS) に代表される一絨毛膜胎盤特有の合併症を生じる。以前は血流不均衡が主な原因とされてきたが、一概に血流量だけでは病態が説明できない場合も多い。また、TTTSとは異なり主に胎盤領域の不均衡を主とする selective intrauterine growth restriction (sIUGR) といった病態も一絨毛膜双胎では比較的多く認めるようになり、それぞれの疾患群における胎児環境の評価がその管理上重要となってきた。

TTTS や sIUGR は一旦発症すると周産期死亡や神経学的後遺症につながるため大きな問題となっていたが、約 20 年前から我が国でも内視鏡的胎児治療を導入することで予後改善が図れるようになってきた。ただし胎児治療を導入したとしても周産期死亡や神経学的後遺症は一定数には認められ、また出生後に肺動脈狭窄症などの先天性心疾患の管理を必要とする場合があることが問題となっている。

近年、TTTS の病態形成メカニズムに対しては、以前から paradoxical renin-angiotensin-aldosterone 系 (RAAS) の役割が注目されていたが、剖検例などのデータによってその説が提唱されるに過ぎなかった。しかしながら近年の超音波検査機器の進歩によって胎児循環における胎児心機能解析が可能となり、また、内視鏡的胎児治療の導入によって羊水などの生体試料の採取が可能となったため、それらのデータと胎児期の内分泌環境の変化との関連性が徐々に明らかとなっている。

本講演では、TTTS などの一絨毛膜双胎特有の病態に対して胎児治療を行った際に収集した超音波学的データや羊水中・臍帯血中の種々の循環作動物質の動態について、長年演者や共同研究者が行った臨床研究データを中心に、TTTS の発症メカニズムを概説すると共に、病態形成メカニズムを念頭においた臨床現場において役立つ胎児評価の方法について解説する。

教育講演 15

周産期における再生医療の現状と課題

北里大学 落合大吾

我々、周産期を専門とする医師は日常診療の中で、早産ハイリスク妊婦に対しては妊娠背景の解析、子宮頸管長の計測、細菌性膣症の診断・治療、あるいは子宮頸管縫縮術による手術介入など様々な方法による早産回避に全力をつくし、残念ながら早産不回避の際にはステロイドを投与し小児科医師と協働した周産期管理を行ってきた。また、胎児超音波や胎児MRIを用いて先天性疾患の胎内診断を行い、胎児の情報をできるだけ正確に捉えて、小児科・小児外科などの関連診療科と情報を共有し治療方針を決定し、その後の妊娠・分娩管理へと繋げてきた。その結果、我が国における周産期医療は世界的に見ても高水準となり、2022年の周産期死亡率は出生1000人あたり3.3人である。しかし、現代の医療では、患児の生存率だけでなく後遺症の有無やその後の生活の質が問われている。そのような視点で考えると、適切な周産期管理を受けた児であっても、出生後には長期間にわたって早産や先天性疾患のため重篤な後遺症に悩んでいる患者さんは依然として多く、根本的な治療方法の開発は急務である。

近年、「幹細胞治療」に関する研究は盛んに行われ、一部で臨床試験が行われている。その中で、臨床応用への課題が少ない細胞として間葉系幹細胞 (mesenchymal stem cell : MSC) が注目されている。本邦でも臨床試験が行われている新生児低酸素虚血性脳症に対する自己臍帯血移植治療もこの範疇に含まれる。これは、周産期脳傷害の治療

や予防として、分娩時に自己臍帯血を採取し簡便な細胞調整作業の後に新生児に投与する手法であり、臍帯血内に含有される幹細胞成分を利用して、MSCは高い抗炎症作用を有していることから、様々な疾患に対する治療効果が検討され、心不全や脊髄損傷などの成人の難治性疾患では治験も行われている。また、周産期疾患でも、周産期脳障害、早産合併症 (早産脳障害、慢性肺疾患、壊死性腸炎)、脊髄髄膜瘤などの先天性疾患、などに対する新規治療法としての期待は大きい。もし、難治性の周産期疾患に対してMSCを用いた幹細胞治療が確立されれば、未来の周産期管理は変貌を遂げる。例えば、出生時にアシドーシスを認めた正期産児や早産児には出生当日から予防的幹細胞治療を行なって脳性麻痺の発症を予防する、脊髄髄膜瘤では胎児幹細胞治療によって脊髄神経障害を治療する、などが考えられる。さらに、早産児の合併症リスクが減少するので間接的に母体の安全性も高まる。すなわち、妊娠高血圧症候群など、妊娠の進行に伴って病状が悪化する疾患では、早期に娩出し母体治療に専念することができる。そして、これまで妊娠禁忌であった合併症妊娠でも、早期娩出を前提とした妊娠許可が可能になるかもしれない。

本講演では、周産期脳障害、早産合併症 (早産脳障害、慢性肺疾患、壊死性腸炎)、あるいは脊髄髄膜瘤などの先天性疾患、に対する再生医療の現状と課題について概説する。

教育講演 17

産婦人科ロボット手術の変遷と新たな展開

藤田医科大学 西澤 春紀

現在、世界で最も臨床導入されているロボット手術は、米国 Intuitive Surgical 社の da Vinci サージカルシステムであり、2022年には世界で約7,500台が導入されて約190万件もの手術が行われたと報告されている。日本におけるロボット手術は、da Vinci サージカルシステムが2009年に医療用機器として承認された後、泌尿器科領域で2012年に前立腺癌に対する前立腺全摘除術が保険収載されたことを契機に全国的にロボット手術の導入が広がり、2018年に産婦人科領域を含めた新たな12術式が追加収載されて以降は、急速に一般医療としての普及が進んでいる。しかしながら、これまでの産婦人科疾患に対するロボット手術の報告では、従来の腹腔鏡手術に比した手術成績や合併症頻度、また腫瘍学的予後に関する明らかな有効性を示す十分なデータは得られていない。デュアルコンソールシステムやシミュレーションプログラムの搭載等により、高い学習効果とラーニングカーブの短縮等は示されているが、臨床成績の向上については、今後の多施設における症例の集積や詳細な検討が必要である。

一方、近年になると世界各国の企業で新しいロボット手術システムが次々と開発され、日本国内でも2020年8月にメディカロイド社のHinotori サージカルシステム、2023年5月にリバーワールド社のSaroa サージカルシステムが国産のロボット手術システムとして製造販売が承認され、既に実地臨床での運用が開始されている。また、これまでのロボット手術システムは、4アームを利用した多孔式アプローチが主流であったが、単孔式手術を可能とする da Vinci SP サージカルシステムが開発され、単孔式ロボット手術への関心や期待も高まっている。こうした状況を鑑みると、次世代のテクノロジーを応用したロボット手術システムは今後も急速に発展すると予想され、内視鏡手術戦略における新たな潮流を築いていくことに疑いの余地はないだろう。

本講演では、これまで運用されてきたロボット手術の変遷や成績を振り返るとともに、新たに導入されたロボット手術の特性や展望について概説する。

教育講演 18

産婦人科における3次元病理学

新潟大学 吉原弘祐

病理学は、光学顕微鏡を用いて組織切片を観察し、細胞あるいは組織の異常を明らかにして、疾患の原因や病態解明につなげていく学問である。組織切片の観察には、ヘマトキシリン・エオジン染色や免疫染色など様々な技法が開発・利用され、疾患の診断精度を高める工夫がなされている。しかし、光学顕微鏡の特性上、観察可能な組織切片の厚さは限りがあるため、得られる情報は「2次元」となる。

近年、脳研究やがん研究分野において、立体的な構造や形態変化が注目されるようになり、「3次元」で観察するための手法が開発されるようになってきた。まず、組織から大量の切片スライドを作成し、1枚1枚をデジタル画像として取り込み、それらの画像を立体像として再構成することが行われるようになったが、膨大な労力と時間を要するなどの課題があった。その点を改善したのが、「組織透明化」と「3次元イメージング技術」の開発である。組織サンプルを光学的に透明化し、薄く平面上に広げたレーザー光照射により、高速に光学的な断層像を取得し、3次元画像を構築することが可能になった。組織透明化は1900年代初めにドイツの解剖学者である Spalteholz 博士によって有機溶媒を使って行われたのが始まりと言われており、2010年代に入って急速に開発が進み、現在では数十種類のプロトコルが利用可能である。組織透明化・3次元イメージング技術の発展に伴い、「3次元病理学」が提唱されるようになったが、その利点として、2次元画像では判別できない「複雑に走行する脈管状・線状構造」、「一

様でない分布をもつ構造」、「疎に分布する構造」を3次元画像では観察できる点がある。その一例として、「子宮内膜の3次元病理学」を紹介する。

子宮内膜を構成している腺管は、コイル状のうねりや、しばしば分岐を伴いながら、表層の開口部から機能層を通過して基底層まで続いており、「分岐単一管状構造」であると考えられてきた。しかしながら、腺管はうねりや分岐を伴う複雑な形態をしているため、その正確な立体構造は明らかになっていなかった。そこで、子宮内膜に病理学的に異常のない婦人科疾患のために子宮摘出手術を受けた方より研究参加の同意を得、摘出子宮から採取した組織の3次元構造解析を行った。数mmから数cm角に切り出した子宮組織を Clear, Unobstructed Brain/Body Imaging Cocktails and Computational analysis (CUBIC) という手法を用いて透明化し、さらに上皮組織のマーカーである CK7 で蛍光染色を行った。シート照明顕微鏡を用いて透明化した標本を撮影し、画像解析ソフトを用いて得られた画像データを3D化し、観察・解析した。その結果、腺管が分岐するだけでなく、網目のような構造を形成し、しばしば複数の腺管が同一の網目構造を共有していることを明らかにした。月経期の子宮内膜においても網目構造が残存していたことから、腺管の網目構造は基底層の主な構成要素であると考えられ、3次元病理学として、正常子宮内膜の組織学的構造の新しい概念を提唱することが可能であった。今後も3次元病理学が発展し、産婦人科領域から新たなエビデンスが発信されることが期待される。

教育講演 19

進行卵巣がんに対する手術療法の意義を再考する

北里大学 加藤 一喜

進行卵巣がんに対する初回治療において、腫瘍減量手術 primary debulking surgery (PDS) においても、術前化学療法 (NAC: neoadjuvant chemotherapy) 後の腫瘍減量手術 interval debulking surgery (IDS) においても、手術により肉眼的残存腫瘍なし (完全切除) の状態になし得たかどうか最も大きな予後因子とされている。しかしながら、「手術により肉眼的残存腫瘍なし」という評価は、術者の主観的 (「肉眼的に完全に切除できた」と思いたいとする希望的な部分もあり得る) 観測に依るところが多分にある。完全切除できた進行卵巣がん症例において予後が良いのは当然で、完全切除出来なかった症例との違いは単に「がん」の悪性度を反映しているに過ぎず、手術の完遂度を反映しているのではないという意見もある。明らかに言えるのは、進行卵巣がんに対して完全切除を目指す手術は、患者に多大な侵襲を与えることである。重大な合併症 (Clavien-Dindo 分類 IIIb 以上) が無ければ、婦人科臓器以外の消化器・泌

尿器臓器の切除・再建といった手術を施行しても構わないとはならない。進行卵巣がん患者が受けるこの多大な手術侵襲を上回る、予後が延長されるという利点が得られないのならば、完全切除を目指した debulking surgery は行ってはならないのである。

一方で、近年、進行卵巣がん治療における術後の維持療法として poly (adenosine diphosphate-ribose) polymerase (PARP) 阻害薬を使用するようになり、PDS で完全切除を達成できた群の予後は良好であり、進行卵巣がんからの根治を望める患者も増えてきた。進行卵巣がんに対する治療において PARP 阻害剤が出現してから、完全切除を目指す手術を行うことが本当に意義があるのかについて、また PDS と NAC→IDS という治療戦略の違いについても、今一度検討すべき状況であると言えよう。本講演では、進行卵巣がんに対して完全切除を目指した debulking surgery の意義を再考したい。

生涯研修プログラム 1 産婦人科における遺伝学的検査

1) NIPT について

昭和大学 小 出 馨 子

非侵襲性出生前遺伝学的検査 (Non-invasive Prenatal Testing : NIPT) とは、母体血漿中に浮遊した核酸を用いて胎児が染色体疾患に罹患している可能性を評価するものである。本邦では日本産科婦人科学会が作成した「母体血を用いた新しい出生前遺伝学的検査に関する指針」に基づき、受検者は染色体トリソミー胎児の妊娠のハイリスク妊婦に限定し、また実施施設は日本医学会の承認を得た、適切な遺伝カウンセリングを提供できる施設に限定する形で2013年に臨床研究として開始された。

近年、日本医学会の承認を受けていない施設がNIPTを行うようになったことに加えて、性染色体異数性、特定の染色体微細欠失症候群、全染色体ゲノム領域の微細変化などの検査が技術的に可能になったことを受けて、それらの検査も無認証施設で行われるようになるなど、NIPTの実施実

態は開始当初とは大きく異なる点があり、それまでの運用体制では十分に対応できない状況となった。このような中、厚生労働省は厚生科学審議会科学技術部会にて今後の出生前検査の在り方について議論し、2021年に出生前検査に関する新たな方向性を示した。これに基づき、2021年11月に日本医学会に出生前検査認証制度等運営委員会が設置され、2022年2月に「NIPT等の出生前検査に関する情報提供及び施設（医療機関・検査分析機関）認証の指針」が発出された。この指針に基づいた医療機関（基幹施設）および検査分析機関の施設認証が2022年6月に開始され、7月からは新しい実施体制によりNIPTは運用されている。

本講演では、NIPTの原理や本邦での実態のほか、2021年に示された厚生労働省の方針や現在の実施体制について概説する。

2) 産婦人科生殖領域における遺伝学的検査法—最近の進歩—

レディスクリニックコスモス高知 桑 原 章

「着床前診断」は長い間、禁止または極めて限定的に実施されてきた。日本産科婦人科学会は「診断する遺伝学的情報は疾患の発症に関わる遺伝子・染色体に限られ、『スクリーニング』を目的としない (2018年版から抜粋)」と「着床前診断に関する見解」に明記した。

PGD : Preimplantation Genetic Diagnosis

PGT : Preimplantation Genetic Test

PGT-M : PGT for Monogenic disorder

PGT-SR : PGT for Chromosomal Structural rearrangement

PGT-A : PGT for Aneuploidy Monogenic disorder

PGDが、症例・家系の重篤度に応じて個別審査を必須とする極めて限定的な運用のなかで行われていた当時、もっとも懸念され、禁止されていたPGT-Aの科学的再検証のため、学会自らが主導する特別な臨床研究が2017年から2022年に実施された。さらに2018年には、網膜芽細胞種に対する

PGT-M申請と患者会からの意見を契機として、これまで日本産科婦人科学会だけで議論してきたPGTに関する仕組みを変え、多種多様な意見を集めた「PGT-Mに関する倫理審議会」が2020-2021年に開催され、これまで見直されることがなかった重篤性に関する考え方を含めた議論が行われた。

2022年1月、日本産科婦人科学会は「着床前診断に関する見解」を「重篤な遺伝性疾患を対象とした着床前遺伝学的検査に関する見解」と「不妊症および不育症を対象とした着床前遺伝学的検査に関する見解」に改め、生殖医療におけるPGT-MとPGT-A/SRの位置づけを明確にして、今後の科学的検討を深化させる準備を整えた。

現在、生殖医療に医療保険制度が適用され、社会的に再度、予測困難な状況に立ち至っているPGTに関連する経緯を紹介しつつ、その意義と今後の課題を説明します。

生涯研修プログラム 1 産婦人科における遺伝学的検査

3) 婦人科がんゲノム医療と遺伝学的検査

岡山大学臨床遺伝子医療学 平 沢 晃

がんゲノム医療は「がん患者の腫瘍部および正常部のゲノム情報を用いて治療の最適化・予後予測・発症予防をおこなう医療（未発症者も対象とすることがある。またゲノム以外のマルチオミックス情報も含める）」と定義される。

これまでのがん治療は、おもに発症した臓器や組織型に基づく分類をもとに治療法の選択が行われてきたが、発症臓器が同じであってもそのゲノム情報は個々の患者や病巣ごとに異なる。セカンドライン以降の確立した標準治療の選択肢が十分でない婦人科癌に対してがん遺伝子パネル検査が実地診療に導入された意義は大きい。

がん遺伝子パネル検査では腫瘍の体細胞病的バリエーションの検出と同時に生殖細胞系列病的バリエーションが検出される場合がある。現在のがん遺伝子パネル検査に搭載されている遺伝子の多くががん関連遺伝子であり、遺伝性腫瘍が推定・検出されることがある。がんのおおよそ1割は生殖細胞系

列病的バリエーション保持に由来する遺伝性腫瘍であると考えられており、とくに婦人科腫瘍はその頻度が高い。

遺伝性腫瘍に関する情報は本人の治療の最適化・予後予測・発症予防において有用であるのみならず、その血縁者に対しても利活用可能な情報となりうる。2020年4月からは遺伝性疾患としての遺伝性乳癌卵巣癌症候群が保険病名として採用され、BRCA1/2の遺伝学的検査、サーベイランス、リスク低減手術などの一部が保険収載されたが、今後はその他の遺伝性腫瘍の診断も目的とした多遺伝子パネル検査（Multi-gene panel testing: MGPT）の臨床実装が求められる。

産婦人科腫瘍領域はゲノム情報を当事者と共有することで、がん未発症者も含めた個別化がん治療や予防が可能となることが多く、今後は全ゲノム解析時代を念頭においた対応が必要である。

生涯研修プログラム2 様々なエストロゲンの生体作用

1) エチニルエストラジオールなど合成Eについて

鳥取大学 谷 口 文 紀

エストロゲンは、主に核内転写因子であるエストロゲン受容体に結合してホルモン作用を示し、性徴の発現、生殖器の形態形成、卵子成熟や妊娠成立・維持をつかさどる。その他、生体作用は全身におよび、骨代謝、尿路系、脂質代謝制御、血液凝固、動脈硬化抑制や脳機能への影響など多岐にわたる作用を有する。

合成エストロゲンとは医薬品として合成された、天然型エストロゲンの類似物質であり、OC・LEPが月経困難症治療薬あるいは避妊薬として広く応用されている。植物中に存在する天然型エストロゲンは、消化管で吸収されたのちに肝臓で不活化される。したがって、治療目的にエストロゲンを投与する場合には、肝臓で不活化されにくいエチニルエストラジオールなどの合成エストロゲンの経口剤や、天然型エストロゲンの用量を増

やした結合型エストロゲンあるいは 17β -エストラジオールの経口・経皮剤が用いられる。

近年の少子晩婚化に伴い、月経困難症に悩む女性が増加している。思春期に月経困難症を有する女性は、将来の子宮内膜症発症リスクが高いと考えられており、OC・LEP等の長期ホルモン療法による管理が重要である。思春期女性の長期OC・LEP服用による獲得骨量低下を危惧する報告もあるが、骨折リスクは不明である。将来の妊孕性低下ならびに症状増悪を防ぐためにも適切な時期に治療介入することが、予防医学的な観点から求められる。今回は、生殖機能を中心に身体機能の維持におけるエストロゲン作用の重要性ならびに合成エストロゲン投与の効果について整理する。

2) 天然型エストロゲン (E1~E3) の生理的作用について

東京大学 平 池 修

天然型エストロゲンとして代表的なものは、エストロン (E1)、エストラジオール (E2)、エストリオール (E3) が知られており、それ以外にも様々なエストロゲンが存在する。E1, E2, E3 は全てコレステロールを最上流とする性ステロイドホルモン代謝経路において産生される物質であり、おのおのの特異的産生酵素が存在する。

エストロゲンの生理学的強度を測るには様々なアッセイがあるが、わかりやすいものとして子宮増殖アッセイがある。子宮増殖アッセイとは、エストロゲンによって雌動物の子宮が肥大する (uterotrophic 作用) ことを利用して、任意の化学物質がどのくらいエストロゲン様作用を有するかを検出する試験法であり、エストロゲン製剤の

uterotrophic 作用はエストロゲンとしての生物作用の指標になる。OC/LEP 製剤に含まれるエストロゲンであるエチニルエストラジオールを1とした場合、同等の作用発現に必要な相対的量は、E2 : 32, 結合型エストロゲン : 32, E3 : 80 倍以上、ということが知られている。

E2の発見以降、各種エストロゲン製剤が開発されてきたが、エストロゲン製剤の投与経路が筋注、内服、経皮、経膣と4通りあるだけでなく、個々の製剤の性質つまりエストロゲンとしての力価が大きく異なること、E3製剤は子宮内膜増殖作用は弱いが生体組織には相対的に強く作用するように、組織によりエストロゲンとして発現する効力が異なることに留意しなくてはならない。

生涯研修プログラム2 様々なエストロゲンの生体作用

3) E4 について

京都府立医科大学 森 泰 輔

天然型エストロゲンにはE1, E2, E3に加えて、第4のエストロゲン（エストロール）があることをご存知だろうか。近年、水酸基を4つ有する第4のエストロゲンであるエストロール（E4）が注目されている。E4は胎児由来のエストロゲンであり、妊娠中に胎児の肝臓で産生され、妊娠9週目より母体尿中に検出されることが知られている。

エストロゲンが及ぼす伝達経路は、核内エストロゲン受容体（ER α や ER β ）を介して標的遺伝子上のエストロゲン応答配列に結合し作用するといったいわゆる古典的経路以外に、最近では膜型ERを介したシグナル伝達経路の存在も報告され

てきた。E4は、これまでの他の天然型エストロゲン（E1-E3）と違い、ER α のシグナル伝達を活性化する一方で、特定の組織では膜型ER α を介するシグナル伝達経路を活性化しないという特徴を有する。E4のこの組織選択性は、子宮内膜、膣、心血管系では従来のエストロゲンが有するような効果を示す一方、肝代謝や、凝固系、脂質、レニン-アンギオテンシン-アルドステロン系、乳房に与える影響は少なく、より安全なエストロゲンである可能性が示唆されている。

本講演では、E4の生体における作用を概説した上で、産婦人科疾患に対する治療選択肢としての可能性について述べる。

生涯研修プログラム3 排卵誘発 新たな方法

1) Progestin-primed ovarian stimulation (PPOS) 法の臨床知見

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医療法人鉄蕉会亀田総合病院生殖医療事業管理部 川井清考

Progestin-primed ovarian stimulation (PPOS) 法は、ゴナドトロピン放出ホルモン (gonadotropin releasing hormone ; GnRH) アゴニストや GnRH アンタゴニストの代替としてプロゲステロン製剤にて早発黄体化ホルモン (luteinizing hormone ; LH) サージを抑制する調節卵巣刺激法である。2015年にKuangらがメドロキシプロゲステロン酢酸エステル (medroxyprogesterone acetate ; MPA) を用いた方法を最初に報告してから、様々なプロゲステロン製剤を用いた PPOS 法が報告されている。卵胞期初期からのプロゲステロン製剤投与のため、子宮内膜の脱落膜化が誘発早期より起こり implantation window は採卵後には消失していることから凍結融解胚移植を前提とした調節卵巣刺激法となる。卵巣過剰刺激症候群 (ovarian hyperstimulation syndrome ; OHSS) の予防、着床前遺伝学的検査 (preimplantation genetic testing ; PGT) の普及、がん・生殖などの

妊孕性温存治療などの全胚凍結を主体とした治療周期が増加により時代に即した調節卵巣刺激であり、国内でも数多くの生殖医療機関で実施されている。2021年に発刊された「生殖医療ガイドライン」では、原因不明不妊患者に対して PPOS 法は①凍結融解胚移植を前提にした卵巣刺激法として GnRH アゴニスト法や GnRH アンタゴニスト法と比較し、採卵数、臨床妊娠率、出生率において同等に有効である (推奨度 A)、②GnRH アゴニスト法や GnRH アンタゴニスト法と比較して、有意に OHSS の発症率が低い (推奨度 A)、③PPOS 法で生まれた児と GnRH アゴニスト法で生まれた児の間に、先天異常の有無、低出生体重、早産率において有意差はみられなかった (推奨度 B) と一定のエビデンスが蓄積した新しい卵巣刺激法と評価している。最新の知見を踏まえて PPOS 法を概説する。

2) 生殖補助医療における卵巣刺激：低刺激法

慶應義塾大学 山田満稔

近年、生殖補助医療 (ART) における卵巣刺激法の進化のなかで、低刺激法における新たな薬剤が注目されている。卵巣刺激には主に2つの目的がある：(i) タイミング法や人工授精における単一卵胞の発育・排卵誘発 (排卵誘発)、および (ii) ART における複数の卵胞発育・排卵抑制 (調節卵巣刺激 COS)。COS は採卵方法や薬剤の使用によって「Natural cycle IVF (nIVF)」、 「Modified natural cycle IVF (mnIVF)」、 「Mild IVF (mIVF)」、 「Conventional IVF (cIVF)」に分類され、特に nIVF、mnIVF、mIVF の3つは自然周期採卵とされ、低刺激法に属する。

クロミフェンクエン酸塩 (Clomiphene citrate (CC))、アロマトラーゼ阻害剤 (Aromatase inhibitor (AI)) および低用量ゴナドトロピン (Gonadotro-

phin (Gn)) を用いた低刺激法は、個別の患者ニーズに合わせて治療プロトコルを構築する際に有用であり、従来の高刺激法と比較して卵巣過剰刺激症候群 (ovarian hyperstimulation syndrome : OHSS) のリスクや費用負担の軽減が期待されている。特に低卵巣予備能の患者群においては、CC 単独または CC に中等量の Gn および GnRH アンタゴニストの併用に基づく mIVF は、cIVF と比較して出生率に差が見られなかったと報告されている。

本プログラムでは、低刺激法が ART 治療においてどのように進化し、患者への影響をどのように改善しているのかについて、最新の動向をお伝えしたい。

生涯研修プログラム 3 排卵誘発 新たな方法

3) GnRH アゴニストまたはアンタゴニスト使用

東邦大学 片 桐 由起子

効率のよい卵子回収を目指して調節卵巣刺激がおこなわれるが、複数の卵胞発育によるエストロゲンの上昇から、卵の成熟に先立って生じる LH サージを回避する方法が考案されてきた。

GnRH アゴニスト (GnRHa) と GnRH アンタゴニスト (GnRHant) は、それぞれ GnRH 作動薬と拮抗薬であるが、いずれも下垂体からの FSH および LH 分泌を抑制し、LH サージを生じさせない。

GnRHa 法は、卵胞発育に伴う血清エストラジオール値の上昇環境下で、LH サージに先立って GnRHant 製剤を投与することで、LH サージを抑制する方法である。GnRHa 法は、GnRHa 製剤が、作動薬として GnRH 受容体に結合するため一時的にゴナドトロピン分泌量が増す(フレアアップ)が、そのまま GnRH 受容体を占拠し続けることで次の刺激が生じない環境が作り出され(ダウンレギュレーション)、FSH および LH の分泌を抑制する方法である。LH サージの抑制が両者の共通

点であり、GnRHa 法では、GnRHant 法では生じないフレアアップが生じることが相違点である。

もう一つの両者の相違点として、トリガーに GnRHa 製剤の選択の可否があげられる。卵胞成熟後に、さらに排卵に至るステージへの卵成熟を目指した薬剤投与をトリガー(引き金)と呼ぶが、トリガーには hCG 製剤と GnRHa 製剤の選択肢がある。GnRHant 法ではいずれも選択可能であるが、GnRHa 法ではダウンレギュレーションが生じているので GnRHa をトリガーとして選択することはできない。

GnRHa 法と GnRHant 法のいずれにおいても、卵巣刺激にゴナドトロピン製剤が使用される。ゴナドトロピン投与量決定には卵巣機能評価が重要となり、また、LH 含有製剤と pureFSH 製剤の別もありその選択は一様ではない。

本講演では、GnRHa 法および GnRHant 法について解説する。

生涯研修プログラム4 ロボット手術の多様性

1) 山梨から発信するロボット手術の工夫

山梨県立中央病院 坂本 育子

婦人科領域でのロボット手術は年々増加している。ロボット手術は安定した3次元の視野、より広い関節可動域、向上した協調性により、手術手技の習得が容易と言われている。安全なロボット手術の導入の後に来る課題として運用コストや教育が挙げられる。ロボット手術のコストは腹腔鏡手術より高額であったという報告が散見され、導入をしたものの、いかに運用するかという問題が現実味を帯びている施設が多い。年間症例数の増加が1症例あたりの維持費減に繋がったという報告もあるが、検討はわずかである。

当院では2018年の保険収載以降手術効率化の取り組みを行い、一日4~5件のロボット支援下手術を可能にしている。また医療費と間接費を考慮

した費用最小化分析も行いロボット支援下手術のコストをいかに削減できるかという検討を続けてきた。さらに術者教育としてロボット手術にStepを設けることで短期目標を明確にし、モチベーションの維持と技術の向上を図っている。これらの工夫により現在経験年数によらず従来手術と同等の利益を計上することが可能となっている。

今回我々がロボット手術を行う上で取り組んできた工夫を紹介し、ロボットの多様性として2023年11月から2台目のロボットとして導入したHugo RASシステムとda Vinci Xiの違いや特性について報告することで、今後ロボット手術が進むべき道への一助になればと思う。

2) 都心部におけるロボット手術

国立国際医療研究センター病院 大石 元

2018年度から保険適応となった婦人科ロボット支援下手術は、現在良性子宮疾患に対する子宮全摘出術、早期子宮体癌に対する子宮悪性腫瘍手術、骨盤臓器脱に対する仙骨陰固定術の3術式が対象となっている。保険適応開始以来、婦人科でのロボット支援下手術の件数は増加傾向ではあるが、施設により導入・普及の状況は異なっている。近年の腹腔鏡手術の普及に伴い婦人科手術の低侵襲化が進んできているが、ロボット支援下手術の導入に伴い出血量のさらなる減少および巨大子宮筋腫や既往手術症例・肥満症例などへの適応拡大

が期待される。また安定した視野が得られるため、再現性の高い術野確保が可能である。本講演では都市部の一般病院でのロボット支援下手術の導入について紹介し、若手医師の教育および再現性の高い術野形成の工夫について供覧する。また今後のロボット手術の方向性として、視覚から得られる触覚(Optical Haptics)の応用、将来的に導入が期待される画像システムの統合によるナビゲーションシステムの搭載、AIの導入によるより安全性の高い手術への展望についても言及したい。

生涯研修プログラム 4 ロボット手術の多様性

3) ロボット手術のこれから

鹿児島大学 戸上真一

2018年から婦人科ロボット手術が保険診療となり、現在では良性子宮疾患(骨盤臓器脱含む)と再発低リスク子宮体癌が施行可能である。ロボット手術の一番の魅力はその低侵襲性とラーニングカーブの短さにあるが、悪性腫瘍手術が最もその恩恵を受けると思われる。しかし2022年には広汎子宮全摘術やPAN郭清などの悪性腫瘍手術を中心に保険術式の適応拡大を目指ものの、残念なことに見送られた。

ロボット手術の低侵襲性とベストマッチな手技の1つに、術中にセンチネルリンパ節(SN)を同定・摘出して術中迅速診断で転移陰性であれば骨盤リンパ節郭清を省略するSentinel Node Navigation Surgery(SNNS)がある。SN生検は2024年の保険収載を目指して継続申請中であるが、共に低侵襲手術であるロボット手術とSNNSの併用は、これからさらに普及していくことが想定される。当科では2018年より再発低リスク体癌に対

するロボット支援SNNSを約160症例に施行しており、本講演会では手術操作等その詳細について概説する。

Da Vinci[®] Surgical System(DVSS)が大きなシェアを占めているが、近年hinotori[™], Hugo[™], Da Vinci[®] SPなどいくつかの手術支援ロボットシステムが承認、導入されている。今後患者や医療機関は、ニーズに合った最適なシステムを選択できるようになり、手術ロボットのコストも軽減していく可能性がある。当院でも国産ロボットhinotori[™]を追加導入し、2022年12月からの婦人科への保険適用と同時に手術を開始した。hinotori[™]ではドッキングフリーデザインなどDVSSと異なるいくつかの特徴があるが、本講演会ではhinotori[™]の特徴やSNNS併用の実際、加えて遠隔医療の可能性を含めた今後の展望について概説する。

生涯研修プログラム5 産婦人科における漢方治療

1) 周産期における漢方療法

かしの葉レディースクリニック, 社会医療法人若竹会つくばセントラル病院, 東邦大学薬学部生薬学

岡村麻子

連綿と続いてきた妊娠分娩は、子孫繁栄のための自然な営みであり、本来は医療の介入を必要としない領域のはずである。昨今は、高齢化、運動不足による筋肉低下、偏食、さらにCOVID-19などのストレスが蔓延しており、いずれも妊産婦のバランスを崩し、自然な営みを阻害する方向につながっている。母児の安全のために、医療の介入がより必要とされるのが現状である。

西洋医学的なアプローチだけではうまくいかない場合やより有効性を求める場合に、漢方薬投与が役に立つことを経験してきた。

漢方薬の温めて補い巡らす作用は臓器の微小循環改善につながる。温める作用を持たない西洋薬の不得意な分野である。また、タイプにあった漢方薬を選択すれば、2種類以上の生薬が協調して作用し、妊産婦をバランスのとれた状態(中庸)にすることが可能となり安胎・安産・良好な産褥経過につなげることができる。

妊婦は、循環血漿量の増加、鉄欠乏性貧血になりやすく、胎児とともに大きくなる子宮を抱えている。これらから、基本的な妊婦のタイプ(証)は血虚・瘀血・水滯ととらえることができる。血を補い、水を動かすことができる当帰芍薬散が安胎薬といわれる理由である。そこに、妊娠前のタイプや現時点の病態も加味して考え漢方薬を選択すると有効となる場合も多い。

分娩(五積散・桂枝茯苓丸)、産褥(芍婦調血飲)などの基本方剤、および重症悪阻、繰り返す腹痛、妊娠をやめたいほどの皮膚症状、抑うつ症状、子宮収縮、便秘などの各論を示す。

漢方薬は、女性の産み育てる力を助け、妊娠分娩を本来の自然な営みに近づけることができる有用な治療法である。漢方治療を合わせて使うことで、世界一安全といわれる日本の周産期医療がより豊かになり、この分野における漢方治療の基礎及び臨床研究が発展することを希望する。

2) 性成熟期女性への漢方療法

東京歯科大学市川総合病院 小川真里子

性成熟期の女性は、妊娠中および出産後をのぞき、女性ホルモンの変動に毎月さらされていることから、月経困難症や月経前症候群(PMS)などの、月経周期にともなう不調への対応が必要となる。これらの治療として、産婦人科では主にOC・LEPなどのホルモン療法が行われるが、妊娠を希望している場合や、OC・LEPが禁忌などの理由で、ホルモン療法が選択しにくいことも多い。一方、漢方療法は古来より、月経随伴症状を含む、女性のさまざまな不調に寄り添うように検討を重ねられてきた。中でも、月経困難症やPMSは、漢方治療のよい適応と言え、妊娠を検討している間も含め、禁忌となる状態は殆どなく、最初の一手としても使用しやすい。

女性の月経に関する不調については、漢方医学で言うところの気・血・水のいずれもが関与しているが、中でも局所的な血の停滞は瘀血と呼ばれ、

月経困難症やPMSの主な原因と考えられている。そのため、瘀血を取り除く、駆瘀血剤が処方を中心となる。実際には、婦人科三大処方と呼ばれる、当帰芍薬散、加味逍遙散、桂枝茯苓丸を基本とし、さらに患者の証や訴えにより、処方の追加や変更を検討すると扱いやすい。他に、温経湯も月経困難症に対するエビデンスを有しており、寒証、虚血、瘀血の症候に効果があることから、月経不順や不妊症の女性にも用いられる。また、近年、月経前の気分変動に対し、抑肝散や抑肝散加陳皮半夏もよく用いられるようになっている。

以上のように性成熟期女性の月経に伴う不調に対して漢方薬は使用しやすいが、発汗作用のある麻黄や、瀉下作用のある大黃、芒硝、利尿作用のある半夏などを含んだ漢方薬については、妊娠中は慎重な使用が求められるとの意見もあり、妊娠後の処方には注意を要する。

生涯研修プログラム 5 産婦人科における漢方治療

3) 婦人科がん治療における漢方療法

富山大学 中 島 彰 俊

婦人科がん診療，特に進行卵巣がん治療は“1. 審査腹腔鏡 2. 術前化学療法 3. 卵巣がん根治術 4. 術後化学療法 5. 維持療法”というステップで治療する患者が増えているが，すべてを完遂するには2年半以上が必要である。難治性である卵巣がんに対し，様々な薬剤開発が行われた結果がこの形であり，それにより予後改善が期待される。他方，卵巣がん患者は薬剤による副作用として“倦怠感・食欲不振”など数値化の難しい症状に悩まされ，体重減少なども合併し治療継続が困難な場合もある。当科では，以前よりがん患者に対し1. 化学療法に伴う副作用に対する支持療法 2. 術後の体力回復 3. 化学療法前後のコンディショニングという3つを目的として漢方薬を使用している。特に近年の長期卵巣がん治療に対し，積極的に漢方薬を導入し，治療完遂に寄与する補助薬と

して使用している。

現在我々は100を超える漢方薬（エキス剤）を使用することが可能であるが，その多くの効能・効果は古典に由来するものであり，我々の治療の拠り所とする Evidence-based Medicine には乏しいものが多い。ただ，その薬剤の適応は患者の訴えを基にしたものであるため，医療面接・病歴聴取は漢方処方診断仮説を立てるうえで最初の重要なステップである。そこで，本プログラムでは，最初に知っておくと良い婦人科がん治療における漢方処方を紹介し，いくつかの患者診察時のポイントを解説する。また最後に，我々が取り組んでいる漢方薬を用いた前向き試験についても紹介し，明日からの婦人科がん診療に役立てていただければ幸いである。

生涯研修プログラム6 話題の感染症と母子の管理

1) 妊婦の新型コロナウイルス感染症

神戸大学 出口 雅 士

新型コロナウイルス (COVID-19) の国内パンデミックでは、妊婦の感染も相次いでいる。そこで、倫理委員会承認のもと全国の周産期センターや日産婦会員に依頼し、オプトアウトにより感染妊婦の情報を収集し、妊婦レジストリを実施している。2023年11月時点で2500件超の症例を集積し、母体の重症化要因、分娩方法の推移、先天性感染等の頻度を調べており、これまでの解析では下記の結果が得られている。

妊婦の感染例は国内での流行者数に比例して増減した。酸素投与が必要な中等症Ⅱ・重症の頻度はデルタ株より前は11%、デルタ株で20%となったが、オミクロン株となってからは1%未満となっている。感染妊婦の2%弱に感染後2週以内を中心に流死産が見られたが、中等症Ⅱ・重症では流死産は見られなかった。

分娩方法は、妊娠36週末満に感染診断された場合、重症でなければ、待機して軽快後に産科的適

応にもとづく分娩方法を取り、重症化傾向があれば妊娠26週以降帝王切開分娩が選択された。36週以降の感染例では重症度にかかわらず当初は帝王切開が選択されることが多かった(軽症でも約6割)が直近では2割程度まで減少している。なお、胎内感染が否定できない新生児感染は0.2%であった。

COVID-19の妊娠への影響として、中等症Ⅱ・重症になると早産、切迫早産が増加したが、他の産科合併症は増加しなかった。COVID-19が中等症Ⅱ・重症となるリスク因子を多変量解析すると、「妊娠21週以降、ワクチン接種歴無し、オミクロン株でない、診断時BMI30以上、年齢31歳以上、デルタ株、併存疾患の既往または現症」が独立したリスク因子であった。妊娠合併症の有無は重症化に関係しなかった。

講演では直近の解析データをもとに報告する。

2) 先天性サイトメガロウイルス感染症の臨床管理の進歩

国際医療福祉大学成田病院 永 松 健

日本における先天性サイトメガロウイルス感染症 (cCMV) は全出生児の0.3%に生じ、症候性感染の頻度が0.1%とされており、種々の母子感染症の中で最大の発生頻度である。妊娠中の初感染では先天感染の発生リスクは高いが、血清学的検査で感染既往と判断される妊婦においても再感染や再活性化により先天感染が生じることが示されている。そのため、母子感染の防止のためには妊婦全体を対象とした予防啓発が重要と考えられる。疫学的な調査では妊婦への感染は育児中の経産婦や保育士などの子供との接触が多い女性において、幼児の唾液や尿などの体液を介した感染経路が推定されている。体液接触を避けて手指衛生を徹底するなどの予防対策の情報提供が有効である。

尿検体を用いた核酸増幅法による先天感染の診断検査および症候性感染児に対するバルガンシクロビルによる治療がそれぞれ保険適用となり先天感染児に対する臨床管理が大きく向上した。一方で、妊娠中の診断および治療については未解決な課題が多い。先天感染のハイリスク妊婦の同定のためのスクリーニング戦略および、感染妊婦に対する薬物的な予防法の確立が求められている。本講演ではCMV特異的IgG avidityを用いた血清学的検査で初感染妊婦の同定、そして特定されたハイリスク妊婦に対する抗CMV高力価免疫グロブリンやバルアシクロビルによる胎児へのウイルス移行を防止するアプローチに関して近年の報告を踏まえて議論を進める。

生涯研修プログラム 6 話題の感染症と母子の管理

3) 梅毒診療のポイントと先天梅毒の現状と母体への適切な治療法

日本大学 川 名 敬

2013年から始まった梅毒の流行は急増ともいわれるほど罹患者が増加し続けている。全数報告が始まって以来初めて年間の罹患者が1万人を超えた。女性の罹患者は、2012年までは年間200人程度であったものが、2022年には20倍の4000人近くになった。この流行とともに梅毒合併妊婦も増加した。その結果、2012年までは日本全国で年間0-2名程度であった先天梅毒が、2019年以降は20名を超えてきている。女性の梅毒罹患者の75%が20-30s歳代であるが要因の1つである。

さらに、日本では従前より経口ペニシリン剤内服（アモキシシリン1.5g/日）を梅毒治療薬として使用してきたが、母子感染予防になるかは不明であった。そこで、日産婦学会女性ヘルスケア委員会で、梅毒合併妊婦の調査を実施した。2010～2018年の172例の梅毒合併妊婦を詳細に追跡した。そのうち43例の先天梅毒児がいた。出産から60日

以上前に治療が開始され、十分に治療が施された妊婦63例中9例（14%）が先天梅毒児となった。経口ペニシリン剤を適切に投与されても母子感染は予防しきれないことがわかった。先天梅毒の症例の属性を見ると、後期梅毒の母体から先天梅毒が発生しやすい。また妊娠週数は関係なく、妊娠初期スクリーニング検査で梅毒と診断されても先天梅毒になった症例が約半数であった。

そこで、治療法として期待されるのが2021年に認可されたベンジルペニシリンベンザチン水和物（ステルイズ®）注射薬である。しかし、ヤーリッシュヘルクスハイマー反応が起こると、全身の炎症反応がおこり、子宮収縮が起こる。妊婦にはペニシリン投与では入院管理下での治療が安全である。本講演では、梅毒の現状と母子感染の予防について詳説したい。

生涯研修プログラム7 よりよい周産期管理のために

1) 妊娠高血圧症候群の周産期管理—発症予測から診断, 治療まで—

東京大学 入山 高行

妊娠高血圧症候群 (HDP) は、母体の重篤な転帰、および新生児死亡や出生児の脳性麻痺を含めた合併症の発生との関連性が高い、重篤な産科疾患である。HDP に対する病態に即した有効な治療法は存在しない。そのため、重症例では超早期期であっても分娩の終了をもって症状の改善を期待するしかないのが実情である。対症療法としての降圧治療が、早期期における1日でも長い妊娠継続の成否の鍵を握るが、降圧療法の開始基準や薬剤の選択、目標血圧値など、至適な管理法について一定の見解が得られていないのが実情である。最近、可溶性 fms 様チロシンキナーゼ-1 (sFlt-1) お

よび胎盤増殖因子 (PlGF) の血中濃度を測定することで妊娠高血圧腎症の短期的な発症予測を行う検査 (sFlt-1/PlGF 比) が臨床の現場で実用化されるに至っている。しかしながら、sFlt-1/PlGF 比によって発症予測や早期診断が実現できても有効な治療には結びつかない、という大きな課題がある。

本講演では、基本的な HDP の診断と治療について概説しつつ、1) 至適な降圧療法についてどう考えるか、2) sFlt-1/PlGF の臨床現場での活用法、最新の知見についても紹介できたら良い、と考えている。

2) 難しくない胎児血流診断

東北大学 齋藤 昌利

意識を消失した成人が目の前にいたら、皆さんはどういった検査をオーダーするでしょうか。何の躊躇いもなく血圧を測定し、同時にパルスオキシメータと心電図を装着の上、採血・採尿を行なって意識に直接/間接的に関連する項目を網羅的にオーダー、あるいは血液ガス分析を行うはずですが、さらには、CT や MRI といった画像検査を実施し、診断と治療計画を立てるかと思えます。しかしながら、対象が「胎児」になると、それらの検査はほとんど行うことができず、「数十分間の心拍数トレース」という成人のそれとは全く違う方法を用いるのが現実です。そういった限定的な武器しか持たない我々にとって、胎児血流診断は心拍数トレース以外に「循環」を推定できる診断補助ツールになるはずですが、特に FGR の評価と管理においては威力を発揮する可能性を有してい

ます。しかしながら、どうしたら波形を描出できるか、どの血流に注意したらいいのか、波形は得られたがそれをどう評価したらいいのか、などなど胎児血流に纏わる疑問は尽きず、有効活用できていないのが現実かもしれません。

我々はパルスドプラ法を用いた胎児血流診断=胎児循環評価を積極的に行い、胎児の「心後負荷」パラメータに注目し娩出タイミングと娩出方法を症例ごとに検討しています。一般的に胎児 well-being の基軸として考えられている「酸素」を指標にしたパラメータフォローではなく、「胎児血圧」を意識したフォローと言えるかもしれません。本講演では、パルスドプラの基本から少し突っ込んだ内容を若手の先生と一緒に考え、「明日から自分達の持っている超音波でできるかも」という視点で私の愚考を披露させて頂ければと思います。

生涯研修プログラム7 よりよい周産期管理のために

3) 妊産婦のメンタルヘルスケア

東北医科薬科大学 松澤 由記子

日本産婦人科医会妊産婦死亡症例検討評価委員会による母体安全への提言 2022vol.13 では、2020年から2022年の3年間の妊産婦死亡の一番の原因が自殺と報告されており、妊娠、分娩および産褥期における妊婦のメンタルヘルスケアは内科的合併症の管理とともに周産期管理の重要な課題である。日本産科婦人科学会産婦人科診療ガイドライン 2023 産科編および日本産婦人科医会による妊産婦メンタルヘルスケアマニュアルでは、妊娠初期の問診内容から妊婦健診の注意点、産褥期の対応や投薬の実際、さらにはプレコンセプションケアに至る妊婦のメンタルヘルスの臨床管理の実際が詳細に解説されており、さらに2017年からは周産期うつ病のスクリーニングを含めた産後2週間健診費用の公的補助が開始され、エジンバラ自己評価票を用いた早期の産後うつ拾い上げの努力も行われてきているが、依然としてメンタルに何

らかの問題を有する妊婦への対応や管理には医師、助産師ともに苦慮する場合が多い。特に、精神科受診既往があり、妊娠初期から定期的な精神科受診がなされ、医療者、家族および地方行政担当者などと良好な信頼関係が構築されている症例については有事の際も多職種連携によるスムーズな臨床対応が可能であるが、ほとんどの場合は患者コミュニケーションに問題を有することが多く十分な早期対応が行えないのが実情である。今回、東北大学産婦人科学教室と共同で実施した宮城県における妊婦のメンタルヘルスケアに関する多施設共同臨床実態調査研究から、妊娠、分娩および産褥期のメンタルヘルスケアの現状を明らかにし、メンタルヘルスに問題点を有する妊婦のよりよい周産期管理のための方策および今後の改善点の提案などについて報告する。

生涯研修プログラム 8 婦人科がんにおける緩和ケア診療

1) 婦人科がんにおける症状緩和

埼玉県立がんセンター緩和ケア科 余 宮 きのみ

婦人科腫瘍医に求められることのひとつとして、緩和ケア部門との緊密な連携が挙げられる。

その理由は、婦人科がんにおける症状緩和には、最も高度なスキルが求められるからである。具体的には、骨盤内腫瘍などによる神経障害性疼痛、腸腰筋症候群、テネスマスなどが挙げられる。いずれもオピオイドの増量だけでは対処が難しい。また、このような痛みを紛れて、骨転移によるオンコロジー・エマージェンシーを合併することも忘れてはならない。例えば、痛みの原因の多くは腹腔内、後腹膜、骨盤内の腫瘍浸潤によるものであるが、これらは、下腹部から下肢に及ぶ痛みを生じる。一方、下位胸椎～腰椎転移による神経根痛や硬膜外伸展においても同じ部位に痛みを生じる。脊椎転移が脊髄圧迫を生じている場合には、緊急的な手術、放射線治療、安静などが必要であり、オンコロジー・エマージェンシーとして対応

しなければ、対麻痺などのさらなる骨関連事象につながる。

加えて婦人科がん患者では、便秘や腸閉塞、腹水による腹部膨満感などを合併するため、多方面からの積極的な緩和ケアが必要となる。特に婦人科がん患者においては、がん治療、腫瘍が腹腔内に及ぶことなどから便秘の難渋例が多い。近年、新規薬剤により便秘治療は大きく進歩している。腎機能障害を合併しやすい婦人科がんでは、漫然とした酸化マグネシウムの投与は避ける必要があり、欧米のガイドラインで第一選択となっているポリエチレングリコールなどの活用が望ましい。

以上のような多様な症状に迅速かつ適切に対処し、質の高いがん治療を提供するためには、単なる紹介状と返書のやりとりにとどまらず、より緊密なチーム医療を実践することが重要である。

2) 鎮痛療法

帝京大学緩和医療学講座 有 賀 悦 子

がん疼痛治療下で治療不十分な患者は50～80%、鎮痛療法が受けられていない患者は、全患者の10～50%存在する(ESMO Guideline, 2011)。一方、2016年ASCOで注目されたITデバイスによる苦痛症状の定期的報告システムを用いたランダム化比較試験では、化学療法期間が延び、約5か月の予後延長を認めたという結果が示された。このことは、Nat Medに報告された除痛により報酬システムが活性化され免疫応答が強化されたマウスの結果と合わせて、苦痛の対処は抗がん治療と併行すべき理由の裏付けといえよう。ところで、うつを合併したがん患者はうつではない患者に比較して2倍オピオイド依存になりやすく、疼痛がある患者はない患者に比較して3.5倍うつになりやすいことや仕事や経済的問題が疼痛悪化に関連しているという報告もある。つまり、良質の鎮痛療法は薬の処方だけでは足りず、包括的アプロー

チが重要なのである。それを踏まえた上で鎮痛薬のトピックスに触れていきたい。子宮頸がん、体がん、卵巣がんでは、局所のCox-2の発現が少しずつ異なり非ステロイド性抗炎症薬の効果も異なることが予測されること、オピオイドは単に疼痛を抑えているだけではなく疼痛メカニズムに関与しているものがあること、慢性腎機能障害下で推奨されるオピオイドはフェンタニル、ブプレノルフィンであるが、注意が必要なものはモルヒネだけではなく、トラマドールが含まれていることはあまり知られていない。糖尿病性末梢神経障害性疼痛ではあるが、Lancetに報告された鎮痛補助薬の比較試験、加えて、オピオイド誘発性便秘症の治療薬による一過性の下痢予防のポイント、オピオイド依存の手前であるケミカルコーピングについて解説を加えていく。

生涯研修プログラム 8 婦人科がんにおける緩和ケア診療

3) 疼痛以外の症状緩和, 緩和ケア教育について

都立駒込病院緩和ケア科 鶴賀哲史

婦人科悪性腫瘍の進行は比較的緩やかで、治療経過は長いことが多い。診断から手術・化学療法・放射線による集学的な治療、経過観察、再発治療の全ての過程で、産婦人科医は主治医であり続ける。結果として婦人科悪性腫瘍患者は産婦人科医に全幅の信頼を寄せようになり、症状緩和や終末期ケアについても多くを期待する。したがって緩和ケアは産婦人科医の必修項目のひとつである。婦人科悪性腫瘍に伴う主な苦痛症状として、腹部膨満感(イレウスやがん性腹膜炎など)、浮腫(リンパ浮腫や血栓症による静脈環流障害など)、呼吸困難(胸水や痛性リンパ管症など)、全身倦怠感(がん悪液質や腫瘍熱など)などがある。一方で身体症状以外に目を向けると、子宮頸癌治療ガイドラインで「遺族ケア」の重要性が明記されているように、患者とその家族の包括的なケア

の重要性が認識されつつある。これらの産婦人科医がおさえておくべき緩和ケア診療について、最新のエビデンスも含めて、報告する。

最後に、産婦人科の終末期ケア教育の現状と課題について考える。DPC制度の導入、在宅医療の普及などにより終末期の療養場所が多様化している。がん治療を受けた病院で最期を迎える患者は少数派となりつつあり、専攻医や修練医に終末期ケア教育をすることが難しくなっている。終末期診療を十分に経験することなく、再発・進行がん患者の治療を計画したり、患者や家族に終末期の迎え方を説明したりすることは難しい。緩和ケアに関する基本的な知識を習得する研修や緩和ケア科の短期ローテート研修、ロールプレイによるコミュニケーション講習など、終末期医療の教育に関する国内外の取り組みを紹介する。

生涯研修プログラム 10 CIN の管理

1) コルポスコピーの pit fall

藤田医科大学岡崎医療センター 藤井 多久磨

子宮頸癌は扁平円柱上皮境界 (SCJ) をその発生源地とするが、特に SCJ の内側すなわち腺領域から発生するものが多いということはあまり知られていない。したがって、コルポ異常所見の最高病変を生検する場合に、このルールに従えば SCJ の内側に異常があればそこが最適の採取ポイントとなる。一方、更年期以降、SCJ は頸管内側に移動するためコルポ検査不適症例が多くなる。この移行期の 35-40 歳以降はそれまでの若年者と比較して異常評価の方法も異なることは注意が必要である。

子宮温存を目的とした円錐切除手術においてはその切除ラインの決定は危機的に重要である。妊孕能温存のためにはコルポを用いた診断能力を高める必要がある。子宮頸がん検診にて異常を指摘された更年期以降のいわゆるコルポ不適例につい

ては、疫学データや視診、触診を含め臨床的感を働かせ、オーダーメイドで管理指針を作成する必要も生じてくる。患者さんにも臨床データを示しながら適格なアドバイスを与え、不安にさせない配慮も重要である。このように、コルポ検査に精通した医師とは単にコルポ機器を用いて生検できる医師を指すものではない。子宮頸部腫瘍の専門医として子宮頸部腫瘍の疫学、分子生物学、病理学に精通し、予防的治療介入 (円錐切除術、蒸散術) の適用やその方法、そして HPV ワクチンを含めて患者さんへの適切な説明ができる医師を指す。専門の医師として重要なことは、患者さん中心の医療が提供できること、特に患者さんの気持ちに寄り添える医師である。子宮頸部腫瘍の臨床はとて奥深く、生涯を通じて研鑽に努める必要があると演者は考えている。

2) CIN2 の適切な管理

国際医療研究センター病院 富尾 賢介

子宮頸部扁平上皮内腫瘍 (cervical intraepithelial neoplasia : CIN) は三段階に区分され、中でも CIN2 は、大半が経過観察のみで自然軽快するものの、一部には前癌病変としての性格を持ち、将来子宮頸がんに進展するものも混在しているため、日常診療における CIN2 の適切な管理を理解しておくことは重要である。

直近の産婦人科診療ガイドライン (婦人科外来編 2023) において CIN2 は、3~6 か月ごとの細胞診とコルポスコピーを併用し、嚴重な経過観察が奨められている。CIN2 の 7~8 割は自然消退するが、ときに CIN3 と判別し難い症例も経験する。基本事項として、細胞診とコルポスコピーの手技に習熟し、過小診断・過剰診断を最小限にとどめることが重要である。2022 年度から日本婦人科腫瘍学会はコルポスコピー研修会を主催しているが、今後も診断精度向上に向けた様々な取り組みが期待される。

近年は、細胞診とコルポスコピーに HPV 検査を併用した管理が確立しつつある。HPV タイピング検査は CIN2 に対して保険適用となっており、上記ガイドラインにおいても、特に進展リスクの高い HPV (16・18・31・33・35・45・52・58 型) 陽性の CIN2 は、陰性例よりも綿密な管理指針が示され、1~2 年の経過観察期間中に自然消失しない場合、患者本人の強い希望がある場合などには、治療も可能とされている。治療として円錐切除術が行われるが、過剰切除は早産リスクにつながるため、切除領域を最小限に抑える配慮が重要である。さらに近年では、HPV 型に基づいた CIN 管理方法が報告されるなど、HPV 感染から病変進展機序の理解が深まるにつれて、より適切なりリスク評価が可能となりつつある。

本講演では、予防・診断・治療の側面から、CIN 2 の適切な管理に必要な知識をまとめた。

生涯研修プログラム 10 CIN の管理

3) CIN の最適な管理法とは

杏林大学 森 定 徹

子宮頸がんは HPV の持続感染がその原因として重要であり、前癌病変としての子宮頸部上皮内腫瘍 (cervical intraepithelial neoplasia : CIN) を経て段階的に発生すると考えられている。この CIN は、子宮頸部異形成および上皮内癌が含まれ、ベセスダシステムにおける扁平上皮内病変 (SIL) とも重なる概念である。CIN の管理について「産婦人科診療ガイドライン～婦人科外来編 2023」では、CIN1 は 6 か月ごとに細胞診と必要に応じてコルポスコピーで経過観察とされ、CIN2 は 3～6 か月ごとに同様に経過観察を行うが、1～2 年の経過観察で自然消失しない場合、患者本人の強い希望がある場合、継続的な受診が困難な場合には、妊娠女性以外では治療を選択できるとされてる。CIN1/2 の進展リスク評価のために行われる HPV ジェノタイプ検査の結果の解釈では、HPV16, 18, 31, 33,

35, 45, 52, 58 は進展リスクが高いため、これらが陽性の場合の CIN2 では治療が選択できる。CIN1/2 の経過観察の場合でも、これらの HPV タイプが陽性の場合には進展リスクが高いため、これ以外の HPV タイプの陽性例とは分けたフォローの仕方が示されている。最近、簡易ジェノタイプ判定のできるハイリスク HPV 検査もいくつか臨床の場で使用できるようになっている。また、病理診断においても CIN1 と CIN2/3 の鑑別に p16, Ki-67 を用いた免疫染色が有用であり、実際の病理診断に使われている。CIN は生殖可能年齢の女性に多く発症することから、より侵襲の少ない治療が望まれ、介入を考える際は妊孕性や周産期予後の観点を念頭に置く必要がある。今回、これら CIN の診断、管理のポイントについて解説する。

生涯研修プログラム 11 生殖医療の標準化と保険診療の現状と課題

1) ガイドラインの改訂について

群馬大学医学部附属病院周産母子センター 北原 慈 和

2022年4月より生殖補助医療の保険適用化され、2年が経過した。それに先立ち、2021年1月に日本生殖医学会学術委員会内のコアメンバーを中心に、生殖医療ガイドライン作成委員会が設立された。保険適用開始前の2022年1月の発刊を目指して、約1年間という短期間でのガイドライン作成とだったため、当時の作成委員のご苦勞は計り知れないものがあったと推察される。

Minds診療ガイドライン作成マニュアルでは、50%のガイドラインが約6年で「時代遅れ」になるとされているため、ガイドラインの改訂は3~5年毎が目安となっている。そのため、初版の生殖医療ガイドライン発刊の直後の2022年9月より、改訂版作成のためのガイドライン作成小委員会が立ち上がり、2025年9月に改訂版を発刊するための準備が始まっている。

改訂版においては、発刊までの時間的余裕があるため、システムティックレビュー (SR) チーム

を立ち上げ、それぞれのCQに関して可能な限りPICOを設定した上でSRを行い、エビデンスに基づいたAnswerの設定、および、解説文の作成を行うこととした。さらに、海外の生殖医療に関連する主要なガイドライン (ESHRE, ASRM, Cochrane review, NICE など) も網羅的に参照し、海外での最新の動向もCQ/Aや解説文に含めるようにしている。

本講演では、今回の生殖医療ガイドライン改訂の概略をお伝えすることを通じて、(1)そもそもガイドラインとは?(2)ガイドライン改訂作業の実際(3)ガイドラインを通じての生殖医療の標準化の3つを中心にお話をさせていただく予定である。さらに、本セッションのタイトルにもなっている、生殖補助医療の保険化の現状とその課題点についても、生殖医療ガイドライン改訂の観点からも触れてみようと考えている。

2) 診療報酬改定を踏まえた保険診療の現状と今後の課題

秋田大学 白澤 弘 光

保険診療を行う上で、医療従事者側、患者側の双方より、保険適用となっていない技術について実施を望む機会は少なくない。しかし、診療報酬改定のハードルは高く、各学会からの提案に対し、2022年(令和4年)度診療報酬改定の採択率は23.9%(175/733)、2020年(令和2年)度は35.5%(264/743)と、各年度により幅はあるものの3割程度となっている。

2022年4月より、種々の制限はあるが、これまで私費診療であった人工授精、体外受精・胚移植が保険適用となった。2024年(令和6年)度診療報酬改定は、不妊治療の保険適用後に初めて迎える診療報酬改定である。本プログラム抄録を作成している2023年11月は、各学会の改定提案に対する中央社会保険医療協議会(中医協)の議論がまさに始まるタイミングである。この後に様々な角度から提案が評価され、2024年4月の本プログラム講演時には、今回の提案で日本産科婦人科学

会、日本生殖医学会、日本産婦人科医会、日本泌尿器科学会などから提案された生殖医療関連の提案(未記載:不妊治療前の夫の感染症結果、不妊治療カウンセリング料、射出精子凍結・融解に関する診療報酬点数の新設/既記載:抗ミューラー管ホルモン測定要件の緩和、Y染色体微小欠失検査実施の施設要件緩和、精巣内精子採取術回収精子を用いた際の加点の回数緩和、流産検体の染色体検査)に対する結果が明らかになっていると思われる。

保険診療で行われる生殖医療において、より良い臨床を実践していくためには、適宜新たな技術の導入も必要である。しかし、私費診療であった際の生殖医療と異なり、新たな技術を臨床に用いるための保険適用を目指す際には、上記プロセスを経ることが必要となる。そのためには高いエビデンス創出が重要であり、学会横断的な取り組みが必須である。

生涯研修プログラム 11 生殖医療の標準化と保険診療の現状と課題

3) 先進医療の現状と課題

東京大学 泉 玄太郎

生殖医療のほとんどが自由診療であった時代は、混合診療の問題を考慮する必要がなかったため、様々な臨床的な試みを導入しやすい環境にあったといえ、実際に新規医療技術が林立している状態であった。しかし、2022年の保険適応の大幅な拡大に伴い、保険適用とならなかった技術に関しては、いわゆる混合診療にまつわる様々なルールを遵守しながら、今後の保険収載に必要なエビデンスを積み上げる必要がでてきた。

先進医療は、保険診療の対象に至らない先進的な医療技術に対して、保険診療との併用を認めるための制度である。ただし、医療技術ごとに定める施設基準を満たしている医療機関必要がある。また、将来の保険収載の可否を検討するエビデンスを集積するために、実施医療機関からは定期的な報告をする義務もある。

先進医療は2023年11月現在で、先進医療Aが28種類、先進医療Bが53種類ある。そのうち、生殖医療に関係するものは、先進医療Aのうち11種類（子宮内膜刺激術、タイムラプス撮像法による受精卵・胚培養、子宮内膜擦過術、ヒアルロン酸を用いた生理学的精子選択術、強拡大顕微鏡を用いた形態学的精子選択術、二段階胚移植術、子宮内細菌叢検査1、子宮内膜受容能検査1、子宮内細菌叢検査2、子宮内膜受容能検査2、膜構造を用いた生理学的精子選択術）、先進医療Bのうち2種類（タクロリムス投与療法、着床前胚異数性検査）である。

ここでは、不妊治療に用いられる先進医療の内容を振り返りながら、そこから見える、受精障害や着床不全などの不妊治療の課題についてレビューをしたい。

医療安全講習会 

患者・家族とともに歩む，患者参加型医療の推進

群馬大学大学院医学系研究科医療の質・安全学 田 中 和 美

近年，医療はますます高度化・複雑化・多様化し，「医療は経済の中で最も複雑な分野であり，病院は人類史上，最も複雑な組織である」と言われるようにまでなった (Drucker P. Managing in the next society, NY, St. martin's Griffin 2002)．医療現場においては，多職種，多診療科，多部門が複雑に相互依存，連携しており，チーム医療の重要性がますます高まってきた．同時に，患者・家族は医療ケアチームの一員であるという考え方も広まり，「患者参画」，「患者家族参画」，「患者参加型医療」，「患者中心の医療」，「共同意思決定」といった言葉をよく耳にするようになってきた．また，それぞれの言葉に対する英語についても「Patient (and family) engagement」をはじめとする多くの表記が存在しており，何となく意味は伝わるものの，具体的にどのようなことを指すのか，どのような場面でどのように取り組んでいけば良いのか，と悩むことも多いのではないだろうか．

「患者とともに考える，患者の意見を聞く」ということは，かねてより医療現場で実践されてきたことではあるが，特に患者安全の側面から，世界的にもますます注目されてきているところである．2021年に世界保健機関 (WHO) から刊行された Global Patient Safety Action Plan 2021-2030 (GPSAP) は，7つの戦略目標で構成され，医療者個人，医療機関，教育機関，国といった様々なレベルでの患者安全行動計画が示されており，戦略目標4として「Patient and family engagement」が掲げられている．また，9月17日はWHOが制定

した世界患者安全の日であるが，2023年は「Engaging patients for patient safety」がテーマとして掲げられ，世界各国で「Patient (and family) engagement」に関する様々な取り組みがなされた．

群馬大学医学部附属病院（以下，当院）においては，2014年に大きく報道された腹腔鏡手術による医療事故以降，様々な改革に取り組み医療安全体制強化に努めてきた．外部委員による医療事故調査委員会からいただいた，医療事故防止再発に向けた提言の中には，「患者参加の促進」という項目も盛り込まれ，日常診療の中で患者との情報共有を図り，患者中心のチーム医療を実現するためのシステムを質の向上を図ること，当院を大切に思い，病院の再生を強く願ってくださったご遺族の思いを改革のエネルギーとして活かすことにより，患者参加型医療を推進していくことが当院の使命であると記載されている．これを受けて，より安全で質の高い医療のあり方を模索しながら，当院における医療事故のご遺族らも委員として参加する患者参加型医療推進委員会を中心として，患者とのカルテ共有，インフォームド・コンセントの録音などについて検討を重ね，全国に先駆けた取り組みを実践してきた．

本発表では，「患者参画」の概念や，患者安全の国際的な動向についても紹介した上で，当院における医療安全体制強化や患者参加型医療の推進に関する取り組みとその成果，実際の患者家族との関わりの中での新たな気づき，今後の展望などについて共有したい．

医療倫理講習会 

医療倫理とイノベーション

東京大学医学部研究倫理支援室 上 竹 勇三郎

医療倫理は医療者の道徳性をめぐる問題から議論が始まったが、科学技術の進歩に伴い、人の健康と厚生に関係する臨床倫理、研究倫理等、様々な問題を扱うようになった。また、最近では「責任ある研究とイノベーション」(RRI: Responsible Research and Innovation)、「倫理的・法的・社会的課題」(ELSI: Ethical, Legal and Social Issues)について議論される機会も少なくない。科学技術の発展においてRRIが重要であり、加えてELSIという課題意識を持ち研究を実施することでポジティブサイクルが生まれるという考え方である。診療から研究まで、「ポジティブサイクルを回すために必要な」幅広い医療倫理的課題に対応する必要性が問われている。

医療倫理は臨床倫理、研究倫理、公衆衛生倫理に大別されるが、本講習会では、主に研究倫理について、はじめに、診療と研究の境界領域の医療行為の取扱いや着床前診断 (PGT: Preimplantation Genetic Testing) 導入時における医療倫理的な考え方等について、実例を踏まえて概説したい。特に、外科的な手技や技術の導入・開発を意味する surgical innovation は外科医特有の命題と考える。surgical innovation は診療か研究かの取扱いが難しいケースも多いが、その評価のための「The IDEAL Framework」の重要性についての報告が散見され、安全性、有効性の検証には適切な臨床研究の実施が求められている。研究倫理については、概念的な面もカバーしたい。医学の進歩は、人を対象とした医学研究にある程度依存せざるを得ないが、第二次世界大戦中にはそれが人体実験の形で行われていた悲惨な歴史がある。そし

て戦後も非人道的な医学研究は後を絶たなかった。その反省から生まれたのが、被験者保護を重視する医療倫理的視点で、その原則に従って国際的なガイドラインが策定され、倫理委員会制度が確立した。どのガイドラインにおいても、被験者の保護を最優先にすること、独立した倫理審査がなされること、研究の科学的合理性が担保されること、十分に情報が提供された上でインフォームドコンセントを受けること、リスクとベネフィットの適切なバランス等の基本的な要項が含まれることについては合意が形成されている。

研究倫理は、研究者の立場に立てば、研究のハードルを上げ、ブレーキをかけるような概念と捉えがちであり、また、どの規制に準拠して研究を実施すれば良いか困惑し、煩わしさを覚えるであろう。さらに、倫理審査は研究計画等の粗探しをされる場のように感じるケースもあるだろう。しかし、実際の倫理審査は、科学的合理性や倫理的妥当性、実施体制等が適切であるかを確認しながら、研究者と審査側とで研究計画をブラッシュアップする建設的な議論の場でもある。いずれにしても、研究者はその善良な目的のすぐ隣に、非倫理性を問われる落とし穴が存在することに留意して研究を進めるべきであるが、研究倫理はより理解を深めれば、研究者自身を守る、研究エコサイクルを制御するための一つの概念と考えることができるはずである。

本講習会では、基本的な医療倫理の考え方、診療からイノベーションの推進までを目的としたポジティブサイクルを回すために必要な医療倫理の考え方まで幅広く概説したい。

感染対策講習会 

感染症・感染対策 Up-to-Date : COVID-19 パンデミック, AMR サイレント・パンデミックから何を学ぶか

東邦大学微生物・感染症学講座 館田 一 博

ペスト, コレラ, インフルエンザ流行の歴史からもわかるように, 感染症はいつの時代も人類の脅威となりうる疾患である。我々は今, “新病原体によるパンデミック”として新型コロナウイルス感染症 (COVID-19) を経験している。約2年半で6億人を超える人が感染し, 約600万人以上の死亡が報告されている。たとえこのパンデミックが収束したとしても, また次のパンデミックが出現することを覚悟しておかなければならない。また, サイレント・パンデミックと称される薬剤耐性菌 (AMR) の問題も喫緊の課題である。インドのニューデリーで見つかったカルバペネム耐性腸内細菌はその1例であり, この細菌から新しい耐性因子 “NDM型 β ラクタマーゼ” が見付き世界を震撼させたことは記憶に新しい。

COVID-19 に対する治療薬・ワクチン開発は欧米がリードする形で進行した。特に世界で初めて開発された mRNA ワクチンは画期的であり, 本ワクチンの開発で何百万人も命が救われたといっても過言ではない。欧米は, 本ワクチンの開発を危機管理の視点で進めており, 10年以上も前からその開発を支援してきた。一方で本邦における mRNA ワクチンの開発はどうか? 医薬創薬技

術において決して劣らない日本企業であるが, 残念ながら欧米諸国に大きく水をあけられている状況となっている。診断法にしても, 本邦における遺伝子検査の普及, 新しい診断法の開発の遅れが明らかとなった。

パンデミック, サイレント・パンデミック感染症に対する治療薬, 診断法等の研究開発の難しさは世界が直面する問題である。投資規模, 開発までの時間, 成功確率の低さ, たとえ成功したとしても利益を回収できないリスクなど, 他の疾患とは異なる問題が存在する。ビジネス原理だけでは進めることのできない感染症治療薬・ワクチン・診断法の開発には, 危機管理と安全保障の視点が重要であり, すでにいくつかの国は新しい政策モデルの導入を検討している。その1例が “プル型インセンティブ” である。2023年5月には広島でG7サミットが開催される。その議題にパンデミック, サイレント・パンデミックが盛り込まれることは確実である。世界に貢献できる感染症治療薬・診断法・ワクチンの開発という視点で, 我々一人一人がどのように活動していかなければいけないのか, ご参加の皆様方と意見交換できれば幸いである。

教育奨励賞/健康・医療活動賞受賞講演 健康・医療活動賞

HPV ワクチンに関する学術的エビデンスの創出と自治体の子宮頸がん対策
および母子保健事業に対する学術的支援

大阪大学 上 田 豊

【目的】

(A) HPV ワクチンに関する学術的エビデンスの創出

本邦においては最近、子宮頸がんが若年層において急増に転じており、子宮頸がん対策は喫緊の課題である。期待された HPV ワクチンは定期接種化されたわずか2か月後に積極的勧奨が差し控えられ、事実上の停止状態となった。当時は、積極的勧奨の再開が再普及の大前提であり、これを訴えかけていくにあたり、HPV ワクチンの重要性和効果を示す学術的エビデンスの構築が必要と考えられた。

(B) 自治体における子宮頸がん対策および母子保健に対する学術的支援

子宮頸がん検診や HPV ワクチンの実務は各自治体が担うことになっているが、多くの自治体では職員が特段の評価などを行わないまま実施されているのが実情である。母子保健の領域においても、育児放棄や虐待といった育児中の女性や子供に関する問題が日々報道される中、実務を行う保健師や自治体職員は様々な指導や対応に追われ、事業の評価などを行って改善を図っていくことが難しい状況と言える。これらの実情を把握し、アカデミアとして自治体が行う事業の効果検証を科学的に行い、課題を自治体職員と共有して改善を図っていくことで、地域住民の身体的・精神的健康の向上に貢献できると考えた。

【方法】

(A-1) HPV ワクチンの有効性調査

全国自治体症例対照研究では全国の自治体からデータ提供を得て、HPV ワクチンによる CIN の予防効果を検証した。また、松山市からデータ提

供を得て、20歳子宮頸がん検診の結果を経年的に観察し、1993年度以前の生まれの HPV ワクチン導入前世代と1994～1999年度生まれの HPV ワクチン接種世代における CIN3+ の頻度を比較した。

(A-2) HPV ワクチン積極的勧奨差し控えの弊害のシミュレーションと実地検証

積極的勧奨差し控えの弊害を示すために、生まれ年度ごとに20歳時の HPV-16・18 型感染相対リスク(導入前世代である1993年度生まれのリスクに対する比)および生涯の子宮頸がん罹患・死亡相対リスクを算出した。また、実地検証として、協力の得られた自治体からデータ提供を得て、20歳の子宮頸がん検診の結果を経年的に観察し、2000年度以降の生まれの HPV ワクチン停止世代の細胞診異常率を、導入前世代および接種世代と比較した。

(B-1) 子宮頸がん検診の受診率向上に向けた取り組み

子宮頸がん検診無料クーポン制度の効果検証を豊中市職員と共同で実施した。すなわち、無料クーポン事業が実施されていた2009～2012年度の各年齢における子宮頸がん検診受診率を事業開始前の2008年度と比較した。また、豊中市・八尾市・枚方市において、母親を介する20歳の子宮頸がん検診受診率勧奨プロジェクトを実施し、20歳の子宮頸がん検診受診率向上を図った。同様に、いわき市、豊中市・茨木市・熊取町において、共同で開発した HPV ワクチン接種環境に応じた子宮頸がん検診受診勧奨リーフレットを用いて勧奨を行い、受診率の上昇効果を検証した。

(B-2) HPV ワクチンの普及に向けた取り組み

豊中市における HPV ワクチン個別案内事業の評価として、2020 年度に市が作成したリーフレットの個別送付の効果を、送付月前と送付月後および 2020 年度と前年度の接種状況を比較することで検証した。

(B-3) 子育て中の女性の孤立感軽減に向けた取り組み

母子保健領域においては、八尾市と共同で4か月健診・3歳半健診の受診者の母親に対してアンケート調査を実施し、育児中の母親の孤独感について検討した。さらに、これを軽減するためのリーフレットを開発した。

【成績】

(A-1) HPV ワクチンの有効性調査

HPV ワクチンによる CIN 1+ および CIN 2+ の有意な予防効果が示された。当調査は厚労省祖父江班の有効性調査を引き継いだものであり、積極的勧奨再開決定時に HPV ワクチンの有効性を示すデータとして引用された。また、松山市の20歳の子宮頸がん検診結果の解析では、本邦の HPV ワクチンプログラムによる CIN 3+ 減少効果を最初に報告した。

(A-2) HPV ワクチン積極的勧奨差し控えの弊害のシミュレーションと実地検証

HPV ワクチン停止世代の20歳時の HPV-16・18 型感染および生涯の子宮頸がん罹患・死亡の相対リスクは、導入前世代と同程度に戻ることが予測された。さらに、全国24自治体(人口規模：1315万人)の各生まれ年度の20歳の子宮頸がん検診において、導入前世代に比して接種世代で低下していた細胞診異常率が、停止世代である2000年度生まれの女性で再上昇していた。これら HPV ワクチン積極的勧奨差し控えの弊害については、多数のメディアで取り上げられ、HPV ワクチンの重要性の認知向上に寄与できたものと考えている。

(B-1) 子宮頸がん検診の受診率向上に向けた取り組み

無料クーポン制度により子宮頸がん検診受診者の掘り起こしの効果は十分認められたが、継続受診には結びついておらず、行政としての課題を明らかにできた。この結果は豊中市職員を共同著者

として論文発表した。また、母親を介する20歳の子宮頸がん検診受診率勧奨プロジェクトおよび、HPV ワクチン接種環境に応じた子宮頸がん検診受診勧奨プロジェクトのいずれにおいても、受診率の上昇が確認できた。

(B-2) HPV ワクチンの普及に向けた取り組み

豊中市において独自に作成した個別案内リーフレットによる HPV ワクチン接種率上昇効果が確認された。厚労省リーフレットを送付していた他の自治体より接種率が高く、独自作成リーフレットの効果が示唆された。さらに、新たに HPV ワクチンの理解を促進するメッセージを開発し、岡山県に提供した。

(B-3) 子育て中の女性の孤立感軽減に向けた取り組み

八尾市で実施した4か月健診・3歳半健診の受診者の母親に対するアンケート調査により、育児中の女性の孤独感が物理的な孤立より精神的な孤立によるところが大きく、自己効力感の低さなどが相関していることが明らかになった。これを基に、自己無力感を低減して市の保健師とのつながりを誘導するリーフレットを開発した。紙面版のリーフレットは八尾市で対象者に送付し、SNS 版リーフレットは Instagram 広告として高槻市内で発信した。

【結論】

HPV ワクチンの有効性およびその裏返しである停止状態の弊害に関しては、一定の学術的エビデンスを提供できたと考えている。今後引き続き、接種率の向上に努めていく必要がある。

子宮頸がん検診の受診率向上や育児中の女性の孤独感の軽減に向けた取り組みも絶えず評価を行いつつ改善を図っていかねば、事業の実効性を高めることは期待できない。これまで各自治体の実務担当職員と長年に渡って情報を共有しあい、アカデミアの立場からできる支援を行ってきた。また、得られたデータを論文にまとめていく作業などを通し、自治体職員の科学的視点も養われたものと考えている。これらは、今後の自治体内部での事業展開などにおいても生かされていくものと信じている。

教育奨励賞/健康・医療活動賞受賞講演 教育奨励賞

1) 近畿大学医学部での10年間の教育活動～医学部生，研修医における産婦人科教育と産婦人科医師に対する内視鏡手術教育の実践

近畿大学 小谷 泰史

大学病院で勤務する以上，臨床，研究，教育の3本柱が大切であると常日頃から考えている。その中で教育に関して，次世代の医師育成のため，自分自身最も重要なものであると思っているが，軽視されがちである。そこで近畿大学医学部産婦人科の医学部生，研修医に対する産婦人科教育と産婦人科医師に対する内視鏡手術の教育の実践を約10年間行ってきたことを報告する。

自分自身まず，医学教育に対しての教育を受けてないことに気付き，積極的に医学教育学に関わる講習会，学会などに参加し，勉強してきた。

当科におけるクリニカルクラークシップの統合責任者を行い，アンケートで約20%程度の医学生が分娩を見学せずに実習を終えていることが判明したため，学生1人1人にPHSを持たし，指導医と密に連携をとる体制とし，分娩の未見学率の低下に貢献した。また自分自身担当している内視鏡手術手技実習で，Virtual Reality Simulators (VR)を用いた子宮全摘術のモデルを用いた実習を従来の手術手技の実習に追加した。前後で婦人科解剖の試験を行った結果，VRを用いた群で有意に知識が増加している結果となり，学生にとって刺激的で知識を増加する実習を実践している。

また産婦人科は初期研修において必修化となり，ローテートしてくる研修医全員と面談を行い，実習で何を勉強したいかというニーズを事前に調査し，それぞれの研修医に対してオーダーメイドのプログラムを作成した。事後のアンケートでも，満足度が従来より上昇しており，一定の効果が得られたと思われた。

産婦人科医に対する内視鏡手術教育として，2013年以降に自分自身が直接指導を行い，12名の内視鏡技術認定医を輩出した。その過程で，自分が直接指導した内視鏡手術に関わる学会発表の件数は237件である。また内視鏡手術に関する指導論文は15編を携わってきた。現在，認定医を取得した医師が，その後輩の指導をするシステムが確立されており，患者に安全に内視鏡手術を提供できる体制となっている。

以上より10年間の教育活動の実践を通じて，医学部生，初期研修医に対して産婦人科に興味をもってもらえるような教育の実践を継続して行ってきた。最終的には産婦人科を専攻してもらい，プロフェッショナリズムを備えた産婦人科に成長し，次世代のリーダーを育成していく教育が出来れば本望である。

教育奨励賞/健康・医療活動賞受賞講演 教育奨励賞

2) 手術教育イノベーション：先端技術による学習効率化の取り組み

国立がん研究センター東病院 竹 中 慎

手術教育イノベーションの取り組みについて報告します。私が各専門医の修練中に常に感じたことは、十分な教育環境や教育教材が足りないことでした。「手術は見て真似よ」の世界で、鏡視下の鉗子操作や縫合結紮の方法や解剖は教科書にほとんど記載されず、悪性腫瘍の修練ではほぼ見えない術野を覗き込みながら、技術を習得することに非常に苦勞しました。このような非効率な学習環境を変えることを模索した結果、一般社会で導入される新規技術を用いて、効率的に学習できるデバイスを開発し、医局の垣根を超えて情報を共有できるコミュニティを形成して外科教育にイノベーションを起こすことを目指しました。

【1 婦人科腫瘍修練医のための二つの子宮モデルの開発】

婦人科腫瘍修練のための二つの種類の子宮モデルを開発し、婦人科手術ハンズオンセミナーを行いました。

1-1：骨盤血管解剖シミュレーターの構築

2017年、針金とスポンジにて3D骨盤血管解剖シミュレーターを工作しました。本モデルをドライボックス内に入れて、鉗子を用いて、腹腔鏡下広汎子宮全摘術の手順のシミュレーションを行うことができます。本モデルと2Dのイラストを比較検討することで修練医の解剖に関する学習デバイスとしての有用性について示し論文化しました。そして同モデルを3Dプリンターにて量産できるように改良して、骨盤解剖ハンズセミナーを行い、全国の医師に対して広汎子宮全摘術および骨盤リンパ節郭清のシミュレーショントレーニングを開催しました。

1-2：腹腔鏡下子宮全摘術・骨盤郭清シミュレーターの構築

2023年、腹腔鏡下子宮全摘術および骨盤郭清の

シミュレーターを企業と共同開発しました。先述のシミュレーターは血管や神経のみを再現しましたが、本シミュレーターではリンパ節や筋膜を見立てたジェルやメッシュを用いることで、リアルに近い形で電気メスやベッセルシーリングシステムを用いて子宮全摘術および骨盤リンパ節郭清のシミュレーションを行えるようにしました。

【2 AIを用いた新たな教育デバイスの開発】**2-1：AIを用いた尿管・膀胱ナビゲーションモデル**

482症例の手術動画から抽出した13191枚の静止画に尿管および膀胱の位置を示した学習データと深部学習の技術を用いて、AIを用いた尿管・膀胱ナビゲーションモデルの構築を行いました。腹腔鏡モニターに尿管や膀胱の位置が光って表示されるシステムであり、レジデントへの骨盤解剖の教育ツールとして活用しました。システムの臨床的有用性を示すため、AIモデルによる医師の臓器認識能の上乗せ効果の検証を行ったところ、どの手術技能レベルにおいても上乗せ効果が示され、特に専攻医の解剖認識能力は技術認定医レベルに向上することが示されました。

2-2：AIを用いた自動手術技能評価モデル

教育において手術技能評価の重要性が高まっている一方、人が評価することでの主観性や多大な労務が課題となっています。この課題を解決するためにAIを用いて自動に客観的な技術評価を行うシステムを構築しました。AIにより15個の手術技能評価パラメーターを構築し、技術評価されたビデオを解析することで、外科医の手術技能を総合的に評価するシステムを構築し、日本内視鏡外科学会の高得点群と低得点群を明確に区別することが可能であることを示しました。

【3 ドライボックスでの縫合結紮トレーニングで

の教育活動】

エキスパート指導による腹腔鏡手術セミナーを卒業することで身につけたドライボックストレーニングの Tips をまとめ、学会発表や教科書、YouTube を用いて発信しました。

YouTube : <https://www.youtube.com/watch?v=HfH-qnAliZI&t=129s>

【4 外科教育プラットフォームの構築】

2020 年 11 月より、長野赤十字病院 堀澤信先生と共同で OSP (Online Surgeons Platform) の運営を開始しました。二人の役割を分担しており、私は主にプラットフォーム全体の運営を行っております。メインコンテンツの OSVD 以外にも Surgeons life (エキスパートの講義、手術のデジタル教科書など)、Learn more (医療機器、トレーニング機器の情報プラットフォーム) など、多くのコンテンツを含む外科医教育の総合プラットフォームを構築しました。現在、医師の会員数は 2900 名を超え、毎月 100 名のペースで会員は増えております。

【5 学会における教育活動】

ロボット技術認定評価ツールの構築

2021-2022 年産科婦人科内視鏡学会ロボット技術認定制度ワーキンググループに所属し、ロボット技術認定評価ツールの原案を作成しました。現在、産科婦人科内視鏡学会の元、ロボット技術認定評価ツールの Validation 試験の研究を計画しています。

【6 その他の教育実績】

・神奈川県産婦人科若手の会 (KTOG) の立ち上げと県内腹腔鏡セミナーの開催

神奈川県内の若手の横断的なコミュニケーションの場の構築のため、神奈川県産婦人科医会の下部組織として神奈川県若手産婦人科の会 (KTOG) を設立し、副会長として 3 年間運営を行いました。特にその中の行事の一つとして神奈川県ラパロセ

ミナーを立ち上げて、2015-2017 年で三回のリーダーを務めて、エキスパートによる講演、ドライボックスおよびウェトラボでの縫合トレーニングを行いました。

・昭和大学腹腔鏡セミナーの主催

2017 年から 2023 年までの 7 年間、毎年 6 月に計 6 回の昭和大学腹腔鏡セミナーを全てオーガナイザーとして開催しました。本セミナーでは、ドライボックスでの縫合結紮の練習だけではなく、手術に必要な「目」「手」「頭」そして「心」のトレーニングをカリキュラムに入れて行いました。また医局の様々なレベルの医師のニーズに対応できるように、レベル別のカリキュラムや選択制のカリキュラムを組んで工夫しました。毎年講師を合わせて 50 名ほどの参加者があり、参加者のモチベーションアップや、トレーニング方法の理解に貢献しました。

・女性医師の手術教育の支援 (イクドクセミナー講師)

育児中の医師を対象とした腹腔鏡トレーニング (イクドクセミナー) の講師を二回務めました。二年間で二回開催し、腹腔鏡の技術指導を行い、5 名の技術認定医を育てました。

おわりに

私の教育に関する行動を振り返ると、私の背景にいつもあるのは「効率的な教育」でした。効率という言葉はけっして聞こえが良くはないですが、私は、新たなデバイスと IT コミュニティで次世代の産婦人科医のラーニングカーブを短縮させることで、確保された時間で医師の QOL を高めることができ、周術期合併症を減少させるができます。医学の進歩に伴い、現在の修練医の習得すべき技術は多岐にわたる一方、働き方改革により医師の働く時間は限られます。新規技術によるイノベーションを教育に積極的に取り入れることが、この状況を打破する一つの解だと考えます。

教育奨励賞/健康・医療活動賞受賞講演 教育奨励賞

3) 初学者に向けた遠隔超音波セミナーの発足と若手サポートメンバーの育成：地域を超えたネットワーク形成を目指して

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田 中 守⁹⁾

はじめに

2020年初頭からのCOVID-19の流行により、オンラインでの遠隔セミナーが普及した。我々はこれを好機と捉え、交通や家庭の都合により実地参加が難しい方に対して、門戸の広い超音波セミナーの受講環境を提供することを目指した。講師陣（以下サポートメンバーとする）は従来の著名な講師ではなく、若手医師やコメディカルとし、サポートメンバーにとっての学びとチーム形成を築くことを目的とした。2020年1月から日本産婦人科超音波研究会が遠隔講座の配信を開始し、委員の先生方の同意を得て、「産婦人科超音波 超ベシクセミナー」が発足した。今回、この遠隔超音波セミナーの取り組みについて報告する。

方法

2020年3月、第1回のサポートメンバー24人は研究会に所属する大学からの推薦により選ばれ、企画を立案した。第2回以降のサポートメンバーは公募も行なった。34名のサポートメンバーが1講義を担当し、15-20分間のプレゼンテーションを作成した。講義形式はzoomを用いたウェビナー形式で行い、人数上限を設けず参加者を募集した。講義の中で大切にすることは遠隔セミナーであっても受講生と「双方向性を持つ」ということである。そこで、イベントツールであるSlidoというアプリケーションを用いて「リアルタイムクイズ」と「質疑応答チャット」を講義の間に実

施した。参加登録者は、メールやSNSなどを通じて全都道府県から募った。

結果

2021年8月、第1回 実施当日の参加登録者は1,050人、最高視聴者数は758人であった。双方向性のセミナーが一体感を産み、3時間のセミナーを飽きずに参加できたという声が多く寄せられた。セミナー満足度(1-5段階で4以上)は97.0%と高い評価を得ることができた。以降、第2回(2022年1月)、第3回(2022年8月)、第4回(2023年3月)に開催し、この2023年8月に第5回を行った。初回からセミナー参加登録者数は累計3,355人(全都道府県含む)、歴代サポートメンバーは47人(秋田から宮崎まで)となった。この活動を通じて、地域を超えたネットワークを形成し、産婦人科超音波の教育の輪ができたと実感している。

考察

この教育活動の重要性には3つの側面がある。

1つに、「教育の地域格差をなくすこと」である。我々は、日本産科婦人科学会主催のサマースクールやPlus One Project 2など過去の経験から、地方の病院までの移動に4-5時間かかることや、少人数の体制で病棟を守っている病院では実地セミナーに参加しにくい現実があった。学びの意欲があるにも関わらず、働く環境の制約で学びの機会が少なくなることを実感し、地域格差がないセミ

ナーの重要性を感じた。このセミナーでは、参加者のみならず、サポートメンバーもオンラインでの参加を可能としている。

2つに、「子育て中でも活動に参加できキャリア形成を止めないこと」である。若手医師が学ぶ時期と妊娠・出産・子育ての時期が重なることは一般的であり、通常の活動では中断が避けられない場合もある。しかし、このセミナーでは自宅から参加可能であり、歴代サポートメンバーの中には妊娠・出産を経験しながら活動した女性医師がいることから、キャリア形成を継続できる環境を提供していると考ええる。

3つに、「サポートメンバーのチーム形成」である。チーム形成には、創造的なアイデアが生まれ

る、リソースの最適活用ができる、モチベーションの向上など様々なメリットを有する。特に産婦人科超音波の分野では講義を共同で作成することで知識の幅が広がる。一施設だけでは知識の偏りが生じやすい中、本セミナーでは異なる経験と意見を共有し、より深い学びが可能となっている。

このセミナーの将来展望は、初学者に対し産婦人科超音波の楽しさや正常例や発生・解剖の理解を促進し、サポートメンバーのチーム形成を強化して国際学会の参加を増進させることである。サポートメンバーと参加者ともに地域を超えたネットワーク形成を進め、今後の更なる教育活動の発展を目指していく。

学術奨励賞受賞講演

1) 生殖補助医療における add-ons 導入と社会医学的課題に関する包括的研究

秋田大学医学部附属病院 白澤弘光

演者は ART における add-ons について、特に IVM (in vitro maturation), TLI (time-lapse imaging), PGT-A (preimplantation genetic testing for aneuploidy) に関する基礎・臨床研究を継続してきた。また近年は ART における laboratory work, 社会医学的な課題についても研究を行っている。本講演では主にヒト配偶子, ヒト胚を用いた add-ons に関する研究, および蛍光免疫染色, 卵子凍結, 胚培養士業務など laboratory work に関連する研究から, ART を基礎・臨床・社会医学の視点から考え, 今後の課題を整理したい。

1. ヒト未成熟卵子を用いた IVM に関する研究

IVM の有用性については evidence が未だ不十分であり, その活用には多くの課題が存在する。演者は約 10 年間 IVM に関する研究を継続してきた。

子宮体がん患者の手術時摘出卵巣から未成熟卵子を得て IVM を施行した (Shirasawa et al. *J Assist Reprod Genet* 2013)。同研究では, non-commercial IVM メディウムを用い, 成熟率 (maturation rate) は 12.6% と低値であったが, その後は IVM media kit を用い, 臨床・研究の両面で maturation rate は 50-60% と改善を認めた。また, 妊孕性温存を目的とした, 開腹術中の未成熟卵子回収, IVM, 成熟卵子凍結を報告した (Shirasawa et al. *Gynecol Oncol Rep* 2017) ほか, 妊孕性温存および研究マテリアルとしての IVM の意義について review を報告した (Shirasawa et al. *Reprod Med Biol* 2017)。また, 研究マテリアルとして, 施設間の卵胞液輸送によるヒト配偶子確保を目的とした研究では, 卵胞液輸送が IVM 成績に与える影響についても検討し, 250km 離れた

施設間における卵胞液輸送を実施し, 非輸送群と IVM 成績比較を行った。結果として, 卵胞液輸送群 (回収卵子個数 8.1 ± 8.4 個, 成熟率 38.6%), 非輸送群 (5.1 ± 5.1 個, 69.2%) の比較において, 輸送群では IVM による成熟率が有意に低下するが, 4 割弱の成熟率が得られること, および年齢と摘出卵巣からの回収卵子個数の間に有意に負の相関を認めることを明らかにした (Shirasawa et al. *Reprod Med Biol* 2019)。また, 卵巣組織凍結時に未成熟卵子を回収し, IVM により成熟卵確保を併用する ovarian tissue cryopreservation-in vitro maturation (OTO-IVM) に関して, OTO-IVM による maturation rate が 59.5%, および第 1 極体放出から引き続いての処置である卵子凍結, ICSI までのタイムラグが平均 13.5 時間であることなどを ASRM で報告し (Shirasawa et al. *Fertil Steril* 2021), 現在追加解析を行い論文投稿中である (Sakaguchi, Shirasawa et al. *under review*)。

上記研究成果から IVM の活用には add-ons 併用, laboratory work を踏まえた検討の重要性が明らかとなった。

2. TLI, PGT-A に関する研究

TLI に関しては, 子宮体がん摘出卵巣から得たヒト未成熟卵子に対する IVM, 単為発生過程を連続的に検討した。成熟率は 55.2% であり, 第 1 極体放出時間 (24 時間以内 53.1%) と, その後の前核発現-消失時間及び卵割過程の関連を検討した。第 1 極体放出が 24 時間以降の群 (46.9%) において単為発生卵割合が高いこと, および単為発生における前核発現時間が, 臨床における ICSI の際の前核発現時間よりも有意に短くなることを見出した (Shirasawa et al. *F S Sci* 2020)。また,

ヒト胚盤胞発育に関わる因子について、胚拡張面積、hatching 有無が内部細胞塊細胞数、栄養外胚葉細胞 (TE) 数と関連することを報告した (Iwasawa, Shirasawa, Terada et al. *PLoS One* 2019). また、TLI による拡張、hatching 所見と、胚発生に重要な Na⁺/K⁺ ATPase における $\alpha 1$, $\beta 1$, $\beta 3$ アイソフォーム局在の関連性を蛍光免疫染色、RT-qPCR を用いて報告した (Hirakawa, Shirasawa, Terada et al. *Hum Reprod* 2022). 近年はマイクロインジェクションを要さない、化学蛍光プローブによるライブセルイメージングを用いた初期胚挙動解析をマウス胚 (Okabe, Shirasawa, Terada et al. *Reprod Med Biol* 2023) からヒト胚に発展させ、紡錘体形状および核異常との関連を検討している (Ono, Shirasawa, Terada et al. *under review*).

PGT-A に関しては TE 生検による PGT-A 結果と、生検後の胚全体を用いた PGT-A 結果における不一致頻度 (37.9%) 及び、モザイクや部分的な染色体異常を認めた症例における不一致頻度を報告した (Takahashi, Shirasawa, Terada et al. *Reprod Med Biol* 2021). また、ヒト廃棄胚を用いた 10 日齢までの長期培養における PGT-A に関する検討では、通常の 5,6 日齢 TE 生検による PGT-A 結果と、培養液中の cell-free DNA を用いた非侵襲性 PGT-A (niPGT-A) 結果を、長期培養後の胚全体による PGT-A 結果と比較した。一致率は、5,6 日齢の PGT-A で 43.8% (感度 87.5%, 特異度 77.8%), niPGT-A で 56.3% (感度 100%, 特異度 87.5%) であった (Shitara, Shirasawa, Terada et al. *PLoS One* 2021).

これらヒト配偶子、ヒト胚を用いた結果から、TLI の有用性および PGT-A の limitation などを引き続き検討している。

3. 生殖医療における社会的問題、laboratory work に関する研究

Laboratory work 改善の観点から、新技術である電界攪拌をマウス卵子の蛍光免疫染色に応用し、紡錘体の微小管に対して、抗体量削減、染色時間短縮を目的とした蛍光免疫染色手法を報告した (Shirasawa et al. *Sci Rep* 2015). また本邦のメデイカル、およびノンメデイカルな卵子凍結の実態について、ウェブから得られるコストに関する比較検討も行い、ヨーロッパ生殖医学会で報告した (Shirasawa et al. *Human Reproduction* 2022). 同検討では、全国 ART621 施設の内、ウェブに卵子凍結実施を明示していた 146 施設 (23.5%) において、88 施設はメデイカルのみ、21 施設はメデイカル+ノンメデイカル、37 施設はノンメデイカルみの卵子凍結であり、ノンメデイカル施設において卵子凍結費用、年間更新料が有意に高額であること等を見出した (Shirasawa et al. *Heliyon* 2023). また、近年は日本産科婦人科学会生殖・内分泌委員会小委員会および、こども家庭科学研究における胚培養士実態調査を踏まえた研究も行っている。本邦では各施設の ART サイクル数と所属胚培養士数に有意な相関を認めるが、ASRM の胚培養士人員基準を満たす施設割合は半数以下に留まること、PGT-A 実施施設で胚培養士人員数が有意に増加すること、胚培養士実施業務は各施設間で大きく異なること等を日本産科婦人科学会や日本生殖医学会で報告し、現在投稿準備中である (Shirasawa et al. *under preparation*).

今後、本邦で IVM, TLI, PGT-A などの add-ons をさらに活用するためには、laboratory work を考慮した人員体制整備が不可欠であり、そのためには本邦の現状を正確に捉える必要がある。基礎的知見を ART 臨床に橋渡しし evidence を構築し、さらに社会医学的な視点から臨床の最適化を試みるのがわれわれの責務であり、今後も幅広い視野から研究を継続していきたい。

学術奨励賞受賞講演

2) 超音波を用いた新たな胎児発育評価

慶應義塾大学 池ノ上 学

出生体重は、周産期予後の重要な予測因子であるだけでなく、児の長期予後とも関連するという、Developmental Origins of Health and Disease (DOHaD)の概念が確立されてきた。DOHaDで当初提唱された、母体の低栄養が胎児に影響を与える「Thrifty hypothesis」に加えて、近年では、母体過栄養や糖代謝異常による胎児プログラミング、つまり過剰な栄養素の供給による脂肪酸酸化や糖新生の抑制および脂肪の蓄積が、小児肥満や早期発症メタボリックシンドロームにつながるという「Fuel overload hypothesis」も注目されている。実際に、約2万人を対象としたHyperglycemia and Adverse Pregnancy Outcomes (HAPO) studyおよび、その後のHAPO follow up studyでは、母体の耐糖能が新生児期さらには小児期の体脂肪率や、小児肥満と関連することが示されている。

脂肪は身体組成の重要な構成要素の一つである。ヒト新生児は他の哺乳類と比較して体脂肪率が高く、出生体重の個体差の46%は脂肪量の差によるとされる。また新生児体脂肪率は、小児期の体脂肪率と有意に相関するため、新生児体脂肪率は小児肥満の有用な予測因子となる。一方で、これまでヒト胎児期における脂肪量やその規定因子に関する報告は乏しい。そこで、胎児脂肪量の計測による新生児体脂肪率の予測や、胎児脂肪量の規定因子の解明を目的として、以下の検討を行った。

(1) 胎児脂肪量の計測による新生児体脂肪率の予測

まず、超音波断層法を用いて、再現性をもって脂肪量を計測可能とされている胎児上腕、大腿、腹部に着目し、妊娠中期、後期に前方視的に計測した胎児脂肪量が、新生児体脂肪率の予測に有用

であるか検討を行った。その結果、妊娠20週における胎児脂肪量は新生児体脂肪率と相関を示さなかったが、妊娠30週における胎児脂肪量は新生児体脂肪率と有意な正の相関を示した。このことから、妊娠20週から30週にかけて胎児脂肪量の個体差が顕在化することが明らかとなった。また、特に上腕における脂肪量が、新生児体脂肪率高値の有用な予測因子であった (Ikenoue S et al. *Pediatr Obes* 2017)。

(2) 胎児肝血流量と新生児体脂肪率の関連

次に、胎児脂肪量の規定因子を明らかにするために、主要な栄養基質の合成・分解の場である、胎児肝臓への血流量に着目した。胎盤から臍帯静脈を通して胎児へ流入した血液は、一部が静脈管を介して心臓や脳へ運ばれ、残りは肝臓に流入する。ヒツジを用いた動物実験では、胎児肝血流量の増加により、Insulin-like growth factor (IGF) など、糖代謝・脂質代謝関連ホルモンの肝細胞での分泌量が増加することが報告されている。一方で、ヒト胎児において肝血流量と脂肪量の関連について検討した報告は少ない。そこで、正常単胎妊婦62例を対象とし、胎児肝血流量と新生児体脂肪率との関連について前方視的検討を行った。その結果、妊娠30週における胎児肝血流量は、新生児体脂肪量および体脂肪率と有意な正の相関を示したが、骨格筋量や出生体重とは相関を認めなかった。このことから、胎児肝血流量は、身体組成の中でも、特に体脂肪量に影響を与えることが示された (Ikenoue S et al. *Am J Obstet Gynecol* 2017)。

(3) 胎盤Corticotrophin releasing hormone (CRH) と胎児肝血流量の関連

さらに遡って、胎児肝血流量の規定因子についても検討を行った。CRHは、生理的ストレス応答により視床下部からの分泌が促進されるが、妊娠

中は胎盤からも分泌され、母体血清中に検出される。妊娠後期には胎盤からのCRH分泌量は約100倍に増加するため、妊娠後期に母体血清中に検出されるCRHは、ほぼ全てが胎盤由来(placental CRH:pCRH)とされる。また、CRHはヒト胎盤において血管拡張作用を有し、胎児期や乳幼児期における発育や肥満と関連することが報告されている。そこで、正常単胎妊婦79例について、妊娠12週、20週、30週における母体血清中のpCRHと、妊娠30週の胎児肝血流量との関連について検討を行ったところ、妊娠30週におけるpCRHが胎児肝血流量と有意に相関した。以上から、妊娠後期のpCRHが胎児肝血流量と関連することが示唆された(Ikenoue S et al. *J Clin Endocrinol Metab* 2021)。

(4) 母体インスリン抵抗性と胎児脂肪量の関連

これまでにHAPO studyにより、母体の耐糖能と新生児体脂肪率が相関することが示されているが、今回さらに、母体の耐糖能と胎児脂肪量との関連について検討を行った。単胎妊婦137例における前方視的検討において、母体インスリン抵抗性(Homeostatic Model Assessment-Insulin Resistance:HOMA-IR)と胎児脂肪量の関連について検討を行ったところ、妊娠20週および30週における母体HOMA-IRが、同時期における胎児脂肪量と有意に相関した。このことから、妊娠20週頃から、母体インスリン抵抗性が胎児脂肪量に影響を与え始めることが明らかとなった(Ikenoue S et al. *Am J Obstet Gynecol* 2023)。

(5) Gestational diabetes mellitus (GDM)における四肢容積の発育についての解析

近年、3D超音波を用いて計測した胎児四肢容積が胎児脂肪量の指標として注目されており、新生

児体脂肪率の予測に有用であることも報告されている。一方で、これまでGDMにおける胎児四肢容積の特徴に関する報告はなかった。そこで、単胎妊婦165例(GDM群:40例、正常耐糖能群:125例)について、妊娠20週から37週に胎児上腕容積および大腿容積を計測し、GDM群および正常耐糖能群における胎児四肢容積の発育について比較検討を行った。その結果、妊娠32週以降で胎児上腕容積がGDM群で有意に高値であり、胎児上腕容積がGDMにおける上肢・体幹優位の特徴的な胎児発育の早期指標になることが示唆された(Akiba Y, Ikenoue S et al. *BJOG* 2021)。

本研究の一連の結果より、妊娠後期の胎児脂肪量から新生児の体脂肪率を予測可能であり、胎児脂肪量は母体インスリン抵抗性や胎児肝血流量の影響を受けること、また胎児肝血流量は胎盤CRHと関連すること、さらに肩甲難産のリスク因子であるGDMでは、妊娠後期に胎児上腕容積が増大することが明らかとなった。今後、胎児脂肪量の規定因子をさらに解明していくことで、胎児期における脂肪蓄積機序が明らかとなれば、胎児発育への臨床的介入や治療戦略の確立が可能となりえる。またこれまでに、新生児期の体脂肪率と、小児期の体脂肪率や肥満との関連が報告されているが、それに加えて、胎児脂肪量に関連した今回の一連の研究により、肥満の起原は胎児期まで遡る可能性が示された。今後、胎児脂肪量や四肢容積、肝血流量などの新たな指標を用いて胎児発育の詳細な評価を行い、さらに出生後は小児科と連携の上で児の長期フォローアップを行っていくことで、児の周産期予後のみでなく長期予後に関連する病態の解明や、早期発症メタボリックシンドロームの一次予防へとつながる可能性がある。

学術奨励賞受賞講演

3) 予防医療への展開を見据えた卵巣癌に対するメバロン酸経路を標的とする予防薬の創出

筑波大学 小林 佑介

【研究背景】

卵巣癌に対する治療戦略は分子標的薬や抗体医薬の臨床応用とその適応拡大、がんゲノム医療や遺伝診療の普及により大きく変容しつつあり、従来の延命的治療から無増悪状態の維持、さらには発生予防へのパラダイムシフトが起きている。特に卵巣癌には遺伝性腫瘍としての側面があり、近年の遺伝性卵巣癌に関する診療の保険収載を背景に普及しつつあるリスク低減卵管卵巣摘出術と同様に、関連遺伝子病的バリエーション保持者などの卵巣癌ハイリスク集団への非侵襲的な予防薬の開発が望まれている。一方、そのような新薬開発は長期間かつ多角的な基礎研究が必要でありかつシーズから承認に至る確率も極めて低いため、国民医療費の高騰を背景に低コストでかつ確実性の高い創薬が可能となるドラッグリポジショニングによる予防薬の創出が期待されている。

【研究内容】

1. メバロン酸経路を阻害する脂質異常症治療薬スタチンによる卵巣癌細胞増殖・腫瘍進展の抑制効果

メバロン酸経路はアセチル補酵素 A からコレステロールを生合成する経路であり、TCGA データベース解析では卵巣癌症例の約 60% でメバロン酸経路関連遺伝子群の発現が上昇していた。メバロン酸経路内を阻害する各薬剤においてそれぞれ濃度依存性の細胞増殖抑制効果を認めた。さらに、同経路の上流に位置するヒドロキシメチルグルタリル補酵素 A 還元酵素を阻害する脂質異常症治療薬スタチンも卵巣癌細胞株に対し細胞増殖抑制効果を示した。動物実験でも、治療モデルとして xenograft マウスで腫瘍形成後にスタチンを

投与したところ対照群と比較し有意に腫瘍の発育を抑制した。予防モデルとして卵管癌を発症する mogp-Tag トランスジェニックマウスに対して漿液性卵管上皮内癌 (STIC) が出現するより前の 3 週齢からスタチンを 8 週齢までの 5 週間投与したところ対照群と比較し有意に腫瘍形成を抑制した。さらに、生後 6 週齢の時点で、対照群の卵管では STIC が発生していた一方で、スタチン投与群では病理組織的に STIC の発生を遅延させていた。また、スタチン投与群において投与期間中における血液検査、生化学検査結果で対照群に対して差を認めなかった。以上より、スタチンの卵巣癌細胞に対する細胞増殖・腫瘍抑制効果が投与安全性とともに確認された。さらに、卵巣癌早期病変の予防効果も確認しており、今後の卵巣癌予防医療に大きく寄与することが期待される。

2. スタチンが抗腫瘍効果を示す作用経路と作用機序

メバロン酸経路に関わる遺伝子群の siRNA による発現抑制実験および化合物を用いた add-back 実験により、タンパクのプレニル化に関わるファルネシル化及びゲラニルゲラニル化をスタチンが阻害することで抗腫瘍効果を示していた。また、マイクロアレイ解析では細胞周期を調節するクロマチン複製関連遺伝子群の発現が最も大きく変化しており、フローサイトメトリーでの検討でもスタチン投与により濃度依存性に G1 アレストが生じていた。メタボロミクス解析から特に注目されたのは、プログラム細胞死を誘導し、また抗癌薬感受性を上昇させるグルタチオンであった。ルシフェラーゼアッセイによりアポトーシスマーカーである caspase3 活性を測定するとスタチン

添加により濃度依存性に上昇していた。また、オートファジーマーカーである LC3 の発現を DsRed で標識されたプラスミドを用いて定量的に確認した実験系でも、スタチン添加培養細胞では LC3 の発現するオートファゴソームの形成が有意に増加していた。さらにスタチン添加培養細胞及びモデルマウスで形成された腫瘍でも、Caspase3/PARP-1, LC3A/3B, とともにスタチン群で有意に発現していた。薬剤感受性についても卵巣癌に対する標準治療薬であるパクリタキセルやカルボプラチンと Isobologram により算出した combination index で 1 以下を示した。以上より、スタチンはアポトーシスとオートファジーを誘導し、かつ細胞周期やエネルギー代謝に干渉することでその抗腫瘍効果を発揮していること、既存抗癌薬との相乗効果を明らかとした。また、メタボロミクス解析の結果を主成分分析で検討すると、スタチン群で TCA 回路に関与する代謝産物が増加しており、増加還元型 NADH と酸化型 NAD⁺ の比率も低下していた。糖代謝のフローからも酸化的リン酸化に関わるアセチル補酵素 A がスタチン投与により増加しており、逆に嫌氣的解糖系に関わる乳酸がスタチン投与により減少していた。以上より、スタチン投与により、がん細胞特異的なワールブルク効果から、TCA 回路が活性化され酸化的リン酸化にシフトしている可能性を明らかとした。

3. スタチンの卵巣癌奏効に関わるバイオマーカーの樹立と臨床検体での奏効実証

既存卵巣癌細胞株 11 種類のスタチン添加培養下の細胞生存率を測定すると、特に漿液性癌と明細胞癌細胞株でスタチンが奏効していた。既存卵巣癌細胞株 11 種類とヒト卵巣癌腹水由来細胞株

4 種類の合計 15 細胞株を、スタチン投与後の細胞生存率より奏効群と非奏効群に分類し、この全細胞株にマイクロアレイ解析をかけて遺伝子発現とスタチン投与による細胞生存率からピアソンの積率相関係数を算出した。その結果、VDAC1 遺伝子の発現はスタチンの奏効と正の相関を、LDLRAP1 遺伝子の発現はスタチンの奏効と負の相関を示した。スタチンの臨床検体での奏効実証を Histo-culture Drug Response Assay 法により卵巣癌 20 症例での増殖抑制率から検討すると、スタチンはパクリタキセルやカルボプラチンと比較しても同等の増殖抑制率を示している症例も認め、特に漿液性癌症例と明細胞癌症例に奏効していた。以上より、スタチンは臨床検体においても卵巣癌増殖抑制効果を示し、特に組織型として漿液性癌と明細胞癌に対しての効果が期待され、VDAC1 および LDLRAP1 遺伝子発現はスタチン奏効の予測マーカーとなることを明らかとした。

【結語】

本研究では卵巣癌に対する脂質異常症治療薬スタチンの抗腫瘍効果の作用機序と作用経路を明らかとし、奏効予測バイオマーカーを樹立し、臨床検体での奏効も実証したことでスタチンが卵巣癌予防薬となり得る可能性を提唱した。本研究成果を踏まえて現在準備中の臨床試験では、樹立したバイオマーカー VDAC1 や LDLRAP1 によるコンパニオン診断でスタチン製剤の奏効を期待できる症例を絞り込み、動物実験で STIC の発生を予防的に抑制していたことから卵巣癌ハイリスク症例に対する予防薬としての有用性を検証する予定であり、今後の臨床への還元が期待される。

学術奨励賞受賞講演

4) ライフコースアプローチとして女性ホルモン分泌機構を維持/制御する多
角的研究

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女性のライフコースにおいて子宮内膜症、多嚢胞性卵巣症候群 (PCOS)、早発卵巣不全 (POI)、更年期障害は主要な健康課題である。各病態は異なるが、月経随伴症状やホルモン分泌異常により女性の Quality of life (QOL) を著しく低下させる。外因性ホルモン製剤投与が治療の中心となるが、副作用や使用禁忌症例、排卵抑制等の問題点もある。これらの解決をめざし、内因性ホルモン分泌機構の維持/制御を主軸とし下記検討を行った。

1. 卵巣機能維持と両立する子宮内膜症治療

子宮内膜症の治療の要はホルモン療法であるが、施行中病変が増大する症例や疼痛が継続する症例もある。また、ホルモン療法は排卵を抑制するため、現在の挙児希望とは両立できずその間病状は悪化する。一方卵巣子宮内膜症性嚢胞 (OE) 摘出術は、卵巣予備能を低下させるというジレンマがあり、卵巣機能への影響を最小限にする治療方法が望まれている。OE 摘出術後に血清 anti-Müllerian hormone (AMH) 値が低下する例と低下しない例があるという検討結果より、周術期のホルモン療法の相違と、術後の AMH 値維持の差異を検討するランダム化比較試験を行った。結果、OE 摘出術前後にジェノゲストを投与した群では、GnRH アンタゴニストを投与した群に比し、術後1年時の血清 AMH 値維持率が良好であること、さらに、ジェノゲスト投与群で血清 IL-6 低下症例が有意に多いことを見出した。周術期におけるホルモン療法の相違が、術後の卵巣予備能維持に影響する可能性が示された。さらに、排卵機能と両立できる子宮内膜症治療法開発をめざし、子宮内膜症の発生要因ならびに非ホルモン性治療に関する基礎的検討を行った。子宮内膜症患者由来

細胞/組織、既存データベースを活用し、子宮内膜症の発生に子宮内膜間質細胞の筋繊維芽細胞への表現型変化が寄与すること、さらにこの表現型変化に子宮内膜への細菌 (フソバクテリウム) 感染が関与することを見出した。逆流説に基づく腹膜病変モデルマウスを用いた検討では、逆流前の子宮内膜に相当するドナーマウス内膜への感染後の抗生剤治療により、成立する内膜症病変数の減少、ならびに成立病変の縮小を確認した。他方、すでに成立した OE に対する非ホルモン性治療法を検討するため、OE モデルマウスを作成、治療ターゲットとして、手術で摘出したヒト OE 組織ならびにマウスモデルの病変部においてインフラマソーム構成分子である NLRP3 発現増強を見出し、モデル動物への NLRP3 阻害薬投与により病変縮小効果ならびに、卵胞数減少の抑制効果を確認した。

2. 若年女性において介入すべき月経異常 (PCOS, POI) の早期診断

若年時からの性ステロイドホルモン分泌異常は、自覚症状として月経周期異常を呈するが、症状があっても受診行動に繋がらず放置されることが多い。若年から病態が開始している PCOS や POI を早期に発見することは、長期間の女性ヘルスケア管理において重要であるといえる。一方で、若年者では正常例でも卵巣の多嚢胞所見を示すことや、高アンドロジェンの指標となるにきび等は多くの思春期女性で見られることが、PCOS の診断を困難としている。また POI は、病態が進行する前の段階でハイリスク例を抽出することは難しく、早期診断に資するマーカーが望まれる。若年女性において、これら疾患の早期スクリーニング

における血清 AMH 値測定役割を検討した。システマティックレビューでは、若年女性の PCOS 補助診断に血清 AMH 値測定が役立つことが示された。実際に女子大学生 528 人の調査により、月経不順の自覚がある例では、AMH 値と LH 値 ($r=0.542$, $p<0.001$) ならびに LH/FSH 値 ($r=0.584$, $p<0.001$) に相関を認めること、さらに血清 AMH 値の PCOS 診断予測カットオフ値 5.30ng/ml (AUC 0.79, 感度 80.0%, 特異度 69.4%) を示した。一方、AMH 値が 1.1ng/ml 以下の卵巣予備能低下例も一定数 (15 人, 2.8%) 存在した。POI では、AMH 値低下後にはすでに病態は進行している。早期診断マーカーにより卵巣予備能低下前に抽出し、妊孕性温存やライフプランの検討を行えることが望ましい。POI 患者は甲状腺自己抗体に代表される既存の自己抗体陽性例が多い一方で、既存自己抗体の有無と AMH 値との相関は認めないという知見を基に、卵巣に対する新規自己抗体検索と POI 診断マーカーとしての検討を行った。POI 患者血清と顆粒膜細胞由来タンパクとの免疫沈降検体のプロテオーム解析により、自己抗体の抗原候補タンパクとして POTEF タンパクを同定した。また、同タンパクの精製を行い、これを抗原とした血清中自己抗体の測定系を開発。POI 患者では正常月経周期を有する女性に比し抗体価が有意に高値であることを確認した。

3. 多能性幹細胞を用いた生殖内分泌中枢の *in vitro* モデル作成による PCOS, 更年期障害の治療開発基盤研究

女性の生殖内分泌機構である視床下部-下垂体-卵巣軸は視床下部キスペプチンニューロンを介したフィードバック機構により制御される。主に動物実験の知見より、ネガティブフィードバックを中継するキスペプチンニューロンは、ニューロキニン B (NKB), ダイノルフィンを共発現し, KNDy

ニューロンと呼ばれ、卵胞発育を担う GnRH/LH パルス状分泌を制御する。同ニューロンについて、更年期におけるホットフラッシュ等の血管運動神経症状や PCOS への関与が指摘されている。後者の検討として血清 LH 値上昇を呈する PCOS ラットモデルを作成、同モデルにおいて KNDy ニューロンが存在する視床下部弓状核におけるキスペプチンならびに、NKB 陽性細胞の増加を示した。ヒトにおける同様の解析は不可能である上に、ヒトキスペプチンニューロンの *in vitro* モデルは存在せず、病態研究や治療薬開発を困難としている。この問題の解決をめざし、ES/iPS 細胞から、立体培養により視床下部・下垂体オルガノイド作成する SFEBq (serum-free floating culture of embryoid-like aggregates with quick reaggregation) 法とその応用により、キスペプチンニューロンの分化誘導を行った。まずより短期間での検証が可能なマウス ES 細胞を用いた誘導法開発を開始、視床下部の分化誘導法の既報を基に腹側化シグナルを強化し、KNDy ニューロンが存在する弓状核への分化を確認、さらに Notch signaling の阻害ならびにその後の平面分散培養により、キスペプチン, NKB, ダイノルフィンを共発現するニューロンの分化誘導に成功した。現在はヒト ES 細胞を用いた分化誘導法の検討を開始、培養法の改良により少数のキスペプチン陽性細胞を確認しており、より効率的な分化誘導法開発に取り組んでいる。

【まとめ】

これらの研究成果は、女性の QOL に関わる各疾患の早期診断・予防ならびに、新規治療開発に寄与しうる。卵巣機能維持と両立する治療や、最上位中枢からのホルモン分泌調整はより生理的であり、多様化するニーズに応え、女性のウェルビーイング実現への寄与が期待される。

J-CIMELS ワークショップ

ディレクター・ミーティング～各地での J-MELS 継続開催の取り組み～

日本母体救命普及協議会の運営するシミュレーションコース (J-MELS) は、分娩の安全性を更に高めるため、そして妊産婦死亡を更に減少させる取り組みとして 2015 年に活動がスタートした。地域ごとに定期的に J-MELS を開催するディレクター、インストラクターの皆様のご尽力もあって、ベーシックコースの受講者はのべ2万人を超えている。本コースは、産婦人科医師のみでなく、救急医、麻酔科医、メディカルスタッフ等との協働を目的とした実践教育、最新の知見に基づいた救命処置を基本にしているため、実際の産科医療に関わる臨床現場においても、関連各科、スタッフとのコラボレーションの醸成に役立っている。コロナ禍も収束し、再び地域ごとに J-MELS の再開

がみられ、発足からもうすぐ10年となるころでもあり、現状の問題点を踏まえたエビデンスに基づいた質の担保された J-MELS が全国で継続的に開催されることが望ましい。本ワークショップでは、各地域で積極的に活躍されている J-MELS のディレクターに、それぞれの問題点と改善点、工夫などをご講演いただき、総合討論として当日参加された全国のディレクターやインストラクターとディスカッションすることを目的とする。全国のディレクター同士の交歓、情報共有をしながら J-CIMELS のアップデートを目指したいと考えている。多くのディレクター、インストラクターの現地参加を期待する。

FIGO President Lecture

Walk hand-in-hand into the expansive future of obstetrics and gynaecology : twinning for development

Kihara Anne-Beatrice¹⁾²⁾³⁾⁴⁾*International Federation of Gynaecologists and Obstetricians (FIGO)¹⁾,**University of Nairobi, Kenya²⁾,**African Federation of Obstetricians and Gynaecologists (AFOG)³⁾,**Kenya Obstetrical and Gynaecological Society (KOGS)⁴⁾***Introduction**

Women and children dyad provide the kaleidoscope of society and nations situation. A review of key performance indicators informing us about maternal health and the ultimate quality of the progeny that carries on into next generations. Globalization has created lessons and revealed challenges : wars / conflict, scarcity of natural resources, a changing landscape for trade and economics, population demographics and dynamics, climate change-food insecurity and malnourishment, environmental pollutants and toxins and weak health systems. Admissions for a multidisciplinary, sector wide, fit-for-purpose obstetrics and gynaecologist will also need our nations twinning to harness health care into as an impactful investment.

Methodology

Scoping literature review that compared Kenya as an example of LMC in SSA and Japan's health landscape looked primarily in Obstetrics and Gynaecology. This was conducted reviewing the international data sets available from WHO, World bank, UNICEF, local demographic health surveys, FP2030, human development and multi-dimensional poverty. Crystalizing from the mapping of advancements in obstetrics and gynaecol-

ogy to addressing the future for a twinned Japan and LMIC.

Results

Comparative analysis of maternal mortality, contraceptive prevalence rate, adolescent fertility rate, human development and multidimensional poverty index done. This reviewed against the obstetric transition model on direct causes of maternal and perinatal morbidity and mortality ; quality of care (KAIZEN model) ; and impactful investment with both social and venture entrepreneurship for development.

Disruption towards universality of healthcare with no one left behind. We must interrogate our valuing of humanity, gender inequality, health inequities with a paradigm shift in public and private sector. Preventive strategies amongst populace employing beneficial practices, art and culture in communities. Examples locally, the calisthenics and Yosakoi dance and green-asia taking centre stage. Evidence embracing diverse group of stakeholders and experts, sector-wide and inclusive of government, academia, civil society. Exemplified in initiatives such as : iFEED, JIR-CAS, SIIF moving effectively from bottom up with communities meaningfully engaged ; making normative adjustments ; innovations and

technologies informed by data driven locally and expanding globally in health, environment, development and with impact investments.

Conclusion

Where is our leadership obstetricians and gynaecologist (FIGO members) yet we address women and perinatal health daily? We must enter politics, economics, take on a societal approach in health delivery, conduct more research, setting up of learning/ development hubs ; and twinning collaboratively with LMIC. Our expertise, divergent exposures, volunteerism, cooperate social responsibility, service above self-placed in a Quanat system to ultimately make a sustainable global difference. Lastly, professional women for women let us break our silence as academia, researchers, mothers and core home-makers surmounting our challenges of gender to make an indelible difference.

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ACOG President Lecture

The Obstetrician-Gynecologist as Leader in The Changing Environment of Women's Healthcare

Hicks Verda

American College of Obstetricians and Gynecologists (ACOG)

As defined by the Oxford dictionary, leadership is the action of leading a group of people or an organization. You may look at this definition and think of a leader as a general, a president, or a business leader. You probably did not think of a leader as YOU!

All obstetrician-gynecologists are leaders of educational teams, patient care teams, advocacy teams. Our patients look to us as leaders for women's health care. No matter where we are in our career path, we are LEADERS.

Unlike all of the evidence based science that we rely on to care for our patients every day, we

do not have a standard curriculum for leadership in our medical training. However, there are evidence-based-guidelines for leadership. We will explore some examples of leadership guidelines.

In conclusion, obstetricians and gynecologists lead everyday in their practices, their families, and their communities. My challenge to each of us is to find an area of Obstetric and Gynecologic practice to lead from where you are in education, research, patient care, advocacy, business, mental health-wellness, or Leadership!

International Symposium 1 **P** : Reproductive medicine

1) Molecular roadmap to embryo implantation

Wang Haibin

Xiamen University, China

Embryo implantation is a critical event during mammal reproduction, which occurred in the uteri and set up both the physical and physiological interaction between the embryo and the uterus for the first time. Successful embryo implantation requires the uterus entering into a receptive state and the blastocyst acquiring the implantation competency. The uterus is just receptive for the embryo in a limited time, called the implantation window, which is mainly under the dominance of steroid hormone estrogen and progesterone. Both the pharmacological and genetic evidence have demonstrated the indispensable role of E2-ER and P4-PR signaling for the establishment of uterine receptivity. However, the molecular diagram for the intra-cellular signal transduction remains unclear. Our recent re-

searches, combined both the genetic mouse model and biochemical approach, revealed that both the expression level and transcriptional activity of hormone receptors are accurately regulated by multiple interactors. Their transcriptional activity is modulated by post-translational modification, such as phosphorylation and ubiquitination, which is regulated through Shp2 and Bmi1. For the protein stability, we uncover that both P38 α and SOX4 knockout would lead to dramatic down-regulation of PR protein in stromal cells, which derails normal uterine receptivity both in mouse and human. In brief, the multiple regulation manners for estrogen and progesterone receptors activity are involved in the establishment of uterine receptivity.

International Symposium 1 **P** : Reproductive medicine

2) Modulating the Aging Ovarian Microenvironment to Improve Reproductive Longevity

Duncan Francesca E.

Feinberg School of Medicine, Northwestern University, USA

The female reproductive system is the first to age in the human body with fertility declining in women in their mid-30s and reproductive function ceasing completely at menopause. In the ovary, reproductive aging is characterized by a decline in both egg quantity and quality which can contribute to infertility, miscarriages, obstetrical complications, and birth defects. Reproductive aging also goes beyond fertility because, as eggs develop within follicles in the ovary, they produce estrogen which regulates bone, cardiovascular, immune, cognitive, and sexual health. The decline in estrogen associated with menopause can have broad impacts on overall health. Thus, there is a need to understand the mechanisms that underlie ovarian aging. We previously reported that the aging ovary assumes a fibro-inflammatory milieu which is associated with increased ovarian stiffness due to collagen I/III accumulation in the ovarian stroma. Therefore, we evaluated whether the systemic delivery of an anti-fibrotic drug (Pirfenidone) has a therapeutic effect on ovarian aging in mice. We first assessed the toxicity and function of Pirfenidone in vitro. Ovaries from 7- and 14-month (N=5/age) old CD 1 mice were isolated and incubated in increasing doses of Pirfenidone or DMSO control for 24h. Then, the explants were collected and tissue architecture, collagen content, and cell death were analyzed. Pirfenidone-treated ovaries did not show signs of toxicity compared to controls.

Next, we tested the ability of this drug to decrease the expression of fibrotic genes in primary ovarian stromal cells. Pirfenidone treatment significantly reduced the expression of collagen 1a1. Given this successful proof-of-concept, we extended studies to an in vivo model in which Pirfenidone was delivered systemically in mice for 6-weeks via mini-osmotic pumps starting at 7-months of age when fibrotic foci are first observed in the ovary. Parameters of reproductive longevity and overall health were assessed in mice in each experimental cohort (control vs Pirfenidone, N=5/cohort) immediately following treatment and 3.5-months post-treatment. Additionally, the ovaries were isolated for histological and RNAseq analysis. Immediately after treatment there were no differences in weight, estrous cycle, hormone levels, and bone mass density between cohorts. H&E-stained ovaries showed a very similar morphology. These results indicate a lack of deleterious side effects immediately following treatment. By 3.5-months post-treatment, mice in the control group showed a reduction in estrous cyclicity with only 40% exhibiting normal cyclicity as expected given their advanced age. In contrast, this reduction was not observed in the Pirfenidone-treated mice (80% had normal cycles). Additionally, Pirfenidone-treated mice did not exhibit an age-associated decline in weight or a reduction in anti-Mullerian Hormone or progesterone levels. Moreover, ova-

ries from Pirfenidone-treated mice showed improved tissue architecture, a greater number of corpora lutea indicative of sustained ovulation, and a more moderate accumulation of collagen with age relative to control mice. Finally, RNAseq analysis revealed that Pirfenidone-treated mice exhibit a decreased expression of

inflammatory genes compared to control ovaries. Overall, these results demonstrate that low-dose anti-fibrotic drugs administered when ovarian fibrosis is first observed may confer beneficial effects on reproductive longevity and healthspan in mice. Methods to translate these findings clinically are ongoing.

International Symposium 1 **P** : Reproductive medicine

3) Noncanonical genome imprinting : A new face of intergenerationally heritable epigenome

Inoue Azusa

RIKEN

Genomic imprinting regulates parental origin-dependent mono-allelic gene expression. It is established during gametogenesis and inherited by embryos. Although it has been long thought that imprinting is controlled by DNA methylation, our recent works have shown that an oocyte-derived histone modification, H3K27me3, can mediate imprinting in a germline DNA methylation-independent manner. DNA methylation- and H3K27me3-mediated imprinting are now referred to as “canonical” and “noncanonical” imprinting, respectively. Noncanonical imprinting is estab-

lishedduring oocyte growth by Polycomb repressive complexes, and maintained through preimplantation and extraembryonic development. Studies of noncanonical imprinting have facilitated our understanding of chromatin regulation in oocytes and early embryos, imprinted X chromosome inactivation (XCI), secondary differentially DNA methylation, and developmental abnormalities in cloned mice. In this talk, I will introduce the regulatory mechanisms and functions of noncanonical imprinting.

International Symposium 1 **P** : Reproductive medicine4) Decoding Human Ovarian Ageing : Genetic Insights into Premature
Ovarian Insufficiency

Chen Zi-Jiang

Shandong University, China

Ovarian ageing is one of the earliest manifestations of female ageing. Premature ovarian ageing can increase the risk of age-related diseases such as osteoporosis, cardiovascular diseases, and neurodegenerative diseases. Therefore, deciphering the mechanisms underlying ovarian ageing is crucial for the management of women's long-term health. Premature ovarian insufficiency (POI) is a common ovarian ageing disorder. The etiologies of POI are highly heterogeneous, and it can be caused by spontaneous genetic defects or induced by autoimmune diseases, infections, or iatrogenic factors. Yet a large proportion of POI cases are idiopathic, with multiple lines of evidence supporting a genetic basis for pathogenesis. In recent years, the widespread use of whole

exome sequencing (WES) expanded our understanding of the pathogenesis of POI. While, the limited sample sizes and inadequate controls, as well as the genetic heterogeneity of POI, have prevented establishment of statistically robust single-gene associations and identification of novel causative genes. Recently, we performed a WES study in the POI cohort with 1,030 cases and depicted the genetic landscape of this disease, which will promote the development of early warning and treatment of POI. Further genetic studies of individuals with differences in ovarian function, such as decreased ovarian reserve, early menopause, and POI, may aid in understanding the common genetic factors in ovarian ageing.

International Symposium 1 **P** : Reproductive medicine

5) Freeze-all Embryos in All IVF Cycles : Pros and Cons

Tarlatzis Basil C.

Aristotle University of Thessaloniki, Greece

Ovarian stimulation represents an important part of the IVF procedure. However, the development of multiple follicles leads to abnormal estradiol (E_2) and progesterone (P) secretion, which may induce abnormal endometrial development in the early luteal phase and adversely affect the probability of embryo implantation. Thus, it has been hypothesized that freezing all embryos in a fresh IVF cycle and deferring embryo transfer in subsequent cycles may provide a more physiological endometrial milieu for embryo implantation when compared to fresh embryo transfer (ET). Additional reasons for utilising this approach include high risk for severe OHSS, premature progesterone elevation in the follicular phase, suboptimal endometrial development, endometrial pathology and PGT-A.

The rapidly increasing use of this strategy, stimulated studies to evaluate the effectiveness of frozen-thawed ET (FET) using a freeze-all policy compared to fresh ET either in high or in normal responder patients. The available evidence from randomized controlled trials (RCTs) and systematic reviews and meta-analyses indicate that overall live birth rates (LBR) were significantly higher after FET as compared to fresh ET. However, sub-group analysis showed that this difference was mainly attributed to hyperresponders, in whom the LBR after FET was sig-

nificantly higher than after fresh ET, while in normo-responders there was no difference. In both cases, the risk of moderate/severe OHSS was significantly lower in the FET cycles than in the fresh ET ones. Nevertheless, FET pregnancies were associated with a significantly higher incidence of pre-eclampsia/PIH and of higher birth weight/macrosomic embryos, as compared to fresh ET. These complications have been attributed to defective decidualization and placentation, probably due to the lack of corpus luteum and the use of hormonal (E_2 and P) preparation of the endometrium. Recent studies have confirmed that FET in the natural cycle is associated with a significant reduction in the incidence of these pregnancy complications.

In conclusion, the freeze-all strategy with subsequent FET, compared to fresh ET, is at least as efficient in terms of LBR in the normo-responders and more efficient in the hyperresponders, with significantly lower risk for OHSS in both groups. Nevertheless, pregnancies after FET in an artificial (E_2 and P) cycle have been associated with a higher risk for pre-eclampsia/PIH and for higher birth weight/macrosomia, as compared to fresh ET, which can be prevented by performing FET in the natural instead of the artificial cycle.

International Symposium 1  : Reproductive medicine

6) Polycystic Ovarian Syndrome (PCOS) —A human model for reproductive longevity?

Huang Zhongwei

NUS Bia Echo Asia Centre for Reproductive Longevity and Equality (ACRLE), National University Health Systems, Singapore/OGSS

Background and Aims : Polycystic ovarian syndrome (PCOS) afflicts 4-20% of all women at reproductive age and is a common cause of infertility. Elevated anti-Mullerian hormone levels (AMH), a clinical marker for ovarian reserve, are routinely associated with PCOS, however, an exact cut-off value has remained elusive. Interestingly, observational studies reported that women with PCOS have purported higher ovarian reserves, implied from higher AMH levels, and later age of menopause delayed by 2 years when compared to women without PCOS. Our study focuses on the Asian population, a demographic frequently under-represented in cohort studies. We posit that our results will bridge the gap in the collective understanding of PCOS and how age and lifestyle affects ovarian reserves in Asian women as well as their reproductive outcomes through Assisted Reproductive Technologies (ART).

Method : A large retrospective study was conducted at a tertiary-care hospital in Singapore from 2016-2020. AMH and clinical demographics from 3,739 Asian women aged 21-53 years were collected. Wilcoxon Rank Sum was used to analyze the data and significance was established if $p < 0.05$. Logistic regression and ROC were generated in R.

Results : AMH (aOR=1.07), age (aOR=0.89) and BMI (aOR=1.12) were significantly associated

with PCOS ($p < 0.001$) in Asian women. AMH declined with age but the decline in the PCOS group was less severe, women in their 40s retaining 80% of AMH levels at a younger age, as compared to controls which retained only 40% of AMH levels at a younger age. Higher BMI > 25 and smoking were associated with lower AMH levels. An ethnic stratification revealed that average AMH levels of Malay women with PCOS were lower than Chinese and Indian women in each age group. The constructed model incorporating all variables had an ROC AUC=0.89. There was also stratification of ART conception outcomes where women with PCOS seek fertility help at a younger age and the chances of conception with advancing age do not depreciate compared to control.

Conclusion : This study highlights the importance of improving the resolution of PCOS diagnosis through AMH profiling, especially in Asian populations. The results from this study suggest potential beneficial effects of lifestyle modifications such as maintaining a healthy BMI and stopping smoking, especially in Asian women with PCOS. Successful conception rate amongst PCOS women with advancing age also suggested the interesting ovarian milieu in these women which can be a human model to better understand reproductive longevity in women.

International Symposium 1  : Reproductive medicine

7) For high responders, mild or conventional stimulation, should we individualize considering general cases, PGT, oocyte cryopreservation, and oocyte donors

Chen Shee-Uan

National Taiwan University Hospital, Taiwan/TAOG

How to perform controlled ovarian stimulation for high responders in IVF is debatable. Mild stimulation uses smaller amount of gonadotrophin and/or oral compound with an aim of limited number of oocytes retrieved. Conventional stimulation apply more gonadotropin dose for obtaining more oocytes, and the pregnancy rates may be improved. Despite the benefits of less pain, less ovarian hyperstimulation syndrome (OHSS) and lower treatment cost, mild stimulation has not achieved overall acceptance, primarily due to the concerns of its lower clinical outcome. Systematic reviews have controversial results regarding clinical and cost effectiveness between these two kinds of stimulation. The GnRH agonist trigger in high responders (antagonist protocol or progestin-primed ovarian stimulation, PPOS) and freezing-all significantly reduce OHSS and achieve high cumulative pregnancy rate. One-and-done strategy has been proposed for completing a family with more than one live births at one cycle of oocyte retrieval. In Taiwan, conventional stimulation is commonly used for high responders instead of mild stimulation. We performed a retrospective analysis and found that the cumulative ongoing pregnancy rate between PPOS and conventional antagonist protocol in high responders does not show statistical significance. PPOS has the benefits of less injections and lower costs. Both of two protocols are

suitable for GnRH agonist trigger to prevent OHSS. However, GnRH agonist trigger may result in an inadequate oocyte yield in a small subset of patients. This failure can range from empty follicle syndrome (EFS) to the retrieval of much fewer oocytes than expected. Dual trigger using GnRH agonist and hCG may overcome the suboptimal response. However, routine dual trigger with addition of hCG may increase the risk of OHSS. LH at the start of ovarian stimulation is a better predictor of the GnRH agonist trigger efficacy than the LH levels on the day of trigger. Patients with low post-trigger serum LH level of <15 IU/l and progesterone levels of <3.0 ng/ml had risk of EFS or lower oocyte yield. We should consider retriggering with hCG and retrieve oocytes at 36 hours after retrigger. Patients treated by the oral contraceptives have risk of suboptimal response to GnRH agonist trigger. High BMI may also be risky of suboptimal response. A basal LH or maximum LH level less than 2.2 is suggested to be a useful predictor of a suboptimal response to GnRH agonist trigger. If dual trigger, hCG dosage should be considered to minimize possibility of OHSS. Before starting the treatments, we may discuss with patients for selecting mild or conventional stimulation regarding the advantages and disadvantages of these two methods. The clinical and cost effectiveness of one-and-done strategy is particularly benefi-

cial in high responders for more than one live donation.
births, PGT, oocyte cryopreservation, and oocyte

International Symposium 2  : Obstetrics

1) How to ensure Equality and Diversity in Research—the OBS UK Methodology for Site Recruitment

Parry-Smith William¹⁾, Elsmore Amy¹⁾, Bell Sarah²⁾*Keele University, UK¹⁾,**Cardiff and Vale UHB, UK²⁾***Introduction**

Obstetric Bleeding Study UK (Obs UK) is a National Institute for Health and Care Research (NIHR) funded stepped wedge cluster randomised controlled trial of a complex intervention for postpartum haemorrhage. This was developed in Wales as a feasibility study, with improvements in maternal outcomes observed. Generalisability of the findings is limited by lack of control data and limited diversity in the population. Obstetric units in Wales are unrepresentative of diversity in the UK, 94% of the Welsh population identifies as white, vs 81% in the UK. Non-white ethnicity and socioeconomic deprivation are linked to increased risk of adverse maternal outcomes.

To investigate the effect of ethnicity and social deprivation on outcomes, we aim to recruit maternity units that represent the ethnic diversity and social deprivation of the UK. This will ensure widespread applicability of the results.

Method

Using routinely collected data we have developed an interactive map that demonstrates the demographics of the population served by each maternity unit in the UK, to inform site recruitment. Data on births/year, ethnic and socioeconomic group of the population for each maternity unit, across the UK were integrated into the map.

Results

The map demonstrates how our sites reflect

the ethnic and socioeconomic diversity of the UK (study vs UK population : White 79.2% vs 81.7%, Asian 10.5% vs 9.3%, Black 4.7 & vs 4%). We ensured variation in site demography, size, and location. Missing data varied across sites & nations and is presented.

Conclusion

Traditionally, decisions regarding site selection are based on desire to complete trials on target, in 'tried and tested' research active institutions. The NIHR equality, diversity, and inclusion strategy states studies must widen participation, facilitating individuals from all backgrounds to engage. The development of this novel interactive map demonstrates an innovative way of achieving this. Future maternity researchers should consider using this to ensure inclusivity and establish results that are clinically relevant and applicable to their geography and populations.

Map and study website : <https://www.obsuk.org/>

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International Symposium 2 **P** : Obstetrics

2) Pregnancy and risks for psychiatric disorders

Kano Shinichi

Heersink School of Medicine, University of Alabama at Birmingham, USA

Pregnancy is a physiological process yet a considerably challenging period for women and babies. Accordingly, women undergoing pregnancy and delivery show worsening of the existing psychiatric disorders, such as schizophrenia and depression, and the onset of new psychiatric disorders, such as postpartum depression. Pre- and peri-natal exposures of children to maternal physical and psychological stress also result in long-lasting alterations of brain development, increasing the risks of neurodevelopmental disorders, such as autism spectrum disorders, and adult-onset psychiatric disorders, such as schizophrenia. Although the links between pregnancy

and psychiatric disorders are well acknowledged, our understanding of physiological and pathological biological mechanisms is still limited. Recent basic biology research has integrated neurobiology, immunology, and endocrinology to provide comprehensive pathobiological mechanisms for pregnancy-related psychiatric disorders. In this talk, I will give an overview of our current understanding of pregnancy-related psychiatric disorders, including several recent topics in the field, and discuss the future perspectives at the interface between obstetrics and psychiatry.

International Symposium 2  : Obstetrics

3) Pravastatin to treat placental vascular dysfunction and prevent adverse pregnancy and neonatal outcomes in rodents and women

Girardi Guillermina

University of Edinburgh, UK

Placental dysfunction is the underlying cause of diverse pregnancy complications, including spontaneous abortions, intrauterine growth restriction, preeclampsia (PE) and obstetric antiphospholipid (aPL) syndrome.

Mouse model have helped the identification of the mediators of placental vascular malperfusion (PVM) and targets for therapy. Using ¹¹¹In-labelled aPL antibodies, SPECT/CT, nanotechnology and MRI we demonstrated the *in vivo* binding of aPL to the placenta was associated with complement deposition. Tissue factor was identified as an important link in the crosstalk between inflammation and thrombosis in several obstetric complications. Statins diminish inflammation and oxidative stress, increase angiogenesis, inhibit the coagulation cascade, and protect the endothelium supporting their use in PVM treatment. Pravastatin improved placental blood flow and prevented recurrent miscarriages and preeclampsia in several animal models worldwide.

Animal studies from our Lab also demonstrated that pravastatin also prevented long term cardiovascular complications in both mothers and offspring. Moreover, pravastatin given during a preeclamptic pregnancy prevented microglia activation in the brains and less anxiety and improved spatial learning and memory was observed in the offspring. Pravastatin also reversed an imbalance in chemical mediators in-

involved in placental function and neuroprotection in OAPS-mice.

Based on these promising preclinical studies and the multiple evidence supporting the safety of pravastatin in pregnant women, several translational studies were conducted to test the efficacy of pravastatin in treating PVM. Addition of pravastatin to standard of care LDA+LMWH increased placental blood flow and improved PE features early after pravastatin treatment. OAPS-patients treated with Pravastatin+LDA+LMWH had full term live births in all patients and all infants are currently healthy.

In another study from our group, pravastatin+L-arginine given at 20weeks improved uteroplacental vascular function, increased fetal growth and prolonged pregnancies preventing neonatal complications. Pravastatin+L-arginine also improved umbilical artery blood flow and neonatal outcomes in dichorionic twin pregnancies through a nitric oxide-dependent vasorelaxant effect.

A pilot study in Australia, suggested that pravastatin can stabilize clinical and biochemical features of preterm preeclampsia. Another pilot study in the USA reported safety of pravastatin during pregnancy and improved obstetrical outcomes in women at high risk of preeclampsia.

A recent meta-analysis showed that pravastatin prolonged pregnancy duration and improved obstetrical outcomes in cohort studies of 1,391

women with uteroplacental insufficiency disorders. Another meta-analysis (1570 women) treated with pravastatin prior to 20 weeks of gestation showed that pravastatin reduced the incidence of preeclampsia by 61%, premature birth by 45%, IUGR by 45% and NICU admission by 77%.

After these successful observational studies,

several RCTs have been organized to test the effects of pravastatin in preventing/treating PE.

Preclinical and pilot studies suggest that treating uteroplacental vascular dysfunction with pravastatin might be a successful strategy to prevent the associated adverse maternal and fetal outcomes. The ongoing RCT are instrumental to the validation of these observations.

International Symposium 2  : Obstetrics

4) The Art and Craft of breech delivery

Louwen Frank

Goethe University & University Hospital, Germany/EBCOG

Even with a policy that strictly defines cesarean section as the preferred mode of delivery for breech at term, vaginal breech deliveries cannot be prevented. Existing studies on complications and risks of breech delivery have so far focused less on the causes of perinatal morbidity and mortality. The results of the FRABAT cohort

with more than 2000 intended vaginal breech births and the possibilities of using skills training to ensure the safety of vaginal birth are evaluated. The FIGO/WATOG skills as part of the “teach the breech” programme are explained in detail.

International Symposium 2 **P** : Obstetrics

5) Prevention of Obstetric Anal Sphincter Injuries

Thakar Ranee

Royal College of Obstetricians and Gynaecologists, UK/RCOG

An obstetric anal sphincter injury (OASI) is any injury to the anal sphincter muscle during childbirth. It can result in medical complications such as faecal incontinence and significant psychosocial problems, as well as long-term financial consequences for the NHS associated with ongoing treatment. There is no single cause of OASI. It is not necessarily the result of poor-quality care, rather it is influenced by a range of factors including advanced maternal age at first birth, larger maternal body mass index and birth weight of the baby, and instrumental delivery. However, as OASI can have a dramatic impact on the short and long-term health of women, influencing decisions about future births, prevention and management of OASI is a priority.

Population-based studies from Scandinavian countries, Australia and England have identified an increase in the occurrence of OASI. One possible reason for this increase is better detection and reporting, but it may also be due to inconsistencies in training, skills and prevention protocols, lack of awareness of risk factors and the

long-term impact of OASI, and variation in practice among health care professionals. In light of these trends, the Royal College of Obstetricians and Gynaecologists (RCOG), and the Royal College of Midwives (RCM) have developed a care bundle to standardise prevention practice. The introduction of this care bundle has led to a 20% decrease in OASI rates.

There are obstetric practices which have been shown to influence reduction in OASI rates. Episiotomy should only be performed when indicated, and a mediolateral episiotomy at 60 degrees angle is preferable to a midline episiotomy. Fewer women with vacuum delivery have anal sphincter trauma compared to forceps delivery. The use of warm compresses on the perineum is associated with a decreased occurrence of OASIS. There is now overwhelming evidence from Scandinavian literature that manual perineal protection during the second stage of labour can reduce OASI by almost 50%. Evidence base for each of these interventions will be discussed.

International Symposium 2 **P** : Obstetrics

6) Conservative Management of Placenta Acreta Spectrum

Kumar Aswath

*Jubilee Mission Medical College & RI Thrissur, India***Introduction**

Placenta accreta spectrum, formerly known as morbidly adherent placenta, refers to the range of pathologic adherence of the placenta, including placenta increta, accreta, and per creta. Rates of maternal death are increased for women with placenta accreta spectrum and are more likely to require hysterectomy at the time of delivery or during the postpartum period.

Aims & Objective :

A series of cases of conservatively managed cases of placenta accreta and per creta.

Primary objective was in conserving the uterus and fertility.

Material & Methods :

Total of 10 cases of PAS were surgically managed in a conservative manner. The method adopted was to preoperatively perform a good sonological assessment of the placenta and its extension and in cases if required by a MRI. During the surgery an incision is made above the adherent part of placenta and baby is delivered out swiftly. Following which depending on the extension and inflow blood channels devascularisation is done either with bilateral internal iliac ligation or with addition of common iliac artery clamp. With these methods the vascularity is reduced and then the placenta is swept out from its extension to bladder and the adherent part is excised along with the uterine wall and removed.

The remaining uterus is reconstructed by suturing the 2 edges, with good approximation and integrity.

Results :

All 10 cases in which the attempt was made were successful in preserving a functional uterus at the end of surgery and, hence retaining future fertility. Bleeding was very low in comparison to traditional methods and these cases required minimal transfusion of blood products. One of the cases managed in 2 laparotomy procedures as to deliver the baby out, a 1-week interval for regression and reduction of vascularity followed by relaparotomy for definitive management.

Conclusion :

This conservative technique with/out modifications can completely change the outlook of PAS management. A lower segment transverse incision over the uterus instead of the classical CS or trans fundal incision in case of Triple P procedure has made a drastic change in the outcome of future fertility and safety. The 2-step procedure done in this series may be extrapolated to such an extent that the baby may be delivered in a primary setup and the abdomen closed and mother shifted with placenta in situ to a tertiary setup for the definitive management. Wide acceptance of such new techniques can change the outlook of high risk obstetrics and improve the maternal health care.

International Symposium 2  : Obstetrics

7) NAFLD, MAFLD, MASLD and adverse pregnancy outcomes

Park Joong Shin

Seoul National University College of Medicine, Korea

Hepatic steatosis in the absence of excessive alcohol consumption or liver disease has been reported to be associated with adverse cardiometabolic complications. Traditionally, non-alcoholic fatty liver disease (NAFLD) has been used to present hepatic steatosis in the absence of significant alcohol consumption. However recent guidelines have suggested that other terminology for hepatic steatosis may be more appropriate to better describe metabolic dysfunction and fatty liver disease. MAFLD was suggested to define metabolic dysfunction-associated fatty liver disease, and recently more definite term, MASLD (metabolic dysfunction-associated steatotic liver disease) has been suggested.

Because pregnancy can be a stress test for further adverse cardiometabolic outcome after delivery, we evaluated if hepatic steatosis could be linked to adverse pregnancy outcomes such as preeclampsia or gestational diabetes mellitus. As


a result, we have reported the relationship between hepatic steatosis and pregnancy outcomes.

1) NAFLD was associated with increased risk of pregnancy complications, such as gestational diabetes mellitus, preeclampsia, and large for gestational age neonates.

2) Any form of hepatic steatosis was a risk factor for pregnancy complications. However, MAFLD was associated with a higher risk for pregnancy complications than NAFLD-only.

3) The presence of MASLD or MetALD (MASLD and increased alcohol intake) during the early pregnancy was associated with an increased risk of adverse pregnancy outcomes.

In conclusion, hepatic steatosis was associated with increased risk of adverse pregnancy outcomes. Further prospective studies should be performed to examine the long-term health outcomes in this population.

International Symposium 3  : Gynecology 1

1) Single-port robotic sacrocolpopexy : Tips to improve outcomes

Lee Sa Ra

University of Ulsan, Asan Medical Center, Korea

Pelvic organ prolapse (POP) is a relatively common condition and the importance of POP is increasing in aging societies. Historically, abdominal sacrocolpopexy (SC) has been recognized as the gold-standard surgical treatment for apical compartment prolapse. The introduction of robotic systems has enabled much easier intracorporeal suturing and deep vesicovaginal and rectovaginal dissections. Therefore, the use of robotic SC continues to increase. Laparoscopic single-port surgery (LESS) has been developed to provide cosmetic benefits via minimal skin incision ; however, difficult angulations and collisions between laparoscopic instruments are the main technical challenges limiting its feasibility. In 2014, the da Vinci Single-Site[®] platform (Intuitive Surgical Inc., Sunnyvale, CA, USA) was developed to overcome the limitations of LESS ; however, the weak power transference achievable by semirigid instruments with limited ranges of motion precludes the application

of the Single-Site system to diverse types of procedures. More recently, the Single-Port[®] system (Intuitive Surgical, Sunnyvale, CA, USA) was developed to overcome the technical limitations of Single-Site and the newer system has been used for more indications than the Single-Site platform. I firstly reported on the feasibility and safety of single-incision single-site robot-assisted laparoscopic SC (SS-RSC) in 2016 and single-port robotic sacrocolpopexy (SP-RSC) in 2019. We compared the surgical time and operative outcomes of SS-RSC and SP-RSC. Single-incision RSC, both SS-RSC and SP-RSC, is a feasible and effective surgical option for treating symptomatic apical POP. In the analysis of the initial 8 cases in each group, all surgical times except the cervix suturing time were shorter in the SP-RSC group. Here I will present the latest surgical outcomes of SP-RSC and will suggest some surgical tips for successful SP-RSC.

International Symposium 3 **P** : Gynecology 1

2) Tumors of the space of retzius

Rao Damodar Raghavendra, Manohar Nimisha, Wangnolim Yingngam

Rao Hospital & CARE, India

Leiomyomas are benign mesenchymal tumours which originate usually from smooth muscle cells, hence can arise at any site where smooth muscle cells exist. In females, most commonly seen in uterus, extra uterine leiomyomas are rare and seldom found in space of retzius. we had 4 cases of tumors of space of retzius, the largest being a retropubic leiomyoma in a 45 year old lady who presented with urinary symptoms and ab-

normal uterine bleeding. Clinical examination and imaging showed uterine leiomyoma with doubtful urethral leiomyoma. all the cases were approached laparoscopically and excision of the mass was done in entirety. Very few cases have been reported in the literature so far. Histopathology showed benign leiomyoma.

International Symposium 3  : Gynecology 1

3) Endometriosis Mapping Scan in Deep Endometriosis and Surgical Planning

Li Ma

National University Hospital, Singapore

Endometriosis is a chronic, inflammatory condition with incidence of 10-15% among reproductive population, one of the most common reasons for debilitating pain and infertility. But still there is a significant delay in diagnosis between the onset of symptoms and a reliable diagnosis averaging between 8-12 years. Diagnosis of deep infiltrating endometriosis is even more challenging. Surgical clearance at the first surgical intervention delivers the greatest benefit, but incomplete diagnosis of deep infiltrating endometriosis lead to incomplete excision of endometriosis, thus persistent or worsening pain, or infertility. 2022 ESHRE guideline stated that laparoscopy is no longer the diagnostic gold standard, and ultrasound scan can be used to accurately diagnose endometriosis including deep infiltrating endometriosis. ENZIAN was implemented in the last decade, and revised Enzian has proved to be

the most suitable tool for staging deep endometriosis including anatomical location and size of all different forms of endometriosis, adhesion, and degree of involvement of adjacent organ. In my lecture I will show recorded video clips of endometriosis mapping scan, including endometriosis in various location following revised Enzian scoring system, in combination with intra-operative findings. I will also show some typical cases of severe endometriosis (bowel endometriosis, ureter endometriosis, endometriosis in rare location etc) I want to highlight the importance of preoperative diagnosis in proper counselling and proper surgical planning. Preoperative planning is equally important as surgery itself, and endometriosis mapping scan provides very good correlation to surgical findings. It's a necessary tool to ensure complete resection of endometriosis.

International Symposium 4 **P** : Gynecology 2

1) Real World Evidence for the evaluation of surgical innovation and medical device surveillance

Prieto Alhambra Daniel

*University of Oxford, UK***OBJECTIVES**

Surgical and device innovation are paramount for the continuous improvement of healthcare. However, a fine balance needs to be struck to ensure patient safety and minimise harm. Real world data, collected in routine clinical practice in the form of electronic medical records, registries, and health claims, can be extremely useful for the monitoring of surgical and device innovations. The main aim of this talk is to review why and how Real World Evidence (RWE) must be generated to facilitate transparent and reproducible research in surgical innovation, with specific clinical examples.

METHODS

I will review previous examples where RWE has proven useful in the characterisation, prediction, and safety surveillance of medicines, medicinal products, devices, and surgeries. I will cover useful data sources, common data models for federated analytics, and methodological advances in the use of these data for public health and regulatory decision making.

RESULTS

We have utilised the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) to facilitate international collaboration into the research of surgery and device safety and effectiveness. I will cover the results of a target trial emulation where we proved how state-of-the-art methods and good quality data can yield results equivalent to those obtained from surgical trials, and how this can be replicated across the globe. Finally, I will explain how such innovation has led to the setting up of international regulatory research networks, including the Data Analysis and Real World Interrogation Network (DARWIN EU)

CONCLUSIONS

RWE will be essential in the characterisation and evaluation of surgical innovation. Obstetrics and Gynecology are no exception to this move, and involved clinicians should learn the basics on how to appraise the resulting research and literature, and how to lead studies in the field themselves.

International Symposium 4 **P** : Gynecology 2

2) Uterine Fibroids : 2024

Stewart Elizabeth A.

Mayo Clinic, USA

Uterine fibroids (leiomyomas) affect up to 75% of all individuals born with a uterus and are a major cause of morbidity for these individuals and society. Hysterectomy has historically been viewed as the “cure” for fibroids. However, our work and that of others, demonstrate increased cardiovascular and mental health morbidity following hysterectomy even with bilateral ovarian conservation. Additionally, some studies demonstrate increased mortality when hysterectomy with ovarian conservation is performed in women younger than age 35.

A series of recent studies also suggests inappropriate overuse of hysterectomy. The first suggested that among women with commercial insurance in the United States, nearly 3 of 5 did not have any conservative therapy for fibroids prior to hysterectomy. A second study suggested that there may be undertreatment of Black or African American women, who clearly have more severe fibroid disease, with uterine sparing options early in their fibroid journey. Finally, despite evidence that nearly 3 in 4 women desire uterine preserving options, nearly 3 in 4 women undergoing surgical therapy undergo hysterectomy. Thus, understanding barriers to alternatives to

hysterectomy for symptomatic fibroids is critical.

The recent introduction of oral gonadotropin hormone releasing antagonist combinations (OGACs) for the treatment of uterine fibroids gives us a powerful new alternative to hysterectomy. These combinations produce robust reduction of heavy menstrual bleeding and bulk symptoms across the entire spectrum of fibroid disease. Research has shown that OGACs are effective across all uterine volumes, all levels of menstrual blood loss, body mass index, and even in the presence of concomitant adenomyosis. Moreover, OGACs produce a very low level of side effects due to either the addition of low physiologic levels of estrogen and progestin or partial antagonism of hypothalamic function.

These two key developments, recognition of the limitations of the hysterectomy even with bilateral ovarian conservation, and effective, well tolerated oral medical therapy will undoubtedly change our future treatment paradigm for uterine fibroids. This lecture will put forward a new vision for treatment of uterine fibroids across the lifespan.

International Symposium 4  : Gynecology 2

3) What's New in Male Infertility — A Comprehensive Overview of Emerging Trends and Innovations

Pai Hrishikesh D.

*Immediate Past President, FOGSI, India***Introduction :**

Infertility is a complex and pervasive issue affecting approximately 17.5% of the global population, as reported by the World Health Organization (WHO) in 2023. This talk delves into the latest developments in addressing male infertility, exploring novel strategies, diagnostic tools, and treatment options. The presentation draws from recent WHO guidelines, advancements in laboratory practices, the integration of artificial intelligence (AI), and cutting-edge therapies that are transforming the landscape of male reproductive medicine.

A key highlight is the public health dimension, emphasizing the prevalence of male infertility as a significant global concern. The WHO's 2023 report provides a comprehensive overview of infertility trends, offering valuable insights into the magnitude of the issue. Moreover, the WHO Lab Manual on Semen Analysis, sixth edition, of 2021, serve as pivotal references for practitioners, both for diagnosis and procedures.

The presentation discusses the impact of AI algorithms in enhancing the precision and efficiency of treatments. Furthermore, automation in the laboratory, including robotic Intracytoplasmic Sperm Injection (ICSI), witnessing systems and automatic vitrification, signifies a paradigm shift in laboratory practices, reducing human errors and optimizing success rates.

The talk scrutinizes the latest advancements

in treatment options for male infertility, emphasizing the role of Microdissection Testicular Sperm Extraction (Micro TESE), spindle check system, and single sperm freezing. Stem cell rejuvenation of the testis emerges as a promising avenue, offering potential solutions for cases of nonobstructive azoospermia. The presentation also explores recent breakthroughs in generating sperm from induced pluripotent stem cells, expanding the scope of therapeutic interventions.

A critical aspect of male infertility assessment involves evaluating DNA fragmentation, and the talk provides insights into the significance of DNA Fragmentation Index (DFI) measurements. It delineates cases where DFI exceeds 30%, exploring its correlation with Recurrent Implantation Failure (RIF), Recurrent Pregnancy Loss (RPL), varicocele, unexplained infertility, and routine evaluations.

The talk scrutinizes criteria for treating varicoceles and reviews the role of varicocele repair in addressing male factor infertility. Additionally, it delves into genetic evaluations in the context of Non Obstructive Azoospermia (NOA) or severe Oligoasthenoteratozoospermia (OAT). It provides a comprehensive overview of empirical treatments available for the treatment for idiopathic oligospermia.

Intrauterine Insemination (IUI) stands as an initial intervention for male infertility. This

method involves placing prepared sperm directly into the woman's uterus during ovulation, increasing the chances of fertilization. We explore the effectiveness of IUI, its success rates, and its potential role in addressing male infertility.

Intra Cytoplasmic sperm Injection (ICSI) has been the gold standard for the treatment of severe male factor infertility. Precision in sperm selection is crucial in improving outcomes in ICSI. Intracytoplasmic Morphologically Selected Sperm Injection (IMSI) represents a significant advancement in assisted reproductive technologies (ART), allowing for the selection of sperm based on their morphological characteristics at high magnification of 6600x. The talk evaluates the benefits and limitations of IMSI, shedding light on its role in enhancing fertilization outcomes. The talk examines the implementation of PCSI (Physiological Intracytoplasmic Sperm Injection) as an alternative to IMSI, designed to improve the selection process, thereby optimizing the chances of successful fertilization.

An innovative technique, Piezo ICSI, involves a more controlled injection of sperm into the egg, using a blunt injection needle in combination with vibration mode. We discuss the advantages of this method in overcoming certain challenges associated with traditional ICSI and its implications for male infertility treatment.

For cases of obstructive azoospermia (OA), Percutaneous Epididymal sperm Aspiration (PESA) emerges as a viable solution. The talk explains the procedure, its success rates, and its

role in offering hope to individuals facing OA. In addressing NOA, microTESE stands as a breakthrough procedure. We evaluate its efficacy, success rates, and its contribution to retrieving viable sperm for assisted reproduction.

The talk highlights the technique of vitrifying individual sperm, using a novel sperm vitrification device, a method with potential applications in preserving male fertility and improving outcomes in patients with severe oligo OAT.

The final part of the talk, examines the intriguing question of whether procedures like ICSI & IMSI can increase the risk of birth defects associated with ART. We explore existing research and contemplate the future implications of these technologies on the health of ART-conceived children.

Conclusion :

In conclusion, this talk encapsulates the dynamic landscape of male infertility treatment, highlighting the intersection of public health, guidelines, technological innovations, and emerging therapeutic modalities. The integration of AI, automation, and advanced diagnostic tools marks a transformative era in male reproductive medicine, offering new hope and possibilities for couples facing infertility challenges. The presentation aims to inspire practitioners, researchers, and policymakers to embrace these innovations, fostering a collaborative approach to address the multifaceted dimensions of male infertility and emphasizing the importance of a multidisciplinary approach in reproductive medicine in the 21st century.

International Symposium 4  : Gynecology 2

4) Hierarchy of the best treatments for endometriosis related pain and infertility - Two systematic reviews with network meta-analyses

Johnson Neil

Repromed Auckland, Auckland Gynaecology Group and University of Auckland, New Zealand / Flinders Fertility, University of Adelaide and Flinders University, Australia

Background and Aims : To determine the relative effectiveness of different treatments for women with endometriosis-related infertility and with endometriosis-related pain.

Methods : We undertook two systematic reviews and network meta-analyses (NMAs) of relevant randomised control trials (RCTs). We searched electronic databases including, MEDLINE, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL) and reference lists to identify eligible studies. We included RCTs comparing any medical/surgical interventions to each other or to no treatment/placebo in women with (a) endometriosis associated infertility and (b) endometriosis associated pain. Trials including only women with endometriomas were excluded.

Results :

First, regarding trials of treatments for endometriosis-related infertility, we included 27 RCTs reporting on 2,195 women with endometriosis-associated infertility undergoing 14 different interventions. The most frequent direct comparison was surgical laparoscopy versus surgical laparoscopy plus GnRHa (7 trials, 686 women). All 27 RCTs reported clinical pregnancy ; only five reported live birth. NMA comparing all treatments to no intervention/placebo showed lipiodol (OR 7.56, 95% CI 1.95 to 29.37) and laparoscopic surgery plus pentoxifylline (OR

3.44, 95% CI 1.08 to 10.93) resulted in more clinical pregnancies ; GnRHa (OR 1.54, 95% CI 0.93 to 2.56) and laparoscopic surgery alone (OR 1.43, 95% CI 0.93 to 2.56) likely resulted in more pregnancies ; dydrogesterone (OR 3.00, 95% CI 0.69 to 13.30), pentoxifylline alone (OR 1.98, 95% CI 0.55 to 7.17) and laparoscopic surgery plus danazol (OR 1.72, 95% CI 0.34 to 8.78) showed imprecise effect sizes. IVF and IUI could not be included in this NMA, as RCTs compared only different ways of undertaking IVF and different types of stimulation for IUI, with no RCT comparing IVF or IUI versus placebo or versus another treatment.

Second, regarding trials of treatments for endometriosis-related pain, considering our primary outcome overall pain, we included 60 RCTs reporting on 2,195 women with endometriosis-associated infertility undergoing 28 different interventions and a total of 75 direct comparisons. The most frequent direct comparison was GnRH agonist versus androgenic agents (14 comparisons ; 1351 patients) then combined oral contraceptive pills (OCP) versus placebo (8 comparisons ; 647 patients). NMA comparing all treatments suggested that the highest ranked treatments for effectiveness in treating overall pain were depot medroxyprogesterone acetate (DMPA), which had an 81% probability of ranking in the top 3 treatments, followed by andro-

genic agents (a 41% probability of ranking in the top 3 treatments).

Conclusions : More RCTs are needed to clarify the relative effectiveness of treatments for endometriosis related infertility, in particular RCTs comparing IVF and IUI to other treatments, including the highest ranked treatment in this fertility NMA, lipiodol. Although many RCTs have contributed to the NMA studying the relative effectiveness of endometriosis related pain, the sheer number of clinically relevant pain

outcomes makes this a vast task. While it is possible to rank treatments (including medical versus surgical interventions), the ultimate choice of treatment may be determined not purely by relative effectiveness but by other factors including treatment availability and adverse events or side effects of treatments, exemplified that the highest ranked interventions for effectiveness in treating overall pain were DMPA and androgenic agents (such as gestrinone and danazol).

International Symposium 4  : Gynecology 2

5) Global events Sexual and Reproductive Health & Rights (SRHR)

Mukhopadhyay Sambit

Norfolk and Norwich University Hospital NHS trust, UK/EBCOG

Sexual and Reproductive health and rights are fundamental to people's health and survival, economic prosperity, and sustainable development. Significant health gains have been achieved since world leaders enshrined reproductive right as basic human right at the ICPD conference at Cairo, Egypt in September 1994. However full attainment of SRHR remains elusive for many nations. In 2015, the international community reaffirmed the commitment of putting "people, planet and prosperity" at the centre of sustainable development and leaving no one behind, when it adopted the 2030 Agenda for Sustainable Development and the Sustainable Development Goals (SDGs). Targets 3.7 and 5.6 explicitly mention sexual and reproductive health rights and it was envisaged that incorporating these targets at national policies and strategies could lead to transformational changes at country level. While efforts by the international community showed favourable trends of SDG, global events like

changes in population size and composition, displacement and conflict, climate change, socio-cultural determinants, COVID pandemic, laws, policies, and programmes affecting health care and technology and innovation in the last decade had significant impact on the progress of SDG.

The European Board and College of Obstetrics and Gynaecology (EBCOG) represents over thirty European countries and is committed to improve health of women and their babies. At global level it is a strong advocate of SRHR and has worked with UNFPA, ESCRH (European Society of Contraception and Reproductive Health) in supporting development of a comprehensive national frameworks for SRH using life course approach from birth to post reproductive years. It is also signatory to FIGO's redline initiative of drawing an end to conflict related sexual violence. EBCOG fully supports UNFPA to achieve its ambitious key SRHR and universal health care targets in SDGs by 2030.

International Symposium 4  : Gynecology 2

6) Defect oriented laparoscopic pelvic floor repair

Noé Günter K.

University of Witten Herdecke, Germany

Pelvic floor surgery is of great importance for women's health. In the last 25 years, after a long period of little progress, a lot has developed in uro-gynecology. Unfortunately, clinical research has been slower than adoption of techniques, leading to many unnecessary complications. The use of meshes has come under criticism, partly justified but partly unjustified. This has unsettled surgeons and patients. Over the last 20 years, we have developed the combination of na-

tive tissue repair and apical fixation using meshes so that the complication rates are very low and the success rates are high. To do this, we use a predominantly laparoscopic, defect-oriented strategy. All pelvic floor defects are treated surgically at their origin without destroying important and uninvolved tissue structures. We attach great importance to easy dismantling in order to avoid long-term problems in the event of complications.

International Symposium 4  : Gynecology 2

7) Preliminary study of the therapeutic effect of human amniotic fluid stem cells-derived exosomes on acute stroke neuronal injury and cell re-generation

Tsai Ming-Song

Cathay General Hospital, Taiwan, Fu Jen Catholic University, Taiwan/TAOG

Human amniotic fluid stem cells (hAFSCs) has been described as multipotent mesenchymal stem cells (MSC) that are similar to embryonic stem cells and express pluripotent markers and exhibit high self-renewal potential. These cells may provide an excellent alternative source of human MSC for cellular therapy in regenerative medicine. Stroke is one of leading causes of death, disability, and healthcare expenses worldwide. Despite adequate engrafting of stem cells, only a few cells can get through to the injured target tissue. Recent research has focused on the paracrine effect of stem cell derived exosomes, which carry proteins, lipids, and genetic materials. Exosomes play essential roles in intercellular communication by transferring their cargo to target cells to enhance tissue repair and functional recovery. We cultured hAFSCs in serum-free culture medium and subsequently separate them into both normoxic and hypoxic conditions and analyzed the characteristics of hAFSCs-

derived exosomes in normoxic and hypoxic conditions. We have successfully characterized miRNA expression profile of hAFSCs and hAFSCs-derived exosomes under normoxia and hypoxia by next generation sequencing (NGS). Additionally, we found that the hAFSCs-derived exosomes could maintain vascular integrity by in vitro human umbilical vein endothelial cells (HUVEC) tube-formation assay. Using size exclusion chromatography (SEC) methods for exosomes purification, we also demonstrated that the neuroprotective effect of hAFSCs-derived exosomes in oxygen-glucose deprivation/reperfusion (OGD/R) -induced neurological injury. We will further investigate the therapeutic effect of hAFSCs-derived exosomes in a cerebral ischemia/reperfusion (I/R) mouse model.

Key word : Amniotic fluid stem cells, Exosomes, Ischemic stroke, Angiogenesis, Neuronal cell viability, Neurogenesis.

International Symposium 5  : PCOS

1) PCOS and AMH : Pitfalls and Management

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In anovulatory women with polycystic ovarian syndrome (PCOS), the growth of antral stage follicles is often arrested at 5-8mm diameter. The origin of PCO is believed to be higher initial population of primordial follicles or slower rate of loss by atresia. This is shown by Webber et al that the median total follicle in anovulatory PCOS is approximately 7 times higher than normal ovulation. In PCOS, there is an increase of AMH production in granulosa cells, prominently found in larger preantral and small antral follicles. AMH plays a disruptive role in folliculogenesis. It can be seen by its inhibitory effects on primary follicles' initial recruitment from resting primordial follicle pool and sensitivity of antral follicles for FSH. This is supported by a reduction of gonadotropin-stimulated aromatase and FSH receptor mRNA expression. This is proven by findings from Wiweko et al that FSH in PCOS patients do not reached its threshold level. In anovulatory PCOS patients, the mean concentration of AMH production is 75 times higher than in normal ovaries. An optimal diagnostic AMH cut-off level is suggested to be 4.45ng/mL and higher levels are 9.35 times more likely to suffer from PCOS. The number of AMH gene promoter mutations is correlated to serum AMH level leading to increased AMH level. Subsequently reduced follicle sensitivity towards FSH and elevated androgen level.

AMH levels serve as a potential indicator for the effectiveness of PCOS treatment, where ele-

vated average AMH levels are linked to unsuccessful ovulation treatment in PCOS patients. Additionally, serum AMH shows a positive association with the HOMA-IR test in PCOS individuals. Notably, the highest AMH values are observed in PCOS phenotype I, which also exhibits the highest incidence of metabolic syndromes compared to other phenotypes. Treatment with metformin or DLBS3233 results in decreased serum AMH levels, with metformin leading to a more significant reduction. These effects are similarly observed in PCOS patients with metabolic syndrome. Moreover, metformin use is reported to cause a notably higher frequency of nausea compared to DLBS3233, potentially increasing the risk of metabolic syndrome in PCOS patients.

Vitamin D regulates FSH receptor and AMH receptor II mRNA levels in human luteinized cells. In addition, vitamin D stimulates progesterone synthesis and release by inducing 3-beta-hydroxysteroid dehydrogenase (3b-HSD) mRNA expression. Because PCOS is caused by hyperandrogenism, insulin resistance, inflammation and metabolic syndrome, a lack of vitamin D leads to anovulation.

In summary, serum AMH can be used to predict PCOS diagnosis, disease severity, and therapy monitoring. In PCOS patients, serum AMH has an indirect link with insulin resistance that may increase the risk of metabolic syndrome. Insulin sensitizer supplements and high-dose vita-

min D supplements are beneficial for the symptoms of PCOS and metabolic syndrome.

International Symposium 5  : PCOS

2) ART in Patients with Polycystic Ovarian Syndrome

Pai Rishma Dhillon¹⁾, Pai Arnav²⁾*Lilavati, Jaslok Hospital & Hinduja hospitals, India¹⁾,**The Everywoman Cliniq, Bandra, India²⁾*

Polycystic Ovarian Syndrome (PCOS) is a highly prevalent condition amongst women in the reproductive age group and is the commonest cause of anovulation affecting about 80% of women diagnosed with PCOS.(1)

The associated problems of irregular menstruation, obesity, mood disorders like depression and anxiety, all contribute to PCOS being a common reason for infertility and for a couple to seek Assisted reproductive technology (ART) treatment. The prevalence of infertility in women with PCOS varies from 70 - 80 % (2)

The elevated AMH in patients with PCOS has a negative impact of FSH signalling and follicle development, the insulin resistance, high LH and hyperandrogenism all contribute to anovulation and poor oocyte and endometrium quality.

If the patient does not conceive with basic oral ovulogens or gonadotrophins and IUI, she often needs to proceed to IVF. Pre IVF, it is important to do a proper assessment of any related medical problems and also have the patient do a lifestyle improvement if necessary, including weight loss for overweight and obese patients.

Pre- preparation with treatment of estrogen before ovarian stimulation using the GnRh antagonist protocol is probably not recommended. Combined oral contraceptive pill pre-treatment is not recommended because of reduced efficacy. (3)

Adjuvent's such as myoinositol can be started (4) which helps reduce dose of gonadotrophins.

Melatonin use has also been found in some studies to improve oocyte quality (5)

Metformin has been used as in insulin sensitizer since years and studies have found reduced risk of ovarian hyperstimulation stimulation (OHSS) with its use (6) Vitamin D supplementation may also help outcomes.

Ovarian stimulation in patients with PCOS needs to be carefully done in order to achieve the optimal number of oocytes and reduce hyperstimulation syndrome. The International Evidence based guidelines 2023 recommends the use of GnRh antagonists protocol with GnRha trigger in IVF cycles, with freezing of all embryos generated if required, without compromising the cumulative live birth rate, to reduce the risk of OHSS. The gonadotrophin of choice is urinary or recombinant FSH.(7)

In patients with a history of severe OHSS or those at a t high risk for it, in-vitro maturation (IVM) and ICSI can be offered, if the expertise is available. It is less effective than standard IVF / ICSI. (8). With different phenotypes of PCOS, the outcomes may differ, with lean PCOS patients having higher cumulative live birth rates (9)

Progestin primed ovarian stimulation, instead of GnRh antagonist has also been used in PCOS patients.(10).

Minimal stimulation protocols are also used in PCOS patients with similar live birth rates and low OHSS risk (11).

The main concern with IVF in PCOS patients has been the risk of OHSS. The use of segmentation technique, GnRha trigger in an GnRH antagonist cycle and freezing all embryos for transfer later in a hormone replacement or natural cycle, will help eliminate OHSS.

Once the patient becomes pregnant after IVF treatment, the pregnancy has to be carefully monitored as, especially the obese PCOS patients, have a higher incidence of gestational diabetes, hypertension, preterm birth and macrosomia.

Overall, ART in patients with PCOS requires good pre-preparation, stimulation protocols carefully chosen and monitored, and frozen thaw embryo transfer followed by regular monitoring of pregnancy when it occurs. This will result in a healthy baby to a healthy mother.

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International Symposium 5  : PCOS

3) Pathogenic mechanisms in PCOS : biological and clinical insights

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Polycystic ovary syndrome (PCOS) is the most common endocrine disorder of reproductive-age women. Although the pathophysiology of PCOS has not been fully elucidated, the reproductive and metabolic abnormalities interact and exacerbate one another. It has been recently recognized that prenatal androgen exposure is involved in the development of PCOS in adulthood. In addition, the gut microbiome in adult patients and rodents with PCOS differs from that of healthy individuals. Moreover, recent studies have suggested that the gut microbiome may play a causative role in the pathogenesis of PCOS.

Based on these findings, we hypothesized that prenatal exposure to high concentrations of androgens would induce dysbiosis of the gut microbiome early in life and that this would lead to the development of PCOS in later life. As the first step in testing this hypothesis, we characterized the temporal relationship between alterations in the gut microbiome and the development of PCOS-like phenotypes between weaning and adulthood using prenatally-androgenized (PNA) female mice (*FASEB J.* 2021). We found that abnormalities in the gut microbiome appear as early as or even before PCOS-like phenotypes manifest in PNA offspring. Then, to clarify which of the prenatal environment or the postnatal nurturing environment contributes more to the etiology of PCOS phenotypes and the alterations in the gut microbiome, or are both important, we used a cross-fostering model and compared the PCOS-like phenotypes and the differ-

ences in the gut microbiome in PNA offspring fostered with a control mother (fostered PNA) and PNA offspring kept with their own mothers vs. control (under review). The results showed that both prenatal androgen exposure itself and the postnatal early-life environment contribute to the development of PCOS-like phenotypes and the alterations to the gut microbiome in PNA offspring. Additionally, the PCOS-like phenotypes in later life, and especially the metabolic phenotype that develops after young adulthood, can be ameliorated by improving their gut microbial composition before adolescence. In order to elucidate the mechanisms by which the alterations in the gut microbiome contribute to the development of PCOS and to identify novel pro/postbiotics and appropriate timing of intervention, we have been conducting metabolomic analysis of the feces. Now we are conducting an intervention study using butyric acid whose content was smaller in PNA offspring compared to control. I'd like to share with you our recent findings in this presentation and provide perspectives regarding the future research to treat and prevent PCOS.

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ing and perspectives regarding future research. *Rep Med Biol.* 2022 ; 21 : e12. Review

International Symposium 5  : PCOS

4) Metformin, Microbes, and More : treatments for hyperandrogenism and PCOS

Chen Mei-Jou

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Women with polycystic ovarian syndrome (PCOS) exhibit characteristics such as hyperandrogenism, chronic anovulation, and a high prevalence of metabolic disturbances. The pathogenesis of PCOS is reported to involve the interplay between hyperandrogenism and obesity. Both extremes of hyperandrogenemia and obesity can contribute to the development of PCOS. Previous literature, including our own, provides substantial evidence that elevated androgen levels and diet-induced obesity can directly contribute to ovulatory dysfunction in women with PCOS, as observed in both in vivo animal and clinical studies.

Medications capable of addressing obesity and hyperandrogenism in women with PCOS may have the potential to restore ovulation. Metformin, an insulin sensitizer, is known to improve pregnancy rates, reduce pregnancy complications and the risk of ovarian hyperstimulation, and enhance the clinical pregnancy rate for women with PCOS undergoing in vitro fertilization (IVF). Our previous studies have indicated that metformin alone not only effectively re-

stores spontaneous ovulation in women with PCOS but also protects the ovaries against chemotherapy-induced gonadal injury. Metformin treatment for up to 6 months in women with PCOS significantly decreases circulating androgen levels, reduces reactive oxygen species (ROS), mitochondrial DNA copy number, and mitigates DNA damage.

Additionally, women with PCOS are recognized to have a higher prevalence of functional gastrointestinal disorders and distinctive gut microbiota compared to those without PCOS. Gut microbes have been reported to be associated with metabolic disorders and hormonal metabolism. Therefore, they could be a potential target in the future for treating patients with hyperandrogenism, such as those with PCOS.

In conclusion, this talk aims to introduce the potential roles of metformin and the gut microbe in the treatment of hyperandrogenemia and PCOS. By unraveling the intricate connections between hyperandrogenism, obesity, and PCOS, we may discuss the future therapeutic strategies for this complex syndrome.

International Symposium 6 **P** : Oncology

1) Epigenetic Approaches to Epithelial Ovarian Cancer

Zhang Rugang

The University of Texas MD Anderson Cancer Center, USA

The past decade has brought unprecedented progress in understanding the genetics of epithelial ovarian cancer (EOC), but cures remain elusive due to the lack of insights into mechanisms that can be leveraged to develop new therapies. EOC is genetically heterogeneous and, therefore, it is imperative that therapeutic strategies become personalized by targeting distinct molecular subsets of EOC. Despite the importance of

epigenetic regulators in EOC, the mechanism of action for these epigenetic regulators and the associated vulnerabilities exposed by their dysregulations have remained elusive for most of them. Here we will discuss our recent work on how to leverage epigenetic mechanisms to address unmet clinical needs in epithelial ovarian cancer through integrated approaches.

International Symposium 6  : Oncology2) Using mass cytometry to dissect human immunity and its application
to research in cancer biologyWing James B.¹⁾²⁾³⁾*Immunology Frontier Research Center (IFReC), Osaka University¹⁾,**Center for Infectious Disease Education and Research (CiDER), Osaka University²⁾,**Center for Advanced Modalities and DDS (CAMaD), Osaka University³⁾*

Human immune responses are complex, often involving interactions of rare cells from multiple branches of the immune system. Additionally immune responses are highly dependent on time and may change radically over just a few days during infection or vaccination. Together these factors emphasize the need for methods that allow simultaneous assessment of finely defined immunophenotypes across time in large longitudinal cohorts. While a variety of single cell methods exist, we find that Mass cytometry (CyTOF) provides an ideal balance of scale and depth. Using this technique, we developed methodology for the large-scale screening of human clinical samples with a workflow termed Mass phenotyping (Massive phenotyping by Mass cytometry) allowing measurement of 100-140 protein markers split across multiple antibody panels designed to provide fine resolution, simultaneous, immunophenotyping of CD4, Treg, Tfh, γ δ T, CD8, NK, B-cells, Monocytes and DCs at a high scale covering hundreds of samples and tens of millions of cells. We have applied it to cohorts of lon-

gitudinal COVID-19, Bacterial Sepsis and mRNA vaccination allowing exact comparison of time dependent changes to immunophenotypes in these diverse settings covering over 600 samples. While this workflow was initially designed to assess the human immune system not all cellular responses can be understood by these methods. To address this point, we have developed a more universal methods for the assessment of the effects of anti-cancer drugs on basic aspects of cell processes such as DNA damage repair, metabolism, cell cycle and histone modifications. Here I will also discuss the application of this technique to the single cell analysis of ovarian cancer cell lines allowing direct comparison of the responses of Clear cell carcinomas (CCC), (ARID1A deficient and proficient) and High-Grade Serous (HGS) cell lines of both HRP and HRD subtypes. Using the depth and scalability of mass cytometry we aim to further develop this approach for the large-scale screening of various drugs in malignancies.

International Symposium 6  : Oncology

3) Multimodal machine learning to risk stratify women with ovarian and breast cancer

Boehm Kevin M.

Memorial Sloan Kettering Cancer Center, USA

Genomic biomarkers have begun to refine therapies for women with cancer. For example, homologous recombination deficiency indicates PARP inhibitors for high-grade serous ovarian cancer, and transcriptomic recurrence scores identify women with early-stage hormone receptor-positive breast cancer who stand to benefit from up-front chemotherapy.

However, clinical imaging data modalities, such as histopathologic and radiologic images, may provide complementary information and are relatively underexplored. Our work posits that integration of histopathologic, radiologic, and clinicogenomic data refines patient stratification and clinical decision support. We will present a framework for multimodal data integration for tumor subtype discovery and inference of response to therapy, with particular attention to appropriate choices around fusion architecture (early, intermediate, and late) and representation learning (engineered features versus deep learning) (Boehm et al., *Nature Reviews Cancer*, 2022).

We will present a demonstrative application of a late-fusion framework with engineered features to a cohort of 444 women with high-grade serous ovarian cancer (Boehm et al., *Nature Cancer*, 2022). From histopathologic images, the model identified nuclear size and stromal morphology as informative features. From contrast-enhanced computed tomography images, auto-

correlation of the gray level co-occurrence matrix was prognostically significant. These two feature sets are subsequently integrated by late fusion with homologous recombination status to stratify women by overall survival after neoadjuvant platinum-based chemotherapy or primary debulking surgery. On this challenging endpoint, only the models integrating both imaging modalities attained statistical significance (permutation $p < 0.05$), stratifying the cohort with a Harrell's concordance index of 0.61 on a withheld test set. Risk groups assigned based on these scores differed by mean overall and progression-free survival (median overall survival of 30 and 50 months, respectively ; $p < 0.05$). This work identifies putative imaging biomarkers for further hypothesis-driven inquiry and empirically demonstrates the benefit of integrating multiple clinical data modalities for patient prognostication.

In addition, we will discuss ongoing work to risk stratify women with early-stage breast cancer. Specifically, we assembled a cohort of over 5,000 women with corresponding whole-slide images of breast tumors stained with hematoxylin and eosin. To infer risk of distal metastatic recurrence, we developed a model to interpret text from the pathologist's report using a large language model and interpret the corresponding whole-slide image using self-supervised vision transformers. Tensor fusion joins the modalities

to infer the Oncotype DX recurrence score. Our model could enable hospitals to rapidly triage the need for genomic risk testing.

Overall, we aim to extend physicians' ability to

care for women with cancer by conceptualizing and empirically validating machine learning models using imaging data acquired during the standard of care.

International Symposium 6  : Oncology

4) Aberrant RNA Splicing Emerges as a Pivotal Cancer Hallmark

Yoshimi Akihide

National Cancer Center Research Institute

Aberrant RNA splicing, driven by genetic alterations in cis-elements or trans-regulatory elements, represents a novel hallmark in cancer. Notable trans-regulatory mutations occur in genes encoding splicing factors such as SRSF2, SF3B1, and U2AF1. Analysis of transcriptomes from 982 acute myeloid leukemia patients revealed a frequent co-occurrence of mutations in IDH2 and SRSF2, jointly promoting leukemogenesis in vivo through coordinated effects on the epigenome and RNA splicing. Functional assessments highlighted INTS3 mis-splicing as a key driver of leukemogenesis in conjunction with mutant IDH2. A pan-cancer analysis of 98 tumors with SF3B1 hotspot mutations identified numerous tumor-specific mis-splicing events. This approach facilitated the identification of novel treatment tar-

gets. Conversely, splice site-affecting genetic mutations act as “cis-acting” regulators, impacting the mutant gene itself. Screening over 230,000 RNA-seq data revealed that splicing-associated variants (SAVs) are enriched in cancer-associated genes. We confirmed correction of aberrant splicing by SAVs using antisense oligonucleotides, offering a potential strategy to target previously “undruggable” gene mutations in cancers. The prevalence of these cis- and trans-regulators in multiple cancers positions the splicing machinery as an appealing therapeutic target. These findings elucidate the functional role of aberrant RNA splicing in tumorigenesis and contribute to the identification of novel and established oncogenic pathways as therapeutic targets in cancers with aberrant splicing.

International Symposium 6 **P** : Oncology

5) Cambodian Society of Gynecology (SCGO) and Obstetrics in Collaboration with Japanese Society of Obstetrics and Gynecology (JSOG) on cervical Cancer in Cambodia

Koum Kanal

President of SCGO

Objective : To illustrate the Cervical Cancer status of Cambodian women and the response of the Cambodian authority and SCGO in collaboration with JSOG.

Cambodia Cervical Cancer Project initiated in 2015 as a collaborative project between SCGO and JSOG with an aim to establish a workable system for early detection and treatment of cervical cancer in Cambodia. The Beneficiaries of the project are the Factory workers at Phnom Penh Special Economic Zone (PPSEZ) and the Staffs as Implementers working at National Maternal and Child Health Center, Khmer Soviet Friendship Hospital and Calmette Hospital. Also with JICA Funding we received a Close Support from NCGM Japan the Program for International Promotion of Japan's Healthcare Technologies and Services funded by Ministry of Health, Labor, and Welfare Japan to Strengthen the capacity of ours Implementer. With the result of the 1st Project SCGO in Collaboration with JSOG has received the 2nd Project to JICA Technical Cooperation Project name Project for Improving the Quality of Comprehensive Cervical Cancer Services through Women's Health Promotion 2019-2022. The output is 1. through Health Education an effective Health Education is provided for the target populations 2. Screening : Capacity of Cervical screening with HIV test is increase 3. Foundation for scaling up : Enabling

environment for scaling up Health education and cervical screening is prepared.

The Beneficiaries of the project are Primary school teachers in Phnom Penh, MOH staff, MOEYS staffs. Unluckily because of Covid19 Epidemic in Cambodia as well as worldwide we cannot achieve our Goals. We JSOG and SCGO propose to JICA an extension of the Project. JICA agreed to extend until June 2024 with the same total budget. Beside of The project we have plan to investigate the applicability of self-sampled HPV testing.

The target population for this is only 1600 Teachers working at the Primary school of Phnom Penh Municipality. The key interventions were conducted in three phases : health education and screening using HPV test for Primary School Teacher using medical sampling and self sampling ; diagnosis and early treatment by loop electrosurgical excision procedure (LEEP) at hospital. The system was successfully introduced with quality by relatively small budget within a short period of time, using existing resources and a new technique. By taking a step-wise quality-focused approach, opportunities and barriers were revealed in each phase as Challenges : physical and financial barriers for access to screening and treatment, replicability of HPV test and screening, limited information system for further development of cancer man-

agement system, and continuous capacity development for pathological services.

International Symposium 6 **P** : Oncology

6) Comprehensive analysis of surgical and oncologic outcomes in endometrial cancer : Population-based cohort study comparing robotic, laparoscopic, and open surgery

Kim Young Tae

Yonsei University College of Medicine, Korea/KSOG

Endometrial cancer is the most common cancer of the female reproductive tract in developed countries. Surgery is the first pivotal step in the management of this malignancy, and the outcomes of surgery can guide the choice of postoperative adjuvant treatment. Various surgical methods including open surgery (OS), laparoscopic surgery (LS), and robotic surgery (RS) have been introduced as option to treat endometrial cancer. Clinical relevance of surgical techniques of minimally invasive surgery (MIS) including LS, 3-arm RS, and 4-arm RS has also been studied recently.

Compared to the OS, the LS provides equivalent oncologic outcomes with reduced surgical and postoperative morbidity. However, the steep

learning curve associated with the LS restricts its widespread application as a surgical treatment for endometrial cancer. The introduction of robot-assisted LS with a relatively shallower learning curve has encouraged more gynecologic oncologists to employ MIS over the OS when treating endometrial cancer, and this has resulted in approximately 80% of patients undergoing hysterectomy for cancer by the RS in the United States.

Therefore, in this presentation, we will discuss studies to compare the perioperative and oncologic outcomes of different surgical approaches with the aim of evaluating the advantages of the RS in the staging of endometrial cancer.

International Symposium 6  : Oncology

7) A confirmatory trial of modified radical hysterectomy for FIGO Stage IB1 cervical cancer patients with tumor diameter preoperatively estimated 2 cm or less : Japan Clinical Oncology Group study, JCOG1101

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[Objective]

The standard surgery for Stage IB1 uterine cervical cancer is radical hysterectomy (RH, Piver class III hysterectomy). However, RH is highly invasive, and there is a need to establish less invasive techniques. We conducted a single-arm confirmatory trial (JCOG1101) to evaluate the efficacy and safety of modified radical hysterectomy (MRH) in patients with tumor diameter ≤ 2 cm Stage IB1 cervical cancer (jRCT : jRCTs031180167).

[Methods]

From January 2013 to August 2017, 240 patients were enrolled from 40 institutions in Japan. Eligibility criteria included : (1) FIGO 2008 Stage IB1 cervical cancer ; (2) histologically proven squamous cell carcinoma, adenocarcinoma (mucinous or endometrioid) or adenosquamous carcinoma ; (3) tumor diameter ≤ 2 cm (measured by MRI or conization speci-

men) ; and (4) neither distant LN metastasis nor distant metastasis in CT. In case that the cancer could be microinvasive, conization was required to exclude Stage IA cases. The protocol surgery involved cutting the anterior layer of the vesicouterine ligament of the uterus and dissecting regional lymph nodes. Only laparotomy was permitted : laparoscopy and robotic surgery were not allowed. Postoperative irradiation was administered in cases where pelvic LN or parametrial invasion was positive, depth in the cervical wall invasion was $\geq 2/3$, or surgical margin was < 1 cm by pathological findings. The primary endpoint was 5-year overall survival (OS). We set the expected 5-year OS of MRH at 95.8% (5-year OS of RH in JCOG0806A, retrospective observational study) and the threshold 5-year OS at 90.8%.

[Results]

Among 225 eligible patients, 193 (85.8%) were

pT1b1 (UICC 7th), and 184 (81.8%) had pathological maximal tumor diameter ≤ 2 cm. Parametrial involvement, lymph node metastasis, $\geq 2/3$ stromal invasion and < 1 cm surgical margin were observed in 3 (1.3%), 16 (7.1%), 30 (13.3%) and 11 (4.9%) patients, respectively. Thirty-nine patients (17.3%) underwent adjuvant (chemo) radiation. Median follow-up was 77.7 months. Five patients (2.2%) died, and 5-year OS was 98.2% (90% CI : 96.0-99.2, $> 90.8\%$). Thirteen patients (5.8%) relapsed (8 local recurrence and 5 distant recurrence), and 5-year relapse-free survival was 94.7% (95% CI : 90.8-96.9%). Self-urination was observed in all patients, and residual urine disap-

pearance up to 56 days after urethral catheter removal was observed in 213 patients (94.7%). Median time to disappearance of residual urine after urethral catheter removal was 1 day. There was no treatment-related death. Grade 3/4 non-hematological adverse events were observed in 17 patients (7.6%), including 8 infection and 4 hemorrhage.

[Conclusion]

In this study, MRH was as effective as RH and less invasive. MRH can be considered a standard surgery for tumor diameter ≤ 2 cm Stage IB1 uterine cervical cancer.

1) 現職女性産婦人科主任教授へのインタビューから

千葉大学 甲 賀 かをり

本シンポジウムでの発表にあたり、現職の女性の産婦人科主任教授である、名古屋市立大学 杉浦真弓先生、九州大学 加藤聖子先生、横浜市立大学 宮城悦子先生、にアンケート形式でインタビューを行った。本講演ではここで得られた回答を筆者の考察を交えてご紹介しながらディスカッションを行いたい。

まず、「教授就任までのキャリアで、女性という理由で不利だったと思われる点」については、「出産・授乳さらに月経困難症等を経験しながらの仕事の継続、特に外科医としての修練の辛さ」といった“生物学的”disadvantageに加え、“社会的”にも「女性という理由での様々な偏見・差別」が多々あったことを(壮絶な具体例とともに!)伺った。ただし、このような風潮は、昨今のコンプライアンス教育等の成果(つまりこれら諸先輩方の戦いのお蔭)により、最近では大幅に減少してきていると思われる。一方、「女性ということが有利に働いた点」として、「女性だという理由で選出されたと言われた」(筆者注:真偽の程は不明だと思います)は極論としても、「希少性から注目されてきた」という点は全ての先生が挙げており、トータルでみると女性医師を取り巻く環境は、以前に比べ大幅に改善してきているように見える(ので最年少である筆者自身は不利だと感じたことは全くありませんでしたし、若い先生にも頑張っていたきたいと思います)。

なお、「教授就任した後で女性であることが不利と感じる点」として、全ての先生が「女性という理由だけで各種委員に任命され会議が増える」と意見されていた。これは他科も含めて女性教授が

増えないと解決しない問題かもしれない。しかし、これは女性という立場を“利用”して大学・病院・学会等で執行部等に入りやすい、意見を通しやすい、“利点”と捉えられることもできる。筆者も含めそのような機会に駆り出された人間は、女性の、そして男女問わず産婦人科の後進が活躍しやすい環境を作るために尽力する使命があると改めて感じる。

一方、「後進を指導する際に感じていること、意識していること」としては、「育児等の苦勞が理解できるだけに強く言えない」「家族のために仕事を犠牲にする女性医師が多いことが残念でたまらない」としながらも「継続は力なり、と支援を継続する」「管理職等に積極的に挑戦させる」「男性優位の組織の意識改革を目指し、国民・行政に働きかける」等、女性医師に寄り添い、職場と家庭での立場を理解し、葛藤を共有しながらも、それぞれのライフステージに合わせて継続的に支援し、他方組織運営においては、職場環境ひいては組織風土自体を変革しようと尽力されているエピソードが多く浮かび上がった。

最後に、「女性医師に対するメッセージ」としいただいた全ての先生の意見をまとめると「継続は力、ライフステージにより緩急はあっても前進を止めないこと」「自分に与えられた社会的使命を果たす自覚を持つこと」「自分に備わった能力を発揮し、医学のプロフェッショナルとして、夢を実現させていく喜びがあるはず、それを信じて自分でも周囲から応援される環境を築き上げて行ってほしい」となる。当日はこれらをもとにディスカッションを深めたい。

会長特別企画シンポジウム 1 全国大学における女性産婦人科主任教授職の増加のために～産婦人科医療改革グランドデザイン 2023 より

2) 私の考える職場環境整備～女性産婦人科医師の活躍を願って～

名古屋大学 梶山 広明

本シンポジウムのテーマは「全国大学における女性産婦人科主任教授職の増加のために」である。私の所属する大学では、たまたま女性が上級教員層（准教授～講師）を占める割合が多い。彼女たちは家事や育児を行いながら臨床、研究指導、そして大学院生や学部学生の教育に尽力されている。全く毎日頭が下がる思いである。それもあってありがたくも今回登壇の機会をいただいた。何か運営の秘訣を話して欲しいということであった。しかしながら特に秘訣もないし、何か努力していることもない。結果としてそうなっているだけである。ただ日頃、心の奥底で想うところがある。

組織運営は何も産婦人科に限った話ではない。強力な長のガバナンスのもとに構成員が同じ価値基準を携えて、同じベクトルの方向に進むことが望ましい。この同じ方向の理念のためには「平等」の精神の元、皆が数多くの「ルール」に従って動く。そして女性の出産や育児における仕事上の「ブランク」をできるだけ埋める必要がある。そのためには組織はその後の女性キャリア支援に精一杯努めなければならない。そのような運営方針は大変素晴らしいものだと考える。しかしながら、個人の価値判断や物差しとして評価軸は時代に伴って移り変わってくる。常識は時代とともに非常識となり、非常識は常識となる。また人にはそれぞれ得意なことに一定の差がある。組織の価値基準が多様で、得意なことを行った方が皆の仕事のモチベーションが維持しやすいのではないだろうか？そのために組織の中では、各人が必ずしも「平等」でなくヘテロな対応でもよいのではないだろう

うか？全体として調和が取れているならば良さそうにも思える。「ルール」とはできるだけ平等を願うように作られた社会的な取り決めである。「ルール」があると“良いこと”と“悪いこと”の間に線が引かれ、行動規範としてわかりやすい。しかし世の中には「グレー」という一定の幅を持った価値基準がある。「グレー」がなくなり「ルール」が多くなり過ぎるとすべてが膠着してしまい、自由闊達な行動の柔軟性が失われてしまう。「ルール」にも良し悪しがある。

確かに強い組織では短期的にはアウトプットが高くなる。しかしながら、短期的に合理的なことほど、長期的には不合理な結果をもたらすことがある。逆に長期的に合理的なことほど、短期的には不合理にみえることは多くの歴史的事実から読み取ることができる。「ゆるくてもしなやかな組織」の方が長期的にはサステナブルのように思える。そして女性産婦人科医にとって出産や育児は仕事上の「ブランク」ではなく「キャリア」であると心の底から思っている。私は立場上、様々な場面で何か分かったようなことを述べる機会が多いが、当然のことながら月経や妊娠、そして出産を自身として経験したことはない。彼女たちはそれぞれ身をもって体験し仕事に活かしているように見える。せっかくの講演の機会をいただいた。当教室の現状や勤務体制を紹介しながら、老若男女、産婦人科医師の活躍を願って、日頃こうした心の中で雑駁に想っていることを述べさせていだきたい。結果的に女性産婦人科主任教授の増加に少しでも結びつくことができたら幸甚である。

3) 臨床医として学術的好奇心を追い求めるには

東京大学 田 口 歩

東京大学の田口歩と申します。私は、大学に属する中堅医師の立場からどのように大学との関係を継続してきたかということについてお話しをさせていただきます。私は2008年卒ですので、2024年3月で16年間産婦人科医として勤務してきたこととなります。大学の医局に所属し、大学を中心とした勤務を継続しております。大学院を2015年に卒業してからも研究活動を継続しており、臨床・研究の2本柱のもと日々の生活を送ってきました。

私の中での原動力は興味のあること好きなことを突き詰めることです。臨床においては、今の治療法での限界や日々の診療で疑問に思うことを明らかにしたいと常に考えています。最近では、JGOGやJCOGの中で、患者の不均一性に注目した解析を行ったり、プラチナ耐性卵巣癌の治療法の標準化を目指した研究をデザインしたりしています。基礎研究においては、まだ誰も見つけていない知見を見出し、病態の解明や予防法・治療法の開発に繋がるような研究を行いたいと考え、HPV関連子宮頸癌をはじめとして婦人科癌に限らず幅広い分野の研究を行っています。幸い、多くの共同研究者に恵まれ、東京大学産婦人科とい

う組織の中で大学院生たちと10年以上研究を継続してこられています。

大学において、産婦人科の臨床医として、臨床、研究、そして教育を実施していくことは時間的にも体力的にも非常に大変なことだと思います。臨床では一人一人の患者さんとしっかりと向き合っていくということを重視しています。そうすると、今の働き方改革の中で時間内に全てを実施していくことはなかなか難しくなると感じています。さらに、女性に限らないことだと思いますが、家庭との両立ということも非常に重要だと考えております。

私にとっては日々の疑問を解決するための手段や体制が大学や学会には多く存在するため、大学を中心とした働き方を行いたいと考えていますが、今後、多くの産婦人科医が大学での臨床・研究・教育を続けるためには体制の整備も必要になってくると感じます。

学術的好奇心を有する多くの若手医師が、臨床と研究を両立していくにはどうすればよいのかを、私の個人的な経験を踏まえながら皆さんと議論させて頂ければ幸いです。

会長特別企画シンポジウム 1 全国大学における女性産婦人科主任教授職の増加のために～産婦人科医療改革グランドデザイン 2023 より

4) 全国大学における女性産婦人科主任教授職の増加のために必要なことは?

横浜市立大学 宮城悦子

産婦人科医療改革グランドデザイン 2023 において、全国大学における産婦人科主任教授職の女性医師の数を 10 名増加が掲げられている。とは言え、現在私を含め現職の産婦人科主任教授は 4 人であり、その中の 3 人は雇用制度が変わらない限り 5 年以内に定年退職となり、このままでは残るは 1 人のみとなる絶滅危惧種である。では、どうしたら複数の産婦人科女性教授がコンスタントに誕生することができるのか?グランドデザインの中で掲げられたこの悲惨な現状の要因は以下の 4 点とされている①キャリアで専門医取得が重要視されており、実際に取得率が高いが学位取得率は低い ②年齢とともに医育機関での勤務者が激減している ③30 代後半から一定の割合で短時間勤務となっている ④就労緩和と産前産後休業はだいたい取得しているが、妊娠出産を契機とした離職は約 20% に認められる。

一方、日本という国の現状を俯瞰すると、毎年公表され報道される、World Economic Forum による Global Gender Gap Report の 2023 年版では、相変わらず日本は底辺にあり 146 カ国中総合 125 位である。重要な各々のインデックスとして、Economic Participation and Opportunity 123 位、Educational Attainment 47 位、Health and Survival 59 位、Political Empowerment 138 位という結果である。この結果は、前述の産婦人科女性医師が最前線で活躍できない現状とも重なる。

では、今後どうしたら 10 人の女性主任教授を産婦人科は排出できるのか? 候補となるべき女性医師がしなやかに自分の強みを発揮し、次々と組織のリーダーとなっていくためには、日本の空気を入れ替えるほどの意識改革が必要であると私は考えている。それは、女性を深く理解している私たち産婦人科医師ならできるのではないかと

思っている。妊娠・出産・授乳という、女性にしかできない役割りを果たす期間に仕事のペースが落ちることは止むを得ない。しかし、その時期を除いては全ての社会的な役割は、男女の区別なく行うべきという意識が、男女とも当たり前のことという教育を受け、その意識が浸透すれば、日本は変わるのではないかと。少子化対策も女性の活躍も、中途半端な手立てしか講じることができないわが日本を嘆いているだけでは始まらない。Global Gender Gap のインデックス上位の多くの国では当たり前である、男女の区別も差別もなく多様性を活かすことができる国になるためには、全てのジェネレーションの仕事への意識や価値観が変わるしかないと考える。

最後に自分の経験も踏まえて、産婦人科の診療や研究に矜持を持って取り組み、奔走している若い医師に男女の区別のないエールを送りたい。まずは、自分が医師として研究者として夢中になれる大好きな何かにすでに出会っているなら、その宝物を大事に育てたい気持ちを愛するパートナーや家族も含めて、周囲の大切な人々と分かち合っていて、前に前に進んでいきたきたい。また、まだその対象が見つからない医師は、その時に備えて研鑽を積んでいただきたい。周囲の理解なしに臨床医としての一流の技術を身に付け、最先端の研究も成し遂げることはできない。前途有望な医師としての大きな夢を持つ若い産婦人科医師が、男女の区別なく産婦人科学という魅力的な学問の進歩の中で、臨床医として研究者としての最大の喜びを得ていくことを願って止まない。そのような産婦人科専門医が増えることが、自然と産婦人科女性主任教授誕生につながるものと考えている。

会長特別企画シンポジウム2 産婦人科領域における産学連携のコツ～AI 研究を通して

1) 医療 AI の社会実装に向けた取り組み：研究の立案から薬事承認まで

国立がん研究センター研究所医療AI研究開発分野 浜本 隆二

近年、深層学習技術の中核とした機械学習技術の発展、GPU など計算機環境が進歩したこと、さらに公共データベースの発展などの理由によりビッグデータを利活用する環境が整備されたことなどを要因として、人工知能 (AI) 技術への期待が高まっている。2016年1月22日に閣議決定された第5期科学技術基本計画において、「Society 5.0」という新しい社会の創成が明文化されたが、その実現にAIが基盤技術として重要であることが明文化されており、AIの研究開発は我が国の科学技術政策の中でも、重要視されてきた。2022年6月3日に閣議決定された統合イノベーション戦略2022においても、引き続き「Society 5.0」が我が国の目指すべき社会であり、その実現に注力することが明文化されており、現在においてもAI研究開発の促進は本邦の科学技術政策において重要な位置付けとなっている。

AI研究の歴史は比較的長く、半世紀以上も前である1956年には、米国ダートマス大学で開催されたダートマス会議において、ジョン・マッカーシーにより「Artificial Intelligence」という言葉が学術用語として使用されている。しかしAI研究の歴史は決して平坦なものではなく、世の中の大きな期待に基づく所謂「ブーム」と呼ばれる期間、また期待に十分応えることができず失望に変わっ

た「冬の時代」と呼ばれる期間を繰り返し、現在は一般的に第3次AIブームと呼ばれる期間であると認識されている。一方、第3次AIブームがこれまでのブームと一線を画するのが、既にAI自体が社会の様々なところで活用されていることが挙げられる。例えば、最近では空港などにおいて顔認証が幅広く導入されており、また自動翻訳・音声認識も社会のあらゆるところで活用されている。その状況は医療分野でも例外ではなく、米国FDAに承認されたAI搭載の医療機器（主にプログラム医療機器）の数は500種類以上にのぼり、日本においても我々の研究成果を含め複数のAIを活用した医療機器が薬事承認を受けている。さらに、2017年にTransformerが登場して以来ChatGPTをはじめとした生成AIに大きな注目が集まっており、社会現象に近い形で幅広い分野で活用が進んでいる。生成AIの台頭に伴い、益々AIへの期待が高まっており、今後も医療AIの社会実装は加速していくと予想している。

本講演においては、CREST、PRISM及びBRIDGEという三つの本邦における大型医療AIプロジェクトを推進し、研究の立案から薬事承認までの全ての過程を取り組んだ経験を基に、医療AIの社会実装に向けた取り組みを紹介する。

会長特別企画シンポジウム2 産婦人科領域における産学連携のコツ～AI 研究を通して

2) 胎児心臓超音波スクリーニング支援 AI システム—産婦人科医の視点—

昭和大学 小松玲奈

先天性心疾患を有する新生児の頻度は、全出生児の約1%と比較的低いが、予後の改善・出生後の治療のための準備・適切な分娩施設の選択・医療経済的利点などの観点から出生前診断は非常に有用である。本邦では、検査者の技術や画像技術の進化によって胎児心エコー検査は大きく進歩している。通常の妊婦健診を担う産婦人科医には基本的な胎児心臓超音波スクリーニングの知識が要求される。しかし、実際には検査者や超音波診断装置によってスクリーニングの成績は異なっており、先天性心疾患の出生前診断率は頭打ちの状態である。出生前診断されない理由としては、① 診断に適さない画像、② 検査者の認識不足、③ 検査者の走査不良などが考えられる。超音波検査はプローブを手動走査することで画像を取得するため、検査者の熟練度によって診断技術の差異も大きくなる。また、超音波画像はアーチファクトの影響を受けやすく、画質劣化および診断精度低下につながるため、その画像精度管理には特有の課題が存在する。これらの課題解決に向けた取り組みの一端として、我々は胎児超音波検査において最も診断技術を要求される胎児心臓を研究対象とした。

人工知能 (artificial intelligence : AI) は大量のデータを効率的に学習することでパターンや関連性を見出すことができる。また、ヒトのような経験や熟練度による個人差はなく、主観的なバイアスを持たずデータに基づいた客観的な判断をすることができる。以上のことから、「ヒトとAIとの協働」によってより正確で効果的な胎児心臓超音波スクリーニングを実現することを目的として、AI

を用いた胎児心臓超音波スクリーニング支援システムの研究開発を進めている。我々の技術は超音波動画からスクリーニングを支援することができる。胎児心臓超音波スクリーニングにおいては、基本断面である腹部断面・四腔断面・左室流出路断面・右室流出路断面・三血管断面・三血管気管断面の確認が推奨されている。しかし、静止画像だけでは正常・異常判定が困難な場合や異常所見を描出できない可能性がある。動画であれば各部位の連続性の確認とともに後方視的な検証も可能となることから、静止画像のみならず動画を用いたスクリーニングが重要と考えている。

AIは「診断に適さない画像」から先天性心疾患を見出すことはできない。画像が診断に適した画像か否かを判断したり、異常所見を認める際に注意喚起したりすることが可能である。さらに、基本断面のチェックリスト表示や胎児評価指標の自動計測などにより検査の効率化にもつながる。

これまで我々が実際に胎児超音波AIの研究開発に取り組んできた経験から、医師単独での研究には限界があり、医師とAI工学者との学際的なコミュニケーションが重要であると言える。胎児心臓超音波スクリーニングの際に、熟練医はどのような視点で検査を行なっているのか、修練医にとって何が困難であるのかなど、臨床的に重要なポイントをAI工学者と共有する必要がある。産婦人科医療における超音波検査の重要性は高く、胎児超音波AIの実臨床応用は今後さらに進むものと思われる。

会長特別企画シンポジウム2 産婦人科領域における産学連携のコツ～AI 研究を通して

3) 胎児心臓超音波スクリーニング支援 AI システム—研究開発者の視点—

理化学研究所革新知能統合研究センターがん探索医療研究チーム、国立がん研究センター研究所医療 AI 研究開発分野

小松正明

超音波検査は簡便性・リアルタイム性に加えて、母体・胎児への非侵襲性に優れているため、産婦人科領域の医用画像診断において最も重要な役割を果たしている。しかし、超音波検査には他モダリティと比較して特有の課題が存在する。まず、超音波画像はプローブの手動走査によって取得するため、検査者や施設間での診断技術の差異が大きく、画像精度管理に問題が生じている。例えば、胎児心臓は拍動を伴う小さく複雑な構造であり、その観察には高度な走査技術と専門知識が必要とされるため、先天性心疾患の出生前診断率はいまだ十分とは言えない。また、超音波画像は空間分解能が低く、ノイズやアーチファクトが出現しやすいことも課題として挙げられる。よって、超音波画像に対する診断支援 AI の研究開発が求められているが、その技術的困難さから、世界的にもこれまで承認を取得した医用画像診断用 AI 搭載医療機器プログラムの対象は CT 検査・MRI 検査・X 線検査に関連するものが多く、超音波検査についてはまだ少ないのが現状である。

本講演では、産婦人科領域における超音波画像 AI の研究開発事例や、私たちの社会実装を志向した取り組みを紹介する。例として、これまでに発表されている胎児超音波画像 AI の主な対象としては、基本診断面の自動抽出、解剖学的構造の自動解析、胎児バイオメトリクスなどの自動評価が挙げられる。私たちは胎児心臓超音波スクリーニング支援技術として、正常胎児データを用いた教師あり学習により、正常からの逸脱を異常所見として検出する手法を開発した。また、超音波動画にお

いて時系列情報を活用することによってノイズを軽減しセグメンテーション性能を向上させる手法も報告している。なお、AI の一つの技術領域である深層学習の問題点として、データから獲得された入出力の関係性が複雑で理解が困難となるブラックボックス問題が挙げられる。そこで、私たちは診断根拠となる出力結果の説明可能性を向上させるため、動画情報を二次元データに変換し、各診断部位の確信度の累積・時間経過を可視化して一覧表示する技術 barcode-like timeline を開発した。さらに、多層構造のオートエンコーダを用いて、超音波プローブの走査速度や前後の戻りといったノイズに依存しない新たな説明可能表現である graph chart についても報告している。

さらに、私たちは医師読影試験を実施し、実際に非熟練医が胎児心臓超音波スクリーニング支援 AI システムを参照することで判定精度の向上が認められるかを検証した。また、深層学習は大量の学習データを必要とするデータ駆動型アプローチであるが、一般的には医療現場で取得できるデータ数には限りがある。一方、データ数を増やすために多施設からデータ収集した場合には、施設間や機種間で学習データとテストデータの分布が一致しないドメインシフトが発生しやすく、モデルの性能低下につながってしまう。よって、超音波画像 AI の実臨床応用に向けては、前述の画像精度管理、説明可能性、ドメインシフトなどの課題解決に向けた基盤技術や研究開発知見を積み上げていく必要がある。

会長特別企画シンポジウム2 産婦人科領域における産学連携のコツ～AI 研究を通して

4) AI 初学者による企業との共同研究の進め方～深層学習による子宮肉腫の術前画像診断システム開発を通して～

東京大学 豊原 佑典

人工知能 (Artificial intelligence : AI) において、深層学習 (Deep Neural Network : DNN) により人間では識別できない多数のパラメータを評価することが可能となり、医療画像の解析の分野でも実装が進んでいる。我々は AI 開発企業、放射線科医師とともに DNN による子宮肉腫の画像診断の検証を行った。

子宮肉腫は予後不良な希少癌であるが、その診断において子宮筋腫と鑑別診断が必要であり、妊孕性温存や腹腔内腫瘍飛散の観点から診断精度の向上は非常に重要である。Magnetic resonance imaging (MRI) が有用となるが、特に変性子宮筋腫では画像的特徴が子宮肉腫と類似することが課題となる。

DNN では一般的に大量のデータの学習が必要な側面があり、子宮肉腫の画像診断においてはその検証がなされていなかった。本発表では、AI 研究における共同研究の具体的な進め方や希少癌に対して症例数を補うための創意工夫について発表する。

隔週のオンラインミーティングを通して、我々産婦人科医師、AI 開発企業、放射線科医師で研究の立案や進捗の報告を行った。症例数を補うためには3施設による共同研究体制を構築し、第一段階として子宮肉腫63例、子宮筋腫200例を後方視的にエントリーした。また、MRI シークエンスを15種類採用することで画像数の確保をおこなった。症例ごとに撮像したMRI シークエンスが異なり、DNN では欠損データの対応が問題となるが、各予測結果を陽性 (子宮肉腫)、陰性 (子宮筋腫) でスコア化し、合計スコアで評価する工夫を行った。データセットはオーグメントを行い、5 : 1

のクロスバリデーションのデータを用意し、MobileNet V2 というネットワーク形状で DNN モデルを生成した (子宮肉腫鑑別 DNN モデル)。さらに DNN モデルの客観的評価指標として、3名ずつの放射線科専門医と放射線科専攻医による読影実験を計画し、1回目の読影実験では、DNN モデルが学習・評価した同一の画像を読影し、子宮肉腫・子宮筋腫の2種類の評価で解答した。1か月の忘却期間の後、2回目の読影実験では、DNN モデルが導き出した評価を付随して、同一の画像を読影した (AI 補助診断)。

結果として、正診率 90.3% の DNN モデルの生成に成功した。1回目の読影実験での放射線科専門医の平均成績は正診率 88.2%、であり、DNN モデルの結果が放射線科専門医相当であったことが示された。1回目の放射線科専攻医の平均は正診率 80.1% であったが、AI 補助診断では正診率 92.2% と成績向上を示し、我々の DNN モデルが診断補助として有用な可能性を示した。

子宮肉腫鑑別 DNN モデルでは、医師が子宮腫瘍を含む画像を抽出する必要があり、実装には課題があったため、我々はさらに開発を進め、子宮腫瘍を判別する DNN モデルを生成した。これを既存の子宮肉腫鑑別 DNN モデルに組み合わせることで、子宮肉腫自動診断 AI システムを構築した。そして未学習の32例のデータセット (子宮肉腫8例、子宮筋腫症24例) を用意し、評価を行ったところ、正診率は92.44% となった。同データセットを放射線科診断医が診断したところ正診率が84.38% であったため、未学習データに対しても高い診断精度が得られることが示唆された。

上記の内容はすでに報告しているが、AI につい

て造詣の浅い一臨床医が AI 開発企業、放射線科
医師と共同研究を行い、データ量の少ない希少疾
患の画像診断の研究を進めていく過程での創意・

工夫を報告し、今後の更なる産学連携の発展に役
立てる。

会長特別企画シンポジウム2 産婦人科領域における産学連携のコツ～AI 研究を通して

5) 希少疾患を対象とした AI の産学連携共同研究における課題への取り組み

サイオステクノロジー株式会社エンジニア・クリエイターCoE 野田 勝彦

産学連携のひとつの形態である完全に対等な関係での共同研究においては、営利活動を目的とした一般民間企業にとって、受託研究とは異なり、研究費用が大きな課題(①研究費用問題)となる。また、産科婦人科領域において特に AI のサポートが期待される希少疾患の研究においては、AI の学習に利用できる症例数が圧倒的に少ないという問題(②データ不足問題)が存在する。さらに、

東大病院 豊原佑典医師らと行った MRI 画像を用いた子宮肉腫診断 AI の研究においては、MRI のシーケンスが不揃いであるという問題(③不揃いデータ問題)が存在した。本講演では、これらの3つの問題(①研究費用問題、②データ不足問題、③不揃いデータ問題)にどのように取り組んだかを報告する。

会長特別企画シンポジウム2 産婦人科領域における産学連携のコツ～AI研究を通して

6) デジタル技術による持続可能な医療

サスマド株式会社 上野 太郎

医師の働き方改革をはじめ医療の効率化が課題となる中、医療分野におけるデジタル技術の活用が求められる。コロナ禍で日本におけるデジタル化の遅れが露見し、デジタル庁の設立やIT人材の育成強化の対策が進められている。睡眠医療においては、不眠症に対する治療法として非薬物療法である認知行動療法が推奨される一方で、医療現場におけるリソース不足から実臨床での普及が課題となっている。近年、薬機法の規定するプログラム医療機器としてモバイル端末を用いた治療用アプリが開発され、疾患治療のために医療現場での普及が進んでいる。英国政府ガイドラインでは不眠症治療において、睡眠薬ではなく治療用アプリを推奨しており、エビデンス・プラクティス・ギャップを埋めるための治療手段として活用されている。我々は日本における不眠障害治療において国内外のガイドラインで推奨する認知行動療法の普及を目指し、不眠障害に対するdCBTを実施するプログラム医療機器を開発してきた。本品は独立行政法人医薬品医療機器総合機構への相談を経て、GCP省令下における治験を実施した。本治験は2021年5月より国内の複数医療機関にて、ICSD-3の診断基準における不眠障害の患者を対象に実施された。同意取得した患者は治療用アプリ群とシャムアプリ群に無作為化され、8週間の治療介入とその後2週間のフォローアップが行われた。主要評価項目であるAIS（アテネ不眠尺度）の変化量（mean ± SD）において、8週時点で治療用アプリが -6.7 ± 4.4 （95% CI -7.6 to -5.8 ）に対して、シャムアプリが -3.3 ± 4.0 （95%

CI -4.1 to -2.5 ）であり、 $p < 0.001$ と有意な治療効果を認めた。さらに治療介入後の10週時点においても、AISの値は治療用アプリで 5.9 ± 4.0 （95% CI 5.1 to 6.7 ）、シャムアプリで 9.7 ± 4.9 （95% CI 8.7 to 10.6 ）、 $p < 0.001$ となっており、睡眠薬で課題となる離脱症状である反跳性不眠の副作用がなく、治療効果が維持されていることが確認された。本邦における治験結果を受けて、2023年2月15日、本品は不眠障害に対するプログラム医療機器として厚生労働省による承認を受けている。さらにアカデミアとの共同研究を通じて、産婦人科領域における早期診断や治療を目指したプログラム医療機器の開発を進めている。

さらに、臨床研究・治験の停滞は、日本において医薬品・医療機器の承認の遅れの原因となり、適切な医療を国民が受ける上での障害となりうる。我々はブロックチェーン技術の医療応用を目的とした研究開発を2016年より行い、複数特許を取得するとともに、システムへの実装と臨床試験での活用を報告してきた。本取り組みは内閣府による規制のサンドボックス制度に認可され、国立がん研究センターとの実証試験を実施した。得られた成果をもとに2020年12月に政府による我々の技術に対する承認通知が発出された。その後、複数のAMED事業を大学病院や国立センターと実施した他、企業治験での活用も開始している。

本講演では、デジタル技術を活用したプログラム医療機器開発や臨床開発の取り組みについて紹介するとともに、その展望について考察する。

会長特別企画シンポジウム3 こども家庭庁を中心とした行政の連携と母子保健の今後のあるべき方向性

1) こども家庭庁の創設と母子保健行政の最近の動向

こども家庭庁成育局母子保健課 木 庭 愛

令和5年4月、こども政策を社会全体で総合的かつ強力に推進していくための包括的な基本法として「こども基本法」が施行され、政府全体のこども関連政策の司令塔として「こども家庭庁」が創設された。こども家庭庁は、「こどもまんなか」をスローガンに、すべてのこどもが健やかに育つ社会を目指し、こどもや子育て家庭の視点に立った政策を進めている。

母子保健分野では、母子保健法等に基づき、妊娠・出産・子育て期にわたる切れ目のない支援を実施するとともに、成育医療等基本方針等を踏まえ、こどもの心身の健やかな成育が確保されるよう、医療・福祉・教育等の幅広い分野との相互連携を図りつつ、科学的知見に基づく成育医療等の提供に関する施策を推進することとしている。

令和5年6月に閣議決定された「こども未来戦略方針」においては、こどもを産み育てることの素晴らしさ、意義を実感できる社会を実現すべく、今後3年間で集中的に取り組むべき施策として、産後の心身の負担軽減を図るとともに、育児をサポートする観点から、産後ケア事業の実施体制の強化や乳幼児健診等の推進等を実施することとされた。

産後ケア事業は、令和3年度より、母子保健法に基づき、市町村が実施体制の整備に努めることとされ、令和6年度中の全国展開を目指している。国においても、産後ケアを実施する施設等に対する施設整備補助を通じて提供体制の強化に取り組むとともに、利用者負担の軽減を図るため、令和5年度からは、産後ケアを必要とするすべての方に利用料減免の対象を広げ、産後ケアがユニバー

サルサービスであることを打ち出している。一方で、実施主体である市町村からは、委託先の確保や、精神的ケアを必要とする方への対応に課題があるとの声もあり、今後は、都道府県に、委託に関して、複数の市町村間での広域調整や、産後のメンタルヘルスケアに関して、行政や精神科医療機関等関係者間での連携の強化等に取り組んでいただけるよう体制整備や支援を行っていくこととしている。

また、母子保健のデジタル化も今後の主要な課題の一つである。妊婦健診や乳幼児健診等母子保健に関する情報について、国民、自治体、医療機関等の中で、効率的に共有・連携できるよう、情報連携基盤を整備する方針であり、令和5年度から、先行的にいくつかの自治体において、情報連携基盤を活用した実証事業に取り組んでいる。将来的に、全国の自治体、医療機関で体制が整備されれば、国民にとっての利便性の向上、医療機関や自治体における事務負担の軽減が図られるほか、里帰り出産をされた妊産婦についても、こうした共通基盤を用いた自治体間での効率的な情報連携により、必要な支援に迅速につなげることができる効果も期待される。

こうした政府方針を着実に実現させるために、地域の実情やニーズに応じたサービスを提供いただく自治体や保健医療福祉の関係者の皆様とともに、こどもや子育て家庭に寄り添った施策を展開してまいりたい。

この機会に、こども家庭庁の創設の意義も含め、母子保健行政の最近の動向について概説する。

会長特別企画シンポジウム3 こども家庭庁を中心とした行政の連携と母子保健の今後のあるべき方向性

2) 厚生労働省における女性の健康に関する取組状況について

厚生労働省健康・生活衛生局健康課 山本英紀

女性は、ライフステージごとに女性ホルモンが劇的に変化するという特性があり、これらを踏まえて、性差に着目して健康に関する取組みの推進する必要があることから、令和6年から開始する健康日本21（第三次）では、女性に多いやせ、骨粗鬆症、女性の飲酒及び妊婦に関する目標を設定しています。

また、厚生労働省では、月経痛や月経前症候群等の月経に関する様々なトラブルについての情報発信や、セルフチェックの結果に基づく医療機関

への受診勧奨等について、女性の健康に関する情報提供サイトである「女性の健康推進室 ヘルスケアラボ」を通じて積極的に実施し、月経に係る問題を抱える女性の支援を推進するとともに、自治体や関係団体等と連携した女性の健康リテラシーの向上に向けた各種の啓発・行事等を展開するために、3月1日から8日の「女性の健康週間」の取組について、ホームページやSNS等の様々なコンテンツを活用した情報発信や、好事例の横展開を図るなどの取組を行っています。

会長特別企画シンポジウム3 こども家庭庁を中心とした行政の連携と母子保健の今後のあるべき方向性

3) 周産期医療提供体制の確保について

厚生労働省医政局地域医療計画課 佐々木 孝 治

我が国では少子化が叫ばれて久しい。こうした中、地域において安心・安全な周産期医療提供体制を構築することは重要な課題である。産科医等分娩を取り扱う医師の数は微増しているものの、出産年齢の高齢化等妊産婦のハイリスク化が生じていることから、分娩医療機関の集約化・重点化は重要な方策の一つと言える。

また、出産時だけでなく、その前後においても母子に対する切れ目のない支援を提供する観点から、医療と母子保健等との連携が必要であり、都道府県、市町村など関係機関による連携体制を構築することが重要である。

以上については、令和6年度から開始される第8次医療計画の策定指針において示しているところである。また、同指針では、分娩医療機関の集約化・重点化によるアクセス面の課題について、

都道府県に対策の検討を要請している。

併せて、産科医等の確保が重要である。医師確保については、各都道府県において医師確保計画を策定し、各種の取組を進めている。具体的には、医学部入学定員に地域枠を設定して修学資金を貸与するほか、専門医資格の取得など本人のキャリアパスに配慮しつつ、医師不足地域等で従事することができるようキャリア形成プログラムによる支援を行っている。また、助産師外来の開設など、産科医以外の職種へのタスク・シフティングやタスク・シェアリングによる勤務環境改善等の取組も挙げられる。

厚生労働省では、地域医療介護総合確保基金等により、こうした取組に対する支援を行っている。これらの取組により、引き続き、周産期医療提供体制の確保を図っていく。

会長特別企画シンポジウム3 こども家庭庁を中心とした行政の連携と母子保健の今後のあるべき方向性

4) こども家庭庁を中心とした行政の連携と母子保健の今後のあるべき方向性～セクシュアルリプロダクティブヘルスアンドライツ (SRHR) の観点から見た連携～

大阪大学 木村 正

こども家庭庁はこれまでの内閣府、文部科学省、厚生労働省こども家庭局が合体して新たに発足した組織である。我々の領域に関しては、これまでの母子に関する福祉・母子保健を主に担当し、地域医療計画を担う厚生労働省医政局、医療保険を担う厚生労働省保険局とは別組織となったわけで、周産期医療をめぐる全貌に関して言うと関係省庁が厚生労働省とこども家庭庁に分かれてしまい、ステークホルダーが増えたともいえる。

妊娠・出産の支援、という文言はあるが、「こどもまんなかの社会を実現する」というスローガンが掲げられている。産む性を有する方々の自己決定の尊重という考えなしには子供を産み育てよう、という意欲が生まれにくい社会の中で今後どのような支援が必要なのか連携して考えてゆきたい。

妊娠の支援、と言う観点でこども家庭庁発足前に最も深く日本産科婦人科学会とかかわりがあったのは厚生労働省母子保健課であった。令和元年に本会は母体血を用いた新しい出生前遺伝学的検査 (NIPT) が非認定施設で十分な情報提供なく広く行われていることを問題視し、NIPTに関する指針の改訂を行った。その改訂に際し、他学会から様々な指摘があり、同年6月21日付の母子保健課からの要望書によりこの改訂に当たり、「国においてもNIPTに関する審議会を設置し必要な議論を行うので、実施についてはその議論を踏まえて対応されたい」との要望を受け、改訂された指

針の運用を一時中止したことは記憶に新しい。その後厚生労働省が設置を後押しした日本医学会出生前検査認証制度等運営委員会において産婦人科医だけではなく小児科医、遺伝専門医などの医師以外に患者団体、一般の方々も含む多くの方々が集まり議論を重ね、こどもを産み育てる方々の意向も汲んだ結論に落ちついたと考える。現在NIPTはこの委員会の指針に基づいて運用がなされている。我々にとってこの時の一連の騒動から得た教訓は、結局本会はプレイヤー(実践者)であって、プレイヤーがルールを決めて審判をするような制度はいくら理にかなったルールを作っても社会的な受け入れは困難である、ということであった。我々は医学医療のプロとして新しい医学を切り開く研究を行い、よい医療を国民に提供し、様々な研究結果から得られた正しい情報やSRHRの考え方を国民に伝えることに徹する。その実践に当たりルールが必要であれば今後はこども家庭庁などが関与する第三者機関で決めていただく、もちろん我々も参画させていただき意見を述べ、その根拠となる適切な情報提供を行う。このようなお互いの連携と幅広い層からの意見聴取が、SRHRの観点から見たより良い妊娠・出産の支援、母子保健の実現に重要となる時代となったと認識している。この時代認識に従い、これまであった様々な本会の見解、すなわちプレイヤーが作ったルールを見直してゆく必要があると考えている。

会長特別企画シンポジウム 4

遠隔医療シンポジウム

近年、医療分野での技術革新や COVID-19 蔓延等により医療を提供する体制が従来に比べ複雑化している。特に外来診療においては、これまで当然のように行われていた対面での診療に対し情報通信技術を用いたオンラインでの診療という選択肢も検討可能な時代となっている。オンライン診療をはじめ、情報通信技術を活用し医療を提供することは、患者満足度を向上させるうえでこれまで以上に重要な選択肢となる可能性がある。

オンライン診療に焦点を絞ると、本邦では平成30年3月に「オンライン診療の適切な実施に関する指針」の発表、令和2年の新型コロナウイルス感染症の蔓延を受けた電話・オンライン診療の特例的・時限的緩和等により、情報通信技術を用いた診療の活用が医療現場で進められてきた。実際にオンライン診療を活用することで、診療に対する患者のアクセシビリティの向上、治療継続率の向上、時間的負担軽減等のメリットを享受できる可能性が考えられている。ただその一方で、オンラインでは安全に治療を実施できないのではないか、治療の有効性が担保できないのではないか、などのような懸念の声も存在する。

本シンポジウムでは、婦人科領域に加えて精神科領域の医療者、オンライン診療普及の国策に関わった国会議員、オンライン診療を実際に活用する患者など様々な立場からの発表をもとに、対面診療の課題からオンライン診療への期待、オンライン診療普及までの展望について議論する予定である。

シンポジウムの5名の演者の講演の概要を紹介する。

まず冒頭2つの講演では、婦人科領域の識者に

加えて、オンライン診療が進む精神科領域の識者が登壇し、対面診療の課題、並びにその課題解決のためにオンライン診療はどのような期待を担うのかについて論じて頂く。

続いて、フェムテック推進・オンライン診療普及の国策に関わった国会議員からの講演として、本邦でのオンライン診療普及のきっかけ、普及施策のための取り組みなどを紹介頂く。医療者の立場ではなく、国がオンライン診療に対しどのような目線を持ち考え行動してきたかを発信することで国の動向を聴講者が理解するのに役立つものと思われる。

続く2つの講演では、オンライン診療を積極的に活用する医療者及び患者の立場より、オンライン診療の重要性やその効果的な使い方などについて説明頂く。医療者からはオンライン診療導入のTipsやオンライン診療の一つのツールである「スマルナ」に対する診療上の位置づけが発信され、患者からは「スマルナ」を使用するに至った背景、使用効果、評価等が発信されることを通じて、オンライン診療導入に障壁を抱える医療者や患者満足度向上に課題を抱える医療者への展望となることが期待される。

5つの講演の後に、婦人科領域にオンライン診療を普及させるための課題と解決策について登壇者間でパネルディスカッションを行う。パネルディスカッションを通じてオンライン診療普及までの課題やその解決策について議論を深める。

会長特別企画の本シンポジウムは、オンライン診療に対する多面的な理解を深め、その活用方法を未来志向で考える貴重な機会であり、多くの先生方の参加・聴講を期待したい。

会長特別企画：教育講演 16+フォーラムディスカッション（クロスオーバー講演） 新時代の産婦人科教育を考える

新時代の産婦人科教育を考える～教育の悩みを共有し、最適解を見つけよう～

岐阜大学¹⁾、鳥取大学²⁾、順天堂大学³⁾、大阪大学⁴⁾、札幌医科大学⁵⁾、岡山大学⁶⁾

磯部真倫¹⁾、小松宏彰²⁾、竹田純³⁾、角田守⁴⁾、
玉手雅人⁵⁾、衛藤英理子⁶⁾

日本産科婦人科学会は、これまでも教育に力を入れる学会の一つとして様々な活動を行ってきた。サマースクールなど産婦人科医を志す学生や研修医に対して産婦人科の魅力伝えるセミナーの開催だけでなく、忙しい指導医にとって便利な医学生、研修医に対する教育ツールを開発してきた。加えて令和2年度からは、卓越した教育活動を行う産婦人科医を表彰する教育奨励賞を創設し、教育を業績として評価している。また、令和5年度からは教育委員会 医学教育活性化小委員会が主催となり Faculty development (指導医養成) が始まり、日本産科婦人科学会の教育は新たなフェーズに入った。現在、産婦人科医の中で教育の熱は確実に高まっている中、これからの産婦人科領域の教育はどこへ向かうのであろうか?本シンポジウムでは、歴代の教育奨励賞受賞者が集い、受賞後の教育活動を共有し、教育に興味のある産婦人科医のキャリア形成について考えるだけでなく、現場の指導医の皆様の教育の悩みを共有し、討論する。参加者全員で教育のコミュニティを形成し、新時代の産婦人科教育を考えるきっかけとなれば幸いである。

第一部 教育を専門とする産婦人科主任教授の

キャリア

医師は臨床・教育・研究を3本柱として日々精進しなければならないとされる。しかし、日本の学会では、臨床、研究に比して、教育は軽視される傾向にある。そのような状況の中、私はこれまで「教育」というものを専門にし、人材育成の中で臨床医として社会に貢献してきた。一連の教育業績が評価され2023年6月1日より、岐阜大学産婦人科学主任教授を拝命することになった。教育を専門とする産婦人科医の私のキャリアを振り返る中で、会員の皆様にとって医師のキャリアにおける「教育」の位置づけについて再考するきっかけとなれば幸いである。

第2部 教育の悩みを共有し、最適解を見つけよう

これまで教育奨励賞を受賞したメンバーが参加し、受賞後の教育活動を発表していただき、教育奨励賞がその後のキャリアに与えた影響を述べていただく。その後の総合討論では、スマートフォンを利用した双方向のオンラインツールを用いて、参加型の討論を行う。現場の指導医の悩みは多種多様である。これらを共有し、会員の皆様と討論を行うことで、明日からの指導につながる教育の最適解を模索できればと考えている。

医会・学会共同企画「生涯研修プログラム」生涯研修プログラム9 P

近年の産婦人科医療の様々な課題を考える・1

1) 日本の性教育の現状と課題

愛育病院 安達知子

性教育は人が生きていくために必須の教育である。あらゆる年齢層に必要な教育とも言えるが、その基本は子どもたちに対する教育で、科学的かつ有効に学ぶために、世界的にも学校での教育が基本となる。日本では主に保健体育の授業で行われている。性教育を通して、子どもたちは子どもから大人へと変化するからだと心の発達、すべての生物に存在する生殖の仕組みを学ぶが、特に人では生殖の手段が性交であること、一方、性交が生殖とは関係のない【人とのコミュニケーション】や【愛情表現】に大切な手段であることなども学ぶ必要がある。現在日本では、学習指導要領の解説に記載されている、いわゆる【歯止め規定】—その主たる内容は中学校の教育では【性交】については取り扱わないとするもの—のため、性交とこれに関連した大切な項目—妊娠を疑う症状

やその時取るべき行動、避妊、人工妊娠中絶、母体保護法など—について義務教育終了までに学校教育の中で学ぶことが困難となっている。しかし、性や性行動を考える上で、人との関わり、相手との距離感、同意の取得、嫌なことは嫌【No】と言えること、相手の【No】を受け入れられること、自分を大切に思うことやそう言える権利、多様性の理解とそのための行動などが必要である。2023年7月に改正刑法で性交同意年齢は明治以来の13歳から16歳未満【13-15歳は条件付き】へと引き上げられた。先進国では性交同意年齢までに通りの人間関係性を含めた包括的性教育を終えるカリキュラムとなっている。本講演では日本における性教育の現状を示すとともに、これからの課題と推進すべき方向性を日本産婦人科医会の活動から解説する。

2) ドメスティック・バイオレンスゲートキーパーとしての産婦人科医の役割

女性クリニック Wel Toyama 種部恭子

ドメスティック・バイオレンス(DV)は、親密な関係にあるパートナーが身体的・精神的・性的暴力を用いて怖がらせ、被害者の自己決定能力を奪い支配するものである。殴る、蹴る、突き飛ばすなどの身体的暴力よりも、怒鳴る、不機嫌、生活費を渡さないなどの精神的暴力が圧倒的に多いためDVに気づきにくく、逃げる選択を決意することも容易でない。長期間支配が続くため複雑性PTSDを発症しやすく、暴力が原因とは気付かないまま被害者は心身に不調を来す。感情の調整や対人関係の困難により社会生活に支障を来しやすく、不眠や慢性疼痛など機能的な身体症状による反復受診も特徴的である。

DVにより望まない妊娠、妊娠合併症、中絶、性感染症などのリスクが高まるため、産婦人科が発見の窓口となることは少なくない。子どもがいる場合、暴力の見聞き(面前DV)が子どもの脳発達

に与える影響は多大であり、被害親は子どもを守ることができないか、虐待に加担している場合もある。面前DVによるトラウマや愛着障害は、対人関係の障害や自己肯定感の低下を来すため、暴力が世代間連鎖するリスクが高い。

2024年4月に施行される改正DV防止法では、DV被害者の安全を守るための保護命令の発令に際して、医師による心身の障害の診断が重要な意義を持つようになる。健康障害や子どもの問題での医療機関受診、また緊急避妊や予期せぬ妊娠による受診がDVに気づき世代間連鎖を止める入口になる可能性は高く、また妊婦への暴力は自殺や重篤な外傷など生命の危険が迫るリスク因子の一つである。被害者支援のゲートキーパーとして、被害者の自己肯定感の回復を支援し逃げる選択を提示するなど、公衆衛生上の重要な課題解決の一翼を担う立場で取り組むことが求められる。

医学会・学会共同企画「生涯研修プログラム」生涯研修プログラム9 P 近年の産婦人科医療の様々な課題を考える・2

3) 産婦人科の視点からのLGBTQ

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中塚幹也

2023年には、LGBT理解増進法が成立、最高裁が戸籍の性別変更のための「性同一性障害特例法」の手術要件（生殖不能要件）を違憲とした。このように、日本社会は大きく変化している。LGBTQ（性的マイノリティ）当事者のうちでも、トランスジェンダー当事者の場合、医療とつながることでメリットの大きい一群があり、ジェンダークリニックにおいて産婦人科医は二次性徴抑制療法や性ホルモン療法、さらに手術療法を行っている。

2022年に発効した国際疾病分類(ICD-11)では、従来の「性同一性障害」を「性別不合」と改称し、「出生時に割り当てられた性と実感する性別とが一致しない状態」とした。また、ICD-10では「精神疾患」に分類されていたが、ICD-11では「性の健康に関連する状態」に分類された。これを機に、疾患への治療という「医療モデル」から、「性と生殖に関する健康と権利」(SRHR)も含めて対応すべき「生活モデル」へと転換することになる。

産婦人科医は従来から、性別不合の診療のみではなく、LGBTQ当事者への生殖医療や養子縁組などの家族形成に関与してきた。また、レズビアンカップルやトランスジェンダー当事者の妊娠や分娩に関わる機会もある。さらに、学校で性教育を行う産婦人科医は「性の多様性」に関する教育を依頼される機会も増えている。今後は、LGBTQの子どもへのライフプラン教育も依頼されるであろう。

「G7の中で同性婚を認めていないのは日本だけ」とされ、全国で同性婚を求める裁判が行われているが、いまだ実現していない。2020年、卵子・精子提供による生殖医療で生まれた子どもの親子関係を定める生殖医療民法特例法が成立したが、LGBTQ当事者を対象に含める議論は遅れている。産婦人科医はこのような議論にも深く関与することになる。

4) 経口中絶薬の実際の使用経験と留意点

医療法人社団こうかん会日本鋼管病院 石谷 健

【目的】

経口妊娠中絶薬（経口中絶薬、メフィーゴ[®]パック）は、2023年5月16日に国内で上市されたが、国内における治験が入院管理下で施行されたことから入院可能な有床施設において2剤目のミソプロストール服用から胎嚢排出まで院内待機する処方条件が課されている。そこで、国内上市後の一般臨床における経口中絶薬の処方症例を検討し、経口中絶薬の臨床運用上の安全性と留意点につき検討した。

【方法】

日本鋼管病院において2023年6月以降に経口中絶薬による初期人工妊娠中絶治療の施行例において、治療週数、中絶完遂率、Hb値の推移、補助療法や時間外受診診療の有無等について調査を行った。併せてラインファーマ株式会社の社内ならびに市販直後調査等のデータについても比較検

討を行った。

【成績】

治療開始時の妊娠週数が8週未満では、全例ミソプロストール服用後6時間以内に胎嚢排出が認められた。過去に人工妊娠中絶手術施行歴のある1例において、胎嚢排出後の腹痛・性器出血の持続を訴え時間外受診となった。輸血や緊急入院を要する大量性器出血や感染症等の重篤な合併症例や他院高次施設への搬送例等は見られなかった。

【結論】

少数例とはいえ、比較的安全に経口中絶薬による初期人工妊娠中絶治療が行われている実態が明らかとなりつつある。症例データを積み重ねて、今後は海外と同様に無床診療所等でも可能な外来治療への適応拡大を検討して、患者アクセスの改善を図ることが望まれる。

医会・学会共同企画「生涯研修プログラム」生涯研修プログラム9 P
近年の産婦人科医療の様々な課題を考える・2

5) 少子化時代における無痛分娩

日本医科大学 鈴木俊治

日本では合計特殊出生率が1.6未満の状態が30年以上継続しており、移民も受け入れていないことが他国にはみられない少子高齢化社会につながっていると分析されている。無痛分娩は次の妊娠率の上昇につながる可能性を示唆した報告があり、多産による少子化対策の一翼を担う可能性があるが、そもそも、出産を回避する以前に結婚が回避されている傾向がある日本においては、特有の価値観あるいは政策に大きな変化がなければ、少子高齢化傾向が改善する見込みはないこと指摘されている。

そのため、妊産婦のさらなる高年化が予測され

るのが現状であるが、例えば高年妊婦に対する無痛分娩に関する検討等は未だ十分でないのが実状である。現時点では、高年初産婦が無痛分娩を希望する率は若年妊婦と比較して高く、一方で、硬膜外麻酔が高年妊婦の分娩に与える影響は一般的なリスクと有意差がなく、以上より高血圧や体力低下が認められやすい高年妊婦は無痛分娩のよい適応ではないかという報告が散見されている。

これらを背景として、特に高年妊婦に対する硬膜外麻酔分娩を中心として、少子化社会における無痛分娩の役割を考察する。

医会・学会共同企画「生涯研修プログラム」生涯研修プログラム9 P 近年の産婦人科医療の様々な課題を考える・3

6) 産科危機的出血による妊産婦死亡の増加傾向の要因分析

聖マリアンナ医科大学 長谷川 潤 一

ここ10年以上、妊産婦死亡率に年次変化はなく中央値4.3(3.9-6.0)/10万分娩で推移している。そのうち、直接産科的死亡が半数以上を占めていたが、年々減少傾向にあり、2021年には初めて間接産科的死亡が上回った。その要因として、日本産婦人科医会の妊産婦死亡報告事業・妊産婦死亡症例検討評価委員会から毎年発刊される母体安全の提言、シミュレーションコースなどによって母体救命の意識が高まり、産科管理が改善されたことが考えられる。しかしながら、産科危機的出血による死亡の割合は2010年29%から漸減し、2019年に7%なった後漸増し、2022年は18%になった。近年の多い原因は、弛緩出血、胎盤早期剝離、子宮型羊水塞栓症など一旦減った原因の再増加と、子宮破裂、癒着胎盤などが目立つ。産科危機的出血の割合の増加の背景には、新型コロナウイ

ルス感染拡大の影響の可能性もあるが、日々の日常臨床における産科危機的出血に対する予防、施設での初期対応などの再考を要する例も少なくない。その一方、子宮破裂や癒着胎盤といったハイリスク妊婦の増加傾向も一因として考えられ、さらにそのような症例の対処の難しい場合の治療戦略など、個人の知識やスキルに関する問題もあると考えられた。これらのことより、産科危機的出血に対し、個人・組織で策を講じる必要があると考える。日々の後産期出血の鑑別、母体急変の感知・初期対応、止血アルゴリズムを徹底すること、保存的止血の限界を認知して外科的止血術への移行をスムーズにすること、フィブリノゲン製剤を含めた正しい輸血管理を再確認すること、社会的背景による産科医療の医療安全の脆弱化へ対応することなどが望まれる。

7) 最多死因となった妊産婦の自殺予防を考える

さがらレディスクリニック 相良 洋子

妊産婦の自殺については、2001年に英国CEMD (Confidential Enquiries into Maternal Deaths) が「妊産婦の死亡原因として最も多いのは自殺を含む精神障害によるものであった」ことを公表して以来、にわかに注目されることになったが、日本においても2015~2017年にかけていくつかの報告があり、妊産婦死亡の原因として自殺がもっとも多い可能性が推測されていた。その後、日本産婦人科医会の妊産婦死亡報告事業において、2020年以降は自殺が死亡原因のトップになり、さらに令和5年版自殺対策白書において初めて妊産婦の自殺数が公表され、2022年に確認された妊産婦の自殺は65人という数字により、自殺が妊産婦死亡の最も多い原因であることが確認された。

自殺の予測・予防は大変に難しく、「こうしておけば予防できた」という確実な方法は存在しない

が、リスク因子や自殺のプロセスを知り、希死念慮を抱く患者にどのように接するかの基本を身につけておくことは重要である。リスク因子としてCEMDの報告では、精神疾患の既往や過去の産褥期精神科入院歴などが挙げられているが、妊産婦死亡報告事業ではさらに精神疾患の悪化に影響を与えた要因として、夫婦の問題や育児不安、早産、身体的不調などがみられていた。また希死念慮を抱く患者に接する際には、傾聴と共感の姿勢で話を聴き、つらい気持ちを受けとめることが重要であるが、さらに多職種連携により患者の負担の軽減や緊急時の対応に備えておくことも重要である。日本産婦人科医会では、これらをまとめた動画を作成してホームページに公開しているが、講演では実際の事例の経過から、特に注意すべきポイントや問題点について整理してみたい。

AOFOG Session : SRHR in Asia & Oceania

1) Violence Against Women : Roles of ObGyn in the hidden epidemic

Jaisamrarn Unnop

Chair of SRH Committee, AOFOG, Thailand

Violence against women (VAW) refers to any act of gender-based violence that results in, or is likely to result in, physical, sexual, or mental harm or suffering to women, including threats of such acts, coercion, or arbitrary deprivation of liberty, whether occurring in public or private life. One in every three women all over the world has been the victim of physical or sexual violence. To eliminate VAW, health sector has an important role to play. Particularly, medical staff in Department of Obstetrics and Gynecology (OB/GYN) play a pivotal role in addressing VAW by detection, providing support and collaborating with various stakeholders. OB/GYN medical staff should be responsible for preventing and responding to VAW during their routine health services.

Prevention education is a preliminary and effective approach to eliminate VAW. OB/GYN team can raise public awareness on this issue by public talks, social media, or specialized training. Education activities can help the patients to increase their perception on gender equality, recognizing the signs of violence, reducing the stigma of abuse, and responding to the trauma of violence.

Detection is another key element of OB/GYN support service on VAW. The medical staff should be aware to both physical signs (such as bruising, swelling and broken bones, etc.) and psychological symptoms (such as anxiety and depression). Delayed care of injuries, or inconsistencies between patients' explanation of injuries

and the nature of injurers should be alerted. Creating a safe and supportive environment, using non-judgmental language and sensitive questioning can help patients to disclose their experiences. Standardized screening tools can be used to build an effective communication and the detection of VAW.

Next, an immediate medical care should be provided, as soon as the VAW victims are identified. OB/GYN staff can conduct a thorough physical examination to assess and treat any physical injuries resulting from the assault. Emergency contraception can be provided to prevent unintended pregnancies, while prophylaxis could be considered for sexually transmitted infections. Additionally, conducting forensic examination, ensuring proper evidence collection, and offering information about available support service (such as counseling, crisis hotlines, and emotional support, etc.) should be done after the essential examination and treatment.

Finally, collaborating with other relevant institutes or organization are crucial. OB/GYN staff can provide crucial medical evidence and documentation to support the legal cases. Work with advocacy organization or local grassroots organization could help to ensure seamless referral and follow-up care.

In addition to direct support services on VAW, OB/GYN staff can contribute to addressing VAW issue through research. Currently, the Sexual and Reproductive Health Committee of AOFOG are conducting two surveys aimed at shed-

ding light on the unknown information of VAW in Asia and Oceania countries, titled “Multi-national Survey on violence against women in Asia and Oceania countries”. The first survey aimed to explore the pattern and prevalence of VAW and the Knowledge, Attitude, and Practice (KAP) towards VAW among reproductive-age women. The second survey focuses on KAP towards VAW and support services among OB/GYN medical staff in Asia and Oceania countries.

As part of these initiatives, AOFOG is committed to conducting more educational campaigns, providing more specialized training, and collaborating with more relevant organizations.

In conclusion, it is imperative to recognize the pivotal role that OB/GYN medical staff play in addressing the hidden epidemic of violence against women. Promoting action on VAW is imperative for creating a safer society.

AOFOG Session : SRHR in Asia & Oceania

2) Preconception and interconception care

Black Kirsten

SRH Committee Member, AOFOG, Australia

The times before conception (preconception) and between pregnancies (interconception) are recognised as vital to improve the health of couples and individuals in ways that can benefit the health of future generations. The range of areas addressed by preconception and interconception care includes lifestyle (smoking, alcohol), nutrition and vitamin supplementation, body composition (overweight and underweight), environmental factors, medical conditions (diabetes) and birth spacing. It will summarise the benefit of optimising these factors to improve maternal and neonatal outcomes and the particular importance of addressing chronic medical conditions such as diabetes and obesity. This presentation will discuss the evidence for the Developmental Origins of Health and Disease (DOHaD) based on the concept that the root of lifestyle-related diseases such as obesity, hypertension and diabetes is formed by the interrelation between genes and the embryonic fetal and neonatal environments. It will highlight the opportunities obstetricians and gynaecologists have to encourage reproduc-

tive life planning both before and between pregnancies and the tools and checklists that are currently available to promote healthy reproduction. However even with increased health care practitioner awareness, implementing preconception and interconception care remains challenging. Globally around half of all pregnancies are unplanned and there is little community understanding about how best to prepare for a pregnancy. Better pregnancy and reproductive life planning may require health care practitioners to enquire regularly about a woman's intention to conceive and, when she is not desiring a pregnancy, to recommend reliable contraception. Enhancing community awareness through public health campaigns as initiated in the United Kingdom and the Netherlands is essential. High quality national and international guidelines on preconception care are currently lacking so developing guidelines, resources and tools for healthcare practitioners will support them to provide optimal care.

AOFOG Session : SRHR in Asia & Oceania

3) Revisiting additional benefits of hormonal contraception

Hiraike Osamu

SRH Committee Member, AOFOG, Japan

In recent years, hormonal contraception has evolved beyond its primary role in preventing unplanned pregnancies. This presentation aims to revisit and highlight the additional benefits associated with hormonal contraceptive methods, shedding light on their multifaceted impact on women's health.

While the primary function of hormonal contraception remains contraceptive efficacy, emerging evidence suggests a spectrum of additional advantages. Firstly, hormonal contraceptives have been shown to ameliorate menstrual disorders, providing relief from dysmenorrhea and menorrhagia. This aspect of hormonal contraception enhances the overall well-being of women and it also addresses the socio-economic burden associated with menstrual-related absenteeism. Secondly, hormonal contraception plays a pivotal role in managing hormonal imbalances, such as polycystic ovary syndrome (PCOS). By regulating menstrual cycles and mitigating androgen excess, hormonal contraceptives contribute significantly to the comprehensive care of women with PCOS, offering therapeutic benefits beyond contraception alone.

Furthermore, hormonal contraceptives have been associated with a reduced risk of certain gynecological cancers, including endometrial and ovarian cancers. This protective effect stems from the hormonal regulation provided by con-

traceptives, offering long-term health benefits for women during their reproductive years. Beyond reproductive health, hormonal contraception exhibits dermatological advantages. It has been linked to improvements in acne severity, making it a valuable therapeutic option for women seeking both contraceptive and skin health benefits. This dual functionality addresses the holistic nature of women's health and emphasizes the interconnectedness of reproductive and dermatological well-being.

Additionally, the use of hormonal contraception has been linked to a lower incidence of benign breast diseases, underscoring its potential protective role in breast health. Understanding these nuanced health benefits contributes to a more informed and comprehensive approach to family planning.

In conclusion, this presentation aims to underscore the diverse and evolving landscape of hormonal contraception. Beyond its primary role in family planning, hormonal contraception offers a spectrum of additional benefits encompassing menstrual health, hormonal balance, gynecological cancer risk reduction, dermatological advantages, and breast health protection. Recognizing these multifaceted advantages is essential for healthcare providers and policymakers to promote informed decision-making and comprehensive women's health care.

AOFOG Session : SRHR in Asia & Oceania

4) Adolescent HPV vaccination : Need of the hour

Gupta Krishnendu

Deputy Secretary General, AOFOG, India

Cervical cancer is a health crisis impacting women and their families across the world - especially in low-resource settings. Here are the facts : ^{1,2}

- In 2020, an estimated 604,127 women were diagnosed with cervical cancer globally, representing 6.5% of all female cancers.
- Cervical cancer is the most common cancer among women in 36 low-and middle-income countries, mainly in sub-Saharan Africa.
- Cervical cancer killed an estimated 341,831 women in 2020, 90% of whom were in less-developed regions of the world, where access to prevention, screening, and treatment services are severely limited.
- Today, more women are dying of cervical cancer than are dying in childbirth.
- A woman diagnosed with cervical cancer is almost twice as likely to die than a woman diagnosed with breast cancer.
- A woman living with HIV is six times more likely to develop cervical cancer than her HIV-negative peers.

These tragic numbers are real, and thankfully, so are the solutions. The objectives of the presentation will be as follows :

- What we already know : Human papilloma virus (HPV), Disease burden, HPV vaccines.
- Counselling and strategies for overcoming barriers to HPV vaccination.
- WHO : “Global strategy” to eliminate cervical cancer.
- HPV vaccines and vaccination : Global and In-

dian scenario.

- HPV vaccination : International recommendations and guidelines.
- Role of professional federations, partner organisations and non-governmental organisations (NGOs)³ to promote HPV vaccination, and, personal experiences.
- HPV vaccines : Newer thoughts and future directions.

In 2020, India alone accounted for 123,907 new cases of cervical cancer being diagnosed, with 77,348 women dying due to the dreaded disease.² With wider access to HPV vaccines, and the recommendation of the cost-effective “one-dose” by the WHO Strategic Advisory Group of Experts on Immunization (SAGE),⁵ along with the continuing cervical cancer screening and treatment, we can end this global epidemic in a generation, but not nearly enough resources are available for these critical programs. In continuation of the changing themes during the Cervical Cancer Awareness Month (CCAM), a global healthcare event to raise awareness of cervical cancer in January every year, the 2024 theme is “Learn, Prevent, Screen” ; these three strategies will help decrease the morbidity and mortality of cervical cancer.⁶

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指導医講習会 サステイナブル産婦人科医療体制確立委員会企画 医師の働き方改革がスタート～産婦人科医療改革グランドデザイン 2023 の
実現に向けて～

医療改革委員会を発展させた形で発足したサステイナブル産婦人科医療体制委員会は、2021年に行われた日本産科婦人科学会学術講演会において医療従事者も含めたサステイナブルな産婦人科医療体制構築に向けて努力していくことを、「新潟宣言」として発出するに至った。その後も、全国民（患者・行政・医療者）と共に学会が目指す取組みとして産婦人科医療改革グランドデザイン2023年を発出した。2024年度からいよいよ医師の働き方改革が開始された。グランドデザイン2023の提言として、1)医師の働き方改革に関する法令を遵守する、2)地域医療提供体制の抜本的な見直し、

3)分娩取り扱い病院の勤務環境改善、4)産婦人科医師数増加、5)男女共同参画の推進、6)自身の働き方と向き合う意識改革を掲げている。本委員会企画では、グランドデザイン2023を具体的に実現するための方策について行政、病院、診療科それぞれのレベルでの情報を厚生労働省、専門家、サステイナブル委員会より講演いただく。今後、サステイナブル産婦人科医療体制委員会としてグランドデザイン2023を実現させていくためには、どのような情報提供や取り組みが必要なのか、パネリストによるディスカッションを通して探っていきたい。

1) 論文投稿の注意点～AEはここを見ている～

九州大学 矢 幡 秀 昭

Journal of Obstetrics and Gynaecology Research (JOGR) は日本産科婦人科学会の英文機関誌であり、Asia and Oceania Federation of Obstetrics and Gynaecology (AOFOG) の機関誌でもある。JOGR に投稿された論文は各担当分野の Associated Editor (AE) にまず割り振られる。この AE は全国の大学病院を中心に約 100 名程度で構成されており、毎月 2-3 本程度の論文対応に当たっている。さて、われわれ AE に送られてきた論文で最初にチェックするのは論文タイトル、著者名ついで Similarity Index (SI) と呼ばれる既に出版された論文との類似性を数値化したデータとなる。この SI は一般的には 20% 前後であるが、40-50% などの数値であればコピー&ペーストした論文ではないかという疑いの目から論文を査読することとなる。まずは SI が高い論文との相同性

を確認し、参考文献に引用もなくコピー&ペーストが主体を占めていれば盗作となり、審議論文の対象となる。また、過去に著者として自分自身が出版した論文をコピー&ペーストして作成された論文も自己剽窃として審議論文の対象となる。また、サラミ論文とは一本の研究論文で報告できる大きな研究を小さい発表論文に分割する行為で分割した各部分は研究の「スライス」と呼ばれ、論文出版の実績を水増しすることになり、不正行為にあたる。最近ではペーパーミルと呼ばれる実在しないデータをもとに論文を量産する手法が登場している。このような論文はデータの相同性もなく SI も高くないため、判別に苦勞することも多い。本講演ではこのような不正論文の実例をもとに論文投稿の注意点について概説する。

編集委員会企画 **P** 明日からの論文作成実践編 Up-to-date

2) 私の考える論文作成のポイント

名古屋大学 梶山 広明

「論文は時空を超える」とある人が言っていた。なるほどの的を射た表現だと思った。時空の「時」は言うまでもなく時間のことである。例えば今でも我々は野口英世や北里柴三郎が100年以上も前に書いた医学論文を普通に読むことができる。学術論文ではないが、日本書紀という奈良時代に成立した日本の歴史書にふれることによって、当時の国内外の状況や天皇の歴史、そして先人がどのような世界観を持って生きていたかがわかる。さらに「栄花物語」という平安時代、約200年間の天皇治世をまとめた歴史物語がある。この中には皇族のお産の状況がよく描写されているが、47人の妊婦のうち11人が出産で死亡したとある(妊産婦死亡率:23.4%)。すなわち著作物は過去に先人が持った観察眼や知性を感じることでできる一種のタイムカプセルのようなものである。

一方、時空の「空」はいうまでもなく空間という意味である。日本語で論文を書けば日本中の人や海外でも日本語に堪能な人の目に留まる。もし英語で論文を書けば地球の裏側にいる人も読むことができる。「論文は時空を超える」という言葉は決して大げさな表現ではない。学会発表ではこうはいかない。我々はまずこの言葉の真髄を理解する必要がある。我々は先人からの知恵をただ受け

とるだけでなく、後世のまだ見ぬ人のために何かを残していかなければならない。現時点ではどれだけ意味があるかわからなくとも子孫の誰かには役に立つということもあるからである。それが世代を超えた知性の橋渡しとなる。

しかしながら論文を執筆するという精神的活動は疲れる。「論文」という言葉には堅いイメージが付きまとう。どうしてもこの潜在意識が作業を行う上で心を固くしてしまう。特に真面目すぎる人は論文が書きにくいような印象をもつ。心理的ハードルが高く、一歩を踏み出しにくいからである。逆にふわっとした人は論文に対する心理的ハードルが低い。結構量産することもある。論文作成は人物像を彫刻する作業に似ている。すなわち、全体を粗く人の形に丸めておいてから部分へと掘り進めるのである。初めから細部にこだわると、途中で疲れてしまい挫折する。全体を俯瞰できるような形にまずは持っていくことが、その後の作業に弾みがつくポイントとなる。私自身、最近論文作成の指導は行うものの、執筆の機会は少なくなってしまった。参考になるか全く分からないが、本講演ではこれまで論文執筆に関する想いや工夫、そして紆余曲折を述べさせていただきたい。

1) PGT-M における現状

長崎大学 三 浦 清 徳

2022年に重篤な遺伝性疾患を対象とした着床前遺伝学的検査に関する見解/細則が改定された。審査に際して、産婦人科医の意見に偏ることがないように、審査小委員会は学会員とそれ以外の委員とで組織されている。また、個々の申請例にお

ける疾患の重篤性の判断には、疾患と関連する学会の意見も参考に様々な視点から審査が行われている。今回、これまでの審査状況と課題について紹介する。

臨床倫理監理委員会企画 PGT-M, PGT-A・SR およびがん・生殖医療施設における現状について

2) PGT-A・SR における現状

国際医療福祉大学成田病院 永 松 健

PGT-A・SRは2022年1月に新たな見解の下で施設認定および臨床での実施が開始されて2年が経過した。この分野における技術の進歩および臨床研究のエビデンスの集積は非常に活発な状況にある。特に、実施対象について反復着床不全、反復流産以外に女性年齢の要素を適応に含めるべ

きか、検査法について外胚葉生検以外の非侵襲的 PGT-A による判定法の取り扱いを認めるべきかなどが論点となっている。今後、国内の臨床研究の結果を見据えながら継続的な議論を行い見解細則の改定の是非を問う必要がある。

3) PGT に対する現行の見解における課題とその論点

東京大学大学院医学系研究科生体物理医学専攻医用生体工学講座,

PGTに関する継続審議小委員会委員長 織田 克利

日本産科婦人科学会では、2022年1月に着床前遺伝学的検査の見解・細則の改定が行われ、PGT-M についての見解・細則と、PGT-SR・PGT-A についての見解・細則が明確に分けられることとなった。しかしながら、いずれの検査においても、その倫理的・科学的・社会的な考え方は時代によ

り変わりうるものであり、継続的に審議していくことが重要となる。今回の発表では、先期から新設された「PGTに関する継続審議小委員会」において議論されている内容を中心に、継続審議を要する課題点について紹介する。

臨床倫理監理委員会企画 PGT-M, PGT-A・SR およびがん・生殖医療施設における現状について

4) がん・生殖医療施設における現状

京都大学 堀 江 昭 史

2021年妊孕性温存治療に対する経済的支援が開始され、がん生殖医療における診療体制の均てん化が加速している。現在、妊孕性温存療法実施医療機関として160を超える施設が登録が行われている。患者が医療費助成を受けるためのシステ

ムは非常に複雑で、医療施設は患者レジストリへの登録など正確な情報提供が求められている。本講演ではレジストリの仕組み、登録状況について解説を行い、今後の本邦における方向性についても言及する。

教育委員会企画 

知ってほしい、始めてほしい「医学教育研究」

～日々の教育活動が研究になる～

産婦人科の教育分野では研究業績が少ないのが現状であるが、その理由は多忙な日常に原因がある一方で、われわれ産婦人科医が、そもそも教育研究とは何かを知らないことも大きな要因であろう。臨床、研究と並んで教育も指導者にとっては多大な時間と労力を要する分野であり、十分評価に値する業務であるが、医師の働き方改革という新たな局面において、時代に即したより効果的な産婦人科教育について討論することは重要である。そこで、教育研究に対する意識の変革、取り組みの契機となるような企画にしたいと考え、2人の教育専門家からご講演いただく。

「働き方改革と医学教育研究の両立を目指して」

2024年4月より医師の働き方について時間外労働の上限規制が始まる。その影響は多方面にわたると考えられ、2023年時点の調査において、全国の大学病院の助教が研究に割く時間は著しく少ないという報告もある。労働時間を短縮すること、自己研鑽と労働時間を明確に区分けすることが求められる中で、診療以外の用務すなわち教育や研究に割くエフォートが切り詰められることは容易に想像でき、現時点からその影響が出始めている。大学病院のみならず、どのような規模の医療機関でも同様の課題に直面しているのではないだろうか。しかし、長い目で見て、このことは我が国の臨床・研究の発展に重大な影響を及ぼしかねない。我々は働き方改革を進めるとともに教育・研究の質と量をいかに担保するかを真剣に考えなければならない局面にきている。このことには様々な解決方法が考えられ、そのキーワードはタスクシェア、タスクシフティングである。メディカルクラークや特定技能を身に着けた看護師の活躍や

一層の多職種連携が期待されている。また、学生や新たな専門職の活躍も期待される。診療参加型実習において学生がより高いレベルで診療参加できるようになれば、医療チームとして学生の能力を診療に活かすことができるようになる。また、臨床研究をサポートする部門の役割や診療看護師なども活躍の場が広がっている。これらの現状を踏まえた課題と今後の展望について述べたい。「学部学生でも“うまくやれば”できる、教育と研究を融合する効率的な医学教育研究手法」

医学教育の受け手である医学生でも十分に彼らの興味に基づいて原著論文を発表することができる。今回は、筆者が特に注目し、医学生達を巻きこみ実施してきた四つの分野に絞ってみる。第一にはAI技術との協働の必要性である。医療分野でのAIの進展は著しく、これを教育プログラムに統合することで、学生たちの学習効果を向上させていかなければならない。第二の課題は、“いかに教員の負担を軽減するか”である。教育の質を保ちながら、教員の業務を効率化し、適切なワークライフバランスを実現することは急務だ。ここで、“引き算の教育”の概念が重要となる。第三には、ジェンダー問題への対応が求められる。わが国では焦点を当てられることが乏しかった多様な性別の学生や教員が公平に扱われ、同等の教育機会を享受できる環境を作ることが不可欠であり、特に女子医学生が不安を抱える課題でもある。最後に、医師としてのプロフェッショナルリズムと共感性教育の重要性である。特に、共感性の育成に焦点を当てることで、初学者にも患者中心のケアを教育していかしなければならない。これらの医学教育上の課題にたいして、どのように医学部学

生に対して研究活動を効率・効果的に教え、成果
をあげてきたかについて具体的な手法を交えつつ
持論を展開する。

災害対策・復興委員会企画 

災害対策ことはじめ～チームづくりと新 PEACE システムの活用～

災害対策・復興委員会はこれまで災害対策の一つとして日本産科婦人科学会大規模災害対策情報システム PEACE (Perinatal Early Assessment and Communication system for Emergencies) を管理し、大規模災害時の医療体制の整備を目的とし活動してきた。東日本大震災、熊本地震等の大規模災害後の対応や、各地での災害対策訓練や研修会を通して表出してきた問題点もあり、今後の課題である。本企画では、前半は実際の現場でのチームづくりを含めた災害対策の実情を、後半は2023年度よりシステム改修を開始し、2024年に全面刷新される新 PEACE の概要について報告し、議論を行う。

1. 『災害に備えて、チーム作りと準備の実際』

当初、災害対応の知識がなく何から備えるか分からなかった。消火設備を見回り、これまでの防災訓練の資料とスタッフへのアンケートから対策・訓練を検討した。防災に興味がありそうな人とチームを作り、年間計画を立て少しずつ備品整備や防災訓練を準備した。訓練は担当スタッフを含め病棟年間計画に組み込み、防災チームは担当が主体的に訓練できるよう支援している。またスタッフが興味ある非常食の試食会を行い病棟の備蓄をすすめ、自宅の備えも充実するよう防災グッズを紹介、楽しみながら学べるゲーム等も実施した。今後は「災害に強い病棟」とスタッフが自信を持つだけでなく、職種を超えた連携から「災害時も頼れる病院」を目指す。

2. 『顔の見える関係づくり：医療・地域・行政の連携方法』

災害医療現場では、各種対応に職種・業種の垣根を越えた連携が必須となる。そのために平時からできる方法として「顔の見える関係づくり」が言われるが、そう容易なことではない。演者の所

属する二次保健医療圏では2015年4月より地域災害医療コーディネーターを中心に災害医療ワーキンググループ(以下WG)を立ち上げ、災害医療体制構築のための活動を行っている。WG所属メンバーは二次保健医療圏5市の行政・医療・民間事業関係者等であり、医療圏全体の訓練の相談役や行政毎の災害医療政策のつなぎ役等を担うことで顔の見える範囲を広げている。当WGの活動を通して、各地域で明日からできる「顔の見える関係づくり」の方法を考えたい。

3. 『新しい PEACE システムの構築～これまでの問題点とどこが刷新されたのか～』

日本産科婦人科学会大規模災害対策情報システム (PEACE) は近年多くの災害や各地の防災訓練にて活用され、小児・周産期領域の災害情報ツールとしてなくてはならないものとなっている。しかし、PEACE 開発当初と比較して、現在までに内閣府訓練やDMATとの合同訓練を通じて、PEACE システムの機能面や他の災害システムとの連携面でアップデートが必要であることが判明した。そのため、2023年度に日本産科婦人科学会災害対策・復興委員会にてPEACEのシステム改修・刷新を行なった。本セッションでは、現在のPEACEの問題点、そして今回改修・刷新される機能について解説する。

4. 『新しい PEACE システムの実際 ～概要と機能紹介～』

新しい PEACE システムでは以下の機能を有している。1) 平時より各施設での診療状況や災害時の担当者連絡先を登録することで、発災時に最小限の情報入力のみで被災状況の報告が完結できる。2) 掲示板でやり取りを行っていた要支援依頼について、施設担当者が物資と患者搬送に分けリスト形式で必要事項を入力できるようになり、

また、小児周産期リエゾン側も要支援情報を一覧で簡便に確認できる。3) 掲示板をより利便性が高い情報交換ができよう刷新するとともに、メール、

SMS 送信による通知機能や、広域災害救急医療情報システム (EMIS) との情報連携機能を設け、災害時の密な情報連携を実現する。

産婦人科未来委員会企画 **P**

組織のソコヂカラを魅せる

～ “心理的安全性を保てる環境づくり” を産婦人科リクルートの鍵に～

日本産科婦人科学会 産婦人科未来委員会

産婦人科医療改革グランドデザイン 2023 では、年間新規産婦人科専攻医数の目標を 625 人と設定し、産婦人科未来委員会は今後もリクルート活動に注力する必要がある。

多くの医療施設では、労働力や能力の偏りがあり、特に産婦人科においては専門分野の細分化やライフステージの多様化により、属人化の解消が組織力の向上に繋がる可能性がある。最先端の設備や、人材が豊富な施設は、研修医や若手産婦人科医師にとって大きな魅力を持つが、規模が小さい施設では個々の技能や特色ある医療技術があれば一つの強みとなるものの、必ずしもすべての組織の中に突出した能力を備えた医師が存在するわけではない。組織力を高めるためにチームビルディングのノウハウを身に付けることで、組織全体の医療技術の向上のみならず、患者満足度、合併症の減少などに貢献できるかもしれない。

近年、チームビルディングにおける課題として、心理的安全性を保てる環境づくりが話題になっている。心理的安全性とは、組織の中でも自然体の自分でいられる環境のことであり、「心理的安全性が高まると、チームのパフォーマンスが向上する」ことを Google 社が発表して以降、注目が集まっている。

自分の意見が言えない専攻医や、専攻医の気持

ちがわからない指導医は、無意識に相手の気持ちを探り、物事をネガティブに捉えることで、組織全体のパフォーマンスの低下につながっているかもしれない。心理的安全性を保つことで、良好なコミュニケーションが生まれ、組織全体のソコヂカラを発揮できるようになり、働き甲斐ややりがいのある魅力的な組織が生まれる。

第1部では、メンタルチャージ ISC 研究所(株)代表取締役である岡本文宏氏より、現場ですぐに活用できる“小さな組織の人”に関する問題解決メソッドや、スタッフを活用して業績アップを実現する『繁盛企業づくり』についてご講演頂く。心理的安全性を保てる環境づくりが、産婦人科業界でどのように活用できるかに焦点を当てる。

第2部のパネルディスカッションでは、多様性のある産婦人科医師に登壇していただき、心理的安全性を保てる環境づくりに関して総合討論を行う。産婦人科の各施設・医局といった小さな組織の中で、各々が抱えるチームに関する問題点や改良点を中心に、聴衆も交えた議論を行う。

この企画によって、組織のソコヂカラを向上させることができ、若手産婦人科医師にとって魅力のある施設づくりの一助となり、ひいては産婦人科のリクルートの鍵となることを期待する。

セクシュアル・リプロダクティブ・ヘルス/ライツ (SRHR) 推進委員会企画 P

セクシュアル・リプロダクティブ・ヘルス/ライツ (SRHR) に関する日本と
諸外国の現状について考える

セクシュアル・リプロダクティブ・ヘルス/ライツ (Sexual Reproductive Health and Right ; SRHR) は、性と生殖に関する健康と権利である。自分のセクシュアリティや望む時に望むだけの子どもを持つことをすべての人が自分で決めることができる。そのためには、避妊の方法や不妊治療について知る事、生殖器のがんや感染症の予防や治療について知る事、そして、母子保健や育児支援が重要である。SRHR は、これらすべてを大切にす理念である。

本学会は 2022 年 6 月には本学会から SRHR 普及推進宣言を発売し、日本及び世界における SRHR に関する課題に対して積極的に関わる事、日本の社会のジェンダー平等の達成に貢献すること、SRHR の侵害を含むジェンダー平等を阻害する課題が提起された場合には専門学会として正面から対応することを宣言し、SRHR の普及・推進に努めてきた。

SRHR をめぐる状況は、世界各国で異なり、経済、災害、紛争などがその状況に影響する。日本

の SRHR に関して抱える課題は多数存在しているのが現状である。本企画では SRHR に関する日本の現状について諸外国の現状と比較しながら考察する。まず、総論として、海外での SRHR に関する活動経験が豊富な国立国際医療研究センター国際医療局の小原ひろみ先生が「SRHR の観点から見た日本の立ち位置～世界との比較から」というテーマで講演する。次に、各論として、種部恭子先生が「女性の自己決定権」、木村正先生が「人工妊娠中絶」、宋美玄先生が「女性と少女の産婦人科へのアクセス」、対馬ルリ子先生が「包括的性教育」というテーマで日本における SRHR の現状について諸外国の現状と比較しながら述べる。

本企画では、世界各国の SRHR に関する現状への理解が深まる事、そして、日本における SRHR に関する現状を国際比較の観点から考える事により、本企画が SRHR に関する課題の改善・解決の一助となり、本学会による SRHR に関する取り組みがさらに推進されることを目指している。

子宮頸がん検診・HPV ワクチン推進委員会企画

子宮頸がん検診・HPV ワクチン普及推進委員会企画

～どうなる?日本の子宮頸がん検診～

日本の子宮頸がん検診におけるHPV検査導入方法提言のためのワーキンググループ

現在、20歳以上、2年毎の細胞診が推奨されている日本の子宮頸がん検診に大きな変革の時がきている。

契機は、国立がん研究センターの研究者による「有効性評価に基づく子宮頸がん検診ガイドライン2019年版」において、細胞診単独法<従来法・液状検体法>の推奨グレードAとともに30~60歳のHPV検査単独法が推奨グレードAとなったことである。HPV検査を含む子宮頸がん検診は、検診の間隔を2~3倍に延長することが可能であるが、細胞診に比べて偽陽性率が上昇する。検診の不利益としての偽陽性率が、細胞診・HPV検査併用法で最大になるとされ、このガイドラインでは、併用法の推奨グレードはCとなった。

また諸外国におけるHPV検査の子宮頸がん検診への導入の状況を鑑みて、日本で子宮頸がん検診実施について影響力を持つ5団体（日本臨床細胞学会・日本産婦人科医会・日本婦人科がん検診学会・日本婦人科腫瘍学会・日本産科婦人科学会）から推薦を受けた各々2人の委員と各団体1人のオブザーバーが参加し、「日本の子宮頸がん検診におけるHPV検査導入方法提言のためのワーキンググループ」を設置し、令和4年4月から令和5年2月までに4回の会議を行った。テーマと

しては、第1回目「HPV検査を含む子宮頸がん対策型検診の推奨年齢設定と検診間隔設定」、第2回目「HPV検査単独検診を対策型検診として採用した場合、子宮頸部腺癌の見逃しが増えるか?」、第3回目「HPV検査自己採取」、第4回目「日本の子宮頸がん検診におけるHPV検査導入方法」について、意見交換を行った。その中で、「HPV検査は30歳以上での導入が妥当である」、「上皮内腺癌と通常型腺癌の検出力においてはHPV検査導入が期待される」、「自己採取のHPV検査は将来の未受診者対策となる可能性はあるが、対策型検診としての導入は時期尚早であり、国内での大規模研究が必要である」とのコンセンサスが得られた。一方で、HPV検査単独法か細胞診との併用法かについて、検診実施のアルゴリズムについては、一定のコンセンサスは得られなかった。

現在、厚生労働省が主催する「がん検診のあり方に関する検討会」において、一定の要件を満たす自治体がHPV検査単独法を導入できるように「がん予防重点健康教育及びがん検診実施のための指針」を改定する動きが見られる中、各団体の代表者とともに再度議論の場を持つため、本セッションを企画した。

感染対策連携委員会企画 **P**

産婦人科にまつわる感染症の課題と対策

～他学術団体との連携をめざして～

1. 日本産科婦人科学会と予防接種推進専門協議会が連携して行う VPD への取り組み

予防接種推進専門協議会は、「予防接種制度について継続的に評価・検討し、全ての年代に必要な予防接種を国内で適切・安全に実施できる体制整備に貢献する」ことを目的として活動している 23 の学術団体からなる協議会で、国や社会に対して様々な要望や提言を行ってきた。産婦人科領域に関係の深い子宮頸がん、風疹、COVID-19 に対する予防接種推進活動について紹介し、今後の課題と問題点について考える。

2. 風疹第 5 期定期接種について

プレコンセンションケアの観点からも、ワクチンで予防可能な風しん対策は重要である。厚生労働省は、1962 年 4 月 2 日～1979 年 4 月 1 日までの間に生まれた男性を対象として、第 5 期定期接種を実施している。しかし利用者は低迷しており、さらに 3 年間の期間延長となっている。近年では、行動経済学を用いた利用率の向上を目指した活動も積極的に行われており、ワクチン接種のみならず有効な教育・啓発活動の手段として注目されている。

3. HTLV-1 感染症

ヒト T 細胞白血病ウイルス (human T-cell leukemia virus type-1 : HTLV-1) は、成人 T 細胞白血病 (adult T-cell leukemia : ATL) など難治性で予後不良な HTLV-1 関連疾患の原因ウイルスである。日本は先進国では唯一のエンデミックエリアであり、2010 年より「HTLV-1 総合対策」が推進されている。その重点対策の一つとして、ATL などの HTLV-1 関連疾患につながる次世代の HTLV-1 キャリアを減少させるため、全国的に妊

婦の HTLV-1 抗体検査が公費負担で実施されている。HTLV-1 母子感染予防対策の現状と今後の課題について、最近の知見をもとに紹介する。

4. 早期梅毒 見逃さないための診療スキル

梅毒は、粘膜の小さな傷からトレポネーマが侵入し、数週間の潜伏期を経て発症する。感染から 1 年以内を指す早期梅毒は、性的接触による感染力が強く、妊婦では母子感染により流産や先天梅毒を引き起こすリスクが高いため早期診断が重要である。梅毒の臨床症状は、陰部の潰瘍性病変や腫瘍性病変が知られているが、性器ヘルペスや尖圭コンジローマと診断され見逃されることが少なくない。「偽装の達人」と称される早期梅毒の診断を今一度確認したい。

5. 婦人科悪性腫瘍における菌血症と抗菌薬戦略

婦人科悪性腫瘍を対象とした血液培養陽性例の起炎菌検索や疫学データは不足している。昨今、がん化学療法が日進月歩で発展を遂げている中、婦人科臓器における解剖学的特徴や微生物背景を考慮した産婦人科医としての抗菌薬戦略の検討が必要と考えられる。自施設における婦人科悪性腫瘍患者の菌血症に対する臨床背景データを用いて、起炎菌やリスク因子を解明し、既報も含め、産婦人科感染症診療の質向上を考察する。

6. 胎児への抗体移行を目的とした妊娠中のワクチン接種

近年、新生児期に重症化しやすい特定の感染症に対する予防戦略として、胎児への抗体移行を期待した妊娠中のワクチン接種が注目されている。特に百日咳含有ワクチンは諸外国において妊娠ごとの接種が強く推奨されているが、我が国での導入は未定である。一方で新生児重症化予防を目的

とした妊娠中のRSウイルスワクチン接種も話題
になっている。妊娠中のワクチン接種に関する世

界・日本の現状と今後の課題を紹介する。

ダイバーシティ・人材育成推進委員会企画 

How can gender equity be achieved in obstetrics and gynecology?

Gender equity has become increasingly important, prompting a critical examination of its implications in various professional settings. In the medical field, promoting gender equity is paramount to facilitating conversations from diverse perspectives, encouraging collaboration, and generating innovative solutions. In this session, the current situation and initiatives to achieve gender equity among OBGYN doctors in Japan, South Korea, and Taiwan will be presented by three speakers and the way forward for gender equity will be discussed.

1. The current situation and challenges for female doctors' work life in Japan : Dr. Michiko Kido (Japan Red Cross Hospital)

In Japan, women work more than five times as long as men for unpaid work. Compared to single female doctors, married female doctors work fewer hours and are more likely to choose a work style without night shifts or on-call duty rather than full-time work. Women themselves are stuck in a gender-role mindset that says "I should save work for the sake of the family." However, when there are time constraints, it is easy to fall into the "mommy track," where the level of difficulty and responsibility is low and there are no career prospects, making it difficult to assume a leadership position. In this session, the efforts of the Japan Society of Obstetrics and Gynecology to increase opportunities for female doctors to demonstrate their abilities and advance their careers during life events will be presented.

2. The promotion of gender equity in obstetrics

and gynecology in South Korea : Prof. Sa Ra Lee (Asan Medical Center, University of Ulsan)

In South Korea, studies on gender discrimination among female doctors are limited, but it was reported that female surgeons faced more gender discrimination than males. Another study on gender's impact on professionalism in female trainees noted challenges in specialty choices and work-life balance due to the training system. Leadership experiences during training influenced career choices. A study on female doctors' leadership concluded practical efforts tailored to Korean culture are crucial for addressing underrepresentation. In-depth interviews with 15 women faculty members in surgery revealed gender inequality as a primary reason for leaving a professorship. Statistical data regarding the growing number of female doctors in the Korean Obstetrics and Gynecological Society will be presented in this session. The growing number of female doctors emphasizes the need for gender equity. Raising awareness of gender biases is crucial, and efforts by female academic OBGYN doctors can change circumstances. Building a support network is vital in reducing gender inequity in our Obstetrics and Gynecological Society.

3. Advancing gender equality in obstetrics and gynecology field : Trends and initiatives in Taiwan : Prof. Mei-Jou Chen (National Taiwan University)

Prof. Mei-Jou Chen will show (1) the gender dynamics in the OBGYN field in Taiwan (trends in the distribution of licensed doctors, the representation of women in leadership roles, and the

potential challenges faced by emerging medical professionals due to gender disparities), (2) the proactive measures undertaken by the Taiwanese government and society to promote gender equality within the OBGYN field, (3) the regulatory frameworks implemented to address gender imbalances, and (4) the advantages provided to

support and encourage female doctors to continue in both clinical work and research. By scrutinizing the current state of gender equality and presenting the initiatives in place, we hope to revisit and open a broader dialogue on creating an inclusive and equitable environment in Obstetrics and Gynecology in Taiwan.

生殖・内分泌委員会企画 **P**

調査・研究を通して知ろう！生殖・内分泌の魅力—保険診療時代の生殖医療エビデンスを求めて

長らく自由診療として行われてきた生殖補助医療ですが、令和4年に基本技術と関連する薬剤が保険収載されました。また、それに先立ち生殖医療ガイドラインが出版されましたが、個々のCQに対するAnswerとその推奨度は、国内外のエビデンスに基づき決定されています。この中には、本学会のART登録の膨大なデータに基づく知見も含まれています。また初版の生殖医療ガイドラインに推奨度Cとして掲載された技術・薬剤の多くは、現在、先進医療として評価されています。さらに月経異常や生殖内分泌疾患の実態および診断基準に関するアップデートも重要です。最近では本委員会を中心にFIGO AUB分類に基づく月

経異常と多嚢胞性卵巣症候群診断の実態調査を行ってきました。これらは、診断プロセスの標準化や診断基準の改定に必須の知見になります。

不妊症の原因疾患およびそれらに関連する月経異常の診断から生殖補助医療まで一連の検査・治療が保険診療として実施可能となった現在、今後のガイドラインと保険の改定に資する調査・研究によるエビデンスの蓄積がますます重要となっていると言えます。今回の生殖・内分泌委員会企画では、データベース研究、先進医療、委員会調査から得られた興味深い結果を紹介するとともに、今後どのような調査・研究が必要かについても議論できればと思います。

新展開が予想される婦人科がん診療を先取りする

本委員会企画は二部構成とする。第一部は2023年に改訂された子宮体癌のFIGO進行期分類について3名の演者より概説いただく。これまでの進行期分類は筋層浸潤の有無と腫瘍の広がり度で評価するものであった。しかしながら、新FIGO進行期分類は従来の腫瘍の広がり度に加えて、組織型、腫瘍パターン、分子分類が混在し非常に複雑化した。この複雑化した進行期分類に関して、3つのテーマで議論する。まず、新FIGO進行期分類改訂によって本会進行期分類はどのように改訂すべきか。次に、新FIGO進行期分類は病理医の負担が大きくなることが予測されるが、病理診断にどのような影響を与えるか。そして日常臨床、そしてガイドラインへ与える影響は大きく、進行期確定はすべての施設で同様に行うことが可能か。さらに術後再発リスク分類をどのように考えるか。

近年、婦人科診療の多様化が際立っている。婦人科がんに対する薬物療法は分子標的薬に加えて、PARP阻害剤、免疫チェックポイント阻害剤が保険適用され、日常的に使用されるようになって

きた。特徴的な有害事象に悩まされることもあり、適正使用、支持療法の重要性が高まっている。またがん遺伝子パネル検査の普及に伴い、遺伝性腫瘍の顕在化、遺伝情報の取り扱いが重要視されており、さらに遺伝子異常の解釈についてはエキスパートパネルの開催によって検討されるようになった。標準治療後のがん遺伝子パネル検査結果に基づいた治療体制の構築によって患者の治療選択が増えているが、治療に結びつくことは必ずしも多くはないのが現状である。また、2018年に早期子宮体癌に対してロボット手術が保険収載され、多くの施設で実施されるようになってきた。さらに婦人科癌におけるセンチネルリンパ節や卵巣癌に対する鏡視下手術の要望も高まり、婦人科悪性腫瘍に対する低侵襲手術の需要が高まってきている。第二部はこの婦人科診療の多様化に関して、薬物療法の注意点、がんゲノム診療の今後の在り方、低侵襲手術の新展開について専門家から講演頂く。

周産期委員会企画 P 周産期医療のトピックス

1) 我が国における分娩遷延の定義の策定

周産期の疾患・病態の基準や管理指針を考える小委員会

微弱陣痛による分娩遷延に対する標準的な介入法の策定を目指した研究ワーキンググループ

横浜市立大学附属市民総合医療センター総合周産期母子医療センター¹⁾、東京大学附属病院女性診療科・産科²⁾、北海道大学

産科・周産母子センター³⁾、岡山大学病院⁴⁾、順天堂大学医学部附属順天堂医院⁵⁾

進藤 亮輔¹⁾、青木 茂¹⁾、入山 高行²⁾、馬 詰 武³⁾、
増山 寿⁴⁾、板倉 敦夫⁵⁾

(背景)

分娩の進行が標準的な進行よりも遅れる場合には陣痛促進などの介入が考慮される。この“標準的な進行”として、わが国では1950年代に提唱されたFriedman曲線が広く用いられてきた。しかし、現代の我が国の分娩進行にはFriedman曲線は一致しないという問題点に注目し、我々は2019-2020年の周産期委員会において、分娩曲線の見直しを行い、わが国における標準的な分娩曲線を策定した。本分娩曲線から、分娩第1期は、子宮口開大5cmまでを潜伏期、5cm以降を活動期と定義した。分娩第1期に分娩の進行が順調でない場合、陣痛促進などの介入が考慮されるが、潜伏期(子宮口開大5cm未満)における分娩進行は個人差が大きいため介入は不要であり、精神的なサポートのみでよいとされている。一方で、活動期(子宮口開大5cm以上)または分娩第2期では、分娩の進行が順調でない場合(分娩遷延)で、その原因が微弱陣痛である場合は陣痛促進の実施が考慮される。しかし、わが国の現状では、①分娩遷延の定義は存在せず、②微弱陣痛の定義も通常使用されない子宮内圧計を用いた基準値しか存在せず、実用的でない。そのため、実際は分娩遷延および微弱陣痛の判断、さらにそれに対する陣痛促進の実施については各医療機関または医師個人の判断・裁量に任せられている。そのため、本来であれば必要のない介入が行われている可能性がある。不適切な陣痛促進剤の使用は、子宮破裂や

産道裂傷などの母体合併症、児の脳性麻痺などの有害事象の発症につながる。不適切な介入による母児の有害事象を減らすために、適切な介入の目安を作成する事は、重要な課題である。本指標が作成されれば、不必要な陣痛促進に伴う母体・新生児の合併症を減少させる事が可能となり、産科医療の質の向上につながるはずである。

本研究の目的は、分娩第1期活動期および分娩第2期における分娩遷延の定義を策定することである。現在の日本産科婦人科学会の用語集および診療ガイドラインでは、分娩所要時間の合計としての“遷延分娩”の定義(分娩所要時間が初産婦で30時間、経産婦で15時間以上)は存在するが、介入の目安とするべき分娩遷延の定義は存在しない。古くはFriedman曲線を基にACOGが作成した分娩遷延の基準が参考にされてきたが、米国では本基準はすでに使われていない。日本の現代の分娩進行のデータから分娩遷延の定義を策定することにより、分娩第1期活動期以降の介入の目安を示すことが可能となると考えられる。

(方法)

本研究は、東京大学医学部附属病院、岡山大学病院、帯広厚生病院、横浜市立大学附属市民総合医療センターで経膈分娩を試み、妊娠37週0日から41週6日までに分娩した症例をとした後方視的検討である。まず、分娩第1期については、分娩方法に依らず子宮口全開大まで到達した症例を収集し、子宮口開大1cmあたりの所要時間について

て検討する。分娩進行データが対数正規分布であると仮定して、ある子宮口開大度から次の開大度への進行の時間の分布を interval censored regression を用いて推定し、中央値と95パーセンタイル値を算出する。所要時間の95パーセンタイル

値を遷延の基準とする予定である。次に、分娩第二期については単純な所要時間のみではなく、所要時間と母児のアウトカムの間連についても検討し、遷延の定義・介入の目安を検討する予定である。

周産期委員会企画 P 周産期医療のトピックス

2) 妊娠貧血に関する管理標準化を目指した調査研究

国際医療福祉大学成田病院 永松 健

循環血液量の増加および胎児胎盤の鉄需要が高まることから非妊娠時に比べて妊娠期全体では約1gの鉄の需要が増加する。しかし、食習慣の個人差もあり必要量の鉄の摂取が追いつかず妊産婦の鉄欠乏性貧血の割合は世界的に高いことが示されてきた。貧血は妊娠期には早産、胎児発育不良に関連が示されており、妊産婦の貧血管理の重要性は高いとされている。しかし、妊娠中の循環血液量の増加において血漿増加が血球増加を上回るため、相対的にヘモグロビン値が低下する変化が生理的に生じる。そのため、妊娠時期に応じてヘモグロビン値の正常範囲は変化すると考えられる。さらに、妊娠高血圧腎症に代表される胎盤機能障害を背景とした周産期疾患においては、生理的な血液希釈が適切に働かないことで正常妊娠よりもヘモグロビン値が高くなるということも指摘されてきた。つまり、妊娠期のヘモグロビン値の解釈や目標については議論の余地があり、妊婦健診において貧血のスクリーニングが行われているが、鉄補充を実施する介入の目安については標準化が

進んでいない。産婦人科診療ガイドライン産科編では2023年版に初めて妊娠中の貧血に関するCQが作成されたが、国内での妊産婦貧血に関するエビデンスはいまだ乏しく、妊娠期の貧血スクリーニング法や鉄補充の方法の標準化には課題が多く残されている。一方で、産褥期の貧血に関しては、分娩期の出血が多く貧血が遷延した場合には、産後うつ頻度が増加し、母乳栄養の確立が阻害されることが知られている。それに対して鉄補充による早期回復を図ることでそれらの負の影響を減らすことができるという報告もあり、鉄欠乏への介入の有効性は妊娠期よりも産褥期についてエビデンスが集積した状況にある。近年、高用量の静注用鉄剤が臨床導入されて治療介入の選択肢は広がったが、内服鉄剤と静注鉄剤の使い分けをどのように行うべきかという新たな課題も生じている。本講演ではそうした視点から国内の妊産婦における貧血の診断、治療介入の問題点を整理し、周産期委員会における妊産婦貧血に関する調査研究の取り組みを紹介する。

周産期委員会企画 P 周産期医療のトピックス

3) フィブリノゲン製剤の適応拡大とその使用実績

順天堂大学医学部附属浦安病院 牧野 真太郎

フィブリノゲンは凝固過程の最終ステップ基質であり、止血に必須の因子である。正常人では血漿中に200~400mg/dL存在するが、止血のためには100~150mg/dL必要で、大量出血では最も初期に枯渇しやすい凝固因子である。フィブリノゲン製剤(乾燥濃縮フィブリン製剤)は1964年に我が国で使用認可されたが、血清肝炎(多くはC型肝炎)多数発生のため、保険適応は1998年から先天性低(無)フィブリノゲン血症に限定され、大量出血に伴う後天性低フィブリノゲン血症は適応から除外された。

2021年8月4日に第46回医療上の必要性の高い未承認薬・適応外薬検討会議が開かれ、ようやく「後天性低フィブリノゲン血症における乾燥人フィブリノゲンの使用に関する今後の取扱い」が取り上げられ、「産科危機的出血、心臓血管外科手術の出血に伴う後天性低フィブリノゲン血症が公知申請」が心臓血管外科での使用は当該調査の後に行うこと、製造販売業者による供給量に限界があることも含めて審議された。これを受け、2021年9月6日開催の薬事・食品衛生審議会は乾燥人フィブリノゲンを産科危機的出血に限定して公知申請を認めた。ただし、漫然と投与することなく、

危機的出血を適切に管理できる日本産科婦人科学会等が定める施設条件を満たし、使用する医療機関は学会調査に協力することが明記されている。輸血細胞治療学会と日本産科婦人科学会をはじめとした関連医学会は、血友病 HIV 感染患者団体と秋野公造議員と共同で大量出血患者救命のため、2010年から学術的社会的活動を開始し2021年に産後の低フィブリノゲン血症がその適応として認可された。

現時点では下記に記したような適正使用が前提となっている。使用例の把握のため、日本産科婦人科学会ホームページをポータルサイトとしたフィブリノゲン製剤の使用について適正使用に関する実態把握及び調査を目的としたシステムを導入(令和4年1月26日)し、令和3年9月6日まで遡っての inputs が現在実施されている。

フィブリノゲン製剤が使用された際には当該調査ページより使用情報が随時入力され、システムに登録される。本登録データを用い各種項目について統計解析が実施されている。使用対象疾患やそれぞれの疾患における本製剤の有効性に加え、より重症例や血中フィブリノゲン値未測定での投与例なども解析中である。

周産期委員会企画 P 周産期医療のトピックス

4) 我が国の産科医療の歩み

大分県立病院¹⁾, 三重大学²⁾, 順天堂大学³⁾, 横浜市立大学⁴⁾, 日本医科大学多摩永山病院⁵⁾
 佐藤昌司¹⁾, 池田智明²⁾, 板倉敦夫³⁾, 倉澤健太郎⁴⁾,
 中井章人⁵⁾

わが国の周産期死亡、妊産婦死亡はともに現在、世界的にも誇れる低率を維持できており、背景には本領域に携わる医療従事者の努力のみならず、行政施策面の拡充や国民の公衆衛生意識の高まりなど、多くの要素が重畳している。この状況は一朝一夕に成し遂げられたものではなく、高度経済成長時代の1960年代にあってはなお、妊産婦死亡率と周産期死亡率は各々90~100(対100,000分娩)および30前後(対1,000出生)と、現在の約10倍の値であった。その後のわが国の産科医療は何を契機に、どのような変遷を経て現在のレベルに至っているのか、そのなかで日本産科婦人科学会および日本産婦人科医会が取り組んできた事業と果たしてきた役割は何かについて、年次を区切りながら評価・検証する。以下、年次ごとに主な事項を羅列する。

●~1980年頃：戦後~高度経済成長期のなか、出産数の増加とともに分娩施設が自宅から施設分娩へ、診療所から病院施設へと変化し、関連法律の整備が進む。生育限界が妊娠24週へと改められ、いわゆる「周産期医療」が提唱され、新生児搬送体制が拡充。本邦および国際的な産科(周産期)医療者の学術団体が設立・発展していく。

主な出来事：優生保護法の施行(1948)、母子手帳発行(1948)、周産期領域の学術団体設立(日本産科婦人科学会/母性保護医協会(1949)、FIGO(1954)、AOFOG(1957)、日本新生児学会(1965)、日本周産期学会(1983))、周産期死亡統計開始(1950)など

●1980年代：出生数の減少が始まる。各地で周産期母子センターの設立が始まり、新生児搬送に加えて母体搬送体制が徐々に拡充。胎児の観察・監視

技術の向上、胎児治療が萌芽。

主な出来事：非加熱製剤肝炎訴訟(1987)、産婦人科認定医制度(1987)、胎児治療の報告(ジギタリス、膀胱羊水腔シャント、腹腔内輸血、血管吻合遮断術など)、分娩監視装置/超音波断層装置の普及など

●1990年代：生育限界の変更、胎児治療の更なる拡充、母体・新生児搬送体制の拡充などを背景に、産科医療の個別化/集約化/階層化の動きが加速。全国の総合・地域周産期母子医療センターが本格的に整備される。

主な出来事：阪神淡路大震災(1995)、母体保護法施行(1996)、周産期母子医療センター設置(1996)、生育限界22週へ変更(1991)など

●2000年代：産科関連の医療事故、訴訟事件などを受け、医療安全への意識が高まり、これを受けて国/学会/医会の取り組みとして周産期救急搬送体制のシステム化、医療事故の予防と対応に関連する諸種の取り組み(ガイドライン、補償制度など)が開始された。

主な出来事：低周産期死亡率世界第1位(2000)、日本産婦人科医会(2001)、日本周産期・新生児医学会(2004)、福島大野事件(2004)、産科医療補償制度(2009)、周産期(全生産)登録(2000)、NCPR事業(2005)など

●2010年代~現在：大災害の発生、新規感染症の蔓延などを経験して、医療過誤の問題のみならず「災害時・緊急時の周産期医療体制」についての準備体制と、実施にあたっての教育・研修体制の確立が喫緊の課題となり、この視点からの取り組みが実施されるようになった。

主な出来事：東日本大震災(2011)、COVID-19

感染症(2020～), 無痛分娩による医療事故(2017), 医療事故調査制度(2015), JALA 設立(2018), 成育基本法成立(2019), NIPT 開始(2013), 妊産婦死亡報告事業(2010), 再発防止に関する報告書(2011), J-CMELs(2015), 母と子のメンタルヘルスフォーラム/研修会(2017), 災害時周産期リエゾン(2017), 産婦重篤合併症報告(2021) など

●産科医療の今後：これらの歴史を踏まえ、新しい医学的・社会的課題(分娩費の保険化・見える化, 産科施設の地域バランスの変化と集約化の問題, 働き方改革の問題(時間外労働, 女性医師の労働環境, 勤務医志向への変化, 救急医療体制), ゲノム医療など)への方策についても論じてみたい。

女性ヘルスケア委員会企画 **P**

婦人科特定疾患治療管理料導入から4年～器質性月経困難症に対する適切なホルモン療法アップデート～

女性ヘルスケア
委員会企画

令和2年度の診療報酬改定で、器質性月経困難症に対してホルモン療法を行う際に、婦人科特定疾患治療管理料が算定可能になった。この管理料を算定する要件に、日本産科婦人科学会と日本産婦人科医会が共同で行っている e-learning の修了があり、今まで7000人を超える先生方にご受講を

いただいている。一方で、管理料が導入されてから4年が経過しており、その間にさらなる知見の蓄積もみられている。ここでは、それらについて、ホルモン療法と制度の2つの観点から振り返ってみる。

1) ホルモン療法アップデート

東京大学 泉 玄太郎

器質的月経困難症の治療戦略は、大きく分けて手術療法と薬物療法に分けられる。薬物療法の目的は、疼痛症状の管理や、病変の縮小、術後再発の予防などであるが、その中心的役割を果たすのがホルモン療法である。

ホルモン療法は原則として長期内服が必要であるが、一方で、副作用のリスクから長期使用できない薬剤もある。また、年齢ごとにリスクを再評価する必要がある薬剤や、排卵を抑制するものであるため挙児希望がある患者には使用できない薬剤も多い。このように、ライフステージに合わせてホルモン治療の選択肢が変わっていく。

そのため、薬物療法を行う際には、患者の症状や器質的疾患の病勢の評価だけでなく、年齢や挙

児希望の有無、挙児努力を始める予定の時期などを考慮する必要がある。さらに、就労状況、経済的背景、など様々な評価が、よりよい治療法の選択のためには必要である。

一方で、薬物療法の選択肢は近年さらに広がりつつあり、GnRH アゴニスト、GnRH アンタゴニスト、低用量エストロゲンプロゲステロン配合薬、内服プロゲステロン製剤（ジェノゲスト、ジドロゲステロンなど）、レボノルゲストレル放出子宮内システムなどの中から適切な薬剤を選択して使用することになる。このセッションでは、このような薬物療法について、特に最近保険適応となった薬剤を中心にその使用方法や注意点について、レビューを行う。

女性ヘルスケア委員会企画 **P** 婦人科特定疾患治療管理料導入から4年～器質性月経困難症に対する適切なホルモン療法アップデート～

2) 婦人科特定疾患治療管理料について

横浜市立大学 倉澤 健太郎

婦人科特定疾患治療管理料は婦人科領域として初めて認められた管理料であるが、正しく運用するためには我が国の保険制度や背景を理解することが重要である。器質性月経困難症の治療については、かつてはいわゆる経口避妊薬を転用しながら自費診療をせざるを得ない時代もあったが、2008年にLEP製剤が保険適用となった。その後もホルモン製剤を用いた内分泌療法は発展を続けており、現在は様々な薬剤が使用可能となっている。一方、器質性月経困難症そのものは、女性の月経回数の増加に伴ういわば現代病でもあり、月経時の苦痛に留まらず、今後の様々なライフイベントにも影響を与えることがわかっている。患者

の症状は痛みや過多月経といった身体的な月経随伴症状にとどまらず、不安やうつなどのQOL指標や労働生産性、不妊や悪性腫瘍に至るまで幅が広く、ニーズもさまざまである。医療者は、器質性月経困難症患者に対して継続的に質の高い医療を提供する責務があるものの、適切に医学管理を継続するためには、一定の水準を担保する必要がある。さらに説明に要する時間については評価がなされるべきである。このような背景のもと本管理料が設定されるに至ったが、本講演では保険診療全般、具体的な運用や留意点についても触れ、月経困難症に対する適切な管理の重要性について共有したい。

婦人科悪性腫瘍統合入力システム up-to-date (JESGO セッション)

婦人科悪性腫瘍総合入力システム (Japan Entry System of Gynecologic Oncology : JESGO) は、婦人科悪性腫瘍症例を施設内で統合的に管理・保管するための施設内サマリシステム (ソフト) で、日本産科婦人科学会 (JSOG)、日本婦人科腫瘍学会 (JSGO)、日本産科婦人科内視鏡学会 (JSGOE) の3学会が共同で開発・運営し、2024年12月より学会員に無料で提供している。

JESGO は日常の診療業務フローに合わせ、各種登録事業を網羅した形で入力できる全国一律のプラットフォームとしての役割を果たしている。特に JSOG や JSGOE 等の各種登録事業へのデータの流し込みを容易にし、入力業務負担を軽減することを目的として開発された経緯がある。

すなわち JESGO を活用することで以下の利点が想定できる。

1) JSOG 婦人科腫瘍登録、JSGOE 症例登録が必要な症例について、JESGO を利用することで必要情報の入力を一括して容易に行うことが可能とな

る。

2) JESGO 使用施設において先進的医療技術の導入などに伴い、厚労省から保険要件としての症例登録・データ解析の提出などの要請があった際に、改めてカルテ調査の必要性が減少し早急な対応が可能となる。

3) JSOG、JSGOE への提出項目以外でも、多施設共同の後方視的調査研究などへの研究活用が可能となる。さらに各施設で追加したい調査項目がある場合には、施設毎に独自にカスタマイズを行うことも可能である。

将来的には JESGO によって本邦の婦人科悪性腫瘍に関連するリアルワールドデータを収集することで、医療レベルの向上を目指している。本学術講演会では JESGO の普及そして利用促進を願って JESGO の活用法とメリットを再確認する。さらに関連する広報活動や問い合わせ体制、そして今後の将来動向を踏まえて各方面の演者から解説する。

厚生労働省企画

出産をめぐる妊婦への経済的支援策の今後の展望

厚生労働省保険局保険課長補佐（公衆衛生学修士）柴田直慧

（概要）

急速に進展する少子化・人口減少に歯止めをかけるためには、若者・子育て世代の所得を向上させるとともに、出産・子育てにおける経済的負担を軽減することが不可欠である。その一環として、本年4月から公的医療保険制度における出産育児一時金の支給額が大幅に引き上げられるとともに、来春以降、全国の分娩取扱施設ごとの特色・サービス内容や出産費用等の見える化が進められる予定である。また、これらの政策の効果検証を行った上で、2026年度を目途に、正常分娩の保険適用の導入を含め、出産に関する支援等の更なる強化について検討を進めることとされている。本セッションでは、これらのトピックについて、政府における現在の議論の状況や、今後の展望について発表を行う。

（出産育児一時金の引き上げ）

出産育児一時金については、出産に係る経済的負担の軽減を図る観点から、厚生労働省社会保障審議会医療保険部会での議論を経て、本年4月から支給額が50万円（産科医療補償制度の対象分娩でない場合は48.8万円）に引き上げられたところである。引き上げ幅については、年々出産費用が上昇している状況を踏まえ、平均的な標準費用を全て賄えるようにするとの考え方に基づき決定されたが、2009年10月に原則42万円に引き上げられて以降、基本的に据え置きとされてきたものが、今回、8万円の大幅増となった。

（出産費用等の見える化）

一方、同部会における議論において、妊婦等が、あらかじめ費用やサービスを踏まえて適切に医療機関等を選択できる環境を整備することが重要であるとの指摘があり、各分娩取扱施設における出

産費用等の「見える化」に取り組むこととなった。

具体的には、全国の分娩取扱施設ごとの特色やサービス内容と、出産費用の平均額等の情報を厚生労働省が収集し、2024年春から、厚生労働省が開設・運営するウェブサイトにおいて妊婦等に情報提供を行うことを予定している。

本セッションにおいては、開設予定のウェブサイトの実際の画面等を用いて、本取組についての紹介を行う。

（正常分娩の保険適用等の検討）

正常分娩の保険適用を含めた出産に関する支援等の更なる強化については、本年6月13日に閣議決定された「こども未来戦略方針」の中で、『2026年度を目途に、出産費用（正常分娩）の保険適用の導入を含め、出産に関する支援等の更なる強化について検討を進める。』とされたところである。

出産の保険適用については、サービスの内容が標準化され、質や安全性が確保されるというメリットがある一方で、全国一律の診療報酬で評価されることになるため、妊婦自身の自由な選択により様々なサービスが利用されている現状から、かえって幅を狭めることのないようにする必要がありと考えられる。

今後、正常分娩への保険適用の導入を含めた支援策について検討を行うに当たっては、こうした点や、出産費用の地域差、地域の産科医療提供体制の確保という観点も念頭に置きつつ、出産に関する保険給付全体の在り方という広い視点から、様々な課題について検討していく必要がある。

本セッションにおいては、正常分娩の保険適用等に関する政府における現在の検討状況や、今後の展望について発表を行う。

専攻医教育プログラム 1

産婦人科と遺伝学

東京大学統合ゲノム学 織田 克利

産婦人科診療において、専門性に関わらず遺伝学の知識が必須となっている。

遺伝性腫瘍においては、遺伝性乳がん卵巣がんやリンチ症候群をはじめ、原因遺伝子の病的バリエーションの検出が、治療法の選択や遺伝診療と密接に関連している。特に腫瘍組織における *BRCA1/2* 遺伝子関連検査、ミスマッチ修復遺伝子の免疫組織染色/マイクロサテライト不安定性検査等、遺伝性腫瘍の診断に関わる情報が得られる機会も増えており、適切な遺伝学の知識と遺伝学的検査、遺伝カウンセリング機会の確保が重要である。治療困難な婦人科がん症例に対しては、がんゲノム医療についての情報提供や検査機会の確保も必要である。

2022年1月に、着床前遺伝学的検査の見解・細則の改定が行われた。重篤な遺伝性疾患を対象とした着床前遺伝学的検査 (PGT-M)、着床前胚染色体構造異常検査 (PGT-SR)、着床前胚染色体異数性検査 (PGT-A) の目的、対象を十分に理解し、本検査を希望されるクライアントに対し、適切な遺伝カウンセリングにつなげられるよう、基礎知識を整理しておく必要がある。NIPT (non-invasive prenatal genetic testing) も遺伝学的知識に基づいたカウンセリング機会の担保が不可欠である。

本セッションでは産婦人科医が知っておきたい遺伝学、遺伝医療の概要について解説する。

専攻医教育プログラム 2

産婦人科と医療保険

帝京大学医学部附属溝口病院 西 井 修

我が国の医療は、全ての国民が医療保険に入る権利と義務を有する国民皆保険制度により運用されている。国民は保険料を保険者に支払い、医療費の3割を医療機関に支払う。医療費の7割は医療機関が保険者に請求する。診療報酬は医療サービスに対する対価として保険から受け取る報酬であり、技術の評価と物の価格よりなる。診療報酬額は医療行為ごとの点数が加えられ、1点を10円として計算される「出来高払い制」である。DPC (Diagnosis Procedure Combination) とは急性期入院医療の包括評価のことである。診断名をもとに手術などの診療行為に応じて、1日当たりの診断群分類点数から医療費を計算する会計方式で包括評価による「定額払い」である。

診療報酬は2年ごとに改定される。改定率は予算編成過程を通じて内閣が決定し、社会保障審議会医療保険部会において、診療報酬改定の基本方針が策定される。この基本方針に基づき中央社会

保険医療協議会（中医協）において審議され、中医協の答申に基づき、厚生労働大臣より告示通知で発出される。

ロボット支援下手術などの新たな医療技術や再評価が必要と考えられる技術は、既存の技術と比較した有効性、安全性、倫理性、普及性等に関して記載した評価提案書を産科婦人科学会等から、外科系学会社会保険委員会連合等を通して厚労省に提出される。提出された提案書は、中医協医療技術評価分科会による評価後、中医協総会を経て、厚生労働大臣から診療報酬改定に係る告示・通知発出され、翌年度の診療報酬から運用される。

少子化対策の一環として2022年に保険適用となった不妊治療や、今後検討されている分娩の保険適用化は、産婦人科診療に大きな影響を及ぼす可能性があり、医療保険に関する十分な理解が必要である。

専攻医教育プログラム3

生殖・周産期診療に関わる遺伝学的検査と生命倫理

国際医療福祉大学成田病院 永松 健

生殖・周産期の領域では、かつては人知を超えた世界であった妊娠成立前の胚のゲノム情報を得ることが可能となっており、妊娠成立後には出生前に胎児の遺伝学的情報を得る方法が確立している。そうした、遺伝学的検査技術は ART 診療における成績の向上、流産の回避、先天性疾患の診断など幅広い目的に応用されている。しかし、こうした検査技術の進歩に対して社会の中での議論が追い付かなければ、優生思想への傾倒、商業主義的な流れに乗った検査の押し付けの状況を生み出しかねない。近年、無侵襲的出生前遺伝学的検査 (NIPT) および着床前遺伝学的検査 (PGT) の臨床導入の過程では、検査へのニーズが高い一方で、先天的疾患を持つ患者に対する社会の理解の後退を生じるという懸念が呈されてきた。

NIPT は、日本医学会の指針に基づく認定施設が少ないことや実施対象の制限などが要因となり、認定外施設での実施が急増する状況が生じて

きた。その後、出生前検査認証制度等運営委員会が設立されて、NIPT を含めた出生前診断全体に関わる情報提供、妊婦のニーズに即した実施体制の構築が進められている。

PGT は着床前診断に関する旧見解に基づいて、重篤な遺伝性疾患および染色体転座による習慣流産のみを適応として行われてきた。しかし、全染色体の数的・構造的分析法の発達により正倍数性胚の選択による ART 診療の治療成績の向上を目的とした PGT (PGT-A) が海外で普及した。国内では、日本産科婦人科学会の PGT に関する新見解が 2022 年 1 月に示され、3 種類の PGT についてそれぞれの目的に即した見解に区分されて、臨床検査としての実施が開始されている。

本講演ではそうした、生殖・周産期領域の遺伝学的検査について現在の実施体制と生命倫理的側面に関して概説する。

専攻医教育プログラム 4

原発性・続発性無月経の診断と治療

東京医科歯科大学 寺内 公一

原発性無月経 primary amenorrhea は「満18歳を迎えても初経の起こらないもの」、続発 [性] 無月経 secondary amenorrhea は「これまであった月経が3か月以上停止したもの」というのが現時点での日本産科婦人科学会の定義である（産科婦人科用語集・用語解説集改訂第4版2018年）。原発性無月経について、アメリカ産科婦人科学会では「15歳までに月経周期の確立しないもの」と定義しており、日本の定義を基にした場合には介入が遅れる可能性がある。そこで、用語集・用語解説集改訂第4版では新たに「初経遅延 delayed menarche」と「遅発初経 delayed menstruation」の用語が導入された。前者は「15歳以上18歳未満で初経の発来していないもの」、後者は「15歳以上で初経の発来したもの」であり、前者が従来の原発

性無月経よりも早期に診断的・治療的介入を行う根拠となる。一方の続発性無月経は、いったんは月経が発来していることから、その病態の基本は排卵障害である。1976年以来用いられているWHO分類では「視床下部下垂体不全」「視床下部下垂体機能障害」「卵巣不全」「先天性・後天性性器異常」「器質性高プロラクチン血症」「機能性高プロラクチン血症」「視床下部下垂体腫瘍」等に分類されている。2022年にFIGOは新しい分類法としての「視床下部性 Hypothalamic」「下垂体性 Pituitary」「卵巣性 Ovarian」「PCOS」を提唱した (HyPO-P)。原発性・続発性無月経を来す疾患の鑑別診断とそれぞれの病態に対応した治療法の選択は複雑で多岐に渡る。本プログラムではこれらについての概説を行う予定である。

専攻医教育プログラム5

月経困難症/月経前症候群の診断と治療

京都大学 江川美保

月経周期に関連して繰り返起こる月経随伴症状には月経期間中にあらわれる月経困難症と月経前の黄体期にあらわれる月経前症候群（PMS）とがある。月経前不快気分障害（PMDD）は精神症状が重篤で生活支障が顕著であるPMSの最重症型を指す精神科的な診断名である。月経困難症は機能性と器質性に分類されるので、まずは詳細な問診と内診、画像診断などで器質性疾患の有無を確認する。一方で、PMS/PMDDには器質性疾患の関与は今のところ示されておらず、また診断に有用な客観的指標も存在せず、前向き症状記録による症状出現時期とその反復性の確認が診断の根拠となる。

機能性月経困難症の対症療法はNSAIDsを痛くなる前に早めに内服することである。その効果が不十分な場合はLEP、プロゲステン製剤、レボノルゲストレル放出子宮内システムを使用する。PMS/PMDDに対しても対症療法（鎮痛剤、利尿

剤、精神安定剤、睡眠導入剤など）を適宜行うが、複数の症状を軽減するにはOC・LEPが有効である。精神症状が強い場合はSSRIかドロスピレノン含有LEPを用い、精神科との併科診療も考慮する。合成プロゲステンを用いた排卵抑制は月経困難症、PMS/PMDD、さらに既存疾患の月経前増悪のすべてに対して効果が期待できる治療戦略であるが、黄体ホルモンに対する忍容性が低い患者もいることに十分な配慮が必要である。

患者が訴える多彩な心身両面の月経随伴症状に気を取られがちだが、本人に過多月経の自覚があるか否かにかかわらず鉄欠乏の評価と対策はすべての有経女性に不可欠であり、その基盤の上でこそ各種薬剤の最大の効果が発揮されると言える。生体機能を整える漢方療法や生活改善指導も取り入れた教育的配慮を伴う包括的なケアと治療を提供することが求められている。

専攻医教育プログラム 6

不妊症の診断と治療

群馬大学医学部附属病院周産母子センター 北原 慈 和

我々の日常診療において、挙児希望はあるが、なかなかお子さんに恵まれないという患者さんに出会うことが多くなっている。不妊症とは、定期的な性交渉を1年間行なっても妊娠が成立しない場合のことを言う。しかし、2019年の我が国のデータでは、女性の初婚年齢の平均は29.6歳とほぼほぼ30歳に達している。さらに、結婚後、第1子出生までの平均期間は2.45年、第2子出生までは4.93年、第3子となると6.96年となっており、その期間は年々上昇傾向にある。そのため、挙児希望で我々産婦人科を受診する時点で、すでに年齢も上昇しているため、Time to pregnancyの観点からも、速やかに不妊症の精査を行い、かつ、適応があれば速やかに不妊症の治療を開始することが重要である。

本講演では、一般産婦人科外来を挙児希望で受診をした患者さん（ご夫婦）に、(1) どのような問診を取ると良いか (2) その問診をもとにどのよ

うな不妊症の精査を行うと良いか (3) それらの問診・精査の結果から、どのような不妊治療（特に、一般不妊治療）を行うと良いのかを中心に実際の外来診療の流れに則した形でお話をできればと考えている。

(1) の問診については、不妊症の原因で多くを占めている排卵障害について、FIGOより発表されている異常子宮出血（AUB）の診断システム、及び、排卵障害の診断システムであるHyPO-Pシステムを中心に説明を行う予定である。(2) の不妊症の精査については、多くの専攻医の先生方が少し苦手意識を持っている生殖内分泌学に基づいた形で、ホルモン検査や子宮卵管造影検査、男性の精液検査などについて説明を行う予定である。(3) の一般不妊治療については、調節卵巣刺激などの排卵誘発法を中心に説明を行う予定である。

専攻医教育プログラム7

生殖補助医療

秋田大学 熊澤 由紀代

生殖補助医療 (Assisted Reproductive Technology : ART) とは、体外受精・胚移植 (IVF-ET)、卵細胞質内精子注入・胚移植 (ICSI-ET)、及び凍結・融解胚移植などの不妊症治療の総称である。1978年に世界初の体外受精児がイギリスで誕生し、日本では1983年にARTが導入された。ARTによる出生児は増加傾向にあり、2021年に日本でARTにより出生した児は69797人と報告されている。

ARTの適応は、1) 卵管性不妊、2) 男性不妊、3) 子宮内膜症、4) 原因不明不妊、5) 免疫性不妊、などが挙げられる。また近年では、悪性疾患に対する化学療法などによる妊孕性の低下に対し、治療前に卵子・受精卵・卵巣組織・精子・精巣組織を凍結保存する妊孕性温存療法にその技術が用いられている。

ARTでは、通常、内因性LHサージを抑制しながら複数の卵胞発育を促すことを目的に調節卵巣

刺激が行われる。具体的には、GnRH agonistを併用するLong法やShort法、GnRH antagonist法などがある。クロミフェンやレトロゾール、FSH/HMG製剤などを投与し卵胞を発育させ、経膈超音波下に採卵を行う。精液所見に異常がなければ調整した精液を媒精し受精を促す。男性不妊では顕微鏡下に直接卵細胞内に精子を注入する顕微授精 (ICSI) を行う。採卵周期で胚移植を行い、余剰卵は凍結保存する。多胎妊娠の防止に、1周期での胚移植は原則1個である。卵巣過剰刺激症候群のリスクが高い場合には、移植は行わず全胚凍結とする。

ARTによる治療は自費診療で行われてきたが、2022年4月より公的健康保険の対象となった。しかしながら保険適応には女性の年齢制限や回数制限があり、また着床前診断などを含む一部の検査については保険の適応外である。

専攻医教育プログラム 8

妊娠と薬

国立成育医療研究センター母性内科¹⁾, 国立成育医療研究センター妊娠と薬情報センター²⁾金子 佳代子¹⁾, 後藤 美賀子²⁾, 村島 温子²⁾

近年の医療の進歩により、高血圧症や糖尿病などの慢性疾患を持つ女性の妊娠や出産が増えている。これらの疾患においては、原則、妊娠中も非妊娠時と同様に適切な薬物治療を行い、疾患活動性をコントロールすることが良好な妊娠転帰を得るためにも重要である。一方で、ウイルス感染症による発熱や上気道症状、妊娠中の頭痛、悪阻による嘔気などに対する症状緩和のために、一時的に薬物治療が必要となることもまれではない。「妊娠しているから」「授乳中だから」という理由で必要な投薬がされず、妊婦や授乳婦に無用な我慢を強いてしまうことがあるとすれば、それは患者のQOL維持の観点からも避けたいところである。

産婦人科診療ガイドライン産科編 2023 には、妊娠と薬に関して5つのCQが設けられている。これらは、産婦人科医が妊娠中・授乳中に適切に薬

剤を使用するために、その道標として設定された項目である。個々の薬物には添付文書が存在するが、添付文書上の「禁忌」は、主に動物実験の結果やヒトでの情報の少なさを理由に定められていることが多く、エビデンスに基づいた安全性情報が十分に反映されているわけではないことに注意が必要である。

国立成育医療研究センター妊娠と薬情報センターでは、科学的根拠に基づいて妊娠中・授乳中の薬物の安全性を評価し、それをもとに妊婦等への医薬品投与に関する情報の添付文書への反映を推進する取組みを行っている。

本講演では、妊娠・授乳中の薬物使用に関する安全性評価の実際について、実例を用いて紹介するとともに、妊娠中の薬物治療に関する基本的な考え方について概説する。

専攻医教育プログラム9

胎児機能不全/胎児発育不全の診断と管理

三重大学 田中博明

胎児機能不全とは、妊娠中あるいは分娩中に胎児の状態を評価する臨床検査において「正常ではない所見」が存在し、胎児の健康であることに確信がもてない場合である。胎児は、母体の子宮内で成育するため、私たちは直接的に胎児の健康度を評価することができない。そのため、これまでに胎児の健康度を評価するため、様々な臨床検査が試みられてきた。しかし、現時点において、高い感度と特異度を持って「胎児の健康度が悪い」ことを示すことができる臨床検査はない。そのため、胎児機能不全の定義が、あえて「臨床検査で正常ではない所見があり、胎児が健康であることに確証がもてない」とされているのである。これまでに、胎児機能不全を診断するためにどのような臨床検査が用いられてきたか、その歴史を振り返り

たいと思う。

胎児発育不全とは、何らかの理由によって胎児の発育が制限されている状態を指す。胎児発育不全は、様々な原因によって起こり得るが、一般的に母体、胎児、胎盤・臍帯因子に分けられる。但し、胎児発育不全は、単因子だけでなく複数の因子によって発症することもしばしばある。現在は、胎盤形成不全に起因した胎児発育不全が、妊娠高血圧症候群の発症とも関連しており、注目されている。この胎盤螺旋動脈のリモデリング不全や trophoblastic plug の早期離脱などによって起こる胎盤形成不全に起因した胎児発育不全の病態を理解することが臨床的に重要であるため、その診断・管理を中心に解説する。

専攻医教育プログラム 10

新生児管理をみすえた胎児管理

国立循環器病研究センター 金川 武司

新生児は、非常に守られた子宮内環境から胎外生活に適応した呼吸循環動態に順応しなくてはならない。そのため、胎内では何事もなく生存していた胎児が、先天性疾患、産科・母体合併症や分娩時の状況によって、新生児期に生死が左右されたり、重篤な合併症が発生したりする。それらの合併症を避けるためには、胎児期から新生児期に起こりうることを予測し、適切な産科管理を行うことが必要になってくる。すなわち、新生児の緊急事態に備えて、適切な胎児診断と管理、そして、場合によっては事前の母体搬送が必要である。しかし、中には急に新生児管理が必要になる病態も存在し、その場合は新生児搬送が必要になってくる。

適切な新生児管理を行うために産科医ができることとして、新生児管理を見越した胎児疾患の診断するスキルを身につけること、また、母体搬送の適応やタイミングを適切に判断すること、そして、急に新生児治療が必要になった場合に適切な新生児搬送ができることである。本レクチャーでは、胎児診断については、胎児循環と新生児循環の違い、その違いのために起こる胎児期は順調に生育しても新生児期に急変する胎児疾患の診断のポイントを解説します。また、母体搬送については、切迫早産における具体的な搬送のタイミングと手順を解説します。さらに、新生児搬送については、搬送の適応と方法について解説します。

専攻医教育プログラム 11

子宮筋腫，腺筋症の診断と治療

奈良県立医科大学 前川 亮

子宮筋腫，子宮腺筋症は月経過多症や月経困難症，慢性的な骨盤痛，また腫大した子宮による圧迫により頻尿等を引き起こして女性のQOLを著しく害する疾患である。

子宮筋腫は主に平滑筋細胞と線維芽細胞で構成される良性の腫瘤性疾患である。診断は超音波検査やMRI等で特徴的な腫瘤像を確認することで得られる。治療は根治的な効果が得られる治療は子宮全摘術であり，妊孕性温存希望がなく手術を許容できる場合の第一選択となる。一方，妊孕性温存希望がある場合は，筋腫核出術や動脈塞栓療法，薬物療法が考慮される。薬物療法においては，GnRH アゴニスト，アンタゴニストによる低エストロゲン・低プロゲステロン状態を目的とした治療のほか，過多月経の改善を目的としてプロゲステロンを含む製剤が使用される場合があるが，プロゲステロンは子宮筋腫の増大に寄与することに留意する必要がある。

子宮腺筋症は筋層内で子宮内膜類似の腺上皮および間質組織が増殖・増殖する疾患である。診断は超音波検査やMRI検査で行われ，びまん性，限局性など種々のパターンを呈する。子宮筋腫と同様に根治的な効果が得られる治療は子宮全摘術である。子宮温存療法として，子宮腺筋症病巣除去術や過多月経改善を目的としたマイクロ波子宮内膜アブレーション療法もある。薬物治療では疼痛改善や過多月経の改善を目的としてGnRH アゴニストの他，プロゲステロンを含有する製剤が選択できる。

子宮筋腫と子宮腺筋症が合併している例も少ない。薬物療法を選択する場合はそれぞれのホルモン応答の違いに留意して治療法を選択し，慎重に経過を観察する必要がある。子宮筋腫と子宮腺筋症の治療と診断について，ホルモン応答の違いにも言及しながら基本的事項を中心に概説する。

専攻医教育プログラム 12

子宮内膜症の診断と治療

高木病院・国際医療福祉大学 北 島 道 夫

子宮内膜症は女性の様々なライフステージにおけるQOLに影響を及ぼし、遅滞ない診断と個々に応じた治療の選択が重要で、ときに領域横断的な対応や長期的な管理を要する。外科的・病理学的な内膜症病変の同定により確定診断されるが、昨今では、臨床的な診断のもと実地的に薬物療法を開始し、症状が改善しない場合に手術を適用することが推奨されている。問診は重要で、痛みに関する事項を詳細に聴取する。内診の診断精度は必ずしも高くないが、重要な診察手技である。経陰超音波断層法はリアルタイムに有痛性部位を確認しながら行うことが可能で、MRIは卵巣病変や深部病変の質的診断ならびに骨盤内の病変の拡がりの評価に有用である。血液検査での診断は困難で病態を反映する各種マーカーの有用性は必ずしも明らかでない。

子宮内膜症性疼痛の第一選択は薬物療法であ

る。長期的な管理が必要であり、副作用を考慮して薬剤を選択、組み合わせる。薬物療法で効果が得られない場合には手術療法が考慮される。重症の子宮内膜症の場合には他科へのコンサルテーションを含めた入念な準備が必要である。子宮内膜症性嚢胞を取り扱う場合には術後の卵巣機能低下を可及的に回避する術式の工夫が必要である。不妊症に対する内分泌薬物療法の妊孕性改善効果にはエビデンスが乏しく、手術療法および生殖補助医療が考慮される。晩婚化、出産年齢の高年齢化から、遅滞ない適切な不妊治療の適用が肝要である。妊娠した場合、周産期合併症が増加することが指摘されており、領域を越えた情報の共有が重要となる。性成熟期以降も子宮内膜症に起因する様々な症状に対する管理において、薬物療法での適切な薬剤の選択、癌化の有無、慢性疾患の有無等に留意してフォローする必要がある。

専攻医教育プログラム 13

卵巣悪性腫瘍の疫学・診断・治療（卵管・腹膜の悪性腫瘍を含む）

慶應義塾大学 千代田 達 幸

卵巣悪性腫瘍は全世界で年間約30万人が罹患し約20万人が死亡する。上皮性、性索間質性、胚細胞に大きく分けられ、90%以上は上皮性である。

近年の解析により、卵巣悪性腫瘍は様々な起源、分子プロファイルを有することが明らかとなった。パラダイムシフトは2001年のPiekらによる予防的卵管卵巣切除検体の卵管に異型細胞が認められるという発見を端緒に、高異型度漿液性癌の多くが卵管由来であることが明らかとなったことである。卵管の異型細胞はすでにTP53変異を有しており、高異型度漿液性癌はTP53変異をベースに染色体不安定性により癌化が進行すると考えられる。漿液性境界悪性腫瘍、低異型度漿液性癌はBRAF、KRAS変異を認め、高異型度漿液性癌とは全く異なる腫瘍であることが明らかとなった。

類内膜癌と明細胞癌は子宮内膜症関連卵巣癌と呼ばれる。卵管結紮、経産はこれらの発がんとは負

に相関しており、月経が密接に発がんに関与している。近年、子宮内膜症のみならず正常の子宮内膜腺管においてもKRAS、PIK3CA変異があることが明らかとなった。類内膜癌と明細胞癌はARID1A、PIK3CA変異を認めるが、形態や化学療法感受性は異なっており、発がん機構の詳細は未だ不明点が多い。

これらからは上皮性卵巣癌において卵巣は“土壌”としての役割が大きいと考えられ、精巣腫瘍の殆どが胚細胞腫瘍であるのと異なり、それが卵巣癌の多彩さ、ユニークさを形成している。

治療においてはpost PARP阻害薬の治療など課題がある。mirvetuximab soravtansineは葉酸受容体 α 陽性のプラチナ抵抗性卵巣癌において化学療法に比較して全生存期間を延長し、抗体薬物複合体の強い効果が卵巣癌においても示された。

本プログラムでは悪性卵巣胚細胞腫瘍、悪性性索間質系腫瘍を含めて概説する。

専攻医教育プログラム 14

性分化異常, LGBTQ, 性暴力

女性クリニック Wel Toyama 種 部 恭 子

【性分化異常】

性分化異常は内外性器の形態, 性染色体の数, 性腺とその機能のバリエーションである。女性として育ち思春期発来の異常で産婦人科医が診断治療にかかわる疾患については, 女性としてのアイデンティティを支持し, 十分なラポール形成を図り, 精神的な発達を見ながら将来のセクシュアリティや妊孕性の見通しについて段階を踏んで理解を促す。女性として生きる上での困難に伴走支援し, 治療の選択肢を提示する。

【LGBTQ】

性自認および性的指向のバリエーションは多様である。うち戸籍に割り当てられた性と性自認が異なるものを性別不合同いう。日本精神神経学会のガイドラインに則り診断治療する場合, 身体的性別の診断および自認する性のホルモン投与等の治療を行い, 社会的受容や生活上の困難の解決に向けて支援する。特例法により一定の条件のもとで戸籍の性別を変更することができるが, 2023

年10月に生殖腺の切除が性別変更の要件であることについて違憲判決が下された。産婦人科医も医学的な視点から社会的な受容を進める議論に加わることが望まれる。

【性暴力】

同意のない性的行為はすべて性暴力である。女性の6.9%は無理やり性交された経験を持っており, 加害者の約9割は顔見知りである。2023年7月の刑法改正により同意のない性交を処罰対象とする構成要件の大幅な見直しが行われ, 性交同意年齢は16歳に引き上げられ, 被害相談が増加している。全都道府県に性暴力被害者のためのワンストップ支援センターが設置されており, 緊急避妊や性感染症の診断治療, および性暴力を証明するためのDNA等資料採取や損傷の診断が産婦人科医に求められる。性暴力はPTSDの発症要因であり, 早期の心身の回復のためにすべての産婦人科医の協力をお願いしたい。

専攻医教育プログラム 15

性感染症

金沢医科大学 藤田 智子

「感染症の予防及び感染症の患者に対する医療に関する法律」に基づいて全数把握対象疾患として HIV 感染症、梅毒が、定点把握対象疾患として性器クラミジア感染症、性器ヘルペス、尖圭コンジローマ、淋菌感染症が調査されている。

これらのうち、報告数最多である性器クラミジア感染症と淋菌感染症は、女性生殖器特有の感染経路で大部分が上行性感染を起こし、自覚症状に乏しいため治療の機会がないまま放置され、子宮頸管炎、子宮内膜炎、子宮付属器炎、卵管卵巣膿瘍、ダグラス窩膿瘍、子宮傍結合組織炎、骨盤腹膜炎、さらには肝周囲炎である Fitz-Hugh-Curtis 症候群へと進展する。長期間放置した場合には卵管周囲癒着、卵管采閉塞、卵管留水腫を起こし、女性の卵管性不妊症、子宮外妊娠の原因となる。また妊娠中に感染した場合には、絨毛膜羊膜炎からの流産の原因となり、産道感染することに

よって、新生児肺炎や結膜炎を引き起こす。治療では薬剤耐性菌が問題となる。さらに、2011 年以降梅毒感染者数が急増しており、特に若年者での感染増加が問題となっている。尖圭コンジローマ感染者数も減少しておらず、HPV ワクチン接種率の高いオーストラリアでは感染者数の減少と、母子感染率も低下しているとの報告がある。

性感染症は性的接触を介して広がり、患者は生殖可能年齢の男女を中心としており、日常診療でよく遭遇する疾患である。そのため、産婦人科医として診断方法・治療方法を熟知しておくことはもちろんのこと、性感染症をどう予防するかについて指導できることが大切である。本講演では性感染症について、産婦人科専門医としての必修知識を、産婦人科診療ガイドラインをまじえて解説する。

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女性アスリートのヘルスケア

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女性アスリート外来では、無月経や月経随伴症状、月経周期とコンディション、不妊症、妊娠期・産後のトレーニングの相談、更年期障害等多岐に渡る相談に対応しており、パラアスリートの診察を行う機会も多い。アスリートの診療を行う際は、アンチ・ドーピングの理念に基づいた対応が必要となるが、受診時に既にドーピング禁止物質を含む産婦人科領域の薬剤を使用していることが明らかとなり、治療使用特例(TUE: Therapeutic Use Exemptions)の申請を含む今後の対応について説明を行う機会も増えている。

無月経については、2014年に国際オリンピック委員会がrelative energy deficiency in sport (REDs: スポーツにおける相対的エネルギー不足)の概念を公表して以来、従来周知されてきた「女性アスリートの三主徴」の概念を包含するREDsの合同声明に沿った医学的介入が行われて

いる。このREDsについては、2023年10月に新たなconsensus statementが出された。今後、REDsの予防、スクリーニング、医学的介入がさらに促進され、スポーツへの参加基準や復帰についても今回更新されたClinical Assessment Tool Version 2が広く適用される可能性がある。また、当センターの調査では、月経随伴症状への治療や月経周期調節目的でのホルモン製剤の使用率は、オリンピック出場選手で年々増えておりEE20 μ g含有かつ連続投与可能なLEPやプロゲステロン製剤使用の割合が高くなっている。

本講演では、婦人科で対応する機会が多い無月経や月経随伴症状への対応について、最新の情報を踏まえて解説するとともに、近年、産婦人科医からの申請が増えているTUEの書き方について情報提供を行う。

IS-AC-1-1

Uterine Necrosis after Uterine Compression Suture for Postpartum Hemorrhage : a Case-control Study Liao Jou Chien, Shih Jin-Chung *National Taiwan University Hospital, Taiwan*

[Objective] Uterine necrosis is one of the rarest but most fatal late complications after uterine compression sutures (UCSs). However, the incidence and the predisposing factors of uterine necrosis remained unknown. Therefore, we aimed to assess the incidence and the risk factors of uterine necrosis after UCS for PPH. **[Methods]** This was a prospective case-control study in Taiwan during a 8-year-period (2015-2022). Our study included women who received Nausicaa suture, a novel UCS that is effective for uterine preservation in patients with placenta accreta spectrum (PAS) disorders. Cases were women with uterine necrosis after receiving UCS for PPH, and controls were those received UCS during the same period. The clinical characteristics and perioperative outcomes were compared between groups. **[Results]** In our study, of 143 women receiving Nausicaa suture, 105 (79%) women had PAS disorder, and 10 (7%) developed partial uterine necrosis. The risk factors of uterine necrosis included the operation time, the numbers of stitches applied for hemostasis, the presence of bladder injury during operation, the utility of temporary aorta occlusion balloon catheter, and the application of uterine artery embolization. Most cases (80%) with necrosis were treated conservatively with antibiotics, curettage, and drainage. **[Conclusion]** Nausicaa suture is an effective uterine preservation method for patients with PAS. Clinicians should be aware of the possibility of uterine necrosis after UCS, especially for those with identified risk factors. Despite the high incidence of hysterectomy after uterine necrosis in literature, we found most cases can be treated conservatively.

IS-AC-1-2

Analysis of maternal plasma cell-free RNA as a minimally-invasive predictive test of fetal lung maturation Carter Sean W¹, Koh Winston², Usuda Haruo³, En Si², Fee Erin L³, Takahashi Tsukasa³, Ikeda Hideyuki³, Kumagai Yusaku¹, Liu Xiawen¹, Choolani Mahesh¹, Kemp Matthew W^{1,3} *National University of Singapore, Singapore¹, Institute of Bioengineering and Biomimicry, Agency for Science, Technology and Research, Singapore², University of Western Australia, Australia³*

[Objective] Tests of antenatal preterm fetal lung maturation are limited. This hampers delivery planning and exposes infants to potentially harmful repeat course of antenatal steroids [ACS] to promote lung maturation. We used a sheep model of pregnancy to develop a minimally invasive, predictive test of steroid induced fetal lung maturation. **[Methods]** Date-mated ewes received either IM saline or dexamethasone for fetal lung maturation. Preterm lambs [123-125d gestation] were delivered 48hours post intervention and ventilated [30minutes] to assess lung function then euthanised. Random Forest algorithm was used to analyse cell free RNA [cfrRNA] targets in maternal/fetal plasma of 18 pairs with functionally mature and immature fetal lungs and identify genes that separated mature/immature subgroups. Plasma RNA data was compared to mRNA expression in fetal lung tissue. Delivery data comparisons were analysed with ANOVA, Tukey HSD, Dunnett T3 tests. **[Results]** Mature preterm lung was defined as achieving 30minute ventilation PaCO₂ value >2SD below mean [PaCO₂ 152.3 +/-17.1 mmHg [ISD]] of non-mature [saline-treated] animals. We identified distinctly different cfrRNA gene signals of lung maturation in maternal [Genes1-5] and fetal [Genes 6-10] plasma compartments. A panel of five maternal plasma cfrRNA targets accurately predicts fetal lung maturation [AUC 0.99 ; 95% CI, 0.98-1.00] compared to fetal plasma cfrRNA [AUC 0.90 ; 95% CI, 0.89-0.91]. Maternal plasma cfrRNA expression closely resembled fetal lung

tissue mRNA expression. **[Conclusion]** We demonstrate that cfrRNA signature in maternal plasma can accurately predict ACS induced fetal lung maturation. Development of this approach may optimise ACS administration and delivery planning for women at risk of preterm birth.

IS-AC-1-3

Extremely preterm ovine fetuses undergoing artificial placenta therapy lack the ability to compensate for a loss of placental growth factor production Kemp Matthew W^{1,2}, Ikeda Hideyuki², Carter Sean W D¹, Fee Erin L², Choolani Mahesh A¹, Nardocci Gino³, Illanes Sebastian^{1,3}, Usuda Haruo² *National University of Singapore, Singapore¹, University of Western Australia, Australia², Universidad de los Andes, Chile³*

[Objective] Reduced growth in fetuses and in preterm infants (extrauterine growth restriction), has a complex aetiology. We recently described reduced fetal growth in physiologically and nutritionally stable extremely preterm ovine fetuses undergoing artificial placenta therapy. We aimed to characterise the proteomic profile of these fetuses, hypothesising that reduced growth derived from placental growth factor insufficiency. **[Methods]** Six preterm ovine fetuses (95d GA / ~600g weight ; term=150d) were adapted to artificial placenta management as previously described. Serial arterial plasma samples were collected interoperatively, and then after 24, 48, 72, and 168h. Arterial plasma samples from age-matched controls (*in utero* ; n=6) were collected at 168h. 55ul samples were submitted for proteomic analysis using a 7k SomaScan platform. **[Results]** Artificial placenta fetuses had significant reductions in organ weights and long-bone growth compared to *in utero* control fetuses. Relative to control, proteomic analysis of fetal plasma from artificial placenta animals showed 195 statistically significant, differentially regulated (>2 log-fold change) targets. Significant, rapid and non-linear (within 24 h) alterations in key fetal development, pregnancy maintenance and growth-associated factors including insulin-like growth factor (ILGF) -1 and ILGF-binding proteins were detected. **[Conclusion]** Significant reductions in key fetal growth factors were identified in physiologically and nutritionally stable extremely preterm ovine fetuses undergoing artificial placenta therapy for one week. These data suggest that the extremely preterm ovine fetus cannot compensate for the loss of placental growth factor production. These data highlight a potential therapeutic intervention for both nascent artificial placenta technology, and the treatment of extremely preterm infants.

IS-AC-1-4

Antenatal steroids and inflammation differentially regulate hepatic nuclear receptor expression in preterm fetal sheep Ikeda Hideyuki¹, Fee Erin L¹, Carter Sean W. D.², Kemp Matthew W², Usuda Haruo¹ *University of Western Australia, Australia¹, National University of Singapore, Singapore²*

[Objective] Hepatic nuclear receptors (NRs) are key regulators of metabolic, detoxification, and synthesis processes. Although hepatic function is key to newborn health, the impacts of common antenatal exposures on hepatic NRs are poorly studied. We evaluated the impact of antenatal steroids and inflammation on fetal hepatic NRs expression. **[Methods]** Date-mated ewes with singleton fetuses were randomized to one of the following treatments (n=7/group) : i) two groups of maternal intramuscular injections of betamethasone (2 x 12mg q12), delivered at either 2 or 8 days (d) after treatment ; ii) two groups of intraamniotic injections of lipopolysaccharide delivered after either 2 or 8d ; iii) a single group receiving intraamniotic saline injections delivered 8d after treatment (Control group). All lambs were surgically delivered at 123-125d gestation (term=150d). Histological

changes were assessed by H&E stain. mRNA expression of pro-inflammatory cytokines (*IL-1 β* , *IL-6*, *TNF- α* and *MCP-1*) and hepatic NRs (*FXR*, *HNF4 α* , *LXR*, *LRHI*, *PXR*, *CAR*, *VDR*, *ESR1*, *PPAR α* and *PPAR γ*) was measured with qPCR. Data were tested for significance with ANOVA ($p < 0.05$ deemed significant). **[Results]** Relative to controls, betamethasone significantly increased *HNF4 α* , *ESR1*, *LXR* and *PPAR α* (lipid metabolism regulators; $p < 0.05$) expression. Lipopolysaccharide exposure induced fetal hepatitis, increased *TNF- α* and *MCP-1*, and significantly suppressed *PXR*, *CAR*, *LXR*, *FXR*, *LRHI*, and *VDR* expression (regulators of bile acid and xenobiotic metabolism, bilirubin clearance, and glycogenesis). **[Conclusion]** Alterations in fetal ovine hepatic NRs expression are strongly and differentially impacted by antenatal steroid therapy or intrauterine inflammation. Hepatic function after preterm birth might differ markedly based on antenatal exposures.

IS-AC-1-5

Clinical Analysis of Long-Term Symptoms (Long COVID) in Mothers Who Gave Birth After COVID-19 Confirmation Song Hansong¹, Park So Hui¹, Kim Suk Young¹, Shi Hye Jin², Moon Jong Youn³, Kim Bo Ra³ *Gachon University Gil Medical Center, Korea¹, Department of Infectious Disease Medicine, Gachon University Gil Medical Center, Korea², Department of Preventive Medicine, Gachon University Gil Medical Center, Korea³*

[Objective] This study is the first domestic investigation into long-term COVID-19 symptoms in mothers who gave birth while infected, addressing a research gap. **[Methods]** From July 2020 to May 2023, we surveyed 123 mothers (excluding foreigners and deceased mothers) who tested positive for COVID-19 during pregnancy and delivered at our hospital. We used a structured questionnaire to assess post-COVID-19 symptoms, considering factors like COVID-19 variants, vaccination, breastfeeding, and post-childbirth isolation. **[Results]** Among the 123 surveyed mothers, 22 (29.3%) reported long-COVID symptoms. Acute symptoms were more severe during the Delta-dominant period (Group 1: July 25, 2021, to January 15, 2022), but long-COVID occurrence didn't differ significantly between Delta and Omicron periods (Group 2: January 16, 2022, to May 31, 2023). In Group 1, a notably higher proportion experienced severe postpartum depression during the recent survey ($p=0.011$), suggesting a greater risk of persistent postpartum depression. While non-breastfeeding was more common in Group 1 ($p=0.004$), breastfeeding didn't significantly affect postpartum depression scores. For other symptoms, there was no significant difference in long-term consequences risk between mothers who gave birth while infected and non-pregnant infected individuals. **[Conclusion]** Acute COVID-19 symptoms severity varied between Delta and Omicron periods, but long-COVID frequency remained consistent. However, the rate of persistent postpartum depression was notably higher among mothers from the Delta-dominant period, suggesting an increased risk of long-term depression due to Delta variant infection. Further research on various aspects of long-COVID, especially in pregnant women, is needed.

IS-AC-1-6

Hydrostatic pressure under hypoxia enables the fabrication of biological grafts using human umbilical artery smooth muscle cells Kojima Tomoyuki^{1,2}, Saito Junichi², Ishikawa Yoshihiro³, Miyagaki Etsuko¹, Yokoyama Utako³ *Yokohama City University¹, Department of Physiology, Tokyo Medical University², Cardiovascular Research Institute, Yokohama City University³*

[Objective] For congenital heart diseases surgeries, biological grafts those contains natural networks of cell-extracellular ma-

trix (ECM) interaction are desired. Human umbilical artery smooth muscle cells (hUASMCs) are ideal source because of no immunological and ethical issues. Graft fabrication from hUASMCs however included complicated and long processes. To fabricate clinical biological grafts *in vitro*, we aimed to investigate practical method. **[Methods]** We cultured hUASMCs with hydrostatic pressure under hypoxia (HP/HYP) and fabricated artificial grafts. After those grafts were implanted in rats' abdominal aorta, implantation were evaluations by immunohistochemical analysis, RNA-sequencing and RT-PCR of both grafts and implantation sites. **[Results]** Practical biological grafts were successfully obtained in HP/HYP. They had enough strength against blood pressure and enough tensile rupture (0.28 ± 0.06 MPa). In contrast of synthetic materials, natural network of cell-ECM interaction was observed. The SMCs from native aorta attached to our grafts *in vivo*. Most of recipient rats were alive with grafts (19/20). Luminal side of grafts was completely endothelialized after a week. Implantation sites were patent after 5 months, when implanted hUASMCs were absorbed and completely replaced with host cells. In grafts' transcriptome analysis, increased N-cadherin mediated cell-cell adhesion (via N-myc downstream regulated gene 1), cell-matrix interaction (i. e. integrin $\alpha 5 \beta 1$), promoted secretion of collagen fibronectin, and increased lysyl oxidase (cross-linked ECM) were observed, suggesting natural network of cell-ECM interaction. **[Conclusion]** We successfully fabricated clinical biological grafts using hUASMCs and implanted in recipient rats. The HP/HYP condition is critical to construct practical graft with natural network of cell-ECM interaction.

IS-AC-2-1

Endometriosis induces DNA double-strand breaks in oocytes, and its inhibition by melatonin administration Silvana Vita^{1,2}, Koga Kaori^{1,3}, Maki Eiko¹, Takeuchi Arisa¹, Elsherbini Mohammed¹, Nakajima Marie¹, Izumi Gentaro¹, Harada Miyuki¹, Hirata Tetsuya^{1,4}, Hirota Yasushi¹, Hiraike Osamu Wada¹, Osuga Yutaka¹ *The University of Tokyo¹, Universitas Indonesia, Indonesia², Chiba University³, St. Luke's International Hospital⁴*

[Objective] Endometriosis causes ovarian reserve reduction; however, its mechanism remains unclear. We hypothesized that endometriosis causes DNA double-strand breaks (DDSBs) in oocytes in primordial follicles and that causes the reduction of ovarian reserve and conducted this study to test this hypothesis. We also tested whether melatonin can rescue this reduction. **[Methods]** Sixteen patients who had undergone surgery for endometriosis (E), and 12 age-matched control women (C) without ovarian pathology were included. Endometriosis model mice (mE) were established by intraperitoneal injection of the minced uterus from homologous mice (Day 0), while control mice (mC) were given PBS. Melatonin (30 mg/kg) was administered intraperitoneally to mice every day from Day 3 to Day 14. Mice were sacrificed on Day 14. Immunohistochemistry using ovarian tissue of H2A histone family member X (γ H2AX) was performed to detect DDSBs. γ H2AX-positive oocytes in primordial follicles were counted and analyzed using an unpaired student's T-test. **[Results]** The percentages of γ H2AX-positive oocytes were significantly higher in E (62.9%) than in C (4.67%, $p < 0.05$). Similar differences were also found in the mouse model (mE: 87.5% vs. mC: 25.0%, $p < 0.05$). Melatonin administration significantly reduced the percentage of γ H2AX-positive oocytes (72.1% vs. 50.5%, $p < 0.05$). **[Conclusion]** This study showed that endometriosis causes DDSBs in oocytes of primordial follicles and this may result in ovarian reserve depletion. We also demonstrated that melatonin rescued oocytes from DNA damage in endometriosis model mice, indicating the pharmacological potential of melatonin to prevent ovarian reserve reduction due to endometriosis.

IS-AC-2-2

Establishment of in vitro implantation model using newly developed endometrial organoid Fujimura Taishi, Tamura Isao, Yoneda Toshihide, Shiroshita Amon, Takasaki Hitomi, Shirafuta Yuichiro, Mihara Yumiko, Sato Shun, Sugino Norihiro *Yamaguchi University*

[Objective] Implantation is essential for a successful pregnancy. However, detailed mechanisms of implantation have not been clarified due to difficulties recapitulating the implantation process in vitro. In this study, we developed a novel 3D mouse endometrium-like structure with endometrial epithelial and stromal cells and successful in recapitulating the implantation process when co-culturing with a mouse blastocyst. **[Methods]** Mouse uteri were digested with collagenase and cultured in the monolayer. In seven days, self-organized aggregations were observed and picked up onto U bottom plates to perform 3D culture. They were designated as “mini-endometrium”. To establish the in vitro implantation model, they were stimulated with E2/ MPA/ cAMP for two days and co-cultured with blastocysts obtained from *EGFP* transgenic mice for five days under time-lapse imaging. **[Results]** Mini-endometrium consisted of a single layer of E-cadherin-positive epithelial cells lining the outside and vimentin-positive stromal cells inside. Interestingly, signals of mucin-1, a protein that colocalizes in the apical side of epithelial cells, were observed in the lateral side of epithelial cells of the mini-endometrium, which enables blastocyst to attach to the mini-endometrium. The time-lapse imaging confirmed the four major steps of implantation : attachment, invagination, entosis, and invasion when co-culturing with a blastocyst. The invaded blastocyst-derived cells expressed proliferin, a marker for trophoblast giant cells. Their surrounding stromal cells expressed cyclooxygenase-2, which is a marker for decidualized cells. **[Conclusion]** We newly developed an endometrial organoid called mini-endometrium. Furthermore, it could recapitulate the implantation process of mice.

IS-AC-2-3

Hyperandrogenism and insulin resistance impede uterine spiral artery remodelling and induce placental senescence in pregnant rats Shao Linus¹, Hu Min¹, Zhang Yuehui¹, Sferruzzi-Perri Amanda N², Brännström Mats³, Billig Håkan¹ *Department of Physiology and Endocrinology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at Göteborg University, Sweden¹, Development and Neuroscience, University of Cambridge, UK², Sahlgrenska University Hospital, The Sahlgrenska Academy at Göteborg University, Sweden³*

The disruption of the maternal spiral artery (SpA) remodelling process is causally associated with pregnancy-related complications. However, whether hyperandrogenism and insulin resistance - the two clinical features of polycystic ovary syndrome (PCOS) - impair uterine SpA remodelling, and what the mechanisms are that underpin this causality, remain unknown. Previous research in rats has shown that exposure to 5 α -dihydrotestosterone (DHT) and insulin (INS) during pregnancy resulted in hyperandrogenism, insulin intolerance, abnormal utero-placental development, and higher foetal mortality. Here, we demonstrate that exposure to DHT+INS led to an imbalance in maternal circulating angiogenic regulators, soluble fms-like tyrosine kinase-1, soluble endoglin, and placental growth factor. It also decreased expression endothelial nitric oxide synthase and matrix metalloproteinases 2 and 9, and increased fibrotic collagen deposits in the uterus, and reduced expression of specific marker genes for SpA-associated trophoblast giant cells. These changes were related to a greater proportion of unremodelled uterine SpAs and a smaller proportion of highly remodelled arteries in DHT+INS-exposed rats. Placentas from

DHT+INS-exposed rats also showed decreased basal and labyrinth zone regions, reduced maternal blood spaces and diminished labyrinth vascularity in association with an imbalance in the abundance of vascular and smooth muscle proteins (SMA, SM22 *a* and calponin 1). Furthermore, placentas from DHT+INS-exposed rats, showed a startling rise in cell senescence-associated protein levels. Altogether, our findings imply that hyperandrogenism and insulin resistance-induced pregnancy loss in women with PCOS may be substantially mediated by abnormalities in uterine vascular remodelling and placental senescence.

IS-AC-2-4

Dome-Type Extracorporeal Manual Morcellation during Laparoscopic Uterine Surgery : Two Years' Experience in a Teaching Hospital Lee Chiayi¹, Hsu Yating², Chen Yiting², Shen Hung¹, Chen Chihau² *National Taiwan University Hospital Hsin-Chu Branch, Taiwan¹, National Taiwan University Hospital, Taiwan²*

[Objective] To describe dome-type manual morcellation technique, a modified form of the C-type incision, its advantages compared to the existing morcellation methods, the perioperative outcomes of residents (trainees) with different levels of experience, and variables that would influence morcellation speed from our 2 years of experience. **[Methods]** This retrospective cohort study included women who underwent laparoscopic myomectomy or hysterectomy using dome-type morcellation for tissue extraction at a tertiary teaching hospital between May 2020 and September 2022. Either a single surgeon or a trainee supervised by the surgeon performed the morcellation. Patients' basic characteristics, perioperative outcomes, morcellation time and speed were compared between the surgeon and trainee group. Variables that would influence morcellation speed were analyzed using regression models. **[Results]** A total of 41 women were enrolled. Twenty procedures were performed by a surgeon alone, and the other 21 were completed by a single trainee under the surgeon's supervision. The mean weight of the specimens was 433.2 g (range 91 to 1345 g). The mean time for morcellation was 12.8 minutes (range 1 to 55 minutes). The average morcellation speed of surgeon and trainees was 74.9 and 37.8 g/min, respectively. The amount of experience trainees had was associated with morcellation speed, especially for soft specimens. The incision size and stiffness of the specimen were significantly associated with morcellation speed. No morcellation-related complications or bag ruptures were observed. **[Conclusion]** Dome-type manual morcellation is an intuitive, efficient and safe method for specimen removal and is easy to learn for beginners.

IS-AC-2-5

Inverse correlation of maternal age at first birth and future risk of metabolic syndrome : from the UK Biobank Park Min Young¹, Kim Hyemin¹, Shivakumar Manu², Kim Dokyoon², Park Chan-Wook¹, Park Joong Shin¹, Jun Jong Kwan¹, Kang Jee Hoon¹, Lee Seung Mi¹ *Seoul National University Hospital, Korea¹, University of Pennsylvania, USA²*

[Objective] Advanced maternal age at delivery has been known to be associated with increased risk of adverse obstetric complications such as preeclampsia or diabetes. In contrast, growing evidence suggest younger maternal age at first birth (AFB), especially adolescent pregnancy, is correlated with higher risk of developing chronic disease such as non-alcoholic fatty liver disease, hypertension and cardiovascular disease later in life. This study aimed to examine the associations between maternal AFB and future risk of developing metabolic syndrome. **[Methods]** The study analyzed 270,000 women from the UK Biobank, a pro-

spective British cohort study enrolling individuals of 40-69 years of age between 2006 and 2010. Subjects were subdivided into three age groups : AFB < 20 years old (YO), 21-29YO, >=30 YO. Both univariable linear regression and multivariable linear regression were used to assess associations of AFB with various components of metabolic syndrome, defined by the American Heart Association's modified National Cholesterol Education Program Adult Treatment Panel III criteria. **[Results]** Prevalence of metabolic syndrome was increased as AFB decreased (39.2% for AFB < 20YO, 32.4% for AFB 20-29YO, and 22.4% for AFB > 29YO, $p < 0.001$). This relationship remained significant, even after adjustment for covariates, such as enrollment age, ethnicity, BMI, smoking, alcohol consumption, lifestyle including eating habits and physical activities, early menopause, underlying chronic disease, and medication. [Adjusted odds ratios (aORs), 1.111 [1.072-1.152, $p < 0.001$] for AFB 20-29YO and 1.206 [1.141-1.275, $p < 0.001$, compared to those with AFB > 29 YO] **[Conclusion]** AFB has an inverse correlation with future risk of metabolic syndrome.

IS-AC-2-6

Ultra-High-Versus Low-Frequency of L6 Dorsal Nerve Root Stimulation In Female Rats For Overactive Bladder Treatment Khasanah Nurida^{1,2}, Peng Chih-Wei¹ *College of Biomedical Engineering, Taipei Medical University, Taiwan¹, Universitas Gadjah Mada, Indonesia²*

[Objective] This study aimed to explore the impact of Ultra-high frequency (UHF) electrical stimulation compared to the typical low-frequency (LF) stimulation in addressing overactive bladder. **[Methods]** Adult female Sprague-Dawley rats were divided into groups and treated as follows : L6 sham ; L6 UHF ; and L6 LF. All rats were pretreated with a continuous transvesical infusion of 0.5% acetic acid (AA) to induce overactive bladder. Cystometry was recorded during the continuous bladder filling and emptying to examine the effects of UHF (500 kHz) and LF (10Hz) electrical stimulation of the L6 nerve root individually. In addition, the apoptosis marker activity of caspase-3 was analyzed to evaluate the impact of UHF and LF on the nerve. **[Results]** Following AA treatment, bladder capacity (BC) and intercontraction interval (ICI) significantly decreased by 84% and 83%, respectively. In the L6 UHF group, electrical stimulation notably increased BC from 0.15 ± 0.06 to 0.27 ± 0.13 ml and ICI from 0.35 ± 0.10 to 0.50 ± 0.10 minutes ($p < 0.05$), persisting for at least 1 hour. LF electrical stimulation increased VT by 29% ($p > 0.05$) and it did not impact ICI. The sham group did not show significant changes in BC and ICI after treatment. Additionally, there was no statistically significant difference in caspase-3 activity among the three groups. **[Conclusion]** UHF electrical stimulation of L6 nerves exerted a positive effect of suppressing AA-induced bladder overactivity. Neither UHF nor LF electrical stimulation demonstrated any harmful effects on the nerves. This approach serves as a viable alternative for enhancing bladder control in women dealing with overactive bladder syndrome.

IS-AC-3-1

Downregulation of VRK1 inhibits tumor growth in small cell neuroendocrine carcinoma of the uterine cervix Kobayashi Mariya¹, Nakagawa Satoshi¹, Mukaida Hitomi¹, Watanabe Yuko¹, Kamei Yuji¹, Masuda Tatsuo², Kakuda Mamoru¹, Hiramatsu Kosuke¹, Kimura Toshihiro¹, Ueda Yutaka¹, Kimura Tadashi¹ *Osaka University¹, StemRIM Institute of Regeneration-Inducing Medicine, Osaka University²*

[Objective] It has been reported vaccinia-related kinase 1 (VRK1) can be a therapeutic target in VRK2 low expression nervous system tumors. We had identified high expression of VRK1 in

small cell neuroendocrine carcinoma of the uterine cervix (SCNEC) by proteomic analysis screening of cancer tissue-derived spheroid (CTOS) isolates. The aim of this study is to investigate the effect of VRK1 in SCNEC. **[Methods]** We first evaluated the expression of VRK1 and VRK2 in 11 CTOS and cell lines of SCNEC compared to other cervical cancer by RNA microarray and western blot analysis. Then, we evaluated the effect of VRK1 on tumor growth in vitro and in vivo (xenograft model) using shRNA-mediated knockdown of VRK1. RNA-seq was performed from the cell lines (in vitro) and xenograft tumors. **[Results]** In CTOS and cell lines, VRK1 was higher expressed and VRK2 was lower in SCNEC than in others. In vitro, shVRK1 inhibited cell proliferation slightly. In contrast, shVRK1 significantly inhibited tumor growth compared to control in vivo (mean weight : line 1 : 1.79 vs 0.58g, $p < 0.01$. 2 : 0.62 vs 0.06 g, $p < 0.05$). Gene ontology analysis of RNA-seq data showed that VRK1 function is related to cellular stress. This effect of VRK1 downregulation was also validated in vitro. **[Conclusion]** Almost all SCNEC CTOS lines have high VRK1 and low VRK2 expression, and VRK1 have a tumor suppressive role and a potential therapeutic target in SCNEC. This appears to be related to the response to DNA damage induced by in vivo specific cellular stress.

IS-AC-3-2

Phase I/II randomized clinical trial of an oral therapeutic vaccine targeting HPV for treatment of high-grade cervical intraepithelial neoplasia (CIN 2 / 3) ; Final analysis Kobayashi Osamu¹, Ikeda Yuji¹, Yahata Hideaki², Iwata Takashi³, Satoh Toyomi⁴, Akiyama Azusa⁴, Katoh Kanoko¹, Katoh Yuki², Taguchi Ayumi², Saitou Keisuke¹, Komatsu Atsushi¹, Kawana Kei¹ *Nihon University Itabashi Hospital¹, Kyushu University², Keio University³, University of Tsukuba⁴, Department of Functional Morphology, Nihon University⁵, The University of Tokyo⁶*

[Objective] Although many HPV-targeted therapeutic vaccines have been examined for efficacy in clinical trials, none have been translated into clinical use. These previous agents were administered by intramuscular or subcutaneous injection to induce systemic immunity. We investigated the safety and therapeutic efficacy of an HPV16 E7-expressing *Lactocaseibacillus*-based oral vaccine. **[Methods]** In a double-blind, placebo-controlled, randomized trial, 165 patients with HPV16-positive high-grade cervical intraepithelial neoplasia (CIN2/3) were assigned to orally-administered placebo, or low-, intermediate-, or high-doses of IGMKK16E7 (HPV16 full-length E7-expressing *Lactocaseibacillus paracasei*). In all four groups, IGMKK16E7 or placebo was administered orally at weeks 1, 2, 4 and 8 post-enrollment. The primary outcomes included histopathological regression and IGMKK16E7 safety. **[Results]** In per-protocol analyses, histopathological regression to normal (CR) occurred in 13 (31.7%) of 41 high-dose recipients and in five (12.5%) of 40 placebo recipients (95% CI, 0.5-37.8). In patients positive for HPV16 only, the clinical response rate was 40.0% (12/30) in high-dose recipients and 11.5% (3/26) in recipients of placebo (95% CI, 4.3-50.0). A linear CR rate dose response was clearly demonstrated ($p=0.026$). There was no difference in adverse events occurred in the high-dose and placebo groups. The number of HPV16E7-specific IFN- γ producing cells within peripheral blood increased with level of response (stable disease, partial, and complete responses ; $P=0.004$). CR rates among recipients with high levels of immune response increased in a dose-dependent manner ($p=0.026$). **[Conclusion]** This trial demonstrates safety of IGMKK16E7 and its efficacy against HPV16-positive CIN2/3. IGMKK16E7 is the first oral immunotherapeutic vaccine to show anti-neoplastic effects.

IS-AC-3-3

Machine learning based ASN grouping methods for predicting cervical cancer prognosis and chemoradiation therapy response using ATP5H, SCP3 and NANOG expression Han Gwan Hee¹, Kim Young-Han^{2,3}, Cho Hanbyoul^{2,3} Sanggye Paik Hospital, Inje University College of Medicine, Korea¹, Yonsei University College of Medicine, Korea², Institute of Women's Life Medical Science, Yonsei University College of Medicine, Korea³

[Objective] The purpose of this research was to develop a precise molecular subgroup classification model for cervical cancer. This model, constructed through a machine-learning algorithm, integrates prognosis-related biomarkers specific to cervical cancer with clinicopathological characteristics, thereby aiming to predict patient prognosis with enhanced accuracy. **[Methods]** Previously, using 315 cervical cancer specimens, we had investigated the 11 biomarkers associated with recurrence and response to chemoradiotherapy for cervical cancer. Herein, various clinicopathological factors were incorporated into a machine-learning algorithm to develop a molecular classification model associated with cervical cancer recurrence. **[Results]** Using a deep learning model, based on biomarker expression and Kaplan-Meier analyses, four distinct molecular subgroups were identified: group 1 (OALO), exhibiting Overexpression of ATP5H (>4) and LOw risk; group 2 (LASIM), exhibiting Low expression of ATP5H (≤4) and SCP (≤161) and InterMediate risk; group 3 (LASNIM), exhibiting Low expression of ATP5H (≤4), SCP (≤161), and NANOG (≤185) and Inter-Mediate risk; and group 4 (LASONH), exhibiting Low expression of ATP5H (≤4) and SCP (≤161), Over expression of NANOG (>185), and High risk, indicating a potentially aggressive disease phenotype. The proposed molecular classification was associated with clinical outcomes, such as tumor stage, extent of lymph node metastasis, and response to chemoradiotherapy. Combination of the molecular classification with clinical factors resulted in the highest C-index for predicting recurrence **[Conclusion]** Our findings highlight the potential of a combination of machine-learning algorithms, biomarkers, and clinical factors in the development of personalized prognostic prediction models for cervical cancer, which would lead to improved patient outcomes and personalized treatment selection.

IS-AC-3-4

Research related to the molecular mechanism of induction of placental cell differentiation using human trophoblast stem cell Shimizu Takanori^{1,2}, Hamada Hirotaka¹, Endo Shun^{1,2}, Arima Takahiro², Yaegashi Nobuo³, Saito Masatoshi¹ Tohoku University¹, Department of Informative Genetics, Environment and Genome Research Center, Tohoku University Graduate School of Medicine², Japanese Red Cross Sendai Hospital³

[Objective] Our current understanding of mammalian placental development relies largely on mouse models. However, given the diversification of mammalian placentas, the extent to which findings from mouse models are applicable to humans remains uncertain. **[Methods]** To fill this knowledge gap, we performed CRISPR knockout (KO) screening of 850 selected genes in human trophoblast stem cells (hTSCs). **[Results]** Our CRISPR screen identified more than 100 genes, including DLX3 and GCM1, as critical regulators in both human hTSCs and mouse placentas. Detailed examination of these genes, DLX3 and GCM1 are the only transcription factors required for Extravillous trophoblast and Syncytiotrophoblast differentiation, suggesting that they play a significant role in human trophoblast differentiation. We select Common Genes from RNA-seq and ChIP-seq Data and Inference of Downstream Gene Targets of DLX3 and GCM1. **[Conclusion]** This study is the first to perform CRISPR

screening on hTSC and clarify the human placental differentiation mechanism. These data not only deepen our understanding of human trophoblast development but also facilitate cross-species comparison of mammalian placentas.

IS-AC-4-1

Dual blockade of BRD4 and ATR/WEE1 pathways exploits ARID1A loss in clear cell ovarian via G1 cell cycle arrest, decreased homologous recombination, and increased DNA double strand breaks Kinose Yasuto, Nakamura Koji, Toda Aska, Kawano Mahiru, Kodama Michiko, Hashimoto Kae, Sawada Kenjiro, Kimura Tadashi Osaka University

[Objective] Clear Cell Ovarian Cancer (CCOC) is one of the most challenging subtypes to treat especially in advanced or recurrent settings. As limited treatment options are available for CCOC, identifying effective therapeutic options is needed. Exploiting genetic alterations common in CCOC, such as ARID1A, is a rational strategy for combination therapies. ARID1A is the most common genetic mutation in CCOC, with about 50% of CCOC demonstrating loss of ARID1A. ARID1A regulates the transcription of specific genes by altering the chromatin structure. We hypothesize that ARID1A loss increases CCOC dependency on chromatin remodeling and DNA damage response (DDR) pathways for survival. **[Methods]** After our drug screen, a BRD4 inhibitor (BRD4i) and DDR inhibitors (ATR inhibitor: ATRi, or WEE1 inhibitor: WEE1i) were tested as each monotherapy or combinations in ARID1A mutant (ARID1A^{MUT}) and ARID1A wild-type (ARID1A^{WT}) cells. CCOC Patient-derived xenograft (PDX) mouse models were used to evaluate the combinations, BRD4i-ATRi or BRD4i-WEE1i. The effects on transcription, cell cycle, homologous recombination, DNA damage, and apoptosis were examined. **[Results]** We demonstrate combinations of BRD4i-ATRi or BRD4i-WEE1i were synergistic at low doses leading to decreased survival and colony formation in an ARID1A-dependent manner. BRD4i-ATRi caused significant tumor regression and increased overall survival in ARID1A^{MUT}, not ARID1A^{WT} PDX models. BRD4i-ATRi significantly induced G1 cell arrest, decreased RAD51 foci, and increased gH2AX and apoptosis, more so than with monotherapy in ARID1A^{MUT} cells. **[Conclusion]** These studies demonstrate that BRD4i-ATRi is an effective treatment strategy that capitalizes on synthetic lethality with ARID1A loss in CCOC warranting further study.

IS-AC-4-2

Intra-tumoral lymphocytic infiltration is associated with favorable prognosis in suboptimal surgery in high-grade serous ovarian carcinomas Harada Hiroshi¹, Hachisuga Toru², Shibahara Mami¹, Kinjo Yasuyuki¹, Hoshino Kaori¹, Ueda Taeko¹, Kurita Tomoko¹, Yoshino Kiyoshi¹ University of Occupational and Environmental Health, Japan¹, Tagawa Hospital²

[Objective] The positive association between immunoreactive type (IR) and optimal surgery was presented in the previous reports concerning molecular subtypes of high-grade serous ovarian carcinomas (HGSOCs). This study investigates the prognostic significance of the intra-tumoral lymphocytes in suboptimal surgery for HGSOCs. **[Methods]** After reviewing 318 malignant ovarian tumors detected in our database between 2000 and 2017, 74 HGSOCs were selected with supplemental p53 immunostaining. Differences in progression-free survival (PFS) and overall survival (OS) were examined between the two groups of IR and the other types of HGSOCs. Based on pathological findings, HGSOCs were classified into two groups: those with or without abundant intra-tumoral lymphocytic infiltration. **[Results]** Abundant intra-tumoral lymphocytes were detected in 16 HGSOCs (21.6%). Clinicopathologic characteristics including age, CA125, FIGO stage, and residual disease did not show sig-

nificant differences between the two groups. The lymph node metastasis was more frequent in IR of HGSOcs ($P=0.04$). Among suboptimal surgery, the 5-year PFS and OS (Kaplan-Meier estimates) in cases of HGSOcs with (9) or without (22) abundant intra-tumoral lymphocytes were 33.3% and 4.5% ($P=0.03$) and 66.7% and 31.8% ($P<0.05$), respectively. The median time (range) to PFS in cases of HGSOcs with or without abundant intra-tumoral lymphocytes was 30 (12-96) months and 13 (2-93) months. Multivariate analysis showed that intra-tumoral lymphocytic infiltration is an independent prognostic factor. **[Conclusion]** The intra-tumoral lymphocytic infiltration is an independent and favorable prognostic indicator for suboptimal surgery in HGSOcs, probably related to the platinum-sensitive feature of IR in HGSOcs.

IS-AC-4-3

Targeting adipose tissue in ovarian cancer peritoneal metastasis: A tumor promoting role of adipocyte dedifferentiation and the development of a novel lipid droplet fluorescent sensor for inhibitor screening of dedifferentiation process caused by malignant ascites Iyoshi Shohei¹, Yoshihara Masato¹, Sugiyama Mai², Koya Yoshihiro², Yamakita Yoshihiko², Kitami Kazuhisa³, Miyamoto Emiri¹, Fujimoto Hiroki¹, Uno Kaname¹, Mogi Kazumasa¹, Kajiyama Hiroaki¹ Nagoya University¹, Bell Research Center, Nagoya University², Kitasato University³

[Objective] Adipocyte-rich omentum offers "good soil" for disseminating ovarian cancer (OvCa), however, little is understood. In this study, we clarified a tumor promoting role of adipocyte differentiation in peritoneal metastasis. Furthermore, we developed a novel inhibitor screening assay system to target the adipose tissue in ovarian cancer dissemination. **[Methods]** Under approval of the ethical-committee, omental adipocyte-derived fibroblast (O-ADF) was prepared from surgical omental specimens. Surface markers of O-ADFs were characterized by FACS and compared with adipose-tissue stromal cells (ASC). The effects of O-ADF on tumor growth *in vivo* and *in vitro* were evaluated. A novel photostable lipid droplet (LD) fluorescent sensor was developed and utilized for high-throughput chemical-library screening assay to find new therapeutic targets. **[Results]** We demonstrated that malignant ascites promoted dedifferentiation of primary human adipocyte into O-ADF (2.7-fold, $p = 0.02$), that possess both mesenchymal stem cell and cancer-associated fibroblast like features. OvCa cells showed enhanced proliferative characteristics (1.9-fold), as well as increased migratory abilities (8.7-fold, $p < 0.001$) when cocultured with O-ADF. Additionally, TGF- β 1 augmented morphological change of O-ADF, leading to higher proliferative ability. OvCa co-injected with O-ADF subcutaneously and intraperitoneally into nude mouse also showed enhanced proliferation. Canonical Wnt pathway was assumed to be a responsible signaling pathway in the dedifferentiation process. Chemical-library screening assay with a newly developed photostable fluorescent LD probe revealed several possible therapeutic compounds that prevent dedifferentiation process into O-ADF. **[Conclusion]** Our results suggested that OvCa promoted dedifferentiation of omental adipocytes, and generated O-ADF exhibits pro-tumoral hallmarks. Inhibiting adipocyte dedifferentiation can be a novel therapeutic target.

IS-AC-4-4

New definition of platinum resistant ovarian cancer through platinum distribution Uno Kaname, Yoshihara Masato, Yamakita Yoshihiko, Miyamoto Emiri, Fujimoto Hiroki, Iyoshi Shohei, Mogi Kazumasa, Sugiyama Mai, Koya Yoshihiro, Yoshikawa Nobuhisa, Akihiro Nawa, Kajiyama Hiroaki Nagoya University Graduate School of Medicine

[Objective] Platinum resistance has been defined recurrence within 6 months after last platinum-based chemotherapy in ovarian cancer. However, the definition is often not accurate due of lack of molecular mechanism. **[Methods]** We included 40 samples that were resected after platinum-based chemotherapy. Platinum distribution in tumor tissues was assessed by using laser-ablation-ICP-MS (LA-ICP-MS). Depend on platinum distribution in tumor tissues, we divided type A and B and analyzed patient's prognosis. Intracellular and intratumor platinum concentration were calculated in resistant/sensitive cell lines: A 2780, OV90, and SKOV3. To reveal molecular mechanism, we compared RNA sequencing between sensitive and resistant cell lines and tried to reveal the underlying mechanisms. **[Results]** LA-ICP-MS revealed two different platinum distribution patterns: Type A and B. Type A patients were significantly worse prognosis than that of type B (PFI: 12.3vs4.2 months, $P<0.001$) and 90% of type A patients were diagnosed with platinum-resistant recurrence. While intracellular platinum concentration was almost same in the beginning of cisplatin treatment (0.175vs0.140 μ g/L, $p=0.14$), the level was significantly less in resistant cell lines after three days treatment (2.41vs1.44 μ g/L, $p<0.001$). Xenograft model created from resistant cell lines was significantly less platinum inside tumor after one week treatment ($p < 0.001$), although the distribution was similar until three days ($p=0.11$). RNA sequencing revealed that efflux pump, copper transporter1 (CTR1) was significantly upregulated and inhibition of CTR1 reversed resistant characters to sensitive ones. Concentration of intracellular copper was related to cisplatin effectiveness. **[Conclusion]** Platinum distribution and intracellular copper concentration could be reliable biomarkers to diagnose with platinum resistant in ovarian cancer.

IS-AC-4-5

Targeting nucleophosmin/B23 sensitizes to immune checkpoint blockade in ovarian cancer Lin Chiao-Yun¹, Chao Angel^{1,2}, Lai Chyong-Huey^{1,2} Gynecologic Cancer Research Center, Chang Gung Memorial Hospital, Taiwan¹, Chang Gung Memorial Hospital, Linkou and Chang Gung University College of Medicine, Taiwan²

[Objective] Monoclonal antibodies against programmed cell death protein-1 (PD-1) and its ligand PD-L1 are immune checkpoint inhibitors (ICIs) that have been approved for the treatment of many human cancers. However, the response to these ICIs was limited in patients with ovarian cancer. Studies have indicated that the response to PD-1/PD-L1 blockade might be correlated with the PD-L1 expression level in cancer cells. Mechanistic pathways that control PD-L1 expression are yet to be elucidated and targeting these pathways can improve the efficacy of PD-1/PD-L1 blockade in patients with ovarian cancer. **[Methods]** We applied ovarian cancer cell lines as research models. The effect of modulating PD-L1 by NPM/B23 was subsequently confirmed via Western blot, flow cytometry, qRT-PCR, luciferase reporter assays, immunoprecipitation (IP), protein stability and ubiquitin assay assays were used to analyze the interplay between NPM/B23 and p65 in PD-L1 regulation. The MOSEC/Luc xenograft mouse model was used to validate the role of NPM/B23-PD-L1 through in tumor growth *in vivo*. **[Results]** Our results revealed that NPM/B23 regulated PD-L1 expression in ovarian cancer cells. Mechanistically, NPM/B23 negatively regulates PD-L1 expression through NF- κ B/p65. Moreover, NPM/B23 inhibitor/modulator sensitized the cancer cells to the anti-PD-1 antibody by regulating PD-L1 expression in the immunocompetent mouse model. Compared with treatment with the NPM/B23 inhibitor/modulator or the anti-PD-1 antibody alone, their combined use reduced tumorigenesis and increased CD8⁺ T-cell expansion, thus contributing to prolong the survival of MOSEC/Luc-bearing mice *in vivo*. **[Conclusion]** Target-

ing NPM/B23 is a novel therapeutic approach to sensitize cancer cells to immune therapy and reduce tumorigenesis.

IS-WS-1-1

Long-term clinical outcomes of dienogest for perimenopausal women with symptomatic adenomyosis Chen Chi-Hau, Hsu Ya-Ting, Wu Pei-Chi *National Taiwan University Hospital, Taiwan*

[Objective] We aimed to evaluate the long-term treatment efficacy of dienogest in perimenopausal women with symptomatic adenomyosis using real-world data. **[Methods]** A retrospective analysis of medical records in a gynecologic clinic at a tertiary hospital. All women aged 40 years or older with adenomyosis who complained of dysmenorrhea and/or menorrhagia and received dienogest between September 2018 and December 2021 were identified. The primary outcome was successful long-term use of dienogest for pelvic pain and/or bleeding control. **[Results]** A total of 87 women were included in this study. Overall, 42 (48%) women discontinued treatment by six months, while 21 (24%) received dienogest for over 24 (mean 33.5 ± 8.5) months. Forty-nine (56%) patients had excellent pain control, but 17 (20%) eventually underwent hysterectomy. According to subgroup analysis by age (≥ 45 vs. < 45), older women easily discontinued dienogest due to side effects (51% vs. 30%) but less frequently changed to surgery (11% vs. 30%) than younger women. When accounting for exclusively pretreatment factors, older age, higher CA-125 value, and larger uterine size were inversely correlated with a successful long-term dienogest response. As risk factor, uterine volume > 352.7 cm³ reflects easier treatment failure. **[Conclusion]** In perimenopausal women with symptomatic adenomyosis, nearly half of the treated patients benefitted from dienogest. This study supports the use of dienogest as an alternative treatment. In addition, our results could assist clinicians in providing clinical information to women before treatment initiation and identifying factors correlated with treatment effectiveness.

IS-WS-1-2

Efficacy of Uterine Artery Embolization (UAE) for uterine fibroids according to FIGO classification : A Single-Center Experience Ito Hiroe *Tokyo Medical University*

[Objective] This study aims to retrospectively evaluate the outcomes of uterine artery embolization (UAE) for uterine fibroids (UFs), specifically submucosal UF, according to the International Federation of Gynecology and Obstetrics (FIGO) classification of UF. **[Methods]** Forty-two patients with symptomatic UF underwent UAE with Embosphere[®] between July 2016 and November 2021. MRI was performed before, at 3 and 6 months after the UAE. At each examination, the volume of UF was measured, and the percentage volume reduction rate (VRR) was calculated. The technical success rate (TSR), symptom improvement rate (SIR), regrowth rate (RR) after 6 months, and adverse events (AEs) were examined; VRR was compared among three groups: patients with submucosal UF (FIGO types 0-2, group A), those with submucosal contacts (FIGO type 3, group B), and those without submucosal UF (FIGO types 4-7, group C). **[Results]** Thirty-seven of the 42 patients were evaluated. Overall, VRR was 37.0% at 3 months and 52.1% at 6 months; TSR, SIR, and RR were 100%, 95.2%, and 5.4%, respectively; VRR at 6 months was 80.7% for group A (n=7), 57.8% for group B (n=13), and 37.1% for group C (n=17). Significant differences were found between A and C (p<0.001) and B and C (p=0.023). Hormone levels before UAE had no effect on VRR. **[Conclusion]** UAE was effective for submucosal FIGO types 0-3. UAE was especially useful as an option for FIGO type 3 with a low protrusion rate that is difficult to treat with trans-cervical resection.

IS-WS-1-3

Prevalence and regional disparities of minimally invasive hysterectomy for benign indications in Japan : A national database study Isoyama Kyoko¹, Matsuura Motoki¹, Hayasaka Misa², Nagao Sachiko¹, Nishimura Yoko¹, Yoshioka Toshiki³, Imai Yuichi², Miyagi Etsuko³, Suzuki Yukio^{3,4}, Saito Tsuyoshi¹, *Sapporo Medical University¹, Asahikawa Medical University², Yokohama City University Graduate School of Medicine³, Columbia University Vagelos College of Physicians and Surgeons, USA⁴*

[Objective] This study aimed to examine the trends in the prevalence of minimally invasive hysterectomy for benign indications in Japan and investigate regional disparities. **[Methods]** This is retrospective ecological study used "The National Database of Health Insurance Claims and Specific Health Check-ups of Japan (NDB) Open Data" We examined hysterectomies that underwent benign indications in Japan from 2014-2020 and analyzed trends in minimally invasive surgery (MIS) through laparoscopic hysterectomies (LH) and robotic-assisted laparoscopic hysterectomy using Cochran-Armitage trend tests and Joinpoint Regression Program. A multivariate regression model explored the association between regional factors of second medical service area (SMSA) and MIS rates. **[Results]** The number of LH has increased from 16,016 in 2014 to 27,755 in 2020. The nationwide MIS rates increased from 29% in 2014 to 55% in 2020 (p<0.001). Even during the pandemic, this increase was consistently observed with an annual percent change of 11.3% (95% CI : 10.0-12.6%). Since 2019, >50% of hysterectomies have been performed as MIS. All age groups had an increasing trend in MIS rates. All prefectures, except one, showed a significant upward trend (p<0.05) in the MIS rates that varied widely (23-84%). In the multivariate model, the MIS was more likely to be performed in the SMSAs in western Japan (p=0.011), wherein the number of laparoscopy-qualified gynecologists is 5-10 (p=0.013) and ≥11 (p<0.001). **[Conclusion]** There is a shift towards MIS in total hysterectomies in Japan. However, significant disparities in MIS hysterectomy prevalence exist, potentially influenced by the number of laparoscopy-qualified gynecologists.

IS-WS-1-4

Laplace Law Controls Pregnancy Intervals, Circadian Timers, and Mode of Delivery Through Exponential Uterine Wall Tension (EUWT) and Hormonal Milieu : A Hypothesis Hegazy Ali A *Regional Hospital Mullingar, Ireland*

[Background] Failure to understand uterine function during pregnancy is a major shortcoming of modern healthcare. **[Objective]** To support the hypothesis. **[Methods]** This study investigated the current evidence-based literature and research that may support the hypothesis. **[Results]** The isthmus of the cervix does not seem to exist embryologically, anatomically, histologically, or functionally. The complex interaction between the gestational sac, uterus, and cervix creates and maintains EUWT. Pregnancy is a state of balance between the two opposing and interactive inhibitory and stimulatory systems secondary to EUWT mechanotransduction and progesterone/estrogen stimulation. Pregnancy is mainly maintained through a stretch-dependent inhibitory system secondary to EUWT. Contractions of the stimulatory system transform the cervix into the lower uterine segment (LUS) through TYVU pattern formation, causing EUWT and inhibitory system failure. Light-dark cycle modulation of interactive inhibitory and stimulatory systems divides gestation into five clinical phases: growth, maturation, transition, parturition, and involution. During the maturation phase (30-40 weeks), nocturnal synchronization and synergy of the inhibitory and stimulatory systems, secondary to light-dark cycle

modulation, transforms the cervix into the LUS, making the cervix lose its strength and eventually causing EUWT failure. Pregnancy intervals and circadian timers are achieved by a single mechanism, namely EUWT failure, secondary to the complete loss of cervical strength nocturnally. An inhibitory system malfunction causes preterm labor. Stimulatory system malfunction causes post-term pregnancy. Combined inhibitory and stimulatory system malfunctions cause labor dystocia. **[Conclusion]** Laplace's law measures EUWT, which might be the law of physics that controls birth timing, pregnancy duration, and mode of delivery.

IS-WS-1-5

The simultaneous assessment of a past history of hypertensive disorders of pregnancy and CDKAL1 genotype potentially predicts the long-term risk for developing type 2 diabetes mellitus Inoue Shota, Sugiyama Takashi, Imai Matome, Onji Hiroshi, Yano Akiko, Inoue Yui *Ehime University*
[Objective] The association between hypertensive disorders of pregnancy (HDP) and the development of type 2 diabetes mellitus (T2DM) remains controversial. Further, there have been no reports investigating the interaction between of HDP and T2DM susceptibility genes on the long-term risk of developing T2DM defined by a 75g-OGTT. **[Methods]** We conducted a population-based study with 978 parous women and investigated the influence of T2DM susceptibility genes on the development of T2DM in individuals with a history of HDP. **[Results]** A history of HDP was identified in 101 participants (10.3%). Compared to the non-HDP group, waist circumference, blood pressure, triglyceride, HbA1c, fasting insulin, HOMA2-IR, HOMA2- β , 1h and 2h-plasma glucose (PG) levels during 75g-OGTT, disposition index and Matsuda index were exaggerated in the HDP group. And the prevalence of hypertension and T2DM were increased in the HDP group. In individuals with HDP who developed T2DM, the C/C genotype at the rs7754840 locus of the human cyclin-dependent kinase 5 regulatory subunit associated protein 1-like 1 gene (CDKAL1) was related to increase of PG values during OGTT, a relative decrease in insulin secretion, and the development of T2DM. Age, and current BMI-adjusted stratified analyses demonstrated an interaction effect between HDP and the CDKAL1 C/C genotype on glucose values during OGTT and an increased risk for developing T2DM (OR =5.03 ; 95% CI : 1.93-13.10, p=0.01). These effects were not observed in individuals with HDP with the non-C/C genotype. **[Conclusion]** The simultaneous assessment of a past history of HDP and CDKAL1 genotype powerfully predicts the long-term risk for developing T2DM.

IS-WS-1-6

Short-, mid-, and long-term outcomes of suburethral slings with concomitant pelvic organ prolapse surgeries in Filipino women Lim Navarro Lilibeth M, Amin · Ong Almira J *Urogynecology and Pelvic Reconstructive Surgery, University of the Philippines, Philippine General Hospital, Philippines*
[Objective] This retrospective cohort study investigated the outcomes of combined surgeries for stress urinary incontinence (SUI) and pelvic organ prolapse (POP) in 31 patients with a follow-up of 7 years. The study aimed to evaluate the success and recurrence rates of POP and SUI, comparing results and identifying predictors for recurrence, while also documenting complications. **[Methods]** The research involved Filipino women with diagnosed urodynamic stress incontinence and pelvic organ prolapse, who underwent incontinence procedures alongside prolapse surgery from 2010 to 2020 using a combination of objective and subjective parameters to evaluate outcomes. Urodynamic SUI was confirmed through office-type

cystometry combined with cough stress test, Pelvic Organ Prolapse Quantification (POPQ) scoring system evaluated prolapse surgery success, and a symptom severity checklist based on King's Health Questionnaire (KHQ) were used. **[Results]** The study demonstrated a 96% objective cure rate for SUI and subjective cure rates of 96% for both SUI and POP. While most patients experienced positive outcomes, some reported persistent symptoms like urine frequency and retention. Mesh erosion was observed in a single patient. The objective cure rate for POP was 67.7%, with recurrence in various compartments. Vault fixation appeared effective against apical prolapse recurrence. The study identified pre-operative age as a significant predictor of POP recurrence. **[Conclusion]** This study supports the durability and efficacy of combined surgeries for SUI and POP, with high patient satisfaction.

IS-WS-1-7

Four conserved amino acids on human papillomavirus E6 predict clinical high-risk types Nishi Masaki, Nagata Koh, Komatsu Nahoko, Niiya Akari, Miura Syouko, Hasegawa Yuri, Miura Kiyonori *Nagasaki University*
[Objective] According to conventional risk classification, over 30 alpha-Human papillomavirus (HPV) s remain unclassified and HPV groups phylogenetically classified using the L1 gene do not exactly correspond to the conventional risk classification groups. Therefore, the aim of this study is to develop novel cervical cancer risk classification based on amino acid sequences coded in alpha-HPVs. **[Methods]** In this study, first, we phylogenetically analyzed the nucleotide sequences of alpha-HPV genes to identify amino acids that can distinguish between conventional high risk HPV (cHRHs) and non-cHRHs. Second, to validate our new HPV risk classification method, we used targeted capture sequencing for the whole genome of alpha-HPVs in specimens obtained from 325 cervical swabs of women who had undergone cervical cancer screening in Japan. Detected alpha-HPV types and their newly classified risks were compared with clinical outcomes for each case. Variations found in HPV genomes were also compared with clinical outcomes. **[Results]** Using four E6 risk distinguishable amino acids (E6-RDAAs), we successfully expanded the conventional classification to encompass alpha-HPVs and resolved discrepancies. We validated our classification system using alpha-HPV-targeted sequence data of 325 cervical swab specimens from participants in Japan. Clinical outcomes significantly correlated with the E6-RDAA classification. Four of five HPV types in the data set that were not conventionally classified (HPV30, 34, 67, and 69) were high-risk according to our classification criteria. **[Conclusion]** We could propose a novel cervical lesion progression risk classification strategy using four E6-RDAAs.

IS-WS-1-8

Performance of Large Language Models and Its Potential in Ob/Gyn Education Eoh Kyung Jin¹, Joon Ho Lee², Inha Lee³, Kim Young Tae², Eun Ji Nam² *Yongin Severance Hospital, Yonsei University College of Medicine, Korea¹, Severance Hospital, Yonsei University College of Medicine, Korea², Gangnam Severance Hospital, Yonsei University College of Medicine, Korea³*
[Objective] Recent substantial advancements in large language model (LLM) technology have heralded a transformative phase in the field of artificial intelligence. This study aimed to assess the performance of ChatGPT, specifically the GPT-3.5 and GPT-4 models, in understanding clinical information and its potential implications for Ob/Gyn education. **[Methods]** Residents affiliated with three hospitals underwent a promotional examination once a year. Analyses were conducted on a total of 116 questions, excluding 54 questions with images, out of the full 170

questions from four years (2020-2023). Scores from GPT-3.5, GPT-4.0, and a total of 100 residents were compared. **[Results]** Across the years, the average scores for GPT-3.5 and GPT-4.0 were 38.76 [standard deviation (SD), 5.65] and 79.39 (SD, 3.67), respectively. For the R1, R2, and R3 groups, the cumulative annual average scores were 79.12 (SD, 9.00), 80.95 (SD, 5.86), and 83.60 (SD, 6.82), respectively. No statistically significant difference was observed between the scores of GPT-4.0 and those of the residents (P value : vs R1, 0.945 ; vs R2 0.915 ; vs R3 0.246). When analyzing questions specific to obstetrics, the average scores for GPT-3.5 and GPT-4.0 were 33.44 (SD, 10.18) and 90.22 (SD, 7.68), respectively. For gynecology-specific questions, the average scores for GPT-3.5 and GPT-4.0 were 43.79 (SD, 12.73) and 72.80 (SD, 4.61), respectively. **[Conclusion]** In terms of problem-solving capacity within the field of Ob/Gyn, the LLM, particularly GPT-4.0, displayed no statistically significant difference compared to the residents. Notably, it exhibited exceptional performance in the obstetrics.

IS-WS-2-1

Factors associated with postpartum depression among Myanmar women in Yangon Yamamoto Eiko, Nishino Kimihiro Department of Healthcare Administration, Nagoya University

[Objective] There has been no policy on postpartum depression (PPD) due to a lack of information on maternal mental health in Myanmar This study aims to identify the prevalence and factors associated with PPD among women in Yangon, Myanmar. **[Methods]** This is a cross-sectional study including 552 women at 6-8 weeks postpartum who visited at a national hospital for postnatal care from September to October 2022. Socio-demographic factors, obstetric and infant factors, family support, and medical history were collected using a structured questionnaire. Myanmar version of Edinburgh Postnatal Depression Scale (EPDS) was used for screening PPD, and all women were divided into suspected-PPD (EPDS ≥ 10) and non-suspected-PPD (EPDS < 10). Chi-square and Fisher's exact tests were used to compare the characteristics of women between suspected-PPD and non-suspected-PPD, and logistic regression analysis was preformed to identify the factors associated with suspected-PPD. Informed consent was obtained from each woman before data collection. This study was approved by the Ethics Committee of the Myanmar Ministry of Health. **[Results]** The mean age of the 552 women was 27.9 years and 176 women (31.9%) were categorized into suspected-PPD. Multiple logistic regression analysis showed that living in a nuclear family, feeling insufficient income, unplanned pregnancy, less than eight ANC visits, low birth weight of the last baby, insufficient support from partners, parents, and parents-in-law, and depressive symptoms during the last pregnancy were associated with suspected-PPD. **[Conclusion]** To prevent PPD, high-risk women should be identified during pregnancy and social support by family members and healthcare workers should be strengthened.

IS-WS-2-2

Comparison of Random Urine Protein—Creatinine Ratio With 24 Hour Urine Protein in Women With Preeclampsia Luqman Sobia, Zulfiqar Anam, Rauf Sidra, Sheikh Bushra, Hina Hadia, Zafar Majida, Naem Shumaila, Javed Nosheela, Batool Mussarat Pakistan Institute of Medical Sciences, Pakistan

[Objective] To determine the diagnostic accuracy of protein creatinine ratio in predicting pre-eclampsia, taking 24 hours urinary protein as gold standard. **[Methods]** A total of 156 women pregnant women with singleton pregnancy (assessed on USG) with suspected pre-eclampsia of 20-40 years were included. Patients having urinary tract infection, GDM, h/o chronic hyper-

tension, CLD and renal disease were excluded. All women, irrespective of the severity of the disease, were asked to provide a 24-hour urine collection for determination of proteinuria. All women were advised to pass urine at 6 : 00 am and collect all the urine subsequently till 6 : 00 am the next morning (24-hour period). The adequacy of urine collection was determined by creatinine excretion. Urine sample for protein-creatinine ratio was collected the next morning after the 24-hour collection was over. Urinary protein quantitation was done by Biuret method, and urinary creatinine estimation was done by modified Jaffe's method. **[Results]** Age range in this study was from 20-40 years with mean age of 29.68 ± 5.32 years. Majority of the patients 83 (53.21%) were between 20 to 30 years of age. Mean gestational age was 26.61 ± 3.15 weeks. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of protein creatinine ratio in predicting pre-eclampsia, taking 24 hours urinary protein as gold standard was 86.96%, 87.36%, 84.51%, 89.41% and 87.18% respectively. **[Conclusion]** This study concluded that diagnostic accuracy of random urine protein creatinine ratio in predicting preeclampsia is very high.

IS-WS-2-3

DELAYED VERSUS IMMEDIATE OXYTOCIN INFUSION AFTER AMNIOTOMY FOR INDUCTION OF LABOR Zainab Paras, Luqman Sobia, Masoom Kausar, Rauf Sidra Pakistan Institute of Medical Sciences, Pakistan

[Objective] To compare the mean amniotomy-to-delivery interval after immediate or delayed oxytocin infusion. **[Methods]** A total of 60 women of age 20-40 years, gestational age $> 37-42$ weeks (on LMP) were included. Females with PROM, previous cesarean section, having any medical disorder (Hypertension, Diabetes, Cardiac disease and Asthma) and Obstetrical complication associated with pregnancy or having fetal compromise were excluded. One group of women after amniotomy with delayed oxytocin infusion (DO) and second group was immediate oxytocin after amniotomy (IO). Amniotomy was performed as planned with the induction appointment. Women in the delayed oxytocin (DO) group were waited for spontaneous contractions for 12 h after amniotomy. Oxytocin was administered according to the local induction of labour protocol. Women in the immediate oxytocin group received standard care and infusion of oxytocin was started immediately (within 30 min). Primary outcome was assessed by amniotomy- to delivery interval. **[Results]** The mean age of patients in early group was 30.20 ± 4.24 years and in delayed group was 29.87 ± 4.28 years. Mean parity in early group was 3.57 ± 0.68 and in delayed group was 3.73 ± 0.69 . In my study the mean amniotomy to delivery interval was 10.60 ± 1.90 hours in early group and 16.03 ± 2.63 hours in delayed group with p-value of 0.0001. **[Conclusion]** This study concluded that immediate oxytocin infusion after amniotomy reduces the delivery time as compared to delayed oxytocin infusion when used for method of induction.

IS-WS-2-4

Abnormal microscopic findings in the placenta correlate with the severity of fetal heart failure Miyoshi Takekazu¹, Yoshimatsu Jun² Clinical Research Center, National Center for Child Health and Development¹, National Cerebral and Cardiovascular Center²

[Objective] This study investigated the association between placental pathology and fetal heart failure. **[Methods]** Singletons with a congenital heart defect (CHD) and/or arrhythmia (n=168) and gestational age-matched controls (n=52) were included in the study. The associations between macro- and microscopic abnormal findings of the placenta and the severity of fetal heart failure were evaluated using the cardiovascular pro-

file (CVP) score. Nine features were microscopically identified and assessed in sections of the placenta : premature villi, edematous villi, fibrotic villi, chorioamnionitis, chorangiomas, fibrin deposition, subchorionic hematoma, infarcted villi, and nucleated red blood cells in villous vessels. **[Results]** Among singletons with CHD and/or arrhythmia, the final CVP score was ≥ 8 in 140 cases, 6 or 7 in 15 cases, and ≤ 5 in 13 cases. Microscopic analysis showed that the frequency and severity of premature and edematous villi and increased nucleated red blood cells in villous vessels were greater in cases of fetal heart failure. These microscopic findings were more common and severe in cases with a final CVP score ≤ 5 than in gestational age-matched controls. The prevalence of abnormal macroscopic findings of the placenta and umbilical cord was similar regardless of the severity of fetal heart failure. **[Conclusion]** Premature and edematous villi and increased nucleated red blood cells in villous vessels were correlated with the severity of fetal heart failure in cases of CHD and/or arrhythmia.

IS-WS-2-5

Prenatal contralateral pulmonary artery diameter is the best prediction of the hernia size in congenital diaphragmatic hernia Yamamoto Yuka, Matsuzawa Nana, Kitamura Eri, Ishida Yuri, Takeda Jun, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] Thoracoscopic repair is one option in cases with congenital diaphragmatic hernia (CDH) in neonate, however it is difficult to estimate whether the thoracoscopic repair is successful because there are no ways to measure the defect size. Our object of this study was to evaluate the defect size of CDH neonates from the prenatal ultrasound parameters. **[Methods]** The data was retrospectively collected between 2016 and 2023, in terms of the demographics, prenatal ultrasound and intraoperative status. The defect size was divided into two groups (more (M) or less (L) 50% of all diaphragms). Ultrasound parameters were evaluated as follow : contralateral pulmonary arterial diameter (mm), observed / expected lung area to head circumference ratio (o/e LHR), pulmonary arterial Doppler in contralateral PA (acceleration time to ejection time ratio=AT/ET, pulsatility index (PI). **[Results]** Twenty-eight cases of prenatally diagnosed CDH were born during the study period, two of which did not result in surgery and died, and two were right-sided CDH. There were 8 cases in which the defect size was $> 50\%$, and all eventually needed open surgery. Contralateral PA size was significantly smaller in group M ($p=0.0002$). o/e LHR was also significantly smaller in group M ($p=0.046$). There was a trend of higher AT/ET ratio in group M ($p=0.080$), but there was no trend in PA PI. **[Conclusion]** Prenatal contralateral pulmonary artery size might be helpful to evaluate the defect size in neonatal left-sided CDH.

IS-WS-2-6

Medullary vein Development in Normal Fetal Brain and abnormal Medullary veins in Cortical malformation cases Using Transvaginal 3D neuro-Doppler Flow Technology PooH Ritsuko *Fetal Diagnostic Unit, CRIFM Prenatal Medical Clinic* **[Objective]** There have been few reports on the development of medullary veins (MV) in the fetal brain. We investigated the normal MV development, and MV in malformations of cortical development (MCD). The purpose of this study is to clarify MVs development in the normal fetuses, and abnormal MV development in MCD. **[Methods]** Between 2018 and 2023, 547 normal singleton fetuses at 15-30 weeks who underwent transvaginal neurosonography (Voluson E10 and Expert22 with 6-12 MHz transvaginal transducer). This study was approved by the Institutional Review Board. 3D HDflow/Slowflow was used to detect

normal development of the medullary veins in anterior coronal section of the brain. Secondly, in 23 fetuses with malformations of cortical development (MCD) beyond 25 weeks, MV was investigated. The length of the superficial medullary veins, subplate and intermediate zone thicknesses were measured in the coronal section and determine a timing when the superficial and deep medullary veins are connected. **[Results]** In normal cases, the length of superficial MV elongates during the second trimester, and superficial MV and Deep MV connect most probably due to the anastomosis veins almost at 25 weeks. The results showed that beyond 25 weeks, if the superficial-deep medullary vein is not connected, which is defined as abnormal MV, the two were not connected in 25 of the 28 MCD cases. **[Conclusion]** Although the present study was limited to a single ethnic group at a single institution, it was thought that the development of MVs may help as an adjunct diagnosis of MCD.

IS-WS-3-1

Distressed Community Index and the Association with Preterm Birth Ghareeb Allen *University of Washington, USA*

[Objective] To determine whether more socioeconomically distressed communities experience higher rates of preterm birth or earlier gestational age at delivery at a tertiary care hospital in Washington state. **[Methods]** We conducted an IRB-approved retrospective cohort study using the Obstetrical Care Outcomes Assessment Program (OBOCAP) at the University of Washington Medical Center. We included the first pregnancy in the dataset for each individual with complete data on gestational age (GA) at delivery and distressed community index (DCI), a tool for measuring the comparative economic well-being of U.S. communities. We evaluated the association between DCI quintile and GA at delivery using linear regression, adjusting for prepregnancy substance use, smoking, diabetes, hypertension, and urban/rural class. **[Results]** A total of 10,143 individuals were included for analysis, with 39.0% of individuals living in the least distressed communities (DCI quintile = 1), and 2.9% in the most distressed communities (DCI quintile = 5). For individuals in the least distressed quintile, gestational age at delivery was 2.5 weeks (95% CI : 2.06, 2.93) later than for individuals in the most distressed quintile, after adjustment for confounders. Individuals in the most distressed communities experienced significantly higher rates of extremely preterm, very preterm, moderate preterm, and late preterm birth compared to the least distressed communities. **[Conclusion]** Our findings indicate that the DCI has the potential to identify patient populations at risk for preterm birth independent of classic risk factors such as smoking, diabetes, substance use, and hypertension.

IS-WS-3-2

Serologic features and dynamics of serum antibodies in Taiwanese pregnant women and infants after COVID-19 vaccination : a longitudinal observational study Chu Ting Yi¹, Chen Yi-Ching², Chiu Cheng-Hsun³, Shaw Steven W.¹, Lo Ling-Ming¹, Hung Tai-Ho^{1,4} *Taipei Chang Gung Memorial Hospital, Taiwan¹, Department of Pediatrics, Taipei Chang Gung Memorial Hospital, Taiwan², Department of Pediatrics, Linko Chang Gung Memorial Hospital, Taiwan³, Department of Medicine, College of Medicine, Chang Gung University, Taiwan⁴*

[Objective] To establish a prospective cohort of pregnant women receiving COVID-19 vaccination to evaluate immunogenicity in different vaccine platforms, duration of antibody waning, efficacy in fetal-maternal antibody transfer, and safety profile in Taiwanese women. **[Methods]** We prospectively collected mother-infant pairs who received at least one dose of any COVID-19 vaccine during pregnancy. Pregnant women without any COVID-19 vaccination or with natural infection were en-

rolled as the negative and positive controls. Maternal sera were collected before delivery, two and six months postpartum, respectively. Blood samples from umbilical vein after clamping the cord and from neonatal peripheral venous circulation at six months old were obtained. Breast milk was collected in breastfeeding mothers. Anti-spike protein antibody was measured by ELISA and neutralization test. **[Results]** A total of 88 mother-infant pairs (74 vaccinated, 14 unvaccinated, two infected) and 29 women of reproductive age (18 vaccinated, 11 vaccinated followed by infection) were included. Anti-spike protein IgG level in sera remained detectable in vaccinated mothers two months after delivery. Sera from umbilical vein in infants of vaccinated mothers generally showed a high level of anti-spike protein IgG, indicating effective placental transportation. However, neonatal anti-spike protein IgG level declined significantly over time. **[Conclusion]** Our results indicate that COVID-19 vaccine, mostly Moderna vaccine, induced a robust humoral response in pregnant women with the efficient placental transportation. However, neonatal anti-S protein IgG levels waned gradually after birth and remained low at six months old. Therefore, a vaccination strategy for neonates after six months warrants attention to achieve effective protection against COVID-19 infection.

IS-WS-3-3

Comparison of Modified 75g Oral Glucose Tolerance Test with 75g Oral Glucose Tolerance Test in Screening of Gestational Diabetes Mellitus Rasheed Shabnum, Batool Mussarat, Rauf Sidra, Javed Nosheela, Sharafat Shirza, Nawaz Farzana, Saeed Qurratulain, Aftab Sadia, Batool Afshan, Jalil Mazhar *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] To compare two diagnostic tests for GDM i.e. modified OGTT 75 g and standard fasting OGTT 75 g. **[Methods]** In this study total 136 pregnant women were selected. This cross sectional validation study was completed in a period of 6 months. Women were between 22 and 26 weeks gestation who were initially investigated with modified OGTT 75 g at 22-24 weeks gestation for glucose intolerance and later at 24-26 weeks they were called again for the fasting OGTT 75 g and glucose test was done in the same patient. The outcome was judged as predictive prevalence of both tests in picking GDM. Ethical clearance was taken from Hospital Ethics Committee. A written informed consent was administered before enrollment of subjects. **[Results]** Women's mean age was 26.6 years in this study. Twenty seven (20.1%) patients were overweight or obese. In 16 (11.8%) patients, a family history of diabetes was there. There were 17 (12.5%) cases with positive findings on modified OGTT (75 g) screening while 13 (9.6%) positive cases on fasting OGTT (75 g). Almost two third of the GDM cases were overweight/obese in this study. The sensitivity and specificity of modified OGTT was found out to be 84.6% and 95.1% respectively. **[Conclusion]** Modified OGTT 75 g and fasting OGTT 75 g have been found equivalent in screening of GDM in women having gestational age of 22 to 26 weeks. Keeping fasting as gold standard method for screening GDM, the modified OGTT test showed a very high sensitivity and specificity in this study.

IS-WS-3-4

Comparison and Efficacy of Auricular Point Acupressure on Lactation in Nulliparous Postpartum Cesarean Delivery Parturient at Thammasat University Hospital : a Randomized Clinical Controlled Trial Suwannarurk Komsun¹, Tungtriratanakul Kitipong¹, Sangwattanakul Paradi², Pichita Prasongvej¹, Junya Pattaraarchachai², Krit Osirichaivait¹, Kornkarn Bhamarapratana³ *Thammasat University, Thailand¹, Chulabhorn International College of Medicine, Thammasat University, Thailand², Department of Preclinical Science,*

Thammasat University, Thailand³

[Objective] This study aimed to compare the lactation enhancing effect of auricular acupressure with or without a magnetic plate on post-cesarean nulliparous parturient. **[Methods]** This randomized controlled trial was conducted at Obstetrics and Gynecology Department, Thammasat University Hospital, Thailand from September 2021 to March 2022. All participants were term primigravida pregnant women who underwent cesarean delivery during the study period. Parturient were randomly allocated into control, magnetic (M) and non-magnetic (NM) groups. Participants in the control group received treatment as per hospital guidelines. M and NM groups were assigned to perform auricular acupressure using auricular patches with and without magnetic plates, respectively. The ear pinna has 5 specific auricular points, namely ; chest (AH10), endocrine (CO18), stomach or Wei (CO4), spleen or Pi (CO13), and sympathetic points (AH6a). Lactation visual assessment (LVA) level was evaluated immediately and daily up to 7 days after delivery. **[Results]** Each group consisted of 25 participants. The mean maternal and gestational ages were 30 years old and 38.5 weeks, respectively. There were more parturient in the M group (20/25), who had onset of lactation within 24 hours, than in the control group (13/25). LVA level 1, 2 and 4 in all three groups were comparable. The onset of LVA level 3 in M group was significantly faster than the control group. Satisfactory lactation and auricular acupressure among M and NM groups were comparable. **[Conclusion]** Auricular acupressure with magnetic plates significantly enhanced lactation onset and lactation visual volume (level 3) in post-cesarean nulliparous parturient.

IS-WS-3-5

Key indicators for early recognition of peripartum cardiomyopathy : Insights from a retrospective analysis of 7 cases Okamura Yu, Kurokawa Yusuke, Muto Megumi, Yokomine Masato, Horinouchi Takashi, Yoshizato Toshiyuki, Tsuda Naotake *Kurume University*

Purpose : Early recognition of peripartum cardiomyopathy (PPCM) is crucial. This retrospective study aimed to clarify key indicators for considering PPCM. **Methods :** Subjects were 7 cases of PPCM encountered at our hospital in 2012-2023. The parameters analyzed were risk factors, timing of diagnosis, subjective and objective signs (except for echocardiography), and the timing of symptom manifestation. **Results :** 1. Risk factors included elderly pregnancy (6 cases), hypertensive disorders of pregnancy (HDP) (3), multifetal pregnancy (3), obesity (3), long-term tocolysis with β_2 stimulants (tocolysis) (2), and a family history of cardiomyopathy (1). 2. The timing of diagnosis was 0-1 day and 9-16 days after delivery for the cases with HDP or tocolysis and without HDP and tocolysis, respectively. 3. Shortness of breath was the solo subjective sign present at diagnosis in all cases. Objective signs comprised tachycardia (101-182 bpm) (6), low levels of SpO₂ (89-93%) (6), and cardiomegaly with a cardio-thoracic ratio of >55% (57-62%) (5), which manifested concurrently with the subjective sign. Notably, in 1 case with HDP, tachycardia preceded the other objective signs by 1 day. 4. The SpO₂ levels at the time of diagnosis showed improvement following oxygen inhalation, ranging from 96-100% within 30 minutes in 5 cases. **Discussion :** In cases with HDP/tocolysis, the clinical course progressed rapidly after delivery. In cases without HDP/tocolysis, the clinical course has a relatively slow progression. In addition to dyspnea, the presence of unexplained tachycardia and normalization in SpO₂ level after oxygen inhalation as well as cardiomegaly can serve as indicators to consider PPCM.

IS-WS-3-6

The risk of preterm birth when fetal fibronectin testing changed from positive to negative Fukuda Toma, Sato Yuki, Matsuoka Ryo, Isogami Hiroataka, Okoshi Chihiro, Yasuda Shun, Yamaguchi Akiko, Fujimori Keiya *Fukushima Medical University*

[Objective] Fetal fibronectin (fFN) is used to predict spontaneous preterm birth within two weeks. Therefore, we measure fFN twice for preterm labor patients, at the time of diagnosis and two weeks later. However, the interpretation is unclear when fFN testing changed from positive to negative. This study aimed to investigate the risk of preterm birth in women whose fFN testing changed from positive to negative. **[Methods]** This retrospective study used data from January 2017 to August 2023. Based on qualitative results (positive : P or negative : N) of the first and second fFN testing, we categorized into four groups : N-N, P-N, N-P, and P-P. The primary outcome was preterm birth. Subgroup analysis was conducted based on the cervical length at the time of diagnosis. **[Results]** A total of 125 women were eligible, and 60 women were categorized in N-N group and 41 women were categorized in P-N group. Multiple logistic regression analysis demonstrated that the P-N group had higher rate of preterm birth compared to the N-N group (aOR 3.1, 95% CI 1.15-8.39). In the subgroup analysis, the P-N group had higher rate of preterm birth compared to the N-N group (aOR 5.01, 95% CI 1.15-21.88) when cervical length longer than 15 mm, whereas there was no significant difference between the P-N and N-N groups (aOR 1.10, 95% CI 0.17-7.60) when a cervical length 15 mm or shorter. **[Conclusion]** In this study, whether fFN changed from positive to negative, the rate of preterm birth remained high.

IS-WS-3-7

Predictive parameters for uterine rupture/dehiscence following prior cesarean section : a prospective longitudinal study using transvaginal ultrasonography Kawakami Kosuke^{1,2}, Yoshizato Toshiyuki², Fujikawa Rie¹, Ono Yumika¹, Shimizu Takahiro^{1,2}, Muto Megumi², Kitagawa Marie^{1,2}, Ishibashi Hiroki¹, Kurokawa Yusuke², Horinouchi Takashi², Okura Naofumi¹, Tsuda Naotake² *National Hospital Organization Kokura Medical Center¹, Kurume University²*

[Objective] To explore the predictive parameters for uterine rupture/dehiscence in pregnancy following prior cesarean section (CS). **[Methods]** The subjects were 87 cases who had undergone CS at term in two hospitals between 2022-2023. Longitudinal observations were conducted at 19-21, 25-27, and 31-33 weeks using transvaginal ultrasonography. Qualitative and quantitative evaluations included classifying the lower uterine segment (LUS) into V-, U- and non-V/non-U-shapes and residual myometrial thickness (RMT). Intraoperative LUS assessment was categorized into four : I (no thinning), II/III (thinning without/with the membranes visible through the myometrium), and IV (uterine rupture). In each age-group, the parameters were compared between two groups with classes I/II (non-uterine scar dehiscence, non-USD) (69 cases) and III/IV (18 cases) (USD). Statistical analysis was performed using the Mann-Whitney test with significance set at $P < 0.05$. **[Results]** The number of cases with V-, U-, and non-V/non-U-shapes was 5/10/3, 0/7/11, and 0/1/17 in the USD group and 45/22/2, 9/36/24 and 0/10/59 in the non-USD group at 19-21/25-27/31-33 weeks. The median value of RMT was different between the groups for cases with a V-shape at 19-21 weeks (USD, 2.5 vs. non-USD, 5.8 mm) and for cases with a non-V/non-U-shape at 31-33 weeks (1.7 vs. 2.4 mm). The cut-off values of RMT for a V-shape at 19-21 weeks and a non-V/non-U-shape at 31-33 weeks were 4.2 and 2.2 mm (AUC, 0.86 and 0.74), respectively. **[Conclusion]** RMT val-

ues for a V-shape of > 4.2 mm at 19-21 weeks and a non-V/non-U-shape of > 2.2 mm at 31-33 weeks can predict the absence of uterine dehiscence/rupture.

IS-WS-3-8

Effect of Barbed sutures versus conventional sutures to prevent Cearerian scar defect following elective Cesarean Section. SPIRAL Trial : A Multicenter, Randomized, Controlled Trial Maki Jota¹, Mitoma Tomohiro¹, Oohira Akiko¹, Ooba Hikaru¹, Eto Eriko¹, Yamamoto Dan², Yamamoto Risa², Kai Kenji², Tamada Takashi³, Akamatsu Kazuyo³, Kawanishi Kunihiko⁴, Masuyama Hisashi¹ *Okayama University¹, Fukuyama Medical Center², Iguchi Perinatal and Obstetrics and Gynecology Hospital³, Yashima General Hospital⁴*

[Objective] The study investigates whether utilizing barbed thread sutures in cesarean delivery (CD) surgeries can help prevent Cesarean scar defects (CSD) and reduce long-term postpartum clinical symptoms. Specifically, we sought to determine the efficacy of barbed sutures in comparison to conventional sutures, examining the ultrasonographic characteristics of the uterine scar area and post-CD clinical symptoms. **[Methods]** Conducted across four Japanese medical centers from May 2020 to March 2023, this multicenter, randomized, controlled trial encompassed pregnant women undergoing their inaugural CD. Participants, meeting all the eligibility criteria, were equally and randomly allocated to two groups : one group was administered the conventional continuous absorbable uterine suture, while the other received barbed thread sutures. The primary point of assessment was the presence of scar niches larger than 2mm, evaluated through transvaginal ultrasonography 6 to 7 months following the surgery. This study is registered under the codes jRCT1062200001 and CRB6180001. **[Results]** From the 220 cases analyzed-excluding dropouts and other exclusions-110 were treated using barbed sutures and 110 with conventional sutures. Six months post-surgery, the barbed suture group demonstrated a considerably lower incidence of uterine niches (29.1% compared to 68.2% in the conventional group), and these were shallower in all measurement points ($P < 0.001$), no difference in menstrual symptoms. Impressively, no large defects with residual myometrium less than 3mm were observed in the barbed suture group. **[Conclusion]** Our findings underscore that employing double-layer barbed sutures during CD surgeries correlates with a reduced occurrence of scar niches, pointing to a positive preventative potential against postoperative complications.

IS-WS-3-9

The exploration of late-onset disease infection route of Group B Streptococcus by polymerase chain reaction (PCR) Yoshida Emiko¹, Takeda Jun¹, Maruyama Yojiro³, Suga Naoko², Makino Shintaro², Itakura Atsuo¹ *Juntendo University¹, Juntendo University Urayasu Hospital², Juntendo University Nerima Hospital³*

[Objective] Group B Streptococcus (GBS) is a pathogen causing life-and-neurodevelopmental-threatening and bacterial infections in newborns. Nationwide surveillance study between 2016 and 2020 in Japan had reported an increase in the number of cases mainly driven by an increase in late-onset disease (LOD). Prevalence of maternal GBS is unstable, so Rapid diagnosis of GBS at delivery is useful as a way to prevent GBS infection. We aimed to reveal the clinical features to explore transmission route of LOD. **[Methods]** Vaginal-and-anorectal specimens were collected from 530 pregnant women at the time of antepartum, delivery or postpartum. Oral/anorectal specimens were collected from their newborns at the time of birth, day3, or day30. Each sample was tested by PCR and/or culture for GBS detec-

tion. The DNA for PCR was purified directly from the buffer that the swab specimens were suspended without enrichment cultivation. **[Results]** The antepartum prevalence of maternal GBS was 18.6% according to PCR, and 16.1% according to cultures. In 9.6% of cases, GBS results on PCR were inconsistent with antepartum and delivery. The ratio of detected GBS capsular types differed between mothers and neonates, type V was the most in mothers and type Ia was the most in neonates. GBS was detected in 4.6% of neonate even from GBS negative mother. **[Conclusion]** As previously reported, PCR showed superior in detection to culture. GBS positive neonate with negative mother suggests horizontal infection after birth. Our method is a direct detection without an enrichment cultivation, suggesting the possibility of point of care testing.

IS-WS-4-1

Change of non-genomic effects of progesterone on rat uterine muscle during pregnancy Yoshida Aya, Yasuda Katsuhiko, Kamiya Akio, Tsuji Shoko, Sumi Genichiro, Okada Hidetaka *Kansai Medical University*

[Objective] We previously investigated the changes in the conflicting nongenomic effects of progesterone (P_4) on rat myometrium during pregnancy and found that P_4 did not cause contraction in the nonpregnant resting-myometrium, but caused contraction in the pregnant myometrium. The contractile response to P_4 and the contractile intensity increased significantly during pregnancy and decreased after delivery. On the other hand, the inhibitory effect of P_4 on high potassium chloride (High-KCl) -induced contractions did not change significantly during pregnancy. In this study, we examined the mechanism of action about the changes in the conflicting nongenomic effects of P_4 during pregnancy using membrane progesterone receptor (mPR) agonist and gene expression of mPRs. **[Methods]** Org OD-02-0 (mPR agonist) was administered at the concentrations of 10^7 to 10^4 M to the resting-myometrium and High-KCL-induced contracted myometrium obtained from the gestational day 20 rats, and their effects were examined. Furthermore, DNA microarray and quantitative real-time polymerase chain reaction (qRT-PCR) were performed for gene analyses. This study was approved by the University's Experimental Animal Committee. **[Results]** Org OD-02-0 mimicked the nongenomic effects of P_4 on myometrium during pregnancy. DNA microarray and qRT-PCR analyses revealed that mPR β gene expression increased significantly during pregnancy and decreased after delivery. However, mPR α , mPR γ , mPR δ , and mPR ϵ expression levels remained unchanged. **[Conclusion]** The stimulatory nongenomic effect of P_4 , which was inducible and mPR β -dependent during pregnancy, may be involved in parturition. The inhibitory effect, which was constitutive and dependent on other mPRs, may be involved in pregnancy maintenance.

IS-WS-4-2

The ability of the ovine fetus undergoing artificial placenta treatment to compensate for acute hypoxia is predictable and determined by gestational age Usuda Haruo¹, Hideyuki Ikeda¹, Yusaku Kumagai², Erin Fee¹, Sean Carter^{1,2}, Matthew Kemp^{1,2} *The University of Western Australia, Australia¹, National University of Singapore, Singapore²*

[Objective] The incidence of perinatal morbidity arising from birth hypoxia has not changed significantly despite better labor management. This may reflect a reduced fetal capacity to compensate for hypoxic insult. We assessed the effect of gestation on hypoxic tolerance in preterm fetuses and investigated predictable factors for fetal hypoxia using an artificial placenta system. **[Methods]** Fifteen ewes with pregnancies were adapted to artificial placenta therapy at 123d (n=7) and 98d GA (n=8). FiO

2 and gas flow volume to the membranous oxygenator were adjusted to maintain fetal SO₂ (about 65%) and pCO₂ (about 40 mmHg), and then reduced by 5% every 30 minutes. Circuit flow : CF, mean blood pressure : mBP, heart rate : HR, arterial blood gas data, ultrasound measurements of cardiac function and pulsatility index (PI) for vessels were assessed hourly. Data were tested with ANOVA and linear regression. **[Results]** Reduction of FiO₂ and gas flow ceased at 50% for 123d-fetuses and 40% for 98d-fetuses as most animals had pH<7.0 and BE<-12. Both groups had progressively elevated HR. Only 123d-fetuses had elevated mBP and CF (p<0.05). There were progressive decreases in pH, BE, pO₂, SO₂, and increases in pCO₂, lactate in both group animals (p<0.05). Cardiac ultrasound showed no significant difference in both groups. Only 123d-fetuses had elevated PI of external iliac artery (ex-IA). PI of ex-IA and HR strongly predicted fetal pH (R²=0.538), BE (R²=0.575), SO₂ (R²=0.641), lactate (R²=0.745) in 123d-fetuses (p<0.05). **[Conclusion]** Mid-gestational fetuses may have mechanism to increase placental flow, and PI of ex-IA and HR may be useful in predicting fetal acidemia and hypoxia. However, it may not be applicable to pre-viable fetuses.

IS-WS-4-3

Dynamic computed tomography in post-partum hemorrhage is useful for the selection of treatment strategy Suemori Ayano, Mitoma Tomohiro, Maki Jota, Nakato Hikari, Ooba Hikaru, Mishima Sakurako, Oohira Akiko, Kirino Satoe, Eto Eriko, Masuyama Hisashi *Okayama University*

[Objective] Postpartum hemorrhage (PPH) is an obstetric emergency that requires prompt action with multidisciplinary care. However, if the treatment of choice is ineffective in controlling bleeding, the situation worsens further : therefore, proper diagnosis and treatment selection is necessary. This study investigates the relevance of extravasation detected in dynamic computed tomography (DCT) and the management choice of PPH. **[Methods]** This retrospective observational study included cases with DCT imaging for the diagnosis of severe PPH from October 2015 to September 2022. Of 90 patients who underwent DCT to diagnose PPH, 60 diagnosed with intractable atonic PPH were surveyed. A comparison was made between the group with contrast extravasation (CE) in the early phase and the other groups. **[Results]** Of the 60 patients with intractable atonic PPH, 21 underwent UAE, 20 of whom had early phase CE on DCT. Pre-DCT clinical parameters and clinical indices were not significantly different in presence of early phase CE. Early phase CE was associated with uterine artery embolisation (UAE) performance, with a sensitivity of 95%, specificity of 87%, positive predictive value of 80%, and negative predictive value of 97%. In cases where UAE was performed after conservative management, there was a significant increase in blood loss and transfusion volume. **[Conclusion]** Early phase CE is significantly associated with UAE for treatment. It is challenging to identify active bleeding by subjective evaluation and laboratory data, and UAE should be selected as soon as possible in the case of active bleeding.

IS-WS-4-4

Therapeutic effects of Human Amniotic Fluid Stem Cell-Derived Extracellular Vesicles (hAFSC-EVs) on Inflammatory Macrophage Polarization Abe Yushi^{1,2}, Otani Toshimitsu¹, Matsumiya Yosuke², Hasegawa Keita¹, Kasuga Yoshifumi¹, Ikenoue Satoru¹, Ochiai Daigo³, Vatish Manu², Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Nuffield Department of Women's and Reproductive Health, University of Oxford, UK², Kitasato University³*

[Objective] Human amniotic fluid stem cells (hAFSCs), a subset

of mesenchymal stem cells (MSCs), are known to have powerful anti-inflammatory effects. It is likely that extracellular vesicles (EVs) derived from hAFSCs alter immune cell function, but the specific mechanisms have not been fully elucidated. This study aims to identify the effects of hAFSCs on macrophages and the mechanisms by which changes occur. **[Methods]** EVs were isolated from hAFSCs (hAFSC-EVs) by ultracentrifugation and their properties and surface antigen markers were investigated. We confirmed that hAFSC-EVs can be taken up by a macrophage cell line (THP-1). Subsequently, we attempted to inhibit the uptake of hAFSC-EVs by blocking key antigens present on EVs with specific antibodies. This allowed us to dissect the effect of specific EV species on macrophages. **[Results]** hAFSC-EVs could be isolated by ultracentrifugation. Their phenotype was confirmed by nanoparticle tracking analysis and western blotting. Comprehensive analysis of surface antigen markers revealed that specific surface antigens were highly expressed. Blocking these surface antigens with functional antibodies reduced their uptake into macrophages. The effect of hAFSC-EVs was also diminished when surface antigens were blocked and uptake was reduced. **[Conclusion]** These results suggest that hAFSC-EVs change the polarity of inflammatory macrophages to anti-inflammatory macrophages and that specific surface antigens may play a central role in this process. hAFSC-EVs may provide a mechanism to promote anti-inflammatory effects in macrophages.

IS-WS-4-5

Limited Fraternal Concordance and Sexually Dimorphic Lung Responses in Twin Preterm Ovine Fetuses Exposed to Antenatal Steroid Therapy Fee Erin L¹, Usuda Haruo¹, Ikeda Hideyuki¹, Carter Sean W. D.², Jobe Alan H^{1,3}, Kemp Matthew W^{1,2} *University of Western Australia, Australia¹, National University of Singapore, Singapore², Cincinnati Children's Hospital Medical Centre, University of Cincinnati School of Medicine, USA³*

[Objective] Individual responses to antenatal steroid (ANS) treatments are variable, and potentially fetus-specific. As natural twin pregnancies in sheep are almost uniformly dizygotic, we aimed to explore the degree of concordance in the physiological and transcriptomic ANS responsiveness of genetically-distinct twin preterm ovine fetuses **[Methods]** 31 twin-bearing ewes at 123 ± 1d gestation received intramuscular injections of either : i) 1 x 0.25 mg/kg betamethasone acetate and phosphate (BM) (n=11 twin pairs) ; ii) 2 x 0.25 mg/kg BM, 24h apart (n=10 twin pairs) ; or iii) 2 x saline, 24h apart (n=10 twin pairs). Fetuses were delivered 24h after their final injection and ventilated for 30mins. Fetal lung (right lower lobe) RNA was subjected to bulk sequencing. Plasma and amniotic fluid cell-free RNA was analysed with qPCR. Plasma and lung betamethasone were analysed by LCMS. Data were tested using Chi-Square tests and McNemar test (p<0.05 significant). **[Results]** Mean PaCO₂ values for male and female fetuses were 97.2 and 76.52 mmHg respectively. Only 52% of twin pairs were concordant for ANS lung responses. Males were significantly more likely to respond to steroids when twinned with a male fetus. Response variability was not a function of number of steroid injections, or tissue/plasma betamethasone levels. **[Conclusion]** Individual variability in fetal ovine responses to ANS depended on the fetus, not maternal or placenta inputs. ANS-treated females had lower PaCO₂ values and their presence was associated with poorer responsiveness in twin males. Pending RNA sequencing and cell-free RNA data may assist in explaining these observed phenomena.

IS-WS-4-6

Critical role of innate immunity in chorioamnionitis-

independent preterm birth Kato Masahiko¹, Negishi Yasuyuki^{1,2}, Watanabe Asako¹ *Nippon Medical School¹, Department of Microbiology and Immunology, Nippon Medical School²* **[Objective]** Chorioamnionitis is a significant factor contributing to preterm birth (PB). However, many cases of PB occur in the absence of chorioamnionitis, possibly due to sterile inflammation. This study conducted immunological analysis on decidua without chorioamnionitis using flow cytometry. **[Methods]** Decidua samples were collected from patients who experienced PB at a gestational age of 24^{wo} to 33^{wo} weeks without pathological chorioamnionitis. The patients were categorized into two groups : those who experienced labor with or without rupture of the membrane (n-CAM-w-LR) and those who did not (n-CAM-w/o-LR). Immune cells from the patients' decidua were isolated from after delivery, and analyzed for accumulation of immune cells, surface marker expression, and the intracytoplasmic levels of HMGB1. Furthermore, we conducted co-culture experiments with immune cells from the decidua and recombinant HMGB1. **[Results]** The accumulation of iNKT cells was significantly higher in the decidua of the n-chorioamnionitis-w-LR group compared to the n-CAM-w/o-LR group. Additionally, increased expressions of toll-like receptor 4, receptor for advanced glycation end products, and CD1d on antigen-presenting cells (APCs) were observed in the n-CAM-w-LR group. The concentrations of HMGB1 in immune and nonimmune cells were elevated in the n-CAM-w-LR group. In the co-culture study, the addition of HMGB1 enhanced the proliferation of iNKT cells. **[Conclusion]** This study revealed distinct dynamics of innate immune cells, particularly in iNKT cells and APCs, in cases of PB without chorioamnionitis. Excessive activation of innate immunity triggered by HMGB1 may play a crucial role in sterile inflammation leading to PB.

IS-WS-4-7

Vaginal microbiota in pregnancy after radical trachelectomy Hasegawa Keita^{1,2}, Kasuga Yoshifumi^{1,2}, Fukuma Yuka¹, Tamai Junko¹, Tanaka Yuya¹, Otani Toshimitsu¹, Ikenoue Satoru¹, Nakabayashi Kazuhiko², Hata Kenichiro^{2,3}, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Department of Maternal-Fetal Biology, National Center for Child Health and Development², Department of Human Molecular Genetics, Gunma University³*

[Objective] Due to the wide resection of the cervix during radical trachelectomy (RT), the vaginal microbiota (VM) may undergo alterations, potentially increasing the risk of preterm delivery in pregnancies after RT. However, there is limited data on the VM during pregnancy after RT. Therefore, we aimed to investigate the VM in pregnancies after RT. **[Methods]** We enrolled pregnant women who had undergone RT (RT group : n =25) and those who had not undergone RT or cervical conization (control group : n=100) and received perinatal care at our hospital between June 2019 and July 2023. Vaginal discharge samples were collected during the first, second, and third trimesters and subjected to microbial analysis by sequencing the V1-V2 region of the 16S ribosomal RNA gene. The α -diversity was calculated using the Friedman rank sum test. **[Results]** Throughout all trimesters, no differences in the incidence of *Lactobacillus* spp. were observed between the two groups. Compared with the control group, the RT group exhibited higher incidences of *Streptococcus* spp., *Enterococcus* spp., and *Prevotella* spp. in the first trimester ; *Prevotella* spp. and *Dialister* spp. in the second trimester ; and *Streptococcus* spp., *Aerococcus* spp., *Prevotella* spp., *Dialister* spp., and *Mycoplasma* spp. in the third trimester. Furthermore, the α -diversity analysis revealed alterations in the VM in the control group but not in the RT group. **[Conclusion]** The VM in the RT group differed from that in the control group. Moreover, the invariance of the VM during

pregnancy after RT could be one of the main causes of preterm delivery.

IS-WS-4-8

A new electrophysiological parameter to predict preterm birth Komatsu Reina¹, Nakamura Hitomi¹, Hosono Takayoshi², Mimura Kazuya¹, Endo Masayuki¹, Kimura Tadashi¹ *Osaka University¹, Biomedical Engineering, Osaka Electro-Communication University²*

[Objective] We focused on local electrophysiological parameters to develop a new parameter with high positive prediction value to predict pre-term labor. The measurements of in-vivo local vaginal bioelectrical impedance (VZ) were assessed using two different types of mouse models of preterm birth. **[Methods]** The transvaginal probe was developed to measure VZ in mice using body composition analyser (MLT-550N, SK Medical Electronics Co. Ltd.). The preterm birth was induced in ICR mice by subcutaneous injection of mifepristone (150 mg) or local intrauterine injection of lipopolysaccharide (LPS) from *Escherichia coli* 0111 : B4 (2 mg or 20 mg). Uterine tissues with vagina including foetuses and placentae were removed 6 hours after the administration of LPS or vehicle, and were histologically assessed. **[Results]** The preterm rates were 100% and 60% after mifepristone (16-20 hrs) and LPS (12-24 hrs) respectively. The measurement value of VZ (at 15 or 10 hrs after mifepristone or LPS treatment respectively) in the group showed preterm birth was significantly lower than in the non-preterm group. Receiver operator characteristic (ROC) curve analysis of VZ as a predictor of preterm birth showed an area under the ROC curve (AUC) of 1.00 and 0.77, respectively. The alteration of sulfation and sialylation of glycoalyx were observed in the spongiotrophoblast and cervix in the LPS group. **[Conclusion]** VZ can determine the alteration of sulfation and sialylation of glycoalyx in the uterus and it might be a useful parameter for predicting preterm birth.

IS-WS-4-9

Verifying the causal relationship of abnormal gut microbiota in spontaneous preterm birth using a mouse model Uchida Azusa¹, Imai Kenji¹, Miki Rika^{2,3}, Aoki Chieko³, Matsuo Seiko^{1,2}, Tano Sho¹, Ushida Takafumi¹, Kotani Tomomi¹, Kajiyama Hiroaki¹ *Nagoya University¹, Laboratory of Bell Research Center², Handa Hospital³, Research & Development Division, Kishokai Medical Corporation⁴*

[Objective] Gut microbiota regulates host immunity via short-chain fatty acid (SCFA) synthesis. Associations have been observed between gut microbiota of pregnant women and preterm birth (PTB), yet causality remains unverified. Thus, we established a mouse model to investigate this causal relationship. **[Methods]** Pregnant mice received non-absorbable antibiotics, categorized into Control (C), Polymyxin-B (P), and Vancomycin (V) groups. On embryonic day 16, anti-CD3 was administered intraperitoneally to compare PTB rates. 16S rRNA and SCFA-concentration analysis (LC-MS) were performed on fecal samples. Flow cytometry (CD8, Treg) with maternal spleen and Multiplex assay with maternal serum was performed. **[Results]** The PTB rates were C : 9.1% (1/11), P : 0.0% (0/11), and V : 56.3% (9/16), significantly increased in V group. In 16S rRNA analysis, V group showed gut microbiota depletion compared to C and P groups, specifically a decreased diversity and occupancy of bacteria, including SCFA-producing bacteria (ex. *Lachnospiraceae*). Fecal SCFA concentrations (butyrate, acetate, propionate) significantly decreased in V group (vs C ; $p < 0.01$, vs P ; $p < 0.05$). Moreover, V group showed significant decreases in regulatory T cells (Treg) and Treg/CD8 ratios, and cytokine concentrations (ex. TNF- α , CCL2) were significantly

increased after anti-CD3 administration. **[Conclusion]** Our results demonstrated that gut microbiota depletion and reduction of SCFA-producing bacteria induce maternal inflammation, potentially leading to PTB. This is the first report of causal relationship between gut microbiota and spontaneous PTB, suggesting the importance of maintaining a healthy gut microbiota in preventing and treating PTB.

IS-WS-5-1

Effectiveness and risks of hysteroscopic metroplasty for uterine septum ; Observational research Nakao Kimihiko¹, Okuda Naofumi¹, Shiraishi Tatsunori¹, Ichikawa Masao¹, Shuichi Ono², Takeshita Toshiyuki³, Suzuki Shunji¹ *Nippon Medical School¹, Surugadai Ladies Clinic², Takeshita Ladies Clinic³*

[Objective] We conducted a retrospective study on the effectiveness and complications of hysteroscopic metroplasty for uterine septum in our hospital. **[Methods]** We extracted 141 cases from January 2011 to April 2022 by reviewing electronic medical records. One hundred seventeen cases (87 with recurrent pregnancy loss (RPL) and 30 with infertility) were available for follow-up at least 1 year after surgery. **[Results]** 70.1% of patients with RPL delivered and the miscarriage rate was 14.9% in the first pregnancies after surgery. Using the McNemar test, the live birth rate significantly improved post-surgery ($p < 0.0001$). The cumulative live birth rate was 84.9%. Logistic regression analysis including age, treatment for thrombotic predisposition, and residual septum as covariates showed that age had a significant negative impact. Although not statistically significant, aspirin treatment and longer residual septal length showed negative tendencies. Of the 30 infertile cases, 76.7% became pregnant after surgery. The live birth rate in the first pregnancy was 56.7%, the miscarriage rate was 20%, and the cumulative birth rate was 66.7%. Perioperative complications included reoperation for residual septum in 4.1% and anemia due to vaginal bleeding in 1 case. There was no uterine perforation or water intoxication. Among 42 cases surveyed for perinatal complications, there were 7 cases of breech presentation, 4 cases of hypertensive disorders of pregnancy (HDP), and 10 cases of postpartum hemorrhage (>1000 mL). **[Conclusion]** Although this study was a case series study, the treatment outcome was considered favorable, similar to previous reports. The risk of postpartum hemorrhage should be elucidated.

IS-WS-5-2

Factors influencing cumulative recurrence rate and pregnancy rate after laparoscopic cystectomy for endometriomas : a single-center retrospective study Yanagihara Yasuho¹, Ozaki Rie², Takeuchi Shiori¹, Kobayashi Mutsumi¹, Ochiai Asako¹, Kawasaki Yu¹, Okada Yukiko¹, Murakami Keisuke¹, Kawamura Kazuhiro¹, Kitade Mari¹, Itakura Atsuo¹ *Juntendo University¹, Tobu Chiiki Hospital²*

[Objective] Laparoscopic cystectomy (LC) for endometriotic ovarian cysts (EMC) requires both preservation of ovarian function to achieve postoperative pregnancy and radical cure to reduce postoperative recurrence rate. The aim of the study was to assess the cumulative recurrence rate and cumulative pregnancy rate after LC for EMC and to examine the factors affecting each rate. **[Methods]** This study retrospectively analyzed 383 patients who underwent LC for EMC from 2012 to 2018. Multivariate logistic regression analysis was used to identify the risk factors for each rate. **[Results]** The mean age of all 383 patients was 33.1 ± 6.2 years, and the mean postoperative observation period was 25.8 ± 19.9 months. The cumulative recurrence rate was 6.4, 10.7, and 20.6% at 6, 12, and 24 months postoperatively, respectively. Significant factors associated with recurrence were postoperative pregnancy (Hazard ratio : HR 0.4,

$p=0.02$), postoperative hormone therapy (HR 0.28, $p=0.002$), rASRMscore > 60 points (Hazard ratio : HR 1.79, $p=0.02$). The cumulative pregnancy rates at 6, 12, and 24 months after surgery were 20.9, 41.4, and 61.1% in the 154 patients (40.3%) who had the desire to present at the time of surgery. Two factors were significantly involved in the cumulative pregnancy rate : presence of postoperative lesion recurrence (HR 0.32, $p=0.001$) and age >35 years (HR 0.86, $p=0.04$). [**Conclusion**] Our data indicated that both postoperative pregnancy and recurrence can be affected each other in LC for EMC. In cases with a desire to achieve pregnancy, aggressive intervention should be considered before recurrence including associated reproductive technology.

IS-WS-5-3

Effective treatments for recurrent pregnancy loss with anti-beta2-glycoprotein I/HLA-DR antibody Tanimura Kenji¹, Deguchi Masashi¹, Saito Shigeru², Tsuda Sayaka², Nagamatsu Takeshi^{3,4}, Fujii Tomoyuki^{3,4,5}, Nakatsuka Mikiya⁶, Kobashi Gen⁷, Arase Hisashi⁸, Yamada Hideto^{1,9} *Kobe University¹, University of Toyama², The University of Tokyo³, IUHW Narita Hospital⁴, Sanno Hospital⁵, Faculty of Health Sciences, Okayama University⁶, Department of Public Health, Dokkyo Medical University⁷, Department of Immunochemistry, Research Institute for Microbial Disease, Osaka University⁸, Center for Recurrent Pregnancy Loss, Teine Keijinkai Hospital⁹*

[**Objective**] It has been discovered that anti- β 2-glycoprotein I/HLA-DR antibody (a β 2GPI/HLA-DR), a neo-self antibody, is a major risk factor for recurrent pregnancy loss (RPL). However, the efficacy of treatments for RPL women with a β 2GPI/HLA-DR-positive test (≥ 73.3 U) have not been evaluated. This prospective, multicenter, observational study aimed to assess whether low-dose aspirin (LDA) or LDA plus heparin (L+H) treatments are effective in improving pregnancy outcomes in a β 2GPI/HLA-DR-positive RPL women. [**Methods**] From August 2019 to August 2023, forty-nine a β 2GPI/HLA-DR-positive RPL women experienced 50 pregnancies. Each attending physician decided treatment modality for these pregnancies. One pregnancy ending in intrauterine fetal death due to chorioamnionitis and 2 ending in miscarriages related to chromosomal abnormalities were excluded. The live-birth rates were compared between a β 2GPI/HLA-DR-positive RPL women treated with LDA or L+H and those without LDA or L+H. [**Results**] Forty-seven pregnancies from the 47 RPL women with a β 2GPI/HLA-DR-positive test were evaluated in the final analysis. All 13 women treated with LDA gave live births, while 21 (80.8%) of 26 women treated with L+H gave live births. On the other hand, 4 (50%) of 8 women treated without LDA or L+H (6 with no treatment, and 2 with steroid) gave live births. The live-birth rates in RPL women with a β 2GPI/HLA-DR-positive test treated with LDA or L+H were significantly higher than those without LDA or L+H (87.2% vs. 50.0%, $p = 0.03$). [**Conclusion**] This study for the first time demonstrated that treatments with LDA or L+H are effective in improving pregnancy outcomes in RPL women with a β 2GPI/HLA-DR-positive test.

IS-WS-5-4

Association between the glucose target range in continuous glucose monitoring and risk of hypertensive disorders of pregnancy and neonatal complications in pregnancies with type 1 diabetes Imafuku Hitomi, Tanimura Kenji, Masuko Naohisa, Uchida Akiko, Takahashi Ryosuke, Deguchi Masashi, Terai Yoshito *Kobe University*

[**Objective**] The aim of this retrospective cohort study was to assess association between the glucose target range in continuous glucose monitoring (CGM) and risk of hypertensive disorders

of pregnancy (HDP) and neonatal complications in pregnancies with type 1 diabetes mellitus (T1DM). [**Methods**] Twenty-eight pregnant women with T1DM using CGM managed at our hospital from January 2015 to August 2023 were included. The time in range (TIR) and time above range (TAR) were calculated by sensor glucose levels of CGM. The associations between the target range (63-140 mg/dL) and risk of HDP and neonatal complications, including large for gestational age (LGA), neonatal hypoglycemia, polycythemia, and hyperbilirubinemia were analyzed by logistic regression. [**Results**] A lower TIR throughout pregnancy (the first trimester odds ratio [OR] 0.93, 95% confidence interval [CI] 0.87-0.99 ; the second trimester OR 0.86, 95%CI 0.76-0.98 ; the third trimester OR 0.71, 95%CI 0.54-0.95), and a higher TAR in the first (OR 1.07, 95%CI 1.00-1.13) and second trimester (OR 1.14, 95%CI 1.02-1.28) were associated with a risk of HDP. A lower TIR in the second (OR 0.91, 95%CI 0.83-0.99) and third trimester (OR 0.84, 95%CI 0.74-0.96), and a higher TAR in the second (OR 1.08, 95%CI 1.00-1.16) and third trimester (OR 1.16, 95%CI 1.04-1.29) were associated with a risk of LGA. There was no association between the target range and other neonatal complications. [**Conclusion**] To prevent HDP and LGA in pregnancies with T1DM, sensor glucose levels should be controlled to achieve high TIR and low TAR from the first trimester.

IS-WS-5-5

Survey on the reproductive outcomes of oocyte and ovarian tissue cryopreservation in Japan Takae Seido¹, Harada Miyuki², Nakamura Kentaro¹, Ono Masanori³, Osuga Yutaka², Suzuki Nao¹ *St. Marianna University School of Medicine¹, The University of Tokyo², Tokyo Medical University³*

[**Objective**] Fertility preservation (FP) is spreading in Japan, as in Western countries, but reproductive outcomes have not yet been clarified. [**Methods**] Under the IRB approval, we conducted a mailed-in questionnaire survey at institutions certified by the JSOG to investigate the number of oocyte cryopreservations (OC) and ovarian tissue cryopreservations (OTC) performed from December 2016 to the end of 2020. In addition, we conducted a detailed investigation of cases in which frozen specimens were used during the investigation period, and made historical comparisons and verifications versus the results of previous nationwide studies. [**Results**] Responses were received from 114 out of 150 facilities (response rate : 76.0%). Breast cancer was the most common reason for both OC and OTC, followed by blood cancer. During the study period, 1237 OCs and 198 OTCs were performed. In addition, 54 cycles of embryo transfer (ET) using cryopreserved oocytes and 12 cases of ovarian tissue transplantation (OTT) were performed. The mean age of patients who underwent ET using cryopreserved oocytes was 34.8 (± 5.8) years, with a median age of 36 years. The pregnancy rate per ET using cryopreserved oocytes was 26.3% and the live birth rate (LBR) was 17.5%. Further, the LBR per patient was 43.3%, and the pregnancy rate following OTTs was 33.3%. Furthermore, controlled ovarian stimulation using the random start method or the combination of aromatase inhibitors had no effect on pregnancy outcome. [**Conclusion**] Performance of both OCs and OTCs have markedly increased over time in Japan, with comparable reproductive outcomes as other reports.

IS-WS-5-6

Current Status of and Issues with Fertility Preservation in Oncofertility Therapy Suzuki Reiko, Horage Yuki, Iwahata Hideyuki, Ito Kaoru, Nakamura Kentaro, Suzuki Yuki, Sugishita Yodo, Takae Seido, Suzuki Nao *St. Marianna University School of Medicine*

[**Objective**] To analyze the current status of cancer patients

who preserved fertility at our hospital and clarify the effectiveness of each fertility preservation method. **[Methods]** A retrospective study of 1457 patients who visited the oncofertility outpatient clinic from 2010 to 2022. **[Results]** Out of 1457 cancer patients, 1207 (906 women, 186 men, and 115 children) wanted to preserve fertility, and their fertility preservation success rates were 49.1%, 92.4%, and 60.0%, respectively. Three methods of fertility preservation were studied in women - cryopreservation of embryos (196), oocytes (131), and ovarian tissues (99) - and their utilization rates after cancer treatment were 35.7%, 4.6%, and 8.2%, respectively. The utilization rate of sperm cryopreservation in men after cancer treatment was 7.0%. The frozen-thawed embryo transfer was performed in 75 cases, with the pregnancy rate per cycle observed at 29.7% (44/148 cycles), the pregnancy rate per patient at 52.0% (39/75), and the live birth rate at 37.3% (28/75). Ovarian tissue transplantation was performed in 14 cases, followed by improved menstrual cycle regularities and increased retrieval of oocytes upon controlled ovarian stimulation. The pregnancy rate per patient was 40.0% (6/15), and the live birth rate was 20.0% (3/15). **[Conclusion]** Herein, we report the outcome of fertility preservation, up to live birth rate, from the utilized frozen-thawed embryo and frozen-thawed ovarian tissue in cancer patients at our hospital. Long-term follow-up studies are necessary to verify the effectiveness of fertility preservation and assure that fertility preservation would not affect cancer recurrence and prognosis.

IS-WS-6-1

Accumulation of plasma cells were in the decidua in patients with adenomyosis : possible association with obstetrical complications Nakajima Marie¹, Koga Kaori², Mohammed Elsherbinielshal¹, Makabe Tomoko¹, Izumi Gentaro¹, Kumasawa Keiichi¹, Iriyama Takayuki¹, Harada Miyuki¹, Hirata Tetsuya¹, Hirota Yasushi¹, Hiraike Osamu¹, Osuga Yutaka¹ *The University of Tokyo Hospital¹, Chiba University Hospital², St. Luke's International Hospital³*

[Objective] Adenomyosis is associated with a risk of a variety of obstetrical complications, including preeclampsia. Chronic deciduitis (CD) is slight inflammation of the decidua found during pregnancy, and recently reported to be associated with preeclampsia. We hypothesized that adenomyosis causes CD, which leads to these disorders. To test this hypothesis, we focused on plasma cells in the decidua and their association with adenomyosis. **[Methods]** A total of 43 patients : 15 with adenomyosis and 28 without adenomyosis matched for maternal and gestational age (the control) were included in this study. The placenta was obtained at cesarean section. All cases were before the onset of labor, and those with inflammatory diseases or endometriosis were excluded. Plasma cells were detected using immunohistochemistry of CD138. The frequency of plasma cells in both decidua basalis and perietalis was compared between patients with adenomyosis and controls. Statistical analysis was performed using the Mann-Whitney test. **[Results]** In the decidua basalis, the frequency of plasma cells in the adenomyosis group was significantly higher (1.66, 0.91 -6.34 (/mm², median, first- third quartile)) than that of controls (0.05, 0-0.34, $p < 0.001$). Similarly, in the decidua perietalis, the frequency of plasma cells in the adenomyosis group (0.53, 0.13-1.28/mm²) was significantly higher than that of controls (0.01, 0-0.11/mm², $p < 0.001$). **[Conclusion]** Our study suggested that patients with adenomyosis are more likely to develop CD, and this may lead to obstetrical complications. Further studies are currently underway to elucidate the mechanism by which adenomyosis causes CD.

IS-WS-6-2

Ferroptosis in Gravid Uterus and Placenta of PCOS-like Rats with Hyperandrogenism and Insulin Resistance : Modulation and Suppression Zhang Yuehui^{1,2}, Hu Min^{2,3,4}, Billig Håkan², Shao Linus R² *Key Laboratory and Unit of Infertility in Chinese Medicine, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, China¹, Department of Physiology and Endocrinology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Sweden², Department of Traditional Chinese Medicine, The First Affiliated Hospital of Guangzhou Medical University, China³, Institute of Integrated Traditional Chinese Medicine and Western Medicine, Guangzhou Medical University, China⁴*

[Objective] 1) To determine the correlation between gravid uterine and placental ferroptosis and maternal hyperandrogenism (HA) -insulin resistance (IR) -induced fetal loss in rats.2) To investigate the efficacy and molecular mechanism of action of the antioxidant N-acetylcysteine (NAC) in reversing gravid uterine and placental ferroptosis in pregnant rats exposed to 5 α -dihydrotestosterone (DHT) and insulin (INS). **[Methods]** DHT and INS were used to create HA-IR phenotype ; quantitative real-time PCR (qPCR), Western blot analyses, glutathione peroxidase 4 (GPX4) immunostaining, Perls' histochemical reaction, assessment of mitochondrial morphology, measurement of glutathione (GSH) and malondialdehyde (MDA), etc. were used to confirm our hypothesis and clarify the related mechanisms of NAC. **[Results]** 1) Maternal exposure to DHT and INS in rats led to changes in the expression of ferroptosis related biomarkers and abnormalities in mitochondrial morphology - especially in uterine tissue, and deregulation of reactive oxygen species (ROS) production.2) NAC could attenuate ferroptosis in uterine and placenta mainly by increasing anti-ferroptosis gene content and GPX4 protein levels, respectively, and partially reverse mitochondria-morphological abnormalities in the placenta.3) NAC could selectively normalized some cytokine levels (such as uterine leukemia inhibitory factor, placental estrogen-related receptor beta) and mRNA expressions (such as homeobox A11, trophoblast-specific protein alpha). **[Conclusion]** 1) Maternal exposure to DHT and INS in rats could trigger GPX4-GSH-linked lipid peroxidation and iron-associated and mitochondria-mediated ferroptosis in the gravid uterus and placenta via different cellular and molecular mechanisms, resulting in oxidative stress-induced pregnancy loss 2) NAC could serve as a potential therapeutic strategy for HA-IR induced uterine-placental dysfunction.

IS-WS-6-3

Nuclear F-actin formation regulates decidualization of human endometrial stromal cells Tamura Isao, Yoneda Toshihide, Takasaki Hitomi, Shiroshita Amon, Fujimura Taishi, Shirafuta Yuichiro, Sugino Norihiro *Yamaguchi University Graduate School of Medicine*

[Objective] Decidualization is a differentiation process of human endometrial stromal cells (ESCs) that is responsible for establishing pregnancy. During decidualization, the actin cytoskeleton is reorganized for the ESCs' morphological and functional changes. Recent reports indicated that actin also exists in the nucleus of some types of cells and forms a polymerized filamentous state (F-actin) upon external stimuli, which regulates gene transcription. This study investigated the nuclear actin dynamics and its role in decidualization of human ESCs. **[Methods]** For visualizing nuclear actin dynamics, ESCs expressing nuclear actin-GFP probe were established. Cells were treated with cAMP to induce decidualization. Nuclear F-actin formation was inhibited by overexpressing the nuclear actin mutant. The transcriptome was analyzed by RNA-sequence. Upstream analy-

sis was performed to identify factors regulating nuclear F-actin formation. *C/EBP β* was knocked down by siRNA. **[Results]** Time-lapse imaging revealed a dynamic formation of nuclear F-actin during decidualization. RNA-sequence analyses revealed that the forced suppression of nuclear F-actin resulted in the suppression of decidualization markers (IGFBP-1 and PRL), accompanied by the abnormal upregulation of cell proliferation genes, leading to incomplete cell cycle arrest. *C/EBP β* , an important regulator for decidualization, was identified as the most significant upstream factor, regulating nuclear F-actin formation. Knockdown of *C/EBP β* suppressed nuclear F-actin formation, cell cycle arrest, and expression of decidualization markers. **[Conclusion]** We revealed that actin exists in the nucleus of human ESCs and nuclear F-actin formation is induced by *C/EBP β* during decidualization. This induces cell cycle arrest to differentiate into decidualized ESCs, which is a novel mechanism for the regulation of decidualization.

IS-WS-6-4

Effects of the prenatal and postnatal early-life environment on the phenotype and gut microbiome of PCOS model mice induced by prenatal androgen exposure: a cross-fostering study Kusamoto Akari, Harada Miyuki, Sakaguchi Nanoka, Koike Hiroshi, Jo Koshin, Tanaka Tsurugi, Urata Yoko, Kunitomi Chisato, Hiraie Osamu, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*

[Objective] Prenatal androgen exposure is critical for the development of polycystic ovary syndrome (PCOS), and the gut microbiome is implicated in the pathogenesis of PCOS. Our recent study revealed that abnormalities in the gut microbiome is already apparent before puberty, followed by the manifestation of PCOS-like phenotypes in PCOS model mice induced by prenatal androgen exposure, suggesting that the gut microbiome in early life represents a potential target for the prevention of PCOS. This study aimed to clarify whether the prenatal or postnatal early-life environment primarily contributes to the change of gut microbiome in early life and the development of PCOS in later life. **[Methods]** A cross-fostering model was used in prenatally androgenized (PNA) offspring. Reproductive and metabolic phenotypes of PCOS and temporal alterations in the gut microbiome were evaluated. **[Results]** Female PNA offspring fostered by control mothers (exposed to an abnormal prenatal environment only, fostered PNA) exhibited less marked PCOS-like phenotypes than PNA offspring, especially with respect to the metabolic phenotype. The gut microbiome of the fostered PNA offspring was similar to that of controls before adolescence, however differences between the fostered PNA and control groups became apparent after young adulthood. Both prenatal androgen exposure itself and the postnatal early-life environment contributed to the development of PCOS and the alterations in the gut microbiome in PNA offspring. **[Conclusion]** Our findings indicate that both pregnant mothers with PCOS and their PNA offspring in early-life could represent targets for the prevention of PCOS.

IS-WS-6-5

Trehalose relieves oxidative stress in ovarian granulosa cells via the downregulation of Rubicon, an autophagy-negative regulator Yamada Kiyotaka, Nunomura Haruka, Furuta Atsushi, Yoshida Mihoko, Ito Masami, Shima Tomoko, Yoneda Satoshi, Nakashima Akitoshi *Toyama University*

[Objective] Granulosa cells play an important role in oocyte growth. Oxidative stress (OS), which causes ovarian functional declines, is believed to increase in ovaries with aging. Autophagy (AtP), whose activity declines with aging, maintains intracellular homeostasis against multiple biological stresses. Tre-

halose (THL), a preservative reagent, activates AtP. Here, we examined the role of THL against OS in granulosa cells via AtP. **[Methods]** All experiments were performed in the human non-leuteinized granulosa cell line, HGrC1. Cell viability was evaluated by WST-1 assay. H2O2 was for OS induction. Tat-Beclin1 (T-B1) was an AtP activator. **[Results]** Cell viability was decreased by H2O2 treatment in a dose-dependent manner. Three types of AtP inhibitors enhanced the H2O2-mediated cytotoxicity; while THL treatment improved the inhibited viability by 55%. We first confirmed THL activated AtP, but THL increased more AtP activity than T-B1 or other reagents. Further examinations newly discovered the downregulation of Rubicon, an autophagy-negative regulator, by THL. It was unknown whether increased AtP activity or declined Rubicon contributed to OS resistance. The downregulation of Rubicon by siRNA improved the H2O2-inhibited cell viability: sole T-B1 treatment also improved the viability, suggesting a synergistic effect of THL. Finally, we confirmed THL analogs had similar effects against OS in HGrC1 cells. **[Conclusion]** THL enhanced OS resistance via activating AtP in granulosa cells. The possible mechanism is to upregulate AtP activity and to downregulate the negative regulator. Rub is reported to increase with aging in some organs of mice. Therefore, THL or analogs could relieve OS in aged ovaries via declining Rubicon.

IS-WS-6-6

CPEB1-dependent disruption of the mRNA translation program in oocytes during maternal aging Takahashi Nozomi^{1,2}, Harada Miyuki¹, Hiraie Osamu¹, Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, University of California, San Francisco, USA²*

[Objective] The molecular causes of deteriorating oocyte quality during aging are poorly defined. Since oocyte developmental competence relies on posttranscriptional regulations, we tested whether defective mRNA translation contributes to the decline in oocyte quality. **[Methods]** RiboTag IP/RNA-Seq were used to measure translation in oocytes from young and old female mice. Using candidate approach, translation was measured by 3'-untranslated region (3'-UTR) YFP reporter assay. To test if haploinsufficiency of cytoplasmic polyadenylation element binding protein 1 (CPEB1) recapitulates the phenotypes associated with oocyte aging, we used oocyte-specific conditional CPEB1 heterozygous (*Cpeb1fl/+; Zp3-Cre*) mice. **[Results]** Using RiboTag IP/RNA-Seq, ribosome loading was altered for 292 mRNAs in old oocytes compared with young oocytes. This defect in translation was confirmed by reporter accumulation driven by the 3'-UTR and altered endogenous poly (A) length. A major regulator of maternal mRNA polyadenylation is CPEB1. Translation of *Cpeb1* mRNA and protein expression are decreased in old oocytes. Decreased CPEB1 level in old oocytes causes precocious activation of Cyclin-dependent kinase 1 (CDK1), and accelerated meiosis reentry. The translation of *Ccnb1*, the regulatory subunit of CDK1, was prematurely activated in quiescent oocytes and its activation was defective in maturing oocytes, suggesting a disruption of the complex driving the meiotic cell cycle. Defective translation of *Ccnb1* is corrected by *Cpeb1* mRNA injection in old oocytes. Oocyte-specific CPEB1 haploinsufficiency in young oocytes recapitulates all the translation phenotypes of old oocytes and decreased fertility. **[Conclusion]** A dysfunction in the oocyte translation program is associated with the decline in oocyte quality during aging.

IS-WS-6-7

Overdue calcium oscillation causes polyspermy but permits normal development in mouse eggs Fukuoka Mio^{1,2}, Yamada Mitsutoshi¹, Kimura Hiroko^{1,2}, Miyado Kenji², Yamagami

Wataru¹, Tanaka Mamoru¹ *Keio University¹, National Center for Child Health and Development²*

[Objective] Fusion of one egg and multiple sperm (polyspermy) induces a robust rise of intracellular calcium ion (Ca^{2+}) concentration in some of non-mammalian eggs. A sperm-derived, dose-dependent Ca^{2+} ion inducer is expected to be required for fertilization. We focused on the extra-mitochondrial citrate synthase (eCS), which has high similarity to mitochondrial citrate synthase (CS) and investigated the role of eCS in male fertility. **[Methods]** eCs-deficient (eCs-KO) mice was produced using C57BL/6J mice. Mitochondria and nuclei were stained with 500 nM MitoTracker Red CMXRos and DAPI, respectively. Eggs were preloaded with the Ca^{2+} sensitive fluorescent dye, Oregon green 488 BAPTA-1 AM, whose fluorescence intensity was measured to calculate the amplitude, interval, frequency, and timing of the first spike, after insemination with sperm. **[Results]** eCS was limitedly localized in the sperm head. The eCS deficiency enhanced polyspermy in both zona pellucida (ZP)-free and ZP-intact eggs. The initiation of the first spike of Ca^{2+} oscillation was substantially delayed in the egg fused with eCs-KO sperm, whereas the elevated sperm concentration normalized Ca^{2+} oscillation initiation. There was no difference both in the blastocyst development rate and litter size between eCS-KO sperm-fertilized eggs and wild-type sperm-fertilized eggs. **[Conclusion]** Our results suggest that eCS contribute to Ca^{2+} oscillation in the mouse eggs, more specifically to the induction of the first Ca^{2+} level increase. eCS deficiency may induce polyspermy to compensate for egg activation failure.

IS-WS-6-8

MicroRNAs derived from fertilized embryos in culture medium may contribute as biomarkers for embryo quality and pregnancy outcomes Shigematsu Yusuke, Nagata Koh, Eishi Chiaki, Kajimura Itsuki, Nagata Ai, Kitajima Yuriko, Hasegawa Yuri, Miura Syouko, Kitajima Michio, Miura Kiyonori *Nagasaki University*

[Objective] Conventionally, morphological classification, e.g. Gardner classification, has performed for selecting better embryo for implantation, but they do not always accurately predict pregnancy outcome. More reliable predictive biomarkers are needed. Recently, it has been reported that microRNAs are detected in embryo culture medium, so we analyzed them to evaluate the character of the fertilized embryo. The objective of this study is to identify microRNAs as molecular biomarkers in the culture medium for selecting the best embryo. **[Methods]** Embryo culture mediums were collected from 122 patients who underwent in vitro fertilization at our hospital in the study. We analyzed and isolated the expression levels of C19MC (Chromosome 19 miRNA cluster) as placental specific microRNA, and C14MC as fetal specific microRNA by relative quantification using RT-qPCR. We compared the variety of microRNA with the pregnancy outcomes. **[Results]** Among 122 cases analyzed, 49 cases were pregnant and 73 cases were non-pregnant. The expression levels of miR-517a, miR-517c and miR-518b among C19MC and miR-433 among C14MC were significantly higher in the non-pregnant group than in the pregnant group. In the case that the grade of trophoblast along Gardner classification is Grade B or more, median value of miR-517a level was significantly lower in the pregnant group than in non-pregnant group (32404 vs 159223, $p < 0.0001$, t-test). **[Conclusion]** Elevated microRNAs that may be leaking from embryos into culture medium suggest that the embryo is not optimal for pregnancy. These microRNAs have the potential as an objective, non-invasive biomarker for assessing the function of fertilized embryos.

IS-WS-6-9

Role and correlations of PROK1, MMP-2 and MMP-9 in plasma of patients with HDP Nonobe Megumi^{1,2}, Goto Shinobu², Kitaori Tamao², Ozawa Fumiko³, Nishikawa Naomi¹, Arakawa Atsushi¹, Ozaki Yasuhiko^{1,2}, Sugiura Mayumi² *Nagoya City University West Medical Center¹, Nagoya City University Graduate School of Medical Science², Research Center for Recurrent Pregnancy Loss, Nagoya City University Graduate School of Medical Science³*

[Objective] Prokineticin1 (PROK1) is an angiogenic factor that is regulated by hypoxia and insulin. PROK1 is produced by decidua and villi, and plays a crucial role in maintenance of pregnancy. Hypertensive Disorders of Pregnancy (HDP) is one of major pregnancy complication which leads to placental insufficiency. PROK1 has been reported to decrease MMP-2 and MMP-9 activity in placenta. In this study, we investigated a role of PROK1, MMP-2 and MMP-9 in the pathogenesis of HDP. **[Methods]** 20 patients of HDP and 17 healthy pregnant women with no complications were included. Blood plasma samples were collected between 10 to 12 weeks of gestation. Clinical outcome of patients was collected from medical record retrospectively. The expression levels of PROK1, MMP-2 and MMP-9 in plasma were measured by ELISA and compared between each group. All samples were collected with informed consent under the approval of the university ethical committee. **[Results]** MMP-2, MMP-9 and MMP-9/PROK1 ratio were not significantly different between groups, but PROK1 was significantly lower [16.7 ± 21.5 (mean \pm SD) ng/ml vs 38.5 ± 53.1 , $p < 0.05$] and MMP-2/PROK1 ratio was significantly higher [20.9 ± 12.8 (mean \pm SD) vs 11.9 ± 7.4 , $p < 0.05$] in patients of HDP than in controls. **[Conclusion]** These findings suggest that decrease of PROK1 level and increased MMP-2/PROK1 ratio during early pregnancy may contribute to the pathogenesis and be a predictive value of HDP.

IS-WS-7-1

Investigation of NK cell immune microenvironment in choriocarcinoma Shibata Mayu¹, Niimi Kaoru¹, Hattori Satomi^{1,3}, Imagawa Takuya¹, Yasui Yuko¹, Nishiko Yuki¹, Oda Yukari¹, Yoshida Kosuke¹, Nishino Kimihiro², Yamamoto Eiko², Kajiyama Hiroaki¹ *Nagoya University Graduate School of Medicine¹, Healthcare Administration, Nagoya University Graduate School of Medicine², Kasugai Municipal Hospital³*

[Objective] The importance of the tumor immune microenvironment has been discussed, but it is still unclear in choriocarcinoma. In this study, we investigated the immune microenvironment focused on NK cells in choriocarcinoma. **[Methods]** Choriocarcinoma cell line (JAR) was co-cultured with IL-2 stimulated NK cells, which were collected from healthy adults. Then, JAR cells were isolated using flow cytometry, and total RNA was extracted to performed mRNA-seq. Moreover, loss-of-function analyses were performed for differentially expressed genes (DEGs) in NK cell-treated JAR cells. Furthermore, peripheral blood and intra-tumoral NK cells were isolated from six choriocarcinoma patients in our hospital, and the expression of receptors on NK cells was analyzed with flow cytometry. **[Results]** mRNA-seq showed that the gene expression profile of NK cell-treated JAR cells was different from that of untreated JAR cells. We focused on DEGs which were related to NK cell suppressor-type receptors and identified that the expression of HLA-E was upregulated approximately 2-fold in NK cell-treated JAR cells. Thus, to evaluate the role of HLA-E in NK-related immunity, the expression of HLA-E in JAR cells was downregulated using two siRNAs and co-cultured with NK cells. As a result, the downregulation of HLA-E significantly decreased the JAR cell viability ($p < 0.001$). The NK cell/T cell ratio in tumor lesions was significantly increased compared with that in pe-

ripheral blood ($p < 0.05$), and the expression of NKG2A and PD-1 on NK cells in tumor lesions was observed. **[Conclusion]** This study suggests that the HLA-E/NKG2A axis may be involved in the NK cell immune mechanism against choriocarcinoma.

IS-WS-7-2

Establishment of etoposide-resistant choriocarcinoma cell lines and their unique gene expression profile Yasui Yuko¹, Yoshida Kosuke¹, Niimi Kaoru¹, Imagawa Takuya¹, Nishiko Yuki¹, Shibata Mayu¹, Nishino Kimihiro², Yamamoto Eiko², Kajiyama Hiroaki¹ *Nagoya University¹, Department of Health-care Administration, Nagoya University²*

[Objective] Chemo-refractory choriocarcinoma is one of the clinical challenges. It is important to elucidate the underlying mechanisms of the resistance to chemotherapy for improving the prognosis of choriocarcinoma. In this study, focusing on etoposide, one of the key drugs for choriocarcinoma, we investigated the molecular characteristics of two etoposide-resistant choriocarcinoma cell lines. **[Methods]** Two choriocarcinoma-derived cell lines, JAR and JEG3, were used for analyses. The cells were cultured in an etoposide-containing medium with gradually increasing the concentration to establish etoposide-resistant cell line. Then, to identify factors involved in resistance, RNA sequencing was performed. **[Results]** We successfully established two etoposide-resistant choriocarcinoma cell lines. The IC50s for etoposide in the parental and etoposide-resistant JAR cells were 0.078 μM and 17.0 μM , respectively, with an approximately 1000-fold difference. Moreover, cross-resistance to CDDP and MTX was observed. The IC50s for CDDP in the parent and etoposide-resistant JAR cells were 0.43 μM and 1.5 μM , respectively, while those of MTX were 0.074 μM and 0.65 μM , respectively. In addition, similar tendencies were also observed in etoposide-resistant JEG-3 cells. RNA sequencing revealed that the expression of CDKN1A and PTK2 was upregulated in the etoposide-resistant JAR cells than the parental JAR cells. Furthermore, pathway analysis showed the potential mechanisms underlying the resistance. **[Conclusion]** Our results showed the successful establishment of etoposide-resistant cell lines with unique gene expression profiles. The resistant cell lines might lead to the development of novel therapeutic agents, and further experiments are essential to overcome the resistance.

IS-WS-7-3

Identification of Driver Mutations in the Development of Endometriosis-Related Ovarian Neoplasms Sohel Hasibul Islam, Nakayama Kentaro, Ishikawa Masako, Yamashita Hitomi, Haraga Hikaru, Kanno Kousuke, Iida Koji, Sultana Razia, Zahan Umme Farzana, Kyo Satoru *Shimane University*

[Objective] The molecular mechanisms through which endometriosis-related ovarian neoplasms (ERONs) develop from benign endometrioma remains unclear. Especially, it is a long-standing mystery why ovarian endometrioma has a potential to develop to two representative histological subtypes, endometrioid carcinoma or clear cell carcinoma. The present study aimed to dissect such molecular mechanisms using our own *in vitro* carcinogenesis model. **[Methods]** The epithelial cells were isolated and purified from surgically removed benign endometrioma samples and immortalized with the overexpression of *cyclinD1/CDK4* in combination with *hTERT*. Immortalized endometrioma cells were confirmed to maintain characteristics of epithelial cells with endometrioma features, and were subjected to various molecular manipulations with knock-out or overexpression of several specific candidate drivers, including *ARID1A*, *KRAS*, *PIK3CA* and c-Myc, based on the pre-

vious comprehensive genome-wide studies, including d TCGA. These cells were then tested for malignant transformation by tumorigenicity in immune compromised mice. **[Results]** Knock-out of *ARID1A* gene in immortalized endometrioma cells, combined with overexpressing *KRAS* oncogenic mutant allele or overexpressing AKT as well as c-Myc overexpression successfully led to efficient tumor formation in nude mice, histologically representing typical endometrioid carcinoma. Interestingly, when these cells were inoculated into SCID mice, they could form tumor as well, but histologically exhibiting clear cell carcinoma. **[Conclusion]** Loss of *ARID1A*, *KRAS* mutation or AKT activation and c-Myc overexpression were found to be the main candidate drivers for the development of ERONs, and tumor immune microenvironment may contribute to determine specific histological subtype.

IS-WS-7-4

Novel BRCA1-BRCT binding partner, mediator complex subunit 1 (MED1) contributes to maintain homologous recombination pathway and suppress R-loop accumulation Honjoh Harunori¹, Tanikawa Michihiro², Hiraike Osamu¹, Oda Katsutoshi³, Miyamoto Yuichiro¹, Mori Mayuyo¹, Sone Kenbun¹, Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital², Division of Integrative Genomics, The University of Tokyo³*

[Objective] Homologous recombination (HR) deficiency has been established as a strong therapeutic target and is closely linked to carcinogenesis. The aim of this study was to elucidate the broad function of a novel HR factor, mediator complex subunit 1 (MED1), in genome stability. **[Methods&Results]** First, the formation of the MED1/BRCA1 complex via BRCT domains was demonstrated by immunoprecipitation. And, the interaction was abolished in the presence of λ -protein phosphatase, DNase, and RNase-the functions as a transcriptional co-factor, demonstrated by Luciferase assay. MED1-deficient cells showed significantly reduced colony-forming ability after IR and CDDP exposure. DR-GFP assays showed that MED1 knock-down significantly reduced HR activity. MED1 knockdown also prolonged IR-induced DNA damage and delayed and prolonged ATM and Chk2 phosphorylation. Pulse-chase BrdU labeling assays showed a decrease in DNA synthesis upon MED1 knock-down. A reduction in C-NHEJ activity was also observed in MED1-deficient cells, and 53BP1 accumulation at sites of DNA damage induced by IR was also reduced. Furthermore, nuclear accumulation of R-loop and R-loop-induced comet tails was observed in MED1 knockdown cells. **[Conclusion]** We conclude that the transcription factor MED1 contributes to genomic stability through the regulation of the HR pathway and R-loop processing. This indicates the possibility of establishing therapeutic strategies targeting genomic vulnerability due to unresolved DNA Double-strand breaks and disruption of replication forks in gynecologic cancers whose function of the mediator complex is impaired.

IS-WS-7-5

Genetic modification of tumor-infiltrating lymphocytes in gynecologic malignancies for optimal adoptive immunotherapy Matsukawa Tetsuya^{1,2}, Yoshikawa Toshiaki¹, Suzuki Shiro³, Kagaya Yuki¹ *Division of Tumor Immunology, Institute for Advanced Medical Research, Keio University¹, Nagoya University², Department of Gynecologic Oncology, Aichi Cancer Center³*

[Objective] Adoptive transfer of tumor-infiltrating lymphocyte (TIL) has demonstrated antitumor efficacy in patients with malignant melanoma. However, TIL therapy has not shown objective response in gynecologic malignancies, mainly due to poor

persistence of the infused TILs. Here, we investigated how to improve the quality of TILs derived from gynecologic tumors by modification of the culture protocol and genetic engineering. **[Methods]** To shorten the culture duration, we obtained a single-cell suspension from surgically resected gynecologic epithelial malignant tumor tissues and directly stimulated them using artificial antigen presenting cells expressing anti-CD3 antibodies and CD80 in the presence of 100 IU/ml of IL-2. Additionally, we retrovirally transduced TILs with our recently developed artificial cytokine receptors that constitutively and selectively activate JAK-STAT pathway through a mutant IL-7 receptor intracellular domain. **[Results]** We achieved significantly better overall proliferation by anti-CD3 antibodies and CD80 stimulation compared to conventional high-dose IL-2 (3000IU/ml) culture of tumor pieces. By optimizing the timing of gene transfer, we were able to achieve more than 60% of transduction efficiency regardless of donor samples. We confirmed that the expression the cytokine receptor of mutant IL7 further enhanced the *in vitro* proliferation and effector functions of TILs. Moreover, the cytokine receptor-engineered TILs showed superior *in vivo* persistence when adoptive transferred into immunodeficient mice compared to those expanded with a conventional protocol. **[Conclusion]** We developed a novel method to produce TILs with improved quality and quantity. Future clinical application for optimal TIL therapy against gynecologic malignancies is warranted.

IS-WS-7-6

A novel epigenetic drug, SUV39H2 inhibitor, can inhibit double-stranded DNA break repair and a combination with poly (ADP-ribose) polymerases (PARP) inhibitor for uterine leiomyosarcoma produces synthetic lethality Toyohara Yusuke, Sone Kenbun, Hachijo Ryuta, Tanimoto Saki, Inoue Futaba, Kukita Asako, Taguchi Ayumi, Miyamoto Yuichiro, Mori Mayuyo, Oda Katsutoshi, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*

[Objective] The prognosis of uterine leiomyosarcoma (uLMS) is poor due to a high recurrence rate and chemotherapy resistance. Therefore, novel therapeutic targets for uLMS require investigation. SUV39H2 is a histone methyltransferase which promotes double-strand DNA break repair by recruiting phosphorylated H2AX (γ H2AX). Herein, we investigated the antitumor efficacy and underlying mechanism of the SUV39H2 inhibitor OTS186935 in uLMS. **[Methods]** First, we analyzed mRNA and protein expression of SUV39H2 in clinical samples of uLMS, normal myometrium, and leiomyoma by real-time polymerase chain reaction and immunohistochemistry, respectively. Next, we conducted drug sensitivity assays of OTS186935 and combination therapy with the PARP inhibitor olaparib using SK-LMS-1 and SK-UT-1 cell lines. We used an annexin assay to investigate mechanisms of cellular death. We also performed western blotting, immunofluorescence, and chromatin immunoprecipitation sequencing (ChIP-seq) to investigate γ H2AX under OTS186935 treatment, in addition to *in vivo* experiments using nude mice. **[Results]** In clinical samples, SUV39H2 expression was significantly elevated in uLMS compared to that in normal myometrium and leiomyoma. OTS186935 showed decreased cell viability in both cell lines and combination therapy showed synthetic lethality in SK-UT-1 (combination index =0.87). Annexin assay revealed that combination therapy induces apoptosis. After treatment with OTS186935, the accumulation of γ H2AX was decreased. ChIP-seq also showed decreased γ H2AX under OTS186935 treatment. Furthermore, OTS186935 showed significant effectiveness *in vivo*. **[Conclusion]** OTS186935 appears to inhibit double-stranded DNA break repair, based on decreased γ H2AX observed with ChIP-seq and other assays. Furthermore, combination therapy with olaparib

showed synthetic lethality in uLMS.

IS-WS-7-7

A novel method for monitoring patients' symptoms and mental status during chemotherapy independent of adherence using heart rate variability Higashiyama Nozomi¹, Yamaguchi Ken¹, Inayama Yoshihide¹, Koike Ayami¹, Ueda Akihiko², Kitamura Sachiko¹, Taki Mana¹, Yamanoi Koji¹, Murakami Ryusuke¹, Hamanishi Junzo¹, Mandai Masaki¹ *Kyoto University Graduate School of Medicine¹, Department of Biomedical Data Intelligence, Kyoto University²*

[Objective] Monitoring patients' symptoms and mental status during chemotherapy with an electric Patient Reported Outcomes (ePRO) can lead to an improvement in quality of life (QoL) and prolong patient overall survival. The biggest problem with ePRO is poor adherence. Heart rate variability (HRV) is related to stress and automatically recorded by mobile devices. The aim of this study was to develop a system that can monitor a patient's condition without being influenced by his/her adherence. **[Methods]** Two-hundred sets of data from 60 patients and 100 datasets from 20 patients with gynecological cancer were used for training and validation data, respectively. HRV and PROs (EORTC qlq-C30, FACT-G, PHQ9, PRO-CTCAE) were collected daily and weekly, respectively. A binary classification model that generates Shapely Additive ExPlanations (SHAP) values was developed to predict whether symptoms related to QoL were severe using HRV. A clustering model was developed by categorizing the SHAP values into three groups using a Parametric Umap. **[Results]** Clustering derived from HRV indicated high, middle, and low QoL groups (Groups A, B, and C, respectively). The total score from the FACT-G was 78.7, 73.1, and 66.9 for Groups A, B, and C, respectively. The score reflecting fatigue and other symptoms was most severe in Group C and mildest in Group A. Monitoring HRV could detect ileus during chemotherapy and pituitary insufficiency during treatment with ICI. **[Conclusion]** Monitoring HRV over time appears to allow early detection of deterioration in a patient's condition, such as complications and side effects of chemotherapy.

IS-WS-7-8

NAC1/ACOX2 axis as a novel therapeutic target for ovarian cancer Sonia Shahataj Begum, Nakayama Kentaro, Ishikawa Masako, Yamashita Hitomi, Haraga Hikaru, Kanno Kousuke, Iida Koji, Sultana Razia, Zahan Umme Farzana, Sohail Hasibul Islam, Kyo Satoru *Shimane University*

[Objective] NAC1, a transcription regulator protein associated with cancer, is highly expressed in ovarian cancer. However, it remains unclear how NAC1 is involved in the ovarian carcinogenesis. Previously found that knocking down NAC1 in ovarian cancer cell lines induces apoptosis and restores their sensitivity to chemotherapy, suggesting NAC1 as a potential therapeutic target. The study aimed to identify molecular pathways how NAC1 is involved in the development of ovarian cancer. **[Methods]** Microarray analyses performed to search the possible target genes upon knockdown of NAC1. Reporter assays conducted to determine if NAC1 regulates the promoters of such downstream targets. Subsequently, a ChIP assay performed to investigate the direct interaction of NAC1 to the promoter regions. **[Results]** Microarray analyses revealed significant over-expression of acyl-CoA oxidase 2 (ACOX2), a known prognostic factor via apoptosis process in ovarian cancer, upon NAC1 knockdown. Computer searching identified a total of 6 consensus motif (CATGs) of NAC1 on the ACOX2 promoter. Reporter assays using ACOX2 promoter demonstrated that NAC1 negatively regulated ACOX2 promoter. We attempted sequential deletions of 6 CATG motifs within the ACOX2 promoter in re-

porter assay, and found that each deletion of 6 CATG motifs significantly attenuated the inhibitory effect of NAC1 on the promoter. Finally, ChIP assay revealed that NAC1 binds to the CATG sequence on the ACOX2 promoter region. **[Conclusion]** The study identified that NAC1 contributes to the development of ovarian cancer by regulating ACOX2 expression via specific binding sites on the promoter, providing insights into NAC1/ACOX2 axis as a potential therapeutic target.

IS-WS-7-9

Initial epigenetic alteration induced by aberrant activation of RAS-MAPK signaling in non-transformed cells Onoyama Ichiro, Yagi Hiroshi, Asanoma Kazuo, Kawakami Minoru, Hachisuga Kazuhisa, Tomonobe Hiroshi, Maenohara Shoji, Kodama Keisuke, Yasunaga Masafumi, Yahata Hideaki, Kato Kiyoko *Kyushu University Hospital*

[Objective] Aberrant activation of RAS-MAPK signaling is known to work as an oncogenic driver in variety kinds of cancer. It is also known that epigenetic changes start soon after RAS-MAPK signaling activation before oncogenic transformation. Epigenetics in cancer cells have been well studied so far, however, initial alteration occurred in oncogene-activated cells has not fully elucidated yet. In this study, we tried to identify early epigenetic changes induced by RAS-MAPK signaling activation in non-transformed cells. **[Methods]** DNA methylation was analyzed by liquid chromatography-mass spectrometry (LC-MS), reduced representation bisulfite sequencing (RRBS) in *Braf600E* KI, *KrasG12D* KI or *Pten* KO MEFs. **[Results]** LC-MS analysis revealed *BrafV600E* or *KrasG12D*-expressing MEFs showed significantly lower 5-mC levels compared to their WT counterparts, indicating endogenous expression of *BrafV600E* and *KrasG12D* promotes genome-wide DNA hypomethylation as seen in cancer cells. RRBS analysis showed several thousand regions at which *BrafV600E* or *KrasG12D* promoted a significant gain or loss of DNA methylation. Interestingly, gain of methylation is more detected than loss of methylation within 500 bp from TSS in both MEFs, but *Pten* KO MEFs, susceptible to transform as *BrafV600E* or *KrasG12D*-expressing MEFs, could not recapitulate this result. As *Dnmt3b* and *Tet3* expression were induced after *Braf* or *Kras* activation, we performed ChIP experiments, and showed that *Tet3* and *Dnmt3B* were bound to representative hypomethylated and hypermethylated regions, respectively, in *BrafV600E*-expressing MEFs identified by RRBS. **[Conclusion]** Our findings elucidate mechanisms of global DNA hypomethylation and local hypermethylation close to TSS promoted by aberrant activation of RAS-MAPK signaling at an early stage of tumorigenesis.

IS-WS-8-1

Application of cellulose nanofiber-based EV sheet for establishing ovarian cancer biomarkers Nagao Yukari¹, Yokoi Akira^{1,2}, Yoshida Kosuke^{1,2}, Kitagawa Masami¹, Uekusa Ryosuke¹, Suzuki Kazuhiro¹, Yoshikawa Nobuhisa¹, Niimi Kaoru¹, Kajiyama Hiroaki¹ *Nagoya University¹, Institute for Advanced Research, Nagoya University²*

[Objective] Extracellular vesicles (EVs) are functionally important for intercellular communication and attracted attention as biomarkers. Since we recently invented cellulose nanofiber (CNF)-based EV sheet for capturing EVs from micro-volume bio-fluids, this study aimed to establish the application of EV sheet for ovarian cancer biomarkers. **[Methods]** During the surgeries for patients with ovarian tumor, CNF-EV sheets were used to collect EVs from ascites on multiple organ surfaces including liver, omentum, pelvic peritoneum, tumor surface, and fallopian tubes, and then small RNA sequencing was performed. qRT-PCR or digital droplet PCR were used for validation procedures. **[Results]** Small RNA sequencing was performed in 250 EV samples from 14 cases by using CNF-EV sheets. miRNA profiles of EVs in distant organs from the tumor, such as liver and omentum, were significantly different from the tumor, and the association fallopian tube derived EVs with high-grade serous carcinoma or serous intraepithelial carcinoma of the fallopian tube was also suggested. Compared to EVs in conventional whole ascites, EVs in tumor surface ascites correlated strongly with tumor tissue miRNA profiles. Differentially expressed EV-miRNAs in the samples from cancer patients were identified in all serum, urine, and ascites, with miR-421 ($p = 0.0059$, AUC : 0.931), let-7f-5p ($p = 0.0008$, AUC : 0.979), and miR-423-3p ($p = 0.0329$, AUC : 0.875). Their miRNA-changes before and after treatment were also confirmed. Candidate EV-miRNAs were validated by both PCRs. **[Conclusion]** EV-miRNAs from CNF-EV sheets could be applied as biomarkers for ovarian cancer diagnosis, staging, and treatment efficacy, which could lead to a new clinical strategy in ovarian cancer.

IS-WS-8-2

Spatial diversity of intraperitoneal extracellular vesicles and its significance on the progression of high-grade serous ovarian carcinoma Hishikawa Risa¹, Yokoi Akira¹, Yoshida Kosuke¹, Suzuki Kazuhiro¹, Nagao Yukari¹, Kitagawa Masami², Yoshikawa Nobuhisa¹, Niimi Kaoru¹, Kitai Miho³, Yamaguchi Satoshi³, Kajiyama Hiroaki¹ *Nagoya University Graduate School of Medicine¹, Bell Research Center, Collaborative Research, Nagoya University Graduate School of Medicine², Hyogo Cancer Center³*

[Objective] High-grade serous ovarian carcinoma (HGSOC) frequently spreads to the peritoneal cavity and produces ascites. Here, we developed a novel method using cellulose nanofiber sheets to capture extracellular vesicles (EVs) from microfluid. This means that we can assess EV profiles on the surface of each organ in the peritoneal cavity. In this study, we investigated a new concept, which spatially diverse EVs are involved in the HGSOC development. **[Methods]** First, we retrospectively reviewed the surgical video of 24 cases with stage III HGSOC who underwent diagnostic laparoscopy. Second, we collected EVs on the liver surface and peritoneum from 36 spots from 12 patients and performed microRNA sequencing. Moreover, we performed *in vitro* analyses to evaluate the function of hepatic cell-derived EVs on ovarian cancer cells. **[Results]** Diagnostic laparoscopy revealed that only one patient (6%) experienced metastasis on the liver surface, whereas 18 patients (82%) had metastasis on the diaphragm. Then, microRNA sequencing showed that the EV microRNA profile on the liver surface was different from that on the peritoneum, suggesting

the spatial diversity of intraperitoneal EVs. Moreover, we confirmed that hepatic cell-derived EVs suppressed the migration and invasion abilities of the ovarian cancer cells ($p < 0.01$) and increased the expression of *CDH1* *in vitro*. **[Conclusion]** We clinically showed that HGSOC rarely spread to the liver surface, which had a unique EV miRNA profile. Moreover, hepatic cell-derived EVs acted as tumor suppressors in ovarian cancer cells. Therefore, spatially diverse EVs might contribute to the formation of peritoneal dissemination.

IS-WS-8-3

The frequency and pathogenicity of BRCA1 and BRCA2 variants in the general Japanese population Mariya Tasuku^{1,2}, Saito Tsuyoshi¹ *Sapporo Medical University¹, Departments of Medical Genetics and Genomics, Sapporo Medical University²*

[Objective] Hereditary breast and ovarian cancer syndrome (HBOC) resulting from pathogenic variants of *BRCA1* or *BRCA2* is the most common and well-documented hereditary tumor. Although founder mutations have been identified in population-based surveys in various countries, the types of variants are not uniform across races and regions. Case-controlled studies have primarily been conducted in Japan, though population-based surveys have been conducted in a few studies. **[Methods]** With the aim of constructing a Japanese genome database, the Tohoku Medical Megabank Organization (ToMMO) began accumulating whole-genome sequence data from the general population of the Tohoku area in 2012. By 2023, approximately 54,000 individuals were included in this database, which was released as 54 KJPN. We analyzed these data and comprehensively identified the prevalence of *BRCA1/2* pathogenic and truncating variants. **[Results]** Our analysis showed that most of the top *BRCA1/2* pathogenic variants believed to be founder mutations do not match reports from other countries. Instead, variants consistent with the cancer patient and family registry data of JOHBOC (Japanese Organization of Hereditary Breast and Ovarian Cancer), such as *BRCA1* : c.188T>A (p.L63*) and *BRCA2* : c.6952C>T (p.R2318*), were identified as founder mutations. The estimated carrier frequency was calculated to be 2.485×10^{-3} for *BRCA1*, 2.873×10^{-3} for *BRCA2*, and 5.350×10^{-3} for *BRCA1* or *BRCA2*. **[Conclusion]** We believe that an accurate understanding of the unique distribution and characteristics of pathogenic *BRCA1/2* variants in Japan through analysis of 54KJPN will enable better surveillance and intervention for HBOC patients, not only in Japan but also worldwide.

IS-WS-8-4

Meflin-positive cancer-associated fibroblasts exhibit anti-tumor effect in advanced ovarian cancer through regulation of inhibition of peritoneal dissemination Miyamoto Emiri¹, Yoshihara Masato¹, Sugiyama Mai², Koya Yoshihiro², Yamakita Yoshihiko², Fujimoto Hiroki¹, Iyoshi Shohei¹, Mogi Kazumasa¹, Uno Kaname¹, Kitami Kazuhisa³, Kajiyama Hiroaki¹ *Nagoya University¹, Bell Research Center², Kitasato University³*

[Objective] In general, cancer-associated fibroblasts (CAFs) are known to play an important role in the acquisition of malignant hallmarks in various malignancies; however, the tumor-suppressive effect of meflin-positive CAFs has been noted in several carcinomas. The aim of this study is to elucidate the function of meflin-positive CAFs in the peritoneal extension of advanced ovarian cancer (aOC/OC). **[Methods]** We subsequently performed histopathological examinations and *in situ* hybridization (ISH) on aOC specimens (N=37) to examine the impact of Meflin-positive CAFs for prognosis. Finally, we performed histological evaluation of OC and stromal cells in peritoneal metastasis using Meflin knock-out mice. We measured ascites volume, tumor weight, fluorescent immunostaining of cells

in ascites, and histological evaluation of disseminated lesions in mice after tumorigenesis. **[Results]** In ISH, we confirmed presence of Meflin-positive CAFs in the peritoneal dissemination of aOC (19/37 : 51.3%). Surprisingly, higher proportion of Meflin-positive CAFs was significantly associated with longer overall survival (OS) [3-year OS rate : positive (N=12) : 63.1%, negative (N=8) : 44.4%, $P=0.0497$]. In addition, allograft tumor on the peritoneum in Meflin KO mice showed desmoplastic tumor. In Meflin KO mice, increased ascites volume and tumor weight were observed. Fluorescent cell immunostaining showed enhanced spheroid formation in KO mice. Histological evaluation showed enhanced inflammatory findings in the omentum adipose tissue in KO mice. These results suggested that Meflin-positive CAFs regulate malignant potential of aOC. **[Conclusion]** The presence of meflin-positive CAFs may regulate peritoneal metastatic potential, and consequently is associated with long-term survival in patients with aOC.

IS-WS-8-5

CircESRP1 promotes cell proliferation of high-grade serous ovarian cancers (HGSOC) via miR-142-3p/HMGA2 pathway Oride Tadashi, Sawada Kenjiro, Oi Yukako, Toda Aska, Nakamura Koji, Kawano Mahiru, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Kimura Tadashi *Osaka University*
[Objective] Circular RNAs (circRNAs) are reported to play pivotal roles in cancer biology, yet their specific functions in HGSOC remain unclear. Our research focuses on identifying highly elevated circRNAs in HGSOC and elucidating their roles in its progression. **[Methods]** To identify highly expressed circRNAs in HGSOC, circRNA microarray analyses were performed on two HGSOC clinical samples and their corresponding normal tissues. Their expression profiles were validated across 24 HGSOC samples using RT-qPCR. To assess the functions of identified circRNAs, in-vitro analyses were executed following siRNA transfection. Further, proteasome analyses were performed, and the mechanism how this circRNA works was identified using in-silico analyses. **[Results]** CircESRP1 emerged as the most highly expressed circRNA, with a Log Fold Change (Log FC) of 3.12 in two HGSOC samples. Subsequently, significant upregulation of its expression was seen, with a Log FC of 5.56, across 24 HGSOC clinical samples as well as HGSOC cell lines, specifically OVCAR3 and Caov3. Suppression of CircESRP1 inhibited cell proliferation by inducing apoptosis. Proteasome analyses revealed the suppression of circESRP1 inhibits HMGA2 expression in HGSOC cell lines, and in silico analyses showed circESRP1 works as a sponge of miR-142-3p, and thereby this miRNA negatively regulates HMGA2 expression. These interactions were validated through dual-luciferase reporter assays and RNA pulldown assays. **[Conclusion]** CircESRP1, specifically elevated in HGSOC, works as a sponge for miR-142-3p, and thereby positively regulates HMGA2 expression, leading to cell proliferation. Our findings shed light on the potential role of a novel circRNA (circESRP1) as a therapeutic target in HGSOC.

IS-WS-8-6

Development and clinical application of a fragment-based BRCA1 methylation detection method Tsuchimochi Saki¹, Taguchi Ayumi¹, Hiraike Osamu¹, Ishizaka Aya¹, Nishijima Akira¹, Sone Kenbun¹, Miyamoto Yuichiro¹, Tanikawa Michihiro², Mori Mayuyo¹, Oda Katsutoshi², Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, Department of Integrated Genomics, The University of Tokyo², Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital³*
[Objective] Methylation of BRCA1 promoter is the second most frequent cause of homologous recombination deficiency (HRD) in ovarian high-grade serous carcinoma (HGSC). BRCA

1 methylation can easily disappear after chemotherapy, leading to chemotherapy resistance. However, no methylation detection methods are clinically available due to their time-consuming and expensive nature. We have developed a convenient and accurate methylation diagnosis method, Fragment Analysis of Methylation (FAM), which combines methylation-sensitive restriction enzymes with fragment analysis. **[Methods]** Clinical samples were obtained from 69 HGSC patients who underwent primary debulking surgery. FAM targeting BRCA1 methylation was performed, and its accuracy was compared to BRCA1 methylation levels calculated using targeted bisulfite sequencing (BIS-seq), a standard method for assessing DNA methylation. The correlation between BRCA1 methylation and mRNA expression was assessed. Methylation rates were compared pre- and post-chemotherapy for 10 cases where paired specimens were available. **[Results]** FAM and BIS-seq identified 21 (30%) and 23 (33%) BRCA1 methylation-positive cases, respectively. Methylation levels calculated by FAM were strongly correlated with BIS-seq results (sensitivity : 93%, specificity : 100%). All cases with a CpG methylation ratio >0.3 in BIS-seq (hypermethylation cases) were detectable by FAM. Cases with BRCA1 methylation had significantly lower BRCA1 expression ($p=0.017$). FAM was also applicable to samples after chemotherapy, and four of the seven patients with BRCA1 methylation pre-chemotherapy were demethylated post-chemotherapy. **[Conclusion]** The newly developed FAM is easy to apply and highly accurate in quantifying BRCA1 methylation levels. Therefore, it can be used to identify patients who develop resistance during treatment by restoring homologous recombination repair functions.

IS-WS-8-7

The combination of PI3K/mTOR dual inhibitor GSK458 and arsenic trioxide As2O3 shows synergistic anti-tumor effects on ovarian clear cell carcinoma via PI3K/mTOR and anti-apoptosis pathways Wang Yan *Osaka University*
[Objective] Ovarian clear cell carcinoma (OCCC) shows a relatively high prevalence in Japan and Asia. As advanced/recurrent OCCC often has resistance to platinum-based chemotherapy resulting in poor outcomes, a novel therapeutic strategy is needed. Given that OCCC represents characteristic activated pathways (PI3K/mTOR, angiogenesis, anti-apoptosis, etc.), we hypothesize a combination of PI3K/mTOR dual inhibitor (GSK458) and As2O3 (arsenic trioxide) has synergistic anti-tumor effects on OCCC. **[Methods]** The effects of each monotherapy and the combination (GSK458-As2O3) on cell viability, colony formation, and apoptosis were studied using 7 OCCC cell lines *in vitro*. We tested the anti-tumor effect using 3D-organoid culture from OCCC patient-derived xenograft (PDX) orthotopic mouse models. The synergistic mechanisms were explored by western blotting regarding PI3K/AKT/mTOR signaling pathway, apoptosis, and autophagy as well as RNA-sequencing. *In vivo* efficacy of the combo was evaluated by TOV21G transduced with firefly luciferase gene and injected into nude mice intraperitoneally. **[Results]** The low-dose combination GSK458-As2O3 synergistically inhibited cell viability and colony formation. The viability of 3D-organoid from PDX tumors treated with the combo decreased to 23.8% compared to control. The combo of GSK458-As2O3 significantly inhibited PI3K/AKT/mTOR signaling pathway, promoted apoptosis (cleaved PARP and cleaved caspase-9), and increased autophagy-related protein LC3B. The combo represented significant tumor suppression and longer survival than other monotherapy groups in TOV21G xenograft. The mean survival in control, GSK458, As2O3, and the combo group was 35, 47, 46 and 59 days, respectively. **[Conclusion]** This new combination of GSK458-As2O3 would be a promising strategy for OCCC.

IS-WS-8-8

High-throughput drug screening using BRCA1-mutated ovarian cancer organoid identified elimusertib as a synthetic lethal drug with olaparib Takahashi Mio, Chiyoda Tatsuyuki, Yoshimura Takuma, Sakamaki Tomomi, Jisaka Mitsuyo, Hirata Momo, Sakai Kensuke, Wada Michiko, Yamagami Wataru, Tanaka Mamoru *Keio University*

[Objective] PARP inhibitors have contributed to prolonging survival, especially in patients with homologous recombination deficient (HRD) ovarian cancer (OC). We aimed to discover the best combinatorial drug with olaparib using patient-derived OC organoid harboring *BRCA1* mutation. **[Methods]** A library of 4560 compounds was used to perform high-throughput drug screening (HTDS) on *BRCA1*-mutated OC organoid. ATP assays were performed to calculate cell viability of each compound, olaparib, and their respective combinations, and the combination index (CI) was examined to confirm synergistic effect with olaparib. To validate the effect of the candidate drug in vivo, olaparib, the candidate drug, their combination, and vehicle were administered to patient-derived organoid xenograft (PDOX) mouse models. **[Results]** In HTDS, elimusertib, ATR inhibitor, was extracted as the best candidate drug. Focusing on ATR-Chk1 pathway, 3 ATR inhibitors including elimusertib, and 2 Chk1 inhibitors were tested for synergy with olaparib using 3 HRD and 1 HR-proficient (HRP) organoids. The CI for elimusertib and olaparib was less than 0.7 for all organoids, and it indicated that elimusertib was synergistic with olaparib for both HRD and HRP organoids, while the other ATR/Chk1 inhibitors were not synergistic with olaparib for the HRP organoid. In PDOX experiment using the *BRCA1*-mutated organoid, post-treatment tumor was significantly smaller in the elimusertib combination group ($p < 0.001$). **[Conclusion]** Elimusertib was extracted in HTDS as the most effective drug in combination with olaparib. Elimusertib was synergistic with olaparib not only for the HRD organoids but also for the HRP organoid and may be useful in clinical practice.

IS-WS-8-9

Metabolome analysis showed that arachidonic acid in high-fat diet promotes mitochondrial metabolism of ovarian cancer Mukaida Hitomi¹, Hiramatsu Kosuke¹, Kobayashi Mariya¹, Watanabe Yuko¹, Kamei Yuji¹, Masuda Tatsuo², Kakuda Mamoru¹, Nakagawa Satoshi¹, Kimura Toshihiro¹, Ueda Yutaka¹, Kimura Tadashi¹ *Osaka University¹, StemRIM Institute of Regeneration-Inducing Medicine, Osaka University²*

[Objective] We demonstrated that High-Fat Diet (HFD) promoted the tumor growth of epithelial ovarian cancer more than Normal-Diet (ND) in vivo. To identify lipid molecules which promote the cell proliferation, we performed metabolome analysis using serum of HFD and ND fed mouse and analyzed which lipid metabolites contribute to the cell proliferation. **[Methods]** We established HFD and ND fed mouse model and performed metabolome analysis using serum sample obtained from HFD and ND mouse and compared their metabolomic profile. Using the lipid molecules which are identified with metabolome analysis, we investigated the metabolic pathway of epithelial ovarian cancer in vitro. **[Results]** The tumor growth of epithelial ovarian cancer cells was significantly promoted in HFD mouse more than in ND mouse (1077mm^3 vs 487mm^3). We detected 210 metabolites by metabolome analysis using HFD and ND mouse serum. Principal Component Analysis showed the obvious different metabolic profiles between them. Partial Least-Squares Discriminant Analysis showed some lipid metabolites, including arachidonic acid (AA) with high variable importance of projection score in HFD mouse. We confirmed AA promoted the cell proliferation and activated MAPK signaling pathway.

We also demonstrated the effect of AA was inhibited by CPT1a inhibitor, suggesting that the cell proliferation is associated with mitochondrial lipid metabolism. **[Conclusion]** Metabolome analysis suggested that arachidonic acid contributes cell proliferation of epithelial ovarian cancer via mitochondrial lipid metabolism.

IS-WS-9-1

Targeted metabolomic analysis of early-trimester serum identifies potential mechanism for late-onset preeclampsia Okoshi Chihiro¹, Kyojuka Hyo², Fukuda Toma¹, Isogami Hirotaka¹, Matsuoka Ryo¹, Murata Tsuyoshi¹, Omoto Takahiro¹, Yamaguchi Akiko¹, Nishigori Hidekazu³, Yasuda Shun¹, Fujimori Keiya¹ *Fukushima Medical University¹, Ohta Nishinouchi Hospital², Fukushima Medical Center for Children and Women, Fukushima Medical University³*

[Objective] Late-onset preeclampsia (Lo-PE) refers to the onset of hypertension with organ damage occurring after the 34th week of pregnancy. It occurs in 2.1% of all pregnancies and can cause serious complications to both mother and child. Identifying the underlying mechanism of Lo-PE is essential for developing preventive measures. We aimed to identify first-trimester maternal serum metabolites indicative of Lo-PE using targeted metabolomic analysis. **[Methods]** This study was conducted as an addendum to the Japan Environment and Children Study. The study cohort comprised 12 patients who experienced Lo-PE and 12 control individuals who experienced healthy pregnancies whose medical background information matched that of the patients in terms of propensity score matching. Capillary electrophoresis-mass spectrometry-based quantitative analyses of charged metabolites were performed on first-trimester maternal serum samples. **[Results]** A total of 183 charged metabolites were identified. The glucosamine peak area was significantly higher in the first-trimester sera of patients with Lo-PE than in that of the controls. Conversely, the serotonin peak area was significantly decreased in the sera of patients with Lo-PE. **[Conclusion]** Glucosamine levels can increase through consumption. It is therefore possible that daily dietary habits are involved in the onset of Lo-PE. Serotonin dysregulation has been reported to potentially be related to both maternal mental health and occurrence of PE. Nutritional intake in early pregnancy and serotonin state reflective of pre-pregnancy dietary habits and mental health are important. Preconception care could potentially prevent Lo-PE onset.

IS-WS-9-2

LC-MS Metabolomic Analysis of Lipid Mediators in Maternal Plasma and Umbilical Cord Blood of Pregnant Women complicated with Preeclampsia and Fetal Growth Restriction Yoshida Tomohiro, Yamamoto Shotaro, Kikuchi Taiki, Shibata Satoshi, Fukuda Eriko, Kitada Kohei, Kurihara Yasushi, Tahara Mie, Hamuro Akihiro, Misugi Takuya, Nakano Akemi, Tachibana Daisuke *Osaka Metropolitan University*

[Objective] Limited reports have explored the relationship between lipid mediators and conditions such as preeclampsia and fetal growth restriction (FGR). The purpose of this study is to analyze the lipid mediators of preeclampsia and FGR in maternal and umbilical cord blood to determine their functions on the fetus and placenta. **[Methods]** This study encompassed two distinct groups: Group 1 consisted of pregnant women who either had preeclampsia-related FGR or delivered infants with birth weights below the 10th percentile, while Group 2 comprised pregnant women who experienced uncomplicated deliveries. Maternal plasma samples were collected before delivery, and umbilical cord blood samples were obtained immediately after delivery. Lipid mediators were extracted from these samples

and subjected to analysis using LC-MS. The study compared the peak values of lipid mediators between the two groups as defined above. **[Results]** Our main findings revealed that 12, 13-DiHOME was significantly elevated in the group with FGR, including preeclampsia. Furthermore, in both groups, a significant negative correlation was observed between the concentration of 12, 13-DiHOME in the umbilical artery and birth weight ($r=-0.70$, $p=0.001$). Additionally, specific lipid mediators, 9, 10-DiHOME, and LysoPAF, were also found to be significantly elevated in the group with FGR in maternal plasma before delivery. **[Conclusion]** 12, 13-DiHOME is known to be involved in the regulation of inflammation and vascular constriction, and its excessive production may potentially impact vascular function and fetal nutrition supply. Therefore, these findings may be valuable in the development of maternal intervention strategies aimed at preventing low birth weight infants and preeclampsia.

IS-WS-9-3

The activation of renin in plasma via placental (pro) renin receptor in preeclampsia model mice Mishima Sakurako, Mitsui Takashi, Nakato Hikari, Suemori Ayano, Ooba Hikaru, Mitoma Tomohiro, Oohira Akiko, Kirino Satoe, Maki Jota, Eto Eriko, Masuyama Hisashi *Okayama University*

[Objective] Recent reports have linked preeclampsia (PE) with prorenin. Previously, we demonstrated the production of Endothelin-1 through the placental (pro) renin receptor (PRR) intracellular signaling pathway in PE model mice. In this study, we investigated the activation of renin in plasma via placental PRR in these PE model mice. **[Methods]** PE model mice were created by performing a reduced uterine perfusion pressure (RUPP) operation, achieved by ligating the uterine artery of ICR female mice on 14.5 day-post-coitum (dpc). The control group comprised normal pregnant mice. Blood pressure was measured on 15.5 and 18.5 dpc using the tail-cuff method. On 18.5 dpc, we collected blood, urine, and placenta, and weighed the fetuses and placentae. Expression of PRR in the placenta was measured using quantitative PCR and Western blotting, and the concentration of soluble PRR in plasma was measured using ELISA. To evaluate the activation of renin, we measured the ratio of des AI/intact angiotensinogen (AGT) concentrations in plasma. Additionally, we administered a PRR inhibitor to the mice via an osmotic pump, and we evaluated the same measurements. **[Results]** PE group exhibited increased blood pressure and proteinuria and decreased fetal and placental weights compared to the control group. Moreover, it exhibited an increase in PRR expression in the placenta, soluble PRR in plasma, and the des AI/intact AGT concentration ratio in plasma. However, PRR inhibitor administration suppressed these changes. **[Conclusion]** Placental hypoxia induced by RUPP increased placental PRR in PE group, suggesting that the placental PRR increased the activation of renin in plasma.

IS-WS-9-4

Chemical modification of angiotensin receptor blockers with polyethylene glycol to inhibit placental permeability and reduce fetotoxicity Inaoka Naoko¹, Iriyama Takayuki¹, Sayama Seisuke², Matsui Haruka¹, Suzuki Kensuke¹, Samejima Taiki¹, Ichinose Mari¹, Toshimitsu Masatake¹, Seyama Takahiro¹, Kumasawa Keiichi¹, Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, Tokyo-kita Medical Center²*

[Objective] Although angiotensin receptor blockers (ARBs) are potentially effective against preeclampsia, their use is contraindicated due to fetotoxicity. Here, we examined whether polyethylene glycol (PEG)-based modification of olmesartan, an ARB, decreases its placental permeability and fetotoxicity. **[Methods]** Olmesartan derivatives were synthesized at the Drug Dis-

covery Initiative of the University of Tokyo. Angiotensin-two-induced mouse model was utilized to evaluate their fetal transfer and drug efficacy. Fetotoxicity was evaluated by administering olmesartan derivatives to pregnant mice. Placental permeability in human was assessed by ex-vivo perfusion model using human placentas. **[Results]** By introducing PEG with insertion of a spacer into olmesartan and further dimerizing, olmesartan derivatives with larger molecular weight and higher hydrophilicity were synthesized. The derivatives were administered to angiotensin-two-treated pregnant mice to screen for placental permeability, and X was obtained whose placental permeability was seven percent of that of olmesartan. Regarding fetotoxicity, although olmesartan displayed renal toxicity at a concentration of one-tenth of its effective dose to ameliorate preeclamptic features in mouse model, X did not cause kidney damage in neonates at its effective dose. Additionally in human, X showed extremely low permeability in placental perfusion model, less permeable than insulin used as a negative control. **[Conclusion]** PEG modification allows olmesartan to inhibit placental permeability and reduce fetal toxicity while retaining its pharmacologic activity. Our findings may provide a breakthrough methodology for drug discovery that can be applied to other drugs whose fetotoxicity is a barrier to treatment during pregnancy.

IS-WS-9-5

The comparison in sFlt-1/PlGF ratio results between preeclampsia with gestational diabetes mellitus and preeclampsia Song Jisue, Kim Suk-Young, An Seon A, Park So Hui, Song Han Song, Kang Jae Hee *Gachon University Gil Medical Center, Korea*

[Objective] Preeclampsia (PE) and gestational diabetes mellitus (GDM) are both significant obstetric complications that can pose risks to pregnant women. This study investigated the sFlt-1/PlGF ratio values and clinical characteristics of mothers experiencing both GDM and PE. **[Methods]** A total of 134 singleton pregnant women who underwent sFlt-1/PlGF ratio testing at our institution from 2019 to 2022 were included in this study. They were categorized into four groups: control group (n=13), GDM-PE group (n=22), and PE group (n=96). The concentration of serum sFlt-1/PlGF ratio is determined through the ELISA (Eitest, Roche, Penzberg, Germany) method and the differences in sFlt-1/PlGF levels was analyzed via ANOVA. Statistical significance has been considered as $p<0.05$. **[Results]** The statistical analysis results indicated significant differences in sFlt-1/PlGF ratio values among the CTRL group, GDM-PE group, and PE group ($p<0.05$). The sFlt-1/PlGF ratio values in PE group was significantly higher than that of CTRL group ($p<0.05$). Additionally, GDM-PE group are meaningfully higher relative to CTRL group ($p<0.05$) and decreased relative to PE group ($p<0.05$). **[Conclusion]** With hyperglycemic exposure in GDM, compensatory mechanisms result in elevated PlGF. However, it was observed that in cases with such GDM situations, there is an increase in the antiangiogenic sFlt-1 when PE occurs. Therefore, despite a milder degree of endothelial dysfunction when compared to PE, the sFlt-1/PlGF ratio test holds significance in GDM-PE mothers, indicating the need for new criteria to be established for its assessment.

IS-WS-9-6

Derivation of Trophoblast Stem-like cells from Pathological Placentas Nakamura Ayano^{1,2}, Chigusa Yoshitsugu¹, Suzuki Naohiro^{1,2}, Mandai Masaki¹, Takashima Yasuhiro² *Kyoto University¹, Department of Life Science Frontiers, Center for iPS Cell Research and Application²*

[Objective] It has been suggested that trophoblast stem (TS) -

like cells in placentas are present, though it has been difficult to isolate them from placentas after the 2nd trimester of pregnancy. Furthermore, it is unclear how TS-like cells in pathological placentas, such as preeclampsia or fetal growth restriction, differ from those in normal placentas. We, therefore, aimed to derive TS-like cells from pathological placentas and to analyze their characteristics. **[Methods]** Villous tissues from the 1st trimester and normal and pathological placentas after the 2nd trimester were subjected to experiments. We sorted cytotrophoblasts (CTs) by flow cytometry. These cells were passaged by the culture method previously developed by us. Representative markers of CT, syncytiotrophoblast (ST), and extravillous trophoblasts (EVT) were assessed by immunofluorescence, flow cytometry, and qPCR. **[Results]** CTs isolated from various villous tissues could be maintained for more than 20 passages and over 180 days. These cells were positive for not only TP63 and TEAD4, CT markers, but also GATA3, TFAP2C, and KRT7, indicating TS-like cells. TS-like cells could be induced to differentiate into ST in which CGB3 and SDC1 were up-regulated. Furthermore, spindle-shaped cells with high expression of HLA-G and NOTUM, suggesting EVTs, were also differentiated from TS-like cells. The efficiency of differentiation into ST or EVTs from TS-like cells in pathological placentas tended to be lower than that of TS-like cells derived from normal placentas. **[Conclusion]** We were able to derive TS-like cells from pathological placentas, but they may have low differentiation potential.

IS-WS-9-7

Establishment of trophoblast stem cells from smooth chorion of term placenta Hoshiyama Takako, Tsuji Shunichiro, Murakami Takashi *Shiga University of Medical Science*

[Objective] Human trophoblast stem cells (TSCs) derived from placental villi in the first trimester have the capacity to differentiate into extravillous trophoblast (EVT) cells and syncytiotrophoblast (ST) cells. However, the efficiency of deriving TSCs from term placenta has been limited. Consequently, this study aims to establish a novel method for deriving TSCs from term pregnancy smooth chorion, with a focus on achieving a higher efficiency compared to placental villi. **[Methods]** Smooth chorion and placental villi isolation was carried out from term placenta, followed by the preparation of single cells through enzymatic dissociation. ITGA6-positive cells were isolated from both smooth chorion and placental villi and cultured in TSC medium. Characterization of chorion-derived TSCs (Ch-TSCs) was conducted through immunocytochemistry and RNA sequence analysis. Additionally, differentiation experiments were performed using Ch-TSCs for EVT and ST cells. **[Results]** TSCs were obtained from smooth chorion of term placenta, despite the inability to derive TSCs from placental villi. Immunocytochemistry of Ch-TSCs confirmed the expression of GATA3, TP63, and TEAD4. Ch-TSCs demonstrated the ability to differentiate into EVT and ST cells, with HLA-G and hCG expression in the differentiated EVT and ST cells, respectively. RNA-seq analysis revealed striking similarities between Ch-TSCs and TSCs derived from placental villi in the first trimester. **[Conclusion]** In summary, we established TSCs from smooth chorion of term placenta. Further research needs to be conducted to utilize our novel methods in deriving TSCs from patients with pregnancy-related diseases, potentially shedding light on the pathogenesis of pregnancy complications.

IS-WS-10-1

Safety of cisplatin short hydration method of concurrent chemoradiotherapy for cervical cancer Kojima Daiki¹, Suzuki Eitaro³, Iwasaki Kota², Nakao Yui², Seki Toshiyuki², Saito Motoaki¹, Takano Hirokuni², Yamada Kyosuke³, Okamoto Aikou⁴

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[Objective] Massive hydration is performed with cisplatin containing chemotherapy for renal protection. Although short hydration (SH) has been increasingly employed recently, few reports have examined the safety of the SH in concurrent chemoradiotherapy (CCRT) with cisplatin for cervical cancer, and we investigated its safety. **[Methods]** We retrospectively reviewed cervical cancer patients undergoing cisplatin-based CCRT at our two hospitals from January 2019 to August 2023, excluding those with poor performance status and pre-existing renal impairment. SH involved within 2 liters of fluid within 5 hours on cisplatin days, while prolonged hydration (LH) exceeded this method. We compared serum creatinine levels (sCr, mg/dL) at baseline, after each cisplatin dose, and 3-6 months post-CCRT (long term) between the two groups. **[Results]** Among 86 patients, 25 received short hydration (SH), and 61 received LH. Mean age of SH group was higher than that of LH group (49, 56 years old, $p = 0.047$). There was no significant difference in body weight, stage, ratio of patient underwent surgery, and total cisplatin dose per body surface area between two groups. No patient in the SH group required dose reduction or discontinuation of cisplatin due to nephrotoxicity, while one and two patients in the LH group, respectively. Mean sCr at baseline, the last cisplatin dose, and the long term were 0.62, 0.56 in SH, and 0.60, and 0.62, 0.59, and 0.63 in LH ($P=0.87$, $P=0.04$, $P=0.16$). **[Conclusion]** SH in CCRT using cisplatin for cervical cancer is safe for renal protection.

IS-WS-10-2

Is Presumed Clinical Stage I Endometrial Cancer, Diagnosed via PET-CT and MRI, Truly Stage I in Surgical Stage? Seon Ki Eun, Je Songhyeon, Lee Young Jae, Lee Jung-Yun, Nam Eun Ji, Kim Sunghoon, Kim Young-Han, Kim Young Tae, Kim Sang Wun *Yonsei University College of Medicine, Seoul, Korea*

[Objective] This study evaluated actual lymph node (LN) metastasis and recurrence rate in patients presumed clinical stage I endometrial cancer using preoperative MRI and PET-CT. **[Methods]** This retrospective study analyzed 423 patients undergoing surgical staging for endometrial cancer between July 2014 and June 2023. The selected patients, assumed to have clinical stage I endometrial cancer, underwent both pelvic and paraaortic LN assessment during surgical staging. Exclusion criteria included a history of other malignancies, radiation therapy, lymphadenectomy, and prior hysterectomy for non-malignant reasons. **[Results]** Postoperative up-staging was observed in 64 patients (15.1%). LN metastasis occurred in 24 patients (5.7%), revealing a 0.943 negative predictive value for imaging. Among these, 20 (4.7%) and 12 (2.8%) patients had PLN and PALN metastasis respectively. Depth of myometrial invasion on MRI (OR 9.2) and BMI of $>25\text{kg/m}^2$ (OR 4.4) emerged as significant PALN metastasis risk factors. Tumors $\leq 2\text{cm}$ in low/intermediate risk groups showed no LN metastasis. During follow-up, 35 patients (8.3%) exhibited recurrence, 3.8% of which were distant organ recurrences. Independent predictors of recurrence were grade 3 endometrioid/non-endometrioid histologic type and myometrial invasion depth. Compared to the low/intermediate risk group ($n=252$), the high-risk group ($n=171$) showed more pronounced up-staging (22.2%), LN metastasis (10.5%), and recurrence (14.6%). **[Conclusion]** Preoperative MRI and PET-CT show limited accuracy in detecting LN metastasis in presumed clinical stage I endometrial cancer, especially in high-risk groups. Notable postoperative up-staging, increased LN metastasis, and higher recurrence rates in this group highlight the critical importance of surgical staging for precise diagnosis and individualized treatment planning.

IS-WS-10-3

Prognostic Significance of Neutrophil-to-Lymphocyte Ratio, Platelet-to Lymphocyte Ratio, or Monocyte-to-Lymphocyte Ratio in Uterine Carcinosarcoma Sakurai Azusa¹, Yamaguchi Ken², Ishida Kentaro³, Honda Tetsuro⁴, Kawai Eri⁵, Kotani Yasushi⁶, Yamanishi Yukio⁷, Kishimoto Naoya⁸, Horikawa Naoki⁹, Tatsumi Keiji¹⁰, Okudate Minami¹¹, Mandai Masaki² *Shiga General Hospital¹, Kyoto University², Osaka Red Cross Hospital³, Kurashiki Central Hospital⁴, Tazuke Kofukai Foundation, Medical Research Institute, Kitano Hospital⁵, Kindai University⁶, Japanese Red Cross Society Wakayama Medical Center⁷, Kyoto Medical Center⁸, Shizuoka General Hospital⁹, Osaka National Hospital¹⁰, Kobe City Medical Center General Hospital¹¹*

[Objective] Immune status affects the prognosis of uterine endometrial cancer. However, it is unclear in stromal malignancies. This study aims to explore the association between pretreatment inflammatory biomarkers (Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Monocyte-to-Lymphocyte Ratio (MLR)) and the prognosis of uterine carcinosarcoma (UCS) and uterine sarcoma (US). **[Methods]** 237 patients (119 UCS, 118 US) treated at fourteen hospitals from 2008 to 2017 were assessed retrospectively. The progression free survivals (PFS) and overall survivals (OS) were analyzed by depicting Kaplan-Meier curves and using the log-rank tests. Cox regression analysis identified independent prognostic factors. **[Results]** Using the median values of NLR, MLR, and PLR as the cutoffs, high NLR and MLR showed significantly poorer PFS ($p=0.003$ and $p=0.01$, respectively); high PLR trended to show unfavorable prognosis ($p=0.09$) in UCS cases. In the US cohort, only a high PLR was significantly associated with poor outcomes, while NLR and MLR did not show a significant difference in prognosis. ROC analysis determined the optimal cutoffs in UCS as 4.0, 220, and 0.3 for NLR, MLR, and PLR, respectively. Univariate analysis indicated significantly worse PFS with elevated NLR, MLR, and PLR in UCS cases ($p<0.05$). When groups were divided based on all biomarker values being above the cutoffs, it revealed significantly poorer PFS and OS, confirming them as independent adverse prognostic factors in UCS. **[Conclusion]** Accumulation of high values of NLR, MLR, and PLR is an adverse prognostic factor, suggesting the association of immunity with the prognosis in UCS but not in US.

IS-WS-10-4

The efficacy of ReAcP53, an inhibitor of p53 aggregation, in treatment for p53-mutated gynecologic cancers Iwahashi Naoyuki, Fujino Megumi, Nishioka Kaho, Yahata Tamaki, Horiuchi Yuko, Ino Kazuhiko *Wakayama Medical University*

[Objective] We previously reported the involvement of p53 aggregates in poor prognosis and in chemotherapy resistance in p53-mutated ovarian cancers. The objective of this study was to investigate the efficacy of ReAcP53, an inhibitor of p53 aggregation, in treatment for multiple types of p53-mutated gynecologic cancers. **[Methods]** To analyze the effect and mechanism of p53 aggregates, we used patient-derived tumor organoids (PDOs) derived from patients with p53-mutated platinum-resistant gynecologic cancers including one ovarian cancer (*TP53* p.G199V), two endometrial cancer (*TP53* p.R213* / *TP53* p.R267W), and one cervical cancer (*TP53* p.Y220C). To analyze the effect of p53 disaggregation on PDO viability, PDOs were cultured with various concentrations of ReAcP53. Total RNA was extracted from vehicle-treated or ReAcP53-treated PDOs for the whole transcriptome analysis (RNA-seq). This study was approved by IRB. **[Results]** We detected the cytoplasmic co-localization of ProteoStat, a reagent for protein aggregation detection, with p53 deposits in all PDOs, which represent the existence of cytoplasmic p53-aggregates. ReAcP53 suppressed proliferation of all p53

aggregate-harboring PDOs. Platinum-resistance was reduced in all PDOs with co-culturing of carboplatin and ReAcP53. To clarify the gain-of-oncogenic function of p53 aggregates, we carried out RNA-seq of the ReAcP53-treated PDOs. Reactome pathway enrichment analysis revealed that ReAcP53 affect multiple pathways including dysregulation of the cell cycle and cell proliferation. **[Conclusion]** We demonstrated that p53 aggregates in p53-mutated gynecologic cancers may be targeted by ReAcP53 so as to inhibit tumor cell proliferation and improve the sensitivity to platinum-based agents. ReAcP53 could be the novel treatment for p53-mutated gynecologic cancers.

IS-WS-10-5

The Correlation of Homologous Recombination Repair Genes mutation and Clinical Outcome of Epithelial Ovarian Cancer Wang Yen-Han¹, Lin Po-Han², Kuo Kuan-Ting³, Tai Yi-Jou¹, Hsu Heng-Cheng⁴, Wu Chia-Ying¹, Chen Chi-An¹, Cheng Wen-Fang¹, Chiang Ying-Cheng⁴ *National Taiwan University Hospital Hsin-Chu Branch, Taiwan¹, Department of Medical Genetics, National Taiwan University Hospital, Taiwan², Department of Pathology, College of Medicine, National Taiwan University, Taiwan³, National Taiwan University Hospital, Taiwan⁴*

[Objective] Identification of homologous recombination deficiency, especially BRCA mutations, is critical to select patients for poly-adenosine diphosphate ribose polymerase inhibitor (PARPi) treatment and as a prognostic biomarker in high-grade serous epithelial ovarian carcinoma (EOC). However, its efficacy in other histology is not clear. **[Methods]** We identified mutation of homologous recombination repair (HRR) genes in EOC patients by a multiple-gene panel via next generation sequencing and correlated it with clinical outcomes. **[Results]** A total of 318 patients, including 177 serous EOC and 141 non-serous EOC were enrolled. HRR gene mutations (including BRCA mutations) were more frequent in serous than in non-serous EOC (25.4% vs. 7.8%, $P < 0.001$). The high-grade serous EOC patients with HRR gene mutations showed increased platinum sensitivity and longer progression free survival and overall survival ($P < 0.01$). However, no significant association was shown between HRR gene mutations and platinum sensitivity or disease survival in non-serous EOC patients. **[Conclusion]** HRR gene mutation is a prognostic biomarker in high-grade serous EOC patients. Further study may be conducted to identify other markers for non-serous EOC patients.

IS-WS-10-6

The application of TCGA endometrial cancer molecular classification gene panel in epithelial ovarian cancer patients and the correlation with clinical outcomes Chiang Ying-Cheng¹, Lin Po-Han², Tai Yi-Jou¹, Heng-Cheng Hsu¹, Wang Yen-Han¹, Wu Chia-Ying¹, Chen Chi-An¹ *National Taiwan University Hospital, Taiwan¹, Medical Genetics, National Taiwan University Hospital, Taiwan²*

[Objective] TCGA endometrial cancer molecular classification by POLE, MMR and P53 has prognostic value in the endometrial cancer, but its application in epithelial ovarian cancer is not clear. **[Methods]** We investigated the somatic mutations of 181 EOC patients using a panel of POLE, MMR and P53 by next generation sequencing. **[Results]** The classification included POLE mutation in 1 patient (0.5%), MMR mutation in 21 patients (11.6%), P53 in 68 patients (37.6%) and NSMP in 91 patients (50.3%). The patterns were significantly different in histology [serous (POLE : 0%, MMR : 6.4%, P53 : 75.7%, NSMP : 17.9%), endometrioid (POLE : 2.8%, MMR : 22.2%, P53 : 16.7%, NSMP : 58.3%) versus clear cell (POLE : 0%, MMR : 11.9%, P53 : 4.5%, NSMP : 83.6%)] ; chi-square test, $p < 0.001$]; FIGO stage [early (POLE : 1.4%, MMR : 11.3%, P53 : 9.8%, NSMP :

77.5%) versus advanced (POLE : 0%, MMR : 11.8%, P53 : 55.5%, NSMP : 32.7%) ; $p < 0.001$] ; tumor grade [low (POLE : 3.8%, MMR : 19.2%, P53 : 11.5%, NSMP : 65.5%) versus high (POLE : 0%, MMR : 10.3%, P53 : 41.9%, NSMP : 47.8%) ; $p = 0.002$] ; recurrence [no (POLE : 1.4%, MMR : 11.3%, P53 : 21.1%, NSMP : 66.2%) versus recurrence (POLE : 0%, MMR : 11.9%, P53 : 47.7%, NSMP : 40.4%) ; $p = 0.002$] and death [alive (POLE : 1.0%, MMR : 9.2%, P53 : 25.5%, NSMP : 64.3%) versus death (POLE : 0%, MMR : 14.5%, P53 : 51.8%, NSMP : 33.7%) ; $p < 0.001$]. There was significant difference in disease free survival (POLE : not reached, MMR : 12.5 months, P53 : 8.5 months, NSMP : 36.5 months ; log-rank test, $p = 0.002$) and overall survival (POLE : not reached, MMR : 41 months, P53 : 47 months, NSMP : not reached ; $p = 0.008$). **[Conclusion]** The pattern of POLE, MMR, P53 and NSMP varied significantly in histological subtypes, FIGO stage, tumor grade, tumor recurrence and tumor-related death of EOC patients. EOC patients with POLE mutation or NSMP had favorable survival than patients with MMR or P53 mutation.

IS-WS-10-7

Effect of Muscle Loss but Not Fat Loss during Primary Debulking Surgery and Chemotherapy on Prognosis of Patient with Ovarian Cancer Ishibashi Tomoka¹, Ishikawa Masako², Yamashita Hitomi², Kondo Yoshimi¹, Sato Rei¹, Kuramoto Yasuha¹, Kurakane Satomi¹, Seki Koichirou¹, Kojima Kazuhisa¹, Murakami Isamu¹, Kyo Satoru², Nakayama Kentaro¹ Nagoya City University East Medical Center¹, Shimane University Hospital²

[Objective] Although the negative effect of muscle loss during invasive treatment has been widely reported in patients with cancer, its value in patients with ovarian cancer is not clear. Therefore, this study was conducted to clarify whether muscle loss during cytoreductive surgery and chemotherapy affects prognosis in patients with ovarian cancer. **[Methods]** We retrospectively recruited 58 patients with ovarian cancer who underwent site reductive surgery and chemotherapy from March 2006 to November 2013 and for whom pre- and postoperative computed tomography were available. Skeletal muscle changes and fat mass volume during primary debulking surgery and chemotherapy were subsequently investigated at the level of the third lumbar vertebra. Muscle and fat mass loss occurred independently in half of the patients. **[Results]** Muscle loss, but not fat loss, was associated with disease-free survival ($p = 0.041$ and $p = 0.794$, respectively) and poor overall survival ($p = 0.033$ and $p = 0.61$, respectively). Cancer therapy is invasive and causes compositional changes in the body, such as muscle and fat loss. **[Conclusion]** During cancer therapy, muscle loss, but not fat loss, may be associated with worse prognosis in ovarian cancer.

IS-WS-10-8

Surgical outcomes after nerve-sparing radical hysterectomy for cervical cancer Kim Jeong Yun, Lim Myong Cheol Uterine Cancer Center, National Cancer Center, Korea

[Objective] To evaluate the surgical outcomes of a nerve-sparing radical hysterectomy (RH) for cervical cancer. **[Methods]** This retrospective cohort study included the patients with 2018 International Federation of Gynecology and Obstetrics (FIGO) stage IA1 to IIIC2 cervical cancer who treated with nerve-sparing RH by a single experienced gynecologic oncologist from May 2012 to March 2023. The postvoid residual volume was measured using ultrasonography after transurethral catheter removal. If necessary, the catheter was reinserted for 24-48 hours. If urinary retention persisted, the patient was educated clean intermittent catheterization (CIC) instruction and

discharged. **[Results]** Of 119 patients, 75 (63.0%) underwent laparotomy, and 44 (37.0%) did minimally invasive surgery (MIS : 23 laparoscopy, 21 robot-assisted surgery). Stage IB2 was most prevalent in the laparotomy group, while stage IA1 was in the MIS group. The time to spontaneous voiding and the postoperative length of stay were significantly longer for patients in the laparotomy group than for patients in the MIS group (median 5 [range : 1-10] and 7 [3-29] days vs 3 [1-7] and 4 [2-10] days ; $p < 0.001$, respectively). 15 (12.6%) women were trained to continue CIC (laparotomy : 12, MIS : 3 ; $P = 0.145$). With a median follow-up time of 44 months, overall survival and recurrence-free survival at 3 years were 98.9% and 91.7%, respectively. **[Conclusion]** Our findings support surgical feasibility and favorable oncological outcomes after nerve sparing RH.

IS-WS-11-1

Comparative Metagenomic Study of Vaginal Microbiota in Women Infected with HPV 16/18 and Other High-risk HPV Subtypes : Multi-kingdom Microbiota Approach Lee Sae Rom¹, Jung Da-Ryung², Kim Jong Mi¹, Lee Yoon Hee¹, Hong Dae Gy¹, Chong Gun Oh¹, Shin Jae-Ho^{2,3} Kyungpook National University Chilgok Hospital, Korea¹, Department of Applied Biosciences, Kyungpook National University, Korea², NGS Core Facility, Kyungpook National University, Korea³

Objective : Recent studies have elucidated that the risk ratio for CIN is clinically higher for HPV 16/18 compared to other hr-HPV subtypes and lower clearance rate of HPV 16/18 infection compared to other hr-HPV infection, this alone does not account for the formation and progression of cervical cancer by HPV 16/18. Therefore, we delved deeply into the role of the vaginal microbiome in influencing the association between HPV 16/18 infection and the progression of CC. **Methods :** In this cross-sectional study, we performed comprehensive metagenome analysis on vaginal swab from 68 women infected with HPV 16/18 ($n = 30$) or other hr-HPV subtypes ($n = 38$), subdivided into normal & low-grade CIN, high-grade CIN, and CC. **Results :** Upon assessing the community state type of VM across groups, both the N/LSIL and HSIL groups showed a lower portion of CST I (dominated by *L.crispatus*) and III (dominated by *L.iners*) in the HPV 16/18 group compared to the other hr-HPV group. Additionally, VM in HPV 16/18 was characterized by higher levels of *S.dysgalactiae*, *G.leopoldii* and *F.vaginae* compared to other hr-HPV. In N/LSIL, *Lactobacillus* spp., which showed high abundance in HPV 16/18, exhibited a strong negative correlation with *C.papillibeta2*. Conversely, in CC, several bacteria recognized as pathogens in female genital health displayed negative correlations with human endogenous retrovirus K and *C.papillibeta3*. **Conclusion :** In our research, through the utilization of metagenomic data, we achieved high-resolution microbiome profiling and therefore provides in-depth and definitive knowledge about the VM composition via multi-kingdom microbiota approach.

IS-WS-11-2

Inhibition of HPV18-dependent cervical adenocarcinoma formation in mice model by an ErbB3 (Her3) inhibitor Sugi Toshihiro, Kamata Saki, Kobayashi Osamu, Okuma Yuki, Nakajima Takahiro, Ikeda Yuji, Matsuda Erina, Aoki Aiko, Kawakami Kaori, Komatsu Atsushi, Saitou Keisuke, Kawana Kei Nihon University Itabashi Hospital

[Objective] Cervical adenocarcinoma is often refractory to radiotherapy and chemotherapy and has a poor prognosis. We have established an induced cervical reserve cell (iRC) from iPS cell and found that ErbB3 is one of the genes that characterize HPV18-dependent adenocarcinoma using adenocarcinoma model with HPV18 E6/E7-transduced iRC (iRC18). Here we ex-

amined whether an ErbB3 inhibitor, pertuzumab, has anti-tumor effect on the mice tumor with iRC18. **[Methods]** iRC18 cells were injected with matrigel subcutaneously into NOD-scid mice. Pertuzumab or saline (control) was administered subcutaneously twice a week in three mice per each group. HPV-dependent glandular structure was identified by immunohistochemistry for E-cadherin instead of p16, because control (iPS) cells are positive for p16. The number and area of glandular structures was analyzed using computer imaging software. Mann-Whitney test was used for statistical analysis. **[Results]** Subcutaneous tumors in mice became enlarged at 12 weeks after injection in both groups. Although the tumor size did not differ between pertuzumab and control groups, the number of glandular structures in the tumors was clearly less in pertuzumab group than in control ($p=0.004$). The proportion of E-cadherin-positive glandular structure area to tumor size was also lower in pertuzumab group than in control ($p=0.047$). **[Conclusion]** Inhibition of ErbB3 pathway led to suppress formation of glandular structures in HPV-dependent adenocarcinoma model. It is suggested that the ErbB3 pathway is closely involved in the formation of adenocarcinoma by HPV18, and its inhibitor may inhibit the growth of cervical adenocarcinoma.

IS-WS-11-3

Assessment of clinical features and immunological desert tumor microenvironment of gastric-type adenocarcinoma of the cervix uteri Matsuda Risa, Nishio Hiroshi, Chiyoda Tatsuyuki, Kimura Yumiko, Matsui Tomoya, Iwata Takashi, Yamagami Wataru, Tanaka Mamoru *Keio University Hospital*
[Objective] Gastric-type adenocarcinoma (GAS) is a rare histological type of cervical cancer with poor prognosis due to resistance to conventional treatments including immunotherapy. In this study, we aimed to clarify clinical features including genomic analysis and assess tumor immune-microenvironment of GAS. **[Methods]** We selected 17 of newly diagnosed patients with GAS and 24 cases of usual endocervical adenocarcinoma (UEA) between 2018 and 2022. We investigated clinical characteristics and cancer gene panel tests undergoing comprehensive genomic profiling (CGP) (FoundationOne® CDx, FoundationOne® Liquid CDx, and PleSSision Rapid). We also established organoids and evaluated T cell infiltration by flow cytometry (FACS). **[Results]** The median observation period among GAS cases was 22 months (range : 4-61 months). GAS cases had higher age at diagnosis compared with UEA cases (years old, median [range], 51 [33-70] vs 40 [29-56] ; p value < 0.001). While clinical stages were comparable between the two groups, progression free survival was shorter in GAS cases (months, 11 [1-41] vs 33 [1-61] ; p value = 0.044). Five GAS cases had CGP testing and tumor mutation burden was low in all cases with microsatellite stable status. 80% (4/5) had *TP53* mutation and two cases revealed druggable variants with *FGF* and *FGFR*, respectively. FACS analysis of three GAS derived organoids showed that the GAS cases had significantly lower levels of CD8⁺ lymphocytes compared to UEA derived organoids. **[Conclusion]** GAS cases have poor treatment outcomes with low tumor mutation burden and low CD8⁺ T cell infiltration within the tumor which could lead to resistance to immunotherapy.

IS-WS-11-4

Quantification of circulating tumor human papillomavirus DNA by digital PCR in cervical cancer patients Matsunaga Asami^{1,2}, Ogawa Miho^{2,3}, Ikeda Yuji¹, Kunita Akiko², Okuma Yuki¹, Kobayashi Osamu¹, Hayashi Nobuki¹, Nakajima Takahiro¹, Komatsu Atsushi¹, Saitou Keisuke¹, Kawana Kei¹, Oda Katsutoshi^{2,3} *Nihon University Itabashi Hospital¹, Division*

of Integrative Genomics, The University of Tokyo², Department of Clinical Genomics, The University of Tokyo³

[Objective] Over 90% of cervical cancers are induced by infection with high risk HPV (human papillomavirus, types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59). Although detection of circulating tumor HPV DNA (ctHPV DNA) may be useful as a specific biomarker, quantitative PCR (qPCR) has difficulty in detecting cell-free HPV DNA due to its low amount. We aim to explore the utility of digital PCR (dPCR) for type-specific, ctHPV DNA detection. **[Methods]** Under written informed consent (Ethical committee approval number : RK-170711-6), blood samples were obtained from 24 cervical cancer patients before the curative surgery (Stage IA1-IIIc1). DNA from plasma was extracted with QIAamp Circulating Nucleic Acid Kit. Type-specific primers, and artificial oligopeptides (as positive controls) were designed for dPCR. HPV-typing of the corresponding FFPE samples was also tested by dPCR. **[Results]** We successfully evaluated 5 high-risk HPV types (16, 18, xx, xx, xx) by dPCR using the control specimens. ctHPV DNA of type 16 and 18 was detected in 3 of 11 samples (27.3%) from 22.0-362.8 copy/ml (2 with HPV-16 and 1 with HPV-18). ctHPV DNA levels were correlated with the HPV copy number from the FFPE samples ($p=0.0005$), tumor size ($p<0.0001$), lymph node metastasis ($p<0.0001$) and vascular invasion ($p<0.0001$). We are currently conducting dPCR of the 5 high-risk HPV types in samples from both FFPE and plasma. **[Conclusion]** Our data suggest that ctHPV DNA can be selectively detected and quantified by dPCR in early-stage cervical cancers, suggesting that ctHPV DNA levels may be useful biomarkers of the disease progression.

IS-WS-11-5

Single-Cell Transcriptomic Analysis Unveils the HPV-Associated Gene Signature and Potential Prognostic Biomarkers for HPV-Associated tumors Kamei Yuji¹, Kimura Toshihiro¹, Mukaida Hitomi¹, Kobayashi Mariya¹, Watanabe Yuku¹, Masuda Tatsu², Kakuda Mamoru¹, Nakagawa Satoshi¹, Hiramatsu Kosuke¹, Ueda Yutaka¹, Kimura Tadashi¹ *Osaka University¹, StemRIM Institute of Regeneration-Inducing Medicine, Osaka University²*

[Objective] The optimal clinical testing method for distinguishing between HPV-associated and HPV-independent cervical cancer, as well as the underlying molecular intricacies influencing the prognostic determinants of HPV, remains under-investigated. The primary objective of this research was to discern potential prognostic biomarkers capable of categorizing HPV-associated and HPV-independent tumors. **[Methods]** We obtained four scRNA-seq data from HPV16-positive cervical intraepithelial neoplasia grade 3 (CIN3). The Seurat package was used for scRNA-seq analysis. Copy number alterations (CNAs) were estimated using the infercnv package. Non-negative matrix factorization (NMF) was utilized to identify cellular programs, and an overall survival prediction model was formulated via univariate Cox and regularized Cox regression. **[Results]** Our study discerned the HPV-related gene signature enriched in HPV-detected cells. Within The Cancer Genome Atlas (TCGA) cervical cervical squamous cell carcinoma (SCC) dataset, the enrichment of this gene signature was an independent favorable prognostic indicator. Fourteen genes in the signature were selected for a survival prediction model. These genes demonstrated efficacy in differentiating HPV-negative and HPV-positive samples in HPV-associated tumors, providing reliable prognostic predictions. **[Conclusion]** The scRNA-seq analysis of CIN3 revealed the HPV-related gene signature and potential prognostic biomarkers for categorizing HPV-associated and HPV-independent tumors. Even though further investigations are imperative, these results could illuminate the favorable

prognostic attributes of HPV-associated tumors and develop new treatment approaches.

IS-WS-11-6

Genomic characterization of coexisting gastric-type adenocarcinoma and lobular endocervical glandular hyperplasia using whole-exome sequencing Kuruma Airi¹, Kodama Michiko¹, Masuda Tatsuo², Komura Naoko², Kawano Mahiru¹, Kinose Yasuto¹, Hashimoto Kae¹, Yokoi Takeshi², Sawada Kenjiro¹, Kimura Tadashi¹ *Osaka University¹, Kaizuka City Hospital², StemRIM Institute of Regeneration-Inducing Medicine, Osaka University³*

[Objective] Gastric-type adenocarcinoma of the cervix (GAS) is a human papillomavirus-unrelated, and aggressive and treatment-resistant cancer. Recently, sporadic reports have emerged regarding the patterns of genetic variation in GAS, using cancer gene panel tests. Lobular endocervical glandular hyperplasia (LEGH) is considered a precursor lesion to GAS, but the mechanism of progression to GAS is not clear. Our study aimed to elucidate the stepwise process involved in carcinogenesis from LEGH to GAS. **[Methods]** Seven patients who had a hysterectomy with a diagnosis of GAS and coexisting LEGH were included in this study. We collected each tissue section of GAS, LEGH, normal endocervical gland, and normal myometrium by laser-microdissection from formalin-fixed, paraffin-embedded tissue blocks and extracted each genomic DNAs, and whole-exome sequencing (WES) was performed. Single nucleotide variants (SNVs) and copy number variants (CNVs) were called by Genome Analysis Tool kit based human reference genome (GRCh38). Phylogenetic tree analysis using SNVs and CNVs, and mutational signature analysis were performed. **[Results]** Previously reported GAS/LEGH-related genes were also identified in our GAS/LEGH data sets. Somatic mutations in TP53 (3/7 ; 42.9%) were most commonly identified in GAS, with other mutations in ERBB2, CDKN2A, STK11, GNAS, and SMAD4. LEGH harbored a somatic mutation in STK11 in one case, the variant allele frequency of which was increased in GAS. Phylogenetic tree analysis showed GAS and LEGH shared common mutations in three cases. Mutational signature analysis showed the majority of GAS/LEGH displayed the aging-related Signature1. **[Conclusion]** WES of co-existing GAS and LEGH suggested the possibility of progression from LEGH to GAS in some cases.

IS-WS-11-7

BHLHE40 regulates energy metabolism mediated by a PPM phosphatase-AMPK axis in endometrial cancer cells Asanoma Kazuo, Yagi Hiroshi, Onoyama Ichiro, Kawakami Minoru, Tomonobe Hiroshi, Hachisuga Kazuhisa, Maenohara Shoji, Kodama Keisuke, Yasunaga Masafumi, Yahata Hideaki, Kato Kiyoko *Kyushu University*

[Objective] Cancer cells are known to dominantly depend on glycolysis for energy production. However, regulatory mechanism of metabolism in cancer cells remains largely unknown. In this study, we studied a regulation of energy metabolism by a tumor suppressive transcription factor, BHLHE40 in endometrial cancer cells. **[Methods]** We used endometrial cancer cells to knockdown or overexpress BHLHE40 to examine their glycolysis and oxidative phosphorylation using a flux analyzer. The expression and activity of AMP-activated protein kinase, AMPK ; lactate dehydrogenase, LDHA ; and pyruvate dehydrogenase, PDH were examined. A PPM family of phosphatase was found to regulate phosphorylation of AMPK α . Transcriptional regulation of PPM family by BHLHE40 was also examined using a reporter assay, gel-shift assay and ChIP assay. Immunohistochemical analysis of BHLHE40, PPM phosphatases

and AMPK α was performed. A microarray and proteomic analysis was also performed to identify downstream of the BHLHE40 pathway. **[Results]** BHLHE40 suppressed glycolysis accompanied by downregulation of LDH activity, and also enhanced oxidative phosphorylation accompanied by upregulation of PDH activity. We found that BHLHE40 enhanced phosphorylation of AMPK α by suppressing the transcription of its specific phosphatase, PPM1F. We also found that the expression of BHLHE40, PPM1F and phosphorylated AMPK α correlated with the prognosis of endometrial cancer patients. **[Conclusion]** BHLHE40 is suggested to regulate the activity of AMPK mediated by PPM1F phosphatase to control the energy metabolic balance between glycolysis and oxidative phosphorylation in endometrial cancer cells. Understanding the mechanism of energy production in cancer cells might lead to a new strategy to control the development of endometrial cancer.

IS-WS-11-8

Advancements in Targeted Therapies Addressing Homologous Recombination Repair Deficiency (HRD) and CDK12 Gene Aberrations in Uterine Serous Carcinoma Kawahara Shunsuke¹, Hamanishi Junzo¹, Murakami Ryusuke¹, Taki Mana¹, Yamanoi Koji¹, Yamakawa Hiroko², Hamada Kohei¹, Watanabe Koichi¹, Takamatsu Shiro¹, Miyamoto Taito¹, Yamaguchi Ken¹, Mandai Masaki¹ *Kyoto University¹, Chordia Therapeutics Inc.²*

[Objective] Uterine serous carcinoma (USC) constitutes a highly aggressive subtype within the spectrum of endometrial cancers, necessitating the exploration of innovative therapeutic strategies. This study aims to elucidate the genetic characteristics of USC, with a specific focus on aberrations in genes associated with homologous recombination repair (HR), particularly CDK12. We seek to investigate the potential link between CDK12 abnormalities, clinical prognosis, and the prospect of novel treatment modalities. **[Methods]** HR deficiency (HRD) scores were computed and compared across different histological types of uterine cancer, utilizing data from The Cancer Genome Atlas (TCGA). In vivo experiments entailed the administration of PARP inhibitors and/or CDK12 inhibitors (specifically, CTX-439) to patient-derived xenograft (PDX) models of USC and human USC cell lines. Subsequent to drug treatment, tumor samples were collected and subjected to RNA sequencing for comparative analysis between the control and CDK12 inhibitor treatment groups. **[Results]** Analysis of TCGA data revealed that HRD scores in USC were significantly elevated when compared to other histological subtypes of uterine cancer. In vivo experimentation demonstrated the efficacy of CDK12 inhibitors in 2 out of 4 PDX patients and 2 out of 2 human cell lines, with enhanced effects observed when combined with PARP inhibitors. Moreover, the CDK12 inhibitor-treated group exhibited decreased expression levels of HR-related genes, as indicated by RNA sequencing, in contrast to the control group. **[Conclusion]** Uterine serous carcinoma is characterized by a high prevalence of HR gene abnormalities, suggesting that CDK12 inhibition may represent a promising therapeutic avenue for this recalcitrant cancer subtype.

IS-WS-11-9

Tumor Microenvironment Assessment Shows TILs as Predictors of OCCC Outcomes, Regardless of ARID1A Alterations Kubokawa Mei, Yoshikawa Nobuhisa, Matsukawa Tetsuya, Iyoshi Shohei, Yoshida Kosuke, Yoshihara Masato, Tamauchi Satoshi, Ikeda Yoshiki, Shimizu Yusuke, Yokoi Akira, Niimi Kaoru, Kajiyama Hiroaki *Nagoya University*

[Objective] To assess the association between tumor-infiltrating lymphocytes (TILs), tumor-associated macrophages (TAMs), ARID1A mutations, and the prognosis in ovarian clear cell car-

cinoma (OCCC) patients, and to identify potential blood biomarkers reflecting local immune responses. **[Methods]** We analyzed 90 OCCC patients with a median observation period of 5 years. Immunohistochemical staining was used to quantify TILs (CD8 positive cells) and TAMs (CD68 and CD163 positive cells) on a scale of 0-2. The presence or absence of ARID1A mutations was classified based on IHC staining. Blood data at the time of diagnosis was also obtained. **[Results]** A significant positive correlation was observed between TILs and both CD68 and CD163 positive TAMs ($p=0.0042, 0.0002$). Within OCCC, we identified two distinct subsets: one with notable TILs and TAMs infiltration, and another with minimal immune cell presence. However, no correlation was found between ARID1A mutations and the infiltration of TILs and TAMs. OCCC patients with a high infiltration score of 2 for TILs ($n=15$) showed a trend toward better prognosis compared to those with scores of 0-1 ($n=75$) ($p=0.1796$). No such trend was observed for TAMs. Integrating peripheral blood data with IHC results, we found that lymphocyte and neutrophil counts in the blood significantly correlated with TIL infiltration ($P=0.0253, 0.0326$). **[Conclusion]** Regardless of ARID1A mutations, the infiltration of TILs may correlate with prognosis. The correlation between peripheral blood lymphocyte and neutrophil counts and TIL infiltration suggests that systemic immune environments might reflect local immune responses in OCCC.

DGGG-1

The edematous change in the placenta as predicting markers of preterm birth in post-Fontan pregnancy : a single-center observational study Watanabe Tomoyuki, Yamaoka Yuika, Suzuki Takashi, Ishikawa Gen, Kakogawa Jun *Tokyo Women's Medical University*

[Objective] Fontan operation is a palliative surgery commonly performed for functional single-ventricular heart diseases. Fontan circulation is characterized by elevated central venous pressure and a low cardiac output, leading to long-term complications with other organ systems, high miscarriages, and premature deliveries. Previous studies have reported that placenta in post-Fontan pregnancies often exhibit edematous changes on ultrasonography. We investigated edematous changes as a risk factor for premature delivery in post-Fontan pregnancy. **[Methods]** We reviewed clinical charts and ultrasonograms in post-Fontan pregnancies who were followed up 2015-2011. During the study period, 15 women with Fontan physiology delivered at our hospital. **[Results]** The mean maternal age at delivery was 28.4 years (20-37) and mean gestational age at delivery was 31.8 weeks (28-37). Edematous change in the placenta were observed in eight pregnancies (53%). Among these, six (75%) experienced premature labor. "Small for gestational age" was observed in one of eight pregnancies (12.5%). In seven pregnancies without edematous placental changes, all deliveries occurred on the pre-scheduled dates determined based on maternal heart condition. **[Conclusion]** Patients who have undergone Fontan operation often exhibit high systemic venous pressure and low cardiac output. These factors may contribute to utero-placental insufficiency, leading to edematous changes of the placenta. Notably, pregnancies with edematous changes in the placenta have a significantly higher risk of preterm delivery than pregnancies without these changes. Therefore, edematous placental changes serve as a valuable predictive marker for preterm birth in post-Fontan pregnancies.

DGGG-2

Forced expression of the angiogenesis regulator vasohibin-1 increases paclitaxel sensitivity of ovarian cancer cells through inhibition of microtubule activity Koyanagi Takahiro, Saga Yasushi, Takahashi Yoshifumi, Tamura Kouhei, Shinohara Miki, Takahashi Suzuyo, Taneichi Akiyo, Takei Yuji, Fujiwara Hiroyuki *Jichi Medical University*

[Objective] An angiogenic inhibitor, vasohibin-1 (VASH1), exhibits detyrosination actions, which are involved in microtubule activity. A core drug for ovarian cancer, paclitaxel, has a point of action on microtubules. We examined the influence of VASH1 on the paclitaxel susceptibility. **[Methods]** 1) VASH1 expression vector was transferred to two serous ovarian cancer cell strains. VASH1 expression was detected using qPCR and Western blotting. 2) The culture supernatant from ovarian cancer cells with forced VASH1 expression was added to human umbilical vein endothelial cells (HUVECs), and the number of viable cells after 48 hours was measured using WST-1 assay. 3) Ovarian cancer cells with forced VASH1 expression were exposed to paclitaxel or cisplatin. The number of viable cells after 48 hours was measured using WST-1 assay, and the IC₅₀ was calculated. 4) Detyrosinated tubulin and cyclin B1, a marker of the middle M phase during which paclitaxel susceptibility reaches a maximum, expressions were examined using Western blotting. **[Results]** 1) Strong VASH1 expression in the VASH1-gene-transferred cells was confirmed. 2) The number of viable cells in the HUVECs to which the culture supernatant from VASH1-expressing cells was added was smaller than in the control cells. 3) The paclitaxel susceptibility of the VASH1-expressing ovarian cancer cells was markedly enhanced in comparison with the control

cells. There was no difference in cisplatin susceptibility. 4) In the VASH1-expressing ovarian cancer cells, detyrosinated tubulin and cyclin B1 expressions were enhanced in comparison with the control cells. **[Conclusion]** Ovarian cancer treatment strategy with VASH1 may inhibit angiogenesis and potentiate the effects of chemotherapy through inhibition of microtubule activity when combined with it.

DGGG-3

CA125 decreasing kinetics is a superior prediction factor in NAC/IDS of advanced ovarian cancer Yasuda Ipppei¹, Matsui Nozomi², Morita Noritsugu¹, Tani Eri¹, Yoshida Mihoko^{1,3}, Takemura Kyoko¹, Shima Tomoko¹, Nakashima Akitoshi¹ *University of Toyama¹, Tonami General Hospital², Saiseikai Toyama Hospital³*

[Objective] Cases of neoadjuvant chemotherapy (NAC) before interval debulking surgery (IDS) increase for unresectable advanced ovarian cancer. The methods of maintenance therapy after chemotherapy can be chosen for homologous recombination deficiency (HRD) status in the cancer tissues. This study investigated the factors, including HRD, to predict complete surgery in NAC/IDS in our hospital. **[Methods]** We evaluated 13 advanced ovarian cancer (serous carcinoma) cases that were received HRD test during NAC/IDS between January 2021 and March 2023. **[Results]** HRD cases were 9 (69%). The comparative study showed no significant differences between HRP and HRD at the factors below : the number of NAC cycles ; 5 (3-6) vs. 5 (4-8), the rate of complete surgery (CS) in IDS ; 1/4 (25%) and 4/9 cases (44.4%), tumor reduction ratio by chemotherapy ; 59.4% (29.1-73.9) vs. 60.4 (55.5-71), the CA125 decreasing kinetics (tumor marker (TM) after 4 cycles / TM before treatment) ; 74.8 (17.4-108.4) vs 46.2 (31.7-217.1), and the KELIM score ; 1.15 (0.66-1.73) and 1.515 (0.93-1.8). When comparing between CS and not CS, CS group showed significantly higher the CA125 decreasing kinetics, 68.9 (55.4-217.1) vs 31.7 (17.4-67.3) ($p=0.0216$), and the KELIM score were 1.52 (1.01-1.8) and 1.05 (0.66-1.55) ($p=0.0538$). **[Conclusion]** HRD status predicts platinum-sensitivity in the clinical field. In addition, our study suggested that CA125 decreasing kinetics was a useful marker for prediction of CS in IDS. Hereafter, we have to find out how to treat the case with lower the CA125 kinetics.

DGGG-4

Hydrostatic pressure under hypoxia enables the fabrication of biological grafts using human umbilical artery smooth muscle cells Kojima Tomoyuki^{1,2}, Saito Junichi², Ishikawa Yoshihiro³, Miyagi Etsuko¹, Yokoyama Utako² *Yokohama City University¹, Department of Physiology, Tokyo Medical University², Cardiovascular Research Institute, Yokohama City University³*

[Objective] For congenital heart diseases surgeries, biological grafts those contains natural networks of cell-extracellular matrix (ECM) interaction are desired. Human umbilical artery smooth muscle cells (hUASMCs) are ideal source because of no immunological and ethical issues. Graft fabrication from hUASMCs however included complicated and long processes. To fabricate clinical biological grafts *in vitro*, we aimed to investigate practical method. **[Methods]** We cultured hUASMCs with hydrostatic pressure under hypoxia (HP/HYP) and fabricated artificial grafts. After those grafts were implanted in rats' abdominal aorta, implantation were evaluations by immunohistochemical analysis, RNA-sequencing and RT-PCR of both grafts and implantation sites. **[Results]** Practical biological grafts were successfully obtained in HP/HYP. They had enough strength against blood pressure and enough tensile rupture (0.28 ± 0.06 MPa). In contrast of synthetic materials, natural network

of cell-ECM interaction was observed. The SMCs from native aorta attached to our grafts *in vivo*. Most of recipient rats were alive with grafts (19/20). Luminal side of grafts was completely endothelialized after a week. Implantation sites were patent after 5 months, when implanted hUASMCs were absorbed and completely replaced with host cells. In grafts' transcriptome analysis, increased N-cadherin mediated cell-cell adhesion (via N-myc downstream regulated gene 1), cell-matrix interaction (i. e. integrin $\alpha 5 \beta 1$), promoted secretion of collagen fibronectin, and increased lysyl oxidase (cross-linked ECM) were observed, suggesting natural network of cell-ECM interaction. **[Conclusion]** We successfully fabricated clinical biological grafts using hUASMCs and implanted in recipient rats. The HP/HYP condition is critical to construct practical graft with natural network of cell-ECM interaction.

DGGG-5

Cancer-associated fibrosis as a potential therapeutic target for peritoneal progression of refractory ovarian cancer Yoshihara Masato¹, Fujimoto Hiroki¹, Iyoshi Shohei¹, Miyamoto Emiri¹, Mogi Kazumasa¹, Uno Kaname¹, Kitami Kazuhisa², Sugiyama Mai³, Koya Yoshihiro³, Akihiro Nawa³, Kajiyama Hiroaki¹ Nagoya University¹, Kitasato University², Bell Research Center, Nagoya University Graduate School of Medicine³

[Objective] Cancer-associated fibrosis (CAFib) is a condition where tumor cells are surrounded by desmoplastic stroma afflicting extra-cellular matrix (ECM). This study focused on the role of CAFib in ovarian cancer (OvCa), especially its contribution to the peritoneal metastatic traits. **[Methods]** Highly metastatic OV-90-IP4 cells were established by 4-times serial intraperitoneal passages in mice using OV-90 cells. Functional analysis of OvCa progression was performed *in vitro* and *in vivo* by comparing OV-90-IP4 and parental OV-90 cells, and extent of CAFib was quantitatively analyzed by Masson-trichrome/Sirius-red staining. We further confirmed the cellular origin of CAFib using conditional knock-in mice with loxP-stop-loxP sequence and tdTomato inserted ($WT1^{CreERT2/+}; ROSA26^{tdTomato}$) and examined their impact on malignant characteristics. **[Results]** Compared with OV-90 cells, mesenchymal phenotype was induced more in OV-90-IP4 cells, and invasive ability and tumor establishment, linked to increased epithelial-mesenchymal transition (EMT) (invasion : 61%-increase ($P < 0.05$), murine peritoneal tumor : 85%-increase ($P < 0.05$)). Also, OV-90-IP4 cells significantly induced CAFib, detected by Masson-trichrome/Sirius-red staining (collagen accumulation : 32%-increase ($P < 0.05$)). We found that CAFib was traced back to EMT-altered peritoneal mesothelial cells (MCs) in the genetically engineered mice. Furthermore, induction of EMT of MCs significantly attenuated invasive ability and cisplatin-resistance (invasion : 94%-increase ($P < 0.05$), apoptosis : 48%-decrease ($P < 0.05$)). Proteomics analysis of the xenograft tumor revealed that alteration of specific ECM-related factors caused modification of microenvironment that induced increased stability of the peritoneal metastatic tumor of OV-90-IP4 cells. **[Conclusion]** As CAFib is an essential biological process in aiding OvCa progression and therapeutic resistance, targeting CAFib could be a potential strategy for OvCa treatment.

DGGG-6

Decellularization and Reconstruction of Ovarian Tissue for Safer Transplantation Wakimoto Yu, Chen Yuekun, Nakagawa Kohei, Fukui Atsushi, Shibahara Hiroaki Hyogo Medical University

[Objective] The autotransplantation of ovarian tissue cryopreserved prior to cancer treatment has been performed for fertility restoration. However, the risk of cancer recurrence due to

minimal residual disease (MRD) in the ovarian tissue is a concern. In this study, we aimed to eliminate the MRD from the ovary by decellularizing the tissue and reconstructing the ovarian tissue by reintroducing isolated follicles for safer transplantation. **[Methods]** Ovarian tissues from ICR mice were decellularized using sodium dodecyl sulfate followed by DNase treatment. These tissues were compared to untreated tissues using HE and Masson's trichrome staining. Follicles were isolated from B6D2F1 mouse ovarian tissue and introduced into the decellularized tissue. We encapsulated them with Matrigel or sodium alginate for ovary reconstruction. We removed either one side or both side ovaries of four SCID mice and transplanted the reconstructed ovarian tissues into the same site. The transplanted SCID mice were mated with ICR mice. For control, in two mice, one ovary was left intact while the other was replaced by the reconstructed tissue. **[Results]** The decellularized tissue retained only the extracellular matrix (ECM) and lacked cytoplasm and nuclei. After transplantation, three SCID mice became pregnant with six fetuses in total. However, none were derived from the B6D2F1 lineage. **[Conclusion]** Decellularized ICR mouse ovarian tissue effectively retains its ECM, demonstrating its potential as a scaffold for ovarian reconstruction. However, the absence of B6D2F1-derived offspring suggests that the reconstructed ovaries did not fully recover their original function. Future studies will explore ovarian stromal cell remodeling.

DGGG-7

Abnormal placental cord insertion increases in the lateral placenta of older pregnancies Shimura Koki, Katayama Akihisa, Tanaka Yukiko, Waratani Miyoko, Mori Taisuke Kyoto Prefectural University of Medicine

[Objective] Lateral placenta and abnormal placental cord insertion (PCI) each exacerbate perinatal outcomes, although the association between the two is unknown. This study evaluated the association between lateral placenta and abnormal PCI. **[Methods]** A retrospective study was conducted on patients who underwent delivery in our institution from 2020 to 2022, excluding those with multiple pregnancies, placenta previa, less than 22 weeks gestation. The placental position was confirmed by ultrasound during pregnancy, and abnormal PCI, including marginal cord insertion (MCI) and velamentous cord insertion (VCI), were verified after delivery. The percentage of abnormal PCI in the lateral and non-lateral placenta was compared. **[Results]** Of the 504 patients included in the study, 92 (18.3%) were diagnosed with the lateral placenta. After delivery, 46 (9.1%) were diagnosed with MCI, 9 (1.8%) with VCI, and a total of 55 (10.9%) with abnormal PCI. The proportion of abnormal PCI was 14/92 (15.2%) in the lateral placenta and 41/412 (10.0%) in the non-lateral placenta, not statistically different ($p = 0.14$). However, abnormal PCI in the lateral placenta increased with age (odds ratio : 1.13, $p < 0.05$), and furthermore, the proportion of abnormal PCI in the lateral placenta was significantly higher than in the non-lateral placenta over 40 years of age (4/8 [50.0%] vs. 2/47 [4.3%], $p < 0.01$). These results were unchanged by excluding assisted reproductive technology pregnancies. **[Conclusion]** Lateral placenta and abnormal PCI were associated in older pregnancies. This may result from abnormal uterine artery blood flow in addition to the trophotropism theory.

DGGG-8

Enhancement effects of adipose-derived mesenchymal stem cell-secreted exosomes on embryonic development and differentiation Hirakawa Toyofumi¹, Nakabayashi Kazuhiko², Urushiyama Daichi¹, Kurakazu Masamitsu¹, Miyata Kohei¹, Hata Kenichiro², Yotsumoto Fusanori¹, Miyamoto Shingo³ Fukuoka

University¹, National Center for Child Health and Development², Iwate Medical University³

[Objective] Adipose-derived mesenchymal stem cells (ASCs) have been reported to be an important contributor to regenerative medicine and cell therapy for damaged ovarian function and infertility treatment. Here, we investigated the impact of ASCs-secreted exosomes on embryonic development and differentiation using mouse blastocysts. **[Methods]** ASCs at early (E-ASCs) or late (L-ASCs) passage stage were co-cultured with ICR murine embryos in transwells. ASC-secreted exosomes within the cell culture supernatant were isolated via ultracentrifugation, and their concentration was evaluated using a Nanosight instrument. Expression analysis of miRNA present in ASCs-secreted exosomes was assessed using an Illumina next generation sequencer (NGS). Gene Ontology analysis using DNA harvested from blastocysts was also performed by NGS. **[Results]** The concentrations of exosomes secreted from E-ASCs or L-ASCs co-cultivated with mouse blastocysts were $2.74 \times 10^9 \pm 1.90 \times 10^8$ particles/mL (mean \pm SD) or $1.98 \times 10^9 \pm 2.75 \times 10^8$ particles/mL, respectively. A significant difference was observed between these values. E-ASCs-secreted exosomes significantly increased the rate of blastocyst development, compared with L-ASCs-secreted exosomes. Notable differences in miRNA profile were observed between E-ASCs and L-ASCs using principal component analysis based on miRNA expression data. Gene Ontology analysis using developed blastocysts incubated with E-ASCs indicated significant augmentations in gene expression associated with pluripotency and embryonic development, compared to those without E-ASCs. **[Conclusion]** ASCs-secreted exosomes may exert positive effects on embryonic development and differentiation and provide new approaches for the treatment of female infertility.

DGGG-9

High-grade serous carcinoma can show squamoid morphology mimicking true squamous differentiation Tomonobe Hiroshi, Hachisuga Kazuhisa, Kawakami Minoru, Maenohara Shoji, Kodama Keisuke, Yagi Hiroshi, Yasunaga Masafumi, Onoyama Ichiro, Asanoma Kazuo, Yahata Hideaki, Kato Kiyoko Kyushu University

[Objective] Tubo-ovarian high-grade serous carcinoma (HG-SC) and ovarian endometrioid carcinoma (EC) can show overlapping morphological features, making their differential diagnosis sometimes difficult. The existence of "squamoid differentiation" tends to lead to a diagnose EC rather than HG-SC. We noticed that HG-SC can contain a "squamoid component". This study was thus established to clarify the nature of this "squamoid component" in HG-SC by investigating its frequency and immunohistochemical features. **[Methods]** We reviewed hematoxylin and eosin (HE) -stained slides of 237 primary untreated cases of tubo-ovarian HG-SC. An immunohistochemical staining panel (CK5/6, CK14, CK903, p40, p63, WT1, ER, and PgR) was used. Fourteen cases of ovarian EC with "squamoid differentiation" were selected as a control. **[Results]** We identified 16 cases (6.7%) of HG-SC with "squamoid component." The "squamoid component" in HG-SC was completely p40-negative and showed significantly lower expression of CK5/6, CK14, CK903, and p63 than the "squamoid differentiation" in EC. The immunophenotype of the "squamoid component" was concordant with the conventional HG-SC component (WT1-positive/ER-positive). Furthermore, all the 16 tumors were confirmed to be truly "HG-SC" by the findings of aberrant p53 staining pattern and/or WT1/p16 positivity, and the lack of mismatch repair deficiency and *POLE* mutation. **[Conclusion]** HG-SC can show a "squamoid component" mimicking "squamous differentiation." However, the "squamoid component" does not represent true "squamous differentiation" and is one part of the morphological spectrum of

HG-SC, which should be interpreted carefully for differential diagnosis. Immunohistochemical panel including p40, p53, p16 and WT1 is a useful adjunct for a correct diagnosis.

DGGG-10

Novel BRCA1-BRCT binding partner, mediator complex subunit 1 (MED1) contributes to maintain homologous recombination pathway and suppress R-loop accumulation Honjoh Harunori¹, Tanikawa Michihiro², Hiraike Osamu¹, Oda Katsutoshi³, Miyamoto Yuichiro¹, Mori Mayuyo¹, Sone Kenbun¹, Hirota Yasushi¹, Osuga Yutaka¹ The University of Tokyo¹, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital², Division of Integrative Genomics, The University of Tokyo³

[Objective] Homologous recombination (HR) deficiency has been established as a strong therapeutic target and is closely linked to carcinogenesis. The aim of this study was to elucidate the broad function of a novel HR factor, mediator complex subunit 1 (MED1), in genome stability. **[Methods]** & **[Results]** First, the formation of the MED1/BRCA1 complex via BRCT domains was demonstrated by immunoprecipitation. And, the interaction was abolished in the presence of λ -protein phosphatase, DNase, and RNase-the functions as a transcriptional cofactor, demonstrated by Luciferase assay. MED1-deficient cells showed significantly reduced colony-forming ability after IR and CDDP exposure. DR-GFP assays showed that MED1 knockdown significantly reduced HR activity. MED1 knockdown also prolonged IR-induced DNA damage and delayed and prolonged ATM and Chk2 phosphorylation. Pulse-chase BrU labeling assays showed a decrease in DNA synthesis upon MED1 knockdown. A reduction in C-NHEJ activity was also observed in MED1-deficient cells, and 53BP1 accumulation at sites of DNA damage induced by IR was also reduced. Furthermore, nuclear accumulation of R-loop and R-loop-induced comet tails was observed in MED1 knockdown cells. **[Conclusion]** We conclude that the transcription factor MED1 contributes to genomic stability through the regulation of the HR pathway and R-loop processing. This indicates the possibility of establishing therapeutic strategies targeting genomic vulnerability due to unresolved DNA Double-strand breaks and disruption of replication forks in gynecologic cancers whose function of the mediator complex is impaired.

DGGG-11

Vaginal microbiota in pregnancy after radical trachelectomy Hasegawa Keita^{1,2}, Kasuga Yoshifumi^{1,2}, Fukuma Yuka¹, Tamai Junko¹, Tanaka Yuya¹, Otani Toshimitsu¹, Ikenoue Satoru¹, Nakabayashi Kazuhiko³, Hata Kenichiro^{2,3}, Yamagami Wataru¹, Tanaka Mamoru¹ Keio University¹, National Center for Child Health and Development², Department of Human Molecular Genetics, Gunma University³

[Objective] Due to the wide resection of the cervix during radical trachelectomy (RT), the vaginal microbiota (VM) may undergo alterations, potentially increasing the risk of preterm delivery in pregnancies after RT. However, there is limited data on the VM during pregnancy after RT. Therefore, we aimed to investigate the VM in pregnancies after RT. **[Methods]** We enrolled pregnant women who had undergone RT (RT group : n =25) and those who had not undergone RT or cervical conization (control group : n=100) and received perinatal care at our hospital between June 2019 and July 2023. Vaginal discharge samples were collected during the first, second, and third trimesters and subjected to microbial analysis by sequencing the V1-V2 region of the 16S ribosomal RNA gene. The α -diversity was calculated using the Friedman rank sum test. **[Results]** Throughout all trimesters, no differences in the incidence of *Lactobacillus*

spp. were observed between the two groups. Compared with the control group, the RT group exhibited higher incidences of *Streptococcus* spp., *Enterococcus* spp., and *Prevotella* spp. in the first trimester; *Prevotella* spp. and *Dialister* spp. in the second trimester; and *Streptococcus* spp., *Aerococcus* spp., *Prevotella* spp., *Dialister* spp., and *Mycoplasma* spp. in the third trimester. Furthermore, the α -diversity analysis revealed alterations in the VM in the control group but not in the RT group. **[Conclusion]** The VM in the RT group differed from that in the control group. Moreover, the invariance of the VM during pregnancy after RT could be one of the main causes of preterm delivery.

DGGG-12

Supply pathway of 3-hydroxybutyrate to the fetus through amniotic fluid for brain development in pregnancy Shibata Takeo, Takata Emi, Takakura Masahiro *Kanazawa Medical University*

[Objective] The human brain can rapidly grow using an energy supply of a “main-ketone body and sub-glucose” system. At least, up to late pregnancy, the human brain could use the ketone body supplied by the placenta. We suspected the existence of an alternative pathway using amniotic fluid to supply the ketone body to the fetus. **[Methods]** We involved nine healthy pregnant women in the study who had C-sections in full-term, without any abnormal glucose tolerance or gestational diabetes mellitus. 3-hydroxybutyrate (3HB) as ketone body was measured in the umbilical vein, umbilical artery, amniotic fluid, and maternal blood. Maternal blood was drawn the day before the C-section. Amniotic fluid, umbilical venous blood, and umbilical arterial blood were collected at C-section. **[Results]** The 3HB concentrations in the amniotic fluid were significantly higher than those in the maternal blood (0.56 ± 0.2 vs. 0.12 ± 0.04 mM, $p = 0.003$, Mann-Whitney U test). In addition, those in the umbilical vein (0.43 ± 0.31 , $p = 0.027$, Mann-Whitney U test) and artery (0.42 ± 0.26 , $p = 0.045$, Mann-Whitney U test) were also higher than those in the maternal blood. **[Conclusion]** Here, we propose that humans have two pathways, an amniotic fluid- and another from placenta to umbilical vein-mediated, for supplying 3HB to the human fetus. These supply pathways are supposedly essential for human brain development during the late phase of pregnancy.

DGGG-13

Comparison of the efficacy and safety of 5-day methotrexate versus pulse actinomycin D for low-risk gestational trophoblastic neoplasia (LRGTN) : A single-center historical study Katayama Eri, Usui Hirokazu, Nakamura Natsuko, Sato Asuka, Otsuka Satoyo, Okuya Rie, Habu Yuji, Matsuoka Ayumu, Nishikimi Kyoko, Tate Shinichi, Koga Kaori *Chiba University*

[Objective] In 2019, our institution changed the first-line treatment regimen for low-risk gestational trophoblastic neoplasia (LRGTN) from 5-day methotrexate (20 mg/body IM) to pulse actinomycin D (1.25 mg/m² IV) every 14 days. We aimed to compare the efficacy and safety of these regimens. **[Methods]** One hundred and five LRGTN cases we managed from 2007 to 2022 were identified. Data on patient background, outcomes, and side effects were retrospectively analyzed using the Mann-Whitney U test, Fisher's exact test, and propensity score matching analyses. **[Results]** Eighty-three patients were treated before 2019 (MTX group), while 22 were treated after 2019 (ACT-D group). Age and pre-treatment hCG levels were comparable, while FIGO scoring was significantly higher in the MTX group ($p < 0.05$). The ACT-D group had a significantly higher complete remission rate (81.8% : 18/22) compared to the MTX group

(38.6% : 32/83) ($p < 0.01$). Drug resistance was observed in 24.1% (20/83) of the MTX group and 18.2% (4/22) of the ACT-D group ($p = 0.78$). These superior effects of ACT-D were also observed in analysis with matched patients' backgrounds, including age, hCG levels, and FIGO scoring ($p < 0.05$). Severe side effects requiring a change in chemotherapy were reported in 37.3% (31/83) of patients in the MTX group, while none in the ACT-D group. **[Conclusion]** As a first-line treatment regimen for LRGTN, pulse ACT-D was more effective and safer than 5-day MTX. Given the patient convenience of fewer hospital visits, pulse ACT-D therapy is considered a better option for patients with LRGTN.

DGGG-14

Body Composition at 32w and mild late-onset (LO) Hypertensive Disorder of Pregnancy (HDP) ; to extract good prognosis HDP Kirino Satoe, Suemori Ayano, Nakato Hikari, Ooba Hikaru, Mitoma Tomohiro, Mishima Sakurako, Oohira Akiko, Maki Jota, Eto Eriko, Masuyama Hisashi *Okayama University*

[Objective] HDP is generally considered caused by placental hypoplasia, however, mild LO Gestational Hypertension (GH) seems more affected by metabolic factors than early-onset (EO). In addition, these days body composition scaler can easily provide us detailed metabolic status compared to BMI, such as % Fat Mass (%FM), Fat to Muscle Ratio (FMR), % Visceral Fat (%VF), % Leg Muscle (%LM). Thus the aim of this study was to evaluate the impact of body composition on LO-HDP prognosis. **[Methods]** We retrospectively analysed association between metabolic status based on body composition at 32w and LO-HDP. 231 HDP patients between September 2014 and December 2022 were included. Excluded cases on low dose aspirin, of multiple pregnancy, or without scanning, 61 patients were finally analysed. Patients were divided into two groups : GH and Preeclampsia (PE), Chronic Hypertension (CH) and Superimposed Preeclampsia (SPE). Multivariable logistic regression model was used to control possible confounding factors of gestational weight gain using STATA version18. **[Results]** In LO-GH group, 38 patients are eligible, resulting in 23 LO-PE, while 20 CH \geq 34w patients proceeding to 9 LO-SPE. LO-GH has significant prognostic factors for mild clinical course : high %FM (OR =0.844, CI : 0.730-0.975, $p=0.021$), high FMR (0.00034 , 4.98×10^{-2} , 0.156, 0.011), high %VF (7.46×10^8 , 7.78×10^{14} -0.071, 0.020), or low %LM (1.32, $16.6-1.04 \times 10^{35}$, 0.036), while CH \geq 34w not. **[Conclusion]** Metabolic status at 32w obtained by body composition scan could be used to distract LO-GH cases with good prognosis, which means less likely to progress for LO-PE with limited impact of placental hypoplasia.

DGGG-15

Feasibility and outcomes of laparoscopic pelvic exenteration compared with open surgery in our hospital Kakuda Mamoru¹, Nakagawa Satoshi¹, Toda Asuka¹, Kinose Yasuto¹, Takiuchi Tsuyoshi¹, Kodama Michiko¹, Hashimoto Kae¹, Mabuchi Seiji², Ueda Yutaka¹, Sawada Kenjiro¹, Kimura Tadashi¹ *Osaka University¹, Osaka International Cancer Institute²*

[Objective] Pelvic exenteration can be a treatment option for patients with recurrent or advanced gynecological cancer. In recent years, there have been several reports of favorable results, such as a lower complication rate for minimal invasive surgery (MIS) compared to laparotomy. This study aims to evaluate the feasibility and outcome of laparoscopic pelvic exenteration compared to laparotomy. **[Methods]** We retrospectively reviewed cases of pelvic exenteration performed at our hospital between 2010 and 2022. **[Results]** 15 cases of laparotomy (OPEN) and 5 cases of laparoscopic surgery (MIS) were extracted. There was no significant difference in patient characteristics between the

two groups. 53% of patients in the OPEN and 80% of patients in the MIS had received prior radiation therapy. The MIS had a longer operative time (734 vs 582 minutes, $P=0.033$), significantly less blood loss (300 vs 2770ml, $P=0.0014$) and less blood transfusion. Intraoperative complications included 1 intestinal injury in the MIS, compared to 4 intestinal injuries and 2 vascular injuries in the OPEN. Serious postoperative complications were observed in 3 cases in MIS and in 13 cases in OPEN, with a tendency to occur more frequently in the OPEN. The 2 year survival rate was 60% in both groups, but recurrence was observed in all patients undergoing MIS, and in 9 patients undergoing OPEN. This may be due to the high number of post-radiotherapy recurrences in MIS. **[Conclusion]** MIS tends to have fewer complications and may be a treatment option, but more cases need to be accumulated to determine prognosis.

RCOG-1

The efficacy of color doppler ultrasound in the first-trimester ultrasound screening of congenital heart disease : a before-after study from a tertiary perinatal center Hashimoto Shin, Tokunaka Mayumi, Takita Hiroko, Yamashita Yuka, Matsuoka Ryu, Sekizawa Akihiko *Showa University*

[Objective] Though color Doppler ultrasound may be useful for screening very small fetal heart in early pregnancy, it is not considered mandatory. Our institution had been implementing a first-trimester screening since 2011. In 2018, we changed our protocol from only B-mode to B-mode with color Doppler. We aimed to assess whether the quality of congenital heart disease (CHD) screening has improved. **[Methods]** We conducted a before-after clinical study to compare the quality of first-trimester (from 11+0 to 13+6 weeks' gestation) CHD screening with and without color Doppler. We included patients who underwent first-trimester screening and subsequently gave birth in our facility. For the safety of the fetus, we complied with the ISUOG guideline and ALARA (As Low As Reasonably Achievable) principle and kept the TIS (thermal index of the soft tissue) below 1. **[Results]** We included 11,448 fetuses, of which 5,015 fetuses were screened using only B-mode (group B), and 6,433 fetuses using B-mode with color Doppler (group B+C). The detection rate, specificity, positive predictive value, and negative predictive value for every CHD in group B and B+C was 33.3% and 54.5% ($p = 0.047$), 99.98% and 99.99% ($p = 0.86$), 93.75% and 96% ($p = 0.74$), 99.40% and 99.69% ($p = 0.021$), respectively. The same value for major CHD in B and B+C was 53.6% and 80.0% ($p = 0.030$), 99.98% and 99.99% ($p = 0.86$), 93.75% and 95.24% ($p = 0.84$), 99.74% and 99.92% ($p = 0.015$), respectively. **[Conclusion]** Using color doppler ultrasound is recommended in first-trimester CHD screening.

RCOG-2

The utility of KELIM for predicting prognosis and indicating therapeutic selection among Japanese patients with high-grade serous ovarian carcinoma : a single-center retrospective observational study Kochi Yuki, Noguchi Daito, Hosoya Satoshi, Kuroda Takafumi, Nagata Chie, Saito Motoaki, Yanaiharu Nozomu, Tanabe Hiroshi, Takano Hirokuni, Yamada Kyosuke, Okamoto Aikou *The Jikei University*

[Objective] Few analyses evaluated CA-125 ELIMination rate constant K (KELIM), a biomarker for assessing prognosis in high-grade serous ovarian carcinoma (HGSOC), among the Japanese population. Meanwhile, dose-dense paclitaxel plus carboplatin (ddTC) is reportedly superior to conventional paclitaxel plus carboplatin (cTC) in patients with poor prognosis defined by KELIM and surgical outcomes. Therefore, we investigated the utility of KELIM among Japanese HGSOC. **[Methods]** We included patients with HGSOC at our institution in 2012-2021. KELIM was calculated online for patients whose CA-125 kinetics during adjuvant chemotherapy (AC) /neo-adjuvant chemotherapy (NAC) could be retrieved and stratified as favorable (≥ 1.0) or unfavorable (< 1.0). We further defined two groups : patients with favorable KELIM and complete surgical outcome (Favorable), and patients with unfavorable KELIM or residual tumors (Unfavorable). Progression-free survival (PFS) /overall survival (OS) were assessed. **[Results]** Of 259 patients with HGSOC, 152 and 107 patients underwent primary debulking surgery (PDS) with AC and interval debulking surgery (IDS) after NAC, respectively. AC/NAC included cTC (n=79) and ddTC (n=180). Patients with favorable KELIM had significantly longer PFS/OS than those with unfavorable KELIM. Conversely, unfavorable KELIM in NAC correlated with residual tumor at IDS (Odds Ratio, 4.53 ; 95% Confidence Interval [CI], 1.71-12). 129

and 130 were in the Favorable and the Unfavorable. In the Unfavorable group, ddTC after PDS showed longer PFS/OS than cTC (Hazard Ratios, 0.595/0.604 ; 95% CIs, 0.354-0.998/0.319-1.143), but not in the Favorable group or those underwent IDS. **[Conclusion]** KELIM could predict prognosis in Japanese HGSOC patients. Moreover, ddTC might be effective in HGSOC with the Unfavorable group.

RCOG-3

Difference in the trajectory of fetal head descent during labor between nulliparous and multiparous women detected by intrapartum transperineal ultrasound : a multicenter prospective study Yano Eriko¹, Iriyama Takayuki¹, Sayama Seisuke¹, Ariyoshi Yu¹, Toshimitsu Masatake¹, Seyama Takahiro¹, Kumasawa Keiichi¹, Kobayashi Koichi², Matsuoka Ryo³, Taketani Yuji³, Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, JCHO Tokyo Yamate Medical Center², Artemis Women's Hospital³*

[Objective] No prior study has evaluated the impact of parity on the fetal head trajectory, the path of the fetal head descent during labor. This study aimed to clarify the difference in the fetal head trajectory between nulliparous and multiparous women using intrapartum transperineal ultrasound (ITU). **[Methods]** This is a multicenter, prospective study performed at three institutions between October 2020 and May 2023. ITU was performed throughout the labor period, and the cases of spontaneous vaginal delivery (SVD) with occiput anterior presentation were included. The cases of operative delivery and cases who delivered with non-occiput anterior presentation were excluded from this study. In the sagittal image, the position of the leading part of the fetal head was plotted using two-dimensional coordinates, (x, y), with the lower edge of the pubic symphysis as origin to mathematically analyze the fetal head trajectory. **[Results]** Of all, 140 cases (64%) met the inclusion criteria : 339 images of nulliparous women (97 cases) and 100 images of multiparous women (43 cases) were evaluated. Trajectory analysis showed that the leading part of the fetal head passed significantly farther from the pubic symphysis, i.e., through the dorsal path of the birth canal, in multiparous women than in nulliparous women. **[Conclusion]** This is the first study to reveal that fetal head trajectory in cases of SVD with normal rotation is apparently different, depending on parity. Differences in the resistance of the soft birth canal, such as the dorsal pelvic floor muscles, due to parity may underlie this result.

RCOG-4

Effects of IGF-I and PGRN on trophoblast cell proliferation Osaka Makoto, Tajima Atsushi, Takemori Satoshi, Watanabe Momoe, Morisada Tohru, Tanigaki Shinji, Kobayashi Yoichi *Kyorin University*

[Objective] Maternal obesity and gestational diabetes mellitus (GDM) share a common insulin resistance condition, increasing the risk of pregnancy and perinatal complications. However, the effects of these maternal backgrounds and maternal weight gain on fetal and placental development are unclear. This study focused on progranulin (PGRN), which has been linked to maternal weight gain, and explored its interaction with insulin-like growth factor-I (IGF-I) using a human choriocarcinoma-derived cell line (JEG-3). **[Methods]** This study examined changes in cell number and proliferative capacity after administering IGF-I (100 ng/mL, 1000 ng/mL) and/or PGRN (1000 ng/mL) to JEG-3. We also analyzed changes in intracellular signaling, including phosphorylation of Akt and Erk1/2 of IGF-I by PGRN using Western blotting. **[Results]** Cell proliferation was significantly increased by IGF-I treatment in JEG-3. However, when IGF-I and PGRN were administered simultaneously, PGRN had an in-

hibitory effect on the proliferative effect of IGF-I at low concentrations of IGF-I (100 ng/mL). No inhibitory effect was observed at high concentrations of IGF-I (1000 ng/mL). Western blotting showed that Erk1/2 phosphorylation was significantly inhibited at low concentrations of IGF-I ($p < 0.05$), while the phosphorylation of Erk1 was not inhibited at high concentrations of IGF-I. Moreover, there was no significant change in Akt phosphorylation in the presence of PGRN. **[Conclusion]** PGRN could have a negative effect on the JEG-3 cell proliferation effects of IGF-I. It appears that PGRN reduces the effects of low concentrations of IGF-I by inhibiting the phosphorylation of Erk1/2 signals. However, high concentrations of IGF-I counteract this inhibition.

RCOG-5

CircESRP1 promotes cell proliferation of high-grade serous ovarian cancers (HGSOC) via miR-142-3p/HMGA2 pathway Oride Tadashi, Sawada Kenjiro, Oi Yukako, Toda Aska, Nakamura Koji, Kawano Mahiru, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Kimura Tadashi *Osaka University*
[Objective] Circular RNAs (circRNAs) are reported to play pivotal roles in cancer biology, yet their specific functions in HGSOC remain unclear. Our research focuses on identifying highly elevated circRNAs in HGSOC and elucidating their roles in its progression. **[Methods]** To identify highly expressed circRNAs in HGSOC, circRNA microarray analyses were performed on two HGSOC clinical samples and their corresponding normal tissues. Their expression profiles were validated across 24 HGSOC samples using RT-qPCR. To assess the functions of identified circRNAs, in-vitro analyses were executed following siRNA transfection. Further, proteasome analyses were performed, and the mechanism how this circRNA works was identified using in-silico analyses. **[Results]** CircESRP1 emerged as the most highly expressed circRNA, with a Log Fold Change (Log FC) of 3.12 in two HGSOC samples. Subsequently, significant upregulation of its expression was seen, with a Log FC of 5.56, across 24 HGSOC clinical samples as well as HGSOC cell lines, specifically OVCAR3 and Caov3. Suppression of circESRP1 inhibited cell proliferation by inducing apoptosis. Proteasome analyses revealed the suppression of circESRP1 inhibits HMGA2 expression in HGSOC cell lines, and in silico analyses showed circESRP1 works as a sponge of miR-142-3p, and thereby this miRNA negatively regulates HMGA2 expression. These interactions were validated through dual-luciferase reporter assays and RNA pulldown assays. **[Conclusion]** CircESRP1, specifically elevated in HGSOC, works as a sponge for miR-142-3p, and thereby positively regulates HMGA2 expression, leading to cell proliferation. Our findings shed light on the potential role of a novel circRNA (circESRP1) as a therapeutic target in HGSOC.

RCOG-6

Prognostic Significance of Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, or Monocyte-to-Lymphocyte Ratio in Uterine Carcinosarcoma Sakurai Azusa¹, Yamaguchi Ken², Ishida Kentaro³, Honda Tetsuro⁴, Kawai Eri⁵, Kotani Yasushi⁶, Yamanishi Yukio⁷, Kishimoto Naoya⁸, Horikawa Naoki⁹, Tatsumi Keiji¹⁰, Okudate Minami¹¹, Mandai Masaki¹² *Shiga General Hospital¹, Kyoto University², Osaka Red Cross Hospital³, Kurashiki Central Hospital⁴, Tazuke Kofukai Foundation, Medical Research Institute, Kitano Hospital⁵, Kindai University⁶, Japanese Red Cross Society Wakayama Medical Center⁷, Kyoto Medical Center⁸, Shizuoka General Hospital⁹, Osaka National Hospital¹⁰, Kobe City Medical Center General Hospital¹¹*
[Objective] Immune status affects the prognosis of uterine endometrial cancer. However, it is unclear in stromal malignancies. This study aims to explore the association between pre-treatment inflammatory biomarkers (Neutrophil-to-Lymphocyte

Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Monocyte-to-Lymphocyte Ratio (MLR)) and the prognosis of uterine carcinosarcoma (UCS) and uterine sarcoma (US). **[Methods]** 237 patients (119 UCS, 118 US) treated at fourteen hospitals from 2008 to 2017 were assessed retrospectively. The progression free survivals (PFS) and overall survivals (OS) were analyzed by depicting Kaplan-Meier curves and using the log-rank tests. Cox regression analysis identified independent prognostic factors. **[Results]** Using the median values of NLR, MLR, and PLR as the cutoffs, high NLR and MLR showed significantly poorer PFS ($p=0.003$ and $p=0.01$, respectively); high PLR trended to show unfavorable prognosis ($p=0.09$) in UCS cases. In the US cohort, only a high PLR was significantly associated with poor outcomes, while NLR and MLR did not show a significant difference in prognosis. ROC analysis determined the optimal cutoffs in UCS as 4.0, 220, and 0.3 for NLR, MLR, and PLR, respectively. Univariate analysis identified significantly worse PFS with elevated NLR, MLR, and PLR in UCS cases ($p < 0.05$). When groups were divided based on all biomarker values being above the cutoffs, it revealed significantly poorer PFS and OS, confirming them as independent adverse prognostic factors in UCS. **[Conclusion]** Accumulation of high values of NLR, MLR, and PLR is an adverse prognostic factor, suggesting the association of immunity with the prognosis in UCS but not in US.

RCOG-7

Surgical and reproductive outcomes in women with cesarean scar pregnancy treated with transabdominal evacuation and cesarean scar defect repair who wish for another baby Goto Yuki¹, Ishikawa Hiroshi¹, Uchiumi Mana¹, Saito Yoshiko¹, Kaneko Meika¹, Yamamoto Keisuke¹, Katayama Eri¹, Nakamura Natsuko¹, Usui Hirokazu¹, Shozu Makio², Koga Kaori¹ *Chiba University¹, Medical Mycology Research Center, Chiba University²*
[Objective] We performed transabdominal evacuation followed by cesarean scar defect repair in women with cesarean scar pregnancy (CSP) who wish for another baby. This study aimed to investigate surgical and reproductive outcomes in the affected women. **[Methods]** We retrospectively analyzed the characteristics, surgical parameters, and reproductive outcomes of eight women who underwent the procedures between 2009 and 2023. Continuous variables were presented at the median (range). **[Results]** Age and BMI perioperatively were 34 years (29-41) and 19.5 (range: 18.8-27.2), respectively. The number of previous cesarean sections was 1 (1-3). Four women were initially treated for CSP, two with transvaginal evacuation, one with systemic methotrexate (sMTX), and two with both transvaginal evacuation and sMTX. The serum hCG level and size of gestational sac or retained products of conception perioperatively were 13,102 mIU/mL ($< 0.2-75,207$) and 20 mm (14.4-37), respectively. Total blood loss was 52.5 mL (30-230) and surgical time was 157.5 min (85-201). The postoperative residual myometrial thickness increased to 7.6 mm (4.3-10.4). None of the women required additional interventions, such as uterine artery embolization, sMTX, and hysterectomy. Three women became pregnant; two underwent elective cesarean sections at term and one is currently pregnant without any complications. **[Conclusion]** Regarding safety, fertility preservation, and subsequent pregnancy outcomes, transabdominal evacuation followed by cesarean scar defect repair is an appropriate option for women with CSP who wish for another baby.

RCOG-8

The association between fetal head malposition and labor analgesia: a propensity score-matched analysis Tamura Nami, Takeda Jun, Mieda Haruka, Yamada Taihei, Sugimura Yusen, Kitamura Eri, Matsuzawa Nana, Yamamoto Yuka, Itakura Atsuo

Juntendo University

[Objective] : Fetal head malposition has a risk of prolonged labor, instrumental delivery, and perinatal complication. Previous studies have suggested the association between fetal head malposition and the use of labor analgesia, but it is still controversial. The aim of this study is to clarify whether fetal head malposition increases with the use of labor analgesia. **[Methods]** : During the period of January 2020 through December 2020 medical records were reviewed. The study subjects were term pregnant women with singleton cephalic fetuses whose cervix were fully dilated. The group without analgesia was considered as a control group (C group) and matched with a labor-analgesia group (A group) by propensity score matching. The primary outcome was the presence of fetal head malposition. The rate of normal vaginal delivery, instrumental delivery, cesarean delivery, and the success rate of attempted manual rotation was considered as the secondary outcome. **[Results]** : During the period, 1370 women were included and 265 pairs were propensity score matched ; 53 and 212 women for C group and A group, respectively. The rate of fetal head malposition was significantly higher in the A group compared to the C group (13.6% vs. 3.7%, $p < 0.05$). There was also a tendency towards higher rates of cesarean delivery (0.5% vs. 0.0%) and instrumental deliveries (21.8% vs. 11.8%) in the A group compared to those of the C group. **[Conclusion]** : We concluded that in women whose cervix is fully dilated, labor analgesia is associated with an increased rate of fetal head malposition, instrumental delivery, and cesarean delivery.

RCOG-9

Therapeutic effects of Human Amniotic Fluid Stem Cell-Derived Extracellular Vesicles (hAFSC-EVs) on Inflammatory Macrophage Polarization Abe Yushi^{1,2}, Otani Toshimitsu¹, Matsumiya Yosuke², Hasegawa Keita¹, Kasuga Yoshifumi¹, Ikenoue Satoru¹, Ochiai Daigo³, Vatish Manu², Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Nuffield Department of Women's and Reproductive Health, University of Oxford, UK², Kitasato University³*

[Objective] Human amniotic fluid stem cells (hAFSCs), a subset of mesenchymal stem cells (MSCs), are known to have powerful anti-inflammatory effects. It is likely that extracellular vesicles (EVs) derived from hAFSCs alter immune cell function, but the specific mechanisms have not been fully elucidated. This study aims to identify the effects of hAFSCs on macrophages and the mechanisms by which changes occur. **[Methods]** EVs were isolated from hAFSCs (hAFSC-EVs) by ultracentrifugation and their properties and surface antigen markers were investigated. We confirmed that hAFSC-EVs can be taken up by a macrophage cell line (THP-1). Subsequently, we attempted to inhibit the uptake of hAFSC-EVs by blocking key antigens present on EVs with specific antibodies. This allowed us to dissect the effect of specific EV species on macrophages. **[Results]** hAFSC-EVs could be isolated by ultracentrifugation. Their phenotype was confirmed by nanoparticle tracking analysis and western blotting. Comprehensive analysis of surface antigen markers revealed that specific surface antigens were highly expressed. Blocking these surface antigens with functional antibodies reduced their uptake into macrophages. The effect of hAFSC-EVs was also diminished when surface antigens were blocked and uptake was reduced. **[Conclusion]** These results suggest that hAFSC-EVs change the polarity of inflammatory macrophages to anti-inflammatory macrophages and that specific surface antigens may play a central role in this process. hAFSC-EVs may provide a mechanism to promote anti-inflammatory effects in macrophages.

RCOG-10

The measurement of term neonatal body movement with a portable piezoelectric meter in relation to body weight Suzuki Tomoo¹, Ono Masanori², Sakai Yousuke³, Kojima Junya², Shimizu Motohiro¹, Nishi Hirotaka² *Tokyo Medical University Hachioji Medical Center, Tokyo Medical University¹, Tokyo Medical University²*

[Objective] Developmental support for newborns is a critical global public health issue. Early identification of developmentally high-risk infants in the neonatal period is important for rapid intervention. Objectively measurable neonatal body movement is an important indicator of overall health status and can also be an important indicator of neurodevelopment. The purpose of this study was to validate the link between body weight at the time of the survey and neonate body movements and cries utilizing a portable, battery-operated instrument. **[Methods]** To measure body movement, we used a device containing piezoelectric sensors, a foot switch, and acceleration as input signals. Body motions were recognized as piezoelectric peaks using Origin software. The connection between daily crying incidents and body motions and body weight was investigated using correlation and regression analysis. **[Results]** There was a positive correlation between body weight and the number of body movements and cries per day. The mean number of body movements per day tended to increase with higher body weight at the time of the study. A strong positive correlation with an R2 value of 0.5804 was found between the mean body weight at the time of the study and the total number of body movements. Regression analysis revealed a linear relationship between body weight and body movements per minute ($p < 0.05$). **[Conclusion]** There is a significant positive relationship between body weight and the number of objective body movements. Our study also has the potential to enable timely early intervention for children at high risk for poor developmental outcomes.

ISP-1-1

Investigation of the cellular origin and differentiation mechanisms of small cell carcinoma of the uterine cervix focusing on intratumor heterogeneity Yoshimoto Daisuke, Taguchi Ayumi, Kusakabe Misako, Ishizaka Aya, Tsuchimochi Saki, Toyohara Yusuke, Kawata Akira, Sone Kenbun, Mori Mayuyo, Oda Katsutoshi, Hirota Yasushi, Osuga Yutaka *The University of Tokyo Hospital*

[Objective] Small cell carcinoma of the uterine cervix (SCCC) accounts for 2% of cervical cancer cases and has a poor prognosis. Human papillomavirus (HPV) infection is often the cause of SCCC, but the mechanisms thereof are poorly understood. In this study, we aimed to elucidate the cellular origin and differentiation mechanisms of SCCC. **[Methods]** Using three cases of cervical mixed carcinoma including SCCC components, whole-exon sequencing and RNA-seq were performed for each histological type. Subsequently, we established organoid cultures from HPV18-positive SCCC and generated a mouse tumor model using SCCC organoids. Single-cell RNA-seq was performed on the mouse tumors. **[Results]** Whole-exon sequencing revealed that mixed carcinoma had a common cellular origin regardless of histological type. Pathway analysis based on RNA-seq showed that the calcium and neurotransmitter signaling pathways were significantly upregulated in the SCCC component. SCCC organoids-derived mouse tumors presented mixed tumors of SCCC and adenocarcinoma. Single-cell analysis of these tumors identified an isolated cluster of enriched neuroendocrine properties. This cluster showed a marked upregulation of calcium channel-related genes, which are associated with cancer stem cell maintenance and drug resistance. **[Conclusion]** Genetic analysis of mixed cancer and single-cell analysis of mouse tumors suggest that SCCC may have the pluripotency to differentiate into various histological types. Newly identified calcium channel-related genes may be associated with carcinogenesis and cellular differentiation of SCCC. These genes may serve as new diagnostic markers for SCCC.

ISP-1-2

Investigation to explore the mechanism of antitumor action of itraconazole via tumor-associated macrophages Takimoto Yumi, Tsubamoto Hiroshi, Narita Sachiyo, Taniguchi Roze, Ueda Tomoko, Shibahara Hiroaki *The Hospital of Hyogo College of Medicine*

[Objective] Itraconazole (ITZ), an antifungal agent, has been reported to have tumor agnostic anticancer effects. We investigated the effects of ITZ on tumor-associated macrophages (TAMs) present in the tumor microenvironment. **[Methods]** Anti-tumorigenic M1 and pro-tumorigenic M2 macrophages were established from THP-1 cells and their phenotypes were determined based on morphology, cell surface antigens by Western blotting, and secreted proteins by ELISA. Bulk proteomic analysis of cell proteins was conducted using liquid chromatography-tandem mass spectrometry. The viability of CaSKi cervical cancer cells was evaluated both in culture with the supernatant and in co-culture with M2 macrophages after treatment with ITZ (10^5 M). Single-cell RNA sequencing (scRNA-seq) with surface labeling of M2 macrophages with and without ITZ was performed, and differential expression analysis and gene list analysis were performed using Reactome. A triple-labeling immunofluorescence study was conducted to detect cholesterol, IL-1 β , and organelles (the endoplasmic reticulum, autophagosome, and lysosome). **[Results]** Itraconazole changed M2 macrophages to an M1-like morphology and protein expression. While co-culture with M2 macrophages promoted cancer cell proliferation, both culture with the supernatant and co-culture with ITZ-treated M2 macrophages significantly inhibited

CaSKi cell growth. scRNA-seq identified newly emerged clusters following ITZ treatment. The clusters expressed M1 markers, including CD8, TLR, IL-6, IL-1 β and GAPDH. Cholesterol metabolism, and lysosome vesicle biosynthesis were identified as significant pathways. Immunofluorescence analysis revealed that the M1-like macrophages had enlarged lysosomes containing cholesterol. **[Conclusion]** Itraconazole repolarized THP-1 derived M2 macrophage to an M1-like phenotype. The mechanism of repolarization involves intracellular cholesterol accumulation via lysosomal dysfunction.

ISP-1-3

Experimental evaluations of alleged findings in HPV vaccine-induced "adverse effects" Shiro Reona, Matsumura Noriomi *Kindai University*

[Objective] Although the Japanese government resumed proactive recommendations for human papillomavirus (HPV) vaccines in 2022, most Japanese still have concerns for their "adverse effects". A line of studies has reported that aluminum adjuvants in HPV vaccines would cause macrophagic myofasciitis (MMF), a systemic disease with inflammation at the injection sites. The immune response to vaccination or molecular mimicry between HPV L1 and human proteins has also been associated with damages in central nervous systems (CNS). Previously, however, we evaluated the manuscripts proposing these hypotheses, and concluded that the experiments had flaws in methods and analyses. Thus, we conducted the experiments to determine the effects of HPV vaccination on mice. **[Methods]** We inoculated female mice intramuscularly with Cervarix, Gardasil, other vaccines containing adjuvants (Bimmugen, HEPTAVAX, and Shingrix), or phosphate-buffered saline (PBS) every 4 weeks. We monitored body weight changes and clinical signs for 12 weeks. We harvested the muscles, general organs, and CNS for pathological assessments. **[Results]** We did not observe clinical signs in all groups, although the Shingrix group had loss of body weight after inoculation. We found MMF-like pathology with inflammatory cell accumulations at the injection sites in the Cervarix, Gardasil, Bimmugen, and HEPTAVAX groups, but not in the PBS or Shingrix group, which contains no aluminum. Neither demyelination nor inflammation was seen in the CNS from all groups. **[Conclusion]** Although we detected the local inflammation at the injection sites following intramuscular inoculation of HPV vaccines and other vaccines containing aluminum adjuvants, we observed neither systemic nor neurological signs.

ISP-1-4

A Potential Therapeutic Method for Uterine Cervical Cancer by Arsenic Trioxide via Inducing Carbonyl Reductase 1 Expression Kajimura Takuya, Takasu Go, Okada Maki, Sueoka Koutarou, Sugino Norihiro *Yamaguchi University*

[Objective] Carbonyl Reductase1 (CBR1) has been reported to be involved in cancer progression. Recently, we reported that CBR1 overexpression repressed malignant behavior of uterine cervical cancer (CC) via epithelial mesenchymal transition. Arsenic trioxide (ATO) is known as an effective chemotherapeutic agent for acute promyelocytic leukemia with a low toxicity. ATO is reported to upregulate CBR1 expression by activating the transcription factor activator protein-1. In this study, we investigated the effect of ATO on the malignant behavior of CC via CBR1 expression. **[Methods]** We investigated the effect of ATO on malignant behavior in CC cell lines (SiHa and SKGII) in vitro by Cell proliferation Assay, Wound healing Assay, and Invasion Assay, and using the mouse models transplanted with CC cells subcutaneously. **[Results]** ATO increased CBR1 expression dose-dependently in the cultured cells. ATO significantly

inhibited the activities of cell proliferation, invasion, and migration. 1.0×10^6 cells of SiHa or SKGII were subcutaneously injected into the back of immunodeficient mice (Bulb-C), and 5.0 mg/kg ATO were given intravenously every two days after the tumor development on the host mice. Seven weeks after injection of ATO, the tumor growth was significantly inhibited in SiHa and SKGII ($P < 0.05$). The CBRI expression level in the tumor treated with ATO was significantly higher than that of control. **[Conclusion]** ATO inhibited the cancer growth and malignant behavior with increased CBRI expression in CC cells. This result suggests that ATO can be the novel agent targeting CBRI in CC treatment.

ISP-1-5

Unclear tumor border in magnetic resonance imaging as a prognostic factor of squamous cell cervical cancer Tamauchi Satoshi, Sato Mamiko, Yoshida Kosuke, Yoshihara Masato, Ikeda Yoshiki, Yoshikawa Nobuhisa, Kajiyama Hiroaki *Nagoya University*

[Objective] Magnetic resonance imaging (MRI) is used for pretreatment staging in cervical cancer. In the present study, we used pretreatment images to categorize operative cases into two groups with their tumor shape and evaluated their prognosis. **[Methods]** A total of 53 cervical cancer patients with squamous cell carcinoma who underwent radical hysterectomy at our institute between January 2009 and December 2013 were included in this study. Based on MRI, the patients were classified into two groups, namely clear and unclear tumor borders. For each patient, the following characteristics were evaluated: overall survival; recurrence-free survival; lymph node metastasis; lymphovascular space invasion; and pathological findings, including immunohistochemical analysis of vimentin, a marker of epithelial-mesenchymal transition (EMT). **[Results]** The clear and unclear tumor border groups included 40 and 13 patients, respectively. Compared with the clear tumor border group, the unclear tumor border group was associated with higher incidence rates of recurrence (3/40 vs. 3/13, respectively), lymphovascular space invasion (24/40 vs. 13/13, respectively), lymph node metastasis (6/40 vs. 10/13, respectively), and positivity for vimentin (18/40 vs. 10/13, respectively). Despite the absence of a significant difference in recurrence-free survival ($p = 0.0847$), the unclear tumor border group had a significantly poorer overall survival versus the clear tumor border group ($p = 0.0062$). **[Conclusion]** According to MRI findings, an unclear borderline in patients with cervical cancer is linked to poorer prognosis, lymph node metastasis, and distant recurrence of metastasis. Vimentin-mediated enhancement of EMT is the underlying of the pathology.

ISP-1-6

Chemical peeling therapy using phenol for the cervico-vaginal intraepithelial neoplasia (CIN/VaIN) Sasagawa Toshiyuki¹, Maehama Toshiyuki², Shimada Sumire¹, Sakamoto Jinichi¹, Shibata Takeo¹, Takakura Masahiro¹ *Kanazawa Medical University¹, Yuuai Medical Center²*

[Objective] This study aimed to validate the use of liquid phenol-based chemical peeling therapy for cervico-vaginal intraepithelial neoplasia (CIN and VaIN), with the goal of circumventing obstetric complications associated with surgical treatment. **[Methods]** Totally 483 eligible women diagnosed with CIN and/or VaIN participated in this study. Participants underwent phenol-based chemical peeling therapy every 4 weeks until disease clearance. Disease clearance was determined by negative Pap tests for four consecutive weeks. HPV genotyping was conducted at the onset of the study and after disease clearance in select cases. **[Results]** CIN1 or VAIN1 ($n = 129$), CIN2

or VAIN2 ($n = 148$), CIN3 or AIS ($n = 112$), CIN1-3+VAIN ($n = 77$), early invasive cervical cancer ($n = 7$), and immunologically suppressed CIN or VAIN (IMM-SUP) ($n = 10$) were included in this study. Among the 476 participants (excluding those with cancer), the number of treatment sessions until CIN/VaIN clearance ranged from 2 to 49 (median = 7 sessions). Forty-five participants (9.4%) underwent surgical treatments. Seven participants (1.5%) experienced recurrence, presenting with CIN 2/VaIN2 or worse lesions; of these, three underwent LEEP, while four repeated the chemical peeling therapy. No obstetrical complications were noted among the 98 pregnancies following this therapy. **[Conclusion]** The findings suggest that phenol-based therapy is safe and effective for CIN, although it requires numerous and lengthy treatments. Factors associated with resistance to this therapy include immune suppression, high-grade lesions, multiple HPV type infection, and direct or passive smoking. Selection of suitable cases are likely to be important in clinical practice.

ISP-1-7

TBX2 expression predicts recurrence of intermediate- and high-risk stage IB-IIB cervical cancer undergoing radical hysterectomy followed by TP as adjuvant chemotherapy Noda Takuya¹, Fukuda Takeshi², Uchikura Eijiro¹, Awazu Yuichi¹, Tasaka Reiko², Imai Kenji², Yamauchi Makoto², Yasui Tomoyo², Sumi Toshiyuki² *Osaka City University¹, Osaka Metropolitan University²*

[Objective] We examined the correlation between TBX2 expression and recurrence of intermediate- and high-risk stage IB-IIB (FIGO2008) cervical cancer undergoing radical hysterectomy followed by TP (paclitaxel plus cisplatin). **[Methods]** We reviewed 100 cases of intermediate- and high-risk stage IB-IIB cervical cancer patients who underwent TP after radical hysterectomy from 2014 to 2020. Cases were divided into two groups, one group in which the patients didn't recur within 2 years after initialization of treatment (group A; $n = 85$), and the other group in which the patients recurred within 2 years (group B; $n = 15$). TBX2 expression was examined immunohistochemically. Multiple logistic regression analysis was performed to identify predictor of recurrence. The effect of the siRNA-mediated knockdown of TBX2 on the sensitivity of cervical cancer cells to cisplatin was investigated. This study was approved by the institutional review board. **[Results]** The expression of TBX2 was significantly higher in group B than in group A ($p < 0.01$). Cases were divided into two groups: low TBX2 expression group (weighted score ≤ 8 , $n = 80$), and high TBX2 expression group (weighted score ≥ 9 , $n = 20$). High TBX2 expression group was more likely to recur after adjuvant TP than low expression group ($p < 0.01$). And multivariate analysis revealed that TBX2 expression was an independent predictor of recurrence ($P < 0.01$). Furthermore, knockdown of TBX2 expression significantly increased cancer cell sensitivity to cisplatin in vitro. **[Conclusion]** High TBX2 expression might be associated with recurrence of intermediate- and high-risk stage IB-IIB cervical cancer undergoing radical hysterectomy followed by TP.

ISP-1-8

Clinicopathological study on patients who had a spontaneous regression based on histopathological assessment by conization Kawatake Rina, Okuma Yuki, Matsuda Erina, Katoh Kanoko, Kobayashi Osamu, Nakajima Takahiro, Aoki Aiko, Ikeda Yuji, Kawakami Kaori, Komatsu Atsushi, Saitou Keisuke, Kawana Kei *Nihon University*

[Objective] HPV-dependent cervical neoplastic lesions often regress spontaneously via an immune response to HPV. In this study, we examined the clinicopathology of cases of spontane-

ous regression of HPV-related tumors using cases with pathological regression in conization specimens. **[Methods]** Of 439 cases with histological CIN3 that underwent conization from 2016 to 2023 at our hospital, 65 cases whose conization specimens were CIN1/2 (CIN1 : 16 and CIN2 : 49 cases) were enrolled in the study. The control group consisted of 374 patients whose conization specimens remained CIN3. Clinical background was examined by logistic regression analysis. Using conization specimens (HE staining), the number of infiltrating lymphocytes (number/HPF) into the submucosa of spontaneous regression areas or non-lesion areas in the same specimen was measured. **[Results]** Spontaneous regression was observed in 15% (65/439) and there was no correlation with preoperative histology, preoperative cytology, or patient age. Positive for surgical margin were negatively correlated with spontaneous regression ($p=0.004$). We focused on 16 cases of spontaneous regression to CIN1. The number of infiltrating lymphocytes at the regression areas was significantly higher than non-lesion areas (80.6 vs. 7.1/HPF) ($p=0.007$). In all cases with spontaneous regression, the number of submucosal lymphocytes was 30-fold (2.3-107 fold) higher than at the non-lesion. **[Conclusion]** Based on pathology of conization specimens, we isolated cases in which CIN3 had apparently regressed to CIN1/2. Infiltration of lymphocytes around regression areas suggest the lesion-specific cellular immunity to CIN3 occurs in some cases with favorable local immune environment.

ISP-1-9

Development of novel tracers for sentinel node identification in cervical cancer Kodama Keisuke, Yahata Hideaki, Tomonobe Hiroshi, Hachisuga Kazuhisa, Maenohara Shoji, Yagi Hiroshi, Yasunaga Masafumi, Onoyama Ichiro, Asanoma Kazuo, Kato Kiyoko *Graduate School of Medical Sciences, Kyushu University*

[Objective] Indocyanine green (ICG) with near-infrared (NIR) fluorescence imaging is used for lymphatic mapping. However, we occasionally experienced ICG fluorescence that does not remain in sentinel lymph nodes (SLNs) but flows to secondary lymph nodes or later. Here we investigated the efficacy and safety of a new fluorescence tracer comprising phytate and liposome-encapsulated ICG (LP). **[Methods]** Coadministration of phytate with LP containing phosphatidic acid promotes chelation mediated by Ca^{2+} in bodily fluids to enhance SLN retention. Uniformly-sized LPs (100 nm) encapsulating ICG under conditions that minimized fluorescence self-quenching during storage were produced. We analyzed the behavior of the new tracer (ICG-phytate-LP) and control tracers (ICG and ICG-LP) in the lymphatic flow of mice in terms of lymph node retention time. We also tested lymphatic flow and safety in pigs that have a more human-like lymphatic system. **[Results]** LPs encapsulating stabilized ICG were successfully prepared. Mixing LP with phytate in the presence of Ca^{2+} increased both the particle size and negative surface charge. In mice, ICG-phytate-LP had the best lymph node retention, with a fluorescence intensity ratio that increased over 6 hours and then decreased slowly over the next 24 hours. In pigs, there were no obvious differences between blood test results for the ICG and ICG-phytate-LP groups, and overall safety was good. **[Conclusion]** We believe that the practical application of this novel tracer will facilitate the identification of SLNs at many institutions and will greatly contribute to the spread of minimally invasive gynecologic malignancy surgery.

ISP-2-1

Evaluation of DNA-loaded Extracellular Vesicles as Novel Diagnostic Biomarker in High Grade Serous Ovarian Carci-

noma Uekusa Ryosuke¹, Yokoi Akira¹, Kitagawa Masami², Yoshida Kosuke¹, Yoshikawa Nobuhisa¹, Niimi Kaoru¹, Kajiyama Hiroaki¹ *Nagoya University¹, Department of Obstetrics and Gynecology Collaborative Research, Laboratory of Bell Research Center²*

[Objective] High-grade serous ovarian carcinoma (HGSOC) is the most common subtype and copy number variations (CNVs) are the dominant genomic event in HGSOC. Extracellular vesicles (EVs) are circulating in body fluids and positively carrying pathological genomic information. Here we evaluated the potential of EV-DNA as novel diagnostic methods for HGSOC. **[Methods]** A total of 124 samples from HGSOC patients and cell lines was analyzed. EVs were isolated using the ultracentrifuge method, and comprehensive CNV statuses were analyzed by whole genome sequencing (WGS). In reference to the Ovarian Cancer Moon Shot database, 30 dominant CNVs in HGSOC were selected as dominant targets for analyzing by droplet digital PCR (ddPCR). **[Results]** CNVs in EV-DNA from both clinical samples and cell lines were correctly detected using WGS, and those CNV status were also detected using ddPCR. Copy numbers of *RAD51*, *BRCA1*, *AKT2*, *CCNE1*, and *MSH6* were significantly higher in malignant tissue than in benign tissue ($p < 0.0001$, $p < 0.0001$, $p = 0.0012$, $p = 0.002$, $p = 0.0328$, respectively), and these were detectable in EV-DNA from ascites. In addition, the amount of DNA in malignant ascites was significantly higher than benign ascites ($p = 0.016$), and increased DNA in ascites itself suggested the presence of malignancy. Furthermore, there was an absolute different CNV status in tissue DNA from patients who treated with olaparib between responder and non-responder groups, and the combination of four genes (*RBI*, *GABRA6*, *CTNBN1*, *MYC*) could predict response to olaparib (AUC : 0.98). **[Conclusion]** CNV status of EV-DNA were correctly evaluated and can be novel diagnostic biomarkers for HGSOC.

ISP-2-2

Plasma Gelsolin inhibits Natural Killer Cell Function and confers Chemoresistance in Epithelial Ovarian Cancer Onuma Toshimichi¹, Inoue Daisuke¹, Tsuyoshi Hideaki¹, Orisaka Makoto¹, Yoshida Yoshio¹ *University of Fukui¹, Ishikawa Prefectural Central Hospital¹*

[Objective] Plasma gelsolin (pGSN) overexpression in ovarian cancer (OVCA) disarms immune function, contributing to chemoresistance. The aim of the study is to investigate immunoregulatory effects of pGSN expression on natural killer (NK) cells function in OVCA. **[Methods]** OVCA tissues from primary surgeries were performed immunofluorescent staining of pGSN and the activated NK-cell marker, natural cytotoxicity triggering receptor 1 to analyze the prognostic impact of pGSN expression and activated NK-cell infiltration. The immunoregulatory effects of pGSN on NK cells were assessed using apoptosis assay, cytokine secretion, immune checkpoint-receptor expression, and phosphorylation of STAT3. **[Results]** In OVCA tissue analyses, activated NK-cell infiltration provided survival advantages to patients. However, pGSN overexpression attenuated the survival benefits of activated NK-cell infiltration. In the in vitro experiment, chemoresistant OVCA cells secreted higher levels of pGSN compared with their chemosensitive counterparts, which induced NK-cell death. pGSN increased T-cell immunoglobulin and mucin-domain containing-3 expression (TIM-3) on activated NK cells. pGSN decreased interferon- γ production in activated TIM-3+ NK cells, responses that attenuated their anti-tumor effects. **[Conclusion]** Increased pGSN expression suppresses the anti-tumor functions of NK cells. The study provides insights into why immunotherapy is rarely effective in patients with OVCA, and suggest novel treatment strategies.

ISP-2-3

Establishment of an artificial intelligence-powered spatial assessment pipeline for intraepithelial and stromal tumor-infiltrating lymphocytes in high-grade serous ovarian carcinoma Hamada Kohei¹, Murakami Ryusuke¹, Ueda Akihiko¹, Kashima Yoko², Miyagawa Chiho², Taki Mana¹, Yamanoi Koji¹, Yamaguchi Ken¹, Hamanishi Junzo¹, Matsumura Noriomi², Mandai Masaki¹ *Kyoto University¹, Kindai University²*

[Objective] Tumor-infiltrating lymphocytes (TILs) are associated with improved survival in patients with epithelial ovarian cancer. However, the quantification of TILs is labor-intensive and has not been applied to routine clinical practice. **[Methods]** We developed two convolutional neural network (CNN) models to detect TILs and to determine their spatial location in whole-slide images (WSIs), and established an artificial intelligence-powered spatial assessment pipeline to objectively define intraepithelial and stromal TILs. **[Results]** The predictions of the established models showed a significant positive correlation with the number of CD8+ T cells and immune gene expressions. A total of 220 advanced cases with adnexa specimens were included in the survival analysis, and we demonstrated that patients with a higher density of intraepithelial TILs had a significantly prolonged overall survival (OS) and progression-free survival (PFS) in multiple cohorts ($p < 0.001$ and $p = 0.003$ for OS and PFS). Based on the density of intraepithelial and stromal TILs, we classified patients into three immunophenotypes: immune-inflamed, excluded, and desert. The immune-desert subgroup showed the worst prognosis ($p < 0.001$ for both OS and PFS). Gene expression analysis of 69 cases with RNA sequencing showed that the immune-desert subgroup had lower immune cytolytic activity (CYT) and T-cell-inflamed gene-expression profile (GEP) scores, whereas immune-excluded subgroup had higher expression of interferon- γ and programmed death 1 receptor (PD-1) signaling pathway. **[Conclusion]** Our established evaluation method provides detailed and comprehensive quantification of intraepithelial and stromal TILs throughout hematoxylin and eosin (H&E)-stained WSIs, and has potential for clinical application for personalized treatment of patients with ovarian cancer.

ISP-2-4

Spatial exosome analysis unveils the location heterogeneity of extracellular vesicles in ovarian cancer Yokoi Akira, Yoshida Kosuke, Kitagawa Masami, Nagao Yukari, Yoshikawa Nobuhisa, Niimi Kaoru, Kajiyama Hiroaki *Nagoya University*

[Objective] Ovarian cancer cells aggressively spread into the intraperitoneal cavity utilizing extracellular vesicles (EVs). In patient bodies, although the EVs in ascites should have heterogeneity and various malignant effects, it has been largely unknown. This study aimed to elucidate unknown ascites-derived EV functions in ovarian cancer. **[Methods]** We developed a unique cellulose nanofiber-based EV sheet that captures EVs from micro-volume fluids, around ten microliters. EVs were captured from ovarian cancer patients and orthotopic ovarian cancer mouse models. The EVs captured by the sheet were analyzed by small RNA sequencing. **[Results]** In the ovarian cancer mouse model, the EV sheet revealed that cancer-related miRNAs were detected from the very early phase at day 4 when the mice did not have apparent ascites. Then, the profiles EVs migrated towards malignant ascites at day 28, which condition is the mimic of the advanced stage. EV sheet analysis in ovarian cancer patients revealed that the tumor surface EVs had distinct profiles from whole ascites. Furthermore, the direct EV sheet attaching method during the surgery of ovarian cancer patients identified the location-based unique EV miRNA profile. Comparing advanced-stage cases, the trajectory analysis re-

vealed that the connection pattern was different in patients with localized disease, and we identified ten cancer-associated miRNAs whose expression level decreased with distance from the primary tumors. **[Conclusion]** EV sheet analysis can provide a whole new concept that the tiny amount of ascites-EVs from ovarian cancer patients had location heterogeneity, which can contribute to understanding the unknown mechanism of ovarian cancer progression.

ISP-2-5

Efficacy of PARP Inhibitors: Insights from a Cancer Genome Profile-Based Model of Malignant Transformation in Mature Teratoma Patients Nakagawa Atsushi, Tamauchi Satoshi, Yoshida Kosuke, Yoshihara Masato, Shimizu Yusuke, Yokoi Akira, Ikeda Yoshiki, Yoshikawa Nobuhisa, Niimi Kaoru, Kajiyama Hiroaki *Nagoya University*

[Objective] Advanced cases of malignant transformation of ovarian mature teratoma are very refractory, and standard chemotherapy has not been established. Although the development of cancer genome profiling (CGP) testing has expanded the use of molecular-targeted agents for these rare cancers, it's difficult to sequentially validate their efficacy in refractory rare cancers in clinical practice. In this study, we established a patient tumor-derived model (PDX) of malignant transformation of ovarian mature teratoma with high loss of heterozygosity (LOH) and tested the efficacy of molecular-targeted agents that were suggested to be effective by the CGP test. **[Methods]** The patient was a 66-year-old woman who was diagnosed with malignant transformation of mature teratoma (squamous cell carcinoma) after an exploratory laparotomy. The tumor underwent CGP testing and was then transplanted into hyperimmunodeficient mice to establish PDX. After three passages, the tumors were divided and transplanted into nude mice, and these mice were divided into 4 groups and treated with control, cisplatin, olaparib, and niraparib. **[Results]** FoundationOne CDx showed a high LOH level of 41.0%. In a dosing study in nude mice ($n = 42$), there was a significant decrease in tumor volume in the olaparib and niraparib treatment groups compared to the control group ($p < 0.05$). No significant tumor volume reduction was observed in the cisplatin group, consistent with the clinical course of platinum resistance. Immunostaining of the tumors after treatment showed increased expression of the cytotoxic marker γ H2AX. **[Conclusion]** The efficacy of PARP inhibitors in the malignant transformation of mature teratomas with high LOH was demonstrated.

ISP-2-6

AMIGO2 is Involved in the Spread of Peritoneal Metastasis in Serous Ovarian Cancer via Promoting Adhesion to the Peritoneal Mesothelial Cells Iida Yuki, Sato Shinya, Yamamoto Koji, Okawa Masayo, Hikino Kohei, Hosokawa Masayo, Sawada Mayumi, Komatsu Hiroaki, Kudoh Akiko, Taniguchi Fuminori *Tottori University*

[Objective] Amphoterin-induced gene and open reading frame 2 (AMIGO2) has been reported to be associated with the prognosis of colorectal, gastric, and cervical cancer. However, the association remains unknown in ovarian cancer. The aim of this study was to clarify the role of AMIGO2 expression in ovarian cancer. **[Methods]** AMIGO2 expression was evaluated by immunohistochemistry in patients with ovarian serous carcinoma. Then we assessed the adhesive association between serous ovarian cancer cell lines and peritoneal mesothelial cells in vitro and murine model studies. **[Results]** The AMIGO2-high group had a significantly shorter progression free survival (PFS) than the AMIGO2-low group. The predictive index of the AMIGO2-high group was considerably higher than that of the AMIGO2-

low group. The rate of complete cytoreductive surgery was lower in the AMIGO2-high group than in the AMIGO2-low group. Moreover, *in vitro* studies revealed that four serous ovarian cancer cell lines were associated between AMIGO2 expression and adhesive rate to mesothelial cell. The adhesion to the mesothelial cell was attenuated by AMIGO2 knockdown in SKOV3 cells. Furthermore, downregulation of AMIGO2 in SKOV3 significantly suppressed peritoneal dissemination in murine model. **[Conclusion]** High expression of AMIGO2 in serous ovarian carcinoma cells contribute to worse prognosis by promoting peritoneal metastasis due to enhanced cell adhesion to mesothelial cells.

ISP-2-7

PTEN Expression in Ovarian Cancer : Impact of PTEN Loss on the Tumor Microenvironment, Treatment Response, and Prognosis Freeman Lina¹, Masuda Kenta¹, Tamura Tomohiro¹, Nagai Shimpei¹, Imaeda Keiyo¹, Akahane Tomoko², Kisu Iori¹, Chiyoda Tatsuyuki¹, Kobayashi Yusuke¹, Banno Kouji¹, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Department of Clinical Laboratory Sciences, Nitobeunika College²*

[Objective] PTEN is a tumor suppressor gene which mutation serves as a driver in the pathogenesis of ovarian cancer. New studies have shown that PTEN expression can affect the tumor microenvironment (TME) of various cancers, however its role within ovarian cancer remains unclear. The aim of this study was to investigate the effects of PTEN expression on ovarian TME and tumor progression. **[Methods]** We performed immunohistochemistry staining for PTEN, CD8, and FOXP3 on 19 tumors with high-grade serous (n=14), clear cell (n=3) and endometrioid (n=2) carcinoma. Clinical stages for high-grade serous carcinoma (HGSC) patients were stage III or IV. We evaluated associations between PTEN expression and both CD8⁺ T cells and FOXP3⁺ cells and explored the correlation between PTEN expression and progression free survival (PFS) for advanced HGSC patients. **[Results]** Tumors were stratified into 2 groups based on PTEN expression : positive (n=4) and negative-to-weak (n=15). There was no significant relation between PTEN and histological type (p=0.277). PTEN positive tumors were associated with higher CD8⁺ T cells (p=0.001) and higher FOXP3⁺ cells (p=0.014). Additionally, HGSC patients with positive PTEN were associated with longer PFS, and all platinum-resistant cases with recurrence less than 6 months after platinum therapy exhibited negative-to-weak PTEN expression. **[Conclusion]** This research suggests that PTEN expression significantly affects T cell infiltration within the TME of ovarian cancer, and could be utilized as a potential biomarker for predicting the efficacy of immune therapy and chemotherapy for ovarian cancer.

ISP-2-8

Establishment of novel immunotherapy by targeting HNF1 beta in ovarian clear cell carcinoma Katagiri Kaede, Nishio Hiroshi, Matsuda Risa, Matsui Tomoya, Sugiyama Juri, Iwata Takashi, Yamagami Wataru, Tanaka Mamoru *Keio University*

[Objective] Transcriptional factor HNF1 β is a diagnostic marker for ovarian clear cell carcinoma (OCCC) and its function has not been clearly clarified. In this study, we investigated the immunological function of HNF1 β and evaluated it as a novel therapeutic target. **[Methods]** We first generated HNF1 β knockdown and overexpression human OCCC cell lines (JHOC-5 and RMG-V) and test their level of immunosuppressive cytokines (IL-6) by ELISA. Next, we screened drug library consisting of 1128 approved drugs and 364 chemical compounds to inhibit HNF1 β . We selected one drug and investigated its transcriptional activity of HNF1 β by chromatin immunoprecipitation

(ChIP) assay. Finally, we evaluated anti-tumor effect by screened drug with syngeneic mouse OCCC model. **[Results]** HNF1 β knockdown OCCC cells significantly decreased IL-6 cytokine production from 4559.4 \pm 559.4 pg/ml to 333.8 \pm 30.2pg/ml and HNF1 β overexpression OCCC cells significantly upregulated IL-6 production from 85.8 \pm 9.8 pg/ml to 611.8 \pm 27.1pg/ml indicating that HNF1 β regulates IL-6 production. With drug screen libraries, we found that BET bromodomain inhibitor (BETi) is capable of inhibiting HNF1 β expression and IL-6 production by OCCC cell lines without affecting cell viability. ChIP assay showed BETi epigenetically suppressed HNF1 β by binding a specific region (-1150bp to -850bp). Finally, we validated anti-tumor effect of BETi with syngeneic OCCC model. BETi oral administration showed anti-tumor effect trend with tumor weight (p=0.139) with reduced HNF1 β expression by immunohistochemistry and IL-6 production in plasma. **[Conclusion]** Inhibitors on the HNF1 β pathway can improve immunosuppressive conditions of OCCC and are useful target of immunotherapy for OCCC.

ISP-2-9

A study of combination therapy with histone methylase EZH2 inhibitor and PARP inhibitor in ovarian mucinous carcinoma Hachijo Ryuta¹, Sone Kenbun¹, Ishizaka Aya¹, Suzuki Eri¹, Tanimoto Saki¹, Tsuboyama Natsumi¹, Toyohara Yusuke¹, Fukuda Tomohiko¹, Taguchi Ayumi¹, Oda Katsutoshi², Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, Department of Clinical Genomics, The University of Tokyo²*

[Objective] The histone methylase EZH2 is an epigenomic factor that has been reported to be a therapeutic target in many cancers. Ovarian cancer is the deadliest gynecologic malignancy, and among them, mucinous ovarian cancer (MOC) is resistant to chemotherapy, including platinum and PARP inhibitors, and has a particularly poor prognosis. In this study, we investigated the efficacy of EZH2 inhibitors and combination therapy with PARP inhibitors in MOC. **[Methods]** EZH2 expression was analyzed by real-time PCR in clinical samples of MOC (n = 13). Three cell lines of MOC were tested for drug susceptibility using Cell Counting Kit -8. The drugs we used were the EZH2 inhibitors GSK126, Olaparib and Cisplatin. Cell lines of MOC were treated with EZH2 inhibitor in combination with PARP inhibitor, and protein expression was evaluated by Western Blotting. **[Results]** In expression analysis, MOC showed significantly higher expression of EZH2 compared to normal ovarian tissue. In MOC cell lines, GSK126 showed a lower IC 50 than cisplatin. A synergistic effect was observed with GSK126 and Olaparib in MCAS, one of the MOC cell lines, and an additive effect was observed with RMUGS in the other. Western blotting of MCAS and RMUGS treated with GSK126 and Olaparib showed a decrease in H3K27me3 protein expression and an increase in cleaved PARP protein expression, suggesting apoptosis. **[Conclusion]** Monotherapy with GSK126 and combination therapy with Olaparib may be a new therapeutic strategy in MOC.

ISP-2-10

Mutation profiles of ovarian seromucinous borderline tumors in Japanese patients Nakayama Kentaro¹, Ishibashi Tomoka¹, Tomita Yasuha¹, Sato Rei¹, Kondo Yoshimi¹, Kurakane Satomi¹, Seki Koichirou¹, Murakami Isamu¹, Ishikawa Masako², Kojima Kazuhisa³, Sasamori Hiroki³, Kyo Satoru⁴ *Nagoya City University East Medical Center¹, Shimane University², Nara Prefecture General Medical Center³*

[Objective] Ovarian seromucinous tumors (SMBTs) are relatively rare, and their carcinogenesis is largely unknown. In this study, the molecular features of SMBTs in Japan were assessed. **[Methods]** DNA was extracted from microdissected paraffin-

embedded sections from 23 SMBT cases. Genetic mutations (*KRAS*, *BRAF*, *PIK3CA*, and *ERBB2*) were evaluated using Sanger sequencing. Immunohistochemistry for p53, ARID1A, and PTEN was also performed as a surrogate for the loss of functional mutations in these tumor suppressor genes. **[Results]** The prevalence of *KRAS*, *BRAF*, *PIK3CA*, and *ERBB2* mutations was 4.3% (1/23), 8.6% (2/23), 8.6% (2/23), and 17.3% (4/23), respectively. Overexpression or loss of p53 expression occurred in 26% (6/23), loss of ARID1A expression in 4.3% (1/23), and none of the cases observed, showed expression of PTEN loss. **[Conclusion]** These findings suggest that *KRAS/BRAF/PIK3CA* and *PTEN* mutations are rare carcinogenic events in SMBTs. The high frequency of positive p53 staining and a low frequency of loss of ARID1A staining suggests that SMBT carcinogenesis may be related to alteration of p53 rather than that of ARID1A. *ERBB2* oncogenic mutations may play an important role in the tumorigenesis of Japanese SMBTs.

ISP-2-11

Identification the role of SETD8, as a newly potential therapeutic target for OCCC Suzuki Eri, Sone Kenbun, Jonouchi Yuri, Fukaya Sayuri, Yoshimoto Daisuke, Ishizaka Aya, Hachijo Ryuta, Tsuboyama Natsumi, Tanimoto Saki, Fukuda Tomohiko, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*
[Objective] SETD8 is Histone 4 lysine 20 (H4K20me1) methyltransferase, and its functions are DNA replication, DNA damage repair, cell cycle progression, and transcriptional regulation. It is reported to be upregulated in various types of cancers including gynecological cancers such as endometrial cancer, ovarian high grade serous carcinoma and ovarian endometrioid carcinoma. However, its role in ovarian clear cell carcinoma (OCCC) has not been understood. In this study, we investigated the expression and function of SETD8 in OCCC. **[Methods]** Using clinical samples (n=46), SETD8 mRNA expression was evaluated by qRT-PCR. MTT assays, Colony formation assay, Western blot method, and Cell cycle assays were performed in three types of OCCC cell lines. **[Results]** Consistent with TCGA datasets for ovarian high grade serous carcinoma and ovarian endometrioid carcinoma, expression of SETD8 was upregulated in OCCC clinical tissues. Using three OCCC cell lines, addition of SETD8 inhibitor resulted in a significant decrease in cell viability compared to Cisplatin addition. Furthermore, the colony formation assay showed a similar trend to the cell viability assay, depending on the SETD8 inhibitor concentration gradient. When SETD8 inhibitor was added, Western blot showed decrease in histone modification, and Cell cycle assay showed increased percentage of cell cycle arrest at G2-M phase. **[Conclusion]** Our results suggest that SETD8 could be a potential therapeutic target for OCCC. Additional studies are needed to determine the mechanisms of SETD8.

ISP-2-12

Fyn expression is associated with sensitivity to platinum-based chemotherapy for ovarian serous carcinoma Uchikura Eijiro, Fukuda Takeshi, Noda Takuya, Awazu Yuichiro, Tasaka Reiko, Imai Kenji, Yamauchi Makoto, Yasui Tomoyo, Sumi Toshiyuki *Osaka Metropolitan University*
[Objective] We examined the correlation between Fyn expression and the sensitivity to platinum-based chemotherapy for ovarian serous carcinoma. **[Methods]** We reviewed 64 cases of ovarian serous carcinoma stage III-IV from 2005 to 2014. Cases were divided into two groups one group in which maximum debulking surgery followed by platinum-based chemotherapy was performed and did not recur within 6 months after completion of chemotherapy (group A ; n=35), and the other group in which maximum debulking surgery followed by platinum-based

chemotherapy was performed and recur within 6 months (group B ; n=29). Fyn expression was examined immunohistochemically. The effect of the siRNA-mediated knockdown of Fyn on the sensitivity of ovarian cancer cells to carboplatin was investigated. This study was approved by the institutional review board. **[Results]** The expression of Fyn was significantly higher in the group B than in the group A ($p < 0.01$). Cases were divided into two groups according to a cutoff value of 6 which was calculated using a receiver operating characteristic curve : one group in which Fyn expression was low level (weighted score ≤ 6 , n=32), and another group in which Fyn expression was high level (weighted score ≥ 8 , n=32). Low Fyn expression group might be sensitive to platinum-based chemotherapy than high expression group ($p=0.003$). There was no significant difference in overall survival between two groups ($P=0.05$). Furthermore, knockdown of Fyn expression significantly increased cancer cell sensitivity to carboplatin in vitro. **[Conclusion]** Expression of Fyn might be associated with sensitivity to platinum-based chemotherapy for advanced ovarian serous carcinoma.

ISP-3-1

The detection of circulating tumor cells in gynecologic malignancies at our hospital Takasaki Kazuki, Ichinose Takayuki, Nishida Haruka, Takahashi Yuko, Hirano Mana, Watanabe Saya, Onodera Takako, Takehara Kohei, Miyakawa Kosuke, Tomiya Hiroka, Hiraike Haruko, Nagasaka Kazunori *Teikyo University*
[Objective] Cancer metastasis via circulating tumor cells (CTCs) correlates with prognosis, and evaluation of CTC in the blood is expected to contribute to early diagnosis, predicting prognosis, and decision for treatment. However, due to the epithelial-mesenchymal transition of CTCs, CTCs cannot be detected by the EpCAM-specific isolation method. We report the methods for detecting CTCs and the results at our institute. **[Methods]** Patients with gynecological malignancies treated at our hospital from April 2022 to August 2023 were included. CTC was detected after removing lymphocytes and mononuclear cells using Dynabeads CD45 (Veritas, Tokyo). We assessed the results of stage, histology, recurrence, and expression of EpCAM in cases with CTCs detection. **[Results]** Blood samples were collected from 20 patients with gynecological malignancies during the study period. CTCs were found in 10 cases : two cases of cervical cancer (IIB-IIIC2, adenocarcinoma/squamous cell carcinoma,) four cases of endometrial cancer (IA only, three of endometrioid carcinoma G2, one of serous carcinoma), three cases of ovarian cancer (IIIC-IVB, high-grade serous carcinoma), and one case of uterine adenocarcinoma (stage IC). The median age was 53 (40-70) years. One case of cervical cancer (stage IIB), one case of endometrial cancer, and two cases of ovarian cancer (stage IIIC-IVB) were EpCAM positive. Of these, one case of ovarian cancer with stage IVB showed a recurrence of pleural dissemination after treatment. **[Conclusion]** The detection of CTCs is minimally invasive and may be useful for preoperative diagnosis. Further studies are needed to examine the prognostic correlation of CTC detection.

ISP-3-2

Atypical mullerianosis of the left adnexa and the left ureter : a case report Yang Hsiang Kuo *National Taiwan University Hospital, Taiwan*
Background : Mullerianosis is a rare choristoma originating from Müllerian tissues, setting it apart from typical endometriosis which involves only endometrial tissue. This condition predominantly affects postpubertal women and can impact the urinary system. Its pathogenesis and optimal treatment remain topics of debate. **Case Presentation :** A 53-year-old female pa-

tient presented with a history of abdominal pain and constipation since late 2021. Initial evaluations revealed bilateral ovarian cysts, nodules on the uterine wall, and left hydronephrosis. When initial interventions, including Gonadotropin-releasing hormone agonist injections from 2023/2-4, failed to alleviate symptoms, she sought for a second opinion at NTUH. Further investigations in 2023 revealed a 6.7cm tumor involving the left ovary, ureter, and surrounding structures, with severe left hydronephrosis and critically impaired left renal function. Following a series of evaluations and treatments, she underwent a laparoscopic surgery which revealed a left ureteral tumor. The final pathology report revealed atypical Mullerianosis over the left adnexa and the left ureter. **Conclusion** : This case underscores the importance of accurate diagnosis and understanding of Mullerianosis. Despite its benign nature, the condition can manifest with significant clinical complications, necessitating timely and appropriate interventions.

ISP-3-3

Microsatellite instability and tumor mutation burden by histological type of gynecological malignancy in Japan Seino Manabu, Sano Shiori, Gonai Yuta, Okui Yosuke, Sakaki Hirotsugu, Oota Tsuyoshi, Nagase Satoru *Yamagata University* **[Objective]** This study determined the microsatellite instability (MSI) and tumor mutation burden (TMB) of gynecological malignancies in Japan. **[Methods]** We assessed the cancer genomic profiling (CGP) data of gynecological malignancy. CGP data were obtained from the Center for Cancer Genomics and Advanced Therapeutics (C-CAT). **[Results]** Regarding cervical cancer, there were 669 squamous cell carcinomas (SCC), 126 endocervical adenocarcinomas, 75 adenosquamous carcinomas, 87 gastric type adenocarcinomas, 118 neuroendocrine tumors, and 429 others. The TMB of SCC (6.86 muts/Mb) was significantly higher than endocervical adenocarcinoma (3.52 muts/Mb). In uterine corpus malignancy, there were 317 endometrioid carcinomas, 129 serous carcinomas, 128 carcinosarcomas, 202 leiomyosarcoma, and 292 others. MSI-high values by histological type were 16.7% for endometrioid carcinoma, which was higher than other histological types. The TMB and TMB-high values in endometrioid carcinoma were also significantly higher than other histological types ($p < 0.01$). In ovarian cancer, there were 1570 high-grade serous carcinomas, 96 low-grade serous carcinomas, 969 clear cell carcinomas, 245 endometrioid carcinomas, 199 mucinous carcinomas, 55 granulosa cell tumors, and 1692 others. The MSI-high value was highest in endometrioid carcinoma (3.3%), and the TMB-high value was higher in granulosa cell tumors (12.7%). **[Conclusion]** The MSI-high and TMB-high values of the uterine corpus endometrioid carcinoma were high among gynecological malignancies, and the MSI-high and TMB-high values of non-SCC of the cervix and ovarian malignancy were low.

ISP-3-4

Analysis of gynecologic cancer patients' subgroup in ONCO DVT study ; Edoxaban for 12 Months Versus 3 Months in Cancer Patients with Isolated Distal Deep Vein Thrombosis Shikama Ayumi¹, Yamashita Yugo², Kawaguchi Ryuji³, Itagaki Hiroya¹, Tasaka Nobutaka¹, Akiyama Azusa¹, Yamada Yuki¹, Iwai Kana³, Kawahara Naoki³, Kimura Fuminori², Satoh Toyomi¹ *University of Tsukuba¹, Department of Cardiovascular Medicine, Kyoto University², Nara Medical University³* **[Objective]** The ONCO DVT study has revealed that 12-month edoxaban treatment for isolated distal deep vein thrombosis (IDDVT) in patients with cancer was superior to 3-month edoxaban treatment in terms of preventing a symptomatic recurrent venous thromboembolism (VTE) or VTE-related death. The ob-

jective of this study is to evaluate the efficiency of 12-month versus 3-month edoxaban treatment for IDDVT in patients with gynecologic cancer frequently accompanied by VTE. **[Methods]** In the ONCO DVT study, the cancer patients with IDDVT were assigned to either a 12-month or 3-month edoxaban treatment. We analyzed the gynecologic cancer patients' subgroup in the ONCO DVT study. The primary endpoint was a symptomatic recurrent VTE or VTE-related death at 12 months. The major secondary endpoint was major bleeding at 12 months. **[Results]** From May 2019 to June 2022, 188 patients with gynecologic cancer were enrolled and randomized (102 patients in the 3-month edoxaban group and 86 in the 12-month edoxaban group). The primary endpoint of symptomatic VTE at 12 months was 0 of 102 patients (0%) in the 12-month group and 8 of 86 patients (7.8%) in the 3-month group ($p=0.008$). No VTE-related death events occurred. The major secondary endpoint of major bleeding events occurred in 8 (9.3%) patients in the 12-month group and 4 (3.9%) in the 3-month group (odds ratio, 0.40 ; 95% CI, 0.12-1.37). **[Conclusion]** In gynecologic cancer patients with IDDVT, 12 months was superior to 3 months for an edoxaban treatment with a symptomatic recurrent VTE or VTE-related death.

ISP-3-5

Therapeutic management of uterine tumors resembling ovarian sex cord tumors including a focus on fertility : Systematic Review Shibahara Mami¹, Kurita Tomoko¹, Harada Hiroshi¹, Takedomi Ruka¹, Hagimoto Marina¹, Higami Shota¹, Tooyama Atsushi¹, Kinjo Yasuyuki¹, Hoshino Kaori¹, Ueda Taeko¹, Matsuura Yusuke², Yoshino Kiyoshi¹ *University of Occupational and Environmental Health¹, Nursing of Human Broad Development, University of Occupational and Environmental Health²* **[Objective]** Uterine tumors resembling ovarian sex cord tumors (UTROSCTs) are extremely rare. Most cases of UTROSCTs underwent hysterectomy and had a benign clinical course. Fertility-preserving surgery should be considered because some cases occur in UTROSCT patients under 40 years. We report the first review of treatment and prognosis including a focus on fertility in the largest number of UTROSCT cases. **[Methods]** We conducted a systematic review of UTROSCT case reports and case series in English till December 2022 and compared initial treatment and recurrence rates. **[Results]** In total, 147 cases (72 articles) reporting the clinical course of UTROSCTs were analyzed. The median age at diagnosis was 50.0 years, and 28 (19.0%) patients were aged under 40 years. Most patients ($n=125$, 85.0%) underwent hysterectomy as the initial surgery, with a recurrence rate of 17.6% ($n=22$). The recurrence rate was 30% ($n=6$) in patients who underwent mass resection ($n=20$). Among the patients, 15 were under 40 years of age, seven had achieved pregnancy (46.7%), and six had successful deliveries (40.0%). No significant difference in the 5- and 10-year disease-free survival (DFS) was found between the hysterectomy and mass resection group ($p=0.123$ and $p=0.0612$). BSO as the additional treatment was not significantly associated with the 10-year DFS ($p=0.548$). **[Conclusion]** While total hysterectomy is the recommended treatment for UTROSCTs based on recurrence rates, mass resection as fertility-preserving surgery is an acceptable treatment option for patients who desire childbearing. We recommend fertility treatment within five years after tumor resection and hysterectomy early after delivery.

ISP-3-6

Treatment outcome of gynecologic cancer patients on hemodialysis in our hospital Oyanagi Ryo, Kakuda Mamoru, Toda Aska, Nakagawa Satoshi, Kinose Yasuto, Takiuchi Tsuyoshi, Kodama Michiko, Hashimoto Kae, Ueda Yutaka, Sawada

Kenjiro, Kimura Tadashi *Osaka University*

[Objective] Treatment for cancer patients on hemodialysis can lead to serious complications because of increased susceptibility to infection, renal anemia and anticoagulation. The aim of this study is to investigate treatment completion rate and prognosis of gynecologic cancer patients on hemodialysis in our hospital. **[Methods]** We extracted gynecologic cancer patients on hemodialysis from our gynecologic database between 2010 and 2023. **[Results]** 11 patients (including 7 endometrial cancer, 2 ovarian cancer and 2 cervical cancer) were extracted. 8 cases were Stage I and 3 cases were Stage II or higher. All 8 patients with stage I disease underwent surgical treatment. All but one patients omitted pelvic lymph node dissection due to concerns about complications. Postoperative treatment was also omitted in all patients for the same reason. As for complication, postoperative bleeding was observed in one patient who underwent pelvic lymph node dissection, and IVR treatment was performed. No recurrence was observed in all patients (median follow-up : 50.8 (20-103) months). All 3 patients with stage II or higher gynecological cancer, including 1 case of uterine cancer stage IVB received systemic chemotherapy, 1 case of ovarian cancer stage IIIC received systemic chemotherapy, and 1 case of cervical cancer stage IIB received CCRT, were discontinued due to serious complications (decreased performance status, septic shock and uncontrolled gastrointestinal bleeding), and best supportive care was introduced **[Conclusion]** While surgical treatment can be an sufficient option for patients with early-stage gynecological cancer, CCRT or chemotherapy for patients with stage II or higher gynecological cancer must be carefully examined.

ISP-3-7

A case of apocrine adenocarcinoma of the vulva Omote Maya, Ueda Tomoko, Oi Katsuhiko, Narita Sachiyo, Taniguchi Roze, Tsubamoto Hiroshi, Shibahara Hiroaki *Hyogo Medical University*

Apocrine adenocarcinoma (AA) of the cutaneous sweat glands is a rare disease. Treatment of metastatic AA was investigated, and in one case, a regimen for triple negative breast cancer (TNBC) was implemented. **[Case]** A 63-year-old woman presented to our hospital with a complaint of a mass sensation in the left vulva and lymphedema of the left leg ; PET/CT scan showed FDG accumulation in the left vulva, pelvis, para-aortic lymph node, and left supraclavicular lymph node. Local excision of the vulvar tumor was performed, and a diagnosis of metastatic AA was made with positive androgen receptor and GCDFP-15. In accordance with previous reports for head AA, paclitaxel and carboplatin were administered as 1st line, and the leg edema improved after the first cycle. However, after 2 cycles, the lower legs were swollen again, and after 3 cycles, the lymphedema extended to the lower abdomen with erythema, warmth, and pain. Serum creatinine and CEA were elevated. Left hydronephrosis was observed and a ureteral stent was placed Based on TNBC, second-line treatment with PTX and bevacizumab (Bev) was administered After second-line treatment (wPTX/Bev), symptoms improved, and PET/CT scan showed no FDG accumulation in the lymph nodes The edema worsened when PTX was reduced, so the patient was started on third line Capecitabine was used as tertiary therapy. However, edema worsened, so low-dose cyclophosphamide + Bev was used for fourth-line treatment, and bicalutamide was used for fifth-line treatment. **CONCLUSION :** wPTX/Bev may be a promising candidate for AA treatment.

ISP-3-8

A Case of Retroperitoneal Hematoma Caused by Ovarian Ar-

tery Rupture Saito Ryotaro, Asada Kayo, Watanabe Tomoya, Oshima Kotaro, Ga Hiroimi, Uetake Nanami, Kurishita Gaku, Ishino Tomomi, Matsumoto Yoko, Kagawa Hideyuki *Kanto Rosai Hospital*

[Introduction] Ovarian artery bleeding is an extremely rare condition, and there have been few reported cases in Japan. In this report, we share a case where coil embolization was performed for a retroperitoneal hematoma suspected to be caused by ovarian artery bleeding. **[Case]** A 50-year-old female with a history of 4 pregnancies and 4 cesarean sections, including 4 cesarean deliveries, and a surgical history of bilateral ovarian cystectomy at the age of 25, presented to our hospital with sudden right lower abdominal pain without any identifiable trigger. She was urgently transported to our hospital due to this acute right lower abdominal pain. Contrast-enhanced CT revealed a retroperitoneal hematoma on the right side, exceeding 10 cm in diameter, suspected to be caused by bleeding from the right ovarian artery. She was urgently admitted, and vascular imaging was performed, revealing a pseudoaneurysm suspected to be caused by bleeding from the right ovarian artery. Coil embolization was performed. On the first day (Day X+1), her hemoglobin level had dropped to 7.6 g/dL, but showed an improving trend thereafter. The hematoma had also decreased in size to 9 cm on the fourth day (Day X+4) after the procedure. Her abdominal pain improved, leading to her discharge on Day X+12. **[Discussion]** Patients who develop ovarian artery bleeding unrelated to the perinatal period often have a history of gynecological surgeries, as was the case with this patient. While there is no established standard treatment for this condition, vascular embolization is considered effective.

ISP-3-9

Ovarian metastasis of thymic carcinoma : a case report Maeda Shinichiro¹, Shiraga Aoi¹, Ogino Atsuko¹, Kawaguchi Yusuke¹, Yamazoe Saeko¹, Matsubayashi Aya¹, Hayashi Nobutaka¹, Tanabe Saeko¹, Ootake Noriko¹, Miki Michiyasu¹, Aoki Takuya¹, Yoshioka Shinya^{1,2} *Kobe City Medical Center General Hospital¹, Okubo Hospital²*

Thymomas and thymic carcinomas are infrequent neoplasms in the anterior mediastinum. Their extrathoracic metastases are uncommon, and metastases to the ovary are exceedingly rare with only 7 cases reported in the literature. We present a young female case of thymic carcinoma with metastasis to her right ovary as well as pericardial dissemination. A 25-year-old woman with no symptoms was referred to our hospital due to a mediastinal abnormality by chest radiograph. Chest CT scan and MR imaging showed signs of mediastinal thymoma with possible invasiveness. Subsequent open thoracic surgery revealed pericardial dissemination and finished with biopsy only. She was thus diagnosed as thymic carcinoma pathologically. Post-operative PET scan showed partial accumulation in her right ovary and our gynecologic department conducted laparoscopic salpingo-oophorectomy for her right adnexa. In due course, pathologic examination demonstrated ovarian metastasis of thymic carcinoma as well as benign ovarian dermoid cyst. As this young nonparous patient wished for fertility preservation before treatment, we quickly referred her to a reproductive clinic and she went through oocyte cryopreservation. She thereupon joined a clinical trial, undergoing chemotherapy (carboplatin and paclitaxel) in combination with immunotherapy by atezolizumab, a humanized anti-PD-L1 monoclonal antibody. Further follow-up is to be made.

ISP-3-10

Laparoscopic surgery for torsion of mature cystic extragonadal teratoma on the mesosalpinx : A case report Suzuki

Yukiko, Shiro Michihisa, Futaki Hitomi, Oki Noriyoshi, Okada Juzo, Yoshida Shigeki *Chibune General Hospital*

Mature cystic extragonadal teratomas are rare and have often been reported in the omentum or Douglas pouch. We herein report a rare case of laparoscopic surgery for torsion of a mature cystic extragonadal teratoma of the mesosalpinx. A 29-year-old woman (gravida 0; para 0), was admitted to our hospital because of strong left lower abdominal pain. She had no history of gynecological disease and had sometimes experienced lower abdominal pain several years previously. Computed tomography showed bilateral ovarian tumors, and both were suspected to be mature cystic teratomas. Emergency laparoscopic surgery was performed due to torsion of the left ovarian tumor. Intraoperatively, the tumor on the left mesosalpinx was found to be twisted with a fallopian tube, and an atrophied left ovary was detected separately from the tumor. The left tumor on the mesosalpinx was resected laparoscopically. Pathological imaging of the tumor showed primordial follicles with mature cystic teratomas. The autoamputated left ovarian mature cystic teratoma was presumably engrafted on the left mesosalpinx, and mature cystic extragonadal teratoma on the mesosalpinx was twisted.

ISP-3-11

Ou MC decrescendo phenomenon as a component of anti-cancer effect by physical activity—based on a new aspect of carcinogenesis by abnormal cell polarity Ou Ming Cheh^{1,2} *Taipei City Hospital, Zhong-Xiao Branch, Taiwan¹, Chung Shan Hospital, Taiwan²*

[Objective] The causal relationship between physical activity and anti-cancer effect are not proved by the current studies. Ou MC (Ming-Cheh) decrescendo phenomenon treatment (OuDPt), an easy self-administered exercise as a component of physical activity, shows an anti-cancer effect. **[Methods]** We review the anti-cancer effects of OuDPt in the context of physical activity and human body anatomical axes (HBAAAs). **[Results]** OuDPt showed to induce normalization of cancer cell polarity, which caused squamous metaplasia, apoptosis and regression of uterine endometrial cancer, suppression of ovarian and pancreatic cancer growth, regression of early suspicious pancreatic cancer, enhancement of chemotherapy effect of pancreatic cancer and stop of cancer-related bleeding. **[Conclusion]** The tumor regression induced by OuDPt may indicate that disruption of cell polarity is not merely a by-product of cancer cells but also a contributing factor in cancer initiation and development. However, such anti-cancer effect by OuDPt shows insufficient efficacy for advanced cancer in long term treatment but may be availed for cancer prevention and adjuvant treatment. Further study is warranted. **Reference :** 1. Ou MC, Ou D, Pang CC. 2nd JCA-AACR precision cancer medicine international conference. Kyoto, Japan, June, 2023, 5-42. Ou MC. Ou MC decrescendo phenomenon as a component of physical activity for cancer prevention. IGCS global meeting, Seoul, Korea, November, 2023.3. Ou, MC., Ou, D., Pang, CC., Ou, YJ. 'The Causal Relationship of Anti-Cancer Effect with Physical Activity Evinced by the Consistent Anti-Cancer Effect of the Ou MC Decrescendo Phenomenon', *Asian Pacific Journal of Cancer Prevention*, 2023, 24 (8), pp. 2869-2874.

ISP-4-1

Retinoic acids tend to suppress endometriotic cell proliferation via G1 cell cycle arrest Azuma Yukihiro, Matsumoto Mei, Nagata Hiroki, Wada Ikumi, Ikebuchi Ai, Sato Eri, Taniguchi Fuminori *Tottori University*

[Objective] As a first step in assessing the role of retinoic acids in endometriotic lesions, we evaluated retinoic acid receptor

(RAR) gene expression in human endometriotic cells. We then examined the antiproliferative activity of retinoids in endometriotic cells. **[Methods]** Endometriotic stromal cells were prepared from endometriotic tissue. RAR gene expression was evaluated using RT-PCR. Primer sets for RARs were prepared using cDNA and genomic sequences in the UCSF genome browser. To test RAR function, cell proliferation capacity was assessed in the presence of all-trans retinoic acid (ATRA) and selective RAR modulators by WST-8 and BrdU assays. Ki-67 expression was examined by Western blotting. By RNA-Seq, differential expression of cell proliferation-related genes was evaluated. **[Results]** Expression of wild-type RAR α , RAR β , and RAR γ mRNA were demonstrated. The cell proliferation rate and Ki-67 expression were repressed in the presence of ATRA. Among selective RAR modulators tested, a selective RAR γ modulator tended to decrease cell proliferation. The administration of ATRA diminished BrdU-positive cells. RNA-Seq demonstrated that retinoids changed several gene expressions related to the G1/S cell cycle transition. **[Conclusion]** We demonstrated the molecular background of RAR expression in the endometriotic cells for the first time. These findings suggested that ATRA suppresses endometriotic cell proliferation via G1 cell cycle arrest.

ISP-4-2

The relationship between the adenomyosis subtype defined by MRI imaging and histories of infertility and pregnancy outcomes : A multicenter retrospective study Tanaka Kota¹, Ono Yosuke¹, Ota Hajime², Miyashita Dai¹, Ogawa Tatsuyuki¹, Sasatsu Satoko¹, Ohgi Maki¹, Ogasahara Eriko¹, Okuda Yasuhiko¹, Wada Shinichiro², Yamada Hideto^{2,3}, Yoshino Osamu¹ *University of Yamanashi¹, Teine Keijinkai Hospital², Center for Recurrent Pregnancy Loss, Teine Keijinkai Hospital³*

[Objective] Few studies have examined the influence of adenomyosis on pregnancy outcomes by classifying morphologically adenomyotic lesion. This study evaluated the relationship between the adenomyosis subtype based on MRI images and histories of infertility and pregnancy outcomes. **[Methods]** Between January 2010 and May 2023, 280 patients with adenomyosis diagnosed by pathological examination after hysterectomy in two institutions were assessed under the approval of IRB. We classified adenomyosis into 4 subtypes (I : intrinsic subtype, II : extrinsic subtype, III : intramural subtype, and IV : indeterminate subtype) according to Kishi classification. The age, BMI, histories of infertility, recurrent pregnancy loss (RPL) and live birth were compared according to the adenomyosis subtype. **[Results]** Adenomyosis were classified as subtype I : 69 (24.6%), II : 77 (27.5%), III : 17 (6.1%), IV : 97 (34.7%), and 20 (7.1%) were unclassifiable. There were no differences in patient backgrounds among I-IV groups. The frequencies of infertility (I : 13.0%, II : 33.8%, III : 4.3%, IV : 24.7%) and ART treatment (I : 5.8%, II : 29.9%, III : 5.9%, IV : 21.6%) were significantly higher in subtype II ($p=0.039$ and $p=0.003$, respectively). The frequencies of RPL (I : 4.3%, II : 10.4%, III : 5.9%, IV : 20.6%; $p=0.028$) was higher, and live birth (I : 90.0%, II : 88.3%, III : 88.2%, IV : 60.8%) was lower ($p<0.001$) in subtype IV. **[Conclusion]** Subtype classification of adenomyosis may be useful in estimating risks for infertility and adverse pregnancy outcomes. Prospective cohort studies are needed to confirm results of this study.

ISP-4-3

Establishment of non-invasive prediction models for diagnosis of subtypes and tissue composition of uterine fibroids by machine learning using MRI data Tamehisa Tetsuro, Sato Shun, Sakai Takahiro, Maekawa Ryo, Sugino Norihiro *Yama-*

guchi University

[Objective] Uterine leiomyomas are classified into two subtypes with or without the MED12 mutation. These subtypes differ in the ratio of smooth muscle cells and fibroblasts and in the amount of collagen fibers (ACF). Thus, the effect of therapeutic drugs (GnRH analogs and selective progesterone receptor modulators) may differ depending on the subtypes and tissue composition, because sensitivities to female hormones differ between smooth muscle cells and fibroblasts. In this study, we established the prediction models for diagnosis of the subtypes and tissue composition of uterine leiomyomas by machine learning using MRI data. **[Methods]** The tumor signal intensity was quantified by five MRI sequences (T2WI, ADC, T1map, T2* BOLD, MTC) for evaluating ACF. After surgery, the MED12 mutations were genotyped, and ACF was estimated by Trichrome staining. These results were used to establish prediction models based on machine learning by applying two classification models (Support Vector Classification and Logistic Regression) to predict uterine leiomyoma subtypes and two regression models (Support Vector Regression and Ridge Regression) to predict tissue composition. **[Results]** Support Vector Classification and Logistic Regression models using five MRI sequence data and MED12 genotyping can highly predict the subtypes (AUC : 0.984 and 0.995, respectively). Support Vector Regression and Ridge Regression models using five MRI sequence data and ACF can highly predict the collagen amount (R2 : 0.570 and 0.525, respectively). **[Conclusion]** We established the non-invasive prediction models for diagnosis of subtypes and tissue composition of uterine leiomyomas by machine learning using MRI data, which support the decision of optimal treatment strategy.

ISP-4-4

Hepcidin as a key regulator of iron homeostasis triggers inflammatory features in the normal endometrium Izumi Yuko, Kataoka Hisashi, Okamura Ayaka, Katayama Akihisa, Shimura Koki, Tarumi Yosuke, Ito Fumitake, Khan Khaleque, Kusuki Izumi, Mori Taisuke *Kyoto Prefectural University of Medicine*
[Objective] Hepcidin is a homeostatic regulator of iron and inhibits iron transport by binding to ferroportin, leading to intracellular accumulation of iron. Menstrual blood containing high iron levels; however, functions of hepcidin in normal endometrium remain unclear. Here, we examined the effects of iron metabolism on normal endometrial cells (NESC). **[Methods]** Hepcidin levels in peritoneal fluid (PF) and menstrual blood (MB) from patients with and without endometriosis were investigated. We also examined the effects of hepcidin on ferroportin expression, iron accumulation, and ROS generation in NESC using immunohistochemistry and immunofluorescence analyses, and evaluated the effects on inflammatory cytokines expression by real-time PCR. **[Results]** There was no significant difference in iron concentrations in MB or PF between women with and without endometriosis; however women with endometriosis had significantly higher hepcidin levels in MB ($P < 0.05$). IL-6 and lipopolysaccharide promoted the hepcidin expression in NESC ($P < 0.05$). Hepcidin reduced ferroportin expression in NESC and promoted iron accumulation ($P < 0.05$). Hepcidin plus iron increased production of ROS ($P < 0.05$) and inflammatory cytokines compared with iron alone; antioxidant monomethyl fumarate suppressed the expression of inflammatory cytokines in NESC ($P < 0.01$). Therefore, local inflammation and bacterial contamination increase hepcidin levels in MB, creating a cycle in which iron overload further promotes inflammatory cytokines expression. **[Conclusion]** Hepcidin may play a critical role in the iron regulation of NESC, implying potential involvement of the hepcidin-ferroportin axis in endometriosis pathogenesis.

ISP-4-5

MicroRNA-210-3p Regulates Development of Ectopic Lesions Through IGFBP3 in Baboons and Women with Endometriosis Kai Kentaro^{1,2}, Aoyagi Yoko¹, Aso Saki¹, Okamoto Mamiko¹, Nasu Kaie¹, Kobayashi Eiji¹ *Oita University Hospital¹, Michigan State University, USA²*

[Objective] MicroRNAs (miRs) play a vital role in the pathophysiology of endometriosis. The mechanisms explaining this role, however, remain to be clarified. This study explores the function of miR-210 and its targets, *IGFBP3* and *COL8A1*, in the growth and development of ectopic lesions. **[Methods]** For the analysis, we obtained matched eutopic (EuE) and ectopic (EcE) endometrial samples from baboons and women with endometriosis. Functional assays were conducted using immortalized human ectopic endometriotic epithelial cells (12Z cells). Meanwhile, endometriosis was experimentally induced in female baboons ($n = 5$), and matched endometrial and endometriotic human tissues were obtained from women ($n = 9$, 18-45 years old) with regular menstrual cycles. Quantitative reverse transcription polymerase chain reaction (RT-qPCR) analysis was performed for *in vivo* characterization of miR-210, *IGFBP3*, and *COL8A1*. *In situ* hybridization and immunohistochemical analysis were performed for cell-specific localization. **[Results]** The *in vitro* functional assays using immortalized endometriotic epithelial cell lines (12Z) revealed that miR-210 expression was decreased in EcE, while *IGFBP3* and *COL8A1* expression were increased. miR-210 was expressed in the glandular epithelium of EuE but attenuated in the EcE cells. *IGFBP3* and *COL8A1* were expressed in the glandular epithelium of EuE and increased compared to EcE. miR-210 overexpression in 12Z cells suppressed expression of *IGFBP3*, and attenuated cell proliferation and migration. **[Conclusion]** Our findings suggest that miR-210 repression and subsequent unopposed *IGFBP3* expression may contribute to developing endometriotic lesions by increasing cell proliferation and migration.

ISP-4-6

Microplastics increased growth of endometriosis in rats via activation of macrophages Katabuchi Misako^{1,2}, Motooka Yashiro², Tashiro Hironori³, Toyokuni Shinya², Kondoh Eiji¹ *Obstetrics and gynecology, Kumamoto University¹, Pathology and Biological Responses, Nagoya University², Women's Health Sciences and Pediatric Nursing, Kumamoto University³*

[Objective] Microplastics (MPs), defined as plastic particles under 5 mm, have been found in various environments such as water, sediments, and air, and detected in the excrement and organs of living organisms. People are exposed to them daily, and the level of exposure is presumed to be increasing. However, the effects on human health remain unclear due to difficulties in identifying individuals who have been exposed. Therefore, we evaluated the effect of MPs on endometriosis, a progressively common disease, utilizing a rat model. **[Methods]** We generated MPs-exposed peritoneal endometriosis model rats by transplanting minced donor uterus and injecting MPs-suspension into the recipient's abdominal cavity. In the control group, the suspension solvent was administered instead of MPs-suspension. Four weeks after transplantation, we compared the number and size of endometriotic lesions and performed histopathological analysis. Additionally, single-nuclei RNA sequencing (snRNA-seq) was performed, and the data were analyzed through Gene Set Enrichment Analysis (GSEA) to identify relevant pathways. **[Results]** A significant increase in the size of lesions was observed in the MP group. Histologically, the endometriotic lesions consisted of endometrial-like glandular epithelium, surrounded by a layer of fibroblasts. MPs were identified in the outermost layer of fibroblasts and were engulfed by macrophages.

The results of snRNA-seq and GSEA indicated increased activation of the epithelial-mesenchymal transition (EMT) pathway in clusters of epithelial cells, stromal cells, and myeloid cells, with potential key factors being secreted by activated macrophages in the MP group. **[Conclusion]** This study suggests that MPs may contribute to the growth of endometriosis by inducing EMT via activation of macrophages.

ISP-4-7

Outcome and risk factors of cesarean myomectomy Na Hyeonjin, Kim Youjin, Ko Youngbok, Lee Ki Hwan *Chungnam National University Hospital, Korea*

[Objective] This study aimed to evaluate and compare the pregnancy outcomes following cesarean myomectomy in both twin and singleton pregnancies. **[Methods]** We conducted a retrospective review of 100 pregnant women diagnosed with myoma, who underwent cesarean myomectomy at Chungnam National University Hospital between January 2012 and July 2022. Of these, 77 were singleton pregnancies and 23 were twin pregnancies. The maternal characteristics, largest myoma size, number of myomas, and surgical outcomes were compared between the two groups. Myomas were further categorized based on size, with large myomas defined as those >5 cm. Maternal characteristics, preoperative and postoperative hemoglobin levels, operative duration, and length of hospital stay were compared between the groups. **[Results]** No significant differences were observed in maternal characteristics, largest myoma size, number of myomas, or surgical outcomes between singleton and twin pregnancies. However, subgroup analysis, based on the largest myoma size (>5 cm or not), revealed significant differences in operative time (95.5 vs. 122.0 minutes, $p < 0.001$) and the need for transfusion (15.6% vs. 36.1%, $p = 0.026$). Otherwise, there were no significant differences in the preoperative and postoperative hemoglobin levels or in the need for massive transfusion ($p > 0.999$), and no patients required interventions such as the insertion of an intrauterine foley balloon, uterine artery embolization, or hysterectomy. **[Conclusion]** Cesarean myomectomy, whether in singleton or twin pregnancies, yielded consistent outcomes. Additionally, performing a cesarean myomectomy on patients with large myomas has proven to be a safe and effective procedure.

ISP-5-1

Twin Pregnancy with One Alive Fetus and Co-Existing Complete Mole Javed Nosheela, Batool Mussarat, Rauf Sidra, Mumtaz Javeria, Nawaz Farzana, Sharafat Shirza *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] We are reporting the case of twin pregnancy of complete hydatiform mole with fetus resulting in live birth and neonatal survival. **[Methods]** Informed Consent was taken from the patient before writing the case report. **[Results]** A 27 year old lady, married for 5 years, Primigravida at 29th weeks gestation conceived with ovulation induction was referred due to twin pregnancy with one alive fetus and other complete mole. Amniotic fluid is reduced with DVP of 2.7 cm. Umbilical artery Doppler shows normal waveform with SD ratio of 1.74. Second complete mole having Placental tissue with cystic changes noted in anterolateral wall of uterus. Her liver function test showed raised ALT OF 162 U/L, AST of 177 U/L and Uric acid of 6.8 mg/dl with normal total bilirubin of 0.4 mg/dl and gamma GT 22 IU/L. Thyroid function test showed hyperthyroidism with TSH of 0.01 uIU/ml, free T3 of 0.8 ng/dl and free T4 of 2.5 pg/ml. Serum human chorionic gonadotrophin level was 429530 mIU/ml. Induction of labor was started with vaginal misoprostol 50 ugm six hourly for two doses. She delivered an alive male of 1.2 kg with good Apgar score. After the delivery of fetus, she re-

ceived general anesthesia and normal Placenta along with complete mole was removed. Suction and curettage was done. Estimated blood loss during procedure was 1200-1500 ml. **[Conclusion]** Twin pregnancy with co-existing molar tissue can be managed conservatively in tertiary care setting where complications can be picked and managed accordingly resulting in live birth of baby.

ISP-5-2

Adenomyosis as a risk factor for placenta accreta spectrum : A retrospective study using causal mediation analysis Wada Yoshimitsu^{1,2}, Takahashi Hironori², Ogozawa Manabu², Horie Kenji², Suzuki Hirotada², Usui Rie², Jwa Seungchik¹, Ohkuchi Akihide², Fujiwara Hiroyuki² *Haga Red Cross Hospital¹, Jichi Medical University²*

[Objective] We aimed to investigate the association between adenomyosis and placenta accreta spectrum (PAS), and to evaluate the mediating effect of assisted reproductive technique (ART) in this association. **[Methods]** We used the perinatal registry database of the Japan Society of Obstetrics and Gynecology between 2013-2019. We conducted a multivariable logistic regression model to analyze the association between adenomyosis and PAS. We also performed a causal mediation analysis, considering ART as a mediator. **[Results]** Of 1,601,932 women, 1,658 (0.10%) had adenomyosis. The number of women receiving ART was 552/1,658 (33.3%) and 135,313/1,600,274 (8.5%) in women with and without adenomyosis. Twenty-two/1,658 (1.3%) and 7,955/1,600,274 (0.5%) women with and without adenomyosis developed PAS. Adenomyosis was significantly associated with PAS (odds ratio [OR], 1.89 ; 95% confidence interval [CI], 1.24-2.88 ; $p = 0.003$). Causal mediation analysis shows that OR (95% CI) of total effect of adenomyosis on PAS was 1.93 (1.14-2.86), natural indirect effect (the effect explained by ART) was 1.16 (1.02-1.44), and natural direct effect (the effect unexplained by ART) was 1.66 (0.87-2.61). The proportion mediated (natural indirect effect/total effect) was 28.7%. **[Conclusion]** Adenomyosis was significantly associated with PAS development. ART was mediated the association ; however, adenomyosis had direct effect on PAS occurrence. Obstetricians should be cautious about PAS in women with adenomyosis regardless of ART.

ISP-5-3

Prolapsed Fibroid in Pregnancy Sharafat Shirza, Batool Mussarat, Rauf Sidra, Rasheed Shabnum, Ahmed Ayesha, Javed Nosheela, Nawaz Farzana *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] This case report highlights rare incidence of prolapsed fibroid during pregnancy. **[Methods]** Informed consent was taken from patient before writing case report. **[Results]** A 38year old, gravida 4 Para 3, with previous 2 normal deliveries followed by one cesarean section was booked at 13weeks gestation. The ultrasound at the time of booking showed an intrauterine gestational sac with CRL of 9+6weeks and a large uterine fibroid arising from the posterior wall of uterus measuring 7.7x7.0 cm. The patient presented at 30+3weeks gestation with history of urinary incontinence and something coming out of vagina for three days. Abdominal palpation showed a symphysio-fundal height of 30cm with a positive fetal cardiac activity. Vaginal examination revealed a 16x16cm degenerated infected, foul smelling fibroid, coming out of the vagina. On investigations, she had a blood group of A+ve and hemoglobin 9.2g/dl. Rest of her baseline investigations was normal. Her ultrasound showed a single alive intrauterine fetus with biometry of 29+0weeks, breech presentation, anterior placenta, absent liquor and normal Doppler indices. There was hypo echoic mass along the posterior

wall of cervix measuring 11x12cm with flow on color Doppler. The patient underwent elective cesarean section and delivered a 1.1kg alive, healthy female baby. EUA showed 16x14cm, prolapsed degenerating fibroid, arising from the posterior uterine wall. Vaginal myomectomy was done and the pedicle was clamped and ligated. **[Conclusion]** Nowadays, cesarean myomectomy has become safer than in the past. Large multicentre studies should be conducted to identify criteria for patient selection, techniques and overall outcome of the procedure.

ISP-5-4

Management of Hypertrophic Scars after Cesarean Section
Hiratsuka Yuki, Osaku Daiken, Kanamori Yasunobu, Sarugami Masako, Tsukihara Satoru, Takaishi Kiyomi, Nam Sungouk, Inoue Kotaro *Japanese Red Cross Yamaguchi Hospital*

[Objective] This study aimed to investigate the occurrence of hypertrophic scars and keloids in patients who underwent cesarean sections, utilizing standardized wound closure techniques and postoperative management. **[Methods]** The study involved 27 patients who underwent cesarean sections and wound follow-ups after their postpartum checkups at our hospital between 2021 and 2022. The wound closure process included the use of 0 STRATAFIX® Symmetric PDS Plus running suture for the fascia profunda, 0 PDS Plus® simple interrupted sutures for the fascia superficialis, and 4-0 STRATAFIX® Spiral PDS Plus running suture for the dermis. Wounds were initially covered with Steri-Strip™ and wound care dressing on postoperative day 7, followed by Atofine™ or steroid tape, depending on the wound condition. **[Results]** Out of the 27 patients, 9 (33.3%) received vertical skin incisions, while 18 (66.7%) received transverse incisions. Among them, 10 patients (vertical incisions : 6 cases (66.7%) ; transverse incisions : 4 (22.2%)) had a history of cesarean sections or uterine surgeries. The median (range) follow-up period after surgery was 113 (32-351) days. Hypertrophic scars were observed in 14 cases (vertical incisions : 6 (66.7%) ; transverse incisions : 8 (44.4%)). The median (range) time from surgery to the occurrence of hypertrophic scars was 36 (18-167) days. Patients with hypertrophic scars were treated with steroid tape, and in five cases (35.7%), there was a significant improvement in their condition. **[Conclusion]** The follow-up of cesarean sections after postpartum checkup may facilitate early detection and effective management of hypertrophic scars.

ISP-5-5

Maternal serum leptin as a possible modulator of fetal adiposity : a longitudinal study
Tamai Junko, Ikenoue Satoru, Hasegawa Keita, Akita Keisuke, Kajikawa Kaoru, Takahashi Marina, Fukuma Yuka, Tanaka Yuya, Otani Toshimitsu, Kasuga Yoshifumi, Yamagami Wataru, Tanaka Mamoru *Keio University*

[Objective] Leptin is one of the adipokines that is associated with birth weight and infant adiposity. However, the association between maternal serum leptin levels and fetal adiposity remains unclear. This study aimed to investigate the association of maternal serum leptin in mid gestation with longitudinal change of fetal adiposity. **[Methods]** A prospective study was conducted in a cohort of 37 singleton pregnancies. Maternal blood sample was obtained at 24 weeks. Fetal ultrasonography was performed at 24, 30, and 36 weeks. Fetal arm and thigh fat area were calculated as difference between the total cross-sectional area and the lean mass area. Fetal abdominal subcutaneous fat was measured as the high-echoic region anterior to the margins of the ribs, proximal to the cord insertion. The association between maternal serum leptin level and fetal adiposity was examined using Pearson product moment correlations. **[Re-**

sults] Maternal serum leptin at 24 weeks was 23.76 ± 17.61 ng/ml (mean \pm S.D.). Maternal leptin was not associated with fetal fat measures at 24 and 30 weeks. Maternal leptin level significantly correlated with fetal arm fat area ($r = 0.35, p < 0.05$) and abdominal subcutaneous fat ($r = 0.40, p < 0.05$), and not with thigh fat area ($r = 0.23, p = 0.17$) at 36 weeks. **[Conclusion]** Maternal serum leptin level at 24 weeks significantly correlated with fetal adiposity at 36 weeks. Maternal serum leptin level in mid-gestation could be a marker for identifying increased fetal adiposity in late gestation.

ISP-5-6

Association Between Gestational Weight Gain and Chronic Disease Risks in Later Life
Kamihara Yuki, Ogawa Kohei, Azuma Hiromitsu, Wada Seiji *Center for Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development*

[Objective] To assess the association between gestational weight gain (GWG) and the risk of developing chronic diseases in later life. **[Methods]** This cross-sectional analysis was conducted between April 2017 and November 2020 at a hospital in Tokyo on 318 women. Data about GWG in the last pregnancy and the development of any chronic diseases of the subjects were retrieved from their maternal health handbook and through a questionnaire survey, respectively. The outcomes were chronic diseases, such as diabetes mellitus (DM), hypertension, hyperlipidemia, and being overweight (body mass index [BMI] ≥ 25 kg/m²). These associations were assessed through a logistic regression analysis after adjusting for maternal height, pre-pregnancy BMI, parity and age at the time of delivery, and the duration from delivery until completion of the questionnaire survey. Further analysis was conducted to adjust for BMI in later life. **[Results]** A significant positive linear association was recorded between GWG and the risk of developing DM, hypertension, and being overweight ($p = 0.013, 0.050$, and 0.017 , respectively). An additional analysis for adjusting for BMI in their later life revealed that a significant association between GWG and DM ($p = 0.025$) remained, while that between GWG and hypertension disappeared, in later life. **[Conclusion]** GWG is significantly associated with DM, hypertension, and being overweight in later life of a pregnant woman. While the association between GWG and DM is partially independent from BMI in later life, the association between GWG and hypertension is mediated by being overweight in the later life.

ISP-5-7

Weight management after the diagnosis of gestational diabetes in severely obese women
Yamashita Hiroshi, Isokawa Satoshi, Yamaguchi Junko, Sugimi So, Koga Megumi, Suga Sachie, Fukuda Masashi, Yasuhi Ichiro *National Hospital Organization Nagasaki Medical Center*

[Objective] Weight management in women with gestational diabetes (GDM) is still controversial. We aimed to investigate whether poor weight gain (WG) following the diagnosis of gestational diabetes mellitus (GDM) was associated with light-for-dates (LFD) infants in severely obese women with GDM. **[Methods]** This retrospective study included singleton severely obese women (BMI ≥ 30 kg/m²) with GDM diagnosed at 24-32 weeks' gestation. All patients underwent self-monitoring of blood glucose for 5 to 7 days and insulin therapy was initiated if their target blood glucose levels did not achieve under nutritional therapy. We investigated the association between maternal weight change after the diagnosis and the newborn birthweight category. **[Results]** Among 51 severely obese patients whose mean prepregnancy BMI was 33.0 (30.0 - 40.1) kg/m² included in this study, 38 (75%) received insulin therapy, and the mean WG

throughout pregnancy was 2.4 kg. In terms of the birthweight category, 5 (10%) and 11 (22%) women had LFD and heavy-for-dates (HFD) infants, respectively. WG (kg) after GDM diagnosis in women with LFD, appropriate-for-dates, and HFD infant was -3.6 ± 1.8 , 1.5 ± 3.1 , and 1.7 ± 3.6 , respectively, with significantly less weight gain in the LFD group ($p < 0.01$) compared with the other groups. The LFD infants were born only to women with decreased WG after the GDM diagnosis (26%, 5/19). **[Conclusion]** In severely obese women with GDM, weight loss after the diagnosis of GDM was associated with the development of LFD infants. Therefore, maternal weight loss after diagnosis should be avoided in those women.

ISP-5-8

Clinic-based evaluation of antigen-based point-of-care tests for genital trichomoniasis infection and bacterial vaginosis among women attending antenatal care facilities in Nchelenge, Zambia Sorano Sumire^{1,2}, Matsui Mitsuaki^{1,3} *School of Tropical Medicine and Global Health, Nagasaki University¹, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, UK², Department of Public Health, Kobe University Graduate School of Health Sciences³*

[Objective] Sexually transmitted infections and/or reproductive tract infections (STIs/RTIs) remain a substantial global health concern, imposing a considerable disease burden. Meta-analysis shows the high prevalence of TV and BV among pregnant women in East and Southern Africa : 29.1% for TV and 50.8% for BV. Trichomoniasis POC test performance was evaluated among symptomatic individuals, but has not been tested among pregnant women in antenatal care settings. The aim of our study is to evaluate the performance of OSOM[®] Trichomonas Rapid Test and OSOM[®] BVBlue[®] and acceptability and operational characteristics of the tests among pregnant women attending antenatal care in the Nchelenge District of Zambia. **[Methods]** We recruited pregnant women attending antenatal care at 4 health centres in the Nchelenge District of Zambia. After acquiring consent, we provided ultrasound scan to confirm pregnancy and to estimate gestational age. We obtained participant background and clinical information including the presence of genitourinary symptoms. Clinical staff collected 4 vaginal swabs from each participant : one swab for each of TV and BV POC test, one swab each for their reference tests. Clinical staff or laboratory staff performed the POC test immediately after sample collection. Results were independently interpreted by two clinical or laboratory staff, each of whom will enter the results in REDCap separately. **[Results]** We will present the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of these test kits. **[Conclusion]** Availability of effective and affordable diagnostic tool would improve the quality of care and the pregnancy outcomes.

ISP-5-9

Single-cell transcriptomic architecture and cellular communication circuits of parametrial adipose tissue in pregnant mice Yano Akiko^{1,2}, Liu Shuang², Suzuki Yasuyuki^{2,3}, Imai Matome^{1,2}, Inoue Shota¹, Inoue Yui¹, Onji Hiroshi¹, Mogi Masaki², Sugiyama Takashi¹ *Ehime University¹, Department of Pharmacology, Ehime University Graduate School of Medicine², Department of Anesthesiology, Saiseikai Matsuyama Hospital³*

[Objective] Adipose tissue is an important endocrine organ essential for whole-body insulin sensitivity and energy homeostasis, whether pregnant or not. The pregnancy-induced adaptation and physiological function of visceral adipose tissue, especially parametrial adipose tissue adjacent to the uterus, have yet to be fully known so far. Therefore, single-cell RNA-sequencing (scRNA-seq) using parametrial adipose tissue (PmAT) was utilized

to examine the changes in cellular composition and functional shift. **[Methods]** PmAT from pregnant and non-pregnant groups was collected and subjected to scRNA-seq. We then examined the differences of single-cell transcriptomic architecture and cellular communication circuits between the two groups. **[Results]** Similar cluster formation was observed in both the pregnant and non-pregnant groups. Changes in cellular composition and functional shift were observed between the pregnant and non-pregnant groups. Furthermore, as a result of cell-cell interaction analysis, a loss of signals from adipocytes to B cells in the resistin signaling pathway network was observed in the pregnant group. Downregulation of resistin-related incoming signaling could contribute to the maintenance of pregnancy and the prevention of diseases related to gestation. In addition, through comparison of significantly enriched extracellular matrix-receptor interactions in non-pregnancy PmAT and in pregnancy PmAT, thrombospondin (THBS) signaling showed the potential capability of mechanical stress-induced adaptive vascular remodeling. **[Conclusion]** PmAT may be involved in maternal-fetal immune tolerance and vascular remodeling processes. Subsequently, these changes may help in the pursuit of new mechanisms in the relationship between general condition and adipose tissue during pregnancy and the development of pregnancy-related complications.

ISP-5-10

The feasibility and efficacy of pemafibrate in the prevention of maternal high-fat intake induced glucose metabolic dysfunction in offspring Imai Matome^{1,2}, Liu Shuang², Yano Akiko^{1,2}, Inoue Yui¹, Inoue Shota¹, Onji Hiroshi¹, Suzuki Yasuyuki^{2,3}, Mogi Masaki², Sugiyama Takashi¹ *Ehime University¹, Department of Pharmacology, Ehime University², Department of Anesthesiology, Saiseikai Matsuyama Hospital³*

[Objective] A maternal high-fat diet (HFD) during pregnancy is critically associated with developmental programming, increased risk of obesity, altered insulin sensitivity, and impaired pancreatic function in the offspring. We have shown that maternal fast-reduced diet intervention may be a promising approach to improve metabolic health and reduce the risk of metabolic disorders in the offspring. In addition, genetic analysis of the pups showed changes in genes related to peroxisome proliferator-activated receptor (PPAR) α and β in the dietary intervention group. The present research investigated the beneficial effects of PPAR- α agonists administered during pregnancy. **[Methods]** C57BL/6N mice were fed either a control diet (CD) or an HFD for 6 weeks from 5 weeks of age until mating. On day 10 of gestation, HFD-fed pregnant mice were randomly divided into control and three doses of PPAR- α agonist-treated groups. Pups were followed and analyzed until 12 weeks of age. During lactation and after weaning, all groups were fed a CD. **[Results]** There was no difference in the number of pups born or birth weight in all groups. A dose-dependent decrease of β cell islet mass and impairment of glucose tolerance and insulin were observed sensitivity in 12 weeks of age offspring suggesting that maternal PPAR- α agonist intervention can prevent maternal HFD-intake-induced diabetes in offspring. **[Conclusion]** PPAR- α agonists may be a potential agent for the prevention of maternal high-fat exposure-induced abnormal glucose metabolism in offspring.

ISP-5-11

Investigation of risk factors for venous thromboembolism in pregnancy using JSOG perinatal registry database : a retrospective study Miyamoto Keisuke, Komatsu Hiroaki, Nagata Hiroki, Kei Nagira, Harada Takashi, Taniguchi Fuminori *Tottori University*

[Objective] This study aimed to clarify the incidence and significant risk factors for venous thromboembolism (VTE) in pregnancy. **[Methods]** We classified 202,607 women registered in 2020 into two groups based on the presence or absence of VTE and extracted risk factors following the Royal College of Obstetricians and Gynecologists guidelines (Green-top Guideline 2015) using multivariate analysis. **[Results]** The incidence of VTE was 0.1%. Univariate analysis revealed VTE risk factors: age >35 years, cesarean section, blood loss, preterm birth <37 weeks, VTE history, fetal growth restriction, multiple gestations, thrombophilia. Independent risk factors for VTE included cesarean section [odds ratio (OR) : 2.1, 95% confidence interval (CI) : 1.4-3.0, $p < 0.001$], preterm birth <37 weeks (OR : 1.6, 95% CI : 1.1-2.5, $p = 0.01$), VTE history (OR : 62.1, 95% CI : 31.2-120, $p < 0.001$), and thrombophilia (OR : 10.4, 95% CI : 4.6-23.3, $p < 0.001$). **[Conclusion]** Preterm birth at <37 weeks was considered a significant risk factor, as were VTE history, cesarean section, and thrombophilia.

ISP-5-12

Effect of SPARC downregulation on BeWo cells fusion Izumi Kenji, Togo Atsuko, Mitsuzuka Kanako, Sato Kenji, Mikami Mikio, Ishimoto Hitoshi *Tokai University Hospital*

[Objective] Syncytiotrophoblasts (STB), which are formed by the fusion of cytotrophoblasts (CTB), play a key role in maintaining pregnancy. Secreted protein acidic and rich in cysteine (SPARC), a non-structural extracellular matrix glycoprotein, is involved in various biological processes such as tissue remodeling, cell proliferation, differentiation, and migration. Previous studies have shown that SPARC is expressed in villous and extra-villous cytotrophoblasts, and that SPARC downregulation by RNA interference significantly attenuated human extra-villous trophoblast HTR8/SVneo cell invasion. To date, however, the involvement of SPARC in CTB fusion (STB formation) remains unknown. **[Methods]** The present study was carried out to investigate placental SPARC protein expression by immunohistochemical analysis, and the effects of SPARC knockdown by small interfering RNA (siRNA) on CTB fusion, using the BeWo choriocarcinoma cell line as a CTB model. **[Results]** Immunohistochemical analysis showed that SPARC expression was high in the first-trimester chorionic villi and low in the late gestational chorionic villi. SPARC knockdown significantly enhanced cell fusion and the expression of human chorionic gonadotropin, a STB marker. Among factors implicated in CTB cell fusion, SPARC gene downregulation significantly increased Ovo-like transcriptional repressor 1 (OVOLI), but not the well-known factors such as glial cells missing transcription factor 1, syncytin-1, and syncytin-2. **[Conclusion]** Thus, our current data indicate that SPARC has a crucial role in suppression of BeWo cells fusion, via a novel pathway involving OVOLI.

ISP-5-13

Effect of sweeping of membranes in onset of labour in pregnancies with previous one scar Intiaz Maleeha, Luqman Sobia, Masoom Kausar, Rauf Sidra *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] To compare the outcome of sweeping of membranes of labor in pregnancies with previous 1 scar vs controls. **[Methods]** A total of 170 women of age 18-40 years of any parity, presenting at gestational age 40 weeks of antenatal checkup with previous 1 C section were included. Patients with chronic or gestational hypertension, diabetes, anemia, liver disease or renal disease, complication (previa, accreta, increta, abruption) or multiple pregnancy, fibroids or PCOS along with fetus, AIF <5cm or >21cm, intrauterine growth restriction, macrosomia and fetal anomaly were excluded. In group A, females with previous 1

caesarean section was undergone sweeping of membranes. In group B, females were followed-up in OPD and were advised to present in labor room if active labor starts. If females were have spontaneous delivery through vagina then it was noted. During delivery, if there was meconium stained liquor observed, then meconium stained liquor was noted. At time of delivery, gestational age was noted and if females delivered 42+1, then post term pregnancy was labeled. **[Results]** In my study, vaginal delivery was seen in 70 (82.35%) group A (sweeping of membrane) compared to 40 (47.06%) group B (controls). Meconium stained liquor and post-term pregnancy were seen in 9.41% and 23.53% group A (sweeping of membrane) compared to 37.65% and 50.59% group B (controls) which has shown p-value of <0.05. **[Conclusion]** This study concluded that outcome of sweeping of membranes is better in onset of labor in pregnancies with 1 previous Caesarean section as compared to controls.

ISP-6-1

The (pro) renin receptor and its intracellular signaling pathway in the placenta of pregnant diabetic mice Mitsui Takashi, Mishima Sakurako, Nakato Hikari, Suemori Ayano, Ooba Hikaru, Mitoma Tomohiro, Oohira Akiko, Maki Jota, Kirino Satoe, Eto Eriko, Masuyama Hisashi *Okayama University*

[Objective] Abnormal glucose metabolism during pregnancies is a risk factor for preeclampsia (PE). Until now, we reported the imbalance between angiogenic and antiangiogenic factors through the activation of protein kinase C in the placenta of pregnant diabetic mice. We also found that endothelin-1 (ET-1) was produced via the intracellular signaling pathway mediated by the (pro) renin receptor (PRR) in the placenta of PE model mice, potentially causing hypertension and proteinuria. Therefore, we examined the PRR and its intracellular signaling pathway in the placenta of pregnant diabetic mice. **[Methods]** In pregnant diabetic mice (KK and BKS.Cg-Dock7m+/-Leprdb/J) and pregnant control mice (C57BL/6), blood pressure was measured on 125 and 155 days-post-coitum (dpc) via the tail-cuff method. Blood samples and placentae were collected from diabetic and control mice on 155 dpc. Placental hypoxia was evaluated by quantitative PCR using hypoxia-inducible factor-1 α (HIF-1 α) as an index. The level of PRR and its intracellular signaling pathway in the placenta were evaluated. **[Results]** Blood pressure on 155 dpc increased in diabetic mice compared to control mice. The level of HIF-1 α was significantly elevated in the placenta of diabetic mice compared to control mice, and levels of PRR, transforming growth factor- β 1, and ET-1 were also significantly increased in the placenta of diabetic mice. **[Conclusion]** The imbalance between angiogenic and antiangiogenic factors lead to increase HIF-1 α in the placenta of diabetic mice. The PRR and its intracellular signaling pathway increased in the placenta might be involved in the development of PE in pregnant women complicated with aberrant glucose metabolism.

ISP-6-2

All-Trans Retinoic Acid Suppresses Ferroptosis in BeWo Cells via HMOX1 Upregulation Matsuoka Tomona^{1,2}, Kajiwara Kazuhiro², Wada Seiji², Samura Osamu³, Sago Haruhiko², Akutsu Hidenori¹, Okamoto Aikou³ *Department of Reproductive Biology, National Center for Child Health and Development¹, Department of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development², The Jikei University³*

[Objective] This study aimed to explore the association between ferroptosis, a newly identified type of cell death, and the role of retinoic acid in the development of pregnancy complications. Therefore, the effects of all-trans retinoic acid (ATRA) on

ferroptosis susceptibility in BeWo cells were assessed to understand abnormal placental development. **[Methods]** BeWo cells were used as surrogates for cytotrophoblasts. The effect of ATRA on ferroptosis sensitivity was assessed by pretreating BeWo cells with ATRA or dimethyl sulfoxide (DMSO ; control), following which the LDH-release assay was performed. The effects of ATRA pretreatment on the antioxidant defense system (including glutathione [GSH], mitochondrial membrane potential, and heme oxygenase-1 [HMOX1]) in BeWo cells were assessed using assay kits, RT-qPCR, and HMOX1 immunostaining. To evaluate the effect of ATRA on it, HMOX1 was silenced in BeWo cells using shRNA. **[Results]** ATRA pretreatment increased ferroptosis resistance in BeWo cells. Although with pretreatment, qPCR indicated HMOX1 upregulation, no significant change was observed in the GSH levels or mitochondrial membrane potential. This was corroborated by intensified immunostaining for heme oxygenase-1 protein (HO-1). Notably, the protective effect of ATRA against ferroptosis was negated when HO-1 was inhibited. Although HMOX1-silenced BeWo cells exhibited heightened ferroptosis sensitivity compared with controls, ATRA pretreatment counteracted ferroptosis in these cells. **[Conclusion]** ATRA pretreatment promotes BeWo cell viability by suppressing ferroptosis and upregulating HMOX1 and this can be used as a potential therapeutic strategy for addressing placental complications associated with ferroptosis.

ISP-6-3

A pilot study of the incidence of ocular trauma in forceps delivery for comparative study of the incidence of ocular trauma during delivery in neonates according to delivery method Maruyama Yojiro¹, Seo Eimi², Fujiyama Koya¹, Lin Ming³, Takahashi Mayu¹, Maeda Chikako¹, Kido Yuka¹, Tanaka Motoki¹, Iwase Koharu¹, Nagasawa Saya¹, Ito Yosuke¹, Ogishima Daiki¹ *Juntendo University Nerima Hospital¹, Juntendo University²*

[Objective] forceps delivery may cause specific injuries including ocular trauma due to direct pressure of the forceps blade on the face. However it has been reported that ocular injuries including retinal hemorrhage have also occurred in normal vaginal delivery and cesarean section infants, the effect of delivery method on ocular trauma during delivery in newborns is not clear. **[Methods]** In our hospital, examinations by an ophthalmologist are performed to screen for ocular trauma of forceps marks over the orbit are found among forceps deliveries. The ophthalmologic examinations are visual examination by an ophthalmologist and fundus examinations using a slit-lamp microscope. **[Results]** The ophthalmologic examinations were conducted in 16 of the 81 forceps deliveries in 2020. Abnormal findings were observed in 3 cases : corneal damage in 1 case and fundus hemorrhage in 2 cases. One case of was bilateral, and one case of fundus hemorrhage was contralateral to the forceps scar. **[Conclusion]** Both of fundus hemorrhage were questionable findings that should be concluded to be caused by forceps injury. To Clear effect of delivery method, a comparative study of the incidence of ocular trauma during delivery in neonates according to delivery method is started on March, 2023.

ISP-6-4

A case of cerebral arteriovenous malformation with cerebral hemorrhage just before pregnancy and craniotomy AVM removal at 13 weeks gestation to continue the pregnancy Yamaguchi Michika, Nakayama Tetsuo, Matsuzawa Satoshi, Yamada Naoshi, Doi Koutarou, Kodama Yuki, Katsuragi Shinji *Miyazaki University*

[Objective] We report the case of a pregnant woman in whom a

residual lesion of cerebral arteriovenous malformation (AVM) was found during pregnancy. The patient wished to continue her pregnancy. She underwent radical surgery in the early stage of pregnancy and was given drug therapy for postoperative epilepsy. She has subsequently had a favorable perinatal course. **[Case]** The patient was 24 years old, gravida 3 para 2. She had a cerebral hemorrhage about 3 months before conception. MRI for follow-up detected an abnormal blood vessel suspected to be an AVM in the left frontal lobe. At the same time, a pregnancy test showed a positive result. The patient was treated surgically at 13 weeks gestation. Antiepileptic drug therapy was given for postoperative epileptic seizures. **[Conclusion and Discussion]** Together with the neurosurgeon, we explained to the patient the advantages and disadvantages of gamma knife therapy, surgery, and standby therapy. We came to the conclusion that surgery was the best treatment for this case. Even after complete removal of the AVM, drug therapy, including treatment of epilepsy, was necessary. The patient is currently at 23 weeks of gestation. The fetus is growing well and a planned delivery is scheduled at full-term pregnancy with pain minimized with epidural anesthesia. We will present the rest of her delivery progress at the conference.

ISP-6-5

Thyroid-stimulating hormone (TSH)-secreting pituitary macroadenoma with first diagnosed during pregnancy Kawabata Ikuno, Ogawa Jun, Kasano Sayuri, Tsunoda Youhei, Kato Masahiko, Ichikawa Tomoko, Kuwabara Yoshimitsu, Satomi Misao, Suzuki Shunji *Nippon Medical School*

[Background] Thyroid stimulating hormone (TSH) secreting pituitary adenoma (thyrotropinoma) is rare occurring at the rate of 0.015 to 0.03 per 100,000 people and extremely rarely identified during pregnancy. **[Case]** We present the case of a 26-year-old primiparous woman diagnosed with thyrotropinoma due to hyperthyroidism during pregnancy. She complained of severe hyperemesis and palpitation in early gestation. Her thyroid work-up at 12 weeks' gestation was as follows : TSH 2.06 μ IU/mL, fT3 8.43ng/dL, fT4 2.86pg/dL (2 steep assays : TSH 1.50 μ IU/mL, fT3 7.78ng/dL, fT4 2.08pg/dL), and the result was SITSH (Syndrome of Inappropriate secretion of TSH). Her family had no thyroid diseases, and she had no TR β genetic mutation. An MRI of her pituitary gland revealed a macroadenoma (12 \times 11mm) extending from the right side of the pituitary into the suprasellar cistern not compressing the inferior surface of the optic chiasm, she was diagnosed with thyrotropinoma. She was monthly treated with a somatostatin analog, lanreotide, from 19 weeks' gestation. At 40 weeks of gestation, she underwent an emergency cesarean section due to severe headache and mild hypertension during labor and delivered a healthy female infant weighing 3216g. She then underwent transsphenoidal resection of the macroadenoma, sparing the normal pituitary 3 months after delivery. **[Conclusion]** Thyrotropinoma in pregnancy is limited evidence to guide management because of exceedingly rare. This case demonstrated that a conservative approach with close monitoring and lanreotide treatment resulted in good outcomes for both mother and child.

ISP-6-6

A perforated appendicitis with decidualis and free air under the diaphragm during pregnancy Kiyose Masumi, Shiro Michihisa, Murakoshi Homare, Okada Juzo, Yoshida Shigeki *Chibune General Hospital*

Acute appendicitis with free air under the diaphragm detected using computed tomography (CT) in pregnant women is rare. Deciduosus of the appendix during pregnancy is a rare condition. We report a case of perforated appendicitis with deciduosus

and free air under the diaphragm during pregnancy. A 28-year-old pregnant woman (gravida 1, para 0) was admitted to our hospital at 31 weeks and 1 day of gestation for right and middle lower abdominal pain. Ampicillin and ritodrine hydrochloride were administered to treat threatened preterm labor and intrauterine infections. Her abdominal pain did not improve; however, abdominal CT tomography showed no signs of conditions that might cause abdominal pain, including appendicitis. The next day (31 weeks, 2 days), contrast-enhanced CT showed free air under the diaphragm, with no evidence of appendicitis. Suspecting that the cause of free air under the diaphragm was idiopathic gastrointestinal perforation, exploratory surgery was performed after cesarean section. Because surgical exploration demonstrated perforated appendicitis with an abscess, an appendectomy was performed. A histological examination of the resected appendix showed that the smooth muscle of the appendiceal wall was completely occupied by decidual cells. As the base structure of the appendix was degenerated by severe decidualosis, there was a high possibility that the base of the appendix was perforated. In the present case, no endometrial glands were identified in the appendix. This case suggests that decidualosis of the appendix should be considered a different clinical condition from normal appendicitis in terms of free air during pregnancy.

ISP-6-7

Association between maternal body fat and the risk of gestational diabetes mellitus Boriboonhirunsarn Dittakarn, Tunkemrat Poramed, Sunaneevithayakul Prasert *Siriraj Hospital, Mahidol University, Thailand*

[Objective] To evaluate relationship between body fat percentage (BFP) and the risk of gestational diabetes (GDM). **[Methods]** A cohort study was conducted in 336 singleton pregnant women attending antenatal care clinic before 14 weeks of gestation. Body compositions of each woman were measured during their first antenatal visit, using a Multi Frequency Segmental Body Composition Analyzer. All women received GDM screening and diagnosis using 50-g glucose challenge test and 100-g oral glucose tolerance test during their first visit and repeated during 24-28 weeks of gestation. Rate of GDM were compared between women with BFP $\geq 30\%$ and $< 30\%$. Correlation between BFP and BMI and their diagnostic ability for GDM were evaluated. **[Results]** A total of 296 women were included in the analysis; 171 had BFP $\geq 30\%$ and 125 had BFP $< 30\%$. Prevalence of GDM was 17.9%. Women with BFP $\geq 30\%$ were significantly older and had higher pre-pregnancy BMI. They also had significantly higher fat percentage, fat mass, free fat mass, muscle mass, and total body water. BFP correlated well with BMI (correlation coefficient 0.956, $p < 0.001$). BFP $\geq 30\%$ and BMI ≥ 25 kg/m² significantly increased the risk of GDM (22.2% vs. 12%, $p = 0.023$ and 26.4% vs. 14.4%, $p = 0.014$, respectively) with sensitivity of 71.1% and 43.3% respectively. Specificity were 45.3% and 73.7%, respectively. Both BFP and BMI had comparable diagnostic ability for GDM (areas under ROC curves of 0.634 and 0.642, respectively). **[Conclusion]** BFP $\geq 30\%$ and BMI ≥ 25 kg/m² significantly increased the risk of GDM. BFP correlated well with BMI and had similar diagnostic ability for GDM.

ISP-6-8

Efficacy of low dose calcium supplementation with standard dose of 1500 mg of calcium intake in prevention of pre-eclampsia in high risk pregnant women Ahmed Ayesha, Rasheed Shabnum, Rauf Sidra, Batool Mussarat *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] To compare the efficacy of low dose calcium supplementation with standard dose of 1500 mg of calcium intake in

prevention of pre-eclampsia in high risk pregnant women. **[Methods]** A total of 212 patients of 16-24 weeks of gestation assessed on LMP, 18 to 35 years of age with singleton pregnancy were included. Patients with chronic renal disease and multiple pregnancies were excluded. Group A received low dose calcium supplementation i.e., 500mg calcium daily and group B was given 1500mg calcium daily as recommended by WHO in three divided doses. Both groups continued taking standard obstetrics care with oral hematinics, loprin and oral antihypertensives, as indicated. Information regarding all the study variables were recorded in a structured proforma. Confidentiality of the data was ensured. BP and proteinuria was checked at 34-36 weeks and at delivery. The frequency of preeclampsia on both groups was compared. **[Results]** The mean age of women in group A was 23.15 ± 6.68 and in group B was 23.41 ± 6.05 years. The mean gestational age in group A was 21.71 ± 4.73 weeks and in group B was 21.42 ± 4.83 weeks. The frequency of recurrence pre-eclampsia without any supplementation is 40%. In my study, frequency of pre-eclampsia was in 07 (6.60%) low dose calcium group compared to standard group was reduced to 19 (17.92%) with p-value of 0.01, which was less than in the standard group. **[Conclusion]** This study concluded that low dose calcium supplementation prevents pre-eclampsia in high risk pregnant females.

ISP-7-1

Menstrual Cycle Prolongation After Receiving the Primary Series and Booster Doses of mRNA Coronavirus Disease 2019 (COVID-19) Vaccination Hosoya Satoshi^{1,2}, Itoi Shiori^{3,4}, Yokomizo Ryo^{1,2}, Hiraike Osamu⁴, Koga Kaori^{1,5}, Osuga Yutaka⁴, Morisaki Naho³ *Center for Regenerative Medicine, National Center for Child Health and Development¹, The Jikei University School of Medicine², Department of Social Medicine, National Center for Child Health and Development³, The University of Tokyo⁴, Chiba University Graduate School of Medicine⁵*

[Objective] Primary series doses (1st and 2nd doses) of coronavirus disease 2019 (COVID-19) mRNA vaccines reportedly cause slight prolongation of menstrual cycles. However, reports on additional doses are limited. To quantitatively evaluate the effect of a booster dose on menstrual cycles, we conducted a retrospective cohort study using a menstrual cycle tracking smartphone application. **[Methods]** Prospectively or retrospectively recorded data, including the start and finish dates of menstruation, were collected using the application. Details on vaccinations, side effects, and participants' characteristics were retrospectively collected from a questionnaire on the app. For the 1st, 2nd, and 3rd vaccinations, within-individual changes in menstrual cycle length up to the 4th post-vaccination cycle were evaluated. **[Results]** Among the 7,376 and 6,873 participants who had the 1st and 2nd doses in different menstrual cycles, menstrual cycles immediately after the vaccination (1st post-vaccination cycle) were an average of 0.22 (95% confidence interval: [0.06, 0.39]) and 0.37 [0.20, 0.54] days longer than the pre-vaccination cycle, respectively. The following post-vaccination cycles returned to the level of the pre-vaccination cycle. However, among the 4,768 participants who had the 3rd dose, the 1st post-vaccination cycle after the booster dose was an average of 1.20 [1.00, 1.40] days longer, with cycle prolongation of 0.27 [0.10, 0.44] to 0.41 [0.22, 0.59] days persisting from the 2nd to the 4th post-vaccination cycles. **[Conclusion]** The booster shot against COVID-19 may have a greater and longer-lasting effect on menstrual cycles than the primary series. Further evidence for effects on menstruation by immunization should be accumulated.

ISP-7-2

The Maternal Health Management and Guidance Card use

and associated factors Namimatsu Kyoko¹, Takeda Jun¹, Ando Hitomi¹, Kitamura Eri¹, Kawasaki Yu¹, Makino Shintaro², Takeda Satoru¹, Itakura Atsuo¹ *Juntendo University¹, Juntendo University Urayasu Hospital²*

[Objective] There is a need to investigate whether the Maternal Health Management and Guidance Card (Maternity Card) is used appropriately and contributes to safe pregnancy management. Our aim of this study is to clarify this card's use rate and the factors associated with its use. **[Methods]** A cross-sectional, multicenter questionnaire survey was undertaken for women who gave birth in four tertiary hospitals. Questions related to clinical, and socioeconomic characteristics were included in the questionnaire. Women who worked during pregnancy were selected and divided into two groups: "Maternity Card users" and "non-users". The factors associated with maternity card use were analyzed with both univariate and multivariate analyses. **[Results]** A total of 975 postpartum women participated in this study with a response rate of 54%. Out of the available data, 652 women were included in the analysis. The Maternity Card was used for 20% of working pregnant women. There is no significant difference in the rate of card use with parity, history of miscarriage or stillbirth, weight change, nor employment status. The rate of card use was significantly higher in those with low family income, without night shift, harassment by colleagues, obstetric complications, high K6 scores, and residence outside of Tokyo. The multivariate-adjusted odds ratio (OR) and 95% confidence intervals (CIs) showed that night shift (2.3, 1.1-4.6), obstetrical complications (2.7, 1.6-4.6), and high K6 score (1.1, 1.0-1.1) were associated with using the Maternity Card. **[Conclusion]** Maternity Card usage was associated with obstetrical complications and work or family status.

ISP-7-3

The effect of switching ferric citrate hydrate tablets for the treatment of iron deficiency anemia: RIO-SWITCH study Hiraie Osamu, Iriyama Takayuki, Mori Mayuyo, Osuga Yutaka *The University of Tokyo*

[Objective] The primary treatment of iron deficiency anemia (IDA) is based on oral intake. The efficacy of switching from existing drugs to ferric citrate hydrate tablets (FCHT) was investigated in IDA patients who had difficulty continuing treatment with existing oral iron tablets due to nausea and/or vomiting (N/V) side effects. **[Methods]** We selected 30 participants with IDA who were intolerant to existing oral iron tablets due to N/V. They were treated by FCHT until resolution of IDA, and laboratory data, impression of intake and patient-reported QoL were investigated. The study was funded by Torii Pharmaceutical Co., Ltd. (JRCTs031210634). **[Results]** All patients included in the FAS analysis completed the medication with no serious adverse reactions and no discontinuations. A patient survey at the end of study treatment showed that switching improved the degree of nausea, with nausea resolving in 11 of 30 patients with nausea at baseline. The number of patients who reported no disruption in their lives due to N/V after taking FCHT increased, and the number of patients who reported psychological stress from the onset of N/V decreased. There was also an improvement in the degree of poor appetite due to N/V after taking FCHT, and treatment satisfaction with FCHT was high compared to the past IDA treatment. The results of EQ-5D-5L and SF-36v2 suggested significant improvement in physical and mental aspects. **[Conclusion]** Considering the improvement of N/V and QoL of the patients, FCHT might be useful both as a first choice drug and as an alternative for IDA.

ISP-7-4

The trends of the visitor numbers to Web articles on eating

disorders Enomoto Yuki, Hiraie Osamu, Tsuchimochi Saki, Furukawa Maho, Makabe Tomoko, Urata Yoko, Izumi Gentaro, Harada Miyuki, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*

[Objective] We run a website to provide accurate information related to health issues for women of all ages since 2017, and we noticed that eating disorder (ED) is one of the most frequently accessed issue. We aimed to examine the trends of people visiting our website related to ED information. **[Methods]** The number of visitors to our website were analyzed using Google analytics from January 2020 to May 2023. We use the Eating Attitudes Test (EAT-26) to identify the risk of ED, and the results of the visitors were also analyzed (cut-off value ≥ 20). Free-text consultations submitted to the Call for Consultations page were also analyzed using a text-mining tool (KH coder) to examine the content of health problems faced by modern women. **[Results]** Total page view (PV) remained at 600,000 visitors/month during the period, but the number of PVs for ED-related pages increased. Those who examined the ED self-check, 55.4% were exceeded the cut-off value and considered to have abnormal eating behavior, with problems related to "Dieting" and "Bulimia and Food Preoccupation." The number of free-text consultations related to ED showed seasonal changes. **[Conclusion]** In women's health care, information on ED has been accessed significantly, reflecting the growing interest about ED. Although there is a limitation that people visiting our website are mostly interested in health care issues, behavioral analysis showed us the distribution of interest from multiple perspectives.

ISP-7-5

Parental Knowledge, Attitudes, and Practices Towards Human Papilloma Virus (HPV) Vaccination for their Children Abad Lara Anjela R, Aquilizan Leo Francis N *St. Luke's Medical Center Quezon City, Philippines*

[Objective] Human papilloma virus (HPV) is one of the most prevalent sexually transmitted infections in the world and is a known causative agent of cervical cancer. HPV vaccination offers an alternative preventive strategy against cancers caused by HPV infection. Studies worldwide have shown that vaccine awareness has waned and the number of children who receive the vaccine and intention to vaccinate has decreased over the years. This study highlights HPV vaccine knowledge, attitudes, and practices among parents being seen in the Department of Obstetrics and Gynecology Outpatient Clinic in a private tertiary hospital in Quezon City, Philippines. Findings of this study may offer possible recommendations for policy making and the way clinicians advise their patients regarding HPV and the HPV vaccine. **[Methods]** A descriptive cross-sectional survey design was conducted on 160 parents. Respondents had at least one son or daughter between the ages of 9 and 17 years. **[Results]** The findings demonstrate that HPV vaccine knowledge is generally poor to fair. Parents generally have a positive attitude toward HPV vaccination. Affordable pricing is important in the acceptance of the vaccine. It is the recommendation of healthcare providers and spouse/partners and family that most greatly influence respondents' decision about HPV vaccine. **[Conclusion]** Socially comprehensive and family-based vaccination campaigns may help improve knowledge on HPV infection and its prevention. Exposure to vaccine-promoting media and suggestions from a healthcare provider could help increase vaccine uptake.

ISP-7-6

HPV-negative lesions in primary HPV testing for cervical cancer screening Hideshima Misako, Umezaki Yasushi, Oishi Shouhei, Yamaguchi Kae, Uriu Yasue, Yoshitake Kaoruko,

Ikedo Masazumi, Kurihara Makiko, Tokunaga Mariko, Fukuda Asako, Okugawa Kaoru, Yokoyama Masatoshi *Saga University*
[Objective] In Japan, primary HPV testing has not been introduced for cervical cancer screening. We evaluate the validity of primary HPV testing in Japan by analyzing CIN2+/hrHPV-cases in cervical cancer screening. **[Methods]** Data from 35,525 cervical cancer screenings with HPV testing and cervical cytology from 2011 to 2019 in S City, were reviewed. The cases with LSIL+/hrHPV- were analyzed in detail. **[Results]** The results of the 35,525 examinees were as follows : 31,123 were NILM/hrHPV-, 2,612 were NILM/hrHPV+, 262 were ASC-US/hrHPV-, 213 were ASC-US/hrHPV+, 291 were LSIL+/hrHPV-, and 1024 were LSIL+/hrHPV+. Of the 256 LSIL+/hrHPV- examinees for whom histology was available, CIN2+ were CIN2 9.4% (24/256), CIN3 3.9% (10/256), cervical adenocarcinoma 0.4% (1/256), uterine corpus cancer 1.2% (3/256) and uterine sarcoma 0.4% (1/256). Overall, the rate of LSIL+/hrHPV- was 0.82% (291/35,525), 0.1% (36/35,525) of which were cervical lesions with CIN2+. Only 1 cervical adenocarcinoma was detected, but gastric-type adenocarcinoma was not included. **[Conclusion]** HPV-negative CIN2+ or cervical adenocarcinoma is not a concern for the introduction of primary HPV screening in Japan. Primary HPV testing in cervical cancer screening is considered a feasible method that can be used in Japan, although an algorithm suitable for Japan needs to be established.

ISP-7-7

Relationship between regular cervical cancer screening and social background in Japan during the COVID-19 pandemic
 Mitoma Tomohiro, Maki Jota, Ogawa Chikako, Masuyama Hisashi *Okayama University Hospital*

[Objective] Japan has one of the lowest cervical cancer screening rates among developed countries. The cancer screening rate has worsened with the COVID-19 pandemic. This study investigated COVID-19 history and socioeconomic background of people who did not undergo on-time cervical cancer screening (CCS) during the two years of COVID-19-related restrictions. **[Methods]** We used data from the Japan COVID-19 and Society Internet Survey, a nationwide, internet-based, self-report, cohort observational study conducted in 2022. The outcome variable was identified by asking whether respondents had undergone on-time CCS within the last two years. This study used multivariate log-binomial regression models to evaluate inequalities during regular checkups for CCS. Adjusted prevalence ratios (APRs) with 95% confidence intervals (CIs) were estimated to incorporate socioeconomic background variables. **[Results]** Of 12,066 respondents, 6469 (53.6%) had yet to undergo CCS within two years. The prevalence ratio (PR) of on-time CCS was 0.70 (95% CI : 0.63-0.79) for those in their 20s and 0.78 (95%CI : 0.70-0.87) for those in their 60s, compared to their 40s. Moreover, socioeconomic inequities were found in the following groups : unemployed/student, unmarried, high school graduate or lower, and household income below 4 million yen. PR of on-time CCS with a history of COVID-19, unvaccinated status, or fear of COVID-19 was not different from underwent CCS. **[Conclusion]** the relationship between socioeconomic inequalities and CCS hesitancy was prevalent among the younger respondents. Our findings will help policymakers identify problems and strategies to improve CCS screening rates in Japan.

ISP-7-8

Effect of Different Educational Interventions on Knowledge of HPV Vaccination and Cervical Cancer among Young Women
 Takahashi Yuko, Nishida Haruka, Miyagawa Yuko, Takehara Kohei, Watanabe Saya, Takasaki Kazuki, Hashimoto Kei, Nishizawa Miki, Ichinose Takayuki, Hirano Mana, Hiraiki

Haruko, Nagasaka Kazunori *Teikyo University*

[Objective] The incidence and mortality rates of cervical cancer are rising among young women in Japan. In November 2021, the Japanese Ministry of Health, Labour, and Welfare reinstated the active recommendation for the human papillomavirus (HPV) vaccine, discontinued in June 2013 due to reports of adverse reactions following vaccination. However, vaccine hesitancy remains. We aimed to conduct a randomized study using different methods of providing educational content to improve health literacy among female students in Japan. **[Methods]** Data was collected three times from students in our university who were divided into three groups : no intervention, print-based intervention, and social networking service-based intervention, using the health literacy scale and communicative and critical health literacy scale. **[Results]** Among the 267 participants, 188 participants have completed the first questionnaires. 148 students (78.7%) were in medical-related faculties, 72 (38.3%) had relatives of medical professionals, 103 (54.8%) had never received the HPV vaccine, and 51 (27.1%) had completed three doses. There were significant differences in the total scores of the health literacy questionnaire depending on the above backgrounds. The scale evaluation between the first and third questionnaires showed no significant differences among the three groups, while students in non-medical faculties tended to show more significant improvement than those in medical faculties. **[Conclusion]** Our analysis indicates that participants' knowledge due to lifestyles is related to health literacy. Therefore, medical professionals must provide accurate scientific knowledge about HPV vaccination and the risk of cervical cancer to improve students' health literacy and subsequently increase the HPV vaccination rates.

ISP-7-9

Questionnaire Survey on the Usefulness of Hands-on Practice of Ectopic Pregnancy Using a Laparoscopic Simulator in Bed Side Learning for Medical Students
 Murakami Keisuke, Yanagihara Yasuho, Takeuchi Shiori, Kawasaki Yu, Ochiai Asako, Okada Yukiko, Kitade Mari, Itakura Atsuo *Juntendo University*

[Objective] Ectopic pregnancy is a condition that medical students need to learn in bed-side learning (BSL), but this opportunity is limited because it is often treated at night or outside of practice hours for students. We incorporate hands-on practice of ectopic pregnancy using a laparoscopic simulator into BSL for medical students. We report on the questionnaire survey for medical students regarding hands-on practice of ectopic pregnancy. **[Methods]** A google forms questionnaire survey about hands-on practice of ectopic pregnancy was administered to 29 medical students who participated in BSL of obstetrics and gynecology from October 2022 to June 2023. **[Results]** The percentages of responses to each question after hands-on practice were as follows : 1) Understanding of ectopic pregnancy (unchanged, 7% ; slightly improved, 45% ; significantly improved, 48%), 2) Understanding of laparoscopic surgery (unchanged, 0% ; slightly improved, 17% ; significantly improved, 83%), 3) Can you consider ectopic pregnancy in the differential diagnosis of women with acute abdomen? (cannot, 0% ; probably can, 66% ; definitely can, 34%), 4) Can you play a role of scopist in actual surgery? (cannot, 7% ; can do with the primary surgeon's instructions, 72% ; can provide appropriate surgical view by oneself, 21%), 5) Can you play a role of primary surgeon? (cannot, 34% ; can do after practice more than 10 times, 59% ; can do after practice a few times, 7%). **[Conclusion]** Hands-on practice of ectopic pregnancy using a laparoscopic simulator for medical students is considered a meaningful practice.

ISP-7-10

Relationship between Urinary Equol Levels and Edinburgh Scores in Pregnant and Postpartum Women Honda Moeka, Taniguchi Hajime, Tokunaga Shuichi, Iwanaga Iwao, Ueno Noriko, Higo Takafumi, Katsuragi Shinji *University of Miyazaki*
[Objective] Decreased estrogen may induce depression in pregnant and postpartum women, while equol has estrogenic activity. Thus, the aim of the study was to examine the relationship of the Edinburgh Postnatal Depression Scale (EPDS) with urinary equol excretion in pregnant and postpartum women.
[Methods] An EPDS test and urinary collection were conducted at gestational week 36, postnatal weeks 2 and 4 from February to July, 2023 in a hospital. Subjects with urinary equol ≥ 1.0 $\mu\text{mol/L}$ in any test were placed in the equol-producing (equol (+)) group and all others were in the equol (-) group. Similarly, subjects with EPDS scores of ≥ 9 points were placed in the high EPDS group and all others were in the low EPDS group. **[Results]** Of 81 subjects, 10 were in the high EPDS group. Equol production rates in the high vs. low EPDS groups were 10.0% vs. 23.9%, 20.0% vs. 28.2%, and 20.0% vs. 31.0% at respective time points, showing less equol production tendency in the high EPDS group. The mean EPDS scores in the equol (+) vs. equol (-) groups were 3.80 ± 4.56 vs. 2.27 ± 3.26 , 3.63 ± 4.01 vs. 2.03 ± 2.77 , and 2.69 ± 3.83 vs. 1.23 ± 1.48 ($p < 0.05$). Subjects with a high EPDS score were also frequently concerned about hair condition in each time point. **[Conclusion]** The results suggest that the EPDS score is related to equol production capacity. Most subjects who did not produce equol had high EPDS scores at gestational week 36, postnatal weeks 2 and 4. Those with a high EPDS score were likely to be concerned about hair condition.

ISP-7-11

The association between PMS/PMDD during preconception and perinatal depression : an analysis of a perinatal medical center database Ohsuga Takuma, Egawa Miho, Tsuyuki Kaori, Ueda Akihiko, Komatsu Maya, Chigusa Yoshitsugu, Mogami Haruta, Mandai Masaki *Kyoto University Graduate School of Medicine*
[Objective] In recent years, several studies have shown an association between PMS/PMDDs (Premenstrual disorders : PMDs) and perinatal depression. However, screening for PMDs during preconception to identify pregnant women in need of support is not yet common in Japan. This study examined the association between PMDs during preconception and perinatal depressive symptoms using the obstetric database of a perinatal medical center. **[Methods]** A total of 379 data on pregnant women from April 2020 - May 2023 extracted from the database were used. PMDs during preconception was assessed by The Premenstrual Symptoms Screening Tool. Perinatal depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS) in mid-pregnancy and at one month postpartum. The cut-off values for EPDS were set at 12/13 in mid-pregnancy and 8/9 at one month postpartum. **[Results]** Among the 27 women with PMDs, the proportions of women with EPDS scores of ≥ 13 in mid-pregnancy and with EPDS scores of ≥ 9 at one month were 25.9% and 40.7%, respectively, compared to 5.7% and 15.1%, respectively, for the 352 women without PMDs. Multivariate logistic regression models showed a PMDs during preconception was associated with an EPDS score of ≥ 13 in mid-pregnancy [adjusted odds ratio (95% confidence interval) : 5.10 (1.63-14.68)] and an EPDS score of ≥ 9 at one month postpartum [2.95 (1.15-7.26)]. **[Conclusion]** PMDs during preconception was associated with depressive symptoms in mid-pregnancy and one month postpartum. The results suggest that screening for history of PMDs may be effective in early identification of pregnant women in need of support.

ISP-7-12

Inter- and Post-Conception Care for Adult Congenital Heart Disease Women Hyodo Hironobu, Nitta Satoshi, Kumazawa Risa, Sue Fusako, Mizuno Yoshiaki, Funakura Midori, Imada Shinya *Tokyo Metropolitan Bokutoh Hospital*
[Objective] The number of adult congenital heart disease (ACHD) has been increasing owing to the progress of medical and surgical management, so the of their pregnancies. They need life-long care but it has still been on the way to be established. Most of them are, however, living uneventful lives and some of them have uneventful pregnancies. Pregnancy can be a good opportunity for the arrangement of future medical care for them, which is no less than their post- (or inter-) conceptional care. The care we have provided at our hospital were reviewed and the better way was discussed. **[Methods]** The medical records of the adult congenital heart disease women whose pregnancies were managed at our hospital from 2014 to 2022 were reviewed. **[Results]** 96 cases and 134 pregnancies were identified. All of them were in NYHA I and VSD was the most major disease. 44 cases were not under regular follow-ups and cardiac evaluations for them were done during and after the delivery. 14 cases were referred to the specialized institute after the delivery. Five cases of simple lesion were pending immediate referral with a view to the next pregnancy. **[Conclusion]** Although the long-term follow-ups of ACHD were not established yet, check-ups every several years may be acceptable for those with simple lesions and preserved functions. Inter-conception visits for them may be, then, altered to the evaluation during the next pregnancy within a couple of years.

ISP-8-1

Association between exercise therapy and sarcopenia during concurrent chemoradiotherapy for cervical cancer Tasaki Kazuto, Yamada Hiroaki, Tasaki Shingo, Yo Takasugi, Nishio Shin, Tsuda Naotake *Kurume University*
[Objective] Although sarcopenia and low muscle mass before cervical cancer treatment have been reported as poor prognostic factors, the effect of rehabilitation intervention during treatment is unknown. In this study, rehabilitation was conducted in cervical cancer patients undergoing concurrent chemoradiotherapy (CCRT), and the association between the rate of implementation, changes in muscle mass, and other factors, as well as prognosis, was examined. **[Methods]** Twenty eligible cervical cancer patients received exercise therapy during CCRT from March 2018 to November 2019. Sarcopenia was diagnosed before and after treatment using the BIA method, and the Psoas muscle mass index (PMI) was calculated by measuring the Psoas muscle area at the L3 level using CT scans. **[Results]** Median patient age was 55 years (33-75 years), median follow-up was 47.3 months (7.1-61.7 months) ; 9 patients relapsed and 8 died ; 5 (25%) had sarcopenia before treatment and 2 (10%) had low PMI. After treatment, sarcopenia increased in 10 patients (50%) but did not correlate with prognosis. Median rehabilitation rate was 66% (19-96) ; PMI was significantly maintained in the high rehabilitation rate group compared to the low group ($p=0.03$), but there was no correlation between PMI and prognosis. Pre-treatment Prognostic Nutritional Index (PNI) was a poor prognostic factor ($p < 0.01$), although it did not correlate with rehabilitation rates. **[Conclusion]** Rehabilitation rates were lower than expected. The high implementation rate group kept the area of the psoas major muscle, but there was no correlation with prognosis. We would like to validate appropriate rehabilitation that contributes to improved prognosis.

ISP-8-2

Differences in cervical cancer survival between prefectures

in Japan—Application of funnel plots in excess hazard model using gynecologic cancer registry data, JSOG Oka Emiko^{1,2}, Yagi Asami¹, Sakakibara Atsuko³, Ueda Yutaka¹, Ito Yuri², Kimura Tadashi¹ *Osaka University¹, Department of Medical Statistics, Research & Development Center, Osaka Medical and Pharmaceutical University², Department of Preventive Medicine, Tazuke Kofukai Foundation, Medical Research Institute, Kitano Hospital³*

[Objective] We examined the association between cervical cancer survival and age, histological type, stage at diagnosis, and treatment volume of hospitals to reveal regional differences by prefecture. **[Methods]** We used data from the gynecologic cancer registry published by the Japan Society of Obstetrics and Gynecology, which included 44,449 patients who started treatment between 2000 and 2013. Funnel plots were used to display the excess hazard ratio (EHR) for each prefecture, defined as the excess hazard of death from each cancer within 5 years of diagnosis relative to the mean excess hazard in all 47 prefectures combined. Good prognosis was defined when the EHR was below the lower 95% control limit, while poor prognosis was defined when the EHR was above the upper 95% control limit. **[Results]** For all stages, EHRs in 10 prefectures with poor prognosis were 1.55 in the univariable analysis and 1.24 in the multivariable analysis adjusted for age, histological type, FIGO stage and case volume, compared to six prefectures with good prognosis. The EHR changed most when adjusted for stage. For stage III or IV, in which differences by prefecture were largest, EHRs in seven prefectures with poor prognosis were 1.47 in the univariable analysis and 1.38 in the multivariable analysis. The EHR changed most when adjusted for stage and case volume. **[Conclusion]** This study revealed inequalities by prefecture in cervical cancer outcome. One reason for this may be the difference in stage. Another could be the case volume of treatment facilities, especially in advanced stage cases.

ISP-8-3

The impact of concurrent chemoradiotherapy on lower-extremity lymphedema in Cervical Cancer—Using the Patient Reported Outcome (PRO) — Kim Ria¹, Tanabe Hiroshi^{1,2}, Sato Chihiro¹, Narui Chikage¹, Takenaka Masataka¹, Saito Motoaki¹, Takano Hirokuni¹, Yamada Kyosuke¹, Okamoto Aikou¹ *The Jikei University¹, National Cancer Center Hospital East²*

[Objective] Although adjuvant concurrent chemoradiotherapy (aCCRT) following radical hysterectomy (RH) for cervical cancer (CC) has been implied to increase the incidence of lower extremity lymphedema (LEL), clinical studies in Japan have been still limited. We aimed to assess the impact of aCCRT on LEL using CTCAE (version 5.0), a conventional physician assessment, and PRO (patient-reported outcome) -CTCAE, a patient self-assessment system. **[Methods]** CTCAE/ PRO-CTCAE data for non-relapsed CCs who received RH were collected as part of a PRO study project conducted at four affiliated institutes from May 2022 to March 2023. Patients were classified into two groups: follow-up group and aCCRT group, and CTCAE/PRO-CTCAE (frequency, severity, interference) in each group were compared. Moreover, we investigated the association with the time from RH and CTCAE/ PRO-CTCAE. **[Results]** There were 41 and 61 patients in the follow-up and aCCRT groups, respectively. Although no significant difference was observed between CTCAE and PRO-CTCAE (frequency, severity, interference) in all patients analysis, the proportion of patients evaluated as no LEL tended to be higher in CTCAE (66.4%) compared with PRO-CTCAE (43%, 45.6%, 70.2%, respectively). There was no significant difference of both CTCAE and PRO-CTCAE between follow-up and aCCRT groups (all $P > 0.2$). Furthermore, no significant association was found between CTCAE/PRO-CTCAE and time from RH. **[Conclusion]** PRO-CTCAE may be

able to detect milder LELs compared to CTCAE. Adjuvant CCRT for CC is likely to have a slight impact on LEL. LEL caused by CC treatment including RH was not considered likely to improve over time.

ISP-8-4

Survival disparities related to age and histology of cervical cancer patients in Japan (2000-2013) Sakakibara Atsuko¹, Ito Yuri², Ueda Yutaka³, Yagi Asami³, Kakuda Mamoru³, Oka Emiko^{2,3}, Terakawa Koichi¹, Konishi Ikuo⁵ *Preventive Medicine, Tazuke Kofukai Foundation, Medical Research Institute, Kitano Hospital¹, Medical Statistics Research & Development Center, Osaka Medical and Pharmaceutical University², Osaka University³, Kansai Electric Power Hospital⁴, Clinical Research Center, Kyoto Medical Center⁵*

[Objective] No study to date has focused on the prognosis of cervical cancer in Adolescent and Young Adult (AYA) patients by excluding the effect of competing risks from other causes of death. Here we investigated the association of age and histology of cervical cancer patients with survival. **[Methods]** Using the Tumor Registry of the Japanese Society of Obstetrics and Gynecology (2000-2013), we identified 44,327 patients diagnosed with and treated for cervical cancer, with a prognostic follow-up rate of at least 80%. Five-year net survival was estimated by stage according to age group [15-39 (AYA-group) /40-49/50-64/≥65 years] or histology (categorized from first to sixth most common type and others) and compared using the excess hazard model. **[Results]** The AYA-group had the poorest prognosis among any age group in stage II and above patients. In particular, prognosis was significantly poorest in stage IIA patients; excess mortality risk was 25-36% lower in age groups ≥40 years compared to the AYA-group. Squamous cell carcinoma (SCC) generally had the best prognosis in any stage compared to other histological types. In stage II and III patients, excess mortality risk was 2.4-4.4 times higher than that of SCC for endocervical adenocarcinoma usual type, adenocarcinoma not otherwise specified, small cell carcinoma, and others. Adjusted for histology, the AYA group had the poorest prognosis at stage II and above. **[Conclusion]** The AYA-group showed the poorest prognosis in patients with stage II and above, and survival disparities were observed for age and histology in this analysis of cervical cancer.

ISP-8-5

Efficacy and safety of taxane/platinum-based therapy and pembrolizumab for recurrent or metastatic cervical cancer Akada Masashi, Kodama Michiko, Kakuda Mamoru, Toda Aska, Nakagawa Satoshi, Kinose Yasuto, Takiuchi Tsuyoshi, Hashimoto Kae, Ueda Yutaka, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] First-line treatment for recurrent and metastatic cervical cancer has been changed to taxane/platinum-based therapy and pembrolizumab, which is the first combination therapy of a cytotoxic anticancer drug and an immune checkpoint inhibitor (ICI) in gynecological malignancies in Japan. We confirm the efficacy and safety of this new treatment for recurrent or metastatic cervical cancer. **[Methods]** We retrospectively reviewed responses and adverse events of 19 cases treated with the combination of paclitaxel, carboplatin, and pembrolizumab and 69 cases treated with paclitaxel and carboplatin (TC) for recurrent or metastatic cervical cancer at our institution between 2012 and June 2023. **[Results]** There were no significant differences in age, histology, or the number of TC cycles between the two groups. In the pembrolizumab group, 10 patients had prior chemotherapy, including TC. The overall response rate (ORR) in the pembrolizumab group was 68% (5 CR, and 8 PR), compared to 45% in the TC group (13 CR, and 18

PR). However, 4 patients experienced serious adverse events (hypopituitarism, colitis and hepatitis, bowel perforation, pulmonary embolus), leading to treatment discontinuation. **[Conclusion]** In our study, the pembrolizumab combination had a better ORR, but was discontinued in 21% due to serious adverse events, including immune-related adverse effects (irAEs). In order to safely continue ICI, it is important to diagnose irAEs early and carefully select cases in which treatment can be resumed.

ISP-8-6

Prognostic Analysis of Lymph Node Metastasis in Cervical Cancer Surgery Ishii Masato, Takeuchi Jun, Ryu Tamami, Iida Serika, Imai Haruka, Endou Hiraku, Kuji Shiho, Ohara Tatsuru, Takae Seido, Tozawa Akiko, Suzuki Nao *St. Marianna University School of Medicine*

[Objective] With the revision of the Cervical Cancer Treatment Regulations in Japan in December 2020, lymph node metastasis was reflected in the new advanced stage classification (FIGO 2018) and classified as stage IIIC. It has conventionally been classified into Stages I-II according to local findings, and surgical treatment has been the treatment of choice in Japan, in comparison to Europe and The United States. **[Methods]** Of the 347 cervical cancer patients treated at our hospital from January 2011 to December 2021 classified as stage I or II according to the old staging system (FIGO 2008), 41 patients newly classified as stage IIIC with surgical treatment were observed retrospectively. **[Results]** During the observation period through September 2022 (median: 95 (7-137) months), the median age of the 41 patients in the new classification IIIC stage was 47 (33-78) years. The median overall survival (OS) was 41 (7-126) months. Of the 26 patients treated through 2017, the five-year survival rate was 65.4% in 17. Postoperative treatment options included concurrent chemoradiotherapy (CCRT group) in 27 patients, chemotherapy (Chemo group) in 11, and no treatment in 3. The result of comparing the OS in the CCRT group against the Chemo group showed no significant difference ($p=0.43$), with a median of 54 (11-124) vs. 24 (9-126) months. **[Conclusion]** The new Stage III classification is considered appropriate for patients with positive regional lymph node metastasis, who are at high risk of recurrence. Although postoperative adjuvant therapy is considered essential, there was no significant difference in OS between concurrent chemoradiotherapy and chemotherapy.

ISP-8-7

Report on Treatment Outcomes of Elderly Patients with Cervical Cancer in Our Hospital Takeuchi Jun, Kuji Shiho, Ryu Tamami, Ishii Masato, Iida Serika, Imai Haruka, Ohara Tatsuru, Takae Seido, Tozawa Akiko, Suzuki Nao *St. Marianna University School of Medicine*

[Objective] To identify treatment methods and identify potential complications particular to elderly patients with cervical cancer. The report aims to identify factors that are important in determining optimal treatment strategy. **[Methods]** The 321 cases of cervical cancer treated at our hospital from January 2011 to December 2020, we conducted a retrospective study of 120 patients which were aged 65 years or older. We analyzed the correlations between age, histopathology, disease staging, overall survival, treatment details, complications, and patient performance status (PS). (Ethical Review No.: 5504) **[Results]** When the treatment for grade B or higher condition according to the Japanese guidelines was considered the standard of care, cytoreduction treatment had been selected for 26/120 patients (21.7%) (cytoreduction treatment group). The median overall survival for the standard of care group and cytoreduc-

tion treatment group was 32 months (5-112 months) and 19 months (1-82 months), respectively ($p<0.001$). Cytoreduction treatment was selected for 12 patients over 85 years of age, 10 patients with poor PS, 3 patients with dementia, 5 patients with cardiovascular complications, 1 patient with ileus, and 3 patients who refused treatment, all significantly more than in the standard of care group ($p<0.01$). **[Conclusion]** In the treatment of elderly patients with cervical cancer, the data indicates a cytoreduction treatment regimen should be considered when the patient is over 85 years old, based on poor PS, presence of dementia, cardiac disease, or ileus, and poor prognosis.

ISP-8-8

A retrospective study of the utility of MRI findings for evaluating pathological factors in stage IBI cervical cancer Kou Kazuhiro, Yamanoi Koji, Taki Mana, Murakami Ryusuke, Yamaguchi Ken, Hamanishi Junzo, Mandai Masaki *Kyoto University*

[Objective] We investigated whether magnetic resonance image (MRI) findings were useful for evaluating pathological factors including tumor size, depth of invasion and lymphovascular invasion (LVSI) status in stage IBI cervical cancer. **[Methods]** Among cases with stage IBI (FIGO2008) cervical cancer who received initial surgical treatment in our institute from 2006 to 2020, we extracted cases in which the tumor was visible on internal examination or detected by MRI. The whole cases were divided into three groups: no detectable tumor on MRI (Undetected group), a maximum tumor diameter <21 mm (U-21 group), a diameter ≥ 21 mm (O-21 group). Several pathological factors were compared among three groups. **[Results]** There were 13 cases in the Undetected group, 37 in the U-21 group, and 59 in the O-21 group. As for the frequency of cases with a pathologically maximum tumor diameter ≥ 21 mm, it was significantly high in the O-21 groups compared to the other two (Undetected: 3/13 cases, 23.1%, U-21: 14/37 cases, 37.8%, O-21: 52/59 cases, 88.1%, $p<0.0001$). As for the frequency of cases with depth of invasion ≥ 10 mm, it was also significantly high in the O-21 group compared to the other two (Undetected: 1/13 cases, 7.7%, U-21: 9/37 cases, 24.3%, O-21: 39/59 cases, 66.1%, $p<0.0001$). As for the frequency of positive-LVSI, it was significantly low in the Undetected group compared to the other two (Undetected: 1/13 cases, 7.7%, U-21: 19/37 cases, 51.3%, O-21: 25/59 cases, 42.3%, $p=0.02$). **[Conclusion]** MRI findings are useful for evaluating pathological factors including tumor size, dept of invasion and LVSI status.

ISP-8-9

Correlation between waiting time from first consultation date to surgery and upstaging in cervical cancer: a single institute retrospective study Yamamoto Shizuka, Yano Mitsutake, Aoyagi Yoko, Aso Saki, Okamoto Mamiko, Obata Eri, Kai Kentaro, Kodama Haruho, Shima Kazuaki, Yamada Tomonori, Kobayashi Eiji *Oita University*

[Objective] Prolonged waiting times for malignant tumor treatment can be associated with unfavorable outcomes. In recent cervical cancer studies, waiting time for surgery or (chemo) radiotherapy did not affect patient overall survival. However, patient survival includes biases such as adjuvant therapy and treatment for recurrence. We, therefore, compared waiting time to surgery and postoperative upstaging rate. **[Methods]** Patients who were newly diagnosed and underwent surgery for cervical cancer between 2018 and 2022 at our hospital were studied. Waiting time (i.e. interval between the first consultation and surgery) was modeled as dichotomized (e.g. ≤ 30 days vs. >30 days). The association with postoperative FIGO upstaging was examined using Pearson's chi-square test. Informed consent was

obtained from patients for the study. **[Results]** Eighty-two patients treated with primary surgery were included. The mean waiting time to surgery was 43.5 days. Postoperative upstaging compared to the preoperative status was observed in 21 cases (25.6%). There was no significant difference in the postoperative upstaging rate between patients who underwent surgery within 30 days and those who did not. There was no significant difference in postoperative upstaging rates when the cutoff was changed to 40 and 50 days. **[Conclusion]** This single institute cohort study demonstrates that a longer waiting time from the first consultation date to surgery in patients with cervical cancer treated with curatively intended surgery does not negatively impact postoperative staging.

ISP-8-10

Two cases of young women onset HPV-independent squamous cell carcinoma with an extremely rapid course Ishikawa Masako¹, Nakayama Kentaro², Yamashita Hitomi¹, Kanno Kousuke¹, Haraga Hikaru¹, Iida Koji¹, Ishibashi Tomoka², Kyo Satoru¹ *Shimane University¹, Nagoya City University East Medical Center²*

Introduction : HPV-independent SCC is advanced at the time of diagnosis, and existing treatment strategies do not work, so there is an urgent need to explore therapeutic targets. We report two cases of extremely rapidly progressing SCC. **Case 1 :** 40 year-old woman, nulligravida, never had sexual intercourse. When she was diagnosed, there were multiple lymph node metastases in pelvic and paraaortic lymph node. First, she had surgery and next she had chemotherapy. 2 courses of adjuvant chemotherapy, although multiple liver metastasis was appeared. She was died 6 months after the onset of the disease. **Case 2 :** 32 year-old woman. She had bone metastasis at the time of diagnosis and underwent concurrent radiation and chemotherapy, but the disease relapsed and she passed away 1 year and 10 months after the onset of the disease. Whole-Exome analysis revealed a genome-wide LOH trend in case 1 and a TMB-High status in case 2. Both showed variants of the SKT11 cancer-suppressor gene, but otherwise they were thought to have undergone completely different carcinogenic processes. **Conclusion :** In the immediate future, whole-exome analysis of a large number of cases may be used to search for causes related to the carcinogenic process, proliferative process, and treatment resistance of HPV-independent SCC.

ISP-8-11

Diagnostic pitfall of recurrence after conization in patients with uterine cervical lesions : A report of two cases Sasa Hidenori, Miyake Taro, Imauji Akari, Ito Tsubasa, Hada Taira, Kato Kento, Miyamoto Morikazu, Takano Masashi *National Defense Medical College*

The uterine cervix may appear different after cervical conization, with a more unsatisfactory colposcopic finding according to the surgical resection. Among six invasive carcinoma cases for past 15 years at our hospital, we present two women with recurrence of invasive carcinoma after conization for intraepithelial neoplasia (CIN). The first case was a 30-year-old woman who underwent colposcopy for cytological diagnosis of atypical squamous cells, which cannot exclude a high-grade squamous intraepithelial lesion (ASC-H), 8 months later after conization for CIN3. She was also pregnant at 9 weeks' gestation. The histological diagnosis was invasive squamous cell carcinoma under unsatisfactory colposcopy and human papillomavirus (HPV) test was negative. Radical hysterectomy performed after pregnancy termination revealed stage IB2, and she underwent chemotherapy. The second case was a 57-year-old woman who was menopausal at 56 years old and referred for cervical cytology of high-

grade squamous intraepithelial lesion (HSIL) after 11 years of conization for CIN3. The colposcopic finding was unremarkable but the biopsy revealed invasive squamous cell carcinoma and she was positive for other high-risk HPV types. Radical hysterectomy was performed, and the clinical stage was IIA. We encountered two invasive carcinoma cases that relapsed after conization in which unclear colposcopic findings and the difficulty of accurate biopsies seemed to be diagnostic pitfalls. When abnormal cervical cytology is indicated after conization, the diagnostic conization, cervical curettage, and measurement of tumor marker could be considered for early diagnosis of recurrence.

ISP-8-12

Case report : A woman of recurrent cervical carcinoma successfully treated by MRI-linac Awazu Yuichiro¹, Yamauchi Makoto², Uchikura Eijiro¹, Noda Takuya¹, Tasaka Reiko², Imai Kenji², Fukuda Takeshi², Yasui Tomoyo², Sumi Toshiyuki² *Osaka City University¹, Osaka Metropolitan University²*

High-field magnetic-linear accelerators (MR-linacs) are linear accelerators combined with a diagnostic magnetic resonance imaging (MRI). Using magnetic resonance (MR) -guided radiation therapy (MRgRT) enables us to visualize target region during radiation therapy. We can daily adapt radiation therapy treatment plan to motion and shape changes. MRgRT provides fewer damage to normal tissue and higher dose of RT to target organ. We experienced a case of 73-year-old woman with cervical carcinoma. Her primary treatment was radical hysterectomy followed by adjuvant chemotherapy. 2 years after, a recurrence in pelvic cavity was pointed out. She underwent 45 gray of MRgRT by using MR-linac. After that, recurrence region had completely disappeared and she did not experience grade 3 or 4 adverse events.

ISP-8-13

Do concurrent multiple infections with high-risk HPVs carry a more malignant potential than a single infection in the uterine cervix? Lee Juhun¹, Lee Hyun-Jung¹, Lee Jieon¹, Lee Sung-Mi¹, Heo Yujin¹, Kim Hee-Jeong¹, Lee Hye-Jin¹, Hong Dae Gy², Kim Jong Mi² *Kyungpook National University, Kyungpook National University Hospital, Korea¹, Kyungpook National University, Kyungpook National University Chilgok Hospital, Korea²*

[Objective] The high-risk human papilloma virus (HR-HPV) has been known as the most important carcinogen in uterine cervical carcinoma. Generally, gynecologists recommend medical interventions for patients diagnosed with HSIL or higher. However, there is limited evidence on the malignant potential of these concurrent multiple infections. **[Methods]** This study included women undergone cervical conization. They underwent an HPV test by cervical swab within 12 months before the surgery. They were divided into two groups : one with a single infection with HR-HPV16 and the other with concurrent multiple infections with HR-HPVs, including genotype 16. They were categorized into two groups based on the pathologic examination : one was HSIL+ to evaluate the risk of the need for medical intervention, including high-grade squamous intraepithelial lesion (HSIL), carcinoma *in situ* (CIS), invasive carcinoma, and the other was CIS+ to evaluate the malignant potential, including CIS, invasive carcinoma. **[Results]** Of the 220 patients infected with HR-HPV16, the single infection group consisted of 120 patients (54.5%), whereas the concurrent multiple infections consisted 100 (45.5%) patients. The rates of HSIL+ or CIS+ were not significantly different between both groups. For HSIL+, the odds ratio was 0.618 (95% CI=0.326-1.173, P=0.141) between the single infection and concurrent multiple infection groups, for CIS+, 1.417 (95% CI=0.831-2.414, P=0.200). **[Conclusion]** The

concurrent multiple HR-HPVs infection did not require a significantly higher frequency of medical intervention for cervical neoplasia. The malignant potential was not significantly different between concurrent multiple infections with HR-HPVs, including 16, and a single infection with 16 in Korean women.

ISP-8-14

A very rare case of cervical squamous cell carcinoma metastasized to both ovaries Jeong Soohwa, Youjin Kim, Youngbok Ko, Ki Hwan Lee *Chungnam National University Hospital, Korea*

Rarely does cervical cancer spread to the ovaries. Among these cases, adenocarcinoma is typically more aggressive, and cases of metastasis to the ovary have been documented. Rare reports of ovarian squamous cell carcinoma (SCC), a more prevalent histological form, have been made. In these extremely rare cases, cervical SCC spreads to both ovaries. The patient in this case was 30 years old and single. She was diagnosed with cervical SCC IA I and was human papillomavirus-16-positive. Therefore, she received conization three times. Then, at follow-up, she underwent vaginal trachelectomy under the diagnosis of a high-grade squamous intraepithelial lesion (HSIL) and invasion suspicion. Total laparoscopic hysterectomy was determined based on HSIL findings at follow-up one year later. SCC in situ of the cervix, with a clear line of resection, was found on histological examination. After about two years without follow-up, the patient visited the hospital with abdominal pain. On examination, a vaginal stump mass of about 1 cm in size was found, accompanied by touch bleeding. Thus, pelvicoscopic bilateral salpingo-oophorectomy and vaginal stump mass excision were performed. The biopsy result was ovarian SCC, and a recurrence of cervical cancer was confirmed on the vaginal stump. Since then, the patient has received systematic chemotherapy and radiation therapy, as a poor prognosis was predicted. According to a review of published research, the incidence of ovarian metastasis from uterine cervical cancer ranges between 0.6 and 1.5%. We report a rare case of cervical SCC with metastasis to both ovaries, which requires further investigation and study.

ISP-9-1

Impact of stage, tumor type, and menopausal status on cancer antigen 125 (CA125), human epididymis protein 4 (HE4), Risk of ovarian malignancy (ROMA) and Copenhagen Index (CHP-I) in the diagnostic workup of epithelial ovarian cancer (EOC) Iizuka Makoto, Hamada Yoshinobu, Kosugi Satoshi, Hiromatsu Ai, Tsuchiya Kei, Kondo Ibuki, Nemoto Kohei, Saito Kanami, Iida Yasushi, Sakamoto Shuichi, Takakura Satoshi *Dokkyo Medical University Saitama Medical Center*

[Objective] To evaluate the impact of FIGO stage (stages I-II vs. III-IV), tumor type (type I vs. II), and menopausal status (premenopausal vs. postmenopausal) on the predicted probability of ROMA and CHP-I as well as CA125 and HE4 serum levels in the diagnostic workup of Japanese women with EOC. **[Methods]** Patients with pathologically diagnosed EOC were enrolled. Multivariable logistic regression analyses were conducted to distinguish between the true positives and false negatives (FNs) by adjusting the above factors for the abovementioned markers and algorithms separately. **[Results]** Among the 140 women, FNs were identified in 22.8%, 45.0%, 27.8%, and 28.5% of women for CA125, HE4, ROMA, and CHP-I, respectively. Stages I-II were independent variables predictive of FN results for CA 125 (odds ratio [OR] 13.9, 95% confidence interval [CI] 2.61-74.10), HE4 (OR 4.53, 95% CI 1.70-12.10), ROMA (OR 15.8, 95% CI 3.41-73.60), and CHP-I (OR 7.77, 95% CI 1.84-32.90). Any tumor type was not independent variables predictive of FN results for those markers and algorithms. Premenopausal status was inde-

pendent variables predictive of FN results for ROMA (OR 4.17, 95% CI 1.69-10.30) and CHP-I (OR 4.16, 95% CI 1.69-10.20). In the premenopausal and postmenopausal women with stages I-II EOC, FNs on ROMA were 57.1% and 33.8%, respectively, and those on CHP-I were 57.1% and 33.8%, respectively. **[Conclusion]** Early stage and premenopausal status are factors that should be independently considered when assessing the above markers and algorithms in Japanese women with EOC to avoid misdiagnosis of benign disease, while any tumor type is not.

ISP-9-2

Impact of age, endometriotic cyst, and renal function (eGFR) on CA125, HE4, risk of ovarian malignancy algorithm, and Copenhagen Index in the diagnostic workup of ovarian tumors Irie Taichi, Iizuka Makoto, Hamada Yoshinobu, Inagaki Risa, Ogasawara Megumi, Nemoto Kohei, Ichikawa Teppei, Saito Yoko, Sakamoto Shuichi, Takakura Satoshi *Dokkyo Medical University Saitama Medical Center*

[Objective] To evaluate the impact of age, endometriotic cyst (EC), smoking, and renal function ([Editor1] estimated glomerular filtration rate) on the predicted probability of the Risk of Ovarian Malignancy Algorithm (ROMA) and Copenhagen Index (CPH-I) as well as cancer antigen 125 (CA125) and human epididymis protein 4 (HE4) serum levels in the diagnostic workup of Japanese women with ovarian cyst or pelvic mass. **[Methods]** Patients with pathologically diagnosed benign ovarian tumors were enrolled. Multivariable logistic regression analyses were conducted to distinguish between the true negatives and false positives (FPs) by adjusting the above factors for the abovementioned markers and algorithms separately. **[Results]** Among the 422 women, FPs were identified in 31.5%, 4.0%, 10.1%, and 10.6% of women for CA125, HE4, ROMA, and CHP-I, respectively. EC was the only variable predictive of FP results for CA 125 (odds ratio [OR] 8.12, 95% confidence interval [CI] 4.75-[Editor1] 13.90). Younger age (OR 0.92, 95% CI 0.88-0.97) and impaired renal function (OR 0.89, 95% CI 0.85-0.93) were independent variables predictive of FP results for HE4. Impaired renal function was the only variable predictive of FP results for ROMA (OR 0.93, 95% CI 0.92-0.96). Older age (OR 1.05, 95% CI 1.02-1.08) and impaired renal function (0.95, % CI 0.93-0.97) were independent variables predictive of FP results for CHP-I. **[Conclusion]** Age, EC, and impaired renal function are factors that should be independently considered when assessing the above markers and algorithms in Japanese women with ovarian tumors to avoid misdiagnosis of malignant disease.

ISP-9-3

Excellent local control of proton beam therapy for recurrent epithelial ovarian cancer Endo Yuta^{1,2}, Yoshimoto Yuki¹, Takagawa Yoshiaki^{3,4,5}, Suzuki Motohisa^{3,4}, Yamaguchi Akiko^{2,6}, Soeda Shu^{2,6}, Watanabe Takafumi^{2,6}, Fujimori Keiya^{2,6}, Murakami Masao^{3,4} *Southern Tohoku General Hospital¹, Department of Regional Gynecologic Oncology, Fukushima Medical University², Proton Therapy Center, Southern Tohoku Proton Therapy Center³, Department of Radiation Oncology, Southern Tohoku General Hospital⁴, Department of Minimally Invasive Surgical and Medical Oncology, Fukushima Medical University⁵, Fukushima Medical University⁶*

[Objective] Several studies have reported the benefit for radiation therapy in patients with recurrent epithelial ovarian cancer (REOC). However, the efficacy and toxicities of proton beam therapy (PBT) remain undetermined. The present study aimed to evaluate the efficacy and toxicities of PBT for REOC. **[Methods]** The medical records of patients who were treated with PBT for REOC at our institution between October 2008 and March 2021 were reviewed. Local control (LC), progression free

survival (PFS) and overall survival (OS) after initial PBT were analyzed using the Kaplan-Meier method, and toxicities were evaluated using the Common Terminology Criteria for Adverse Events version 5.0. **[Results]** Thirteen patients with 34 irradiated sites were included. The median age at initial PBT was 62 (range, 42-82). Eight patients had stage III or IV disease, and seven patients had serous carcinoma. Ten patients had platinum-resistant recurrence. Of the irradiated sites, 20 were lymph nodes and nine were pelvic or abdominal masses. The median tumor size and SUVmax of 18F-FDG-PET/CT were 25 mm (range, 9-83 mm) and 13.1 (range, 3.9-25.1), respectively. The median total dose was 65 Gy (RBE) (range, 45-72 Gy). The 1-year and 2-year LCs were 91.5% and 71.3%, respectively. The median PFS and OS after initial PBT were 9.4 months and 30.1 months, respectively. No grade ≥ 3 PBT-induced adverse events were observed. **[Conclusion]** PBT was associated with excellent local control for REOC and the toxicity level was acceptable.

ISP-9-4

Relationship between hematological toxicities during maintenance treatment and during chemotherapy before maintenance treatment in patients with platinum-sensitive relapsed ovarian cancer Matsuoka Hirofumi¹, Nakamura Keiichiro¹, Yorimitsu Masae², Ogawa Mariko³, Kozai Ayumi⁴, Nakamura Hiroko⁵, Haruma Tomoko⁶, Shiroyama Yuko⁷, Hayata Yuu⁸, Sugii Hirokazu⁹, Ueda Akiko¹⁰, Masuyama Hisashi¹ *Okayama University Hospital¹, Hiroshima City Hiroshima Citizens Hospital², Fukuyama Medical Center³, Kagawa University Hospital⁴, Kure Medical Center and Chugoku Cancer Center⁵, Okayama Saiseikai General Hospital⁶, Hiroshima Prefectural Hospital⁷, Kagawa Prefectural Central Hospital⁸, Iwakuni Clinical Center⁹, Onomichi General Hospital¹⁰*

[Objective] To determine whether PARP inhibitors (Olaparib or niraparib) as maintenance treatment can be performed effectively and safely in patients with platinum-sensitive relapsed ovarian cancer. **[Methods]** We carried out a multi-center study to investigate progression-free survival (PFS) and adverse events (AEs) in 229 patients receiving maintenance treatment for platinum-sensitive relapsed ovarian cancer. All patients started taking PARP inhibitors (Olaparib or niraparib) as maintenance treatment from January 2019 to March 2023. The primary endpoint was the incidence of maintenance therapy-induced hematological toxicities (anemia, neutropenia, thrombocytopenia). The incidence of \geq grade 3 AEs was reviewed in detail. We investigated the correlation between hematological toxicities occurring during maintenance treatment and during chemotherapy given before maintenance treatment. **[Results]** The median PFS in the 229 patients with maintenance treatment was 14.0 months (95% confidence interval 10.3-17.6 months). The hematological toxicities included \geq grade 3 anemia in 33.2% of cases. Anemia during maintenance treatment was significantly more common than anemia during chemotherapy given before maintenance treatment ($P < 0.001$). Anemia during chemotherapy prior to maintenance treatment significantly increased the risk of anemia during maintenance treatment, compared with other clinical features (area under the curve=0.586, $P=0.035$). **[Conclusion]** Maintenance treatment can be performed safely and effectively in patients with platinum-sensitive relapsed ovarian cancer. Anemia during chemotherapy given before maintenance treatment increased the risk of developing anemia during maintenance treatment in patients with platinum-sensitive relapsed ovarian cancer.

ISP-9-5

The impact of clinical staging and bevacizumab on outcome in 373 cases of ovarian clear cell carcinoma Osone Fumimasa,

Tabata Junya, Shiota Yasuhiro, Koba Takuhiro, Kochi Yuki, Hosoya Satoshi, Nagata Chie, Saito Motoaki, Yanaihara Nozomu, Yamada Kyosuke, Takano Hirokuni, Okamoto Aikou *The Jikei University*

[Objective] Prognostic factors and effective chemotherapy regimens for ovarian clear cell carcinoma (OCCC) patients are undetermined. This study aimed to identify prognostic stratification factors in patients with OCCC and to evaluate the prognostic significance of bevacizumab (Bev). **[Methods]** We retrospectively analyzed OCCC patients initially treated at our affiliated four institutions between 2012 and 2021. We performed log-rank tests on several prognostic factors and multivariate Cox proportional hazards analyses, including factors that prolonged progression-free survival (PFS). In addition, the prognosis of those who received platinum-based chemotherapy (PC) alone or in combination with Bev as adjuvant or neoadjuvant therapy was analyzed. **[Results]** Of 373 patients, univariate analyses showed that surgical completion, clinical stage (III vs. III/IV), CA-125 elimination rate constant K (KELIM), and CA125 at first visit were associated with prolonged PFS with statistically significant differences. However, in multivariate analyses, the clinical stage was the only factor that significantly prolonged PFS. Among stage III or IV patients, 67 underwent PC treatment without Bev, while 26 received Bev combination therapy. Notably, the combination therapy with Bev was linked to extended PFS ($p < 0.05$), a finding confirmed by propensity score matching ($p < 0.05$). **[Conclusion]** Clinical staging emerged as the sole significant prognostic factor in OCCC. Including Bev in primary chemotherapy appears promising to improve PFS in patients with advanced OCCC. Broader research with a more extensive case series is required to establish personalized medicine for OCCC.

ISP-9-6

Diagnostic performance of the MR relaxometry-independent tool for distinguishing between ovarian endometrioid cysts and endometriosis-associated ovarian cancer (modified e-NARA Index) Yamanaka Shoichiro, Kawahara Naoki, Yamamoto Konosuke, Nishikawa Kyohei, Matsuoka Motoki, Fukui Yosuke, Maehana Tomoka, Sugimoto Sumire, Iwai Kana, Yamada Yuki, Kawaguchi Ryuji, Kimura Fuminori *Nara Medical University*

[Objective] We have previously shown that the R2 value measured by magnetic resonance relaxometry and the e-Nara Index calculated using this value as a factor can accurately distinguish between ovarian endometrioma (OE) and endometriosis-associated ovarian cancer (EAOC) with a high degree of accuracy. However, since the R2 value can only be measured by a limited number of devices, we developed a value that approximates the R2 value (The R2 Predictive Index) using tumor diameter and CEA. We tested whether the modified e-Nara Index (Me-Nara Index), which substitutes The R2 Predictive Index into the e-Nara Index formula, is useful for differentiating OE from EAOC. **[Methods]** The Me-Nara Index was calculated for 142 patients with suspected OE or EAOC who underwent MR relaxometry at our institution between December 2012 and October 2019, and compared with other indices. **[Results]** The area under the curve of the receiver operating characteristic curve was measured, and the R2 value : 0.870, e-Nara index : 0.898, The R2 Predictive Index : 0.822, Me - Nara Index : 0.862. The sensitivity and specificity of the Me- Nara Index were 88.2% and 72.5%, respectively, when the cutoff value of the e-Nara Index was 20.40. The correlation coefficient between the e-Nara Index and the Me Nara Index was 0.954. **[Conclusion]** The Me-Nara Index has the potential to differentiate OE from EAOC more easily than conventional methods.

ISP-9-7

A massive single-cell image-based quantification of platelet aggregation in ovarian cancer patients Fukaya Sayuri¹, Taguchi Ayumi¹, Yamaguchi Kohei¹, Ishizaka Aya¹, Tsuchimochi Saki¹, Miyamoto Yuichiro¹, Sone Kenbun¹, Tsuruga Tetsushi¹, Mori Mayuyo¹, Koga Kaori², Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, Chiba University²*

[Objective] Cancer-associated thrombosis (CAT) has garnered significant attention as a poor prognostic factor in ovarian cancer. Although platelet aggregation is essential for CAT formation, the absence of appropriate statistical tools has hindered the precise early-stage assessment of this phenomenon. Recently, a cutting-edge single-cell image-based profiling system has been developed. In this study, we employed this innovative technology to characterize platelet aggregation in patients with ovarian cancer. **[Methods]** Blood samples were procured from patients with ovarian tumors for surgery (45 with ovarian cancer and 70 with benign tumors), and platelet aggregates were quantified using the advanced single-cell image-based profiling system. We assessed the ratio of platelet aggregation (Th_48) based on malignancy and histological type. Furthermore, we conducted a comparative analysis of inflammatory markers, such as serum albumin (Alb) and CRP, between histological types, focusing on cases exhibiting platelet hyper-aggregation. **[Results]** Th_48 was significantly higher in patients with ovarian cancer than in those with benign tumors ($p=0.0019$). In the overall analysis, despite significantly elevated D-dimer levels in high-grade serous carcinoma (HGSC) than in endometriosis-associated ovarian cancer (EAOC), patients with platelet hyper-aggregation were more frequently observed in EAOC group (HGS vs EAOC : 11% vs 35%). HGSC patients with platelet hyper-aggregation displayed significantly lower Alb levels than EAOC ($p=0.048$), indicating a potential association between the hyperinflammatory state induced by tumor progression and platelet hyper-aggregation in HGSC patients. **[Conclusion]** Platelet aggregation was markedly enhanced in ovarian cancer, and the mechanism varied by histology. Therapeutic interventions may be tailored to address the specific mechanisms of platelet aggregation.

ISP-9-8

The Prognostic Predictive Score around Primary Debulking Surgery (PPSP) enhances diagnostic accuracy for predicting ovarian cancer prognosis Kawahara Naoki, Yamamoto Konosuke, Matsuoka Motoki, Nishikawa Kyohei, Maehana Tomoka, Fukui Yosuke, Yamanaka Shoichiro, Sugimoto Sumire, Yamada Yuki, Iwai Kana, Kawaguchi Ryuji, Kimura Fuminori *Nara Medical University*

[Objective] In recent years, it has been found that the inflammatory responses prior to treatment can predict the prognosis. However, there has been no analysis of the combined inflammatory responses before and after surgery. The aim of the current study is to identify the factors that predict the recurrence and develop new predictive scoring. **[Methods]** This study was conducted at our institution from November 2006 to December 2020, with follow-up until September 2022. We collected demographic and clinical data from women who underwent primary debulking surgery. We developed a scoring system called the Prognosis Predictive Score around Primary debulking surgery (PPSP) to predict progression-free survival (PFS). We performed univariate and multivariate analyses to evaluate its effectiveness in predicting PFS and overall survival (OS). We used Cox regression analyses to assess its time-dependent efficacy. Finally, we compared the survival rate using Kaplan-Meier and the log-rank test. **[Results]** In the present study, 235 patients were included. The scoring system had a cut-off value

of six. Multivariate analyses showed that advanced International Federation of Gynecology and Obstetrics (FIGO) stage ($p < 0.001$ for PFS ; $p = 0.038$ for OS), decreased difference in white blood cell count ($p = 0.026$ for PFS), and high-PPSP ($p = 0.004$ for PFS ; $p = 0.002$ for OS) were independent prognostic factors. Cox regression analysis also supported these results. **[Conclusion]** The PPSP demonstrated excellent prognostic efficacy in predicting both PFS and OS of ovarian cancer patients, comparable to FIGO staging.

ISP-9-9

Preoperative serum CA72-4 in stage IC ovarian clear cell adenocarcinoma as a predictor of recurrence Suzuki Hironori¹, Yokoi Akira², Kimura Mariko³, Yoshida Kosuke^{1,2}, Yoshihara Masato¹, Tamauchi Satoshi¹, Shimizu Yusuke¹, Ikeda Yoshiki¹, Yoshikawa Nobuhisa¹, Niimi Kaoru¹, Kajiyama Hiroaki¹ *Nagoya University¹, Institute for Advanced Research, Nagoya University², Okazaki City Hospital³*

[Objective] Serum CA72-4 is widely used as a diagnostic biomarker for ovarian cancer, but its role as a prognostic biomarker is not fully understood. This study aims to re-evaluate the usefulness of serum CA72-4 in stage IC ovarian clear cell adenocarcinoma for predicting recurrence. **[Methods]** Between 2004 and 2021, 152 cases of ovarian clear cell adenocarcinoma treated in our institute were identified, 77 cases of which were in stage IC and 73 cases were eligible. Clinical and prognostic information was obtained from their medical records. The cutoff value of serum CA72-4 at the initial visit was set at 6.9 U/ml. The cases were divided into two groups : the serum CA72-4 positive and the serum CA72-4 negative. Several clinical covariates were adjusted for baseline balance, using an inverse probability of treatment weighting (IPTW). Progression-free survival (PFS) of the two groups were then compared. **[Results]** Of the cases studied, 19 cases (26%) were serum CA72-4 positive. Median follow-up period was 63.4 months. 12 cases (16%) had recurrence during the study periods. The Kaplan-Meier curves showed the serum CA72-4 positive group to have poor prognoses (log-rank $p=0.032$). Even after the adjustment using IPTW, the group was still shown to have poor prognoses (log-rank $p=0.032$). CA125 was also analyzed following the same procedures, with the cutoff value at 35 U/ml, which showed no significant difference in prognoses (log-rank $p=0.242$, $p=0.43$, before and after the IPTW adjustment respectively). **[Conclusion]** Preoperative serum CA72-4 in stage IC ovarian clear cell adenocarcinoma is useful in predicting recurrence.

ISP-9-10

Safety and Efficacy of Olaparib in Patients with Platinum-Recurrent Ovarian Cancer Ryu Tamami, Takeuchi Jun, Ishii Masato, Iida Serika, Kanamori Ryo, Imai Haruka, Endo Hiraku, Kuji Shihou, Ohara Tatsuuro, Takae Seido, Tozawa-Ono Akiko, Suzuki Nao *St. Marianna University School of Medicine*

[Objective] The purpose of this study was to evaluate the implementation of olaparib administration to patients with recurrent platinum-sensitive ovarian cancer from a retrospective perspective and to discuss factors related to safety, efficacy and others. **[Methods]** We retrospectively verified 29 patients with recurrent platinum-sensitive ovarian cancer, who received olaparib, between June 2018 and July 2022 in our hospital. The observation period (from initial treatment) was from August 2005 to January 2023 with a median of 80 months (41-209 months). **[Results]** The median duration of olaparib in 29 patients was 16 months (1-39 months). In addition, 6 patients were positive for BRCA pathological variants, 3 were negative, and 20 were untested. Adverse reactions led to a period of drug withdrawal in

16 patients, of which the most common cause was anemia, and one patient continued on taking medication during 10 drug withdrawal cycles, ultimately resulting in prolonged PFS. On the other hand, in 6 patients, the dosage was reduced from the beginning in consideration of the patient's general condition; therefore the medication could be administered without a drug withdrawal. In addition, no drug withdrawal or dose reductions were made in 6 patients. And chemotherapy was performed in all patients after PD. The median PFS was 23 months (4-55 months) and the median OS was 74 months (26-209 months). **[Conclusion]** We were able to verify that safe olaparib administration with appropriate drug withdrawal and dose reduction contributes to prolonged PFS.

ISP-9-11

Impact of postoperative residual disease on survival in epithelial ovarian cancer with consideration of recent frontline treatment advances : A systematic review and meta-analysis
Kim Ji Hyun¹, Kim Se Ik², Park Eun Young³, Ha Hyeong In¹, Kim Jae-Weon², Coleman Robert L⁵, Bristow Robert E⁶, Park Sang-Yoon¹, Fotopoulou Christina⁷, Lim Myong Cheol¹ *Gynecologic Cancer Center, National Cancer Center Korea, Korea¹, Seoul National University College of Medicine, Korea², Biostatistics Collaboration Team, National Cancer Center, Korea³, Pusan National University Yangsan Hospital, Korea⁴, Gynecologic Oncology, SVP & Chief Scientific Officer, US Oncology Research, the Woodlands, USA⁵, Irvine Medical Center, USA⁶, Department of Surgery and Cancer, Imperial College London, UK⁷*

[Objective] The study aimed to investigate the impact of residual disease after cytoreductive surgery for EOC on survival outcomes within the recent paradigm of frontline ovarian cancer treatment. **[Methods]** We searched relevant literature from the MEDLINE, Embase, and Cochrane Library databases to identify randomized controlled trials and prospective clinical trials of primary EOC published between 1 January 2000 and 22 September 2022. To evaluate the impact of postoperative residual tumors on progression-free survival (PFS) and OS, we constructed a linear regression model for log-transformed median PFS and OS. Patients who did or did not receive first-line maintenance therapy were examined. **[Results]** A total of 97 trials with 43,260 patients were included: 2,476 received poly (ADP-ribose) polymerase (PARP) inhibitors and 6,587 received bevacizumab. Multivariable analysis of the linear regression model of all studies revealed that the median OS increased by 12.97% for every 10% increase in complete cytoreduction rates, independent of the use of systemic maintenance. In the subgroup analysis of patients receiving maintenance therapies, the effect of complete tumor clearance was potentiated, with a median OS increase of 19.13% for every 10% increase in complete cytoreduction rates. **[Conclusion]** Total macroscopic tumor clearance at the initial presentation of EOC significantly prolongs OS. Our results establish the importance of complete surgical cytoreduction, even after the introduction of recent advances in frontline treatment for EOC.

ISP-9-12

The benefits of additional intensified treatments to liver metastases in recurrent epithelial ovarian cancer Li Yingxuan¹, Chin Hsu¹, Kuan-Ju Huang², Wen-Chun Chang³, Lin-Hung Wei³, Bor-Ching Sheu³ *National Taiwan University Hospital Hsinchu Branch, Taiwan¹, National Taiwan University Hospital Yun-Lin Branch, Taiwan², National Taiwan University Hospital, Taiwan³*
[Objective] Observing the impact of additional treatment of metastatic liver tumors on the prognosis of recurrent epithelial ovarian cancer (tubal cancer, peritoneal carcinoma). **[Methods]** A retrospective cohort study to collect the patients who had re-

current epithelial ovarian cancer with liver metastasis at National Taiwan University Hospital between January 1, 2010 and December 31, 2021. To treat the disease, the patients would receive an additional local liver tumor treatment (LT) followed by chemotherapy or chemotherapy alone. Then the progression free survival (PFS) and overall survival (OS) of additional local liver tumor treatments followed by chemotherapy and chemotherapy alone were analyzed via Kaplan-Meier survival analysis and Cox proportional model. **[Results]** 131 patients had treatments to recurrent epithelial ovarian cancer with liver metastasis. 63 patients had received LT, and 68 patients had not. The PFS was longer if receiving LT ($p=0.049$), and the hazard ratio was 0.68. The OS was not significantly different between two groups. Furthermore, we found that the recurrence risk decreased more obviously within those patients who were free of chemotherapy more than 6 months and had no residual liver tumor after LT ($p=0.001$, HR=0.45). However, the recurrence risk elevated within those patients who were free of chemotherapy more than 6 months but had residual liver tumors after LT ($p=0.068$, HR=1.93), and the death risk significantly increased ($p=0.008$, HR=3.69). **[Conclusion]** LT provide benefits to PFS, especially to the patients who were free of chemotherapy more than six months and had no residual liver tumors after LT.

ISP-9-13

The outcomes of women treated for adult-type granulosa cell tumor of the ovary Ju Uchul, Kim Seokmo *Chonnam National University Medical School, Korea*

[Objective] Granulosa cell tumor (GCT) of the ovary are a rare malignant tumor with a relatively favorable prognosis. We investigated the characteristics of adult-type GCT of the ovary and the outcomes of women received the primary treatments. **[Methods]** We retrospectively reviewed the clinical data of patients who were treated for adult-type GCT of the ovary from 1999 to 2021. **[Results]** Seventy-eight patients were identified. The median age was 53 years (range, 17-80 years). All women firstly received a primary surgery. Endometrial carcinoma was detected in 7 (9.0%). The majority of patients had FIGO stage I ($n = 68$, 87.2%), while 7 patients (9.0%) had stage II and 3 (3.8%) had stage III. The patients with stage IC or more disease ($n = 14$, 17.8%) received adjuvant platinum-based chemotherapy. In the median follow-up period of 92 months, 10 women (12.8%) relapsed with a median time to recurrence of 68 months (range, 23-140 months). All patients with recurrent disease received debulking surgery and some received postoperative platinum-based chemotherapy. No patients are died of the disease. **[Conclusion]** Adult-type GCT of the ovary have good outcomes, however, require long-time follow-up. Secondary debulking surgery with adjuvant treatment is indicated to recurred diseases.

ISP-10-1

On the development of a minimally invasive surgical navigation system for gynecological cancer using deep learning
Jonouchi Yuri, Sone Kenbun, Tanimoto Saki, Honjoh Harunori, Fukuda Tomohiko, Eguchi Satoko, Miyamoto Yuichiro, Mori Mayuyo, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*

[Objective] Recently, minimally invasive surgeries such as laparoscopic and robot-assisted surgery have been widely performed for gynecological malignancies. In order to achieve safe and stable surgical operations, we aimed to develop a minimally invasive surgical navigation system by learning from surgical videos of gynecological malignancies using deep learning. **[Methods]** We used surgical videos of laparoscopic and robot-assisted total hysterectomy in gynecological tumor cases. First, we identified uterine artery and ureter, which are the two vital

organs in the gynecological field, and aimed to display each of them separately. Videos of each procedure were taken as still images, annotated with organs and connective tissue, and learnt using deep learning. The recognition performance of the developed deep learning model was then verified in another surgical video. In practice, 617 images 14 case videos were analyzed and evaluated in 7 case videos. A modified version of PIDnet was used for deep learning. **[Results]** In the judgement of three obstetricians and gynecologists, the recognition and distinction between uterine artery and ureter was reasonable in the current model. It was also possible to recognize uterine artery and ureter in images in that the full view of them was not visible. **[Conclusion]** The deep learning model developed in this study needs to be improved in the future, but it could enable navigation systems for all surgical procedures in the future. The system has a high potential to contribute to safe and stable surgical operations when used in actual clinical practice.

ISP-10-2

—Fusion of Robotic and Laparoscopic Surgery—Examination of New Procedure Hybrid Hysterectomy Using Hugo Sawada Mayumi, Komatsu Hiroaki, Wada Ikumi, Taniguchi Fuminori *Tottori University*

[Objective] The Hugo™ robot-assisted surgery system consists of four arms and offers versatile configurations. We report the development of a novel surgical technique, robot-assisted hybrid hysterectomy (HyH), which combines robotic and laparoscopic approaches. **[Methods]** The HyH procedure involves port placement on the left side and midline of the lower abdomen for surgeon manipulation, with the Hugo port positioned at the umbilicus and on the right side. The assistant operates the camera and auxiliary forceps using a Hugo system. We compared the surgical time and precision of forceps manipulation between total laparoscopic hysterectomy (TLH) and HyH, with both procedures performed by the same surgical team within one week. **[Results]** The total surgical times were 2 h, 3 min for TLH and 1 h, 53 min for HyH. The time required to initiate intraperitoneal procedures was 13 min, 28 s for TLH and 15 min, 50 s, for HyH, with no significant time increase due to Hugo docking. The number of times the needle and thread were grasped missed during suturing was 32 in TLH and 14 in HyH. In tissue grasping, there were 27 missed grabs in TLH and 12 in HyH. The number of swing misses during tissue incisions using monopolar instruments was 8 for TLH and 3 for HyH. Both types of error were less frequent in HyH. **[Conclusion]** HyH demonstrated superior surgical accuracy in comparison to conventional TLH. It has the potential to be a safe and effective addition to surgeon training systems.

ISP-10-3

Development of a selection system using multimodal artificial intelligence for the optimal surgical procedure in minimally invasive surgery Shigekawa Koichiro, Miyata Kohei, Ishida Tomohiro, Hirano Tomoka, Kurakazu Mariko, Yoshikawa Kenichi, Kimura Ibuki, Noguchi Yukiko, Kiyoshima Chihiro, Kurakazu Masamitsu, Yotsumoto Fusanori *Fukuoka University* **[Objective]** In this study, we used highly accurate artificial intelligence (AI)-based predictive models to analyze the perioperative outcomes of robot-assisted hysterectomy (RAH) and total laparoscopic hysterectomy (TLH). **[Methods]** This comparative study included 116 patients who underwent RAH and 231 patients who underwent TLH for benign uterine disease at our hospital. The patient characteristics, blood tests, and imaging data were reviewed from their medical records. The machine learning platform TensorFlow was used to create the predictive models and cross-validation was applied to evaluate

their generalization ability. **[Results]** Analysis using TensorFlow showed that in addition to age, the body weight and preoperative serum albumin level were significant contributors to blood loss. Other factors that contributed significantly to the efficacy of RAH were height, blood loss, postoperative pain, postoperative serum albumin level, and postoperative hospital stay, whereas factors that contributed significantly to the effectiveness of TLH were the postoperative serum CRP level, operation time, body mass index, and body weight. With regard to the accuracy of the predictive models, the area under the receiver operating characteristic curve based on clinical information alone and clinical information in addition to blood tests and imaging data was 0.603 and 0.819, respectively. **[Conclusion]** The important preoperative factors for creating a predictive model were age, height, body weight, and preoperative serum albumin level, and a highly accurate predictive model could be created by integrating data from multiple modalities. Therefore, a multimodal AI-based diagnostic system can potentially contribute to the optimal selection of the RAH and TLH surgical procedures.

ISP-10-4

The learning curve of Transvaginal Natural Orifice Transluminal Endoscopic Hysterectomy (vNOTES) in the Hands of skilled Japanese Gynecologist Deguchi Satoki, Mabuchi Seiji, Sakata Mina, Maeda Michihide, Kakubari Reisa, Matsuzaki Shinya, Hisa Tsuyoshi, Kamiura Shoji *Osaka Medical Center for Cancer and Cardiovascular Diseases*

[Objective] To evaluate the feasibility, safety and a learning curve of vNOTES conducted by a skilled surgeon with experiences of vaginal surgery and laparoscopic surgeries. **[Methods]** Eleven patients who had been scheduled to undergo vNOTES hysterectomy from August 2022 to September 2023 were identified and their clinical data were retrospectively reviewed. After excluding two cases whose vNOTES hysterectomies were converted to a conventional laparoscopic hysterectomy and a case in which vNOTES hysterectomy plus simple vulvectomy were performed, the remaining nine cases were included for the analyses. All surgeries were performed by a single gynecologist. The primary outcome was operation time. Secondary outcomes had intraoperative blood loss. **[Results]** Surgical procedures performed were vNOTES hysterectomy plus bilateral salpingectomy (n=6) or oophorectomy (n=2). Median age was 51 years (range 33-79). Median hysterectomy time was 86.5 minutes (59-155), and no intraoperative or postoperative complications occurred. When the first 4 hysterectomies were compared with the 4 subsequent procedures, surgical time was significantly decreased [median : 125 minutes (range : 91-155) vs. 70 minutes (range : 59-82), P=0.04], but intraoperative bleeding did not decrease [median : 67.5ml (range : 0-290) vs. 80ml (range : 0-150), p=0.77]. **[Conclusion]** vNOTES hysterectomy can be safely performed and improved in a short period when surgeons have enough experiences of vaginal hysterectomy and laparoscopic surgery.

ISP-10-5

Predictors of prolonged operative time for total laparoscopic hysterectomy Narumi Megumi¹, Igasaki Mari², Todo Yusuke¹, Itoh Toshiya¹, Mastumoto Masako¹, Matsuya Madoka¹, Shibata Toshiaki¹, Murakami Hirotake¹, Abe Masakazu¹, Nakayama Takeshi², Itoh Hiroaki¹ *Hamamatsu University School of Medicine¹, Shizuoka Kosei Hospital²*

[Objective] Total Laparoscopic Hysterectomy (TLH) is on the increase in Japan, but few studies have examined the factors that prolong the operative time. Preoperative identification of the risk of prolonged operative time would lead to safer perioperative management. We aimed to identify preoperative fac-

tors associated with prolonged operative time. **[Methods]** We retrospectively reviewed patients who underwent TLH at our institution from April 2018 to February 2022. Patient background, preoperative MRI findings, and findings at surgery were extracted from medical records, and factors associated with prolonged TLH time among items that could be assessed preoperatively were analyzed. Multivariate analysis was performed using linear and logistic regression analysis. **[Results]** There were 227 eligible patients, mean age 51.4 years (± 9.4 SD), mean BMI 22.8 (± 3.4 SD), the majority of preoperative diagnoses were uterine myoma (78.4%), and the preoperative MRI rate was 96.5%. The mean operative time was 171.9 minutes (± 51.4 SD). Multivariate analysis revealed that the factors considered to prolong operative time were 1) BMI, 2) history of endometriosis, 3) maximum myoma diameter, and 4) uterus exceeding the cape angle. Furthermore, the two factors with the highest positive predictive value for risk of operative time longer than 180 minutes were 4) alone (73.8%) and two or more items from 1) to 4) (78.1%). **[Conclusion]** The factors that could be evaluated preoperatively for prolonged TLH surgery time were BMI, history of endometriosis, maximum myoma diameter, and uterus exceeding the cape angle, and their positive predictive value was also high.

ISP-10-6

Actual incidence of thromboembolism after gynecologic surgery for malignant diseases Obata Eri, Aoyagi Yoko, Aso Saki, Okamoto Mamiko, Kai Kentaro, Kodama Haruho, Shima Kazuaki, Yano Mitsutake, Yamada Tomonori, Yamamoto Shizuka, Kobayashi Eiji *Oita University*

[Objective] Information regarding actual incidence of thromboembolism after gynecologic cancer surgery is limited. The aim of this study is to evaluate incidence of the post operative thromboembolism after gynecologic cancer surgery. **[Methods]** Using an electronic health record, cross-sectional study was conducted in a university teaching hospital. Since 2018, we have routinely performed contract-enhanced computer tomography (CECT) pre and postoperatively after gynecologic malignancies as an institutional policy. We investigated the incidence of post operative thromboembolism detected by CECT one week after surgery. **[Results]** Chest-to-lower-extremities CECT was conducted in 290 (72.0%) of the patients, and 43 (14.8%) of the 290 patients experienced one or more postoperative vascular complications : thrombosis (n=35, 81.4%), vascular lesion, i.e., stenosis or an arteriovenous aneurysm (n=5, 11.6%), and renal infarction (n=33, 7.0%). Pulmonary thrombosis occurred in 12 patients, deep venous thrombosis in 11, pulmonary-deep venous thrombosis in five patients, and other vessels in seven : internal iliac vein, external iliac vein, ovarian vein and descending aorta. Of patients with thrombosis, 30 (85.7%) of these 35 patients received anticoagulation therapy. There were no deaths due to thrombosis. The patients with stenosis, aneurysm, or renal infarction received no medical intervention. **[Conclusion]** This study reveals the actual incidence of post operative thromboembolism after gynecologic cancer surgery. This incidence is higher than the previously report in Japan.

ISP-10-7

Study on the Drainage Volume and Timing of Drain Tube Removal after Retroperitoneal Lymph Node Dissection Kawarai Yoshimasa, Horiguchi Tatsuya, Fukuda Shiho, Hirose Masaki, Kuno Tatsuya, Obayashi Satoshi, Mitsuhashi Akira *Dokkyo Medical University*

[Objective] After retroperitoneal lymph node dissection, drainage tubes are placed to facilitate the early detection of postoperative bleeding and prevent lymphocele formation. However,

because there are no clear guidelines for the timing of drain removal, we retrospectively examined this aspect in this study. **[Methods]** We included 37 patients who underwent pelvic and para-aortic lymph node dissection during ovarian cancer or uterine corpus cancer surgery. Of these patients, 17 were obese (BMI ≥ 25 kg/m²). Drains were placed in both retroperitoneal cavities. The drainage volume was measured every 24 hours, and the decision for removal was made during outpatient visits. In addition to the drainage volume, data were extracted from medical records and analyzed. **[Results]** The average postoperative day and drainage volume at the time of drain removal were respectively 3.3 days and 90.8 mL for the first drain and 6.6 days and 191.9 mL for the second drain. In 24 patients, the volume at the time of second drain removal exceeded 150 mL. The obese group had significantly fewer patients with a volume of 150 mL or more at the time of second drain removal than the non-obese group ($p=0.0075$, Fisher's exact test). One patient (BMI 19.2 kg/m²) had lymphocele infection with drain removal on the 12th day and a volume of 170 mL. None of the patients developed lymphatic fistulas. **[Conclusion]** Removing a drain with a high volume may not change the occurrence of complications. On the contrary, prolonged drainage may pose a risk of lymphocele infection.

ISP-10-8

Comparison of surgical outcomes between robot-assisted and laparoscopic hysterectomy for endometrial cancer in patients with obesity class II or III Takemoto Yuki, Kodama Michiko, Kakuda Mamoru, Toda Aska, Nakagawa Satoshi, Kinose Yasuto, Takiuchi Tsuyoshi, Hashimoto Kae, Ueda Yutaka, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Introduction] The number of robot-assisted surgeries for endometrial cancer has gradually increased. In obese patients, robot-assisted surgeries may achieve better outcomes than laparoscopic surgeries ; however, there is no conclusive consensus. **[Objective]** To review the safety and efficacy of robot-assisted and laparoscopic surgery for endometrial cancer in obese patients. **[Methods]** We retrospectively extracted the patients with early-stage uterine cancer with obesity class II or III (body mass index ; BMI ≥ 35 kg/m²) in our hospital from April 2018 to March 2022 from electrical medical records. Operation was performed by 9 gynecologists. Operation time, blood loss, postoperative hospital stay, and perioperative complications were compared between robot-assisted and laparoscopic surgery. **[Results]** Of the 25 cases who underwent hysterectomy, 7 underwent robot-assisted hysterectomy and 18 underwent laparoscopic hysterectomy. Median BMI for robot-assisted and laparoscopic hysterectomy was 40.2 (min-max ; 35.5-54.7) and 38.6 (35.1-49.8) ($p=0.47$), respectively. Mean operative time was 268 min and 285 min ($p=0.70$), median blood loss was 25 (10-60) ml and 35 (0-1400) ml ($p=0.70$), and median postoperative hospital stay was 8 (6-9) days and 7.5 (6-26) days ($p=0.66$), respectively. In the laparoscopic surgery group, complications were observed in four patients (22.2%) : two cases of ileus, two cases of pelvic infections, one case of surgical site infection, and one case of conversion to open surgery. In the robot-assisted group, one (14.3%) required conversion to laparoscopic surgery. **[Conclusion]** Robotic hysterectomy for obese patients might be comparable in surgical outcome and safe to laparoscopic surgery. We are planning further studies to explore the potential benefits of robotic surgery for obese patients.

ISP-10-9

Partial vaginectomy assisted by laparoscopy combined with transvaginal endoscopic surgery for isolated vaginal recurrence of low-grade uterine endometrial stromal sarcoma af-

ter hysterectomy Yoshikawa Kenichi, Miyata Kohei, Ishida Tomohiro, Hirano Tomoka, Shigekawa Koichiro, Kurakazu Mariko, Kimura Ibuki, Noguchi Yukiko, Kiyoshima Chihiro, Yotsumoto Fusanori *Fukuoka University*

Severe tissue fibrosis and adhesions or anatomical deviation are often seen in the pelvic floor after hysterectomy, potentially affecting the quality of the surgery for vaginal recurrence. Here, we present a patient who underwent partial vaginectomy with concurrent transvaginal endoscopic surgery and laparoscopy for recurrence of low-grade uterine endometrial stromal sarcoma (LGESS). The patient was 41 years old, para 4, gravida 2, with a history of myomectomy and hysterectomy for myoma uteri and LGESS. A 24-mm single tumor was found in the vaginal stump without distant metastasis nine months after hysterectomy. Hence, we planned surgical excision for this isolated recurrent tumor using two cameras from the abdominal side and vaginal sides. The transabdominal approach was performed via four ports, with one 12-mm trocar in the umbilicus and three 5-mm trocars in the lower abdomen. The transvaginal approach was performed via GelPOINT Mini Advanced Access Platform (Applied Medical) with one 12-mm and two 5-mm trocars. The total operating time was 244 min, and the estimated blood loss was 50 mL. Complete resection was achieved without any complications. The postoperative course was uneventful; the patient was discharged on postoperative day 8. This hybrid technique offers the major advantages of better surgical radicality, continuous protection of the bladder and rectum, and less intraoperative bleeding in cases when the tumor invades the pelvic organs or there are severe abdominal adhesions.

ISP-10-10

A case of peritoneal tuberculosis diagnosed with laparoscopy Yamada Takashi *Pathology, Osaka Medical and Pharmaceutical University*

[Background] Peritoneal tuberculosis is often misdiagnosed as peritoneal carcinomatosis preoperatively. We report a case of peritoneal tuberculosis diagnosed with laparoscopy. [Case] A 53-year-old, gravida 3, para 2, woman complained of abdominal distention of one month's duration. The serum levels of tumor markers were positive for CA125; 1181 U/ml and CA19-9; 202 U/ml. Magnetic resonance imaging (MRI) showed thickened peritoneum with large amounts of ascites, peritoneal carcinomatosis was suspected. Laparoscopic surgery was performed. With the patient under general anesthesia and in the lithotomy position, an incision was made in the umbilicus, and a 12-mm port for camera was inserted. There were 1200 ml of ascites and diffuse nodular lesions along the surface of normal-sized ovaries, fallopian tubes, uterus, intestinal loops, omentum and peritoneum. Laparoscopic bilateral oophoro-salpingectomy and partial omentectomy was performed. The specimens in the bag were pulled out from the umbilicus. Intraoperative cytology of ascites was negative for malignancy, and intraoperative diagnosis of frozen section was suspicious of tuberculosis. In immunohistochemical findings, vimentin was positive, and AE1/AE3, CK7 and CK20 were negative. Ziehl-Neelsen staining showed no acid-fast bacilli. Final histological diagnosis was peritoneal tuberculosis. **[Conclusion]** Laparoscopy can be an effective approach for diagnosis of peritoneal tuberculosis.

ISP-10-11

A Concept Paper : Real Time Linked 3-Dimensional Headset and 360 Degrees Bilateral Full-Flexi Toggle Controlled Micro-Minituarised Operating Bots (MMOB) in Selected Benign/Need to Confirm Benign Gynaecological Surgery Weng Kong Eugene Leong^{1,2,3} *Taylor's University School of Medicine, Malaysia¹, KeyHole Surgery/GynaeOncology/Com-*

plex Surgeries Fellowship Trained Singapore, Klinik Pakar Wanita Imperial NewLife-Precious Obstetrics & Gynaecology, Malaysia², KeyHole Surgery/GynaeOncology/Complex Surgeries Fellowship Trained Singapore, Sri Kota Specialist Medical Centre SKSMC, Malaysia³

[Objective] : To discuss- Real Time Linked 3-Dimensional Headset & 360 degrees Bilateral Full-Flexi Toggle Controlled Micro-Minituarised Operating BOTS (MMOB) in selected Gynaecological Surgery. An Innovative Concept Paper. **[Methods]** : In the years to come - Micro-Minituarised Operating BOTS (MMOB) and Specialised Specimen Recovery Vehicles (SSRV) with non-spillage precepts, that operate in coordinated seamless fashion controlled by an expert trained Specialist Gynaecologist (Linked Headset/Toggles with powerful micro-processors & clear vision) & special slimfit atraumatic smooth agile with controlled movements that have sheathed operating arms either singly or in pairs or threes can perform selected operations in gynaecological surgeries under anaesthesia. They will outperform in terms of pain, post-operative recovery, adequacy of operation, specimen recovery, safety, achievement of operating objectives and other aspects including being scar-less. Entry is designed via the fallopian tubes or vagina. Specimen recovery with the SSRV may require small precise vaginal exit. Designed for fast dis-assembly for sterilising and cleaning and re-use. Software uploads enabled. Specific very strict case selection/filters crucial (Tumour Board). Pneumoperitoneum is an option for clearer vision and to avoid surgical clutter. Not for Advanced/Large/Adherent/Bulky cancers or unfit patients. Advanced nontoxic biomechanics, waterproof microcircuits, harmless 100hour batteries, great optics. **[Results]** : Good less pain and safe operations in specific selected gynaecology can be further accelerated. **[Conclusion]** : In the years to come, it will be a reality with MMOB and SSRV in specially trained expert Specialist Gynaecologists with headsets/toggles as described in selected scenarios only.

ISP-11-1

Establishment of a Method for Human ES Cell Differentiation into Kisspeptin Neurons Seki Tomomi, Osuka Satoko, Takeda Takehiko, Kaseki Satoshi, Yabuki Atsushi, Tanaka Hideaki, Miyake Natsuki, Sonehara Reina, Muraoka Ayako, Nakamura Tomoko, Kajiyama Hiroaki *Nagoya University*

[Objective] The hypothalamic-pituitary-gonadal axis is regulated by kisspeptin, which plays a role in follicle development, ovulation, and sex hormone secretion. However, an in vitro model of human kisspeptin neurons is nonexistent, and their developmental features remain unexplored. We aimed to elucidate the developmental mechanism of human kisspeptin neurons which localized in hypothalamic arcuate nucleus (ARC) by inducing kisspeptin neuron differentiation from human pluripotent stem cells. **[Methods]** According to our previous reports, feeder-free human embryonic stem cells (hESCs) in serum-free floating culture of embryoid body-like aggregates with quick reaggregation were used to induce kisspeptin neuron differentiation in medium supplemented with 5% KnockOut™ Serum Replacement with Wnt signal inhibitor, Activin signal inhibitor, sonic hedgehog signal agonist and bone morphogenetic protein4. Fluorescence immunostaining of pituitary-hypothalamic organoids (PHOs) was conducted at several points to confirm marker gene expression. **[Results]** Aggregates on days 30, 60, and 100 were collected, and differentiation into PHOs was confirmed through a positive fluorescent immunohistochemistry of E-cadherin, PRO1, PITX1, LHX3, and RAX for Day 30; E-cadherin, PRO1, PITX1, LHX3, adrenocorticotropic hormone (ACTH), RAX, and POMC for Day 60; E-cadherin, PITX1, LHX3, POMC, and ACTH for Day 100. Culture without JNK-IN-8, used from day 0 to day 30 in the organoid with pituitary con-

tents differentiation protocol, yielded the Agouti-related peptide positive cell differentiation, a marker of the ARC. Furthermore, on Day 100, organoid immunostaining revealed kisspeptin-positive neurons. **[Conclusion]** We confirmed that kisspeptin neurons can be differentiated from hESCs. We will continue to explore more efficient differentiation methods to evaluate kisspeptin neuron function.

ISP-11-2

Expression of virus-like particles from germ cells Kobayashi Mutsumi¹, Shioda Toshihiro², Kitade Mari¹, Itakura Atsuo¹, Kawamura Kazuhiro¹ *Juntendo University¹, Center for Cancer Research, Massachusetts General Hospital, USA²*

[Objective] Human endogenous retroviruses (HERVs) are remnants of ancient infection by retroviruses, comprising nearly 8% of the human genome. In the human primordial germ cell-like cells (hPGCLCs), we reported that the methylation level in long terminal region 5 Hs (LTR5_Hs) was significantly decreased. Because the LTR-5_Hs is the LTR of HERV-K which has been integrated into our genome most recently, we investigated the HERV-K and the other endogenous retrovirus expression in primordial germ cell-like cells. **[Methods]** Bulk RNAseq and proteomics analysis were performed on hPGCLCs and iPS cells to detect the HERV-K expression. To check the HERV-K expression in human fetuses and embryos, re-analyses of previously deposited single-cell RNAseq data were performed. **[Results]** Using RNAseq analysis, it was shown that HERV-K was significantly expressed in hPGCLCs, but not in human iPS cells, following that the HERV-K protein was detected by proteomics and western blotting. Because it is known that the HERV-K sequences have the potential to compose the virus-like particle (VLP), transmission electron microscopy revealed that hPGCLCs expressed the VLP containing HERV-K protein. Finally, it was confirmed that the HERV-K was highly expressed in human embryos by re-analysis of previously reported single-cell RNAseq analysis. **[Conclusion]** HERV-K sequences were highly expressed in human germ cells and composed of the VLP. The function of the VLP in human reproduction has not been clarified yet. The VLP might play an important role in germ cell development or embryo implantation.

ISP-11-3

Cellular senescence contributes to pathogenesis of polycystic ovary syndrome Tanaka Tsurugi, Harada Miyuki, Urata Yoko, Kunitomi Chisato, Aoyama Akari, Koike Hiroshi, Jo Koshin, Sakaguchi Nanoka, Hiraike Osamu, Hirota Yasushi, Osuga Yutaka, Takahashi Nozomu *The University of Tokyo*

[Objective] Cellular senescence, is a permanent state of cell cycle arrest, contributes to the pathogenesis of various diseases. The combination of Dasatinib + Quercetin (DQ) has been extensively used as a senolytic, which selectively eliminate senescent cells. Polycystic ovarian syndrome (PCOS) is a common endocrine disorder, but its pathology and treatment strategy remain unclear. We hypothesized that cellular senescence plays a pivotal role in pathology of PCOS and aimed to investigate the effect of a senolytic on PCOS pathogenesis. **[Methods]** We obtained ovaries and granulosa cells (GCs) from patients with or without PCOS. Human GCs were stimulated by testosterone and treated with DQ. PCOS model mice were established by injection of dehydroepiandrosterone and treated with DQ. The expression of senescence markers (p16^{INK4a}, p21, p53, and γ H2AX) and a senescence-associated secretory phenotype (SASP) factor interleukin-6 (IL-6) in ovaries were examined by immunohistochemistry and qPCR. The accumulation of senescence markers and a SASP factor in human GCs were examined by western blotting, ELISA and senescence-associate β -galactosidase stain-

ing. **[Results]** The expression of senescence markers were elevated in ovaries from PCOS patients and PCOS model mice. In human GCs, senescence markers and IL-6 were upregulated by testosterone stimulation and DQ treatment mediated the upregulation. In PCOS model mice, DQ treatment mitigated the upregulated expression of senescence markers and IL-6 in the GCs and improved the ovarian morphology, specifically, reduced the number of atretic follicles. **[Conclusion]** Cellular senescence plays a pivotal role in PCOS pathology and represents a novel target in treatment of PCOS.

ISP-11-4

Crosstalk between Mitochondrial and Endoplasmic Reticulum in Oocytes Nakamura Fumihiko, Takehara Isao, Hine Saki, Sato Ai, Nakai Nanako, Matsukawa Jun, Nishi Michi, Nagase Satoru *Yamagata University*

[Objective] Aging adversely affects oocyte quality and fertility, with oxidative stress playing a role. While efforts to enhance mitochondrial function have shown partial success, controlling endoplasmic reticulum (ER) stress has improved blastocyst and pregnancy rates but not overall livebirth rates. This study investigates the relationship between mitochondrial dynamics and ER in oocytes. **[Methods]** Mouse MII oocytes were left untreated, exposed to mitochondrial hypofunction-inducing CCCP (15 μ M), or subjected to ER stress through thapsigargin (5 μ M). Signal intensity of MitoSOX[®] (indicating mitochondrial ROS) and GRP78 (an ER stress marker) was measured using Confocal Laser Scanning Microscopy. A post-ovulatory 'aging' model was employed to simulate reduced oocyte quality. 'Aging' oocytes and, treated with the mitochondrial enhancer 5-ALA (10 μ M), the ER stress regulator Salubrinal (5 μ M), or both were also examined. **[Results]** Significant increases in MitoSOX[®] occurred in CCCP- and thapsigargin-treated oocytes compared to untreated (P<0.01). GRP78 also significantly rose in CCCP- and thapsigargin-treated oocytes (P < 0.01), suggesting mitochondria-ER interaction in oocytes. In 'aging' model, 5-ALA significantly reduced MitoSOX[®] (P<0.01), while salubrinal showed a trend toward reduced MitoSOX[®]. Salubrinal significantly decreased GRP78 (P<0.01), while 5-ALA did not demonstrate any discernible influence. 5-ALA and Salubrinal tended not to mutually enhance mitochondrial and ER function. **[Conclusion]** Unfertilized oocytes exhibit mutual influence between mitochondrial and ER function. In 'aging' oocytes, 5-ALA enhances mitochondrial function, while salubrinal boosts ER function. However, crosstalk between mitochondria and ER was only partially observed. We'd like to further our research by devising the timing of these drugs use during embryonic development.

ISP-11-5

Differences in the sex steroid hormone-induced feedback mechanisms in ovariectomized or ovary intact female rats Tumurbaatar Tuvshintugs, Kanasaki Haruhiko, Zhuoma Cairang, Batjargal Lkhagvajav, Oride Aki, Okada Hiroe, Kyo Satoru *Shimane University*

[Objective] Hypothalamic-pituitary gonadal axis regulates sex steroids-induced feedback mechanisms. We examined the difference in sex steroids-induced feedback mechanisms in pituitary and hypothalamus depending on the presence or absence of ovaries. **[Methods]** Seven weeks-old female rats were ovariectomized and supplemented with estradiol (E2), progesterone (P4) and dihydrotestosterone (DHT). Seven-week-old ovary-intact female rats were also treated with E2, P4, and DHT. Changes in hypothalamic Kiss-I and pituitary gonadotropin subunits gene expression were determined. **[Results]** Kiss-I gene expression in hypothalamic region including the arcuate nucleus was increased by ovariectomy and decreased by E2 supplementation.

The increase in Kiss-1 gene by ovariectomy was also suppressed by P4 and DHT supplementation. Pituitary gonadotropin α , LH β and FSH β subunit gene expressions were significantly increased by ovariectomy. E2 supplementation after ovariectomy suppressed the ovariectomy-induced increase in all gonadotropin subunits gene expression. P4 failed to suppress the increase in gonadotropin subunits, and DHT had partial suppressive effects on α and FSH β subunit. Kiss-1 gene expression in hypothalamic regions including the arch nucleus was markedly suppressed by E2 treatment in ovary-intact female rats, but was unchanged by P4 and DHT treatment. Pituitary α , LH β and FSH β subunits were significantly suppressed by E2 and P4 administration in ovary intact rats, but were unchanged by DHT administration. **[Conclusion]** The effects of sex steroid hormones on the hypothalamus and pituitary gland might be differ depending on the presence or absence of ovaries.

ISP-11-6

Effect of Endoplasmic Reticulum Stress on Human Endometrial Stromal Cell Decidualization Ito Tomomichi, Watanabe Norikazu, Yamaguchi Risako, Fukase Mika, Yamanouchi Keiko, Nagase Satoru *Yamagata University*

[Objective] In the decidua, mild endoplasmic reticulum stress (ERS) contributes to the implantation and maintenance of pregnancy. While ovarian hormones regulate ERS in human endometrial stromal cells (HESCs) even before decidualization, the precise significance remains uncertain. Our study investigated the ERS effect on HESCs before decidualization. **[Methods]** We cultured HESCs obtained from patients who had undergone hysterectomy for benign conditions. HESCs were cultured with or without ERS inducer thapsigargin (Tg) and decidualized for 48 h with medroxyprogesterone acetate and cyclic adenosine monophosphate. We assessed these cells based on morphological changes, cellular viability, and mRNA expression of the decidualization marker, PRL. Additionally, we conducted co-culture experiments involving decidualized HESCs and trophoblast cells (Bewo). We measured the extent of Bewo sphere infiltration into monolayers of decidualized HESCs pretreated with or without Tg. To elucidate the involvement of Inositol requiring 1 (IRE1) pathway of the ERS reaction, we used STF-083010, an IRE1 pathway inhibitor. **[Results]** HESCs cultured with high concentrations of Tg exhibited cell atrophy, reduced cell viability, and decreased PRL expression compared to control group. Contrastingly, HESCs cultured with low concentrations of Tg displayed morphological changes and cell viability similar to control group, with a tendency towards increased PRL expression. In co-culture experiments, HESCs decidualized after low-concentration Tg treatment exhibited increased Bewo infiltration compared to control. However, the IRE1 inhibitor added during low-concentration Tg treatment significantly reduced Bewo infiltration compared to Tg treatment alone. **[Conclusion]** Mild ERS in HESCs before decidualization may enhance post-decidualization functionality through the IRE1 pathway, increasing their receptivity to trophoblast cell invasion.

ISP-11-7

Cabergoline has inhibitory effects on FSH-induced granulosa cell differentiation and hormone secretion in primary cultures of rat ovarian granulosa cells Mori Yusuke, Kishi Hiroshi, Kasahara Yuta, Okamoto Aikou *The Jikei University*

[Objective] Cabergoline is used as a preventive medicine for ovarian hyperstimulation syndrome, but it is not clear what effect cabergoline has on the changes induced by FSH stimulation. In this research, we investigated the effects of cabergoline on ovarian granulosa cell function using a primary culture system. **[Methods]** We used a primary culture system of ovarian

granulosa cells obtained from immature female rats treated with diethylstilbestrol. FSH or cabergoline were added alone or co-added to this system, and the following changes induced by these additions were examined. (1) mRNA expression of *Lhcgr*, *Cyp19a1*, *Star*, and *Cyp11a1* by RT-PCR (2) estradiol (E_2), testosterone (T), and progesterone (P_4) concentrations in the culture medium (3) cAMP concentration **[Results]** Co-addition of FSH and cabergoline suppressed each of the following changes compared to FSH alone. Cabergoline was added at 1 μ M and 10 μ M. (1) *Lhcgr*, *Cyp19a1*, and *Cyp11a1* mRNA expression decreased by up to 59%, 32%, and 44%, respectively, in a concentration-dependent manner. *Star* expression did not show any significant change. (2) The concentrations of E_2 and P_4 decreased by up to 51%, and 60%, respectively, in a concentration-dependent manner. (3) Cabergoline suppressed the cAMP production induced by FSH stimulation by 52%. **[Conclusion]** Cabergoline inhibited gene expression and hormone secretion induced by FSH stimulation. These changes are caused by decreased cAMP production. Further research is needed to elucidate the mechanism by which cabergoline suppresses cAMP production.

ISP-11-8

Impact of Polyunsaturated Fatty Acids on Chronic Endometritis : Novel Insights from a Mouse Model with Modified Lipid Metabolism Regulation Matsuda Shigeru¹, Kuwabara Yoshimitsu¹, Sugita Yosuke¹, Oishi Yumiko², Suzuki Shunji¹ *Nippon Medical School Hospital¹, Department of Medical Biochemistry, Tokyo Medical and Dental University²*

[Objective] Chronic endometritis (CE) adversely affects reproduction ; however, its underlying mechanisms remain unclear. For patients resistant to antibiotic therapy, effective treatment remains elusive. We speculate a connection between polyunsaturated fatty acids (PUFA), critical for in vivo resolution of chronic inflammation, and CE condition. Utilizing a systemic knockout mouse model of *Srebf1* (Sterol regulatory element-binding factor 1), encoding a key regulator of fatty acid metabolism, we examined PUFA's impact on the pathology of CE. **[Methods]** To construct a mouse CE model, lipopolysaccharides (LPS) were administered to the uterus of female C57BL/6 mice, resulting in the accumulation of CD138-positive plasma cells, mirroring human CE. This model was studied in wild-type mice (WT) and *Srebf1*^{-/-} mice (*Srebf1*^{-/-}) to investigate the plasma cell number, reproductive impact, and influence of eicosapentaenoic acid (EPA) supplementation. **[Results]** RNA-seq analysis revealed upregulation of lipid metabolism-related genes in the uterus from CE-induced WT mice. Mass spectrometry-based lipidomic analysis showed increased PUFA levels in WT uteri, whereas decreased in *Srebf1*^{-/-} uteri, particularly in EPA. Compared to WT, *Srebf1*^{-/-} exhibited significantly increased plasma cells within the endometrial stroma. Mating of *Srebf1*^{-/-} with male mice after LPS administration resulted in an increased pregnancy loss compared with WT. Notably, the changes by CE induction improved through oral EPA supplementation in both WT and *Srebf1*^{-/-}. **[Conclusion]** The pathology of CE and its negative effects on reproduction are exacerbated by PUFA deficiency and improved by its supplementation. EPA may be a novel treatment option for CE that does not rely on antibiotics.

ISP-11-9

Circadian clock gene BMAL1 positively correlates with genes regulating steroid biosynthesis in human granulosa cells Kutsuna Tomomi¹, Ono Masanori¹, Kikuchi Takayuki¹, Yamanaka Akina¹, Ueno Keiko¹, Kojima Junya¹, Fujiwara Hiroshi², Kuji Naoaki¹, Nishi Hirotsuka¹ *Tokyo Medical University Hospital¹, Kanazawa University Graduate School of Medical*

Sciences²

[Objective] Circadian clocks have an essential role in the daily physiological regulation. The transcription factor *brain and muscle arnt-like protein-1 (BMAL1)* is a principal driver of a molecular clock in mammals. Importantly, disruption in circadian clock function have been implicated in reproductive physiology, including ovulation, embryonic implantation, parturition and reduced progesterone production. *Bmal1* knockout mice were found to have significantly reduced ovulation and be infertile. However, few investigations on the correlation between fertility and clock abnormalities in humans have been conducted. In this study, we analyzed the circadian clock gene expression and its effect on genes regulating steroid biosynthesis in human granulosa cells. **[Methods]** We used small interfering RNA (siRNA) to knock down the expression of *BMAL1* in KGN cells, a steroidogenic human ovarian granulosa cell line. We measured the expression levels of the genes regulating steroid biosynthesis and circadian clock genes in human granulosa cells using reverse transcription-quantitative real-time polymerase chain reaction (RT-qPCR). **[Results]** We demonstrated that expression of *BMAL1* positively correlates genes regulating steroid biosynthesis in human granulosa cells. We found that circadian clock genes exhibited rhythmic change and were further enhanced by dexamethasone synchronization in granulosa cells. *BMAL1* knock down disrupted ovarian steroidogenesis enzyme genes, and furthermore reduced estradiol and progesterone production in KGN cell line. **[Conclusion]** We investigated the role of the key circadian clock gene, *BMAL1* on human granulosa cells. *BMAL1* plays a critical role in steroid biosynthesis of human granulosa cells.

ISP-11-10

Proteomic changes in human uterine fluid-derived small extracellular vesicles during implantation window Ohara Tsutomu, Horie Akihito, Nakamura Mitsuhiro, Imakita Sachi, Ikeda Asami, Shitanaka Shimpei, Yanai Akihiro, Kitawaki Yoshimi, Okunomiya Asuka, Mandai Masaki *Kyoto University*
[Objective] Small extracellular vesicles (sEVs) released by various cells transfer cargos such as microRNAs or proteins for cell-cell communication. It is suggested that endometrial cell-derived sEVs, which promote the adhesion and invasion of trophoblast cells, are involved in embryo implantation, but it is still unclear how endometrial cell-derived sEVs contribute to embryo implantation in vivo. We investigated proteomic change of human uterine fluid-derived sEVs (UF-sEVs) during implantation window to identify proteins contribute to embryo-endometrium crosstalk. **[Methods]** UF samples were collected on the day of oocyte pick-up (ovulatory-phase group) or 5 days after oocyte retrieval (implantation-phase group) from 5 women each, with a history of delivery. Proteins were extracted from sEVs isolated from UF by size exclusion chromatography and were identified and quantified by liquid chromatography-mass spectrometer. **[Results]** We identified 2041 and 1386 proteins from the ovulatory- and implantation-phase UF-sEVs, respectively. These data showed more identified proteins than previously reported. Compared with the ovulatory-phase group, 318 proteins (140 up-regulated, 178 down-regulated) were expressed significantly in the implantation-phase group ($|\text{Fold change}| > 2$, $p < 0.05$). Among these proteins, we focused on galectin-3. Galectin-3 is involved in cellular processes such as adhesion, proliferation, and apoptosis, which are important for embryo implantation. We found galectin-3 was up-regulated in the implantation-phase UF-sEVs and increased in sEVs derived from human endometrial carcinoma cell line, Ishikawa, treated with hormones to mimic the implantation-phase. **[Conclusion]** Our proteomic analysis of UF-sEVs showed higher quality of proteins. These identified proteins changed during implantation

window and galectin-3 increased in the implantation-phase.

ISP-11-11

Macrophage infiltration and fibrosis induced by alkylating agents may cause chemotherapy-induced ovarian insufficiency Yamamoto Gaku, Kawano Mahiru, Toda Aska, Nakamura Koji, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Sawada Kenjiro, Kimura Tadashi *Osaka University*
[Objective] The exact mechanism of chemotherapy (CTx) - induced premature ovarian insufficiency (POI) has not been fully understood. In addition to the direct cytotoxicity to follicular cells, CTx have potential effect on tissue remodeling that negatively affect the ovarian function. The aim of this study is to investigate the role of ovarian macrophages and fibrosis in CTx-induced POI. **[Methods]** CTx-induced POI mouse model was established by peritoneal injection of alkylating agents, Cyclophosphamide and Busulfan, to C57BL/6 female mice. The ovaries were harvested at different time point and histologically examined for follicles (HE), macrophages (Immunohistochemistry) and fibrosis (Masson's trichrome staining). Macrophage population was assessed by flowcytometry. Chemokine expression was quantified by qPCR. Clinical samples from patients who underwent oophorectomy at our hospital under 45 years were examined histologically. **[Results]** CTx to mice led to depletion of follicles, loss of estrous and infertility, which is consistent with POI. In CTx-treated ovaries, the proportion of macrophages was increased (day0 : 32.4%, day10 : 53.0% among leukocytes, $p < 0.05$). Especially, Ly6C⁺ monocyte-derived inflammatory subtype was expanded. Expression of CCL2, which is the major chemoattractant for monocytes, was upregulated in advance (4.46 fold increase at day6). Histologically, enlarged macrophages were associated with apoptotic follicular cells. Extensive fibrosis was also observed in CTx-treated ovaries at day 30. Ovaries from patients with CTx (n=5) showed less follicles (0.29 vs 0.93 /mm²), increased macrophage infiltration and more extensive fibrosis of ovarian cortex than ovaries from controls (n=5). **[Conclusion]** Monocyte-derived macrophages were recruited to CTx-treated ovaries, which might contribute in fibrosis and depletion of follicle reserve.

ISP-11-12

The effect of pyrroloquinoline quinone (PQQ) on serum AMH level Tsuji Saori, Takiuchi Tsuyoshi, Handa Mika, Goto Takeshi, Honda Hidemine, Miyake Tatsuya, Kimura Tadashi *Osaka University*
[Objective] Oocyte maturation requires large amount of ATP and it might produce excessive oxygen radical, which inhibits development of follicles. Pyrroloquinoline quinone (PQQ) is reported to protect mitochondria and promote development of ovarian follicles. In this study, we prospectively investigated the effect of PQQ on serum AMH level as an indicator of development of follicles. **[Methods]** This study was approved by IRB. (IRB No. 17000161) The subjects were 25 to 42 years old, healthy female with regular menstrual cycles and serum levels of 0.5 ng/mL \leq AMH $<$ 3.0 ng/mL [R1] (N=50). They orally took PQQ 20 mg daily for 90 \pm 10 days. Their blood samples were collected from the first to seventh day of menstrual cycle, before and after administration of PQQ. **[Results]** The median age of the subjects was 38.5 years old and median AMH level before administration was 1.555 ng/mL. The average AMH levels of before and after administration were 1.561 ng/mL and 1.439 ng/mL, respectively, which did not change significantly ($p = 0.182$). Although not significantly ($p = 0.056$), the average AMH levels increased from 1.121 ng/mL to 1.361 ng/mL among those who were under 38.5 years old and with AMH of under 1.555 ng/mL before administration (N=7/35). In this population, oxidative

stress marker, d-ROMs significantly decreased ($p=0.009$). **[Conclusion]** PQQ might be effective for improvement of ovarian function in relatively young females whose ovaries were affected by oxidative stress.

ISP-11-13

Human microbiomes from follicular fluid in women with endometriosis Chon Seung Joo¹, An Sunah¹, Yoon Meesup² *Gachon University, Gil Hospital, Korea¹, Gachon University, Korea²*

[Objective] The follicular fluid of human oocyte is important for follicle growth, ovulation and maturation of the oocyte, and it eventually affects pregnancy. There are micro-organisms in follicular fluid and they could affect the quality of oocytes and be causative factors of *in vitro* fertilization (IVF) outcomes. Therefore in this study, we are to identify specific micro-organisms in follicular fluids in women with endometriosis. **[Methods]** We enrolled women undergoing IVF and divided them according to presence of endometriosis, Group 1 (N=15) with endometriosis, Group 2 (N=15) without endometriosis. Follicular fluid samples were collected during oocyte pick up, and 30 samples were analysed by DNA sequencing, and further analysis was done using culture for microbiomes. **[Results]** Micro-organisms and cytokines were detected and compared in between the two groups. Specific colonizing micro-organisms were detected in endometriosis group compared to non-endometriosis group ($P = 0.005$) and it was related to lower fertilization rates. There were no definite differences in follicular fluid cytokine profiles in between the groups. **[Conclusion]** Micro-organisms which are present specifically in follicular fluids of endometriosis patients seem to exist and this could be related to reproductive outcome in assisted reproductive technology.

ISP-12-1

The process of acquiring heart rate variability in extremely low birth weight infants by Poincaré plot analysis Yamada Naoshi¹, Ikenoue Tsuyomu², Fukumoto Takuro¹, Obata Shizuka¹, Nakayama Tetsuo¹, Goto Tomoko¹, Matsuzawa Satoshi¹, Yamashita Rie¹, Doi Koutarou¹, Kodama Yuki¹, Kaneko Masatoki¹, Katsuragi Shinji¹ *University of Miyazaki¹, Miyazaki Medical Association Hospital²*

[Objective] Fetal electrocardiography has made it possible to analyze and display heart rate variability as a numerical value. We speculated that the concept of variability of fetal heart rate could be applied to neonates to measure the course of neurological development in the neonatal period. **[Methods]** The ECG waveforms of neonates were output in analog form, and the neonatal heart rate variability (Short term variability (STV) and long term variability (LTV)) were calculated for each beat from the waveform data using IKE1 software. 6 extremely low birth weight infants born at 25-27 weeks of gestation were measured STV and LTV from birth to 40 weeks of corrected gestation, and the variation in heart rate variability during neonatal development were examined using scatter plotting (Poincaré plot analysis). **[Results]** We measured the acquiring process of STV increasing first, followed by LTV. We found that scatter plotting with STV and LTV is gradually spreading out during the neonatal period. **[Conclusion]** We were able to measure variations in neonatal heart rate variability in extremely low birth weight infants for the first time. In particular, we could use Poincaré plot analysis to find out the process of gradual acquisition of STV and LTV, respectively.

ISP-12-2

delta pH (subtraction of UmVpH from UmApH) predicts very short-term prognosis for births with UmApH<7.2 Sugeno Misa¹, Yasuda Shun², Ishibashi Makiho¹, Hiraiwa Tsuyoshi¹

Iwase General Hospital¹, Fukushima Medical University²

[Objective] UmApH<7.2 is a concern in neonates, with some cases requiring no resuscitation while others demand intensive measures. Identifying predictive factors in such situations is essential. **[Methods]** We collected data from 1990 singleton full-term vaginal deliveries with UmApH<7.2 from April 2017 to December 2022 in our institution, conducting binomial logistic regression analysis to identify risk factors for UmApH<7.2. Additionally, among the 117 cases with UmApH<7.2, we examined the relationship between delta pH and other variables in 39 cases requiring neonatal resuscitation. **[Results]** Among UmApH<7.2 cases, the sole risk factor for needing resuscitation measures was delta pH<0.05. **[Discussion]** The relation between delta pH and neonatal prognosis remains underreported. This study suggests that delta pH is related to very short-term neonatal outcomes and can be a valuable marker when combined with postnatal clinical conditions for assessing physiological backgrounds. **[Conclusion]** delta pH is associated with very short-term neonatal prognosis in UmApH<7.2 cases, proving to be a useful marker for evaluating neonatal health outcomes. This research emphasizes the importance of considering delta pH as a predictive factor for the need for resuscitation measures in neonates with UmApH<7.2.

ISP-12-3

Study of circulating blood volume after placenta delivery in CS using 3D echocardiography Higashi Marie, Gi Kayo, Yoshimoto Nozomi, Nakayama Tetsuo, Matsuzawa Satoshi, Yamada Naoshi, Doi Koutarou, Katsuragi Shinji *Miyazaki Medical College Hospital*

[Objective] Pregnant women with severely reduced cardiac function often feel discomfort just after removal of the placenta. We sought to evaluate the phasic changes in the venous return during elective cesarean section in low-risk mothers using transthoracic echocardiography. **[Methods]** We used EPIQ with X5-1 probe (Philips) for 2D/3D image acquisition and Dynamic Heart Model (Philips), Auto-RV (TOMTEC) for the quantitative 3D analysis. Measurements were made in nine mothers without cardiac disease in scheduled Cesarean section at full term. Mean velocity of the right ventricular inflow spectrum (RVIF-meanV), right ventricular stroke volume by Doppler equation (2 D RVSV), 3D RVSV were serially measured at the timing of 1) After epidural-spinal anesthesia, 2) incision of peritoneum, 3) incision of myometrium, 4) delivery of the fetus, 5) delivery of the placenta, 6,7) suturing the 1st and the 2nd layer myometrium, 8) uterus is returned into the abdominal cavity. **[Results]** RVSV measured in 2D and 3D tended to increase after placental delivery. They returned to preoperative values at the time of uterine suture. **[Conclusion]** In this study, venous return maximized after placenta delivery, that may explain the post-delivery symptoms in high-risk mothers. This phenomenon might occur due to 1) autologous blood transfusion from the uterine myometrium into systemic circulation when uterus contracted, and 2) physical load reduction to inferior vena cava after uterine involution.

ISP-12-4

A case of Vogt-Koyanagi-Harada disease (VKH) with visual field abnormality in the postpartum period following preeclampsia Yada Takahiro, Magawa Shoichi, Kato Maya, Tamaishi Yuya, Takakura Sho, Maki Shintaro, Nii Masafumi, Toriyabe Kuniaki, Ikeda Tomoaki *Mie University*

Case : 23 years old, G1P1, no abnormality was noted after the pregnancy was established. During a prenatal checkup at 36 weeks of pregnancy, maternal weight gain, significant edema, urinary protein, and elevated blood pressure were observed, and the patient was hospitalized for management, and cesarean sec-

tion was performed on the same day. Patient continued to have hypertension after surgery. The visual field disturbance was observed in the left eye on the first postoperative day, and the symptoms persisted, so the patient was brought to our hospital for further examination. On admission, she had a pulse of 121 beats/minute, blood pressure of 142/101 mmHg, body temperature of 37.2°C, and an abnormal visual field in the left eye. MRI of the head showed no abnormality. Fundus examination revealed edematous changes around the optic nerve papillae and fluid retention in both eyes, and optical coherence tomography showed polycystic serous retinal detachment and choroidal thickening. Fluorescein angiography showed macular leakage of contrast medium around the optic nerve papillae in both eyes. On the fourth postoperative day, headache and fever were observed, leading to a diagnosis of incomplete type of VKH. Treatment with steroids was started on postoperative day 6. After steroid treatment, ophthalmologic findings improved and symptoms became milder. **Clinical Significance** : It is sometimes difficult to distinguish visual field abnormalities related to pregnancy-induced hypertension from those caused by VKH, and because VKH can cause rapid vision loss, treatment with steroids is necessary as soon as the diagnosis is made.

ISP-12-5

Study of 390 cases of water birth at our hospital Nonaka Yuri, Seki Akihito, Kido Michiko, Arima Kaori, Hosokawa Satsuki, Watanabe Michiko, Yamada Manabu, Kasai Yasuyo, Miyauchi Akito *Japanese Red Cross Medical Center*

[Objective] In recent years, an increasing number of women are choosing epidural labor for pain relief, but water birth is also an effective option for relaxation and pain relief. Although few hospitals offer water births in Japan, our hospital has been offering it since 2006. In this study, we summarized the characteristics of water birth at our hospital and the results regarding the maternal and neonatal safety. **[Methods]** We conducted a retrospective study using our medical records from 2006 to 2022. At our hospital, we perform water births on healthy full-term pregnant women without complications with informed choice and with smooth delivery progress. We extracted the data of the cases which completed delivery in water, and examined maternal characteristics and maternal and neonatal outcomes. **[Results]** There were 390 cases which delivered in water from January 2006 to December 2022. 251 were multiparous, average of the first and second stage of labor was 10 hours and 3 minutes and 5 hours and 48 minutes for the nulliparous and multiparous women respectively. 119 had 2nd degree perineal laceration, 3 had 3rd degree perineal laceration, the average amount of bleeding was 355g, the average five-minute Apgar score was 9.6, the average umbilical artery blood pH was 7.298, and the neonatal intensive care unit admission rate was 1.7%. There were no infections caused by legionella among mothers or infants, and were no infant drowning. **[Conclusion]** By evaluating the risks during pregnancy and labor and selecting appropriate cases, deliveries in water can be performed safely.

ISP-12-6

Below or above the limit of weight gain during pregnancy and delivery outcome Kumagai Asako, Oshima Naoki, Hirayama Yuichiro, Iwagaki Anna, Hoshino Masaki, Ijichi Kouji, Kuki Saki, Tanaka Satomi, Yata Shotaro, Kaneda Hiroshi, Tanaka Toshitaka *Juntendo University Shizuoka Hospital*

[Objective] Appropriate intake of nutrition is essential to reduce maternal and fetal comorbidity during pregnancy. The modification of ideal weight gain during pregnancy (WGDP) was issued in 2019. This study is aimed to investigate the correlation between the delivery outcome (DO) and WGDP in underweight

and overweight population. **[Methods]** DO with body mass index below 18.5 (LBMI) and above 30 (HBMI) were overviewed retrospectively between July 2022 to May 2023. Full-term, singleton, and nulliparous women were divided into two groups by WGDP, either within or over the recommended range (group R, group O, respectively). Birth weight (BW) and the rate of emergency cesarean section (ReCS) were investigated. BW was divided into three groups, small for date (SFD), appropriate for date, and large for date (LFD). **[Results]** LBMI and HBMI were 39 and 20 cases. In LBMI, 17 and 22 cases were group R and O, respectively. In HBMI, 8 and 12 cases were group R and O, respectively. In LBMI, BW distribution of SFD and LFD was 5.9%, 11.8% in group R and 9%, 0% in group O. In HBMI, 25%, 12.5% in group R and 16.7%, 33.3% in group O. ReCS was none in group R and 9% in group O of LBMI and 25% in group R and 41.7% in group O of HBMI. **[Conclusion]** Regardless of BMI, recommend WGDP was hard to reach, SFD · LFD were born independent of WGDP, and ReCS was independent of WGDP. ReCS and Rate of LFD between LBMI and HBMI were significantly different.

ISP-12-7

The prenatal management to the pregnant woman with limb-girdle muscular dystrophy type 2A Miyamoto Kaede¹, Takesawa Ami², Fujii Ayano², Mitani Takahiro², Kadooka Mizuho², Furusawa Yoshiaki², Suemitsu Tokumasa² *Post Graduate Education Center, Kameda Medical Center¹, Kameda Medical Center²*

[Introduction] Limb-girdle muscular dystrophy (LGMD) is a neuromuscular disease that causes progressive muscle weakness starting. Pregnancy with LGMD type 2A (LGMD-2A), an autosomal recessive disorder, is extremely rare, and prenatal management is unclear. We report a challenging case of perinatal management involving vaginal delivery in a patient with LGMD-2A. **[Case]** A 39-year-old primigravida with LGMD-2A was referred to our hospital in the first trimester. She could walk indoors with a cane before pregnancy, but her muscle weakness in the lower extremities gradually worsened during pregnancy as she gained weight, and rehabilitation was implemented in the second trimester. Her cardiopulmonary function was regularly evaluated as tolerable for vaginal delivery. The trial vaginal delivery with epidural anesthesia was planned to prevent irrecoverable muscle damage caused by straining or cesarean section. We had a multidisciplinary simulation in the third trimester for her safe delivery to confirm her lithotomy position and the number of staff required. At 38 weeks of gestation, we induced labor with epidural anesthesia and achieved instrumental delivery after a four-hour second stage. The male neonate weighed 2848 g, with an umbilical cord artery pH of 7.27 and Apgar scores of 8 and 9. With continuous postpartum rehabilitation, the muscle strength in her lower extremities recovered to the same level as pre-pregnancy. Her creatinine kinase level was abnormally high, but it was not different than her perinatal level. **[Conclusion]** We managed safe obstetrics management for a patient with LGMD-2A with multidisciplinary teamwork, but further cases are needed to establish the proper management strategy.

ISP-12-8

Factors associated with spontaneous preterm birth after physical examination-indicated cerclage : An 10-year retrospective cohort study Lee Huinisol, Kim Youjin, Ko Youngbok, Lee Ki Hwan *Chungnam National University Hospital, Korea*

[Objective] This study aimed to assess the factors related to the occurrence of spontaneous preterm birth (sPTB) after physical examination-indicated cerclage (PEIC) and determine corre-

sponding risks. **[Methods]** This 10-year retrospective cohort study was conducted at a Chungnam National University Hospital. All singleton pregnancy women with bulging membranes in the second trimester of pregnancy who were admitted to Chungnam National University Hospital from January 2013 to January 2022 were included. Out of the 62 patients who underwent PEIC, we conducted an analysis on 54 of them for whom we have delivery outcome. **[Results]** After underwent PEIC, 30 patients gave birth at 34 weeks or later, while 24 delivered before 34 weeks. When analyzing these two groups, no significant differences were observed in maternal characteristics, the frequency of amnioreduction, the presence of amniotic fluid sludge, occurrences of intra-amniotic infection, use of macrolides, or results from pre-operative serum inflammatory. **[Conclusion]** The hypotheses emerging from this study shed significant light on potential factors associated with cerclage failure, enhancing our understanding of its etiology. Nonetheless, to gain a deeper insight into these factors, further research with larger sample sizes and more comprehensive investigations is essential.

ISP-13-1

Identification of novel biomarkers in amniotic fluid that enable to assess fetal maturation Eishi Chiaki, Nagata Koh, Shigematsu Yusuke, Murakami Toru, Nagata Ai, Kitajima Yuriko, Miura Syouko, Hasegawa Yuri, Miura Kiyonori *Nagasaki University Graduate School of Biomedical Sciences*

[Objective] Microbubble and shake tests have been used to evaluate fetal maturation of lungs, but there is no method that can evaluate fetal maturation of other organs. The objective of this study is to identify novel biomarkers that reflect fetal maturation using mRNAs present in amniotic fluid. **[Methods]** Amniotic fluid samples for this study were collected from pregnant women at 16 and 38 weeks of gestation who underwent perinatal care at our hospital. Total RNAs were extracted from the amniotic fluid and RNA sequencing was performed to compare mRNA expression levels at 16 and 38 weeks of gestation. **[Results]** The following five mRNAs, which were not expressed in amniotic fluid at 16 weeks of gestation but were expressed at 300 TPM (transcripts per million) or more at 38 weeks of gestation, were identified as biomarkers reflecting the functional maturation of the fetus : CALML5 distributed in skin and salivary glands, IFITM3P6 distributed in adrenal, thyroid and salivary glands, NAA10 distributed in fat tissue and appendix, SFTPC distributed in lung, and SMIM29 distributed in brain and skin. **[Conclusion]** We identified five novel biomarkers in amniotic fluid that enable to evaluate fetal maturation. We are currently investigating whether these biomarkers can be evaluated in maternal plasma. We are also comparing the expression levels of these biomarkers in normal pregnancy group and in perinatal disease to examine whether they are useful in predicting fetal maturation associated with perinatal diseases.

ISP-13-2

Involvement of Ferroptosis in Placental Ischemia-Reperfusion Injury in Cases of Twin-to-Twin Transfusion Syndrome Kajiwara Kazuhiro¹, Matsuoka Tomona^{2,3}, Murotomoto Jin¹, Sugibayashi Rika¹, Ozawa Katsusuke¹, Akutsu Hidenori², Wada Seiji¹, Sago Haruhiko¹ *Center for Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development¹, Center for Regenerative Medicine, National Center for Child Health and Development², The Jikei University³*

[Objective] This study aimed to investigate the possible involvement of ferroptosis, an iron-dependent cell death associated with lipid peroxidation, in placental ischemia-reperfusion injury (IRI) in the context of twin-to-twin transfusion syndrome

(TTTS). **[Methods]** We analyzed placental tissues from uncomplicated monochorionic diamniotic (UC-MD) twin pregnancies and TTTS cases diagnosed between 2021 and 2023. Our assessments included villous capillary diameter (VCD), malondialdehyde (MDA) levels and immunohistochemistry for 4-hydroxynonenal (4HNE) as a marker of lipid peroxidation, and quantitative PCR (qPCR) for placental differentiation markers : syncytin-1, HLA-G, HCG ; potential IRI-related genes : ferroportin (FPN), transferrin receptor 1 (TFRI), and heme oxygenase-1 (HO1) ; and ferroptosis-related genes : ferroptosis suppressor protein-1 (FSP1) and glutathione peroxidase 4 (GPX 4). **[Results]** This study included 8 UC-MD cases and 8 TTTS cases, with 6 TTTS cases undergoing fetoscopic laser photocoagulation. Histopathological analyses showed no significant differences in VCD (TTTS : 188 μ m vs UC-MD : 194 μ m). Although the MDA level in TTTS placentas was higher (TTTS : 1.2 μ mol/L vs UC-twin : 0.85 μ mol/L), it was not significant. In both UC-MD and TTTS placentas, 4HNE was detected in the trophoblasts. qPCR revealed a significant reduction in HO1 and FPN expression and a significant upregulation of Syncytin-1, HLA-G and HCG levels in TTTS placentas, especially in the donor region, suggesting altered antioxidant defense system and placental morphogenesis. Surprisingly, we detected a significant decrease in GPX4 and FSP1 expression levels in TTTS placentas. **[Conclusion]** IRI-mediated ferroptosis may be involved in TTTS-associated placental pathology and potentially impact placental function. Further research may provide new strategies for placental dysfunction in TTTS.

ISP-13-3

Viral infection impairs placenta function by inhibiting differentiation of human cytotrophoblasts Motomura Kenichiro^{1,2}, Matsubara Keiko³, Wada Seiji², Sago Haruhiko^{2,4} *Department of Allergy and Clinical Immunology, National Research Institute for Child Health and Development¹, Center for Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development², Division of Diversity Research, National Center for Child Health and Development³, Center for Medical Genetics, National Center for Child Health and Development⁴*

[Objective] Pregnant mothers are exposed to multiple pathogens, which can cause adverse pregnancy outcomes. Recently, we showed that the syncytiotrophoblast (STB) specifically expresses double-stranded RNA (dsRNA) receptors to protect the fetus from viral infections by eliciting anti-viral responses. Such receptor signaling can also harm the placenta by inducing trophoblast apoptosis. However, we have a poor understanding of the effects of dsRNA on cytotrophoblasts (CTBs), which differentiate and fuse into the STB to maintain its functions. Here, we investigate whether dsRNA hampers placenta function by affecting CTB differentiation. **[Methods]** Primary human CTBs were isolated from the placentas of uncomplicated women who delivered at term. The CTBs were exposed to synthetic dsRNA (poly (I : C)) for 24 h. The poly (I : C) was washed out, and CTB culture was continued for 120 h to facilitate their spontaneous differentiation into STB-like cells (differentiated CTBs, dCTBs). dCTB viability, gene expression, and hormone concentration of the culture media were evaluated by WST-8 assay, qPCR, and ELISA, respectively. **[Results]** Poly (I : C) exposure reduced the dCTBs' expressions of fusogenic genes (*syncytin-1*, *syncytin-2*, and their transcription factor, *GCMI*), indicating a poor differentiation of dCTBs. A placental enzyme (*HSD11B2*) and human chorionic gonadotropin (*CGB*) gene expressions as well as the release of hCG- β protein of dCTB were reduced by poly (I : C), suggesting the impairment of its functions. Moreover, poly (I : C) downregulated placental growth factor (*PGF*) expression. The effect of poly (I : C) on dCTB viability

was minimal. **[Conclusion]** Virus-derived dsRNA can cause poor STB formation by impairing CTB differentiation, leading to altered placental function and adverse pregnancy outcomes.

ISP-13-4

Progesterone Receptor Membrane Component 2 attenuation promotes cell invasion and angiogenesis in the extravillous trophoblasts Konishi Tae^{1,2}, Kanagawa Takeshi¹, Ogawa Noriko¹, Ebisu Shuhei¹, Konagai Nao¹, Ogawa Ayana¹, Temukai Mai¹, Sawada Masami¹, Nakanishi Atsushi¹, Kakigano Aiko¹, Iwanaga Naoko¹, Yoshimatsu Jun¹ *National Cerebral and Cardiovascular Center¹, Duke University School of Medicine, USA²*

[Objective] Although Progesterone Receptor Membrane Component 2 (PGRMC2) is expressed strongly in placentas, the role of PGRMC2 in placental development is unknown. We discovered that PGRMC2 was highly expressed in syncytiotrophoblast but decreased in extravillous trophoblasts (EVT) in the first trimester. The aim of this study is to investigate the role of PGRMC2 in EVT invasion and angiogenesis during placentation. **[Methods]** PGRMC2 knockdown (KD) and overexpression (OE) cells were established in HTR8/SVneo cells, a first trimester EVT-derived cell model, by transfection with small-interfering RNA or PGRMC2 plasmids. The proliferation, invasiveness, and angiogenesis of HTR8/SVneo cells were assessed using an MTS assay, invasion assay, and a tube formation assay, respectively. Hypoxia inducible factor 1 α (HIF1 α) pathway was examined. HIF1 α KD and PGRMC2/HIF1 α double KD HTR8/SVneo cells were established, and their invasiveness was assessed. **[Results]** The cell proliferation and invasiveness were significantly promoted in PGRMC2 KD (Relative absorbance ratio : 1.000 vs 1.154, $p < 0.003$; Invasion index : 1.00 vs 5.28, $p < 0.0001$) and inhibited in PGRMC2 OE (Relative absorbance ratio : 1.000 vs 0.7771, $p < 0.0001$; Invasion index : 1.00 vs 0.58, $p < 0.05$) compared with their controls. PGRMC2 KD led to cellular morphological changes and enhanced tube formation. The PGRMC2 KD upregulated the mRNA and protein levels of HIF1 α . Inhibition of HIF1 α counteracted the enhanced cell invasion by PGRMC2 attenuation. **[Conclusion]** The attenuation of PGRMC2 plays a role in placentation by promoting cell proliferation, invasion, and angiogenesis in EVTs. This function is regulated by the activation of HIF1 α signaling.

ISP-13-5

Macrophages transform amnion mesenchymal cells into myofibroblasts in subchorionic hematoma during pregnancy

Yasuda Eriko, Mogami Haruta, Matsuzaka Sunao, Matsuzaka Yu, Inohaya Asako, Takakura Masahito, Chigusa Yoshitsugu, Mandai Masaki *Kyoto University Graduate School of Medicine*

[Objective] Subchorionic hematomas (SCH) increases the risk of preterm prelabor rupture of membranes and preterm birth. Here, we investigated the effects of hematoma on fetal membranes. **[Methods]** The amnion of 9 cases of SCH (the SCH group) and 7 cases of cesarean delivery (the control group) were histologically compared. Human amnion mesenchymal cells (AMCs) were co-cultured with the M2 macrophages (M2 M ϕ) differentiated from THP-1 cells by IL-4 and IL-13. **[Results]** In immunofluorescence, the number of α -smooth muscle actin, a marker of myofibroblasts, expressing cells in AMCs was increased in the SCH compared to control (86.1 vs 57.5%, $p < 0.05$). In Trichrome stain, collagen layer in the fetal membranes tended to be thickened in the SCH group (59.4 vs 39.4 μ m, $p = 0.055$). Iron-laden macrophages migrated to the amnion of the SCH (3.2 vs 0.0 cells/field, $p < 0.01$), and these macrophages were CD163⁺, CD206⁺ and CD86⁺ M2 phenotype. In vitro, mRNA expression of ACTA2 and COL1A1 in AMCs were increased by co-culture with M2 M ϕ (x3.46, x2.09, respectively, $p < 0.01$). The

treatment of AMCs with TGF- β increased the ACTA2 (x3.08, $p < 0.01$) and COL1A1 (x2.11, $p = 0.12$) mRNA. TGF- β receptor blocker inhibited the increase of ACTA2 (x0.59, $p < 0.01$) and COL1A1 (x1.15, $p = 0.12$) mRNA in AMCs co-cultured with M2 M ϕ . In immunoblots, co-culture with M2 M ϕ increased phosphorylation of nuclear Smad3 in AMCs. **[Conclusion]** M2 macrophages migrated to the amnion of SCH, which may transform amnion mesenchymal cells into myofibroblasts presumably via TGF- β . These myofibroblasts may contribute the fibrosis of the fetal membranes in SCH.

ISP-13-6

The effectiveness of GnRH antagonist for the management of retained products of conception (RPOC) Sasatsu Satoko, Ono Yosuke, Miyashita Dai, Tanaka Kota, Ogawa Tatsuyuki, Ohgi Maki, Ogasahara Eriko, Okuda Yasuhiko, Yoshino Osamu *University of Yamanashi*

[Objective] In the patients with RPOC who wish to have a next baby, minimally invasive and surgical radicality is necessary to preserve fertility, especially. Therefore, efforts to reduce the risk of bleeding are required before surgery. The impact of the use of GnRH antagonist preparations, which are expected to decrease uterine blood flow, on RPOC management was studied. **[Methods]** With the approval of IRB and the consent of the patients, this retrospective study included 103 RPOC cases managed at our hospital between January 2011 and August 2023. We categorized patients who were treated with (Group A ; N=11) or without (Group B ; N=92) oral GnRH antagonist, and examined the clinical course until the next pregnancy permit is granted between two groups from electronic medical records. **[Results]** There were no differences in background of patients, operative time, and amount of blood loss between two groups. We checked the loss of blood flow in RPOC in all cases of Group A by preoperative ultrasound examination. The number of days from postoperative period to permit for next pregnancy was significantly shorter in the group A (45.6 \pm 20.4 days) than that of B (94.4 \pm 78.6 days ; $p = 0.005$). And multivariate analysis showed that GnRH antagonist was associated with a lower risk of postoperative pregnancy after 60 days (OR 0.14 ; 95% CI [0.01-0.80] ; $p = 0.024$) **[Conclusion]** GnRH antagonist may decrease RPOC blood flow and contribute to a smoother transition to the next pregnancy. Further validation with a larger number of cases is needed.

ISP-13-7

Ultrasound Doppler findings in fetal vascular malperfusion due to umbilical cord abnormalities Saji Shota¹, Hasegawa Junichi², Takae Seido¹, Tozawa Akiko¹, Suzuki Nao¹ *St. Marianna University School of Medicine¹, Department of Perinatal Developmental Pathophysiology, St. Marianna University School of Medicine²*

[Objective] Fetal Vascular Malperfusion (FVM) is one of pathologic condition in the umbilical venous flow due to a chronic vasooclusive disorder. Microthrombi made by umbilical blood flow deficiency in congested umbilical vein secondly affect to microvascular damage to fetal organs, especially brain resulting in cerebral palsy, and the placenta resulting in fetal growth restriction and fetal hypoxia. However, FVM is considered only after delivery so far. The aim of the present study was to clarify whether FVM could be detected using antenatal ultrasound. **[Methods]** Prospective observational study was performed in pregnant women who diagnosed by antenatal ultrasound screening as umbilical structural anomaly. Additional detail ultrasound and Doppler examinations and pathological examinations of the delivered placenta were attempted. In cases within criteria of FVM according to pathological findings such as avas-

cular villi, particular ultrasound findings in FVM were evaluated. **[Results]** Regarding morphology, excessively long cord, hyper-coiled cord and single umbilical artery were associated with FVM. In cases suggested decrease in preload due to umbilical venous blood flow insufficiency, umbilical venous flow velocity and flow volume were decreased without venous pulsation, additionally MCA-PSV was elevated. In evaluation using microvascular Doppler imaging, congested stem villi and absence of dendritic villous vessels were observed. **[Conclusion]** This is the first report to demonstrate clinical relations between antenatal evaluation of the umbilical cord abnormalities and pathological findings of FVM. We believe ultrasound diagnosis of umbilical cord abnormality and particular Doppler velocimetry will suspect FVM condition antenatally.

ISP-13-8

Clinical features of vasa previa according to placental types—80 cases in single institution Kikuchi Taiki, Kitada Kohei, Yamamoto Shotaro, Shibata Satoshi, Yoshida Tomohiro, Fukuda Eriko, Kurihara Yasushi, Tahara Mie, Hamuro Akihiro, Misugi Takuya, Tachibana Daisuke *Osaka Metropolitan University*

[Objective] Vasa previa (VP) is categorized by placental types, and clinical features are vary depending on those categories. The aim of this study is to evaluate validity of classifying VP based on placental types. **[Methods]** Cases of VP managed in our hospital between 2010 and 2022 were collected. VP cases were classified into two groups by placental type, type 1 group (VP with velamentous cord insertion) non-type 1 group (VP with multilobed or succenturiate placenta or with vessels branching out from the placental surface and returning to the placental cotyledons). Clinical characteristics and outcomes were extracted from medical records. **[Results]** We found 80 cases, with 58 cases of type 1 group and 22 cases of non-type 1 group. Type 1 group showed a significantly higher association with assisted reproductive technology, compared with non-type 1 (55.1% v.s. 27.2%, $p=0.027$). Period of diagnosis was significantly earlier in type 1 group (23.4 weeks v.s. 27.5 weeks, $p=0.018$). Period of hospitalization and termination was not significantly different between two groups. Perinatal outcomes were almost same in both groups and no severe complications were found. **[Conclusion]** Non-Type 1 group tend to be diagnosed at later term of pregnancy. It seems to be important to perform transvaginal ultrasonography in order to detect vasa previa at later term even if it is not found in earlier term of pregnancy.

ISP-13-9

A Study on Unsuccessful Bleeding Control in Placenta Previa Cases Treated with Prophylactic Intrauterine Balloon Tamponade and Prolapse Prevention Measures Arakaki Tatsuya, Matsuoka Ryu, Takita Hiroko, Yamashita Yuka, Tokunaka Mayumi, Sekizawa Akihiko *Showa University*

[Objective] We previously reported the effectiveness of prophylactic intrauterine balloon tamponade with prolapse prevention for controlling intraoperative and postoperative hemorrhage in placenta previa (PP). This study aims to investigate the cause of unsuccessful bleeding control in PP using prophylactic balloon. **[Methods]** We subjected PP cases in which a prophylactic intrauterine balloon insertion protocol was performed at our hospital. The protocol included cervical clamping to prevent balloon prolapse before the operation, balloon insertion during the operation, and leaving it in place overnight post-operation. We analyzed the cases where bleeding control was unsuccessful. **[Results]** There were 119 cases, of which 62 (52%) were major PP and 57 (48%) were minor PP. Bleeding control failed in 11 cases (9.2%), 7 due to clinical placenta accrete spectrum

(PAS) and 4 due to atonic hemorrhage post-operation. These cases required additional treatments of total hysterectomy, uterine artery embolization, hemostatic suture, or bimanual compression. None of the included clinical PAS were successfully managed with this protocol. All four cases of atonic hemorrhage were minor PP, and the bleeding site was in the uterine body where compressing the balloon was challenging. **[Conclusion]** I Prophylactic balloon tamponade is ineffective in clinical PAS, even with balloon prolapse prevention. Therefore, making an intraoperative decision regarding additional treatment for bleeding control is crucial. In the case of minor PP, attention should be paid to the infusion volume and postoperative uterine contraction control, as the balloon may not provide adequate compression at the bleeding site.

ISP-13-10

A case of the new Type 3 vasa previa with central umbilical cord insertion at the upper uterine segment and aberrant branched vessels on the broad membrane Sano Yuka, Shiro Michihisa, Kiyose Masumi, Suzuki Yukiko, Ikagawa Shota, Yoshida Shigeki *Chibune General Hospital*

Recently, a new type of vasa previa (Type 3) was proposed. Several reports regarding Type 3 vasa previa have described the characteristics as resolution of placenta previa in the second trimester of pregnancy, low-lying placenta, umbilical cord insertion at the lower uterine segment, and only one fetal aberrant vessel on the membrane, similar to the orbit of a boomerang. We herein report a case of Type 3 vasa previa with no findings of low-lying placenta that showed central umbilical cord insertion at the upper uterine segment and aberrant branched vessels on the broad membrane. A 35-year-old multigravid pregnant women was diagnosed with vasa previa by transvaginal ultrasound with color Doppler at 26 weeks' gestation. Placenta previa and low-lying placenta were not detected during pregnancy. Caesarean section was performed at 34 weeks' gestation due to vasa previa. A gross examination of the placenta showed Type 3 vasa previa with two aberrant fetal vessels with branching on the broad membrane and central cord insertion, located farther from the longitudinal center of the placenta than the running vessels on the membrane. These characteristics differed from those described in past reports of Type 3 vasa previa. Careful screening for vasa previa by transvaginal ultrasound is required, even if cord insertion is normal at the upper uterine segment and placenta previa or low-lying placenta is not detected in the second trimester of pregnancy.

ISP-13-11

Clinical characteristics of placenta accreta spectrum at Calmette Hospital Ly Chhiv Ieng¹, Walch Robert¹, Korn Aun^{1,2}, Chhun Samsorphea¹, Koum Kanal², Mori Mayuyo³, Matsushita Tomomi⁴, Fujita Noriko^{4,5}, Osuga Yutaka³ *Calmette Hospital, Cambodia¹, Cambodian Society of Gynecology and Obstetrics, Cambodia², The University of Tokyo³, Bureau of International Health Cooperation, National Center for Global Health and Medicine⁴, School of Tropical Medicine and Global Health, Nagasaki University⁵*

[Objective] Placenta accreta spectrum (PAS) describes the clinical disease spectrum in which a placenta does not separate spontaneously at delivery and cannot be removed without causing abnormal and potentially life-threatening bleeding due to varying degrees of placental invasion into or through the myometrium. The PAS has great impact on the pregnancy outcomes with high maternal morbidity and mortality rate even though pre-operation diagnosis has been done. Our study aimed to show the clinical characteristics of PAS at Calmette Hospital. **[Methods]** A retrospective study was conducted in 2021 using

Epi-info7 registry. A total of 25 cases (among 7414 births) with information on age, gestation, parity, history of cesarean, antenatal diagnosis, graduation of PAS, treatment, blood loss and blood transfusion were analyzed. **[Results]** In 2021, we had 25 cases of PAS. The mean age was 33.9, gestation 4, parity 2, no history of c-section 4 (16%), gestational age 37 weeks (34-40), pre-operative diagnosis 21 (84%), 0 maternal death. For our treatment of PAS, caesarean-hysterectomy was performed in 16 cases (64%) and caesarean-fetal extraction/uterus in place 9 cases (36%). Total blood loss estimated was less than 1000mL in 6 cases (24%), less than 2000mL in 9 cases (36%) and more than or equal 2000mL in 10 cases (40%). **[Conclusion]** PAS is a serious complication of pregnancy with high morbidity and high risk of mortality to women. Pre-operation diagnosis and multi-disciplinary team approach is important to reduce the risks during operation and better outcomes for women.

ISP-14-1

A study of interventional radiology failure for obstetric hemorrhage Shimada Tetsuro, Ogoyama Manabu, Horie Kenji, Suzuki Hirotsada, Usui Rie, Ohkuchi Akihide, Takahashi Hironori, Fujiwara Hiroyuki *Jichi Medical University*

[Objective] Interventional Radiology (IVR) is a useful treatment for obstetric hemorrhage associated with retained products of conception (RPOC) and uterine artery pseudoaneurysm (UAP). However, rebleeding after IVR (IVR failure) sometimes occurs requiring additional hemostatic treatments. We investigated the characteristics of such cases in our institution. **[Methods]** We retrospectively collected information on patients who underwent IVR for obstetric hemorrhage from January 2013 to November 2022 in our institution. Of those, data in patients with IVR failure were analyzed. **[Results]** IVR was employed in 151 patients, of those, 17 (11.2%) showed IVR failure. The background diseases that caused IVR failure were RPOC (5 : 29.4%), UAP (4 : 23.5%), atonic bleeding (4 : 23.5%), clinical amniotic fluid embolism (2 : 11.7%), cesarean scar pregnancy (2 : 11.7%) and others (duplicate causes existed). Median time from bleeding event to first IVR was 5.5 (1-15) hours, and median blood loss until the first IVR was 2000 (425-8870) mL. The content of the additional treatment included re-IVR (9 : 52.9%), hysterectomy (6 : 35.2%) and others. Of re-IVR cases, hemostasis finally achieved in 5 patients (55.5%) and the other patients required additional treatments. No maternal death was noted, and the uterus could be preserved in 7 patients (41.1%). **[Conclusion]** IVR failure accounted for approximately 10% of the cases. Of re-IVR cases, hemostasis achieved in only about 50%, and, thus, the indication for re-IVR should be judged carefully. To clarify the details of IVR failure cases, we plan to compare them with IVR success cases.

ISP-14-2

Transcatheter arterial embolization for postpartum vulvovaginal hematoma reduces blood transfusion compared to surgical treatment Takahashi Tsukasa, Tomita Hasumi, Hamada Hirotsuka, Iwama Noriyuki, Saito Masatoshi *Tohoku University*

[Objective] The management of postpartum vulvovaginal hematoma has not yet been standardized. The aim of this study was to determine adequate treatment case by case. **[Methods]** We undertook a retrospective cohort study of women who were transferred to our hospital from January 2016 to September 2023 for management of postpartum vulvovaginal hematoma. All patients received either i) conservative treatment, ii) surgery, or iii) transcatheter arterial embolization (TAE). Shock index, hemoglobin concentration at arrival, hematoma size, existence of extravasation determined by computed tomography, and

amount of blood transfused were recorded. The factors influencing the clinical decision for therapeutic intervention (surgery or TAE) were analyzed by a logistic regression model in primary analysis. Then, risk factors for increased blood transfusion during therapeutic intervention were analyzed by a multiple linear regression model. **[Results]** 19 patients received conservative treatment, 11 patients received surgery, and 27 patients received TAE. In primary analysis, only the existence of extravasation (50.93 [5.55, 467.46]) was significantly associated with the choice of therapeutic intervention. Shock index (adjusted odds ratio [95% confidence interval] 1.47 [0.76, 2.84], hemoglobin concentration (0.94 [0.57, 1.56]) and hematoma size (1.84 [0.89, 3.83]) were not significant factors influencing clinical decision. In secondary analysis, surgery instead of TAE ($p=0.01$), lower hemoglobin concentration at arrival ($p<0.01$), and larger hematoma ($p<0.01$) were significantly associated with increased blood transfusion. **[Conclusion]** When vulvovaginal hematoma does not have extravasation, conservative treatment regardless of hematoma size, appears reasonable. When therapeutic intervention is required, TAE may reduce blood transfusion compared to surgery.

ISP-14-3

Pathological evaluation of intrauterine tissue in retained products of conception with severe postpartum hemorrhage Kurakazu Mariko, Kurakazu Masamitsu, Ito Tomohiro, Shigekawa Koichiro, Hirakawa Toyofumi, Yoshikawa Kenichi, Kiyoshima Chihiro, Sanui Ayako, Izuchi Daisuke, Urushiyama Daichi, Miyata Kohei, Yotsumoto Fusanori *Fukuoka University*

[Objective] This study aims to clarify the relationship between the histopathological findings of retained products of conception (RPOC) and the risk of severe postpartum hemorrhage (PPH). **[Methods]** 43 patients diagnosed with RPOC who underwent surgical procedures were included. Subjects were divided into RPOC with severe PPH ($n=5$) and without severe PPH ($n=38$). In addition, the characteristics of the histopathological finding of the uterine contents were compared between the two groups to evaluate the risk of severe PPH. **[Results]** The histopathological findings of RPOC have four distinct types : necrotic chorionic villus (A), fibrous exudate (B), inflammatory infiltrate (C), and ectopic calcification (D). Logistic regression analysis showed that the risk of RPOC with severe PPH in the combination of A, B, C, and D : 24.7 (crude odds ratio, $p=0.02$), that of A, B, and C : 17.5 ($p<0.01$), that of A, B, and D : 12.0 ($p=0.04$), that of B, C, and D : 24.7 ($P=0.02$), that of B and C : 12.8 ($p=0.02$). There were no significant differences in the risk of RPOC with severe PPH in the combination of A, C, and D, that of A and B, that of A and C, that of A and D, that of C and D. No significant difference in a single factor A, B, C, and D, respectively. **[Conclusion]** The combination of multiple histopathological findings, including inflammatory infiltrates, significantly increased the risk of RPOC with severe PPH. Evaluating the relationship between specific pathological findings of intrauterine tissue may reduce the risk of RPOC with severe PPH.

ISP-14-4

A Retrospective Study of the Cases of Uterine Artery Embolization (UAE) for Perinatal Disease Takahashi Kyokusho, Kihira Chikara, Kido Koichiro, Terashima Tsuyoshi, Yatsuki Keita, Nishizawa Miki, Takahashi Yuko, Kamata Hideo, Hiraike Haruko, Sasamori Yukifumi, Ryo Eiji, Nagasaka Kazunori *Teikyo University*

[Objective] The purpose of this study was to evaluate the efficacy of uterine artery embolization (UAE). **[Methods]** We retrospectively reviewed 61 cases of UAE performed for perinatal diseases at our hospital from April 2014 to August 2023. **[Re-**

sults] The mean age at delivery was 36 years (22-43 years) ; 28 were primipara, and 33 were multipara. Vaginal delivery was performed in 32 cases (8 by aspiration and two by forceps) and cesarean section in 15 cases. The gestational age was less than 22 weeks in 14 cases and more than 22 weeks in 47 cases (37 more than 37 weeks). The mean bleeding volume was 1867.5 mL (183-8480 mL), except in 15 cases where the volume was not measured. UAE was performed for retained products of conception (RPOC) in 26 cases (8 cases of placenta accreta), pseudoaneurysm in 17 cases, atonic bleeding in 9 cases, hematoma in 8 cases, and so on. After UAE, total hysterectomy was required in 6 cases (9.8%), including 4 cases of placenta previa accreta. Hemostasis was achieved after a single UAE in 52 cases (85.2%) and more than twice in 4 cases. There were no complications such as necrosis or intrauterine adhesions due to UAE. Pregnancy after UAE was confirmed in 15 cases. Menstruation resumed in 13 cases. **[Conclusion]** UAE is effective in treating various causes of abnormal bleeding. However, many patients undergo hysterectomy due to placenta previa accreta, requiring careful case selection. Further study of reproductive function after UAE is also needed.

ISP-14-5

The timing of rebleeding after uterine artery embolization for postpartum hemorrhage was divided into two groups : A retrospective study in our institution Yasui Yuki, Okada Aiko, Kawanishi Yoko, Nakamura Koji, Miyake Tatsuya, Kawano Mahiru, Hiramatsu Kosuke, Mimura Kazuya, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University*

[Objective] Uterine artery embolization (UAE) is an effective alternative to surgery and fertility-preserving treatment for postpartum hemorrhage (PPH). However, it is difficult to determine option of treatment for unsuccessful UAE. Here we retrospectively analyzed the cases of unsuccessful UAE for PPH. **[Methods]** We retrospectively reviewed 83 patients who underwent UAE for postpartum hemorrhage from January 2014 to August 2023 in our institution. We obtained their information from our electronic health records. **[Results]** The clinical success rate of first UAE was 86% (71 of 83). Among the 12 failed cases, 1 case underwent balloon tamponade, 2 cases repeat UAE and 9 cases total hysterectomy. In failure cases, the timing of additional treatment was divided into two groups. In 7 cases, postpartum hemorrhage was uncontrolled after primary UAE (early group). In 5 cases, rebleeding occurred during outpatient management after primary UAE (late group). Median time from primary UAE to rebleeding was 3 hours (range 1-7 hours) in early group vs 27 days (range 10-44 days) in late group. Among the late group, all cases had RPOC (retained product of conception), and 1 of them was also complicated by infection. The rate of cases performed total hysterectomy in late group was 80% (4 of 5). In outpatient management with RPOC after primary UAE, the rate of total hysterectomy because of rebleeding was 16% (4 of 25). **[Conclusion]** The successful rate and the complication rate were compatible with previous reports. For outpatient management with RPOC after primary UAE, the possibility of total hysterectomy should be fully explained at the time of rebleeding.

ISP-14-6

The reference range of parameters for rotational thromboelastometry (ROTEM sigma®) in Japanese singleton pregnant women at term gestation Nagao Takeshi, Tsuruoka Yuto, Hasegawa Akihiro, Inoue Momoko, Ito Yuki, Takahashi Ken, Miya Michiko, Samura Osamu, Okamoto Aikou *The Jikei University*

[Objective] To establish baseline rotational thromboelastometry parameters in singleton pregnant women at term gestation.

The secondary aim was to explore the potential of these parameters before onset of labor in predicting postpartum hemorrhage (PPH). **[Methods]** This study is a retrospective, single-center investigation involving Japanese pregnant women at term gestation. We conducted ROTEM sigma® testing, excluding women with any coagulation-affecting conditions. Blood tests were administered prior to planned delivery or elective cesarean section to assess the following parameters : FIBTEM, and EXTEM, including coagulation time (CT), and amplitude at 5, 10 minutes (A5) (A10). The main outcome is to determine the median and interquartile ranges (IQR) of each parameter. Subsequently, the parameters were compared between PPH patients (CS>1,500 mL, vaginal delivery>800 mL) and non-PPH patients. **[Results]** One hundred women met the inclusion criteria with a median gestation of 39.4 weeks. The median values of each parameter were : FIBTEM CT 53 seconds (50-56 seconds), A5 16 mm (IQR 15-19 mm), A10 18 mm (IQR 16-21 mm), EXTEM CT 49 seconds (47-53 seconds), A5 54 mm (IQR 51-55 mm), A10 64 mm (IQR 61-66 mm). The PPH group had 26 individuals, and the non-PPH group had 74 individuals. No significant differences in parameters between groups. **[Conclusion]** This study provides the reference values for ROTEM parameters in Japanese pregnant women. While predicting PPH by ROTEM parameters may be challenging, the potential for improving PPH management as a point-of-care tool has already been suggested, and further research is warranted based on these reference range.

ISP-15-1

Potential Impact of Modulating Glucose Deprivation and xCT/SLC7A11 Expression on Cisplatin Resistance in Endometrial Cancer Aoyama Kohei, Yoriki Kaori, Tarumi Yosuke, Kataoka Hisashi, Kokabu Tetsuya, Mori Taisuke *Kyoto Prefectural University of Medicine*

[Objective] The tumor microenvironment, including glucose deprivation, contributes to chemoresistance. Oxidative stress induced by cisplatin activity is associated with this phenomenon. Although xCT (SLC7A11), a redox-involved transporter, is induced under glucose-deficient conditions, the resistance mechanism of remains unclear. This study aimed to elucidate this mechanism in endometrial cancer. **[Methods]** The HEC-1A and AN3CA endometrial cancer cell lines were cultured under glucose deprivation and treated with cisplatin. We evaluated the effect of siRNA and the xCT inhibitor HG106 on cisplatin sensitivity as well as on cell proliferation, ROS production, and xCT expression. Cisplatin-resistant cells were created for comparative analysis based on a previous report. **[Results]** Glucose deprivation decreased cisplatin sensitivity and increased xCT expression in both the cell lines (HEC-1A : $p=0.031$; AN3CA : $p<0.01$). xCT inhibition using siRNA or HG106 enhanced the cisplatin-induced cell proliferation inhibitory effect ($p<0.01$) and decreased the IC50 (μM) for cisplatin (HEC-1A : 8.44 vs. 4.14, AN3CA : 5.20 vs. 3.86). ROS levels were reduced by glucose deprivation and increased by xCT inhibition ($p<0.01$). The combination of cisplatin and HG106 increased ROS production. Cisplatin-resistant cells exhibited higher cisplatin IC50 (μM) (HEC-1A : 10.1 vs. 22.8, AN3CA : 4.53 vs. 16.1) and xCT levels (HEC-1A : $p=0.029$, AN3CA : $p<0.01$). HG106 ameliorated cisplatin-induced ROS increase and cell growth inhibitory effect, even in cisplatin-resistant cells. The addition of N-acetylcysteine negated this effect. **[Conclusion]** Glucose deprivation and xCT expression are crucial factors in the chemoresistance of endometrial cancer cells. This suggests that targeting xCT could enhance sensitivity to cisplatin in the tumor microenvironment.

ISP-15-2

Establishment of immortalized endometrial cell lines using Sendai virus Hikino Kohei, Komatsu Hiroaki, Yamamoto Koji, Okawa Masayo, Iida Yuki, Hosokawa Masayo, Sawada Mayumi, Kudoh Akiko, Sato Shinya, Taniguchi Fuminori *Tottori University*

[Objective] To establish endometrial immortalized cell lines using the Sendai virus and analyze their characteristics. **[Methods]** The study included patients with benign ovarian tumors and endometrioid carcinoma who had regular menstrual cycles. Endometrial cells were collected and separated into epithelial and non-epithelial cells using MACS® (CD326 (EpCAM) MicroBeads, an anti-fibroblast antibody). Furthermore, the isolated cells were infected with Sendai virus carrying three immortalization genes (Bmi-1, hTERT, and SV40T) to create immortalized cell lines. The cells were characterized as epithelial cells by immunocytochemistry (ICC) and flowcytometry (FCM), and receptor expression was assessed by reverse transcription PCR (RT-PCR). Non-epithelial cells from the patients with endometrial carcinoma were evaluated using ICC. **[Results]** The immortalized cell lines were capable of more than 20 passages. Immortalized endometrial epithelial cells tested positive for anti-Keratin and anti-E-cadherin antibodies and negative for anti-Vimentin antibodies by ICC. Additionally, FCM detected these cells as positive for anti-EpCAM antibody, confirming that they were epithelial cells. RT-PCR confirmed mRNA expression of estrogen α -receptor and progesterone receptor after 20 passages, establishing an endometrial epithelial immortalized cell line. Non-epithelial cells isolated from patients with endometrial carcinoma tested positive for anti- α -smooth muscle actin and anti-Vimentin antibodies by ICC, indicating their characterization as cancer-associated fibroblasts. **[Conclusion]** We successfully established an immortalized cell line of endometrial epithelial cells using Sendai virus and generated cancer-associated fibroblasts.

ISP-15-3

Inhibition of amino acid transporter SNAT2 suppresses cell proliferation and increases p21 expression in endometrial cancer cells Kaneko Meika¹, Ishikawa Hiroshi¹, Goto Yuki¹, Katayama Eri¹, Okuya Rie¹, Saito Yoshiko¹, Nakamura Natsuko¹, Habu Yuji¹, Usui Hirokazu¹, Mitsuhashi Akira², Koga Kaori¹ *Chiba University¹, Dokkyo Medical University²*

[Objective] To investigate the effect of amino acid transporters on the cell proliferation and expression of p21, which regulates cell cycle progression and cyclin dependent kinase 4 (CDK4), which is regulated by p21 in endometrial cancer cells. **[Methods]** We measured expression levels of eight genes (*SLC1A5*, *SLC7A5*, *SLC7A8*, *SLC38A1*, *SLC38A2*, *SLC38A3*, *SLC38A4*, *SLC38A5*) encoding amino acid transporters in endometrial cancer cells, Ishikawa and HEC1B, using RT-qPCR. Then we suppressed genes that were highly expressed in these cells using siRNA transfection and measured cell proliferation using Cell Counting Kit-8. We extracted total RNA and protein 72 hours after siRNA transfection, and measured expression levels of p21 and CDK4. Further, we examined the effect of V9302, a small neutral amino acid transporter 2 (SNAT2) inhibitor, for the proliferation in these cells. **[Results]** Out of the eight genes, *SLC38A1* coding SNAT1, *SLC38A2* coding SNAT2, *SLC7A5* coding LAT1, and *SLC1A5* coding ASCT2 were expressed in both Ishikawa and HEC1B cells. Inhibition of *SLC38A2* suppressed cell proliferation, while inhibition of *SLC38A1*, *SLC7A5*, and *SLC1A5* had no effect on cell proliferation in both cells. Inhibition of *SLC38A2* increased p21 mRNA expression two-fold and decreased CDK4 protein levels. Administration of V9302 to the culture medium inhibited cell proliferation in a concentration-

dependent manner. IC₅₀ was 10.5 ± 2.4 μM for Ishikawa and 17.0 ± 3.9 μM for HEC1B. **[Conclusion]** Inhibition of SNAT2 suppressed cell proliferation and increased p21 expression in endometrial cancer cells. SNAT2 may be a potential target for the control of endometrial cancer.

ISP-15-4

Effects of epithelial-mesenchymal transition on tumor immune microenvironment in uterine carcinosarcoma Okamoto Haruko, Taki Mana, Hamada Kohei, Suzuki Haruka, Kitamura Sachiko, Yamanoi Koji, Murakami Ryusuke, Yamaguchi Ken, Hamanishi Junzo, Mandai Masaki *Kyoto University*

[Objective] Uterine carcinosarcoma (UCS), which shows the poorest prognosis among endometrial cancers, is a rare and biphasic malignant tumor composed of carcinoma and sarcoma components arising from a single clone. The genomic profiles of UCS showed the upregulation of epithelial-mesenchymal transition (EMT)-related gene expression in sarcoma component, whereas no genomic alteration is related to sarcoma differentiation. The purpose of this study is to elucidate what EMT-related factor affects tumor immune microenvironment in UCS. **[Methods]** We evaluated immune status of carcinoma and sarcoma components in UCS human samples by immunohistochemistry. We also extracted the EMT-related gene associated with tumor immunity of UCS using TCGA dataset and analyzed how the gene works tumor immunity using UCS mouse model. **[Results]** We found that CD206 (immunosuppressive M2 macrophages) were more abundant in sarcoma component than in carcinoma component by immunohistochemistry. Cases with high numbers of M2 macrophages in sarcoma component had a poorer prognosis. TCGA dataset showed that EMT signature was correlated with immune-related signature in UCS. We detected that the EMT-related gene, SPARC, was highly expressed in sarcoma component and SPARC overexpression increased tumor growth in mouse model. **[Conclusion]** These results suggest that EMT affects the tumor immune microenvironment causing miserable prognosis in UCS.

ISP-15-5

Clinical significance of p53 abnormal immunohistochemical expression in low-grade endometrial cancer Hachisuga Kazuhisa, Kawakami Minoru, Tomonobe Hiroshi, Maenohara Shoji, Kodama Keisuke, Yagi Hiroshi, Yasunaga Masafumi, Onoyama Ichiro, Asanoma Kazuo, Yahata Hideaki, Kato Kiyoko *Kyushu University*

[Objective] In the cancer genome atlas (TCGA) analysis, endometrial cancer subdivided into four molecular subtypes. Inspired by these findings, a molecular classification of endometrial cancer was developed. In this molecular classification, p53 abnormal group showed the poorest prognosis and this group was characterized by p53 abnormal immunohistochemical expression. However, the molecular classification may not be required in low-risk endometrial cancer. In this study, we investigated the clinical significance of p53 abnormal immunohistochemical expression in low-grade endometrial cancer. **[Methods]** We obtained 9 frozen samples of endometrial cancer (low-grade endometrial cancer with p53 wild-type expression : n=3, low-grade endometrial cancer with p53 abnormal expression : n=3 and high-grade endometrial cancer : n=3). RNA-sequencing was performed for each samples. All samples passed RNA quality control. Our institutional review board approved this study and informed consent was obtained in all cases. **[Results]** Differentially expressed genes (DEGs) identified in the RNA-sequencing result (1088 genes between low-grade endometrial cancer with p53 wild-type expression and p53 abnormal expression, 1811 genes between low-grade endometrial cancer with p

53 abnormal expression and high-grade endometrial cancer). In principal component analysis (PCA), low-grade endometrial cancer with p53 abnormal expression was more similar to that with p53 wild-type expression than high-grade endometrial cancer. **[Conclusion]** In this study, the RNA-sequencing results revealed that low-grade endometrial cancer with p53 abnormal expression was more similar to that with p53 wild-type expression than high-grade endometrial cancer. Furthermore, we will report immunohistochemistry for formalin-fixed paraffin-embedded (FFPE) samples, adding the cases from our previous study.

ISP-15-6

Preoperative Serum Tissue Factor Pathway Inhibitor-2 Level as a Prognostic Marker for Endometrial Cancer Maehana Tomoka, Kawaguchi Ryuji, Yamamoto Konosuke, Nishikawa Kyohei, Matsuoka Motoki, Fukui Yosuke, Yamanaka Shoichiro, Sugimoto Sumire, Kawahara Naoki, Iwai Kana, Yamada Yuki, Kimura Fuminori *Nara Medical University*

[Objective] Advanced endometrial cancer (EC) often recurs and has a poor prognosis. Therefore, identifying new biomarkers is vital. This study aimed to investigate whether the tissue factor pathway inhibitor-2 (TFPI2) level is elevated in the preoperative serum of patients with EC and if it can be a prognostic factor. **[Methods]** This retrospective study included 207 patients who had a confirmed pathological diagnosis of EC and received surgical therapy as the initial treatment between January 2011 and December 2017. Survival analysis was performed using Kaplan-Meier analysis and the Cox proportional hazards regression model. **[Results]** The 5-year disease-free survival and overall survival (OS) rates were 73.3% and 83.7%, respectively. The cut-off value for predicting OS for TFPI2 level was 177 pg/ml as determined from the receiver operating characteristic curve. A TFPI2 value ≥ 177 pg/mL was significantly correlated with age ≥ 65 years ($p < 0.001$), diabetes ($p = 0.035$), stage ($p < 0.001$), myometrial invasion ($p < 0.001$), lymphovascular invasion ($p = 0.004$), lymph node metastasis ($p = 0.010$), distant metastasis ($p < 0.001$), cancer antigen (CA) 125 ≥ 36 U/mL ($p < 0.001$) and CA 19-9 ≥ 38 U/mL ($p < 0.001$). In multivariate analysis, high-grade carcinoma (hazard ratio [HR] : 2.439, $p = 0.041$), lymph node metastasis (HR : 2.116, $p = 0.038$), distant metastasis (HR : 3.604, $p = 0.009$) and TFPI2 level ≥ 177 pg/mL (HR : 2.42, $p = 0.043$) were significant prognostic factors affecting OS in patients with EC. **[Conclusion]** The preoperative serum TFPI2 level, along with its histological type, lymph node metastasis and distant metastasis, was a prognostic factor for OS in patients with endometrial cancer.

ISP-15-7

LIMI contributes to the malignant potential of endometrial cancer through CREB signaling Kato Hiroaki¹, Murakami Sakiko¹, Yasuoka Toshiaki¹, Morimoto Akemi¹, Usami Tomoka¹, Matsubara Yuko¹, Fujioka Toru¹, Matsubara Keiichi¹, Matsumoto Takashi¹, Sugiyama Takashi¹, Imai Yuuki², Saeki Noritaka³ *Ehime University¹, Division of Integrative Pathophysiology, Ehime University Proteo-Science Center², Division of Medical Research Support, Advanced Research Support Center, Ehime University³*

[Objective] To discover new therapeutic targets molecule for endometrial cancer. **[Methods]** RNA sequence data registered in The Cancer Genome Atlas (TCGA) were compared between stage I and stage 2-4 (2008 FIGO classification). We then performed LIMI gene suppression (LIMI-KD) against the endometrial cancer cell line HEC50B corresponding to grade 3 endometrial cancer, and the ability to proliferate, migrate, and invade was compared between control and LIMI-KD cell lines. Us-

ing female nude mice, control and LIMI-KD HEC50B cells were inoculated subcutaneously and performed xenograft experiments. IPA (Ingenuity Pathway Analysis) analysis of RNA-seq data using both cell lines was performed. We analyzed protein levels of phosphorylated CREB (pCREB) by immunoprecipitated with CBP. Tumor tissues extracted from a xenograft model using both cell lines and evaluated by immunostaining against pCREB. We performed Kaplan-Meier plotter analysis for prognosis of endometrial cancer by LIMI expression. **[Results]** TCGA analysis showed that LIMI expression was significantly elevated in stages 2-4. LIMI-KD suppressed proliferation, migration, and invasive ability. In the Xenograft model, tumor growth was significantly suppressed in the LIMI-KD cell line. IPA analysis predicted suppression of CREB-related gene expression and we found reduced pCREB in the LIMI-KD cell line. Expression of pCREB in concert with CBP was decreased in the LIMI-KD cell line. Immunostaining analysis showed that decreased expression of pCREB in tumors derived from LIMI-KD cell line. Kaplan-Meier plotter analysis showed that the high LIMI expression associated with poorer prognosis. **[Conclusion]** LIMI in endometrial cancer cells associate with proliferation via CREB signaling, and also contributes to migration, invasion ability.

ISP-15-8

Analysis of molecular profiles of synchronous endometrial and ovarian cancers and metastatic ones Tsukamoto Hiroyuki, Yoshida Emiko, Terao Yasuhisa, Itakura Atsuo *Jun-tendo University*

[Objective] It is difficult to distinguish between independent primary tumors and metastatic diseases (MDs) from synchronous endometrial and ovarian carcinoma (SEOs) on clinical and pathological features alone. We examined MDs and SEOs by molecular analyses and attempted to find out differences in the RNA-seq and methylation pattern. **[Methods]** Patients were recruited from the Department of Obstetrics and Gynecology, Juntendo University Hospital from 2010 to 2020. During this period, 5 cases are diagnosed as MDs and 10 cases are did as SEOs. Each case samples were collected both ovarian tumor and endometrial tumor in pair. Tumor portions of the FFPE specimens were selectively collected for DNA extraction. Frozen tissue of the tumor were collected for RNA/DNA extraction without dissection. 4 frozen cases were applied to RNA-seq and 15 cases are applied to DNA-methylation analysis. **[Results]** In comparison of gene expressions of 4 frozen cases, gene expression patterns between ovarian cancer and endometrial cancer of MDs indicated more similarity than SEOs. DNA methylation patterns of the same 4 frozen cases showed the same trend as RNA-seq. In the methylation patterns of 6 cases from FFPE samples, two MDs cases located in close proximity. The other two MDs located in the ovarian cluster. One case of SEOs located in endometrium cluster. Only one case of MDs plot divided into two cluster. These results suggest that methylation patterns reflects the originality of the primary site. **[Conclusion]** Methylation profiles may help to expect the benefit for distinguish between SEOs and MDs.

ISP-15-9

Relationship between Skeletal Muscle Mass and Prognosis in Stage IV Uterine Cancer Akira Kazutaka, Mimura Takashi, Higuchi Daiki, Asami Yuka, Hirose Yusuke, Shimada Kanae, Nagashima Minoru, Onuki Mamiko, Matsumoto Koji *Showa University*

[Objective] Numerous reports have identified sarcopenia as a risk factor for poor prognoses in various cancers, yet there remains a lack of standardized evaluation methods. The psaos

muscle index (PMI), calculated as the psoas muscle area in L3 region (cm²) divided by the square of height (m²), can be assessed using pre-treatment CT scans. In Japanese women, a PMI value below 3.92 is indicative of low muscle mass. This study aims to investigate whether low muscle mass is associated with a poor prognosis in uterine endometrial cancer patients. **[Methods]** We conducted a retrospective analysis of 33 patients diagnosed with stage IV uterine endometrial cancer between 2018 and 2021. We categorized patients into three groups: normal muscle mass (NM), low muscle mass (LM), and very low muscle mass (very LM) - those falling below the 50th percentile of the low muscle mass group. The prognosis was using the log-rank test. **[Results]** Seven patients were classified in the NM group, 11 out of the 26 patients in the LM group fell into the very LM group (PMI<2.97). The median survival time was not reached in the NM group due to the limited observation period. In the LM group, the median survival time was 30 months, whereas in the very LM group, it was only 5 months, indicating a substantial decline in prognosis. **[Conclusion]** CT-based measurement of PMI serves as an objective indicator of a patient's overall condition. Particularly in cases of low PMI, a more meticulous approach to treatment planning is warranted.

ISP-16-1

A review of cases in which surgical intervention aiming at complete resection for diaphragmatic disseminated ovarian cancer Yasui Hiroaki¹, Mizuno Sho¹, Shinoda Mami¹, Kojima Ryuji¹, Watanabe Eri¹, Mori Masahiko¹, Asano Tomonari², Okuno Masataka², Natsume Seiji², Shimizu Yasuhiro², Suzuki Shiro¹ *Aichi Cancer Center¹, Department of Gastroenterological Surgery, Aichi Cancer Center²*

[Objective] The diaphragm is a common metastatic invasion site of advanced ovarian cancer. We review the most recent cases of advanced ovarian cancer in which diaphragmatic surgery was attempted at our hospital. **[Methods]** We assessed diaphragmatic disseminated epithelial ovarian cancer patients who were estimated to be eligible for complete surgery by primary debulking surgery or neoadjuvant chemotherapy followed by interval debulking surgery, between April, 2021 and September, 2023. We reviewed cases in which a diaphragmatic approach was performed in patients who were presumed to be candidates for complete surgery based on the findings at laparoscopy or laparotomy. **[Results]** A total of 12 cases were included. We successfully obtained complete surgery for eight cases. However, the four cases were incompletely resected, two of which underwent optimal surgery and two of which underwent suboptimal surgery. In the optimal cases, small multiple tumor dissemination was a factor in the failure to completely resection. On other hand, in the suboptimal surgery cases, tumor invasion was so close to the inferior vena cava (IVC), leading to be a factor for the non-complete surgery. There is currently no way to evaluate in advance whether the close region of IVC has been invaded by cancer using either imaging and laparoscopy. **[Conclusion]** In total, we could not perform complete surgery in four cases. Especially, there is no best method to evaluate the vast diaphragmatic metastasis with close invasion to IVC, and a certain number of cases are assumed to become suboptimal surgery after performing the diaphragmatic approach.

ISP-16-2

PARP inhibitors as maintenance therapy in patients with primary ovarian cancer: A single institutional retrospective study Tamai Kana, Fukuda Tomohiko, Yamaguchi Shogo, Yamaguchi Kohei, Kawata Yoshiko, Honjoh Harunori, Eguchi Satoko, Miyamoto Yuichiro, Sone Kenbun, Mori Mayuyo, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*

[Objective] PARP inhibitors including Olaparib and Niraparib have been used as maintenance therapy in patients with primary ovarian cancer in Japan. We generally used Olaparib for patients carrying *BRCA1/2* mutation, Niraparib for homologous recombination proficient (HRP) patients. Bevacizumab was added to Olaparib depending on the surgical outcome. **[Methods]** We analyzed the patient prognosis and adverse events of PARP inhibitors up to August 2023 retrospectively. **[Results]** 36 primary advanced ovarian cancer patients were treated with PARP inhibitors (Olaparib 15, Niraparib 21) between May 2019 and August 2023. MST and median PFS were 14 months and 25 months for Olaparib, 8 months and 24 months for Niraparib respectively. The CTCAE grade 3 or higher adverse events were 5 anemia, 3 neutropenia and 3 interstitial pneumonia for Olaparib, compared with 2 anemia, 2 interstitial pneumonia, 1 neutropenia and 1 gastrointestinal event for Niraparib. **[Conclusion]** Although Niraparib was used for patients without *BRCA* mutation who are expected to have poor prognosis, Niraparib's OS has so far been similar to Olaparib's. Fewer cases of discontinuation due to adverse events occurred with Olaparib than with Niraparib. Four patients (26.7%) in the Olaparib group stopped taking the drug due to interstitial pneumonia, but only four (26.7%) required dose reductions. In contrast, 11 patients (52.3%) in the Niraparib group required dose reduction due to adverse events. However, no patient had to stop taking Niraparib with appropriate dose reduction.

ISP-16-3

First-line Maintenance Therapy for Ovarian Cancer at Our Institution Otsuki Maya, Nakagawa Satoshi, Kakuda Mamoru, Toda Aska, Kinose Yasuto, Takiuchi Tsuyoshi, Kodama Michiko, Hashimoto Kae, Ueda Yutaka, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] Advanced ovarian cancer (OC) treatment is improving with the introduction of new agents, but drug selection is becoming more complex. In our hospital, where there is short turnover interval of physicians, we have created a flowchart of initial maintenance therapy (MT) to assist the physicians choice. This study aims to review the selection, efficacy, and side effects of initial MT at our hospital and to assist in future selection. **[Methods]** Retrospective study of patients diagnosed with advanced OC between January 2021 and December 2022 at our hospital. **[Results]** During that period, 53 patients were newly diagnosed with advanced OC. Among them, 43 underwent HRD testing, with an HRD positivity rate of 55.8%. Among HRD-positive or gBRCA-positive patients, 24 received first-line MT. Nineteen of them used bevacizumab plus olaparib. Fourteen cases continue MT, averaging 13 months in treatment duration. Among HRD-negative or unclear cases, 15 received initial MT, with 8 choosing bevacizumab and 7 selecting niraparib. In the bevacizumab group, one case changed to a different MT due to side effects, three experienced platinum-resistant relapse. In the niraparib group, four cases had to discontinue or switch MT due to side effects. **[Conclusion]** Many HRD-positive cases have undergone initial MT with bevacizumab plus olaparib, showing a high continuation rate, suggesting the need to maintain the current approach. However, for HRD-negative or unclear cases, while bevacizumab and niraparib were equally selected, considering potential new treatment options in the future, updates may be necessary.

ISP-16-4

The ovarian cancer patients with BRCA2 R2318X variant may be resistant to PPAR Inhibitors Isayama Mizuki, Shikama Ayumi, Ayuzawa Moe, Iwata Narushi, Itagaki Hiroya, Tenjimbayashi Yuri, Tasaka Nobutaka, Akiyama Azusa, Nakao

Sari, Kobayashi Yusuke, Minaguchi Takeo, Satoh Toyomi *University of Tsukuba*

It is known that the efficacy of PAPR inhibitors in ovarian cancer (OC) patients with BRCA variants is high. We report OC patients with the BRCA2 R2318X variant who received Olaparib as maintenance therapy but developed early recurrence. (Case 1) A 43-year-old woman with high-grade serous OC (stage IIIC) received neoadjuvant chemotherapy (NAC) with paclitaxel and carboplatin (TC) followed by interval-debulking surgery (IDS). The tumor was surgically removed to less than 1 cm. Genetic testing revealed that the patient had BRCA2 R2318X variant. After four courses of chemotherapy, the patient began maintenance therapy with Olaparib. Six months later, she developed peritoneal dissemination. She received chemotherapy with Pegylated liposomal Doxorubicin and Carboplatin (PLD-C), but her disease progressed. (Case 2) A 70-year-old woman with high-grade serous OC (stage IIIC) received NAC with TC, followed by IDS. At the time of IDS, the tumor lesion remained more than 1 cm. The patient received four courses of chemotherapy and had a complete response on the imaging study. Genetic testing revealed that the patient had BRCA2 R2318X variant. Seven months after initiation of maintenance therapy with Olaparib, she developed peritoneal dissemination and received PLD-C, but the disease progressed. It has been reported that the cumulative risk of developing OC in women with the R2318X variant has been reported to be higher than BRCA2. The present cases may indicate that the location of the BRCA1/2 variant may be related to the efficacy of PAPR inhibitors.

ISP-16-5

Spontaneously ruptured ovarian carcinoma presenting as acute abdomen-A report of five cases Onuma Kazuya, Bando Takuto, Tajima Yui, Matsumoto Manayo, Aoyagi Ryo, Watanabe Remi, Uzawa Yoshie, Mizuno Izumi, Fukuda Takanori, Kohata Yutaka, Inoue Hiromi *Shonankamakura General Hospital*

[Introduction] Although spontaneous rupture (SR) is documented in some ovarian tumors such as granuloma cell tumors and germ cell tumors, SR of ovarian carcinomas is uncommon initial presentation and its clinical features are not well described. We report five cases of spontaneously ruptured ovarian carcinoma (OCA) presenting as acute abdomen and describe their clinicopathological characteristics. **[Case]** Five cases were documented in a five-year period at our institution, comprising 2.5% of OCAs in the period. The patient's age ranged from 29-59 year-old, and 3 were postmenopausal. The tumor size ranged from 7.3-15cm. The tumor was of the right ovary in 3 and left in 2. CA125 was elevated in all patients and the mean was 398.6 IU/ml. CA19-9 was elevated in 4 patients and markedly elevated up to 6880 IU/ml in 1. Three patients underwent emergency adnexectomy and staging laparotomy subsequently. Two patients underwent staging laparotomy in non-emergency setting because of subsidence of the symptom. The histologic type was clear cell carcinoma in 4 patients, and endometrioid carcinoma with a minor component of undifferentiated carcinoma in 1. All tumors were associated with endometriotic cysts. While three patients are free of tumor recurrence and alive, two died of tumor recurrence and progression in 9 and 23 months respectively. **[Conclusion]** SR can be an initial presentation in a minority of patients with OCA. It exclusively occurred in endometriosis-related OCAs in our experience. SR alone does not appear to have prognostic significance. Emergency adnexectomy and subsequent complete staging laparotomy may be reasonable approach.

ISP-16-6

Strumal carcinoid of the ovary mimicking ovarian epithelial malignancy-A case report Tajima Yui, Onuma Kazuya, Bando Takuto, Matsumoto Manayo, Watanabe Remi, Uzawa Yoshie, Mizuno Izumi, Fukuda Takanori, Kohata Yutaka, Inoue Hiromi *Shonankamakura General Hospital*

[Introduction] Strumal carcinoid of the ovary (SCOV) is a rare and unique germ cell tumor histologically characterized by co-existence of thyroid and carcinoid components. It may be difficult to plan proper surgical treatment because the diagnosis is usually made in permanent histologic section. We report a case of SCOV which was radiologically highly suspicious for ovarian carcinoma and managed accordingly. **[Case]** A woman of her 40's was referred to our institution for a multilocular cystic mass of the left ovary which was incidentally detected. MRI showed a 66mm cystic mass with thickened septum exhibiting restricted diffusion, indicating high suspicion of ovarian carcinoma. CT showed no findings of lymph node or distant metastasis. Tumor markers were within normal range. She underwent laparotomy and it showed a left ovarian tumor with smooth surface without intraperitoneal spread. Intraoperative pathologic examination was reported to be most likely ovarian carcinoma and staging laparotomy was performed. Final pathologic examination showed relatively monotonous atypical cells growing mostly trabecular and insular pattern but occasionally in glands. The tumor cells were positive for neuroendocrine markers, and only focally positive for CK7, consistent with carcinoid. A minor component of thyroid follicles was identified in the periphery of the tumor. The right ovary showed miniature mature cystic teratoma. The uterus, momentum, and lymph nodes were free of specific pathology. **[Conclusion]** SCOV, in particular when carcinoid component is predominant, can mimic ovarian carcinoma radiologically as well as pathologically. This case illustrates difficulty in surgical management for this tumor which is mostly benign in nature.

ISP-16-7

A Case of a Malignant Wolffian Tumor Experienced at Our Institution Sugi Haruka, Terada Atsumu, Ryu Tensei, Sakata Kotaro, Tetsuo Aki, Ishiguro Hajime, Morishita Yushi, Hori Hironobu, Seike Takashi, Gondo Kanako, Park Jongmyung, Shimomura Takuya *St. Mary's Hospital*

[Introduction] The Wolffian tumor is an extremely rare tumor originating from Wolffian duct-derived tissues, with approximately 100 reported cases to date. While these tumors often follow a benign course, around 10-20% of cases may exhibit metastasis or recurrence, and there have been reports of malignant tumors. In this report, we present a case of a malignant Wolffian duct tumor and provide a literature-based discussion. **[Case]** The patient was a 78-year-old woman with a history of two pregnancies and two deliveries. She presented with abdominal distension and was initially seen by a local physician. She was subsequently referred to our hospital with a diagnosis of a pelvic tumor. Pelvic MRI revealed a multilocular mass measuring 17 cm in the pelvic cavity, with cystic components showing a stained glass-like appearance and areas of low ADC values. A malignant tumor originating from the left adnexa was suspected. Contrast-enhanced CT scan revealed right pleural effusion, ascites, and peritoneal dissemination. Cytological examination of the pleural effusion identified adenocarcinoma. She underwent laparoscopic exploratory surgery. Pathological diagnosis suggested the possibility of serous carcinoma or endometrioid carcinoma, but a definitive diagnosis was not reached. The patient received four cycles of TC + Bevacizumab therapy as neoadjuvant chemotherapy. Due to a partial response, interval debulking surgery was performed, achieving complete resection. The final pathological

diagnosis was malignant Wolffian duct tumor. Postoperative chemotherapy with TC + Bevacizumab was administered for four cycles. Recurrence was observed 4.5 years after the initial treatment. **[Conclusion]** we describe a case of malignant Wolffian tumor.

ISP-16-8

Effective Proton Beam Irradiation for Adrenal Metastasis from Peritoneal Cancer : A Case Report Mori Atsushi, Fujino Shotaro, Honda Riku, Kamiyo Kyosuke, Sano Megumi, Imai Takashi, Muramoto Tsutomu, Kobayashi Yaeko *Nagano Municipal Hospital*

The efficacy of proton beam therapy for peritoneal cancer is not well-established. We present a case in which proton beam therapy was employed to treat recurrent peritoneal cancer with adrenal metastasis, achieving local control. **Case Presentation :** A 60-year-old patient presented to our institution with the chief complaint of left axillary lymph node enlargement. No abnormalities were detected in the breast. CT and PET scans revealed abnormal findings in the left axillary lymph node, right adrenal gland, retroperitoneal lymph nodes, left inguinal lymph node, and peritoneum. Adenocarcinoma was confirmed through inguinal lymph node biopsy, with immunohistochemical staining showing positivity for PAX8, WT-1, and P53, leading to a diagnosis of serous adenocarcinoma. While no significant ovarian enlargement was observed in imaging, peritoneal dissemination was evident, resulting in a diagnosis of stage 4B peritoneal cancer. The patient underwent seven cycles of dose-dense Paclitaxel/Carboplatin therapy, achieving complete remission. Six months later, a recurrent tumor measuring 56×39 mm was observed in the right adrenal gland. Docetaxel/Carboplatin therapy were administered. During treatment, significant bleeding occurred within the right adrenal tumor, necessitating transcatheter arterial embolization (TAE) for hemostasis. Upon the patient's request, proton beam therapy (72.6 Gy in 22 fractions) was administered to the right adrenal gland. Before irradiation, the tumor measured 93×72 mm, but three months after irradiation, it had reduced to 59×44 mm. CA125 levels also decreased from 237.5 IU/ml to 27.7 IU/ml. The patient is currently undergoing additional chemotherapy. Proton beam therapy may hold potential efficacy for serous adenocarcinomas of the ovary and peritoneum.

ISP-16-9

A case of Serous Tubal Intraepithelial Carcinoma diagnosed by laparoscopic Risk Reducing Salpingo Oophorectomy Inoue Yuta, Hashiguchi Yasunori, Nakahira Rie, Yamamoto Akira, Koyama Masayasu, Yamamoto Kumio, Tamura Kazutomi *Ishikiriseiki Hospital*

Introduction : We report a case of serous tubal intraepithelial carcinoma (STIC) diagnosed by laparoscopic risk-reducing salpingo-oophorectomy (RRSO) for a patient with hereditary breast and ovarian cancer syndrome (HBOC). **Case :** The patient is a 48-year-old woman with gravida 0 para 0, and 43 years of menopause. She underwent laparoscopic right ovarian cystectomy for a right ovarian endometriotic cyst at the age of 36. Her family history includes bilateral breast cancer in her mother and great-aunt (maternal side). She presented to our hospital with a complaint of a lump in her left breast, and was diagnosed as HBOC with stage I left breast cancer, cT1N0M0, triple negative, and BRCA1 (c.4986+1G>A) pathological variant. After left total mastectomy, right risk-reducing mastectomy, and 4 courses of adjuvant chemotherapy (docetaxel and cyclophosphamide), the patient underwent laparoscopic RRSO. Although there were no obvious abnormal findings intraoperatively and intraperitoneal cytology was negative, a diagnosis of STIC was

made on pathological examination. After careful consultation and counseling to the patient and her family, the patient underwent a total hysterectomy, a complete omentectomy, and a peritoneal biopsy. Since no malignant findings were found on pathological examination, the patient was placed under observation, and she has passed one year and two months after the surgery without any evidence of recurrence. **Conclusion :** RRSO should be performed aggressively in patients with HBOC who do not wish to preserve the fertility.

ISP-16-10

Assessment of the Accuracy and Safety of Ultrasound-Guided Tru-Cut Biopsy in a Tertiary Hospital from January 1, 2021 to December 31, 2022 : A Retrospective Study Panganiban Arienne C *Department of Obstetric and Gynecology, Section of Ultrasound, Rizal Medical Center, Philippines*

[Objective] To assess the accuracy and safety of tissue diagnosis of advanced ovarian carcinoma using Tru-Cut biopsy. **[Methods]** We used Retrospective Descriptive Purposive sampling technique and 33 patients diagnosed with ovarian malignancy in a tertiary hospital from January 2021 to December 2022 were included. **[Results]** The adequacy rate of the Tru-cut biopsy size for histological findings was determined to be 100% while the detection rate was 81.8%. The observed agreement between ultrasound-guided Tru-Cut biopsy and cytopathology (Kappa=83.3%, p=0.03) was higher than what would be expected by chance alone (Kappa=55.6%). This ultrasound-guided Tru-cut biopsy has a sensitivity of 87.5% (95% CI : 47.4%, 99.7%), specificity of 75.0% (95% CI : 19.4%, 99.4%), positive likelihood ratio of 3.5 (95% CI : 0.63, 19.50), and a negative likelihood ratio of 0.17 (95% CI : 0.02, 1.14). There were no reported complications which deems Tru-cut biopsy as safe procedure. **[Conclusion]** Tru-Cut biopsy is an accurate and safe alternative procedure with high adequacy rate and detection rate. It is a safe procedure with no complications observed.

ISP-16-11

Rationale and Study Design of the KOV-HIPEC-02 : A Randomized, Multicenter, Open-label Phase III trial of Hyperthermic Intraperitoneal Chemotherapy in Platinum-Resistant Recurrent Ovarian Cancer Lim Myong Cheol¹, Kim Ji Hyun¹, Lee Yoo-Young², Jeong Dae Hoon³, Lee Sung Jong⁴, Park Eun Young⁵, Lee Taek Sang⁶, Park Jeong-Yeol⁷, Jeon Seob⁸, Kim Ki Hyung⁹, Chang Suk-Joon¹⁰, Park Sang-Yoon¹ *Gynecologic Cancer Center, National Cancer Center Korea, Korea¹, Samsung Medical Center, Korea², Busan Paik Hospital, Inje University, Korea³, Seoul St. Mary's Hospital, Korea⁴, Biostatistics Collaboration Team, National Cancer Center, Korea⁵, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Korea⁶, Asan Medical Center, Department of Obstetrics and Gynecology, Korea⁷, Soonchunhyang University Cheonan Hospital, Korea⁸, Pusan National University Hospital, Korea⁹, Ajou University School of Medicine, Korea¹⁰*

[Objective] Hyperthermic intraperitoneal chemotherapy (HIPEC) during cytoreductive surgery has emerged to achieve a higher concentration of chemotherapeutic agents and treat micro-metastases on peritoneal surfaces. At advanced staged ovarian cancer treated with neoadjuvant chemotherapy, HIPEC during interval cytoreductive surgery with cisplatin 75-100mg/m² increases progression-free survival and overall survival (OV-HIPEC-01 and KOV-HIPEC-01). **[Methods]** This trial (KOV-HIPEC-02) is currently actively enrolling, a multicenter, open-label, 1 : 1 randomized, phase III trial that will enroll 140 patients in platinum-resistant recurrent epithelial ovarian cancer. The trial is registered on ClinicalTrials.gov (NCT05316181). Institutional review board approval was obtained. The first pa-

tient has been enrolled Apr 07, 2022. The experimental arm will receive HIPEC followed by standard chemotherapy, and the control arm will receive standard chemotherapy without HIPEC until disease progression. If patients are assigned to the HIPEC group, the HIPEC procedure is carried out using the open or closed technique, infusing 41.5-42.0°C doxorubicin 35mg/m² and mitomycin 15mg/m². Enrolled patients will receive physician-choice non-platinum compound systemic chemotherapy until progression. The primary objective of the trial is to evaluate progression-free survival (PFS) between the HIPEC group and the control group. Assuming that the enrollment period is three years and the follow-up period is two years, the total number of events required is 121. Based on the log-rank test, the total number of subjects required to prove HR 0.6 with a two-sided alpha of 0.05 and 80% power is 126. One hundred forty patients are finally studied, considering 10% drop-out. **[Results]** **[Conclusion]** No available at the time of submission.

ISP-16-12

Malignant Brenner tumor with uterine involvement : A case report Limbo Catherine Loren C, Reyes Maria Lilia *Section of Ob-Gyn Ultrasound, University of the East Ramon Magsaysay Memorial Medical Center, Inc., Philippines*

Background : Malignant brenner tumor is a rare type of neoplasm that accounts for approximately < 0.05% of ovarian malignancy. Due to paucity of cases, our knowledge on disease presentation, behavior, treatment and prognosis has been limited. We present our encounter with this rare ovarian malignancy. **Case :** A 37-year-old presented with vague abdominal pain associated with gradual increasing abdominal girth and a palpable pelvoabdominal mass. Transvaginal with transabdominal ultrasound revealed a multilocular solid pelvoabdominal mass measuring 22 x 17 x 10 cm in dimension together with a uterus compatible with sonologic features of adenomyosis with a pedunculated fibroid measuring 7 x 7 x 5 cm. She then underwent exploratory laparotomy with subtotal hysterectomy with bilateral salpingoophorectomy and biopsy of cervical and parametrial masses that revealed malignant Brenner tumor in both ovaries with no capsular invasion. The uterus was found to be positive for malignancy with extensive lymphovascular involvement. Biopsies on both the cervix and peritoneum were also positive for malignancy however peritoneal fluid cytology was negative for malignancy. Postoperative plans included chemotherapy using epithelial ovarian malignancy protocols. **Conclusion :** Malignant Brenner tumor poses both a diagnostic and treatment challenge even with the wide availability of diagnostic imaging and advances in medical knowledge. Its rare occurrence and non-specific symptomatology and ultrasound presentation compound to the difficulty in clinching its diagnosis. Treatment is still surgical excision and further studies are still needed to establish guidelines both for its diagnosis with imaging and chemo-radiation therapy regimens.

ISP-17-1

Single Institute Comparative Analysis of Gestational Trophoblastic Disease (GTD) Treatment in Cambodia : INCa 2010 vs. FIGO 2012 Treatment Strategies Huy Vinnika¹, Uy Kyna^{1,4}, Chhit Maryan¹, Koun Linka¹, Matsushita Tomomi², Mori Mayuyo², Fujita Noriko^{3,5}, Osuga Yutaka², Koum Kanal¹ *Khmer Soviet Friendship Hospital, Cambodia¹, University of Tokyo², Bureau of International Health Cooperation, National Center for Global Health and Medicine, Japan³, Cambodian Society of Gynecology and Obstetrics, Cambodia⁴, School of Tropical Medicine and Global Health, Nagasaki University⁵*

[Objective] In Cambodia many facilities are using the guideline from the Institut National du Cancer (INCa) 2010 for GTD man-

agement. Since 2017, Gynecology department of Khmer Soviet Friendship Hospital (KSFH) has adapted FIGO cancer 2012 guideline. This report aims to compare and evaluate the outcomes of GTD treatment by analyzing two distinct groups. **[Methods]** The study was conducted using retrospective data analysis of GTD cases of 66 patients between 2017 and 2019 treated under FIGO guideline, and 107 cases between 2009-2015. The old treatment group was using 8days Methotrexate regime, while the new treatment group received 5 days regime. Key parameters assessed in this comparative analysis include treatment efficacy, duration of therapy, mortality rates, and abandonment rate. **[Results]** Among 66 patients, 28 received chemotherapy. Compared to the INCa guideline, the FIGO group showed shorter hospitalization days (7 days vs 4 days). Lesser average doses are required to normalize HCG level (4 doses Vs 3 doses). Between 2nd and 5th doses, remission rate is 37% and 86% respectively. Furthermore, the new treatment modalities were associated with very few adverse effects. **[Conclusion]** This report sheds light on the evolving landscape of GTD management in Cambodia, highlighting the potential benefits of transitioning to FIGO treatment approaches. The outcomes of this study emphasize the importance of early diagnosis, multidisciplinary care, and the adoption of evidence-based therapeutic strategies. Further research and long-term follow-up are essential to refine and optimize the management of GTD in Cambodia.

ISP-17-2

Hemostatic Radiotherapy on a Bleeding Vaginal Metastatic Lesion of Gestational Trophoblastic Neoplasia : A Case Report Garcia Dayanara Mae C *Southern Philippines Medical Center, Philippines*

Gestational trophoblastic neoplasia (GTN) is the malignant end of the gestational trophoblastic spectrum which arises from the abnormal proliferation of placental trophoblasts. These placental tumors are characterized clinically by their propensity to widely metastasize. The vagina, next to the lung, is the second most common metastatic site in trophoblastic tumors. Profuse vaginal bleeding is the most common clinical presentation of patients with vaginal metastasis and this is due to the abundance of venous plexus and thin-walled fragile vessels of the invasive tumor. This report describes a case of a 41-year-old G5P4 (4014) with gestational trophoblastic neoplasia who presented with vaginal metastasis and profuse vaginal bleeding which was resolved with after three (3) sessions of hemostatic radiotherapy. **Keywords :** gestational trophoblastic neoplasia, vaginal metastasis, hemostatic radiotherapy

ISP-17-3

VCAM-1 is involved in the progression of preexisting endometriosis Kitano Saki, Hashimoto Kae, Toda Aska, Nakamura Koji, Kawano Mahiru, Kinose Yasuto, Kodama Michiko, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] NF κ B activation has been reported to be involved in the progression of endometriosis lesions, and NF κ B regulates the release and expression of cytokines, which are involved in the persistence of endometriosis inflammation and the migration and invasion of endometriosis cells. Herein, we investigated the relationship between NF κ B and adhesion factor, and its involvement in the progression of already formed endometriosis lesions. **[Methods]** Endometrial stromal cells were obtained from patients in primary culture. The effect of NF κ B inhibitor (IMD-0560) on adhesion factors was examined using PCR arrays. Nuclear migration of NF κ B was examined using fluorescent immunostaining for NF κ Bp65 ; and Adhesion Assay was used for the effect of NF κ B on adhesion capacity. Fluorescence intensity analysis was used to confirm cell adhesion

ability. Western-blot assay was used to measure protein level of VCAM-1. **[Results]** The effect of IMD-0560 on adhesion factors was confirmed by PCR array, and VCAM-1 was decreased. Therefore, we examined the relationship between NF κ B and VCAM-1, and their involvement in the development of endometriosis. Fluorescent immunostaining for NF κ B p65 in endometrial stromal cells showed that IMD-0560 treatment inhibited nuclear migration of NF κ B. IMD-0560 treatment decreased VCAM-1 expression and inhibited endometrial stromal cell adhesion. In q-PCR-2 of VCAM-1, we found that VCAM-1 was increased in endometriotic cyst wall, but not in eutopic endometrium neither with or without endometriosis. **[Conclusion]** These findings suggest that VCAM-1 may be involved in the development of preexisting endometriosis rather than initiation of endometriotic lesion.

ISP-17-4

Establishment of a novel 3D spheroid culture system of uterine leiomyoma cells Sakai Takahiro, Sato Shun, Takasu Go, Tamehisa Tetsuro, Kajimura Takuya, Tamura Isao, Sugino Norihiro *Yamaguchi University*

[Objective] To establish three-dimensional (3D) spheroid culture system of uterine leiomyoma (ULM) cells that responds to estrogen (E) and progesterone (P). **[Methods]** Monolayer and spheroid cultures were done on MED12-mutation positive and negative ULM cells. ULM cells were confirmed to be smooth muscle cells with 80% purity and to have progesterone receptors by immunocytochemistry. The cells were preincubated for 2 days, and used for the following experiments. For monolayer culture, cells were incubated with E+P, E alone, P alone, and control (without E+P) for 7 days. For 3D culture, cells were incubated in the low attachment well dish, and after 24 h, floating cell aggregates were identified as spheroids of ULM cells. Then, the ULM-spheroids were incubated with E+P, E alone, P alone, E+P+selective progesterone receptor modulator (SPRM), and control for 7 days. **[Results]** In the monolayer culture, ULM cells in both MED12-mutation positive and negative ULMs did not proliferate by any female hormones. In the 3D spheroid culture, the cross-sectional area of the spheroid in E+P and P alone was larger than that in E alone, E+P+SPRM and control in both MED12-mutation positive and negative ULMs. The morphology of the spheroid of E alone, E+P+SPRM and control showed the shrink of smooth muscle cells. These results suggest that the growth of the ULM-spheroid is maintained by progesterone, and that the responsiveness of the spheroid to progesterone did not differ between MED12-mutation positive and negative ULM cells. **[Conclusion]** We established the 3D spheroid culture system of ULM cells that responds to progesterone.

ISP-17-5

A Study on the Anatomy of submucosal fibroid pseudocapsule from TCR with low protrusion rate myoma Oki Toshimichi¹, Uchida Natsuko², Sameshima Hirotsugu³, Kawahara Yuji¹, Karakida Noriko², Sakihama Mika², Oki Chie², Kobayashi Hiroaki² *Department of Reproductive Health Care Nursing, School of Health Sciences, Kagoshima University¹, Kagoshima University Medical and Dental Hospital², Ibusuki Medical Center², Psychiatry, Fukuyama Hospital¹, Fiore Daiichi Hospital²*

[Objective] To elucidate an anatomy around a pseudo-capsule of a myoma nodule that can be observed during TCR-M of low protrusion rate. **[Methods]** This study included 27 cases of TCR-M with a protrusion rate of 50% or less. After informed consent, surgical videos were retrospectively reviewed. Our technique was as follows : 1) Expose a myoma nodule, 2) Detach a nodule at an inner layer of a pseudo-capsule 3) Identify feeding vessels 4) Avoid vascular plexus and proceed deep area between a fi-

broid and myometrium from other directions 5) Enucleate a nodule from lower uterine segment to fundal area, 6) Cut vascular plexus inside a pseudocapsule and release a nodule into uterine cavity 7) Remove a myoma nodule. **[Results]** A myoma nodule have a protruding portion (protruding area) and a buried portion in myometrium. In addition, a buried portion is divided into a shallower layer (shallow area) and a deeper layer (deep area) than the maximum diameter of a myoma nodule. Step1) 2) a pseudo-capsule is thin and appears as a translucent film wrapping a nodule, Step3) -6) In deep area, a pseudo-capsule exists sparsely. Around vascular plexus and shallow area, a pseudo-capsule is dense. A detached pseudo-capsule change from firm to a honeycomb or cord-like structure. Inside area of pseudo-capsule has only negligible vessels. **[Conclusion]** A pseudo-capsule of a myoma nodule is literally loose connective tissue separating the fibroid tissue from myometrium. Correct recognition of these anatomy contributes to complete removal and safe procedure.

ISP-17-6

Consideration of postmenopausal shrinkage of uterine myomas—from a retrospective study of 98cases followed for 10years after menopause— Oue Kenta¹, Ichimura Tomoyuki², Murakami Makoto³, Matsuda Makiko¹, Kawamura Naoki³, Sumi Toshiyuki² *Osaka City University¹, Osaka Metropolitan University², Osaka City General Hospital³, Izumi City General Hospital¹*

[Objective] The trend of postmenopausal uterine myoma is of interest to both patients and gynecologists, but there are no data on changes after a long period of time. We aimed to elucidate clinical findings related to postmenopausal myoma shrinkage. **[Methods]** We included 98patients with myomas (between 50 and 160mm in long diameter) who had been followed for 10years after menopause. The diameter was measured by ultrasonography before menopause and every year until 10years after menopause, and reduction rate for each year after menopause was calculated. The reduction rate after 10years was defined as 10R. The period taken to reach to half of 10R was defined as half reduction period (H). The relationship between 10R and H and clinical findings was examined retrospectively by the Spearman rank correlation coefficient test and Mann-Whitney test. **[Results]** 10R ranged from 73.6 to -3.7%. A significant weak negative correlation (correlation coefficient = -0.204, p = 0.048) was found between 10R and BMI, and a significant weak negative correlation (correlation coefficient = -0.239, p = 0.018) between 10R and number of nodes. H of one nodule was 2years and that of four or more nodules was 4years, and there was a significant difference between the reduction rate of one nodule and that of four or more nodules for each year until 3years after menopause (p=0.038, 0.001, 0.025). **[Conclusion]** It was suggested that BMI and number of nodules may be involved in postmenopausal shrinkage rate. The results also suggested that spontaneous shrinkage may begin earlier after menopause in cases with smaller number of myoma nodules.

ISP-17-7

A case of parasitic myoma with endometrial tissue after laparoscopic hysterectomy Kusakabe Ai¹, Narita Sachiyo¹, Komoike Satoshi¹, Yano Mizuho², Shimada Takahiro¹, Taniguchi Roze¹, Ueda Tomoko¹, Wakimoto Yu¹, Tsubamoto Hiroshi¹, Shibahara Hiroaki¹ *Hyogo Medical University¹, Meiwa Hospital²*

A multigravida woman with uterine leiomyoma underwent total laparoscopic hysterectomy and bilateral salpingectomy at the age of 47 years. The uterus was removed from the umbilicus with an extended incision by manual morcellation, and the specimen was diagnosed as leiomyoma. At the age of 50 years,

she had right-sided abdominal pain with mild elevation of white blood cells on blood test and was treated with antibiotics for suspected diverticulitis. Her symptoms improved within four days. Abdominal pain recurred every 3 to 5 months. After four episodes at the age of 52 years, contrast-enhanced CT showed a mass lesion approximately 2.5 cm in diameter with a central low-density area in the ascending region. A lower gastrointestinal endoscopy was performed, but no lesions were found in the intestinal tract. Laparoscopic resection of the mass was performed for the diagnosis and treatment. The tumor originated from the omentum and was firmly adhered to the abdominal wall. The internal abdominal oblique muscle and omentum were incised and the tumor was removed by en bloc resection with a sufficient surgical margin. Histopathological examination revealed endometrial-like components with internal hemorrhage surrounded by increased smooth muscle cell proliferation. Part of the tissue containing both the endometrium and smooth muscle appeared to fall into the abdominal cavity during manual morcellation. The tissue adhered and increased as both ovaries remained intact. One year later, at the age of 53, her blood endocrine tests showed menopause. She had no recurrence two years after tumor resection.

ISP-18-1

Exploratory research of the 3D-printed graft of autologous mesenchymal stem cells for uterine regeneration in a cynomolgus macaque model Shiraiishi Tetsuro¹, Kisu Iori¹, Matoba Yusuke^{1,2}, Yanokura Megumi¹, Hayashi Ryoma¹, Nogami Yuya¹, Tsuji Kosuke¹, Masuda Kenta¹, Kobayashi Yusuke¹, Banno Kouji¹, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Vincent Center for Reproductive Biology, Massachusetts General Hospital, USA²*

[Objective] Uterine regeneration has been studied to solve uterine factor infertility. However, current methods using various scaffolds have not become practically feasible yet. Bio-3D-printing, a cutting-edge technology, has recently been developed to fabricate tissue-like fragments using only cells for tissue regeneration. An exploratory study was conducted to assess the feasibility of this technology for uterine regeneration using cynomolgus macaque, which has uteri anatomically similar to human. **[Methods]** A sexually matured six-year-old macaque was used. Mesenchymal stem cells (MSCs) were isolated from macaque bone marrow, and MSC-spheroids were assembled using a Bio-3D-printer to construct a cylindrical graft with a diameter of 5 mm. Under general anesthesia, a full-thickness defect was surgically created in the macaque uterus, and the graft was implanted. Laparoscopic observation of the implantation site was performed at two, four, and eight-week after implantation. On day 130 after transplantation, the macaque was euthanized, and the uterus was removed for further examination. **[Results]** Isolated cells from the macaque bone marrow were validated as MSCs by multipotency and surface markers. The 3D-printed graft was firm enough to be suture-fixed. Laparoscopic observation after implantation revealed no adhesions around the implanted site or graft failure. The menstrual cycle was recovered after 117 days post-transplantation. Macroscopically, no endometrial adhesion or myometrium defect was observed in the removed uterus. Furthermore, histological assessment by hematoxylin and eosin (HE) staining revealed complete wound healing and no obvious fibrogenesis. **[Conclusion]** While further investigation is required, the MSC-graft generated by Bio-3D-printing may be an attainable approach for uterine regeneration.

ISP-18-2

Impact of preexisting chronic endometriosis before assisted

reproductive technology Sakai Kazuyoshi¹, Takehara Isao², Hine Saki², Sato Ai², Nakamura Fumihiko², Nakai Nanako², Takahashi Kyoko³, Nishi Michi², Matsukawa Jun², Nagase Satoru² *Yamagata Prefectural Shinjo Hospital¹, Yamagata University², Saiseikai Yamagata Hospital³*

[Objective] An example of infertility treatment without assisted reproductive technology (ART) includes intrauterine insemination. We investigated the impact of preexisting chronic endometriosis (CE) on infertility treatment without ART to determine the necessity of the diagnosis and treatment of CE prior to ART. **[Methods]** This study was approved by the ethics committee in our institution. We included patients who underwent infertility treatment without ART in our facility between April 2020 and March 2022. CE was diagnosed by the presence of CD 138-positive cells in the endometrial tissue at the start of infertility treatment. We retrospectively evaluated whether CE affected the outcomes of infertility treatment before ART. **[Results]** Among the 45 women undergoing 145 treatment cycles who met the inclusion criteria, 28 (54.9%) were CE-positive. No significant differences were observed in the backgrounds of the CE-negative and CE-positive groups. Positive pregnancy rates were 14.1% (9/64 cycles) and 13.6% (11/81 cycles) in the CE-negative and CE-positive groups, respectively. Clinical pregnancy rates were 12.5% (8/64 cycles) in the CE-negative group and 13.6% (11/81 cycles) in the CE-positive group. Ongoing pregnancy and live birth rates were 12.5% (8/64 cycles) in the CE-negative group and 12.5% (10/81 cycles) in the CE-positive group. No significant differences were observed between the two groups. **[Conclusion]** In the present study, the existence of CE did not significantly impact infertility treatment outcomes prior to ART. Therefore, the diagnostic workup and treatment of CE should be continued in patients undergoing ART.

ISP-18-3

The presence of adenomyosis is associated with poor pregnancy outcome in patients with recurrent implantation failure Fukui Yamato, Matsuo Mitsunori, Hiratsuka Daiki, Iida Rei, Ishizawa Chihiro, Hiraoka Takehiro, Izumi Gentaro, Harada Miyuki, Hiraike Osamu, Osuga Yutaka, Hirota Yasushi *The University of Tokyo*

[Objective] Recurrent implantation failure (RIF) is one of the major problems in assisted reproductive technology, and it remains unclear which gynecological diseases are involved in the occurrence of RIF. Recent studies suggested that chronic endometritis (CE), uterine fibroid, adenomyosis and endometriosis are associated with infertility. This retrospective study aimed to analyze whether the presence of these gynecological diseases is linked to pregnancy outcome in RIF patients. **[Methods]** One hundred and sixty-two RIF patients who had more than two failed embryo transfer cycles younger than 43 years were included in the study (36.7 ± 3.9 years old, mean ± SD). They underwent hysteroscopy and endometrial biopsy for detection of CE and MRI for detection of uterine fibroid, adenomyosis and endometriosis. Patients diagnosed with CE was treated with antibiotics. Post-examination embryo transfers (ETs) were performed in all patients, and the factors contributing to the outcome of clinical pregnancy in post-examination ETs were analyzed using univariate and multivariate analyses. Experimental procedures were approved by the institutional review board and written informed consent was obtained from all patients. **[Results]** Univariate analysis showed that the presence of adenomyosis was associated with poor pregnancy outcome ($P=0.0215$), and younger age ($P=0.199$) and the presence of CE ($P=0.159$) were linked to favorable pregnancy outcome. In multivariate analysis, the presence of adenomyosis was also associated with poor pregnancy outcome ($P=0.035$). **[Conclusion]** We found that the presence of adenomyosis is linked to poor preg-

nancy outcome. These findings suggest that adenomyosis is a predictor of poor pregnancy outcome in RIF patients.

ISP-18-4

The prevalence of chronic endometritis and clinical outcomes following antibiotic treatment in infertile women with ART treatment : retrospective study in our hospital Goto Takeshi¹, Takiuchi Tsuyoshi^{1,2}, Tsuji Saori¹, Honda Hidemine¹, Handa Mika¹, Okada Aiko¹, Miyake Tatsuya¹, Kawano Mahiru¹, Kimura Tadashi¹ *Osaka University¹, Department of Clinical Genomics, Osaka University²*

[Objective] Association between implantation failure and chronic endometritis (CE) has been reported. The objective of this retrospective study was to investigate the prevalence of CE in infertile women undergoing ART treatment and to evaluate clinical outcomes following antibiotic treatment. **[Methods]** Thirty-nine infertile patients, who underwent a biopsy for CE following failure of one or more IVF attempts between June 2019 and April 2023, were evaluated. CE was diagnosed as five or more CD138-positive endometrial stromal plasmacytes in 20 high-power fields (HPF). **[Results]** Of the 39 patients, 20 (51.3%) were diagnosed as CE. The rates of CE in the groups of patients with IVF failure between one and more than one cycles were comparable (54.5% and 50.0%, respectively). Among all the patients, 79.5% had endometriosis, uterine fibroids, or other medical conditions, and the proportion of patients with underlying conditions in the groups of IVF failure with one and more than one cycle were 81.8% and 78.6%, respectively. Following the first-line doxycycline treatment, the cure rate was 60.0%. Following the second-line metronidazole/ciprofloxacin treatment, the overall cure rate was 85.0%. The live birth rates in the first ET cycle following treatment in the cured-CE group and non-CE group were 15.0% and 21.1%, respectively. The difference was not statistically significant. **[Conclusion]** Our data suggested treatment of CE may improve the clinical outcomes of infertile women. As high prevalence of CE was observed even in patients with single IVF failure, the timing of CE evaluation should be considered based on the patient's medical condition.

ISP-18-5

A retrospective study of 95 patients with endometriosis underwent reproductive counseling Takeuchi Arisa¹, Saitoh Karin^{1,2}, Ogaki Yoko^{1,3}, Koizumi Yayoiko¹, Ichiyama Takuhiko¹ *Torch Clinic¹, Sanwa Hospital², Kohsei Chuo General Hospital³*

[Objective] Endometriosis not only causes intractable infertility but also carries perinatal risks. Recently the importance of preconception reproductive care has been noted. For patients with endometriosis, it is necessary to propose appropriate treatment plans based on ovarian reserve and family planning at the appropriate time. This study aimed to clarify the decision trends in treatment choices and pregnancy outcomes among patients with endometriosis who underwent reproductive counseling and to utilize for future treatment strategies. **[Methods]** We retrospectively reviewed 95 patients with endometriosis who visited our clinic between May 2022 and August 2023 for advice on whether they could conceive. Their background, ovarian reserve, treatment choices, and pregnancy outcome were analyzed in detail. **[Results]** The mean age of the patients was 33.7 ± 0.5 years. The mean size of the endometrial cyst was 26.6 ± 1.6 mm. The mean serum AMH level was 3.4 ± 0.4 ng/ml. 69 patients out of the 95 wanted to conceive immediately, and 52 of them started the fertility treatment cycle. Among the 52, 26 patients began with general fertility treatment and the remaining 26 began with ART treatment due to poor ovarian reserve and male factors. We could confirm clinical pregnancies in 16 of them (61.5%). **[Conclusion]** We were able to identify a high

pregnancy rate among patients with endometriosis, those who appropriately chose fertility treatment cycle by preconception reproductive counseling. In light of these considerations, appropriate therapeutic intervention may facilitate patients with endometriosis to achieve their family planning.

ISP-18-6

The current status of fertility treatment using donor sperm at our facility and the right to know the origin of the offspring Miyazaki Kaoru, Kamoshita Keiko *Fertility Center, Hara Medical Clinic*

[Objective] Our facility started artificial insemination with donor sperm (AID) in 1997, and currently performs approximately 800 cycles per year. Although AID has been performed in Japan since 1948, there have been problems with AID, such as the fact that offspring have no right to know the origin. Moreover, IVF using donor sperm (IVF-D) cannot be performed even for couples with multiple unsuccessful AIDs, due to the Health Sciences Council's statement in 2003. In 2020, a special law was enacted to clarify the parent-child relationship of children born through assisted reproductive technology, guaranteeing the parent-child relationship between the child born through AID and the patient couple. However, since legislation allowing IVF-D has not yet been submitted to the Diet, azoospermic couples repeat AID dozens of times, causing them both financial and mental complications. **[Methods]** We decided to implement IVF-D in our own way to address the remaining issues that have not yet been legislated, and we have created a system that guarantees the children's right to know their origins by using sperm donors who can be contacted by the children after the age of 18. **[Results]** As of July 31, 2023, we have performed IVF-D on 75 patients (90 cycles in total). 83 cycles of embryo transfer were performed, and implantation was confirmed in 41 cycles, and the fetal sac in 38 cycles. Twenty-nine ongoing pregnancies were confirmed up to 8 weeks. **[Conclusion]** To continue to provide adequate medical care using donor sperm throughout Japan, it is essential that a national system be established.

ISP-18-7

Non-invasive AI Prediction of Blastocyst Ploidy from Embryo Culture Time-Lapse Images Yanai Akihiro, Horie Akihito, Imakita Sachi, Nakamura Mitsuhiro, Ikeda Asami, Shitanaka Shimpei, Ohara Tsutomu, Kitawaki Yoshimi, Okunomiya Asuka, Mandai Masaki *Kyoto University Graduate School of Medicine*

[Objective] PGT-A is commonly used for repeated failure in ART, but invasiveness is main issue. AI ploidy prediction from embryo time-lapse images can be a non-invasive alternative. However, previously reported models are inadequate for clinical use, because either of the following reason : 1) ROC-AUCs are not sufficiently high ; 2) manual annotation of time-lapse parameters requires great deal of effort. Besides, in these models, image/video AI is in a black box. In this study, we aimed to create accurate and explainable AI ploidy prediction models appropriate for clinical applications. To achieve this, we developed a novel AI time-lapse image auto-annotator, created prediction models from only human-recognizable features, and visualized the basis of AI decisions with SHAP. **[Methods]** First, we created a dataset of 28,000 images with 20-class supervised labels including developmental stages and grades. Then, we fine-tuned 12 excellent pre-trained image AIs with data augmentation. Next, 2728 sets time-lapse images of blastocysts with PGT-A results were annotated by our best fine-tuned AI for each image. Final ploidy prediction models were created by analyzing each-time annotations, AI calculated time-lapse parameters and clinical features, using various machine-learning methods (SVM,

XGBoost, Transformer, etc.). **[Results]** The fine-tuned ConvNeXt-Large model achieved the highest accuracy of 86%, with 96% stage accuracy. Test ROC-AUCs of our best models were 0.82 for euploid prediction and 0.81 for euploid + low mosaic prediction. **[Conclusion]** We created the most clinically useful AI prediction models for blastocyst ploidy compared to previous studies. Our novel models enabled highly accurate prediction without manual annotation.

ISP-18-8

Deep learning models using time-lapse imaging data to predict successful clinical pregnancy and embryo euploidy Maekawa Ryo¹, Takasaki Hitomi¹, Shiroshita Amon¹, Fujimura Taishi¹, Shirafuta Yuichiro¹, Yoneda Toshihide¹, Mihara Yumiko¹, Tamura Isao¹, Kuramoto Takeshi², Tanaka Atsushi², Sugino Norihiro¹ *Yamaguchi University¹, St. Mother Hospital², Kuramoto Women's Clinic³*

[Objective] In single embryo transfer, it is important to select good-quality embryos. Also, there is currently no technique to distinguish embryos with euploidy based on their morphological features. Here, we established two deep-learning models to determine good-quality embryos and embryos with euploidy based on morphological features obtained by time-lapse imaging. **[Methods]** This retrospective study analyzed time-lapse videos of 2,494 embryos with clinical pregnancy outcomes and 1,645 embryos with karyotype outcomes examined by preimplantation genetic testing for aneuploidy (PGT-A). Two deep learning models were trained: the clinical pregnancy (CP) model, which predicted the probability of clinical pregnancy, and the euploid (EP) model, which predicted the probability of euploidy, confirmed by PGT-A, using time-lapse video sequences and patients' ages. The models' performances were evaluated using the average area under the curve (AUC) of the receiver operating characteristic curve with ten independent experiments. **[Results]** The CP model achieved an AUC of 0.670 with a 90th percentile range of 0.656-0.683 in predicting clinical pregnancy, while the EP model achieved an AUC of 0.672 with a 90th percentile range of 0.659-0.684 in predicting embryo euploidy. **[Conclusion]** We established two deep learning models, CP and EP, to select good-quality embryos and embryos with euploidy. The CP model can potentially increase pregnancy rates in patients undergoing assisted reproductive technology, while the EP model can help to reduce miscarriages caused by embryo aneuploidy.

ISP-18-9

Impact of the microbial metabolites D-amino acids on preimplantation development Sakuma Moeko¹, Yamada Mitsutoshi¹, Fukuoka Mio¹, Matsuzawa Yuichi¹, Ooka Reina¹, Iwai Maki¹, Kamijo Shintaro¹, Sasabe Junpei², Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Department of Pharmacology and Chiral Biology, Keio University²*

[Objective] Symbiotic microbiota in reproductive tract of model organisms influences embryo development. We have displayed a correlation between species-level microbiome profiling and the *in vitro* fertilization outcomes. This study aimed to clarify the microbiota metabolism and their role in preimplantation development. **[Methods]** PICRUSt analysis using 16S rRNA gene sequences was performed to predict biological functions of microbiota in the human vagina. D-/L-amino acids (D-/L-AA) were analyzed using a two-dimensional HPLC system. To test the contribution of D-AA to preimplantation development, B6D2 F1 mouse embryos were subjected to culture AA-depleted medium. To explore the role of D-AA oxidase (DAO), immunocytochemistry was performed using a polyclonal antibody to DAO, and litter size of mice carrying a natural point-mutation (G181R) lacking DAO activity was observed. **[Results]** PICRUSt analy-

sis predicted abundance of metabolic genes for phenylalanine in the microbiota from pregnant group (P-group), whereas enriched metabolic genes for other amino acids in that from unpregnant group (U-group). AA analysis detected D-Serine, D-Alanine, D-Asparagine, and D-Proline, known as the *Lactobacillus* metabolite, in the vaginal, uterine, and follicular fluid of P-group. Follicular fluid that developed into blastocysts (N=3) contained more D-AA than that of arrested embryos (N=2). All of the embryos cultured in AA-depleted media (0.0% : 0/78) arrested, whereas 41% (25/61) of the embryos with D-AA supplemented to the AA-depleted medium developed into blastocysts. Mouse oocytes and blastocysts expressed DAO. DAO-null mice had fewer births than wild type. **[Conclusion]** Microbiota-derived metabolites D-AA may be involved in preimplantation embryo development.

ISP-18-10

Letrozole has a prophylactic effect on ovarian hyperstimulation syndrome in controlled ovarian stimulation: a randomized controlled study Takeda Takehiko, Osuka Satoko, Seki Tomomi, Kaseki Satoshi, Yabuki Atsushi, Tanaka Hideaki, Sonehara Reina, Miyake Natsuki, Muraoka Ayako, Nakanishi Natsuki, Nakamura Tomoko, Kajiyama Hiroaki *Nagoya University*

[Objective] Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening complication of controlled ovarian stimulation. Cabergoline or aromatase inhibitors are administered to prevent OHSS; however, only a few studies have directly compared these medications. We conducted a randomized controlled trial to compare the effects of cabergoline and letrozole on patients at high risk for OHSS. **[Methods]** From April 2020 to October 2022, patients who underwent oocyte retrieval (OR) for assisted reproductive technologies whose E2 levels were $\geq 3,000$ pg/mL were randomly assigned to receive cabergoline (0.5 mg) or letrozole (5 mg) for 5 days from the day of OR at our hospital. The severity of OHSS and blood sampling data after OR were evaluated. **[Results]** In total, 34 patients (cabergoline group, n = 16; letrozole group, n = 18) were included in this study. No significant differences were noted in patient characteristics (age, BMI, and the number of oocytes retrieved) or incidence of moderate-to-severe OHSS between the cabergoline and letrozole groups (80.0% vs. 82.3%, p = 0.56). Rates of hospitalization for severe OHSS (20.0% vs. 0%, p < 0.05) and incidence of nausea 1-3 days after OR (33.3% vs. 0%, p < 0.05) were significantly lower and serum albumin levels were significantly higher (3.78 vs. 3.85 g/dL, p = 0.036) in the letrozole group than in the cabergoline group. **[Conclusion]** This study demonstrated that letrozole was associated with lower hospitalization rates, nausea prevention, and better albumin levels than cabergoline. Letrozole can be an important option for OHSS prevention.

ISP-18-11

A Comparative Study of In Vitro Maturation Rates at Our Institute: Ovarian Tissue Oocytes vs. Punctured Follicle-Derived Oocytes Nakagawa Kohei, Wakimoto Yu, Sugimoto Mayuki, Nakayama Kana, Wakimoto Ken, Iwamoto Maiko, Korosue Maiko, Yamaya Ayano, Fukui Atsushi, Shibahara Hiroaki *The Hospital of Hyogo College of Medicine*

[Objective] This study investigates the efficacy of oocyte cryopreservation using ovarian tissue oocytes-in vitro maturation (OTO-IVM) for fertility preservation. We compared the maturation rates of punctured follicle-derived oocytes (p-FDO) and OTO. **[Methods]** Oocytes were laparoscopically retrieved from an ovary using a 23G needle. Retrieved immature oocytes, termed as p-FDO, underwent in vitro maturation. Simultane-

ously, the ovary's cortex was sliced for ovarian tissue cryopreservation. Detached cumulus-oocyte complexes (COC) from the ovarian tissue were cultured under the OTO-IVM protocol. Medical records were retrospectively reviewed to determine patients' age, maturation rates, and the number of cryopreserved oocytes. **[Results]** A total of 47 patients, with a mean age of 19.1 years (range : 2-43 years), underwent unilateral oophorectomy for fertility preservation. Out of these, 25 underwent IVM. From the ovarian tissues, 46 cumulus-oocyte complexes (COCs) were retrieved. The maturation rate for p-FDO was 35.8% (66/184), and oocytes were cryopreserved in 16 out of 25 cases. In contrast, the maturation rate for ovarian tissue oocytes (OTO) was 19.5% (9/46), with oocytes cryopreserved in 2 out of the 6 cases. Furthermore, immature oocytes were categorized based on the quantity of surrounding cumulus cells with maturation rates of 20% for naked oocytes, 17.6% for small COSs, and 21.0% for large COSs. **[Conclusion]** The maturation rate of p-FDO was higher than that of OTO ($p=0.034$). Even with residual cancer lesions in frozen ovaries, successful live births can be achieved without cancer recurrence concerns. OTO-IVM shows potential for better fertility preservation outcomes.

ISP-18-12

Sperm Mieap plays a critical role in in vitro fertilization and embryo development under in vitro culture conditions

Orisaka Makoto, Yoshida Yoshio *University of Fukui*

[Objective] In human assisted reproductive technologies (ART), the influence of sperm quality on embryo development during in vitro fertilization (IVF) is poorly understood. Mitochondria-eating protein (Mieap), also known as SPATA18, controls mitochondrial quality in cells and is involved in spermatogenesis. Here we report a critical role of Mieap in sperm function during IVF. **[Methods]** To investigate the physiological functions of Mieap, we generated Mieap-deficient (Mieap-KO) mice. We evaluate the morphology, motility, and reactive oxygen species (ROS) production of Mieap-KO spermatozoa derived from Mieap-KO male mice. We also conducted in vitro fertilization and intracellular ROS detection in embryos by using Mieap-KO spermatozoa. **[Results]** Mieap was highly expressed in the midpiece of flagellum, where sperm mitochondria are localized. Mieap-KO spermatozoa exhibited abnormal morphology, significantly decreased motility, and increased ROS production in mitochondria. Although Mieap was not involved in in vivo fertility, Mieap-KO spermatozoa reduced fertilization rates in IVF and arrested embryo development under in vitro culture conditions. Mieap-KO spermatozoa increased 2-cell block of embryo growth and induced oxidative stress in embryos during IVF. The 2-cell block of embryo growth induced by Mieap-KO spermatozoa was suppressed by hypoxic environment and antioxidant supplementation. **[Conclusion]** The present results suggest that sperm Mieap plays a critical role in in vitro fertilization and embryo development during IVF by preventing mitochondrial oxidative stress. Sperm Mieap may play a protective role in embryos under stressful culture conditions, such as IVF.

ISP-19-1

Clinical characteristics and pregnancy outcomes of incarcerated gravid uterus

Yamamoto Shotaro, Kurihara Yasushi, Kikuchi Taiki, Shibata Satoshi, Yoshida Tomohiro, Fukuda Eriko, Kitada Kohei, Hamuro Akihiro, Tahara Mie, Nakano Akemi, Misugi Takuya, Tachibana Daisuke *Osaka Metropolitan University*

[Objective] Incarcerated gravid uterus (IGU) is a rare obstetric complication and can lead to devastating obstetric complications if uterine retention persists during delivery. However, no definitive management for IGU has been established. The aim of

this study is to reveal the diagnosis, natural course and outcomes of IGU. **[Methods]** We examined IGU cases managed at our hospital from April 2011 to December 2022. IGU was defined as a retroverted or retroflexed uterus after 16 weeks of gestation. We observed natural courses of IGU without any manual reduction. **[Results]** There were sixteen cases of IGU among 8,301 pregnant women. Five cases (31%) were referred to our hospital with suspicious of placental malposition, eight cases were referred because of complication with myoma. Twelve cases (75%) were observed cervical deviation and/or extension. Spontaneous resolution of IGU after 16 gestational weeks was observed in eleven cases. Five of eleven cases resulted in vaginal delivery, while six cases required cesarean section for obstetrics indication. Five cases persisted IGU until delivery were performed cesarean section. One case was misdiagnosed as placenta previa, and uterine cervix was subsequently injured during cesarean delivery, resulting in massive hemorrhage. The newborn's condition was favorable in all cases. **[Conclusion]** In IGU cases, abnormal placental position and cervical changes (deviation and/or extension) were observed, which served as the diagnostic trigger. After diagnosis, expectant management with careful attention to the IGU may be one option in situations where there are no severe symptoms.

ISP-19-2

A discussion on possible influence of location of subchorionic cysts on a risk of fetal growth restriction based on a case of recurrent subchorionic cysts

Nakajima Hazuki, Moriyama Yoshinori, Naito Kana, Mitani Takeji, Sakabe Yoshiko, Noda Yoshiteru, Nakamura Masamitsu, Sekiya Takao, Nishizawa Haruki *Fujita Health University*

[Introduction] Subchorionic cysts are reported to be a risk factor of fetal growth restriction (FGR) when large or multiple, but causality of their location and FGR has not been established. Here we discuss it with a case of recurrent subchorionic cysts. **[Case]** A 37-year-old primipara was referred to our hospital due to FGR and GDM at 27 weeks' gestation. The first surveillance revealed FGR (-2.2 SD) and multiple placental cysts including one sized 3 cm at the cord insertion site (CIS). At 32 weeks she underwent an emergent C-section for fetal distress and delivered a healthy baby weighing 942 g (-3.0SD). Her placenta had a 3-cm cyst at 1 cm from CIS and a 5-cm cyst away, and showed infarction and paucity of villi. Two years later she came up at 21 weeks' gestation. Ultrasonography showed normal fetal growth and multiple placental cysts with one of them near CIS. At 35 weeks she delivered a 1,920-g (-1.6SD) healthy baby. Her placenta contained a 3-cm cyst at 2 cm from CIS and five cysts sized up to 4 cm away. **[Discussion]** Subchorionic cysts would cause FGR by cord compression when larger than 4.5 cm or more than three near CIS. In our case, a 3-cm cyst at 1 cm from CIS led to FGR, while a cyst of the same size at 2 cm did not. Thus, a cyst nearer than 2 cm from CIS can be a risk factor of FGR and a closer observation should be followed.

ISP-19-3

CASE REPORT : Mirror Image Artifact—A Heterotopic pregnancy copycat

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Background : Mirror image artifacts are created when ultrasound waves pass through a structure and encounter a strong and smooth interface that functions like a mirror, resulting to a copy of the same image. This artifact is commonly encountered by radiologists, but rarely seen in obstetric imaging. A lack of awareness can result in incorrect diagnoses and unnecessary surgeries. **Case :** 28-year-old G2P2 (2002) at 10 weeks age of ges-

tation was referred for an ultrasound to assess fetal viability. The patient was asymptomatic and had no previous ultrasound. A transvaginal ultrasound revealed an intrauterine pregnancy with crown rump length compatible with her last menstrual period. Sagittal and transverse views of the uterus showed the presence of another gestational sac containing a fetal pole located posterior to the uterus. Differential diagnosis was heterotopic pregnancy. Assessment of the extrauterine fetus was difficult because clear images of the entire fetus could not be obtained. Slightly delayed fetal movements were observed within the second gestational sac compared to the fetus within the uterus. A transabdominal ultrasound was performed, which showed the absence of the extrauterine fetus, thus confirming the presence of a mirror image artifact. **Conclusion :** Mirror image artifacts can lead to diagnostic inaccuracies. This case highlights that a thorough examination with awareness of the mirror image artifacts phenomenon, can facilitate accurate diagnosis and appropriate treatment. A potential factor contributing to the mirror image artifact could be the thin and flat posterior uterine wall, which functioned as an ideal reflector owing to the heightened acoustic interface.

ISP-19-4

Cesarean Section Scar Pregnancy : A Case Report Gonzales Gilana A, Diaz Ma. Rosario Laarni *Mandaluyong City Medical Center, Philippines*

Cesarean Scar Pregnancy is a rare type of ectopic pregnancy where the blastocyst is implanted in the myometrium and fibrous tissue of the scar after a previous cesarean section. A 35 year old Gravida3Para2 (2002) was admitted due to vaginal bleeding of one week duration. She had history of 2 Low Segment Cesarean Sections. For the present pregnancy, Transvaginal Ultrasound showed Early Intrauterine Pregnancy 5 weeks and 3 days Age of Gestation versus Ectopic Uterine Scar Pregnancy. She was eventually admitted with an impression of Cesarean Section Scar Pregnancy 5 weeks and 5 days age of gestation, unruptured for Methotrexate therapy. Ultrasound showed irregular gestational sac without cardiac activity attached within the cesarean section scar with a thin residual myometrium. Initial beta hCG determination result was 1271.24 mIU/mL. Methotrexate 87.7mg (3.5mL) by intramuscular route was given based on a 50mg per meter square of body surface area. With decreasing beta hCG and ultrasound examination showing less than 50% of the gestational sac, patient was sent home in good condition. After discharge, beta hCG monitoring showed the following results : 158.75, 82.02, 55.8, 34.4, 26.75, 20.48, 18.27 mIU/mL. She was then readmitted for a second dose of Methotrexate. On discharge, bHG was 8.75 mIU/mL. Due to the rarity of Cesarean Scar Pregnancy, the treatment remains to be undefined. Systemic administration of Methotrexate has proven to be effective but requires longer period for follow up until the beta hCG returns to normal and the gestational mass resolve completely.

ISP-19-5

Successful reduction of tocolytic drugs for twin pregnancies after fetoscopic laser surgery using indomethacin Tachihara Mayu, Takano Mayumi, Kamiya Mio, Kotaki Hikari, Shimabukuro Makiko, Nagasaki Sumito, Nakata Masahiko *Toho University Omori Medical Center*

[Objective] Preterm labor is a severe problem after fetoscopic laser surgery (FLS), which requires high doses of tocolytic drugs and sometimes multiple doses. This study investigated the utility of indomethacin for reduction of tocolytic drugs after FLS. **[Methods]** This study included monochorionic diamniotic twin pregnancies who underwent laser surgery for twin-to-twin

transfusion syndrome or selective fetal growth restriction at our hospital from 2015 to 2023. Medical records of all cases were reviewed retrospectively. Since indomethacin were used from 2020, all cases were divided into the control group (without indomethacin) and treated group (with indomethacin). Indomethacin was administered until 48 hours after surgery. This study was performed under the approval by the ethics committee of our hospital, and written informed consent was obtained from all patients. **[Results]** Seventy-eight patients were in the treatment group and 126 were in the control group. There were no cases of fetal adverse effects in the treatment group. The median of gestational age at delivery and the number of live births did not differ between the groups ($p > 0.05$). The treatment group required less median magnesium sulfate administration days than the control group (3 days [2-21 days] vs 9 days [2-119 days], $p < 0.01$). The use of nifedipine was significantly lower in the treatment group (44%) than in the control group (75%) ($p < 0.01$). **[Conclusion]** The administration of indomethacin did not associate with fetal adverse events, and it may be useful in the postoperative management because the simultaneous use of tocolytic drugs can be reduced.

ISP-19-6

Developmental process of fetal hypoxic/ischemic brain injury described by sequential ultrasound observations : Insights from a case of a donor fetus with twin anemia-polycythemia sequence Aoki Rumiko, Inoue Asami, Kurokawa Yusuke, Muto Megumi, Yokomine Masato, Horinouchi Takashi, Yoshizato Toshiyuki, Tsuda Naotake *Kurume University*

Introduction : We aimed to describe the developmental process of fetal hypoxic/ischemic brain injury by sequential ultrasound observations in a case of a donor fetus with twin anemia-polycythemia sequence (TAPS). **Case presentation :** A 34-year-old Japanese woman, gravid 3, para 2, was referred to our hospital at 23+5/7 weeks for the management of twin-to-twin transfusion syndrome (TTTS), which had developed at 21 weeks. Fetoscopic laser photocoagulation was not performed due to technical difficulties. Upon referral, the estimated body weights of the donor/recipient twins were 268/652 grams (-3.9/+0.1SD), indicating selective fetal growth restriction. The maximum systolic velocities of middle cerebral artery (MCA) were 48.4/23.8 cm/sec (1.58/0.78 MoM) with placental dichotomy, consistent with stage 3 TAPS. The resistance indices of the umbilical artery and MCA were 0.74/0.82 ($< 90 / < 10$ percentile), respectively with a normal brain morphology. At 25 weeks, no diastolic flows of MCA were observed in the donor fetus followed by the detection of diffuse hyperechoic patterns in the periventricular regions at 26 weeks. By 28 weeks, diastolic MCA flows returned to normal values, however bilateral ventriculomegaly was observed, which remained unchanged thereafter until the pregnancy was terminated at 34 weeks due to hypertensive disorders of pregnancy. TAPS was confirmed by umbilical arterial Hb levels of 14/18.0 g/dL. **Conclusions :** Profound anemia caused by TAPS initiated at 23 weeks, combined with preceding systemic hypoperfusion due to TTTS, resulted in irreversible hypoxic/ischemic brain injury. This injury was characterized by diffuse periventricular hyperechoic patterns which developed by 26 weeks, progressing to ventriculomegaly within approximately 2 weeks.

ISP-19-7

A case report : monochorionic diamniotic twin pregnancy with double velamentous cord insertion Tanaka Narumi, Shimura Koki, Katayama Akihisa, Tanaka Yukiko, Waratani Miyoko, Mori Taisuke *Kyoto Prefectural University of Medicine*

[Introduction] Although velamentous cord insertion (VCI) is

associated with adverse perinatal events, its association with twin-to-twin transfusion syndrome (TTTS) in monochorionic diamniotic (MD) twins remains unclear. [Case] A 30-year-old primiparous woman with MD twins was admitted at 26 weeks' gestation with persistently absent end-diastolic flow in the umbilical cord artery of twin A. No TTTS or selective fetal growth restriction (sFGR) was observed; however, VCI was detected in both twins. At 28 weeks' gestation, sFGR (type 2) was diagnosed in twin A due to fetal growth restriction (-1.7 standard deviation (SD)) without any abnormalities in either twin's amniotic fluids. Twin B was observed cardiac enlargement from 31 weeks' gestation and excessive amniotic fluid from 33 weeks' gestation. An emergency cesarean section was performed due to non-reassuring fetal status at 33 weeks' and 3 days' gestation. Twin A was a male weighing 1464 g (-1.9 SD) with Apgar scores of 5 and 8 at one and five minutes, respectively, and an umbilical artery blood pH of 7.318. Twin B was a male weighing 1687 g (-1.1 SD) with Apgar scores of 3 and 7 at one and five minutes, respectively, and an umbilical artery blood pH of 7.290 without anemia or hyperemia. The placenta revealed anastomotic vessels and VCI in both twins. Twin B had TTTS recipient-like changes after birth. [Conclusion] It may be important to identify placental cord insertion in MD twins to predict sFGR and TTTS.

ISP-19-8

Clinical outcomes of twin vaginal delivery with non-cephalic presentation of the second twin Ishii Yusuke, Hiramatsu Kosuke, Kawanishi Yoko, Okada Aiko, Nakamura Koji, Miyake Tatsuya, Kawano Mahiru, Mimura Kazuya, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University*

[Objective] Vaginal delivery (VD) of twins, especially of second twin being non-cephalic presentation should be managed by a team consisting of the experienced obstetrician. Thus, cesarean section (CS) for twin pregnancy with non-cephalic presentation of second twin is often chosen. This study focuses on the presentation of second twin and clinical outcomes when we attempted VD. [Methods] This is a retrospective study of 120 twin pregnancies with the vertex position of the first baby those attempted VD at our hospital from 2010 to 2023. All VD was managed by supervised residents. Clinical outcomes including success rate of VD were evaluated. [Results] Among 120 cases, 88 (73.3%) resulted in VD, 10 (8.3%) received CS for second twin, and 22 (18.3%) delivered both twins by CS. After VD of first twin, 65 second twin were in cephalic position and 60 (92.3%) resulted in VD, while 33 second twin were in non-cephalic position and 28 (84.8%) resulted in VD. There was no significant difference in the success rate of VD between these two groups (92.3% vs 84.8%; $p = 0.30$), as well as the time interval for delivery between two twins (mean minutes, 22.4 vs 17.1; $p = 0.37$). In addition, there were no significant differences in the 5-minute Apgar scores ($p = 0.86$) and umbilical artery blood gas analysis ($p = 0.33$). [Conclusion] In the case of VD for twin pregnancies, second twin presentation at delivery does not affect clinical outcome. Thus, twin VD could be attempted more.

ISP-20-1

Symphysial fundal height versus ultrasound estimated fetal weight in predicting small for gestational age Machimura Sakaaki¹, Masuda Tatsuo², Mimura Kazuya¹, Endo Masayuki¹, Kimura Tadashi¹ *Osaka University¹, StemRIM Institute of Regeneration-Inducing Medicine, Osaka University²*

[Objective] Symphysial fundal height (SFH) is used to screen for fetal growth retardation (FGR). Although ultrasound estimated fetal weight (EFW) is used in many centers in Japan, its accuracy in screening is not clear. The aim of this study is to de-

termine whether changes in SFH and EFW with pregnancy differ in their ability to predict small for gestational age (SGA). [Methods] This is a retrospective cohort study of singleton pregnant women who delivered at our hospital from January 2016 to August 2023 and had their SFH and EFW measured. SFH was measured at every antenatal examination after 16 weeks. Fetal ultrasound was performed by obstetricians and technicians, both trained by supervisors certified by the Japanese Society of Ultrasound Medicine, and EFW was basically measured at 18, 28, and 36 weeks. The Z-score was calculated for SFH and EFW. Infants who fell below the cut-off at least once during pregnancy were predicted to have SGA. Birth weight below -1.5 SD was considered SGA and ROC curves were constructed for each. [Results] There were 4073 singleton pregnancies and 258 cases of SGA. The median and interquartile range of gestational age were 39+0 and [38+0 - 40+1]. The AUC for predicting SGA using SFH and EFW were 0.724 and 0.905, respectively. The p-value obtained by Delong's test was <0.01. [Conclusion] In our setting, EFW was a better predictor of SGA than SFH. Because SFH is less variable between institutions, we recommend using SFH as a reference to confirm the accuracy of EFW.

ISP-20-2

Predicting severity of small for gestational age cases using fms-like tyrosine kinase receptor-1/placental growth factor ratio Yamashita Yuka¹, Matsuoka Ryu¹, Koide Keiko¹, Makino Koki¹, Goto Minako², Takita Hiroko¹, Arakaki Tatsuya¹, Tokunaka Mayumi¹, Kawashima Akihiro¹, Matsuura Rei¹, Komatsu Reina³, Sekizawa Akihiko¹ *Showa University¹, Showa University Northern Yokohama Hospital², Showa University Koto Toyosu Hospital³, Ebara Hospital¹*

[Objective] To analyze the characteristics of fms-like tyrosine kinase receptor-1 (sFlt-1) /placental growth factor (PIGF) ratio (FPR) in small for gestational age (SGA) and examine whether it can predict the severity of SGA. [Methods] This retrospective study included cases of singleton pregnancies in which the FPR was measured based on a common protocol at our affiliated institutions, from January 2022 to June 2023. First, we examined the patients diagnosed with SGA with regard to cause and severity. Second, we calculated the cutoff value to extract severe SGA cases and examined whether it was useful as a risk factor. Statistical analysis was performed using the χ -square test and logistic regression analysis. [Results] The total number of cases extracted was 135, of which 49 were SGA with a birth weight of -1.5 standard deviations (SD) or less. SGA due to placental factors was the most common (65.7%) and tended to have higher FPR and lower PIGF compared with SGA due to other causes. In severe SGA (-2SD or less), preeclampsia incidence and FPR were significantly higher than in SGA from -2 to -1.5 SD or less, and PIGF was also significantly lower. The cutoff value was 21.0 when calculated from the ROC curve with severe SGA as the outcome of all cases (area under the curve 0.75, 95% confidence interval 0.64-0.85). For a cutoff of 21.0 or higher, the odds ratio for severe SGA was 5.56 (95% confidence interval 2.1-14.7, $P < 0.001$). [Conclusion] FPR can be used to predict the severity of SGA.

ISP-20-3

Inflow pattern of fetal hepatic veins can differentiate between conducted and non-conducted premature atrial contractions Kaji Takashi, Shirakawa Aya, Minoda Ayuka, Yoshida Atsuko, Iwasa Takeshi *Tokushima University*

[Objective] Fetal hepatic venous (HV) Doppler has been used to diagnose fetal premature atrial contractions (PACs) due to the ease of recording the flow. However, fetal HV Doppler is

now considered to be impossible to differentiate between conducted PACs and non-conducted PACs. This study aimed to evaluate the use of inflow patterns of fetal HV Doppler in the differentiation of conducted PACs from non-conducted PACs. **[Methods]** This was a retrospective study of fetuses with PACs seen at our hospital between 2016 and March 2023. We used stored images of simultaneously recorded pulsed-wave Doppler signals in the fetal HV and descending aorta with the dual-gate Doppler. The inflow patterns of fetal HV Doppler wave following the PAC were divided into two patterns (monophasic or biphasic). Conducted PACs were differentiated from non-conducted PACs due to the presence of an aortic ejection wave following the PACs. **[Results]** Forty-six PACs (21 fetuses) were studied, including 25 conducted and 21 non-conducted PACs. On the inflow patterns of fetal HV Doppler, 25 PACs showed monophasic pattern, and 21 PACs showed biphasic patterns. All PACs with the monophasic pattern were non-conducted. Seventeen out of 21 PACs (81%) with the biphasic patterns were conducted, and the remaining 4 PACs were non-conducted. **[Conclusion]** The inflow of fetal HV Doppler following PACs showed different patterns by the presence of conducted ventricular contraction in fetuses with PACs. Monophasic pattern indicates non-conducted, and biphasic pattern indicates non-conducted. Fetal HV Doppler can diagnose not only PACs but also differentiate between conducted PACs and non-conducted PACs.

ISP-20-4

AI-based automated evaluation of the PLAS index/LAPSD ratio for the TAPVC detection Aoyama Rina^{1,2}, Komatsu Masaaki^{1,3}, Harada Naoaki¹, Komatsu Reina², Sakai Akira⁵, Matsuoka Ryu⁴, Sekizawa Akihiko² *Division of Medical AI Research and Development, National Cancer Center Research Institute¹, Showa University², Center for Advanced Intelligence Project, RIKEN³, Solution Transformation Unit, Fujitsu Ltd.⁴, Artificial Intelligence Laboratory, Fujitsu Ltd.⁵*

[Objective] Total anomalous pulmonary venous return (TAPVC) is one of the severe congenital heart diseases (CHD) requiring early diagnosis for improved prognosis. The PLAS (post-left atrium space) index and LAPSD (left-atrial posterior-space-to-diagonal) ratio are known indicators for the TAPVC detection (PLAS index > 1.0 and LAPSD ratio > 0.35 in TAPVC) in fetal cardiac ultrasound. In this study, we aimed to develop a fully automated evaluation method for these indicators using deep learning. **[Methods]** We enrolled 162 normal cases, 25 CHD cases (without TAPVC), and 6 TAPVC cases. YOLOv7 was used for automatic image extraction including the four-chamber view (4CV) from fetal cardiac ultrasound videos. DeepLabv3+, UNet3+, and SegFormer were used for segmentation and 5-fold cross-validation was performed. We evaluated segmentation performance using the mean Dice coefficient (mDice). The PLAS index/LAPSD ratio was calculated using each point-to-point distance automatically measured in pixels by the program. We then compared the performance of 3 deep learning-based models with 17 obstetricians in the area under the curve (AUC) of a receiver operating characteristic curve. **[Results]** SegFormer achieved the highest mDice for the aorta, heart, and crux: 0.845, 0.934, and 0.808, respectively. The PLAS index/LAPSD ratio were 0.495/0.202 in normal cases, 0.449/0.167 in CHD cases, 1.232/0.554 in TAPVC cases, respectively. SegFormer showed the highest AUC of 0.940/0.940, superior to obstetricians of 0.815/0.816 in the PLAS index/LAPSD ratio. **[Conclusion]** Our novel method achieved an accurate and automated evaluation of the PLAS index/LAPSD ratio in fetal cardiac ultrasound videos. It can lead to effective TAPVC detection.

ISP-20-5

Congenital diaphragmatic hernia coexisting with bronchopulmonary sequestration; their incidence and prognosis Hamamoto Eriko, Mimura Kazuya, Okada Aiko, Kawanishi Yoko, Nakamura Koji, Miyake Tatsuya, Hiramatsu Kosuke, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University Hospital*

[Objective] Congenital diaphragmatic hernia (CDH) and bronchopulmonary sequestration (BPS) are both rare diseases, but they have been reported to occasionally coexist. We report cases of CDH with coexistent BPS. **[Methods]** We retrospectively reviewed cases delivered and diagnosed as CDH or BPS at our institution from January 2010 to July 2023, and analyzed coexisting cases of CDH with BPS. **[Results]** There were 46 cases of CDH, all of which were prenatally diagnosed. There were 24 cases of BPS, of which 12 cases were prenatally diagnosed. There were 9 cases of CDH with coexistent BPS. Two of the 9 cases had a prenatal diagnosis of coexistence by fetal sonography and MRI, and one of them resulted in termination of pregnancy and the other survived after birth. Seven of the 9 cases were considered as CDH alone prenatally, and coexistent BPS was found incidentally during postnatal surgery. Four neonates of them were survived, and the other 3 died with postnatal circulatory failure. The mortality rate of BPS alone, CDH alone and coexisting cases was 0%, 17% and 37.5%, respectively. **[Conclusion]** It was not rare that CDH had coexistent BPS. Furthermore, the coexistent BPS may be a prognostic factor of CDH. Although difficult to detect prenatally, it is important to keep in mind the possibility that CDH has coexistent BPS.

ISP-20-6

Fetal lung size and survival in children undergoing fetoscopic endotracheal occlusion for severe congenital diaphragmatic hernia Ozawa Katsusuke¹, Kajiwara Kazuhiro¹, Muromoto Jin¹, Sugibayashi Rika¹, Wada Seiji¹, Sago Haruhiko² *Division of Fetal Medicine, National Center for Child Health and Development¹, Center for Medical Genetics, National Center for Child Health and Development²*

[Objective] The present study reports survival in children with severe congenital diaphragmatic hernia (CDH) undergoing fetoscopic endotracheal occlusion (FETO) and investigated the correlation between the survival of children and lung size after FETO. **[Methods]** The study included fetuses with severe left-sided CDH with observed/expected lung-to-head ratio (o/e LHR) < 25% who underwent FETO at our hospital between 2014 and 2023. The study excluded fetuses with chromosomal abnormalities, those that died in utero, and those in whom balloon occlusion failed. The primary outcome was survival 6 months after birth. The present study retrospectively reviewed data showing the observed/expected total fetal lung volume (o/e TFLV) measured using magnetic resonance imaging (MRI) and o/e LHR measured ultrasonographically before FETO and balloon removal. **[Results]** The study included 18 fetuses, of which 6 (33%) survived. FETO was performed at 27-29 weeks gestation in cases of severe left-sided CDH. Median gestational age at delivery was 36⁺¹ (30⁺⁵ to 39⁺¹) weeks. The median pre-FETO o/e TFLV and o/e LHR were 17% (9-35%) and 20% (8-24%), respectively. The median o/e TFLV and o/e LHR before balloon removal were 19% (10-89%) and 28% (14-62%), respectively. The o/e TFLV and o/e LHR were higher in survivors than in non-survivors before balloon removal (41% vs. 17%, p=0.01 and 47% vs. 24%, p<0.01). **[Conclusion]** Fetal lung size after FETO was greater in survivors vs. non-survivors. FETO led to an increase in fetal lung size and improved the survival of children with severe left-sided CDH.

ISP-20-7

A case of prenatally diagnosed fetal cardiac capillary hemangioma Shinagawa Masahiro, Maekawa Ryo, Sueta Mitsuo, Tamura Yuji, Matsui Fuka, Murata Susumu, Sugino Norihiro *Yamaguchi University*

[Introduction] The incidence of fetal cardiac tumors is reported to be 0.14 - 0.17% of congenital heart disease and 0.002% of all births. Hemangiomas are reported to be quite few, accounting for only about 2% of primary cardiac tumors in children. Here, we report a case of fetal cardiac capillary hemangioma diagnosed prenatally and resulting in emergency cesarean section due to fetal tachyarrhythmia and hydrops. **[Case]** 31-year-old pregnant woman, gravida 2 para 1, no significant family history. Ultrasonography at 28 weeks' gestation showed a 22*19 mm mass in the right atrial wall and pericardial effusion. Fetal MRI suggested cardiac teratoma or hemangioma. The mass gradually increased in size. At 32 weeks 5 days, the mass reached 37*35*29 mm, with extrasystoles and ascites. At 33 weeks 0 day, tachyarrhythmia was observed, resulting in fetal hydrops, and emergency cesarean section was performed. The neonate weighed 2,430 g and the Apgar score was 3 at 1 min. The neonate was intubated for asphyxia and admitted to the neonatal intensive care unit. Because treatment-resistant atrial tachycardia, atrial flutter and hemodynamic instability were observed, urgent resection of the tumor was performed at 2nd day after birth. Histopathology revealed a diagnosis of capillary hemangioma. **[Conclusion]** Fetal cardiac tumors, especially fetal cardiac capillary hemangioma, are very rare. Since cardiac hemangioma can cause fetal arrhythmia, leading to fetal hydrops and eventually fetal death, the fetal condition should be evaluated frequently by using ultrasonography.

ISP-20-8

Retrospective Analysis of 4 Cases of Intracranial Hemorrhage with Fetal Ventriculomegaly in Our hospital Tanaka Yukiko, Katayama Akihisa, Shimura Koki, Waratani Miyoko, Mori Taisuke *University Hospital, Kyoto Prefectural University of Medicine*

[Objective] Fetal intracranial hemorrhage (ICH) is rare. Diagnosing ICH during the fetal period is challenging due to the dynamic nature of hemorrhage, often resulting in ventriculomegaly. We examined the four cases with fetal ventriculomegaly that were diagnosed with ICH after birth. **[Methods]** This retrospective study included 24 singleton fetuses with fetal ventriculomegaly who were delivered in our hospital between 2020 and 2023. Among the 24 cases of fetal ventriculomegaly, four cases (16.7%) were diagnosed with ICH after birth. We evaluated prenatal management and adverse neurological outcomes in these four cases. **[Results]** Among the four cases, one fetus was diagnosed with ICH based on prenatal ultrasound and MRI studies. In the remaining three cases, ICH was not evident on prenatal examination, but was confirmed on postnatal MRI. In one of these cases, fetal ventriculomegaly was mild, but genetic testing revealed Sotos syndrome, and developmental delay was observed at age 1. In the other two cases, MRI showed no obvious abnormality and no developmental delay at 1 year of age, despite a severe fetal ventriculomegaly diagnosis and undergoing VP shunting procedures. **[Conclusion]** The prognosis of fetal ICH depends on the presence of underlying hemorrhagic disease, which do not correlate with the severity of fetal ventriculomegaly. This makes it challenging to predict the prognosis during pregnancy. Even in cases where fetal ventriculomegaly is mild, careful prenatal management and postnatal evaluation are essential.

ISP-20-9

Prenatal diagnosis and evaluation of congenital diaphragmatic hernia ; early evaluation did not predict its prognosis Komatsu Naoto, Nakamura Koji, Kawanishi Yoko, Okada Aiko, Miyake Tatsuya, Hiramatsu Kosuke, Kawano Mahiru, Mimura Kazuya, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University*

[Objective] The severity of congenital diaphragmatic hernia (CDH) is usually determined at initial prenatal diagnosis, however, it does not always correlate with the postnatal prognosis. Here we aim to identify the optimal timing to evaluate the severity of CDH to predict postnatal prognosis. **[Methods]** We retrospectively analyzed left CDH cases who were prenatally diagnosed at our Hospital and delivered at 34 0/7 weeks of gestation or later between January 2016 and December 2022. According to the previous representative studies, the severity of CDH was categorized into three groups ; mild, moderate, and severe based on the value of observed/expected lung area to head circumference ratio and liver position. The severity of CDH was evaluated at the initial diagnosis and reassessed at the last prenatal visit. The postnatal outcome was evaluated by mortality rates. **[Results]** 23 cases were included in this study. The median of initial and last evaluation of CDH severity were 27 and 37 weeks of gestation, respectively. At each evaluation, the number of cases and mortality rate were as below (death/cases) ; initial (mild 2/14, moderate 3/8, severe 0/1), last (mild 0/12, moderate 3/7, severe 2/4). The CDH severity changed between initial and last evaluation in 12 cases (52%). Four of 8 cases died whose severity worsened at the last evaluation, whereas all of 4 cases survived whose severity became milder. **[Conclusion]** The last prenatal visit might be superior to the initial visit as the timing of CDH evaluation to predict postnatal outcome.

ISP-20-10

Retrospective review of the cases with hypospadias in five years Ishida Yuri, Yamamoto Yuka, Mieda Haruka, Yamada Taihei, Sugimura Yusen, Seyama Rie, Kitamura Eri, Matsuzawa Nana, Takeda Jun, Itakura Atsuo *Department of Obstetrics & Gynecology, Juntendo University*

[Objective] Hypospadias can be diagnosed on fetal ultrasound by characteristic findings such as the penis being buried in a bifid scrotum or tulip sign, but it is still difficult to detect hypospadias prenatally. We aimed to improve the detection of prenatal hypospadias by reviewing maternal and disease characteristics of hypospadias delivered at our hospital, including two cases with prenatal diagnosis. **[Methods]** We retrospectively reviewed cases delivered at our hospital and diagnosed with hypospadias after birth between Jan. 2018 and Dec. 2022. Maternal characteristics, classification of hypospadias and characteristics of external genitalia were compared. Only fetal second trimester ultrasound screening is performed around 20 weeks in our hospital. **[Results]** There were 6103 deliveries during the study period, and 7 cases (0.11%) were diagnosed with hypospadias after birth. The maternal age was 33.8±4.3 years, the gestational age at birth was 36.1±3.1 weeks, and the birth weight was 11±8.32 percentile. Three cases with fetal growth restriction (FGR), 3 (42.9%) hypertension induced pregnancy (HDP) and 2 trisomy 21 were complicated. The type of hypospadias was 6 scrotal (85.7%), 1 proximal, and 3 cases with bifid scrotum (42.9%). Both prenatally diagnosed cases were found to have bifid scrotum and tulip sign on fetal ultrasound which led to the prenatal diagnosis without FGR or other complications or chromosomal abnormalities. **[Conclusion]** In cases of FGR, HDP, and chromosomal abnormalities, a detailed fetal evaluation, including careful observation of the vulva, may lead to the prenatal diagnosis of hypospadias.

ISP-20-11

Investigation of the obstructive site and prenatal ultrasound features in fetal small bowel atresia Matsuzawa Nana, Yamamoto Yuka, Mieda Haruka, Seyama Rie, Kitamura Eri, Ishida Yuri, Takeda Jun, Itakura Atsuo *Juntendo University* [Objective] In this study, we compared the ultrasonographic findings of prenatally diagnosed small bowel atresia (SBA) with the site of obstruction confirmed by postnatal surgery to determine whether prenatal ultrasonographic findings can predict the site of obstruction. [Methods] We retrospectively reviewed 11 cases diagnosed with fetal SBA at our hospital between 2019 and 2022. The width and length of the dilated intestinal tract and the number of cysts were evaluated by horizontal and sagittal sections of prenatal ultrasound images. We also extracted records about the time of diagnosis, amniotic fluid volume, and course of the disease. The postnatal outcome was referred to the operative record. [Results] There were 6 jejunal atresias (JA), 3 ileal atresias (IA), and 2 cases that did not require postnatal surgery. The timing of the diagnosis was at 28 (22-32) weeks in JA, and 28 (24-30) weeks in IA. The number of bubbles increased significantly as the occlusion site became lower ($p < 0.01$). The dilation was 28.65mm (10-30.4) and 30.9mm (21.4-38.8), the length was 83.85mm (35.5-149.6) and 71.95mm (66.8-77.1) in JA and IA, respectively. There was no significant correlation between the obstruction site and dilated condition. Polyhydramnios was significantly more common in JA than IA. [Conclusion] It was difficult to evaluate the position of the obstructed site according to the combined length and dilation of the bowel on ultrasound in SBA cases. The number of bubbles on ultrasound and clinical course during pregnancy might help distinguish between JA and IA.

ISP-20-12

Posterior urethral valves with patent urachus, allantoic cyst, bilateral hydroceles and bladder rupture : A rare presentation of urinary tract malformations Plenty Nicole L¹, Efeadue Latoya¹, Batiste Kierra² *Wellstar Health System, USA¹, Lincoln Memorial University-DeBusk College of Osteopathic Medicine, USA²*

Introduction : Posterior urethral valves (PUV) are the most common cause of fetal lower urinary tract obstruction typically presenting with oligohydramnios, keyhole sign, and hydronephrosis. A third of these cases have a patent urachus resulting in normal amniotic fluid. Few cases of a combination of bladder rupture with PUV exist but no cases associated with a patent urachus or our associated findings. **Case description :** We present a 27-year-old primigravida initially seen during the 28th week of pregnancy for the indication of fetal hydronephrosis. Bilateral UTD-A2/3 observed with what was initially suspected to be a large right hydroureter. During her subsequent scan, the size of the cyst increased in size with the bladder still appearing without a keyhole sign. Due to social issues, she re-presented five weeks later with fetal ascites, decrease in size of the cystic structure, now with connection seen to the abdominal wall. Bilateral hydroceles were also observed. Fetal MRI was done in the 34th week, confirming suspicion of PUV, patent urachus, with urinary ascites caused by fetal bladder rupture. Bilateral hydroceles were also seen. Due to cholestasis and lack of compliance, the patient was delivered via C-section in the 36th week with observation of an allantoic cyst at the cord insertion in addition to antenatal findings. **Discussion :** This case demonstrates the rare combination of urinary tract abnormalities and the importance of keeping PUV with patent urachus and bladder rupture in the differential with fetal presentations of worsening hydronephrosis, ascites and normal amniotic fluid or even polyhydramnios.

ISP-20-13

A Case of Costello Syndrome Diagnosed by Whole-Genome Sequencing in Nonimmune Hydrops Fetalis with Increased Nuchal Translucency Kim Su Mi^{1,2}, Lee Ru Mi², Hong Seung Hwa^{1,2}, Ji Il Woon^{1,2}, Jeong Eun-Hwan^{1,2} *Chungbuk National University, Korea¹, Chungbuk National University Hospital, Korea²*

[Objective] We present a case of nonimmune hydrops fetalis (NIHF) with increased nuchal translucency (NT) diagnosed with Costello syndrome (CS) using whole-genome sequencing (WGS). [Case description] A 26-year-old nulliparous woman was referred at 12 5/7 weeks of gestation due to increased NT, which measured 4 mm. Non-invasive prenatal testing was performed, yielding low-risk results. At 21 6/7 weeks of gestation, bilateral ventriculomegaly was detected. At 28 2/7 weeks of gestation, right-sided pleural effusion developed. At 32 6/7 weeks of gestation, polyhydramnios, bilateral pleural effusion, hepatomegaly, and anemia (MCA PSV >1.5MoM) were detected. A cesarean section was performed at 33 2/7 weeks of gestation. The female infant had a birth weight of 2790 grams (98th percentile) and a head circumference of 34 cm (100th percentile), indicating macrosomia and macrocephaly. She was diagnosed with Persistent Pulmonary Hypertension of the Newborn through echocardiography. Despite receiving ventilation support, she died four days after birth due to multiple organ failure. WGS was undertaken for diagnostic investigation. A de novo heterozygous HRAS variant (NM_005343.4 : c.37G>T, p. Gly13Cys) was detected, and the diagnosis of CS was established. [Discussion] CS is a rare genetic condition, part of the RASopathies caused by HRAS mutations. Traditional genetic tests like karyotyping or chromosomal microarray only ascertain the cause in 25% of NIHF cases and do not detect single-gene disorders. Establishing a precise diagnosis of NIHF improves the accuracy of counseling, including prognosis, recurrence risk assessment, and clinical care. [Conclusion] To enhance perinatal outcomes, accurate diagnosis through WGS is necessary for NIHF.

ISP-20-14

Observations on the detection and management of fetal anomalies at a community clinic : Insights from three cases Huang Sing Ying *WS Mombaby Clinic, Taiwan*

A detailed fetal anatomic ultrasound, often referred to as level II sonography, is not a routine prenatal examination for all pregnancies. Nevertheless, due to the widespread availability of ultrasound facilities and its relatively affordable cost in Taiwan, a significant proportion of pregnant women opt to undergo level II sonography. This has resulted in a notably high detection rate of fetal anomalies, providing an early opportunity for additional examinations such as genetic testing, such as karyotyping and array CGH, as well as the possibility of termination if deemed necessary. This trend is particularly prominent in urban areas and extends to minor anomalies. In this context, I would like to present three cases of fetal anomalies that were detected through level II sonography at the obstetrics and gynecology clinic where I practice. These cases involve the identification and management of a duplicated collecting system, sacrococcygeal teratoma, and pulmonary valve stenosis. This encompasses the entire process, from the initial diagnosis to patient explanation, referral to a tertiary referral hospital for precise evaluation, coordination of further examinations and postnatal treatment, and the ongoing monitoring of each case's prognosis.

ISP-21-1

Laparoscopic fixation of a prolapsed neovagina created using atelocollagen : A case report Kamada Yasuhiko,

Kawaguchi Yurika, Okamoto Ryota, Kashino Chiaki, Kubo Kotaro, Mitsui Takashi, Masuyama Hisashi *Okayama University*

Neovaginal prolapse often occurs in women following sigmoid vaginoplasty for vaginal defects, such as those associated with Mayer-Rokitansky-Küster-Hauser Syndrome (MRKHS). However, no studies have reported neovaginal prolapse after vaginoplasty using atelocollagen (artificial dermis). Herein, we report a rare case of recurrent neovaginal prolapse after vaginoplasty using atelocollagen following laparoscopic fixation during each event. [Case] A woman in her 20s diagnosed with MRKHS underwent laparoscopic-assisted vaginoplasty using atelocollagen. She experienced difficulty with intravaginal prosthesis removal four years postoperatively. Laparoscopic fixation was planned for a later date for managing the neovaginal elongation and vaginal blind-end drooping. The patient returned with genital bleeding and abdominal pain four years and seven months postoperatively. An intestinal prolapse from the vaginal introitus was suspected and managed via emergent surgery. Perioperative vaginal reassessment revealed an inverted neovagina, rather than intestinal prolapse. Laparoscopic evaluation revealed a finger-sack shaped neovaginal apex. To prevent re-drooping, the neovagina was fixed in the pelvic cavity with six single ligations using 4-0 PDS sutures bilaterally on the rudimentary uterus. However, she returned eight months later with difficulty in self-management. Her vaginal length measured 15 cm, and laparoscopic neovaginal shortening and re-fixation were performed. Considering her youth and the possibility of a future repeat operation, the neovagina in the pelvic cavity was fixed without a mesh, using non-absorbable sutures. The neovaginal apex was purse-string sutured twice and fixed to the right ovarian ligament and the right round ligament. No neovaginal prolapse was observed at the 9-month follow up.

ISP-21-2

A retrospective study of abdominal wall and umbilical adhesions after abdominal surgery Kawasaki Yu, Murakami Keisuke, Okada Yukiko, Ochiai Asako, Takeuchi Shiori, Yanagihara Yasuho, Kitade Mari, Itakura Atsuo *Juntendo University*

[Objective] Complications during the first puncture are a concern in laparoscopic surgery in patients with previous abdominal surgery. There is a lack of studies on how much abdominal wall adhesions from abdominal surgery affect laparoscopic surgery. The frequency and trends of umbilical and abdominal wall adhesions due to previous abdominal surgery are analyzed. [Methods] The abdominal wall and umbilical adhesion rates were compared retrospectively in 3902 patients (previous abdominal surgery, group P : 792 patients ; no previous abdominal surgery, group N : 3110 patients) who had undergone laparoscopic surgery. In addition, the association between previous wound site, previous operative technique, number of previous operations, and umbilical bowel adhesions was assessed. [Results] The intestinal adhesions in the umbilical region, which are a risk of organ injury during the first puncture, were significantly more common in the P group [P group : 10/792 (1.3%) ; N group : 1/3110 (0.03%)]. Furthermore, intestinal adhesions in the umbilical region were found in 6/15 (40%) patients with an upper midline abdominal incision and 6/15 (40%) patients with previous gastrointestinal surgery [upper gastrointestinal region (laparotomy) : 6/15 (40%), laparoscopic surgery : 2/20 (10%) ; lower gastrointestinal region (laparotomy) : 7/196 (3.6%)]. The frequency of umbilical adhesions tended to increase with increasing number of previous operations (1 : 3.7%, 2 : 9.7%, 3 : 16.7%). [Conclusion] Intestinal adhesions in the umbilical region are predominantly increased in upper midline abdominal incisions and gastrointestinal surgery and in multiple previous operations.

ISP-21-3

Efficacy of flexible hysteroscopy for cases diagnosed with endometrial thickening by transvaginal ultrasound Maebayashi Aki¹, Shimogawa Saori², Yoshida Yukihiko^{1,2}, Ajioka Hiromi^{1,2}, Kawatake Rina², Nagaishi Masaji¹, Kawana Kei² *Nihon University¹, Nihon University Itabashi Hospital²*

[Objective] Endometrial thickening during menopause is suspected to be cancer or endometrial hyperplasia, and uterine body cytology is often performed. Uterine body cytology has a sensitivity of 79% and specificity of 99%, and because the accuracy of a single test is low, examinations are sometimes performed repeatedly and followed up over a long period. We investigated the efficacy of flexible hysteroscopy for cases diagnosed with endometrial thickening by transvaginal ultrasound. [Methods] From March 2022 to September 2023, patients were referred to our hospital for detailed examination of endometrial thickening. Age, menopause, symptoms, endometrial thickness, follow-up period, hysteroscopy findings, and histopathological diagnosis were retrospectively studied. [Results] The age range was 47-65 (median 50) years, 53% (7/13) were menopausal, and 30% (4/13) had irregular bleeding. Endometrial thickness ranged from 8 to 20 (median 15) mm, and follow-up period ranged from 0 to 60 (median 10) months. Hysteroscopy revealed endometrial polyps in all cases, and hysteroscopic surgery was planned and performed. At the same time, abnormal findings suggestive of malignancy, such as abnormal blood vessels and papillary masses, were observed in 23% (3/13) of the cases, all of which were patients taking tamoxifen. Postoperative pathological diagnosis results were benign endometrial polyps in all cases. [Conclusion] Flexible hysteroscopy is valuable for determining treatment strategies, as it prevents repeated examinations over a long period. In addition, patients taking tamoxifen may show abnormal findings on flexible hysteroscopy, and although the lesion in this case was benign, caution may be required.

ISP-21-4

Robot-assisted total hysterectomy using Force Bipolar in the 3rd arm—Triple bipolar method— Kanno Toshiyuki, Motohashi Takashi, Funamoto Hiroshi, Kumakiri Jun, Tabata Tsutomu *Tokyo Women's Medical University*

[Objective] In robot-assisted total hysterectomy (RAH), the hemostasis and coagulation by bipolar forceps manipulated by left hand is commonly performed ; however, the technique is occasionally difficult to perform for the right-side pelvic cavity of patient. Moreover, switching forceps during robot-assisted surgery is occasionally inefficient for surgical duration. Against the background, we devised a novel method of triple bipolar placement for being possible to multidirectionally perform hemostasis and coagulation. [Methods] From November 2021 to January 2023, the author operated 19 cases of RAH by the TB (triple bipolar) method. Two "Force Bipolars" were inserted to the trocars with first arm manipulated by surgeon's left hand and third arms with the arm manipulated by the surgeon's right hand. "Maryland bipolar" was inserted to the trocar with the arm manipulated by the surgeon's right hand. [Results] The hemostasis and coagulation for right-side of pelvic cavity was freely and effectively achieved by the method. Especially, it was easier to perpendicularly apply the "Force bipolar" inserted to the trocar with 3rd arm to the right uterine artery. In addition, the grasping system by the "strong mode" of "Force bipolar" is equivalent performance to that of "ProGrasp forceps". Therefore, surgical field was appropriately obtained by pulling uterus even when the uterine manipulator was not effective. There was no difference in the surgical outcomes of 19 cases compared to the surgery previously performed by our conventional method. [Con-

clusion] We suggested that the TB method is useful in RAH for multidirectionally manipulations including hemostasis and coagulation.

ISP-21-5

Comparing peri-operative outcomes between minimally invasive hysterectomy with specimen extraction versus abdominal hysterectomy Cochrane Caroline¹, Thomas Jonathan¹, Burns Jersey¹, Morgan Samuel E², Zdroik Anna¹, Moulder Janelle K¹ *Wake Forest University Health Sciences, USA¹, Wake Forest University, USA²*

[Objective] Minimally invasive (MIS) hysterectomy is the recommended modality for gynecologic surgery given known benefits of decreased hospital stay and wound infections. Various methods of specimen extraction have been utilized to achieve a minimally invasive approach, however, comparisons between MIS hysterectomy with specimen extraction and abdominal hysterectomy (AH) are not well-reported. The purpose of this study was to compare MIS hysterectomy with specimen extraction to AH with regard to intraoperative and postoperative outcomes. **[Methods]** A retrospective chart review was performed on patients undergoing hysterectomy for benign indications at an academic tertiary medical center from 2017-2021. Patient demographics, modality of surgery, and perioperative outcomes were collected. Outcomes included intraoperative data and composite adverse events (AE) within 90 days. Descriptive, bivariate, and multivariate analyses were performed. **[Results]** Patients underwent 109 MIS hysterectomies with specimen extraction : 450 AH. Mean uterine weight was smaller with MIS hysterectomy (225g vs 522g, $p < 0.01$). MIS hysterectomy had shorter length of stay (1.4 vs. 3.3 days, $p < 0.01$) and fewer intraoperative adverse outcomes (AOR 0.41, 95% CI 0.19-0.89). A composite of medical and surgical 90-day outcomes were less likely to occur among MIS hysterectomy when compared to AH (AOR 0.38, 95% CI 0.17 - 0.87). **[Conclusion]** MIS hysterectomy remains the preferred route of surgery. Our data support that MIS hysterectomy with specimen extraction by any modality is a safe alternative to abdominal hysterectomy for benign indications. Patients have fewer rates of intraoperative complications and shorter hospitalizations, as well as fewer 90-day postoperative adverse outcomes.

ISP-21-6

Vaginal Agenesis—A modified and simplified Laparoscopic Vaginoplasty Dixit Kamad¹, Chaube Sanjay², Claube Jyoti³, Nigam Parul¹ *Surgery, Nirmla Hospital, India¹, Division of Minimally Invasive Surgery, St. Jude's Hospital, India², Division of Radiology, St. Jude's Hospital, India³, St. Jude's Hospital, India⁴*

[Objective] Vaginal atresia is rare but it has devastating consequences on the social and mental health of the patient. To rectify the problem of vaginal agenesis many procedures are described. They are expensive with high morbidity. Due to poor economic and social status they are not able to go under costly procedures. **[Methods]** A modified laparoscopic with the help of locally available materials was designed to cut the cost and make it available for the socially, economically and mentally devastated patient and her family. It was performed with the help of locally developed olive and traction device. A glass olive was put at the vaginal dimple and a traction thread was passed with the help of atraumatic safety needle between the vesico-uterine fold and taken out at suprapubic region and a locally developed traction device was attached to it. Daily traction was increased and it created a space within the rectovaginal space. **[Results]** In total twelve cases this modified and cost effective procedure was performed which gave good functional space over a period of 5 to 7 days. There was no major morbidity except some pain due

to traction which was controlled with oral analgesics. **[Conclusion]** This was a very simple procedure can be performed with common laparoscopic instruments and locally made olive and traction device. This gives good functional results with minimum morbidity and high rate of satisfaction to the patients.

ISP-21-7

Trends of Fistula Management During Covid 19 Pandemic in a Tertiary Care Hospital Zafar Majida, Luqman Sobia, Rauf Sidra, Naeem Shumaila, Nasir Sannia, Akram Iqra, Hina Haadia, Batool Mussarat, Jalil Mazhar *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] To highlight the trends of fistula management during and after the COVID-19 pandemic. **[Methods]** This retrospective study was conducted for a period of around 3 years i.e. 2020, 2021 and 2022. **[Results]** In this study a total of 203 women were enrolled. Most of the cases 159 (78.3%) had iatrogenic causes of fistula while 44 (21.7%) had obstetric causes. There was a decreasing trend of iatrogenic and an increasing non-linear trend of obstetric causes in our patients from 2020 to 2022 (p -value, 0.04). In two-third cases of type of fistula was VVF while one-third had RVF. The type of fistula was VVF in 41 (61.2%) cases in the year 2020, 56 (83.5%) had so in 2021 whereas 50 (72.5%) had VVF in 2022. Similarly, there were 26 (38.8%) cases of RVF in 2020, 11 (16.4%) in 2021 whereas 31 (44.9%) in 2022. This non-linear trend was also found statistically significant between the three years (p -value, 0.003). Very few cases 26 (12.8%) were abdominally repaired in the study while most were managed via vaginal repair 105 (51.7%) and RVF repair (33.5%). There was a decreasing trend of abdominal repair and vaginal repair noted in the study while RVF repairs were on the rise from the year 2020 to 2022. There was a significant linear trend of repair techniques noted year wise (p -value, < 0.001) **[Conclusion]** maternity services need to be continuously educated regarding up scaling of routine skills, so that iatrogenic and obstetric fistula could be reduced.

ISP-21-8

Laparoscopic Management of Acute Abdomen in Female Patients with Pelvic Masses Chaube Jyoti¹, Nigam Parul³, Chaube Sanjay² *Radiology, St. Jude's Hospital, India¹, Division of Minimally Invasive Surgery, St. Jude's hospital, India², St. Jude's Hospital, India³*

[Objective] Acute abdomen due to gynecological causes are mainly due to ectopic gestation, torsion of adnexa, rupture of ovarian tumour or ovarian bleeding. Diagnostic modalities are inconclusive or some time not available. Laparotomy was the main part for confirmation and treatment. Laparoscopy was offered as diagnostic and therapeutic modality. **[Methods]** Laparoscopy was performed in 108 of acute abdomen of gynecological problems. Laparoscopy not only clinched the diagnosis of acute abdomen but also have a therapeutic benefits. Majority of patients were of ectopic gestations. Eleven were of twisted adnexa, two were of pyosalpinx, one was of ovarian bleeding and four were of nongynecological causes. Laparoscopic management was performed in ectopic gestation in form of salpingostomy, salpingectomy or electrocautery of unruptured ectopic. Salpingectomy was performed in pyosalpinx. Twisted adnexa were detwisted and cystectomy was performed. **[Results]** in our study ectopic gestation is the major cause of acute abdomen of gynecological causes. **[Conclusion]** Laparoscopy is not only a good tool for confirmation of cause of acute abdomen but it can manage the etiology of the acute abdomen with minimum morbidity.

ISP-21-9

Laparoscopic management of Iatrogenic Uterine Perforations Singh Anupama¹, Singh Rajesh², Chaube Sanjay³ *Singh Hospital, India*¹, *Division of Minimally Invasive Surgery, Singh Hospital, India*², *Division of Endoscopic Surgery, St. Jude's Hospital, India*³

[Objective] Uterine perforation is a dreaded complication of D& C performed to evacuate uterine pathology or to terminate the early pregnancy. If the breach of the uterine wall occurs during the procedure leads to severe morbidity and mortality sometime. We frequently encounter uterine perforations at our peripheral hospital. The traditional approach was formal laparotomy to manage it. **[Methods]** laparoscopy was performed in such case in whom uterine perforation was diagnosed or suspected. In total five patients of suspected uterine perforations with stable vitals laparoscopy was done. In three patients there was breach at the fundus with minimal collection no bowel or major injury was noted In one patient patient was having ectopic gestation with breach of uterine wall salpingectomy and closure of rent was done, In one patient there was breach of uterine fundus with perforation of small bowel and contamination of the peritoneal cavity with bile. Formal laparotomy with repair of small bowel and uterine breach done peritoneal lavage done. **[Results]** All patients completely recovered patients treated with laparoscopic modality were discharged after 72 hrs. **[Conclusion]** Laparoscopy should be tried in patients of suspected uterine perforation as this give good results with less morbidity and laparotomy can be avoided.

ISP-21-10

A longitudinal study on metabolic profiling of menopause : a large-scale population-based cohort study in Japan Miyake Atsuko^{1,2}, Iida Miho², Takebayashi Toru², Banno Kouji¹, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University*¹, *Department of Preventive Medicine and Public Health, Keio University*²

[Objective] Various health risks including metabolic syndrome (MetS) increase rapidly after menopause. Metabolomics studies reporting differences in metabolic profiles of pre- and post-menopausal women suggest their potential associations with such elevated risks. However, few reports have investigated them in a longitudinal design. We aimed to investigate metabolite changes induced by menopausal transition and their associations with MetS using a longitudinal study. **[Methods]** Participants were premenopausal women enrolled in the baseline survey of a large-scale population-based cohort study in Japan and had data from at least one of two follow-up surveys. At each survey, menopausal status and data on MetS were collected, and plasma metabolites such as amino acids were profiled with capillary electrophoresis mass spectrometry. Thirty-one metabolites were investigated for their associations with menopausal transition using a mixed-effects model. Discriminant analysis was performed to examine whether these metabolites could determine later development of MetS. **[Results]** A total of 938 women (43.9 ± 5.3 years old) were included in the analysis, and 318 (33.9%) reached menopause during follow-up (5.0 ± 1.1 years). Sixteen metabolites significantly increased from pre- to post-menopause during follow-up. In the analysis on MetS, 310 women were MetS-free at baseline, of whom 16 (5.2%) subsequently developed MetS. Discriminant analysis showed that glutamate concentration greatly contributed to the determination of MetS onset, with a variable importance in projection score > 1.5. **[Conclusion]** Our longitudinal study showed plasma concentrations of numerous metabolites increased as women shifted from pre- to post-menopause. These changes may reflect the mechanism of increased MetS risk with menopause.

ISP-22-1

Preoperative Platelet/Lymphocyte Ratio and Hemoglobin Level as Predictors to Estimate Lymph Node Metastasis in Endometrioid type Endometrial Cancer Wang Shao Chi *Gynecology Oncology, Kaoshiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan*

[Objective] Previous studies had investigated that higher level of neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) were found in patient with cancers. Besides, some studies announced NLR and PLR had positive association with myometrial invasion and as a prognostic factor of endometrial cancer (EC). Our aim is to find predictor from preoperative hemogram in order to predict lymph Node Metastasis (LNM). **[Methods]** We retrospectively investigated patients with endometrioid EC who underwent complete staging surgery during January 2015-June 2022 in our hospital. We collected hemogram data before surgery. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values by determining the point with the maximal Youden index. Multivariate logistic regression analyses was used to find the impact of different variables on LNM. **[Results]** Total 510 cases of endometrial cancers underwent staging surgery from January 2015 to June 2022. Ultimately, 355 patients were included in this study. The optimal cut-off values for the PLR, NLR, and hemoglobin (Hb) were determined to be 127.5 (AUC 0.611, p=0.010), 1.65 (AUC 0.580, p=0.041), and 13.25 g/dL (AUC 0.608, p=0.011), respectively. Multivariate analysis revealed that PLR > 127.5 (OR : 2.508 ; 95% CI : 1.105-5.689) and Hb < 13.25 g/dL (OR : 2.586 ; 95% CI : 1.095-6.106) were independent predictors. If both PLR ≤ 127.5 and Hb ≥ 13.25 g/dL, the predicted risk of LNM is 3.186%. The negative predictive value is 97.1%. **[Conclusion]** We could simply use pre-operative hemogram to estimate the risk of LNM in patients with endometrioid EC. This could serve as a reference to avoid routine complete lymphadenectomy.

ISP-22-2

Management of over forty-year-old women with atypical endometrial hyperplasia or endometrial cancer after fertility-sparing therapy Okuya Rie¹, Habu Yuji¹, Otsuka Satoyo¹, Katayama Eri¹, Nakamura Natsuko¹, Matsuoka Ayumu¹, Nishikimi Kyoko¹, Tate Shinichi¹, Ishikawa Hiroshi¹, Usui Hirokazu¹, Mitsuhashi Akira², Koga Kaori¹ *Chiba University*¹, *Dokkyo Medical University*²

[Objective] There is no established standard protocol for atypical endometrial hyperplasia (AEH) and well-differentiated endometrial cancer (EC) patients who achieve complete remission (CR) after high-dose medroxyprogesterone acetate treatment. This study provides the outcomes of patients who underwent fertility-sparing therapy at our institution and continued to be managed over the age of 40. **[Methods]** We retrospectively examined 35 patients (14 AEH, 21 EC) who achieved CR during their initial treatment and continued follow-up after the age of 40 out of 83 cases treated between 2010 and 2021 at our institution. **[Results]** The median age at the last observation was 45 years (range : 40-53), and the median duration of follow-up after remission was 120 months (range : 14-150 months). Two patients were still undergoing infertility treatments, while eight patients achieved live births. Among the 21 patients who initially presented with EC, 13 experienced recurrences, with a median age of recurrence at 40 (range : 33-48). Thirteen patients finally underwent hysterectomy at median age 43 (range 40-50), of which six had EC and two had AEH identified in the excised uterus. No recurrences were observed in initial AEH cases. Ten patients had their ovaries removed during hysterectomy. Among the 19 patients still under observation, 14 had

menstrual regulation with progestins, and one decided to follow off without recurrence after 12 years-follow duration. **[Conclusion]** Regardless of recurrence status, hysterectomy may be considered for EC patients when they no longer want children. Conversely, in AEH cases, it might be reasonable to pursue expectant management with menstrual regulation using progestins till menopause.

ISP-22-3

A real-world multicenter observational study of lenvatinib plus pembrolizumab in Japanese patients with endometrial cancer: interim analysis of GOGO-EM4 study Nagase Yoshikazu^{1,2}, Nakagawa Satoshi², Ueda Yutaka², Kobayashi Mariya², Shiomi Mayu³, Kakubari Reisa⁴, Otake Akiko⁵, Watanabe Masahiro⁶, Takata Tomomi⁷, Matsuzaki Shinya¹, Yokoi Takeshi¹, Kimura Tadashi² *Kaizuka City Hospital¹, Osaka University², Osaka Police Hospital³, Osaka International Cancer Institute⁴, Minoh City Hospital⁵, Hyogo Prefectural Nishinomiya Hospital⁶, Kansai Rosai Hospital⁷*

[Objective] There are limited researches on the efficacy and safety of lenvatinib plus pembrolizumab (LP) in Japanese patients with endometrial cancer (EC), and further studies in real-world settings are warranted. **[Methods]** This is the first multicenter, retrospective and prospective cohort study of LP for EC with the largest sample size in Japan, with a planned enrollment of 100 patients (GOGO-EM4, UMIN000049997). We performed an interim analysis when 56 patients were enrolled. EC patients who had progressed after at least one platinum-containing chemotherapy were enrolled. The primary endpoint was progression-free survival (PFS). The secondary endpoints included overall survival (OS), objective response rate (ORR), disease control rate (DCR), and safety. **[Results]** At data cutoff, median follow-up period was 184.5 days. Median PFS and OS were 224 days (95% confidence interval [CI]: 108-280) and 371 days (95% CI: 254-not reached). ORR was 32.6% and DCR was 78.3%. Common adverse events (AEs) were hypertension (67.9%), hypothyroidism (64.3%), fatigue (58.9%), thrombocytopenia (53.6%), proteinuria (50.0%), decreased appetite (44.6%), and hand-foot syndrome (39.3%). AEs of grade ≥ 3 were hypertension (21.4%), hand-foot syndrome (14.3%), thrombocytopenia (10.7%), proteinuria (10.7%), and fatigue (10.7%). AEs with a delay of ≥ 2 weeks from first onset to most severe grade onset were anemia, proteinuria, hand-foot syndrome, hypothyroidism, decreased appetite, and weight decreased. **[Conclusion]** The therapeutic effect of LP was consistent with that of the prior clinical trial. The frequency of AEs in Japanese patients tended to be higher than in patients from other countries, and the final analysis of this study is awaited.

ISP-22-4

Relative dose of lenvatinib may be a predictor of treatment with lenvatinib and pembrolizumab for advanced or recurrent endometrial cancer Urugou Kohei, Nishio Shin, Yoshikawa Hideaki, Kataoka Nene, Aoki Rumiko, Yamada Hiroaki, Tasaki Shingo, Yo Takasugi, Tasaki Kazuto, Katsuda Takahiro, Tsuda Naotake *Kurume University*

[Objective] It has been reported that relative dose maintenance is important for the therapeutic efficacy of lenvatinib (LEN) in hepatocellular carcinoma. Therefore, we investigated whether the relative dose of LEN in Lenvatinib and pembrolizumab (LP) therapy for advanced or recurrent endometrial cancer (arEC) could be a predictive factor for treatment. **[Methods]** Twenty-eight patients (pts) who received LP therapy from November 2018 to July 2023 were included. Relative dose intensity (RDI) and body surface area-corrected DI/BSA ratio (DBR) were used as indices of relative dose, and the association between RDI and

DBR and efficacy was examined. **[Results]** The median age was 58.9 years, and the histologic types of endometrioid carcinoma were G1, G2, and G3, 10 pts, 8 pts, and 5 pts, respectively, and other histologic types, 5 pts. Micro instability status testing was performed in all pts, and only 1 pts had dMMR. The median progression-free survival (PFS) was 5.7 months and median overall survival was not reached. The RDI cutoff value was 0.81. The overall response rate (ORR) was statistically significant in the high RDI group (16 pts) compared to the low RDI group (12 pts) ($p=0.02$). PFS was not significantly different. The DBR cutoff value was 606. The ORR was significantly higher in the high DBR group (14 pts) than in the low RDI group (14 pts) ($p=0.05$); PFS showed no statistically significant difference, but the high DBR group tended to have a better prognosis. **[Conclusion]** Relative dose of LEN may be a predictor for treatment with LP in arEC.

ISP-22-5

Evaluating the long-term prognostic factor in the overall population of patients with advanced stage endometrial carcinoma Yusuke Shimizu *Nagoya University*

[Objective] This study aimed to evaluate the clinical characteristics, prognosis according to initial treatment, and impact of the role of cytoreduction in the overall population of patients with advanced-stage endometrial carcinoma. **[Methods]** All patients with advanced-stage endometrial carcinoma diagnosed between 2010 and 2020 were identified from tumor registry databases in our institution. Individual patient data were collected retrospectively. **[Results]** Eighty-five patients underwent surgery as primary therapy or after chemotherapy for stage III or IV endometrial carcinoma. The median overall survival (OS) of all cases was 30 months (range 3-85). 70 (82.5%) patients were treated with primary surgery followed by chemotherapy and 15 (17.5%) with primary chemotherapy followed by surgery. Complete cytoreductive surgery (no residual tumor) was accomplished in 52 patients (61.2%), while 33 patients (38.8%) were left with residual disease. Postoperative intra-abdominal residual tumor significantly differed statistically in OS (complete surgery groups and residual disease OS 63.14 months $p<0.001$). No other characteristics showed statistical difference in OS except for the extra abdominal metastasis and therapy with or without surgery treatment. Eleven cases (12.9%) showed more than 3 years of survival which 10 cases were treated with no residual tumor after surgery. **[Conclusion]** From our result completely debulking abdominal disease regardless of primary treatment appears to be the most important determinant of long-term survival in patients with advanced-stage endometrial carcinoma. With the recent indication for immune checkpoint inhibitors, further improvement in outcomes is expected in conjunction with treatment strategies that include complete resection of the tumor.

ISP-22-6

Diagnostic accuracy of preoperative magnetic resonance imaging in early stage endometrial cancer Kodama Haruho, Aso Saki, Shima Kazuaki, Yamada Tomonori, Yamamoto Shizuka, Obata Eri, Aoyagi Yoko, Yano Mitsutake, Okamoto Mamiko, Kai Kentaro, Kobayashi Eiji *Oita University*

[Objective] Preoperative assessment of myometrial invasion in early-stage endometrial cancer alters the type of hysterectomy and the area of lymphadenectomy in our clinical setting. However, the diagnostic accuracy of preoperative contrast-enhanced magnetic resonance imaging (CE-MRI) is controversial. This study aims to investigate the diagnostic accuracy of preoperative MRI on myometrial invasion in early stage endometrial cancer in our institution. **[Methods]** This was an electronic health

record-based descriptive study conducted in a university teaching hospital. We retrospectively reviewed the radiological and pathological reports of with stage I-II endometrial cancer patients who underwent definitive surgery at our institution between 2018 and 2022. **[Results]** 152 patients were identified. Preoperative MRI-based diagnosis by the radiologist on myometrial and stromal invasion was concordant with pathological evaluation in 121 (79.6%), but discordant in 31 (20.4%). Among those with discrepancies, eight patients (25.8%) were up-staged postoperatively (from IA to IB in all eight patients), and the other 23 patients (74.2%) were down-staged postoperatively : from IB to IA (n=19), from II to IA (n=3), and from II to IB (n=1). **[Conclusion]** The accuracy of preoperative diagnosis of uterine cancer is still limited and problematic. We will report the results from our own institution and a review of the literature.

ISP-22-7

Investigation of Incidentaloma in Uterine Corpus Cancer Surveillance Kato Asami, Soeda Shu, Okabe Chikako, Sato Tetsu, Miura Hideki, Furukawa Shigenori, Watanabe Takafumi, Fujimori Keiya *Fukushima Medical University*
[Objective] Although there is limited evidence regarding the effectiveness of imaging tests in the surveillance of malignant tumors, there have been reported cases where tumor lesions (incidentalomas) have been incidentally detected through imaging tests. The aim of this study was to elucidate the details of incidentalomas detected during malignant tumor surveillance. **[Methods]** In one year of 2014, we studied 42 patients who were diagnosed with and treated for endometrial cancer at our hospital. Our investigation focused on the types, diagnostic methods, and treatment approaches for incidentalomas. **[Results]** The follow-up period ranged from 5 to 9 years, the median age of 42 patients was 55 years (range : 30-88 years). All cases underwent imaging surveillance, and an incidentaloma was detected in 21 cases (50%). Fourteen cases (66%) were identified during preoperative imaging, while seven cases (33%) were detected during surveillance. Twenty cases (95%) were benign tumors (liver, kidney, adrenal gland, thyroid, thymus), and one case (5%) underwent surgery. One case (5%) was a rectal malignant tumor, and treated with no recurrence since. **[Conclusion]** Our study revealed cases where incidentalomas were identified through routine imaging tests even in asymptomatic patients, leading to treatment. To address lesions outside the primary site is necessary.

ISP-22-8

Clinical outcomes of lenvatinib plus pembrolizumab for uterine corpus cancer in our hospital Ito Yosuke, Fujiyama Koya, Lin Ming, Maeda Chikako, Kido Yuka, Tanaka Motoki, Mera Riho, Iwase Koharu, Mori Yusuke, Nagasawa Saya, Maruyama Yojiro, Ogishima Daiki *Juntendo University Nerima Hospital*
[Objective] To clarify the appropriate use of lenvatinib and pembrolizumab combination therapy for unresectable advanced/recurrent endometrial cancer that has progressed after cancer chemotherapy. **[Methods]** Clinical data were retrospectively collected using electronic medical records from six patients with endometrial cancer who received combination therapy with lenvatinib and pembrolizumab from April 2021 to September 2023. **[Results]** Two patients had to reduce the dose of Lenvatinib to 10 mg, but maintained PR status for 1 year and 2 months. Lenvatinib was discontinued in 1 patient after 3 months, but PR status was maintained for 1 year and 2 months with pembrolizumab monotherapy. One patient showed PD after 5 months and treatment was discontinued, but the patient remained in SD status for 3 months. One patient discontinued Lenvatinib after 1 month and was considered to have had PR status

for 1 year and 2 months, but subsequently developed PD and died. **[Conclusion]** Lenvatinib and pembrolizumab combination therapy is used after platinum drugs have been determined to be ineffective, so the timing of chemotherapy introduction must be appropriately determined. On the other hand, there are some patients who are markedly effective and have a prolonged prognosis.

ISP-22-9

The hysteroscopic findings of the uterine adenocarcinoma (UA) Hamada Yoshinobu¹, Kouroku Yasumasa¹, Saito Yoko¹, Saito Kanami¹, Irie Taichi¹, Iizuka Makoto¹, Matsushima Jun², Iida Yasushi¹, Sugimoto Kouhei³, Sakamoto Shuichi¹, Takakura Satoshi¹ *Dokkyo Medical University Saitama Medical Center¹, Department of Pathology, Dokkyo Medical University Saitama Medical Center², Center for Reproductive Medicine, Dokkyo Medical University Saitama Medical Center³*

[Introduction] Uterine adenocarcinoma (UA) is a rare mixed tumor composed by benign epithelial glands and malignant stromal elements. In some cases of UA, the pathological findings are not malignant. Furthermore, the characteristic hysteroscopic finding is unclear. Hence, the preoperative diagnosis of UA is considered as difficult. Two cases of UA diagnosed using hysteroscopy was reviewed. **[Case 1]** Fifty-one years old woman, G3P3 presented because of abnormal genital bleeding. The finding of the vaginal speculum examination was the red-colored and irregular-shaped mass, 63 mm in diameter, aborting outside the external os. The pathological finding of surface tissue of mass was only atypical cells. The hysteroscopic resection was performed. Observing with hysteroscopy, the stalk of the mass existed on the lower uterine cavity. The uterine cavity without the stalk was not dirty. The pathological finding was adenocarcinoma. Hysterectomy was undergone, the pathological diagnosis was same. **[Case 2]** Fifty-two years old woman, G0P0 presented because of abnormal genital bleeding. The finding of the vaginal speculum examination was not particular. The sonographic examination revealed the endometrial thickness, 21 mm. The results of endometrial cytology were negative. Observing with hysteroscopy, there were irregular polypoid lesions with vascular proliferation in the endometrium, however the uterine cavity was not dirty. The polypoid lesions were collected by aspiration with hysteroscopy. The pathological finding was adenocarcinoma. Hysterectomy was undergone, the pathological diagnosis was same. **[Conclusion]** In two cases, the same hysteroscopic finding was "not dirty" uterine cavity with irregular-shaped lesion. It may be characteristic of UA.

ISP-22-10

Is safe omitting pelvic lymphadenectomy in patients with grade-3 endometrioid endometrial cancer staged IA? Kim Seokmo, Ju Uchul *Chonnam National University Medical School, Korea*

[Objective] We investigated the effect of pelvic lymphadenectomy (PL) on prognosis in patients with grade-3 endometrioid endometrial cancer (EEC) staged IA. **[Methods]** Of 612 patients who received surgery for EEC from 2004 to 2017, 108 patients finally diagnosed with grade-3 EEC staged IA according FIGO system were enrolled to this study. We divided 108 patients into non-PL group (n=31) not received PL because they had low-risk disease and PL group (n=77) received PL. Low-risk disease was defined grade 1 or 2 disease on preoperative endometrial biopsy and the tumor confined in the uterine corpus and invaded to < 1/2 of myometrium on preoperative images. All patients in two groups received postoperative radiation. **[Results]** There was no statistical significance when the groups were compared in patients' age, obesity, tumor size, lymphovascular space inva-

sion, positive pelvic washing cytology and surgical approach (laparotomy vs. laparoscopy). Only one patients in PL group had positive pelvic lymph nodes. Disease-free and overall survival rates did not show significance differences in two groups. **[Conclusion]** Pelvic lymphadenectomy did not affect the prognosis of patients with grade-3 EEC staged IA. Omitting pelvic lymphadenectomy might be safe for patients with low-risk EEC before primary surgery even if the tumor is finally diagnosed with grade-3 disease after surgery.

ISP-23-1

Analysis of gynecological tumors with PGPV identified from comprehensive genomic profiling Hayashi Ryoma¹, Masuda Kenta¹, Nakamura Kohei², Tsuji Kosuke¹, Kisu Iori¹, Chiyoda Tatsuyuki¹, Nishio Hiroshi¹, Kobayashi Yusuke¹, Iwata Takashi¹, Banno Kouji¹, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Genomics Unit, Keio Cancer Center, Keio University²*

[Objective] Comprehensive genomic profiling (CGP) sequences DNA from cancer tissue or ctDNA in order to identify gene variants that may become therapeutic targets. We recommend genetic counseling for patients with a presumed germline pathogenic variant (PGPV), but the frequency of such cases is unknown. Therefore, we reviewed cases of PGPV identified in gynecological cancer patients who underwent CGP at our hospital. **[Methods]** We observed patients with gynecological cancer who underwent CGP at our hospital between September 2019 and July 2023, which includes 132 cases of FoundationOne[®] CDx (F1), 13 cases of FoundationOne[®]Liquid CDx (FIL), 16 cases of OncoGuide[™]NCC Oncopanel System (NOP). We extracted the data from medical records and analyzed retrospectively. **[Results]** As a result, this research included the following: 66 ovarian/fallopian tube/peritoneal cancers, 43 cervical cancers, 34 uterine cancers, and 18 others. Within those cases, 91 cases (186 variants) of F1, 11 cases (32 variants) of FIL, and 12 cases (18 variants) of NOP showed ClinVar pathogenic variants. PGPV was identified in 21 of F1, 5 of FIL, and 1 of NOP patients, and genetic counseling was provided in 8/21 of F1 (38%), 3/5 of FIL (60%), and 1/1 of NOP (100%) patients. From here, *BRCA1* in 7 patients (6 ovarian and 1 cervical cancer), *BRCA2* in 2 patients (1 ovarian and 1 cervical cancer), and *MLH1* in 1 patient (1 ovarian cancer) were identified as germline variant. **[Conclusion]** In conclusion, hereditary breast ovarian cancer and Lynch syndrome were diagnosed by genetic testing from PGPV. However, only limited number of patients with identified PGPV received genetic counseling, and this should be improved.

ISP-23-2

Development and validation of Japanese version of cancer risk assessment system in primary care (JCRAS-PC) Narumoto Keiichiro¹, Shibata Ayako² *Department of Family and Community Medicine, Hamamatsu University School of Medicine¹, Yodogawa Christian Hospital²*

[Objective] Hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome (LS) are the most common hereditary cancer syndromes, increasing cancer risk across organs and generations. Identifying at-risk individuals based on personal and family health history in primary care is recommended but challenging. We developed the web-based, Japanese version of Cancer Risk Assessment System in Primary Care (JCRAS-PC) to address this gap. **[Methods]** After reviewing 12 relevant guidelines and articles, we identified 155 criteria indicating genetic testing or referral to genetic professionals. We finally selected 50 items by panel review with EviQ and NICE guideline used as the primary references because these were aimed for primary care providers. JCRAS-PC features family tree creation with instant HBOC/LS risk assessment based on the 52 items,

factsheets and collection of example sentences for communication with patients, a list of cancer surveillance strategies for HBOC/LS, and self-learning resources on clinical genetics. Regarding validation, we examined the extent to which JCRAS-PC identified cases appropriate for referral to genetic professionals against genetic counselors' assessments in de-identified 35 cases where genetic consultations had occurred. We calculated kappa, sensitivity, and specificity using IBM SPSS version 25 statistical software. **[Results]** JCRAS-PC showed substantial agreement (kappa= 0.91) with 96.6% sensitivity and 100% specificity for HBOC/LS risk assessment. In one case, JCRAS-PC determined "no risk" while genetic counselors suggested "refer." **[Conclusion]** We developed a validated, web-based HBOC/LS risk assessment system. Its feasibility and utility in primary care warrant further investigation.

ISP-23-3

A Case of spontaneous Pregnancy Following Prophylactic Total Colectomy for Familial Adenomatous Polyposis Aoyagi Yoko, Kai Kentaro, Nishida Masakazu, Kobayashi Eiji *Oita University*

Introduction: Familial Adenomatous Polyposis (FAP), an autosomal dominant disease, is primarily caused by *APC* gene mutations. Prophylactic total colectomy is performed in adolescents and young adults to prevent colorectal cancer, yet reports concerning postoperative perinatal outcomes are scarce. **Case Presentation:** The patient was a 22-year-old nulliparous woman diagnosed with FAP, with a family history of colorectal cancer. At 17-year-old, she underwent laparoscopic total colectomy and ileal pouch-anal anastomosis. At 22-year-old, she conceived spontaneously. But at 20-week gestation, she was diagnosed with peritonitis due to small intestinal perforation and referred to our hospital. She underwent partial resection of small intestine and intraperitoneal lavage and drainage. At 21-week gestation, the perforation recurred, and jejunostomy was performed. At 24-week gestation, due to fetal dysfunction, she had an emergency cesarean section delivery. The newborn, a girl weighing 822 g, exhibited severe neonatal asphyxia, congenital anemia, and intracranial hemorrhage. Despite multidisciplinary treatment, the infant died at one day old. Two months post-emergency cesarean, the patient underwent closure of stoma, and 24 months later, removal of an intraperitoneal desmoid tumor. She continues tamoxifen therapy with no disease progression. **Conclusion:** The perinatal outcomes of prophylactic total colectomy are essential for genetic counseling, necessitating further accumulation of similar cases.

ISP-23-4

A case of Lynch syndrome with double cancer of the uterus and ovary with different genetic characteristics Ohta Mamiko, Miyagawa Chiho, Nakai Hidekatsu, Matsumura Noriomi *Kindai University*

[Introduction] The risk of double cancers is high in Lynch syndrome. Recently, genetic analysis using exome sequencing has shown that double cancers that develop in the uterus and ovary in non-Lynch syndrome have identical genetic characteristics. We report a case of Lynch syndrome, in which double cancers of the uterus and ovary with different genetic characteristics were found. **[Case]** A 45-year-old nulliparous female was diagnosed with endometrial carcinoma. Surgical staging was performed and the histopathology confirmed the diagnosis of endometrial carcinoma at FIGO stage IB and dedifferentiated ovarian carcinoma at FIGO stage IIIB. Immunohistochemistry showed deletion of PMS2 and MLH1 in both tumor components. Foundation One[®] CDx Cancer Genome Profiling was performed on the ovarian component, which revealed a pathological mutation in the MLH

1 (E178*). Germline testing revealed an exon5 deletion in the MLH1 gene, leading to a confirmed diagnosis of Lynch syndrome. In the endometrial cancer component, genetic analysis using the tumor mutation load panel test revealed a pathological mutation in the MLH1 (R226Q), and many other genetic mutations that were completely different from those in ovarian cancer, indicating that both tumors have different genetic characteristics. **[Discussion]** In this case, the patient had Lynch syndrome with MLH1 mutation in the germ line, and the pathological mutation as a different second hit was added in the uterus and ovary, respectively. This case suggests that patients with double cancers of the uterus and ovary with different histologic subtypes are more likely to have Lynch syndrome.

ISP-23-5

Is there molecular homology between HPV L1 and human proteins? Nishioka Kazuhiro¹, Matsumura Noriomi², Hashiguchi Yasuhiro¹, Kishimoto Sachiko¹ *Kindai University Nara Hospital¹, Kindai University²*

[Objective] HPV vaccine lawsuit claims that HPV and human proteins are homologous and HPV vaccination will produce autoantibodies and cause organ damages. To substantiate no existence of HPV L1 epitopes used in HPV vaccine in human proteins. **[Methods]** We analyzed whether the type 16 HPV L1 epitopes registered in Immune Epitope Database, are found in human proteins using NIH BLAST. This analysis followed the method of Kanduc et al. and examined not only the full linear epitopes but its five amino acid sequences. Gene ontology analyses are performed on the identified proteins. Similar analyses were performed for random sequences with the same number of peptides of HPV and for the epitope of hepatitis B virus (HBV). **[Results]** 22 linear epitopes were registered for type 16 HPV L1 and not found in human proteins. 16 proteins were found in humans at 7 residues, 106 at 6 residues and 1282 at 5 residues. No statistically significant gene ontology enrichment was observed in those proteins : 14, 10 and 5 at 7 residues : 57, 88 and 42 at 6 residues : 1014, 1282 and 846 at 5 residues in the three sets of random sequences : 16 at 7 residues, 127 at 6 residues 1677 at 5 residues in the HBV. **[Conclusion]** The epitope for HPV L1 is not present in the human proteins. The data that the HPV L1 epitope sequences of 5 residues have common in the human proteins are also found in random sequences and the epitope of HBV. No evidence that components of the HPV vaccine can produce autoantibodies.

ISP-23-6

Analysis of chemotherapy-induced febrile neutropenia for gynecologic malignancy chemotherapy in our hospital Shimizu Yusaku, Takiuchi Tsuyoshi, Kakuda Mamoru, Toda Aska, Nakagawa Satoshi, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Ueda Yutaka, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] Chemotherapy-induced febrile neutropenia (CIFN) frequently leads to a life-threatening course. We investigated the incidence and clinical features of CIFN in patients who received paclitaxel and carboplatin (TC) or gemcitabine and carboplatin (GC) for gynecologic malignancy. **[Methods]** Between March 2022 and April 2023, we retrospectively reviewed all gynecologic malignancy patients in our hospital and analyzed the cases of CIFN by TC or GC. We excluded with immune checkpoint inhibitors. This study was approved by the ethics committee of our institution. **[Results]** A total of 63 patients received 326 cycles of chemotherapy during the study period. Chemotherapy-induced FN occurred in 8 (12%) patients over 9 (2.7%) chemotherapy cycles. The median age of FN cases was 57 years (range,45-76). 4 (50%) patients developed FN during

the first or second course of chemotherapy. Among the FN cases, recurrent cancer patients were observed in 2 (25%) patients and 2 (22%) cycles ($p=1.000, p=1.000$). 5 (62%) patients received concomitant Avastin, as did 5 (62%) cycles ($p=0.241, p=0.315$). There was a trend of higher FN incidence in stage III and higher, with 6 (75%) cases and 7 (78%) cycles, but no statistically significant difference was observed compared to the non-FN group ($p=0.224, 0.325$). **[Conclusion]** It was difficult to predict the incidence of FN. By identifying risk factors for FN, the safe management of chemotherapy-induced FN may be possible in patients with gynecologic malignancy. We need further studies to better understand the risk of FN.

ISP-23-7

Lipschütz ulcer after COVID-19 infection : Acute aphthous vulvar ulcers developed on the same day in 21-year-old and 17-year-old sisters after COVID-19 onset Koizumi Mai¹, Kinose Yasuto¹, Kakuda Mamoru¹, Toda Aska¹, Kodama Michiko¹, Sawada Kenjiro¹, Shimizu Takashi², Kimura Tadashi¹ *Osaka University Hospital¹, Shimizu Women's Clinic²*

Background : Acute aphthous nonsexually vulvar ulcers, known as Lipschütz ulcers, can occur mostly in adolescents and young women and cause severe vulval pain. Dozens of reports represent cases of women with Lipschütz ulcers after COVID-19 infection or COVID-19 vaccination. Here we report cases of two females who are sisters developed vulvar ulcers on the same day after COVID-19 infection. **Cases :** A 21-year-old older sister and a 17-year-old younger sister both recognized sore throat and fever. The younger sister tested positive for COVID-19, and the older sister living together had similar symptoms. Three days after the COVID-19 symptom onset, they both felt vulvar pain and visited a gynecologic clinic. The older sister had experienced sexual intercourse whereas the younger sister had never experienced it. The patients were referred to our hospital for further evaluation. Clinical examination revealed the older sister had a 5-mm ulcerative scar on the left labia minora and the younger sister had 10-15 mm kissing ulcers with pain on both sides of the labia minora. The older sister showed negative results of any sexually transmitted infection and spontaneously recovered without any treatment in a week. The younger sister needed 2-week of urinary catheter management due to the difficulty in urination and received topical steroids for a month until her ulcers healed. **Conclusion :** Based on the two sisters developed Lipschütz ulcer after COVID-19 infection, it is suggested that genetic or environmental factors might be involved. Further study is needed to reveal the pathogenesis of Lipschütz ulcer after COVID-19.

ISP-23-8

Two cases of patients diagnosed with isolated ACTH deficiency during immune checkpoint inhibitor treatment Tomiya Hiroka, Nishida Haruka, Miyakawa Kosuke, Takehara Kohei, Onodera Takako, Watanabe Saya, Takasaki Kazuki, Takahashi Yuko, Ichinose Takayuki, Hirano Mana, Hiraike Haruko, Nagasaka Kazunori *Teikyo University Hospital*

[Introduction] Immune checkpoint inhibitors (ICIs) are now commonly used to treat gynecological malignancies. Here, we describe two cases of patients diagnosed with isolated ACTH deficiency (IAD) during ICI treatment. **[Case]** A 52-year-old woman was diagnosed with MSI-positive uterine endometrial cancer and treated with pembrolizumab. Two months after the treatment, she developed hyperthyroidism. Six months after the treatment, she had stiff joints, general malaise, anorexia, and weight loss. The diagnosis of rheumatoid arthritis was not made, and both ACTH and cortisol levels decreased to 1.5 pg/ml and 0.2 µg/dL, respectively. After an ACTH stress test, we diag-

nosed her with IAD, and the patient was started on hydrocortisone. After her symptoms improved, pembrolizumab was resumed. A 53-year-old woman had recurrent cervical cancer and was treated with cemiplimab. One month after the treatment, she developed hyperthyroidism, and two months later, it turned out to be hypothyroidism, and she was treated with levothyroxine sodium. Three months later, her medical check-up showed a decrease in ACTH to 10.3 pg/ml and cortisol to 1.0 µg/dL without symptoms such as fatigue. She was diagnosed with IAD, started on hydrocortisone, and has received cemiplimab since then. **[Discussion]** The incidence of pituitary dysfunction is rare in treated with ICIs. IAD is often associated with thyroid dysfunction, and early detection may be possible by paying attention to symptoms of adrenal insufficiency in patients with thyroid dysfunction. **[Conclusion]** It is essential to measure blood ACTH and cortisol regularly when ICI is used and to intervene early when IAD is suspected.

ISP-23-9

Clinical features of cerebral stroke in gynecologic cancers of Korean women Lee Jongmin, Kwon Ji Young, Park Kena, Song Jeong Min, Pyeon Seung Yeon, Chung Young Shin *Kyung Hee University School of Medicine, Kyung Hee University Hospital at Gangdong, Korea*

[Objective] Stroke in cancer patients is expected to be more critical as oncologists occasionally face medical challenges in managing patients who experience stroke during cancer treatment due to increasing life expectancies and cancer prevalence rates. This study aimed to evaluate the risk factors and prognosis of stroke in patients with gynecological cancers. **[Methods]** A retrospective cohort study was performed on patients with cervical, endometrial, and ovarian cancers. Patients were classified into three groups based on the period of stroke onset: at least one year before cancer diagnosis, within one year before cancer diagnosis to six months after the last treatment date, and six months after the last treatment date. **[Results]** Among the 644 patients, 54 (8.4%) had experienced stroke in the process of treatment of gynecologic cancers: 29 patients before cancer treatment, 19 during treatment, and 6 after treatment. Old age and high blood pressure were significant risk factors of stroke. Stroke did not significantly affect progression-free survival but did affect overall survival. However, in multivariate analysis, stroke was not independent prognostic factor of overall survival. **[Conclusion]** It is important to build up an appropriate management plan for patients with stroke and gynecologic cancers rather than excessively concerning about the adverse effects of stroke on cancer prognosis.

ISP-23-10

Paratubal cyst in an adolescent female: A case report Chung Sun Wook¹, Oh Sang Yup², Chung U Rim³ *Ulsan Medical Center, Korea¹, Busan Maryknoll Hospital, Korea², GVCS, Campus of Mungyeong, Korea³*

[Background] It is difficult to differentially diagnose acute abdominal pain in adolescence. Because of the intra-abdominal presence of female reproductive organs, the differential diagnosis of abdominal pain includes disease of the ovaries, fallopian tubes, and uterus in addition to the typical diseases considered in other patients presenting with acute abdominal pain. Among these causes, it's worth paying attention to torsion of gynecologic organs. Paratubal tumor comprises about 10% of uterine adnexal tumor and if probably of paramesonephric, mesothelial or mesonephric origin. The tumor usually occurs in perimenopausal woman and rarely in adolescents. Torsion of the paratubal cyst is rare but significant cause of acute lower abdominal pain in adolescent females that is difficult to recognize preop-

eratively. Early diagnosis is very important in adolescent because of the risk of decreased fertility if it is not treated at an early stage. **[Case presentation]** A 12-year-old patient presented with 1-month history of worsening nausea and increasing abdominal pain. When visiting the emergency room, abdominal imaging revealed a 10cm-sized adnexal mass, so we recognized ovarian cyst torsion, so, emergency single port laparoscopic surgery was performed and after it turned out to be with para tubal cyst torsion, conservative surgery was performed with cyst removal while preserving the ovaries and tubes. **[Conclusion]** This case suggests that a paratubal cyst should be included into the differential diagnosis of pelvic masses, especially in the adolescent age. Careful inspection during surgery is necessary and cystectomy should be the first consideration in the management of paratubal cysts.

ISP-24-1

Impact of frozen-thawed embryo transfer on the development of placenta accreta spectrum: An analysis of 213,923 cycles in the assisted reproductive technology registry of Japan from 2017 to 2020 Fujita Tomoyuki¹, Yoshizato Toshiyuki¹, Murotani Kenta², Obara Hitoshi², Tsuda Naotake¹ *Kurume University¹, Biostatistics Center, Kurume University²*

[Objective] To investigate whether frozen-thawed embryo transfer (FET) is associated with an increased risk of developing placenta accreta spectrum (PAS). **[Methods]** Data of 213,923 embryo transfer (ET) cycles resulting in pregnancies with live births were retrieved from the assisted reproductive technology registry of Japan for the period 2017-2020. Cohorts of FET and fresh ET cycles were selected at a 1:1 ratio through propensity score matching. Using logistic regression modeling with variables related to confounders for the development of PAS as covariates, a propensity score was calculated for the FET group from the full analysis set. The primary endpoint was the presence of PAS. The odds ratio (OR) of the development of PAS in FET versus fresh ET was estimated through propensity score-based analysis. **[Results]** There were 188,338 and 25,585 cycles for FET and fresh ET, respectively. After establishing a 1:1 propensity score-matched cohort, 15,034 cycles (7,517 cycles each for FET and fresh ET) were analyzed. The adjusted OR for FET with fresh ET as the reference was 5.83 (95% confidence interval [CI], 3.53-9.63). Using the inverse probability of the treatment weighting, the adjusted OR was obtained as 6.63 (95% CI, 5.62-7.80). With fresh ET as the reference, programmed FET was associated with PAS (OR, 8.35; 95% CI, 6.20-11.23) whereas natural FET (crude OR, 1.00; 95% CI, 0.68-2.11) and stimulated FET (crude OR, 1.28; 95% CI, 0.77-2.11) were not. **[Conclusion]** Compared with fresh ET, FET, especially programmed FET, is a risk factor for the development of PAS.

ISP-24-2

Histopathological analysis of the placenta in a mouse model of endometriosis: a study on the causes of fetal growth restriction Mohammed Elsherbinielshal¹, Koga Kaori², Nakajima Marie¹, Silvana Vita¹, Maki Eiko³, Kumasawa Keiichi¹, Izumi Gentaro¹, Harada Miyuki¹, Hirata Tetsuya¹, Hirota Yasushi¹, Hiraike Osamu¹, Osuga Yutaka¹ *The University of Tokyo¹, Chiba University², Yaizu City Hospital³, St. Luke's International Hospital⁴*

[Objective] Previously, we have shown that pregnancy in a mouse model of endometriosis results in fetal growth restriction (FGR). The aim of this study was to examine the histopathology of placenta in order to determine the cause of its complication. **[Methods]** Endometriosis was induced by intraperitoneal injection of homologous mouse minced uteri (ENDO). Vehicle was injected for the control (CONT, n = 4 in each group). Mating was

started 43 days after the endometriosis induction. On 18 dpc, dams were sacrificed, and the placenta were removed. Histological analysis was performed using hematoxylin and eosin (HE) staining followed by Image J analysis. The thickness of the decidua (DC) and the labyrinth (LB) and the total surface area of the junctional zone (Jz-area) were measured. The width of the entire junctional zone (Jz) and the width of the interrupted zone (JzI) were measured, and the ratio (JzI/Jz) was calculated. **[Results]** DC and LB were comparable between the groups. Jz-area was significantly smaller in ENDO (ENDO : 0.8 ± 0.1 , CONT : 1.1 ± 0.1 , mean \pm SD, mm², $p < 0.05$). JzI/Jz was significantly higher in ENDO (ENDO : 0.1 ± 0.04 , CONT : 0.03 ± 0.03 , mean \pm SD, %, $p < 0.05$). Disrupted junctional zones were observed mainly in ENDO. **[Conclusion]** The current study suggests that chronic exposure to endometriosis may have an adverse effect on placental microenvironment, especially on the junctional zone, which may result in FGR. Further molecular biological analysis is warranted to elucidate the mechanism.

ISP-24-3

Pregnancies by frozen-thawed embryo transfer using hormone replacement therapy cycles increase placenta with velamentous umbilical cord insertion Furuya Satoshi^{1,2}, Yamaguchi Takashi², Kubonoya Kiyoshi¹ *Kubonoya Women's Hospital¹, Infertility, Kubonoya IVF Clinic²*

[Objective] We have reported on the study that pregnancies achieved by assisted reproductive technology had more cases of placenta with velamentous umbilical cord insertion (VCI) than spontaneous pregnancies. Amid a recent continuous increase in the number of frozen embryo transfer (FET), FET needs be performed either in a natural cycle (NC) or a hormone replacement therapy cycle (HRT). Our study objective is to determine whether the different endometrial preparation protocols for FET might affect the incidence of VCI. **[Methods]** We reviewed the medical records of 1002 singleton FET-conceived and delivered cases in our facility during 8 years since 2016. Our study population was divided into two groups according to the method of endometrial preparation : FET cases using HRT (Group A : $n = 737$), and FET cases in NC (Group B : $n = 265$). Odds ratio for VCI in Group A, compared to Group B was calculated, using multivariate logistic regression. **[Results]** The incidence of VCI was 5.9% (59/1002) in all. The incidence of VCI in Group A and B was 7.1% (52/737) and 2.6% (7/265), respectively, that showed statistically significant difference ($P < 0.01$). Adjusted OR for VCI of Group A, compared to Group B was 2.81 [95% CI : 1.34-6.87, $P = 0.01$]. **[Conclusion]** It can be concluded that pregnancies achieved by FET using HRT are more likely to have placenta with velamentous umbilical cord insertion. In order to secure the safety for both mother and fetus, we need to identify the umbilical cord insertion site more proactively by ultrasound, especially for the FET cases using HRT.

ISP-24-4

Recurrent and Persistent First Trimester Bleeding : A Report and Review of Literature for a Case of Uterine Arteriovenous Malformation Co-existing with a Placenta Accreta in a 30-year-old Post Curettage for Missed Miscarriage Mascarinas Mark John Arnel G, Carlos Marcela Dianalyn S *Angeles University Foundation Medical Center, Philippines*

This unique case report outlines the complexities surrounding a 30-year-old woman experiencing recurrent and persistent first-trimester vaginal bleeding after undergoing two curettages for missed miscarriages. The distinctive nature of this case is marked by the co-existence of uterine arteriovenous malformation (UAVM) and placenta accreta, both rare conditions, infrequently found to be the underlying causes of early pregnancy

bleeding. The persistent vaginal bleeding initiated a series of diagnostic interventions, leading to the primary consideration of retained products of conception and gestational trophoblastic neoplasia. However, after an equivocal hysteroscopy, the utility of advanced diagnostic modalities, including transvaginal ultrasonography with Doppler studies and pelvic angiography, facilitated the confirmation of a UAVM diagnosis. Embolization therapy was subsequently implemented successfully, culminating in cessation of the vaginal bleeding. Unexpectedly, a month later, the vaginal bleeding recurred. A subsequent transvaginal ultrasound revealed focal placenta accreta, a condition known for its implications on fertility. In response to this, methotrexate therapy was initiated, which led to the ultimate cessation of vaginal bleeding. This case accentuates the critical value of comprehensive diagnostic methodologies, particularly Doppler ultrasonography and pelvic angiography, in managing complex and rare obstetric conditions like UAVM and placenta accreta. It underscores the importance of clinical vigilance, thorough evaluation, and the formulation of individualized treatment plans that align with patients' fertility preservation goals. The insights gleaned from this case may contribute significantly to the understanding and management of complex obstetric conditions. **Keywords :** Placenta Accreta ; Uterine Arteriovenous Malformation (UAVM) ; Doppler Ultrasonography ; Pelvic Angiography ; Methotrexate Therapy ; First-Trimester Vaginal Bleeding ; Fertility Preservation.

ISP-24-5

Perinatal outcomes of women conceiving at age 43 or older by freeze-thawed embryo transfer~A survey using the database of the Japan Society of Obstetrics and Gynecology~ : Ministry of Health, Labor and Welfare Scientific Research Group Yasuoka Toshiaki¹, Yokoyama Maki¹, Iwama Noriyuki², Suzuki Nao³, Sugiyama Takashi¹ *Ehime University Hospital¹, Tohoku University Hospital², St. Marianna University School of Medicine³*

[Objective] This study aimed to clarify the perinatal outcome of pregnancies resulting from frozen-thawed embryo transfer at the age of 43 years or older. **[Methods]** The study included cases of singleton pregnancies resulting in delivery at 22 weeks gestation or later, conceived by frozen-thawed embryo transfer between January 2016 and December 2019, and aged 43 years or older, from the ART Registry Project database of the Japan Society of Obstetrics and Gynecology (JSOG). Furthermore, singleton cases aged 43 years or older who experienced spontaneous pregnancies or non-ART pregnancies and deliveries after 22 weeks of gestation during the same period using the perinatal registry database of the JSOG were considered as the control group. Logistic regression analysis was performed on 4,828 pregnancies in the frozen-thawed embryo transfer group (FET group) and 11,191 spontaneous/non-ART pregnancies (NA group), using the NA group as the reference group. **[Results]** The adjusted odds ratios for perinatal outcomes in the FET group were as follows : low birth weight at term : 0.60 [95% CI : 0.52-0.69] ; preterm delivery < 37 weeks : 0.68 [95% CI : 0.61-0.77] ; stillbirth : 0.32 [95% CI : 0.19-0.51] ; and gestational hypertension : 0.65 [95% CI : 0.65]. 65 [95% CI : 0.57-0.73] ; gestational diabetes : 0.54 [95% CI : 0.48-0.61] ; placental abruption : 0.15 [95% CI : 0.08-0.25] ; and placenta previa : 0.57 [95% CI : 0.43-0.75]. **[Conclusion]** The results suggest that frozen-thawed embryo transfer pregnancies at age 43 years or older may not be more risky than those in the NA group from the perspective of perinatal outcome.

ISP-24-6

p32 can be associated with autophagy function in trophoblast

Morishita Hiroki, Kiyokoba Ryo, Sugiura Takako, Nakahara Kazushige, Hachisuga Nobutaka, Sakai Atsuhiko, Fujita Yasuyuki, Kato Kiyoko *Kyushu University*

[Objective] Preeclampsia (PE) has been attributed to reduced placental function, but its detailed etiology and treatment have not been established. There are several reports that decreased expression of p32 is associated with placental function. The p32 is mainly found in the mitochondrial matrix, important for mitochondrial translation, and for oxidative phosphorylation. It has also been reported that impaired autophagy leads to placental dysfunction. On the other hand, p32 is involved in autophagy, especially lysosomal acidification, in p32 knockout mice. In this study, we investigated the relationship between p32 and autophagy in placentas and trophoblast cell lines. **[Methods]** We collected placentas from 13 normal and PE placentas and evaluated p32 expression, autophagy-associated proteins in comparison with normal placentas. In addition, we used siRNA to control p32 expression in HTR8svneo, trophoblast cell line, and we evaluated autophagy-associated proteins, and lysosomal function. **[Results]** In parturient placentas, the expression of p32 was decreased in PE compared to normal placentas, and autophagy-associated proteins accumulated. Restriction of p32 expression in HTR8svneo resulted in impaired lysosomal acidification and accumulation of autophagy-associated proteins. **[Conclusion]** Our results suggest that decreased p32 expression in placentas may impair lysosomal function and cause autophagy dysfunction. p32 may be an interesting model because it is thought to be upstream of autophagy dysfunction in the placenta. In the future, we will explore the mechanism by which p32 expression is downregulated during pregnancy and conduct experiments in a model that more closely resembles pregnancy environment to investigate the relationship between p32 and placental function.

ISP-24-7

Identification of shared pathophysiological pathways of PCOS and ASD by RNA-seq datasets Caglayan Ahmet O^{1,2}, Bozkurt Fatma B³, Cakir Tunahan³ *Dokuz Eylul University, Turkey¹, Institute of Health Sciences, Dokuz Eylul University, Turkey², Department of Bioengineering, Gebze Technical University, Turkey³*

[Objective] Polycystic ovary syndrome (PCOS) is used as a model to investigate the relationship between high prenatal androgen exposure and neuropsychiatric disease in children. ASD is more common in boys than girls. This difference suggests that various factors involved in sex development and steroidogenic pathways, are also important in ASD evolution. **[Methods]** : The RNA-seq datasets used for the analysis of PCOS and ASD (6 for PCOS, 6 for ASD) were downloaded from Gene Expression Omnibus database. Differential gene expression analysis of each RNA-seq dataset was performed in R via edgeR package. To create a list of differentially expressed genes (DEGs) for PCOS and ASD datasets, we searched for genes that were identified as differentially expressed in at least 2 datasets. **[Results]** : The intersection between the PCOS DEGs identified in at least two PCOS datasets and the PCOS-related genes list was found as 44. The intersection between the PCOS DEGs and the ASD-related genes were detected as 83. Among the ASD DEGs, 94 genes were found to be PCOS-related, whereas 90 genes of them were found as ASD-related. The number of genes that were common in PCOS DEGs & ASD DEGs was found as 79. The related phenotypes for these genes were mostly associated with immunodeficiency, autoimmunity, autoinflammatory syndrome, diabetes, etc. **[Conclusion]** : We have successfully identified candidate genes that play significant roles in the shared pathophysiological pathways of PCOS and ASD. Some of them can be potential drug targets which is an important goal of this study.

ISP-24-8

Effect of galanin-like peptide (GALP) on hypothalamic kisspeptin expression in female Zucker fatty rats Sakata Akiko^{1,2}, Iwata Kinuyo², Nakao Kimihiko¹, Suzuki Shunji¹, Ishii Hirotaka² *Nippon Medical School¹, Department of Anatomy and Neurobiology, Nippon Medical School²*

[Objective] Kisspeptin neurons in the arcuate nucleus (ARC) of the hypothalamus are involved in pulsatile LH secretion via GnRH neurons. Galanin-like peptide (GALP) neurons in the hypothalamus also promote GnRH/LH secretion. Zucker fatty (ZF) rats with leptin receptor gene abnormalities exhibit obesity and suppression of pulsatile LH secretion. In ZF rats, GALP and kisspeptin expression levels are low in the hypothalamus, and GALP administration induces LH release. In this study, we performed histochemical analysis to determine whether GALP-induced LH release is mediated via activation of kisspeptin neurons in ZF rats. **[Methods]** ZF rats were ovariectomized and E2 tubes were implanted to eliminate the effects of endogenous sex steroid hormones. GALP or vehicle was administered into the third cerebroventricle, and blood samples were taken every 10 minutes to measure plasma LH concentration. After the administration, the animals were perfused with 4% paraformaldehyde solution and the brain was harvested for staining. *In situ* hybridization and immunohistochemistry were performed, and the number of *Kiss1* (the gene encoding kisspeptin) cells, Fos-positive *Kiss1* cells, and cFos-positive GnRH neurons were counted. **[Results]** GALP administration increased the plasma LH concentration in ZF rats. There was no significant difference in the number of *Kiss1* cells or the percentage of Fos-positive *Kiss1* cells between the GALP- and vehicle-treated groups. The number of cFos-positive GnRH neurons was significantly increased in the GALP-treated group. **[Conclusion]** GALP may promote LH release by activating GnRH neurons without mediating activation of kisspeptin neurons in the ARC.

ISP-24-9

Kamikihito contributes to visceral fat reduction and appetite suppression in PCOS model rats through effects of oxytocin and leptin Yamamoto Yuri, Takeda Asuka, Uchishiba Maimi, Minato Saki, Kamada Syuuhei, Iwasa Takeshi *Tokushima University*

[Objective] Polycystic ovary syndrome (PCOS) is an endocrine disorder that causes infertility as well as obesity and other metabolic abnormalities. Oxytocin (OT), a neuropeptide involved in appetite and fat metabolism, may be therapeutically beneficial for PCOS. However, there is currently no oral OT drug available. Kamikihito (KKT), a traditional herbal medicine consisting of 14 herbs, is often prescribed in clinical settings to women going through menopause. Furthermore, KKT has been shown to up-regulate the expression of OT in the hypothalamus and exert various physiological effects. The present study investigated the anti-obesity effects of KKT in relation to OT using a PCOS model rat. **[Methods]** Female rats were implanted with dihydrotestosterone to induce PCOS and divided into a normal food group (NF group) and food containing KKT group (KF group). After surgery, rats were fed normal food for four weeks, followed by food containing 3% KKT for another four weeks. The anti-obesity effects of KKT and its impact on the ovarian morphology in PCOS were examined. **[Results]** The results obtained showed that KKT supplementation reduced food intake, the size of visceral adipocytes, and ovarian weight. No significant differences were observed in the hypothalamic gene expression of OT and related factors. In contrast, the KF group showed increased mRNA expression levels of OT receptors and leptin in visceral fat and slightly increased serum levels of OT and leptin. **[Conclusion]** These results suggest the potential of

KKT as a therapeutic agent for PCOS via the modulation of adiposity, potentially through effects on OT and leptin signaling pathways.

ISP-24-10

Etonogestrel Subdermal Implant Continuation Rates and Associated Factors among Post-partum Adolescents in a Tertiary Government Hospital Ico Jennieffer Kristine M, Nuñez - Sangcate Jewell P. *East Avenue Medical Center, Philippines*

[Objective] : To determine the association of sociodemographic and clinical factors with continuing use of etonogestrel subdermal implant among post-partum adolescents in a tertiary government hospital **[Methods]** : Forty-one (41) adolescents who had etonogestrel subdermal implant insertion post-partum or post-operatively were followed-up via telemedicine online interview. Association of socio-demographic characteristics, clinical history, contraceptive related factors and presence of side effects to continuation rate was analyzed. Reasons for early discontinuation were identified. **[Results]** : The overall continuation rate had a mean duration of 30.39 months. Sociodemographic, obstetric characteristics and contraceptive factors were not found to be associated with the continuation rate of etonogestrel subdermal implant. The most common reason for removal was perceived side effect (84.7%). Patient-reported occurrence of side effect of weight loss was found to be significantly associated with etonogestrel implant continuation rate of less than 36 months. **[Conclusion]** : The continuation rate among post-partum adolescents is high, hence it should be offered to adolescents as one of their contraceptive options. Raising awareness on the possibility of side effects, specifically, the risk of weight loss-- should also be done, as this was found to be associated with early etonogestrel subdermal implant removal.

ISP-25-1

Immunohistological evaluation of MMP-2 and periostin in pathogenesis of recurrent pregnancy loss Ozawa Fumiko¹, Goto Shinobu^{1,2}, Yoshihara Hiroyuki^{1,2}, Kitaori Tamao^{1,2}, Ozaki Yasuhiko^{1,2,3}, Sugiura-ogawara Mayumi^{1,2} *Research Center for Recurrent Pregnancy Loss, Nagoya City University¹, Nagoya City University², Nagoya City University West Medical Center³*

[Objective] Matrix metalloproteinases -2 (MMP-2), which degrade protein of extracellular matrix, is important for forming placenta in early pregnancy. Periostin is cell adhesion protein that allows the maintenance of cancer stem cells and upregulated MMP-2 expression by inhibiting MMP-2 binding to the cell surface or by its degradation. We previously reported that in plasma, the expression of MMP-2 and periostin were significantly lower with RPL patients than healthy controls ($p < 0.05$). In this study, we investigated a roll of MMP-2 and periostin in pathogenesis of recurrent pregnancy loss (RPL). **[Methods]** With informed consent, decidual tissues were collected from idiopathic RPL patients with normal fetal chromosome (NC) (n=5) or with abnormal fetal chromosome (AC) (n=5) and patients of artificial abortion as healthy controls (n=5). Sections were stained by fluorescent immunohistochemistry. Eight to ten fields were evaluated at x400 magnification. We quantified the expression levels of MMP-2 and periostin by normalizing the integrated intensity to the number of DAPI-stained cells. **[Results]** The normalized intensity per DAPI count of MMP-2 and periostin in decidua, the one-way ANOVA detected significant differences between groups [MMP-2 : F (2,12) =14.2, $p < 0.01$, periostin : F (2,12) =4.08, $p < 0.05$]. The normalized intensity per DAPI count of MMP-2 and periostin in decidua with NC was significantly lower than in AC ($p < 0.01$) or in healthy controls ($p < 0.01$). **[Conclusion]** The results in this immunohistological

study suggested that decreased MMP-2 and periostin in decidua and in plasma play an important role in pathogenesis of RPL and they can be one of the predictive factors with RPL.

ISP-25-2

Role of PROK1 in decidua and in plasma of patients with unexplained recurrent pregnancy loss showing insulin hypersecretion Goto Shinobu¹, Ozaki Yasuhiko², Ozawa Fumiko³, Kitaori Tamao¹, Sugiura Mayumi¹ *Nagoya City University Graduate School of Medical Sciences¹, Nagoya City University West Medical Center², Research Center for Recurrent Pregnancy Loss, Nagoya City University Graduate School of Medical Sciences³*

[Objective] Prokineticin1 (PROK1) is an angiogenic factor that is regulated by hypoxia and insulin. PROK1 is produced during endometrial decidualization and plays an important role in embryonic implantation and placentation. In this study, we investigated the role of PROK1 in decidua and in plasma in patients with unexplained recurrent pregnancy loss (RPL) showing insulin hypersecretion. **[Methods]** The decidua and villi of the patient were surgically collected under a diagnosis of miscarriage from unexplained RPL patients. Fasting blood glucose and insulin levels were measured, and HOMA- β was calculated. Using IHC and ELISA, the expression of IGFBP-1, and PROK1 in the decidua and IGF-2 in the villi were analyzed in patients with euploid miscarriage with a high HOMA- β index (n=8) and compared to controls (euploid miscarriage with normal HOMA- β : n=12 ; aneuploid miscarriage with normal HOMA- β : n=12). Circulating PROK1 were measured using plasma of non-pregnant unexplained RPL patients (euploid miscarriage with high HOMA- β : n=10 ; normal HOMA- β : n=14, aneuploid miscarriage : n=10). All samples were collected with informed consent under the approval of the university ethical committee. **[Results]** The co-localization of PROK1 and IGFBP-1 in decidua was observed by IHC. Although circulating PROK1 was not significantly different between groups, PROK1/IGFBP-1 ratio in decidua was significantly higher and IGF-2 expression in villi was significantly lower in RPL patients with high HOMA- β compared to that of the controls. **[Conclusion]** Impaired decidualization and excessive PROK1 production may have pathological implications in patients with unexplained RPL with insulin resistance, especially under the state of hyper insulin production.

ISP-25-3

Unsuccessful cases of low-dose aspirin administration for thrombophilia other than antiphospholipid antibody syndrome in recurrent pregnancy loss Ichikawa Tomoko¹, Matsuda Shigeru¹, Kasano Sayuri¹, Yokote Ryouko¹, Yonezawa Mirei¹, Ouchi Nozomi¹, Kawabata Ikuno¹, Kuwabara Yoshimitsu¹, Satomi Misao^{1,3}, Takeshita Toshiyuki^{1,2}, Suzuki Shunji¹ *Nippon Medical School¹, Takeshita Ladies Clinic², Higashifuchu Hospital³*

[Objective] Low-dose aspirin (LDA) is often selected as an antithrombotic therapy for patients with recurrent pregnancy loss, and with thrombophilia other than antiphospholipid antibody syndrome (APS). Such LDA administration may be unsuccessful in preventing pregnancy loss. Therefore, this study aimed to examine the characteristics of these unsuccessful cases. **[Methods]** From 2017 to 2023, among a total of 3,291 patients, the 673 patients with thrombophilia other than APS who underwent LDA and whose pregnancy outcomes were confirmed were divided into two groups : live birth and unsuccessful. Cases with abnormal parental karyotypes or chorionic chromosomal abnormalities were excluded. The patient backgrounds were retrospectively analyzed. **[Results]** The live birth

rate based on the number of pregnancies while taking LDA were as follows : 1st : 67% (451/673), 2nd : 62.5% (40/64), 3rd : 12.5% (1/8), 4th : 20% (1/4). The live birth rates were significantly lower in cases with positive anti-cardiolipin IgG (anti-CL IgG) than in cases with transient or weakly positive anti-CL IgG or where antibody levels were strongly positive but did not match the clinical findings of obstetric APS (anti-CL IgG positive : 41.3% vs anti-CL IgG negative : 58.6%, $P=0.0017$). The antibody levels were significantly higher in the pregnancy loss group (live birth group : 2.84 ± 0.19 IU vs pregnancy loss group : 3.54 ± 0.35 IU, $P=0.0081$). **[Conclusion]** If live births cannot be obtained after LDA administration in two pregnancies, and/or if anti-CL IgG is positive in cases other than APS, alternative treatment approaches should be considered.

ISP-25-4

Clinical utility of next-generation sequencing method with short tandem repeat analysis for evaluation of products of conception Honda Hidemine¹, Takiuchi Tsuyoshi^{1,2}, Tsuji Saori¹, Goto Takeshi¹, Handa Mika¹, Miyake Tatsuya¹, Kimura Tadashi¹ *Osaka University¹, Clinical Genomics, Osaka University²*

[Objective] Genomic evaluations of products of conception (POC) play a crucial role in determining causes of pregnancy loss (PL). We conducted a comparison between next-generation sequencing (NGS) and karyotyping to identify the causes of PL. **[Methods]** Genomic evaluation of POC was performed using both NGS and karyotyping. We assessed the ratio of cases in which the genetic abnormalities of miscarriage (gestational age <12 weeks) or intrauterine fetal demise (IUFD, gestational age ≥ 12 weeks) could be found. Short tandem repeat (STR) analysis with maternal germ line DNA to confirm the presence of maternal cell contamination (MCC). **[Results]** We included 47 cases consisting of 42 miscarriages and 5 IUFDs. Among these, 4 used frozen specimens, and 16 expelled vaginally and non-sterilely due to spontaneous abortion or IUFD. NGS estimated genetic abnormalities 57% of cases (27/47), while karyotyping did in 40% of cases (19/47). NGS can more accurately estimate genetic abnormalities of PL compared to karyotyping ($p < 0.05$). In karyotyping, 26% (12/47) of cases failed to yield results due to culture failure, and among those cases, 50% (6/12) exhibited genetic abnormalities through NGS. Among POC analyzed using NGS, 27% (13/47) exhibited a 46 XX, and within this group, 38% (5/13) showed maternal nucleic acid levels above 80%, indicating MCC. **[Conclusion]** POC using NGS is more effective approach than karyotyping for determining the cause of PL, and addition of STR analysis could speculate MCC.

ISP-25-5

Association among NK cell, zinc, and vitamin D in reproductive failures Yamaya Ayano, Ogino Nana, Yamaguchi Momoko, Omote Maya, Saeki Shinichiro, Kamei Hidetake, Takeyama Ryu, Wakimoto Yu, Fukui Atsushi, Shibahara Hiroaki *Hyogo Medical University*

[Objective] Immune abnormalities have been reported as a cause of reproductive failures. We have reported that high CD16⁺/CD56^{dim} or low NKp46⁺ NK cells in endometrium are related to reproductive failures. In recent years, it has been reported that vitamin D has the function of regulating immune function and its deficiency is associated with reproductive failures. In addition, zinc plays an important role in maintaining cell function, and it also works to assist the vitamin D functions. In this study, we investigated whether zinc and vitamin are associated with immune states. **[Methods]** Peripheral blood and endometrium were collected from patients with recurrent pregnancy losses (RPL) (n=190) and repeated implantation failures (RIF) (n=32) in mid luteal phase. NK cell cytotoxicity, zinc level, and 25-

hydroxyvitamin D3 level of peripheral blood were measured. The percentage of CD16⁺/CD56^{dim} cells in uterine endometrial NK cells was measured using flow cytometry. **[Results]** There were no significant differences in the items measured in RPL and RIF. The percentage of endometrial CD16⁺/CD56^{dim} NK cells greater than 18% was considered the high group and less than 18% the normal group. 25-hydroxyvitamin D3 was significantly lower in the high group in RIF ($p=0.017$). 25-hydroxyvitamin D3 was strongly negatively correlated with endometrial CD16⁺/CD56^{dim} NK cells in RIF ($r=-0.836$, $p=0.001$). In the case of RPL, zinc and 25-hydroxyvitamin D3 showed weak positive correlations, but no other correlations were observed. **[Conclusion]** Vitamin D deficiency was associated with endometrial NK cell abnormalities in RIF, predicting a therapeutic effect of vitamin D supplementation.

ISP-25-6

The presence of chronic endometritis detected by endometrial microbiome test is associated with favorable pregnancy outcomes at subsequent embryo transfer in patients with recurrent implantation failure Hiratsuka Daiki, Matsuo Mitsunori, Fukui Yamato, Ishizawa Chihiro, Iida Rei, Hiraoka Takehiro, Izumi Gentaro, Harada Miyuki, Hiraike Osamu, Osuga Yutaka, Hirota Yasushi *The University of Tokyo*

[Objective] Hysteroscopy, endometrial CD138 test, and endometrial microbiome test are used for the diagnosis of chronic endometritis (CE) in patients with recurrent implantation failure (RIF). However, it remains unclear which methods are effective in improving pregnancy outcomes. This retrospective study investigated the correlation of populations diagnosed with CE by each method and their contribution to RIF treatment. **[Methods]** Sixty-eight RIF patients who underwent all three tests at our hospital were included. RIF was diagnosed with more than two failed embryo transfer cycles using good-quality embryos. Patients diagnosed with CE by each method received antibiotic therapy and/or lactobacillus supplementation before post-test embryo transfer (ET). In 29 of 68 cases, post-test ET was performed. We examined the correlations of the patient populations diagnosed with CE by these tests, and the correlations between the presence of CE and good pregnancy outcome in post-test ET. **[Results]** Of the 68 cases, CE was diagnosed in 32, 34, and 33 cases by hysteroscopy, CD138 test, and microbiome test, respectively (47, 50 and 48.5%). There was no clear correlation among CE-positive individuals from these tests. The correlation coefficients between the presence of CE and post-test pregnancy on hysteroscopy, CD138 test, and microbiome test were 0.19 ($P=0.30$), 0.14 ($P=0.46$), and 0.39 ($P=0.04$), respectively. Abnormal endometrial microbiota was significantly linked to successful pregnancy outcomes in the subsequent ET. **[Conclusion]** Each CE detection method has the potential to detect different RIF populations. Among these methods, endometrial microbiome test may be the best one for improving fertility in RIF patients.

ISP-25-7

Laparoscopic management of Ectopic Gestation—A Scenario in the primary care hospital of a developing country Singh Rajesh K¹, Nigam Parul¹, Chaube Sanjay², Chaube Jyoti³ *Endoscopic Surgery, Singh Hospital, India¹, Division of Minimally Invasive Surgery, St. Jude's Hospital, India², Division of Radiology, St. Jude's Hospital, India³, St. Jude's Hospital, India⁴*

[Objective] Ectopic pregnancy is a common gynecological problem that causes significant morbidity mortality in the women of reproductive age. Diagnosis of ectopic gestation is usually delayed in the developing countries and most patients come in ruptured state. Bleeding ectopic leads to shock and poor general

condition. Retrospective study of ectopic gestation patients managed with laparoscopic methods from Jan. 19 to July 23 to evaluate the outcome of the laparoscopic management. **[Methods]** total 28 patients of ectopic gestation were managed with laparoscopic method. Laparoscopy revealed unruptured tubal gestation in 3 patients other patients had ruptured ectopics and free blood in the pelvis. Different procedures like electrocoagulation, Methotrexate injection, milking of the tubal pregnancy, salpingostomy or salpingectomy was performed according to the site and size of the ectopic gestation or future need of pregnancy. Postoperative period was uneventful all patients were discharged after 72 hrs. **[Results]** Laparoscopic method is a good option in ectopic gestation patients where we can confirm the diagnosis and simultaneously manage it. **[Conclusion]** We advise to do laparoscopic management in patients of ectopic even if it has ruptured but haemodynamically stable.

ISP-25-8

RECURRENT ABDOMINAL PREGNANCY : A CASE REPORT Nasser Halija, Pelupessy Nugraha, Chalid Maisuri Hasanuddin University, Indonesia

Abdominal pregnancy is a rare condition that may cause a significant threat to maternal life. This kind of pregnancy is the most-uncommon kind of ectopic pregnancy. It can cause significant morbidity because of its impact on vital organs to ability to reach an advanced gestational age if not promptly diagnosed and managed. Advanced abdominal pregnancy is extremely rare. Abdominal pregnancy occurs when a fertilized ovum implants within the abdomen but outside the female reproductive organs, either primarily or secondarily. The gestational age at presentation varies based on symptoms, location of implantation, and ability of the patient to access care. Treatment is most often surgical, but image-guided vessel embolization or direct injection of methotrexate may also be used in certain clinical situations. In cases in which placental extraction is performed, a good separation technique and adequate vascular management will provide the best results.

ISP-25-9

A case of ectopic pregnancy implanted on pelvic peritoneum and managed by laparoscopic surgery Kang Jae Hee, Kwon Kyeong Yeon, Shin Jin Woo Gil Medical Center, College of Medicine, Gachon University, Korea

[Objective] This case report describes an ectopic pregnancy implanted on pelvic peritoneum and managed by laparoscopic surgery. **[Case Report]** 31-year-old female presented to the emergency department, with a preliminary diagnosis of ectopic pregnancy with Beta-hCG level of 10733 mIU/ml and an sonographically undetectable intrauterine gestational sac. Ultrasound examination revealed an empty uterine cavity, normal both ovaries and fallopian tubes, a small quantity of fluid in the anterior and posterior cul-de-sac, along with a mass adjacent to the posterior uterus showing an active color doppler signal. Diagnostic laparoscopy was conducted. Bilateral normal ovaries and fallopian tubes were observed upon laparoscopic inspection. An abdominal pregnancy implanted on the pelvic peritoneum of posterior aspect of the uterus. Surgical excision of conception products was accomplished with minor bleeding control. Subsequently, serum Beta-hCG levels declined rapidly and surgical biopsy was confirmed as an ectopic pregnancy. The patient recovered with a general postoperative course. **[Conclusion]** Intraabdominal pregnancy should be considered when an ectopic pregnancy with empty uterine cavity and unremarkable finding of both adnexa on ultrasound examination. Operative laparoscopy is a secure and effective method for managing patients of early abdominal pregnancies.

ISP-25-10

Ectopic gestation in incisional sac—A case Report Chaube Rohan¹, Chaube Sanjay², Chaube Jyoti³, Nigam Parul¹ *Radiology, M. M. Institution of Medical Sciences, India¹, Division of Minimally Invasive Surgery, St. Jude's Hospital, India², Division of Radiology, St. Jude's Hospital, India³, St. Jude's Hospital, India¹*

28 years old female patient presented with complain of pain abdomen and distension. She has a history laparotomy in the past. Clinical examination reveals obstructed incisional hernia. X-ray abdomen was suggestive of intestinal obstruction. USG abdomen showed a live fetus of 10 weeks in the hernial sac with dilated loops of small bowel. Emergency exploration was performed with removal of the ectopic gestation, Reduction of the contents small bowel done and simple closure of the hernial defect done. Postoperative period was uneventful and patient was discharged with complete recovery on 5th post operative day. Ectopic gestation in pelvis or abdomen encountered frequently but abdominal gestation is rare. This ectopic gestation in hernial sac is one of the rarest case.

ISP-25-11

Novel function of inflammatory IL-18 for the prevention of murine miscarriage Horii Yumi^{1,2}, Ino Hajime^{1,2}, Negishi Yasuyuki^{1,2}, Suzuki Shunji², Morita Rimpei¹ *Department of Microbiology and Immunology, Nippon Medical School¹, Nippon Medical School²*

[Objective] Inflammatory cytokines, such as IL-1 β , TNF- α , and IL-6, induce reproductive failure along with excessive inflammation. IL-18, despite being an inflammatory cytokine, is unique with diverse functions such as angiogenesis. However, the role of IL-18 during pregnancy is still unclear. Thus, this study aimed to investigate the role of IL-18 during pregnancy in mice. **[Methods]** Lipopolysaccharides (LPS, 1 or 2 μ g/body) were administered intraperitoneally on the gestational day 8.5 (Gd 8.5) in B6 \times B6 syngeneic pregnant mice. Certain mice were treated with anti-IL-18 antibody to neutralize IL-18. The pregnancy outcomes, cytokine production levels, and immune cell kinetics were analyzed using immunostaining, flow cytometry, and western blotting. **[Results]** The administration of 2 μ g of LPS resulted in significantly higher murine abortion. Interestingly, although 1 μ g of LPS did not induce abortion, IL-18 neutralization resulted in significant abortion in the mice. It suggests that the inflammatory cytokine IL-18 has a protective role against murine miscarriage. We discovered that IL-18 neutralization inhibited IFN- γ and IL-4 production as well as their signaling pathways in the decidua and myometrium. Furthermore, we found that IL-18 was produced by not only macrophages but also the myometrium. **[Conclusion]** IL-18 has a protective role against murine miscarriage induced by minor infection caused by IFN- γ and IL-4 production, which may be associated with placental development and anti-inflammatory effects. We propose that appropriate inflammation related to IL-18 is required for a successful pregnancy outcome.

ISP-25-12

Role of laparoscopic surgery in ovarian pregnancy Chaube Sanjay, Nigam Parul, Chaube Jyoti *Division of Minimally Invasive Surgery, St. Jude's Hospital, India*

[Objective] Ectopic gestation is a fatal complication of pregnancy goes unnoticed. In the developing country they presents late when it has ruptured and leads to haemoperitoneum. ovarian ectopic is only 2% cases of ectopic gestations. **[Methods]** We performed laparoscopic management of ovarian gestation in four cases out of total 198 cases of ectopic gestation presented in our hospital in last eight years. Diagnosed on sonography patients of ectopic gestation were taken for laparoscopic interven-

tion. Laparoscopy revealed free blood and blood clot in the pelvis. clots and blood evacuated wedge resection of the ovary was performed with energy source. Haemoperitoneum was established. Peritoneal lavage with saline. Excised gestation taken out from 10 mm port. Port closed after putting a drain. **[Results]** The laparoscopic procedure was completed successfully without any complication and minimal morbidity. All patients discharged on 72 hrs. with complete recovery. **[Conclusion]** Laparoscopic management gives satisfactory results in ovarian ectopic gestation.

ISP-26-1

Rapid inflammatory responses and subsequent migration of macrophages to fetal membranes in the mouse model of intrauterine infection Matsuzaka Yu, Mogami Haruta, Matsuzaka Sunao, Yasuda Eriko, Inohaya Asako, Takakura Masahito, Chigusa Yoshitsugu, Mandai Masaki *Kyoto University Graduate School of Medicine*

[Objective] Some pregnancies are threatened to bacterial invasion but not all the cases lead to preterm birth. We investigated the protective functions of fetal membranes against bacterial infection using mouse model of intrauterine infection. **[Methods]** Laparotomy was performed in pregnant mice on day 15 post coitum under general anesthesia and 10 ng of lipopolysaccharide (LPS group, n=3) or PBS (PBS group, n=3) was injected into each gestational sac. Fetal membranes were collected 4, 24, and 48 hours after injection. **[Results]** The expression of inflammation related genes such as *IL1B*, *IL6*, *PTGS2*, and *TNF* mRNA was increased in the LPS group compared with the PBS group at 4 h ($x620.0 \pm 160.5$, $x94.61 \pm 24.25$, $x6.41 \pm 1.82$, and $x181.4 \pm 36.36$, respectively, $P < 0.01$). The inflammatory responses reached their peak at 4 h and returned to the basal levels 48 h after injection. At 4 h, immune cells were rarely observed in both groups. However, more immune cells migrated to the fetal membrane in the LPS group than the PBS group at 24 h (98 ± 73.8 cells per section in the LPS group, 20 ± 14.6 cells per section in the PBS group, $p = 0.02$). The number of F4/80 positive macrophages was also increased in the LPS group than the PBS group at 24 h (36.8 ± 23.5 cells per section in the LPS group, 6.2 ± 8.9 cells per section in the PBS group, $p < 0.01$). **[Conclusion]** Fetal membranes rapidly respond to endotoxin stimuli which is followed by migration of macrophages to fetal membranes. These migrated macrophages might have a defensive function against bacterial pathogens.

ISP-26-2

Porphyromonas gingivalis enhances the expression of inflammatory cytokines in human amnion mesenchymal cells Teraoka Yuko, Uyama Takuto, Sugimoto Jun, Kudo Yoshiki *Hiroshima University*

[Objective] We generated a dentally infected mouse model using *Porphyromonas gingivalis* (*P.g.*), a periodontal pathogen, and reported its usefulness as a preterm birth model. In this model, the expression of inflammatory cytokine was upregulated in the fetal membranes. Additionally, *P.g.* was localized in the placenta and fetal membranes, suggesting that local inflammation caused by *P.g.* could be one of the factors leading to preterm birth. However, it is not clear whether *P.g.* induces inflammation in the human fetal membranes. In this study, we investigated the effects of *P.g.* using primary cultured human amnion mesenchymal cells (hAMCs). **[Methods]** Under the approval of the Institutional Ethics Committee and with patient consent, we obtained amniotic membranes from the placentas after cesarean section. We isolated and cultured human amnion mesenchymal cells (hAMCs) using trypsin-collagenase treatment. After adding *P.g.* suspended in culture medium, we measured the gene

expression of inflammatory cytokines and COX-2 in real-time RT-PCR. The activation of the NF- κ B pathway was verified using Western blot analysis with anti-phosphorylation antibodies. **[Results]** In hAMCs, stimulation by *P.g.* resulted in an upregulation of inflammatory cytokines such as IL-1 β and IL-6, as well as COX-2 gene expression, with a significant increase observed at an MOI of 10. Furthermore, in hAMCs, proteins involved in the NF- κ B pathway were phosphorylated. **[Conclusion]** In hAMCs, the upregulation of inflammatory cytokine gene expression, such as IL-1 β , in hAMCs suggested their involvement in cytokine production in the amniotic membranes. *P.g.* may activate the NF- κ B pathway and induce inflammation in human amniotic membranes.

ISP-26-3

A qualitative and quantitative assessment of placental alpha microglobulin-1 (PAMG-1) for predicting spontaneous preterm birth in asymptomatic women with a short cervix Nozaki Yuki¹, Imai Kenji¹, Ohori Yukiko¹, Miki Rika^{2,3}, Matsuo Seiko¹, Tano Sho¹, Ushida Takafumi¹, Kotani Tomomi¹, Kajiyama Hiroaki¹ *Nagoya University¹, Bell Research Centre for Reproductive Health and Cancer, Medical Corporation Kishokai², Collaborative Research, Nagoya University Graduate School of Medicine, Laboratory of Bell Research Centre³*

[Objective] As a potential predictor of spontaneous preterm birth (PTB), PAMG-1 measurement in cervicovaginal fluid (CVF) is conducted internationally. However, no report had evaluated the PAMG-1 ability in Japan. The purpose of this study is to determine whether qualitative/quantitative assessment of PAMG-1 improves predicting ability of PTB in Japanese clinical settings. **[Methods]** During May 2020 to March 2023, we collected 244 CVF samples (24-35 gestational age, cervix \leq 25 mm). Multivariate logistic regression analysis was performed to reveal the relationship of PAMG-1 to PTB within 1- or 2-week after CVF sampling (termed "Impending PTB"). The risk of Impending PTB was stratified by predetermined thresholds by quantitative evaluation of PAMG-1. Moreover, we compared the predictive ability of PAMG-1, fetal fibronectin (FFN), and their combination using Receiver operating characteristic (ROC) analysis. **[Results]** Positive PAMG-1 was independently associated with Impending PTB (within 1-week: OR 7.84, 95% CI 2.02 - 30.5, $p = 0.003$; within 2-week: OR 7.34, 95% CI 2.75 - 19.6, $p < 0.001$). For impending PTB within 1-week, quantitative evaluation of PAMG-1 improved the predicting accuracy (4.3% at < 1000 pg/mL to 50.0% at ≥ 3000 pg/mL), and no PTB occurred when both PAMG-1 and FFN were negative. When PAMG-1 > 3000 pg/mL, the rate of PTB within 2-week reached 90%, regardless of FFN value. Combining PAMG-1 and FFN showed highest AUC values (0.821 for PTB within 1-week and 0.804 for PTB within 2-week). **[Conclusion]** The qualitative and quantitative assessment of PAMG-1 improved the accuracy of predicting PTB, which is first evaluation in Japanese clinical settings.

ISP-26-4

The umbilical cord blood microRNA profiles in preterm birth Pyeon Seung Yeon, Kena Park, Ji Young Kwon, Jeong Min Song *Kyunghee University Hospital at Gangdong, Korea*

[Objective] The aim of this study was to compare microRNA profiles in umbilical cord blood between preterm and term births. Using this approach, we attempted to elucidate the pathophysiology of preterm birth at the microRNA level. **[Methods]** Venous blood from umbilical cord was obtained from 10 patients (5 preterm birth, 5 term birth). Quantification and analysis were performed using the Nanostring nCounter system in PhileKorea. Then, validation of differentially expressed mi-

croRNA in Nanostring nCounter system was done by quantitative real time PCR. **[Results]** Nanotstring analysis found the expressions of 5 microRNAs were significantly altered in patients with preterm birth compared to those with term birth. Quantitative real-time PCR confirmed that level of let-7i-5p in preterm birth was declined compared to term birth. **[Conclusion]** This study demonstrated that the microRNAs in cord blood are altered in preterm birth group and it might be related to pathophysiology of preterm birth. This assumption needs to be further studied.

ISP-26-5

Efficacy of modified short-term tocolysis for the management of threatened preterm labor Kawamata Mari, Shimura Koki, Katayama Akihisa, Tanaka Yukiko, Waratani Miyoko, Mori Taisuke *Kyoto Prefectural University of Medicine*

[Objective] In 2020, our hospital changed its management protocol for threatened preterm labor from long-term tocolysis to "modified short-term tocolysis": a protocol we devised in which ritodrine hydrochloride is aggressively reduced and discontinued but can be resumed and continued if uterine contractions recur. This study aimed to evaluate the effectiveness of our "modified short-term tocolysis" protocol. **[Methods]** A retrospective study was conducted on patients with threatened preterm labor of less than 34 weeks' gestation who were managed in our hospital between 2017 and 2022. Patients with multiple pregnancies, fetal anomalies, placenta previa, premature rupture of the membranes, and therapeutic cervical suture were excluded. Patients were divided into long-term tocolysis (long group) and modified short-term tocolysis (modified group) and compared for perinatal outcomes. **[Results]** There were 61 and 35 patients in the long group and the modified group, with no difference in gestational age at admission (long group : 29 [22-33] weeks, modified group : 30 [22-33] weeks, $p = 0.522$). There was no difference in the preterm delivery at less than 34 weeks' gestation between the two groups (long group : 6 cases [9.8%], modified group : 5 cases [14.3%], $p = 0.522$). On the other hand, the number of days of intravenous ritodrine hydrochloride infusion was significantly shorter in the modified group (long group : 68 days, modified group : 6 days, $p < 0.01$). These results were unchanged after adjusting for patient background. **[Conclusion]** It would be effective to change from long-term tocolysis to modified short-term tocolysis for threatened preterm labor.

ISP-26-6

Urgency of the McDonald cerclage : A case-control study Tanaka Ikko, Urushiyama Daichi, Nagata Koshiro, Hirano Tomoka, Ishida Koko, Hirakawa Toyofumi, Sanui Ayako, Izuchi Daisuke, Ito Tomohiro, Miyata Kohei, Kurakazu Masamitsu, Yotsumoto Fusanori *Fukuoka University*

[Objective] Cervical cerclage for cervical incompetence is reportedly effective in preventing preterm births. Little evidence exists regarding the urgency of the McDonald cerclage in unexpected cervical incompetence cases. This study aimed to examine the relationship between the time from diagnosis of cervical incompetence to surgery and perinatal outcomes. **[Methods]** Twenty-three women who underwent the McDonald cerclage for cervical incompetence at less than 26 weeks' gestation at single institution from 2015 to 2023 were included. A case-control study was conducted with 12 patients undergoing emergency surgery on the day of diagnosis as the emergency surgery group (group E) and 11 patients undergoing elective surgery on or after the day after diagnosis as the elective surgery group (group W). The perinatal outcomes were miscarriage or preterm birth at less than 34 weeks' gestation (PB<34w), extended pregnancy

duration, perinatal death, and developmental disability at 1.5 years of age (DD1.5y). **[Results]** Overall, the median (range) gestational age (GA) at which cervical incompetence was diagnosed was 21.9 (13.7-24.4), and the median (range) GA at which the McDonald cerclage was performed was 22.4 (15.7-24.9); there was no significant difference between the two groups ($P=0.324, 0.076$; respectively). The prevalence of PB<34w/perinatal death/DD1.5y was 83/42/75% and 22/0/0% in groups E and W, respectively ($P=0.009, 0.045, 0.003$; respectively). The median extended pregnancy duration in groups E and W was 47.5 and 40.0 days ($P=0.049$). **[Conclusion]** The McDonald cerclage had better outcomes in group W than in group E.

ISP-26-7

Time interval from antenatal corticosteroids to delivery was associated with complication rates in very preterm infants Fuma Kazuya¹, Kotani Tomomi¹, Tsuda Hiroyuki², Tano Sho¹, Ushida Takafumi¹, Imai Kenji¹, Kajiyama Hiroaki¹ *Nagoya University¹, Japanese Red Cross Aichi Medical Center Nagoya Dai-ichi Hospital²*

[Objective] The optimal time interval from antenatal corticosteroids administration to delivery (ACS-to-delivery interval) is recommended as 1-7 days to prevent complications in preterm infants. However, its association with non-respiratory complications is unclear. **[Methods]** We retrospectively investigated very preterm infants (<32 weeks) in 2012-2020 at two tertiary centers. Eligible infants were classified into four groups : the no ACS (A, n=155), partial ACS (B, n=96), ACS-to-delivery interval 1-7 days (C, n=320), and ACS-to-delivery interval ≥8 days groups (D, n=96). Adjusted odds ratio (aOR) for neonatal complications was compared using logistic regression analysis with covariates of gestational age, small for gestational age, sex, chorioamnionitis, and delivery mode. **[Results]** Compared with group A, groups C and D showed significantly lower aORs for respiratory distress syndrome (RDS, 0.36 [0.23 to 0.57], and 0.38 [0.22 to 0.68], respectively); but higher aORs for chronic lung disease (CLD, 1.86 [1.06 to 3.29], and 3.11 [1.53 to 6.31], respectively). Group C also showed a significantly lower aOR for intraventricular hemorrhage (IVH, 0.21 [0.07 to 0.63]) and patent ductus arteriosus (PDA, 0.47 [0.29 to 0.75]), and possibly a lower aOR for retinopathy of prematurity (ROP, 0.51 [0.26 to 1.01]). There was no significant difference in aOR for sepsis, necrotizing enterocolitis, periventricular leukomalacia, and death; however, the incidence of these complications was minimal. **[Conclusion]** The ACS-to-delivery interval of 1-7 days appears to be advantageous for preventing IVH and PDA. Optimal timing of ACS could maximize the preventive effect for complications in very preterm infants.

ISP-26-8

The incidence of preterm birth after cervical conization by Shimodaira-Taniguchi instrument : a single center retrospective cohort study Tabuse Mari, Kawanishi Yoko, Okada Aiko, Nakamura Koji, Miyake Tatsuya, Hiramatsu Kosuke, Mimura Kazuya, Kimura Toshihiro, Ueda Yutaka, Sawada Kenjiro, Endo Masayuki, Kimura Tadashi *Osaka University*

[Objective] The incidence of preterm birth (PTB) after conization is higher than general pregnant population, and the PTB risk is different among resection procedure. We use Shimodaira-Taniguchi (S-T) instrument. Here we report relationship between S-T conization and PTB in our institution. **[Methods]** We had 855 cases of S-T conization for reproductive aged women from 2010 to 2022. There were 65 pregnancies and we analyzed the 37 cases of first pregnancy after S-T conization. **[Results]** PTB occurred in 10 cases (27%), in which preterm premature rupture of membranes occurred in 8 cases. Seven were nullipar-

ity and no one had previous PTB history. The remaining cervical length (CL) in the second trimester was 27.5 mm (18.3-41.3) in PTB group, while 36.6 mm (19.9-66.0) in term birth (TB) group ($p=0.09$). PTB group had 3 (30%) of adenocarcinoma in situ (AIS), and all their CLs were less than 25 mm in second trimester, in which 2 underwent re-conization. TB group had 9 (33%) of AIS or Ia1 stage cancer, but all their CLs were more than 25 mm in second trimester, in which 4 underwent re-conization. **[Conclusion]** The PTB rate at our institution was higher than the general incidence of 8-15% after conization. However, a previous report has shown that the PTB risk after S-T conization is not high, and this was probably because our institution deal with high-risk patients. Care must be taken in cases of AIS or cancer in which the resected lesion is large and causes cervical shortening.

ISP-26-9

Therapeutic outcomes of ultrasound—and physical examination-indicated cerclage in low-risk pregnant women Goto Ryota, Nagao Takeshi, Tsuruoka Yuto, Hasegawa Akihiro, Inoue Momoko, Ito Yuki, Takahashi Ken, Miya Michiko, Samura Osamu, Okamoto Aikou *The Jikei University*

[Objective] To investigate the efficacy of ultrasound- and physical examination-indicated cerclage. **[Methods]** We conducted a single-center, retrospective study from 2018 to 2023. First, patients with cervical length (CL) <25 mm less than 25 weeks without bulging membrane were divided into cerclage and non-cerclage groups. Cerclage was performed upon request by patients after explaining the associated risks. The primary outcome was delivery before 37 weeks. Second, patients with dilated cervix and bulging membranes under 25 weeks were also divided into cerclage and non-cerclage groups. Cerclage was performed at the obstetrician's discretion. The primary outcome was the diagnosis-to-delivery duration. We excluded women with a history of preterm deliveries from both cohorts. **[Results]** Thirty-six patients with CL <25 mm were divided into cerclage ($n=17$) and non-cerclage ($n=19$) groups. The median CL did not differ at diagnosis (cerclage : 13.5 mm, non-cerclage : 13.0 mm, $p=0.69$). Delivery before 37 weeks occurred in 47.0% of cerclage and 47.3% of non-cerclage cases ($p=0.98$). Delivery before 34 weeks (cerclage : 35.2%, non-cerclage : 36.8%, $p=0.92$) and diagnosis-to-delivery duration (cerclage : 66.0 days, non-cerclage : 100.5 days, $p=0.54$) also showed no significant difference. Eighteen patients with bulging membranes were divided into cerclage ($n=10$) and non-cerclage ($n=8$) groups. Baseline characteristics were similar between groups. The cerclage group had a significantly longer median duration to delivery (cerclage : 55.5 days, non-cerclage : 4.5 days, $p=0.02$). There were one case of rupture of membranes within 48 h postoperatively. **[Conclusion]** Ultrasound-indicated cerclage may not effectively prevent preterm birth. Physical examination-indicated cerclage may potentially extend the duration of pregnancy.

ISP-26-10

The investigation of patients with preterm labor using cervical pessary therapy in our hospital Kondo Emi¹, Ozaki Yasuhiko¹, Tokioka Ayana¹, Kawamura Yuji², Nonobe Megumi¹, Kawabata Shunichi¹, Arakawa Atsushi¹, Nishikawa Naomi¹, Kumagai Kyoko³, Sugiura Mayumi³ *Nagoya City University West Medical Center¹, Inazawa Kosei Hospital², Nagoya City University³*

<Objectives> Short cervical length (CL) is one of the risk factors for preterm labor (PL). Cervical pessary (CP) has been reported to be a relatively minimal invasive option for the prevention of PL. We report on cases in which we used CP for the prevention of PL in our hospital. **<Methods>** We retrospectively

examined 105 patients with short CL who underwent CP insertion. The mean weeks of gestation was 27 (15-34), and the mean CL was 18.0 mm (0-39) at the time of CP insertion. 73 patients needed to be hospitalized from CP insertion to delivery, and the mean hospitalization period was 18.4 (1-74) days. **<Results>** In the 93 patients delivered in our hospital, 36 patients were PL, 22 of 71 in singleton pregnancies (30.9%) and 14 of 22 in twin pregnancies (63.6%). 3 of 8 (37.5%) in cervical incompetence and 1 of 7 (14.2%) in after uterine conization were PL. In PL, 21 patients were PROM, 8 were uterine contractions, 5 were elective cesarean section for twins, 1 was TTTS, and 1 was intra-abdominal hemorrhage due to endometriosis. 2 patients were required hospitalization because of the increasing of vaginal discharge which was difficult to differentiate from PROM, and 1 patient was removed CP due to vaginal pain. **<Conclusion>** Using CP may prevent shortening CL and reduce hospitalization period. And it may also be useful in twin pregnancies, cervical incompetence and pregnancies after uterine conization.

ISP-26-11

Deciphering an indispensable role of uterine epithelial SHP2 in parturition initiation at single cell resolution Deng Wenbo, Liu Meng, Ji Mengjun, Cheng Jianghong, Wang Haibin, Zhongxian Lu *Xiamen University, China*

[Objective] The timely onset of parturition is a critical determinant for pregnancy success. The highly heterogenous maternal decidua has been increasingly recognized as a vital factor in setting the timing of labor. Despite the cell type specific roles in parturition, the role of the uterine epithelium in the decidua remains poorly understood. **[Methods]** We unravel the previously unappreciated role of epithelium in parturition initiation leveraging genetic, molecular and pharmacological approaches. **[Results]** Our major finding including 1) Unravel the Cell heterogeneity of maternal epithelium by scRNA-seq ; 2) Investigate the dynamic changes in the epithelium on days 16 and 19 of pregnancy ; 3) Genetic evidence show that uterine epithelium *Shp2* deficiency contributes to dystocia ; 4) Epithelial *Shp2* directs epithelial COX1/COX2 expression and PGF2 α production ; 4) There is significant changes of genes in different cell types in the absence of epithelial *Shp2* uterus ; 5) *Shp2*-deficient uteri show dysregulation in decidua before labor ; 6) There is extensive interactions between epithelium and other cell types. **[Conclusion]** Our studies elucidate the role of epithelial *Shp2* in regulating PGF2 α level and decidua at term to determine the onset of parturition.

ISP-26-12

Home telemedicine for preterm labor using mobile cardiocography : A case series Suemitsu Tokumasa¹, Kadooka Mizuho¹, Hosokawa Mayu¹, Yasuda Koya¹, Kanamoto Yoshihisa¹, Mitani Takahiro¹, Furusawa Yoshiaki¹, Tajima Atsushi² *Kameda Medical Center¹, Kyorin University²*

[Objective] Cardiotocography (CTG) assessment can now be performed at home owing to innovations in information and communication technologies. We have reported on home care for high-risk pregnancies and fetal growth restriction using a mobile CTG system (iCTG). However, its effectiveness in monitoring patients with preterm labor (PTL) remains unclear. We investigated the clinical impact of telemedical home care with iCTG for PTL. **[Methods]** Nine patients with admitted PTL were enrolled in a single-center retrospective case series. iCTG home care was implemented for patients who had not delivered after hospitalization and had concerns about moving to outpatient management directly because of PTL symptoms. iCTG was performed at home for 1 hour twice daily, and the physician assessed the findings on the cloud. Uterine contractions and

perinatal outcome were evaluated on iCTG. **[Results]** For patients discharged with iCTG, the median hospital stay was 17.0 days. For all iCTGs, the trace numbers were 258, with median and minimum compliance rates of 91.2 (IQR, 85.7-94.4) and 75.0, respectively. The median and minimum validity rates were 100.0 (IQR, 94.5-100.0) and 65.0, respectively. iCTG data detected uterine contractions 181 times (80.8%). Eight patients completed iCTG home care and six delivered at term after outpatient care. One patient required emergency visits owing to vaginal bleeding and underwent an emergency cesarean section for premature rupture of membranes after admission. **[Conclusion]** Our study demonstrated the efficacy of iCTG home care for PTL, with a shorter hospital stay than 25.0 days without iCTG and a reduced economic burden of hospitalization.

ISP-27-1

Fetal macrophages induce parturition Matsuzaka Sunao¹, Mogami Haruta¹, Kawamura Yosuke², Matsuzaka Yu¹, Yasuda Eriko¹, Inohaya Asako¹, Takakura Masahito¹, Chigusa Yoshitsugu¹, Mandai Masaki¹ *Kyoto University Graduate School of Medicine¹, Shiga General Hospital²*

[Objective] Initiation of parturition is thought to be associated with sterile inflammation. However, the precise mechanism of the regulation of parturition by the immune system is unclear. Here, we investigated the role of macrophages in the initiation of parturition. **[Methods]** We made fetal macrophage-depleted mice by *Cre/loxP* systems. *Cx3cr1^{CreER/CreER} Csf1r^{flax/flax}* male mice were mated overnight with *Cx3cr1^{+/+} Csf1r^{flax/flax}* female mice, and thereby *Cx3cr1^{CreER/+} Csf1r^{flax/flax}* fetuses ("Cre+ fetuses") were generated. As a control, we used *Cx3cr1^{+/+} Csf1r^{flax/flax}* fetuses ("Cre- fetuses") born from breeding pairs of *Cx3cr1^{+/+} Csf1r^{flax/flax}* mice. At 15 and 17 days post coitum (dpc), 4 mg of Tamoxifen (TAM) or vehicle (Veh) was injected intraperitoneally into both genotype pregnant mice. After injection at 17 dpc, continuous video monitoring of the pregnant mice was started, and the date and time of the delivery of the first litter was recorded among 4 groups (Cre⁻ TAM, Cre⁻ Veh, Cre⁺ TAM and Cre⁺ Veh, respectively). **[Results]** *Cx3cr1⁺* macrophages were successfully depleted in the fetal membranes of Cre⁻ TAM fetuses compared to those of Cre⁺ Veh fetuses. Cre⁻ TAM macrophage-depleted fetuses were born significantly later than Cre⁻ Veh fetuses (22.9 ± 1.0 and 19.6 ± 0.9 dpc, respectively, *p* = 0.0028, *n* = 6 in each group). In contrast, the pregnancy period of Cre⁺ TAM and Cre⁺ Veh mice was not significantly changed (20.7 ± 0.6 and 19.7 ± 0.4 dpc, *p* = 0.34, *n* = 6 in each group). **[Conclusion]** The depletion of fetal macrophage resulted in the delay of the onset of parturition in mice. This implies that fetal macrophages might induce the labor onset.

ISP-27-2

Kielland's rotational forceps delivery has fewer ophthalmic injuries than non-rotational forceps delivery Masaoka Shun, Takeda Jun, Itakura Atsuo *Juntendo University*

[Objective] Non-rotational forceps delivery (NRFD) has possibility of ophthalmic injuries due to improper forceps setting in the case of oblique sagittal suture. To overcome this and improve success rate of forceps delivery, we have started using Kielland's rotational forceps delivery (KRFD) since 2016 that can perform vaginal delivery in the case of malposition; However, reports about safety of KRFD are limited and controversial. To make sure the safety and availability of KRFD, we aimed to compare the perinatal complication between KRFD and NRFD. **[Methods]** We investigated the cases of forceps delivery from 2016 to 2023 and allocated into NRFD and KRFD group. The cases of failure of forceps delivery and use of both forceps were excluded. The number of harmful ophthalmic inju-

ries such as corneal damage and hemorrhage around anterior chamber were set as primary outcome. Additionally, the number of ophthalmological consultation due to forceps marks on orbit, amount of bleeding, and umbilical artery pH were analyzed. **[Results]** We collected 1924 cases in NRFD and 145 cases in KRFD respectively. No case had primary outcome in KRFD, while 8 cases in NRFD (0.4%). Although there were significant differences about ophthalmological consultation and umbilical artery pH, bleeding was lower in NRFD (606g in NRFD and 725 g in KRFD, respectively, *p* = 0.0006). **[Conclusion]** KRFD reduced harmful ophthalmic injuries rather than NRFD, while in KRFD we have to pay attention bleeding, but not clinically significant difference. Proper use of Kielland's rotational forceps with good practice would be valuable option to achieve safer delivery.

ISP-27-3

The success rates and perinatal outcomes of external cephalic version at 36 or 37 weeks of gestation : a retrospective study in our institution Hirose Rikuto, Okada Aiko, Kawanishi Yoko, Nakamura Koji, Miyake Tatsuya, Kawano Mahiru, Hiramatsu Kosuke, Mimura Kazuya, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University*

[Objective] The timing of external cephalic version (ECV) is generally recommended after 36 weeks of gestation (WG), however American College of Obstetricians and Gynecologists has revised its recommendation after 37 WG due to prevent late preterm birth. We changed the timing of ECV to after 37 WG since 2017 and investigated its influences of the change of our practice. **[Methods]** We retrospectively reviewed the clinical data of patients who underwent ECV at our hospital between January 2013 and August 2023. We compared the success rates and perinatal outcomes of ECV at 36 and 37 WG. Data were analyzed by Fisher's exact test, Mann-Whitney test, or Chi-squared test. **[Results]** We included 162 patients. Before 2017, all the 46 cases were performed at 36 WG. After 2017, 95 of 116 cases were at 37 WG. There were no significant differences in the patient background. The success rates were 58.7% and 69.5% in 36 and 37 WG groups, respectively (*p* = 0.2). The rate of re-rotation to non-cephalic presentation was significantly higher in 11.1% of 36 WG group than 1.5% of 37WG group (*p* < 0.05). The preterm delivery occurred only in 36 WG group in 1/46 (2.2%). Other perinatal outcomes were not significant between the both groups. **[Conclusion]** The success rates of ECV at 36 and 37 WG were not different. Re-rotation rate was higher after ECV was performed at 36 WG than at 37 WG. Therefore, we support the recommendation of ECV at 37 WG to prevent iatrogenic preterm delivery.

ISP-27-4

Risk reduction of Cesarean scar defect by barbed suture for uterine myometrial closure Moriyama Yoshinori, Nakajima Hazuki, Mitani Takeji, Noda Yoshiteru, Nakamura Masamitsu, Sekiya Takao, Nishizawa Haruki *Fujita Health University*

[Objective] Cesarean scar defect (CSD) is one of long-term complications of C-section including Cesarean scar syndrome and difficulty in the next C-section. Obstetricians have been engaged in its prevention, mainly by elaborating suture technique of uterine myometrial closure, but it has not been settled. We aimed to solve it by using barbed suture at C-section. **[Methods]** This is an observational study. Women were recruited who underwent C-section with double-layered uterine myometrial closure by a single operator (YM) at our hospital between April 2020 and August 2023. They were divided into two groups by closure method : inner-interrupted outer-interrupted (Int), inner-barbed outer-interrupted/barbed (Bar). At a month or

later postpartum, the residual myometrial thickness (RMT) was evaluated by transvaginal ultrasonography. Excluded were those who already had CSD due to a previous C-section, underwent an atypical procedure including three-layered myometrial closure, or lacked RMT data. **[Results]** A total of 81 women were included consisting of 33 and 48 for Int and Bar, respectively. Background characteristics of the groups showed no clinically significant difference. Operation time was 51.8 ± 25.3 and 38.0 ± 12.4 min ($P = 0.003$), and RMT was 11.1 ± 3.0 and 12.0 ± 3.5 mm ($P=0.108$) for Int and Bar, respectively. No postoperative complications were observed. **[Conclusion]** Barbed suture could reduce a risk of CSD and subsequent complications.

ISP-27-5

High level of intrapartum fetal heart rate pattern evaluated using the Japanese 5-tier classification is correlated with low neonatal Apgar score Watanabe Norikazu¹, Watanabe Mariko², Yamaguchi Risako¹, Ito Tomomichi¹, Fukase Mika¹, Yamanouchi Keiko¹, Nagase Satoru¹ *Yamagata University¹, Yonezawa City Hospital²*

[Objective] The fetal heart rate pattern on cardiotocography is usually categorized into five levels in Japan ; however, studies on the 5-tier classification of cardiotocography are limited. We aimed to confirm whether there is a correlation between the 5-tier cardiotocography levels at delivery and neonatal Apgar scores using the perinatal registry database. **[Methods]** This retrospective study used data obtained from the 2018 Perinatal Registry Database of the Japan Society of Obstetrics and Gynecology. Apgar scores were compared between patients with intrapartum cardiotocography levels 1-2 and those with levels 3, 4, and 5 as described by the Japan Society of Obstetrics and Gynecology level classification. **[Results]** A total of 240,987 cases were registered. The 114,201 full-term deliveries included 84,703 vaginal and 29,498 cesarean deliveries. In cases of vaginal delivery, the crude odds ratios (ORs) of 1-min Apgar score ≤ 3 for levels 3 (OR 1.7, 95% confidence interval [CI] 1.4-2.0), 4 (OR 5.9, 95% CI 5.1-6.9), and 5 (OR 49.2, 95% CI 37.5-64.5) were significantly higher than those for levels 1-2. Similarly, in cases of cesarean delivery, the crude ORs of 1-min Apgar score ≤ 3 for levels 3 (OR 2.6, 95% CI 2.3-3.0), 4 (OR 4.4, 95% CI 4.0-5.0), and 5 (OR 19.3, 95% CI 16.1-23.2) were significantly higher than those for levels 1-2. **[Conclusion]** Our results confirmed that the levels of the 5-tier evaluation of cardiotocography can serve as a predictor of severe neonatal asphyxia.

ISP-27-6

The evaluation algorithm of cardiotocography to improve detection of decelerations Terao Junna, Ando Hitomi, Takeda Jun, Sugimura Yusen, Mieda Haruka, Yamada Taihei, Matsuzawa Nana, Kitamura Eri, Yamamoto Yuka, Makino Shintaro, Takeda Satoru, Itakura Atsuo *Juntendo University*

[Objective] Fetal heart rate (FHR) monitoring with cardiotocography (CTG) is important to evaluate fetal condition during labor. However, CTG interpretation can result in significant variabilities between and within observers. To solve this problem, classification of CTG tracing has been standardized and several computer analysis systems has been developed to ensure objective reading. However, computer analysis is not superior to human interpretation in perinatal outcomes and detection of deceleration, so technological enhancement is awaited. Previously we succeeded to establish the better way to detect late deceleration using a technique of change point detection. In this presentation, we report an algorithm to detect deceleration which improves the interpretation of CTG traces. **[Methods]** The FHR and uterine contraction are provided from the monitoring device as inputs, and the baseline, variability, decelerations, and the peak of

uterine contraction are detected by the algorithm. Each deceleration is classified for early, variable, late, and prolonged deceleration, and mild or severe deceleration based on JSOG. To validate the accuracy of the interpretation, the same CTG was also checked by a perinatologist, a general obstetrician and a trainee, and the results were compared to that by the algorithm. **[Results]** The number of decelerations detected by each method and the concordance rate are currently being validated. **[Conclusion]** Our algorithm can improve the way of CTG interpretation which had previously low reproducibility, and the results is verified comparing to that of the clinicians.

ISP-27-7

A case of necrotizing fasciitis after cesarean section Morishita Yushi, Shimomura Takuya, Sakata Kotaro, Ryu Tensei, Ishiguro Hajime, Tetsuo Aki, Sugi Haruka, Seike Takashi, Hori Hironobu, Gondo Kanako, Park Jongmyung, Terada Atsumu *St. Mary's Hospital*

Background Necrotizing fasciitis is a rapidly progressive necrotizing soft tissue infection. We report a rare obstetric complication of necrotizing fasciitis after cesarean section, based on a review of the literature. **Case** 35-year-old female. An emergency cesarean section was performed due to fetal dysfunction at a local clinic, and on the 6th postoperative day, she developed fever and blood tests showed elevated inflammatory response. A diagnosis of endometritis was made, and CTRX was administered intravenously. On postoperative day 7, the cesarean section wound was found to be erythematous, tender, and indurated, and on the 10th postoperative day, blisters appeared around the wound, and the patient was referred to our hospital because a severe wound infection was suspected. Contrast-enhanced CT was suspicious for necrotizing fasciitis. An emergency wound incision and debridement under general anesthesia was performed with plastic surgeon. The patient was admitted to the ICU with an open wound and discharged from the ICU the next day. MRSA was detected in the wound culture, and the antibiotic was changed to MEPM + VCM. Thereafter, the wound was cleaned daily, VACulta therapy and hyperbaric oxygen therapy was started 14 days after reoperation, and the wound was closed 30 days after reoperation. Infection and general condition improved, and the patient was discharged 50 days after reoperation. **Discussion** Necrotizing fasciitis occurs at a rate of 1.8 per 1000 patients undergoing cesarean section. Necrotizing fasciitis is an extremely lethal disease with a mortality rate of 8%-76%.

ISP-27-8

Efficacy of music therapy and Zingiber officinale Roscoe aromatherapy for reducing pain during the first stage of labor : A randomized controlled trial Chanthasenanont Athita, Paoin Pontip, Prasongvej Pichita, Niumpradit Tichayakorn, Pongrojpaew Densak, Suwannanurk Komsun *Thammasat University, Thailand*

[Objective] To study the pain reducing effect of music therapy and ginger essential oil (GEO : Zingiber officinale Roscoe) aromatherapy on the first stage of labor. **[Methods]** This randomized controlled trial was conducted at the labor room of Thammasat University Hospital, Thailand from May to October 2022. Subjects were nulliparous pregnant women who came with true labor pain and 3 cm cervical dilatation. They were allocated into three groups : control, music and aromatherapy. The control group received intrapartum care following hospital care guidelines while participants in the music group listened to a music playlist "Musical Journey through Pregnancy" and the aromatherapy group inhaled GEO. Visual analogue scale was used for pain evaluation every 2 hours and the interventions and pain evaluation were done until the end of the first stage of labor or

cesarean section was indicated. **[Results]** Three hundred pregnant women were recruited. The mean age of participants was 27.7 years old. Subjects in the music and aromatherapy groups had statistically significantly less labor pain than those in the control group during cervical dilatation between 4 and 7 cm ($p < 0.001$). Both intervention groups also had a significantly shorter time of labor and less estimated blood loss during vaginal delivery than the control group ($p < 0.001$). **[Conclusion]** Music and aromatherapy decreased labor pain, labor time and estimated blood loss than the control group.

ISP-27-9

Prevalence of Anal Sphincter Injuries Identified Using Endoanal Ultrasound Among Primipara Women : A Cross-Sectional Analytical Study Remo Joy Christine M *Department Obstetric and Gynecology, Section of Ultrasound, Rizal Medical Center, Philippines*

Introduction. Perineal lacerations result from the trauma induced by various factors such as a weak or a prior damaged anal sphincter, leading to a third- or fourth-degree tear of the anal sphincter which are then called as Obstetric Anal Sphincter Injuries (OASIS).^{1,3} This study is one of the first studies to determine the local prevalence of anal sphincter injuries in primipara women who delivered by normal spontaneous delivery in a tertiary hospital from March 2023 to April 2023. **Methods.** We used a cross-sectional descriptive design. A total of 48 primipara women were included in the study. **Results.** All 48 participants were initially found to have a perineal injury. Thirty (62.5%) patients had second-degree tear while 18 (37.5%) suffered a third-degree tear. At 6 weeks follow-up, all underwent endoanal ultrasound to determine the extent or severity of tears or injuries to the anal sphincter complex and it was determined that only 1 out of 48 (2.1%) had internal anal sphincter injury while 97.9% are in normal condition. Only the weight of the newborn was significantly associated with anal sphincter injuries. The diagnostic accuracy of endoanal ultrasound was 64.58% (95% CI). **Conclusion.** There is a prevalence of 37.5% for anal sphincter injuries in primiparous patients who underwent NSD in our institution. Endoanal ultrasound accurately confirms the extent of these injuries and symptoms at 6-week follow-up is consistent with the characteristic of the injuries.

ISP-27-10

Competency Level in Performing The Atencio Technique of Delivering Impacted Fetal Head at C-Section Among Residents at A Tertiary Level Hospital Gabasa Kate Sarah P, Maglaya-Ang Hermie F *East Avenue Medical Center, Philippines*

[Objective] To determine the surgical competency level of the 3rd year and 4th year OBGYN residents in performing the Atencio technique to deliver an impacted fetal head at C-section using the modified Objective Structures Assessment of Technical Skills (OSATS) scoring system in a tertiary government hospital. **[Methods]** Monocentric descriptive cross-sectional study among nineteen (19) residents who were anonymously video recorded while doing the Atencio technique for three trials. Training consultants graded each resident using the modified OSATS Scoring system, which included the mean delivery time and maternal blood loss. **[Results]** 17 out of 19 (89%) residents passed the OSATS scoring sheet for the Atencio technique in the third trial. The mean delivery time was 2 : 52 mins, 2 : 02 mins, and 1 : 36 mins in the first, second, and third trials, respectively. The mean maternal blood loss was 545.78 ± 245.63 ml, 463.15 ± 185.839 ml, and 458.94 ± 147.268 ml in the first, second, and third trials respectively. **[Conclusion]** Despite being a novel technique, the Atencio technique can successfully be taught to residents-in-

training. The majority of the residents succeeded in correctly performing the technique, with improvement in delivery time, and with no excessive blood loss in all trials.

ISP-28-1

Changes in Prescription of GnRH Analogs following the Start of Relugolix Prescriptions in Japan : National Database of Health Insurance Claims and Specific Health Checkups of Japan Miyake Natsuki, Osuka Satoko, Takeda Takehiko, Seki Tomomi, Kaseki Satoshi, Tanaka Hideaki, Yabuki Atsushi, Sonehara Reina, Muraoka Ayako, Nakamura Tomoko, Kajiyama Hiroaki *Nagoya University*

[Objective] GnRH analogs were widely used for uterine myoma and endometriosis treatment, and GnRH agonists have been the standard treatment for several decades. However, in March 2018, Relugolix, a GnRH antagonist, was incorporated into insurance coverage list. This study examines the changing landscape of GnRH analog prescriptions, particularly in response to Relugolix availability across Japanese prefectures, using public databases. **[Methods]** We retrieved GnRH analog prescription data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan. We compared prescription trends during two periods : April 2020 to March 2021 (period A) and April 2021 to March 2022 (period B). Additionally, we extracted data on female population aged 20-54 from government statistics for each prefecture. **[Results]** During period B, Relugolix prescriptions significantly increased from 4,792,566 in period A to 6,476,916. Conversely, total nafarelin and busererin prescriptions decreased from 67,334 to 58,028. Prescription rates per thousand women aged 20-54 varied among prefectures, with the highest rate at 355.4 and the lowest at 140.2. **[Conclusion]** The rise in Relugolix prescriptions and decline in busererin and nafarelin prescriptions indicate a notable shift towards Relugolix due to its immediate efficacy. The inclusion of endometriosis as an approved indication for Relugolix in December 2021 is expected to drive further increase Relugolix prescriptions. In contrast, GnRH agonist prescriptions are expected to increase with the start of insurance reimbursement for assisted reproductive technologies. Considering the unique characteristics of each drug, tailoring GnRH analogs to individual patient needs becomes increasingly essential.

ISP-28-2

The Impact of Japanese Government Introduction of Financial Incentive on the Management of Secondary Dysmenorrhea Ishida Risa¹, Koga Kaori^{1,2}, Izumi Gentaro¹, Osuga Yutaka¹ *The University of Tokyo¹, Chiba University²*

[Objective] In April 2020, the Japanese government introduced a financial incentive for the appropriate management of secondary dysmenorrhea. The purpose of this study was to determine the impact of this policy change on the practice of dysmenorrhea. **[Methods]** Using a large Japanese nationwide claims database (JMDC claims database), we identified women between the ages of 10 and 60 as the source population and outpatient visits with secondary dysmenorrhea from April 2018 to March 2022. We used an interrupted time-series analysis, defining the period before April 2020 as pre-introduction and after April 2020 as post-introduction. Outcomes were the proportion of outpatient visits and those prescribed hormonal drugs among the source population and outpatient continuation among outpatient visits with secondary dysmenorrhea. **[Results]** There were significant upward slope changes between pre- and post-introduction in the proportion of outpatient visits (1.21% vs. 1.24% ; +0.29% per year ; 95% confidence interval [CI], +0.20% to +0.38%) and those prescribed hormonal drugs (0.14% vs. 0.17% ; +0.038% per year ; 95% CI, +0.030% to +0.045%) among the source popu-

lation. Similarly, there was a significant upward level change in the proportion of outpatient continuation (66.8% vs. 69.0% ; +2.68% per month ; 95% CI, +0.87% to +4.49%). **[Conclusion]** This policy change for the management of secondary dysmenorrhea was associated with increased proportions of patients diagnosed with secondary dysmenorrhea, hormonal drug prescriptions, and continued outpatient care.

ISP-28-3

The change of glycoprotein on the eutopic endometrial cell from endometriosis patients Matsumoto Yuka, Hashimoto Kae, Toda Aska, Nakamura Koji, Kawano Mahiru, Kinose Yasuto, Kodama Michiko, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] Endometriosis is a common gynecological disorder affecting 10 to 15 % of women during their reproductive years, however, the cause of endometriosis remains unclear. According to Sampson's transplacental theory, we hypothesized the eutopic endometrium of endometriosis has some differences from that without endometriosis. In this study, we focused on glycoproteomics and clarify the differences in glycosylation of eutopic endometrium between with or without endometriosis. **[Methods]** Eutopic endometrium were collected from patients undergoing hysterectomy or endometrial biopsy in our institution. Written informed consent was obtained. Endometriosis cases are confirmed by transvaginal ultrasound or histopathological diagnosis and control cases had no history of the endometriosis and no gynecological malignancies. Endometrial stromal cells were obtained from primary culture of collected endometrium. We analyze glycoprotein profile of cultured cell lysate with Lectin microarray and decide the target glycoprotein and further confirmed by lectin blotting. **[Results]** We analyzed two cases each from endometriosis group and control group with lectin microarray. We found lectins recognizing Sia a 2-6 Gal/GalNAc, Man a 1-3 Man, GlcNAc oligomers and Gal β 1-3 Gal/NAc were increased in endometriosis group than control group. SNA, lectins recognizing Sia a 2-6 Gal/GalNAc, showed about two times higher fluorescence intensity. We selected the Sia a 2-6 Gal/GalNAc as our target and lectin blotting confirm the increase of Sia a 2-6 Gal/GalNAc in endometriosis group than control group. **[Conclusion]** We observed that Sia a 2-6 Gal/GalNAc was increased in eutopic endometrium of endometriosis cases. The role of Sia a 2-6 Gal/GalNAc in the development of endometriosis will be further investigated.

ISP-28-4

Clinical demarcation between the indications for uterine fibroid embolization and minimum invasive hysterectomy : a single center cohort study in Japan Kyojuka Hyo *Ohta Nishinouchi Hospital*

[Objective] Uterine fibroid embolization (UFE) and total laparoscopic hysterectomy (TLH) are minimally invasive approaches for treating women with symptomatic UF. However, no reports on the clinical indications for UFE treatment exist. This study aimed to establish the clinical indications for UF treatment where UFE or TLH was performed for symptomatic UF at a single institution. **[Methods]** This study was conducted at a single center and included 35 and 39 women who underwent UFE and TLH, respectively between 2021 and 2023. First, the clinical findings between the UFE and TLH groups were compared. The MRI findings included the length of the uterus (LU), and depth of the uterus (DU). Receiver operating characteristic (ROC) curves were also generated using the UFE as the outcome. **[Results]** The ratio of history of delivery was significantly higher among the TLH cases (57.1% vs. 94.9% for UFE and TLH, respectively). Regarding the MRI findings, significant

differences were observed in the median LU (129 vs 94 mm, $p < 0.01$), DU (88 vs 70 mm, $p < 0.01$), for UFE and TLH, respectively. In the ROC analysis, the AUC for LU and DU was 0.75 ($p < 0.01$), and 0.70 ($p < 0.01$), respectively. The cut-off value for LU indicating suitability for either UFE or TLH were 107 mm. **[Conclusion]** This study analyzed the data of gynecologists who performed both UFE and TLH as the main surgeons. Our study demonstrated a clear distinction between the indications for UFE and TLH. Our findings could assist gynecologists in identifying candidates for UFE among patients with UF.

ISP-28-5

Clinical outcomes of laparoscopic myomectomy with vasopressin Tumenjargal Amartuvshin^{1,3}, Oyunchimeg Erdenee², Gantumur Dolgormaa⁴, Davaatseren Munkhtsetseg¹ *Mongolian National University of Medical Sciences, Mongolia¹, Department of Academic Research, National Center for Communicable Diseases, Mongolia², Department of Gynecological Surgery, Mongolia Japan Hospital, Mongolian National University of Medical Sciences, Mongolia³, Department of Hepatobiliary and Pancreatic Surgery, Gunma University⁴*

[Objective] To evaluate clinical outcomes of vasopressin in laparoscopic myomectomy **[Methods]** We retrospectively analyzed 110 myoma patients treated with laparoscopic surgery in the gynecological surgery department between January 2022 and January 2023. We evaluated the safety of vasopressin in 45 patients undergoing laparoscopic myomectomy ; 28 were treated with an intraoperative intra-myometrial injection of dilute vasopressin (group1), and 17 were treated without the use of any vasoconstrictive agent (group 2) compared in terms of size, number, and type of myomas ; estimated blood loss (EBL) ; and procedure length. **[Results]** The Baseline demographics were similar between groups. The most common indication for surgery was pelvic pain in 27 patients (60%), infertility in 2 patients (4.5%), followed by abnormal bleeding in 23 patients (52%). The size of mass below 10 cm was 35 (82%) and above 11 cm was 10 (23%) in both groups. The mean EBL in group I compared with 272 ± 171.8 mL in group II 318 ± 141.8 , respectively ($p < .001$). Additionally, EBL was significantly lower in the vasopressin group in all of the study's subgroups of patients stratified according to the size and number of myomas. However, procedure length and the mean hospital stay did not differ significantly. **[Conclusion]** Laparoscopic myomectomy with vasopressin reduced blood loss during surgery and is likely to decrease the procedure time.

ISP-28-6

Share, Care, and a Better Life : TWSDM.com for Better Management of Endometriosis Huang Kuanju^{1,2}, Yang Ihjane^{1,2}, Chang Wenchun², Sheu Borching² *National Taiwan University Hospital Yunlin Branch, Taiwan¹, National Taiwan University Hospital, Taiwan²*

[Objective] TWSDM.com is a multilingual, evidence-based shared decision-making website incorporating three techniques, including multimedia learning design, communication skills, and artificial intelligence for the management of endometriosis. TWSDM.com aims to reduce cognitive overload by empowering patients and medical professionals to stand on the same knowledge base. This allows for the discussion of the most suitable treatment options, helps to reduce unnecessary surgeries, and improves reproductive outcomes. (Please see the advertising video at : <https://youtube.com/shorts/Qig1Phv7dIU>, or the TWSDM.com Japanese version at : <https://twsdm.com/ja-JP>, or English version at : <https://twsdm.com/>) **[Methods]** Retrospectively collecting and analyzing data from TWSDM.com for satisfaction via the 9-Item Shared Decision Making Questionnaire

(SDM-Q-9) and website sessions via Google analysis. **[Results]** Since our beta version went live in August 2023, there had been 124 users from 5 countries resulting in 219 sessions and 1267 views. The mean time surfing TWSDM.com is 2 minutes 33 seconds. Further analyses of satisfaction data based on users' age, education level, and area of residence will be available when our formal version is online. **[Conclusion]** TWSDM.com is a promising patient decision aid tool on shared decision-making for the management of endometriosis, targeting international users including patients and medical professionals. Further clinical results and updates of current guidelines will improve our website, enhance satisfaction on treatment outcome, and help to balance and allocate medical resources across different socioeconomic backgrounds.

ISP-29-1

Functional analysis implicates oncogenic potential of SNIP1 in 1p34 risk locus in ovarian cancer Ishii Saki, Nakamura Koji, Toda Aska, Kawano Mahiru, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] Previously we identified chromosome 1p34.3 as an ovarian cancer risk locus in which several putative oncogenes including SNIP1. Here we performed functional validation of SNIP1 as a novel oncogene in ovarian cancer development. **[Methods]** The relationship between SNIP1 expression and the prognosis of ovarian cancer patients was evaluated using Kaplan-Meier plotter. SNIP1 expression of ovarian cancer cell lines was compared with that of immortalized ovarian surface and fallopian tube epithelium cell lines by RT-qPCR and immunoblot. We transiently silenced SNIP1 expression in several ovarian cancer cell lines and tested the effect of SNIP1 on ovarian cell proliferation and colony formation. Since SNIP1 had been reported as a co-activator of c-Myc which is frequently activated in ovarian cancer patients, c-Myc expression after SNIP1 silencing was tested in ovarian cancer cells. **[Results]** Kaplan-Meier plotter revealed increased SNIP1 expression was associated with shorter survival in ovarian cancer patients. SNIP-1 expression was generally upregulated in ovarian cancer cell lines such as OVCAR3, OVCAR8, OVKATE and Kuramochi compared to benign cell lines in both protein and mRNA level. SNIP-1 silencing impaired proliferation and colony formation in ovarian cancer cell lines. c-Myc protein expression was downregulated by SNIP1 silencing. **[Conclusion]** Our results suggest that SNIP1 can work as one of oncogenes in 1p34 risk locus. We will further investigate the functional role of SNIP1 focusing on its association with c-Myc oncogene.

ISP-29-2

Screening for the drugs that increase the efficacy of poly ADP-ribose polymerase inhibitor by the FDA-approved compounds library Okui Yosuke, Ohta Tsuyoshi, Sano Shiori, Gonai Yuta, Sakaki Hirotsugu, Seino Manabu, Nagase Satoru *Yamagata University*

[Objective] Ovarian cancer, the most lethal gynecologic cancer, has seen improved prognosis in patients with homologous recombination deficiency (HRD), including BRCA mutations, due to poly ADP-ribose polymerase (PARP) inhibitors. However, some ovarian cancer patients with HRD still develop resistance to PARP inhibitors. This study aimed to identify drugs that enhance the efficacy of PARP inhibitors by screening a compound library developed by our University. **[Methods]** The library contains 2334 FDA-approved drugs. In the primary screening, we treated A2780 cell lines with olaparib alone or combined with each library drug to assess cell proliferation through the MTS assay. Drugs that inhibited cell growth by 50% or more

were defined as candidate drugs. Furthermore, we calculated the IC_{50} values of these drugs and investigated their clinical C_{max} values for secondary screening. Drugs with a $C_{max} > IC_{50}$ were identified as potential candidates enhancing the efficacy of olaparib, and we further investigated in other ovarian cancer cell lines. **[Results]** Out of 2334 drugs, 70 demonstrated over 50% cell growth inhibitory rates when combined with olaparib compared to olaparib treatment alone in the primary screening. Secondary screening revealed six Japanese-approved oral drugs, including a proteasome inhibitor, HDAC inhibitor, rheumatism medicine, antimetabolite, microtubule inhibitor, and anti-alcoholic drug. Among these, the proteasome inhibitor and microtubule inhibitor increased the efficacy of olaparib in other cell lines. **[Conclusion]** We identified proteasome and microtubule inhibitors as potential candidate drugs for enhancing the efficacy of PARP inhibitors using our compound library.

ISP-29-3

Cancer-associated mesothelial cells as a source of intratumoral vessels are potential therapeutic targets for ovarian cancer Mogi Kazumasa^{1,2}, Yoshihara Masato¹, Miyamoto Emiri¹, Fujimoto Hiroki¹, Uno Kaname¹, Iyoshi Shohei¹, Sugiyama Mai³, Koya Yoshihiro³, Yamakita Yoshihiko³, Nawa Akihiro³, Kajiyama Hiroaki¹ *Nagoya University Graduate School of Medicine¹, Department of Tumor Pathology, Gifu University Graduate School of Medicine², Bell Research Center, Nagoya University³*

[Objective] Cancer-associated mesothelial cells (CAMs) have been reported to promote ovarian cancer progression in the peritoneal microenvironment, however, their dynamics have remained unclear. We investigated CAMs in peritoneal dissemination using a conditional knock-in mouse model. **[Methods]** For lineage tracing of mesothelial cells, we generated the *Wt1*- and *Krt19-CreERT2/ROSA26-LSL-tdTomato* mice and, which selectively express tdTomato (red-fluorescent protein) in mesothelial cells. We administrated tamoxifen to these mice. Then, these mice were intraperitoneally injected with ovarian cancer ID8 cells, the disseminated tumors were analyzed for immunofluorescence. Next, tdTomato-positive (Tomato+) cells were collected from normal and disseminated models using digestive enzymes and flowcytometry, and analyzed. **[Results]** This analysis showed that mesothelial cells specifically express RFP in both mice, but mesothelial cells were recruited more into the tumor (20.6% area) in *Wt1-Cre* mice than *Krt19-Cre* mice. These Tomato+ cells were co-stained with fibroblast markers, and some showed vessel structure and co-stained with endothelial and mural cell markers. These Tomato+ cells were also localized on functional intratumoral vessels labeled with delineated with perfused fluorescent-labeled lectin (maximum 52.9% per 100 μ m² view). Real-time PCR showed that higher expression of the mesenchymal markers α -SMA and FN1 in Tomato+ cells from the disseminated models than from the normal models (α -SMA : 1.30, FN1 : 4.45 fold-change relative to control). **[Conclusion]** Our data indicated that *Wt1*-positive mesothelial cells transform readily into CAMs and tumor stromal cells, and some of which are recruited as a source of intratumoral vessels in peritoneal dissemination. These findings provide a potential therapeutic target for peritoneal dissemination.

ISP-29-4

Overcoming platinum resistance of high-grade serous ovarian cancer targeting the activated JAK/STAT pathways via extracellular vesicles Suzuki Kazuhiro¹, Yokoi Akira¹, Yoshida Kosuke¹, Kitagawa Masami¹, Matsuo Seiko¹, Uekusa Ryosuke¹, Nagao Yukari¹, Watanabe Eri², Yoshikawa Nobuhisa¹, Nagao Shoji², Yamaguchi Satoshi¹, Kajiyama Hiroaki¹ *Nagoya University*

sity¹, Aichi Cancer Center², Okayama University³, Hyogo Cancer Center⁴

[Objective] The molecular definition of platinum-resistant ovarian cancer (PROC) is still unclear, and overcoming PROC has been the biggest challenges. Extracellular vesicles (EVs) are essential in cell-to-cell communication, and this study aims to identify molecular mechanisms of PROC via EVs to suggest novel therapeutic strategies. **[Methods]** A total of 60 samples from 20 high-grade serous ovarian cancer (HGSOC) cases were analyzed, and each sample of tissues and ascites was collected before initial therapy. RNA-sequencings were performed to investigate the molecular profiles of PROC and validated by *in vitro* and *in vivo* experiments. **[Results]** Comprehensive gene expression analyses of tissue mRNA-seq revealed that the JAK/STAT pathway was significantly activated in the PROC group ($p < 0.001$), and the protein expression was validated by immunohistochemistry in HGSOC tissues. *In vitro* analyses, JAK inhibitors (JAKi) had equivalent efficacy for platinum-sensitive/resistant HGSOC cell lines, and suppression of JAK in PROC cell lines by siRNAs significantly increases sensitivities for cisplatin. JAKi also had the synergistic effect with cisplatin for PROC cell lines. *In vivo* analyses, JAKi significantly inhibited tumor growth in the PROC mouse model ($p = 0.019$). Small RNA-seq for tissues and ascites-EVs revealed miR-135a-5p and -221-5p highly expressed in PROC. Overexpression of miR-135a-5p and -221-5p in HGSOC cell lines by miRNA mimics resulted in higher expression of the JAK family and resistance to cisplatin. **[Conclusion]** Our results demonstrated novel molecular mechanisms of PROC via EVs and provided the rationale for JAK-targeted therapy for PROC. EVs regulate the PROC and can be diagnostic and therapeutic biomarkers for PROC suggestions and JAKi indications.

ISP-29-5

Direct evaluation of homologous recombination repair activity in human ovarian cancer cells Yagi Hiroshi, Onoyama Ichiro, Asanoma Kazuo, Kawakami Minoru, Tomonobe Hiroshi, Hachisuga Kazuhisa, Maenohara Shoji, Kodama Keisuke, Yasunaga Masafumi, Yahata Hideaki, Kato Kiyoko *Kyushu University*

[Objective] In the current treatment strategy for advanced ovarian cancer, it is critical to evaluate the activity of homologous recombination repair (HR) in cancer cells. However, HR deficiency (HRD) test in clinical practice indirectly evaluate HR activity based on genomic instability of cancer cells. In this study, aiming for clinical application of the direct evaluation of HR activity in the future, we verified whether HR activity can be directly evaluated *in vitro*. **[Methods]** Fifteen human ovarian cancer cell lines were used in this study. To directly evaluate HR activity in these cells, we took advantage of a system called Assay for Site-specific HR activity (ASHRA). In this assay, site-specific CRISPR/Cas9 and a HR donor sequence containing a marker gene were introduced to cancer cells. To increase the efficiency of gene transfer, we subcloned lentiviral vectors expressing these genes. Subsequently, genomic integration of marker gene was quantified by qPCR. **[Results]** Five cell lines were HRD, four were HR proficient, and remaining six cell lines had decreased HR activity. Among four HR proficient cells, OVAS had the highest HR activity. In SHIN3 cells, knock down of BRCA1 induced a decrease in HR activity, suggesting that this assay properly evaluate HR activity. **[Conclusion]** A modified ASHRA assay allowed direct evaluation of HR activity in human ovarian cancer cells. It is important to take into account the difference in HR activity when performing experiments using human ovarian cancer cells.

ISP-29-6

Examination of LAT1 expression and leucine transport in clear cell ovarian carcinoma Nakamoto Kosuke, Koh Iemasa, Teraoka Yuko, Oomori Yuriko, Nosaka Suguru, Sekine Masaki, Tomono Katsuyuki, Yamazaki Tomomi, Mukai Yurika, Sugimoto Jun, Banno Kouji, Kudo Yoshiki *Hiroshima University*

[Objective] It is known that cancer cells have enhanced uptake of glucose and amino acids necessary for their active cell proliferation. In amino acid uptake, L-type amino acid transporter 1 (LAT1) has attracted attention as an important transporter that supplies nutrition to cancer cells by transporting essential amino acids including leucine. LAT1 is highly expressed in various cancers, and efficacy and safety of nanvuranlat, LAT1-selective inhibitor, as monotherapy has been reported in biliary tract carcinoma. We have confirmed that LAT1 is also expressed in ovarian clear cell carcinoma. Therefore, we investigated the relationship between LAT1 expression and leucine transport in ovarian clear cell carcinoma using nanvuranlat. **[Methods]** Several ovarian clear cell carcinoma cell lines were used to confirm the expression of LAT1, and tracer experiments were performed for leucine transport using [³H] leucine as a substrate. The effect of nanvuranlat on leucine transport was also analyzed. **[Results]** In ovarian clear cell carcinoma cell lines, time-dependent, Na-independent, and concentration-dependent saturation of leucine transport were observed, suggesting leucine was transported via transporters. Leucine transport was also inhibited by nanvuranlat in a concentration-dependent manner. The expression of LAT1, which is involved in leucine transport, differed among cell lines, and was strongly inhibited in cell lines with high expression of LAT1. **[Conclusion]** In ovarian clear cell carcinoma cell lines, nanvuranlat inhibited intracellular transport of leucine. The expression of LAT1 was suggested to be involved in leucine transport and LAT1 selective inhibitors are expected to inhibit cell growth in ovarian clear cell carcinoma with high expression of LAT1.

ISP-29-7

Synthetic lethality by targeting a histone methyltransferase, EHMT2 through immune activation in ARID1A-deficient ovarian endometrioid carcinoma Tanimoto Saki^{1,2}, Sone Kenbun¹, Ishizaka Aya¹, Suzuki Eri¹, Hachijo Ryuta¹, Tsuboyama Natsumi¹, Fukuda Tomohiko¹, Taguchi Ayumi¹, Mori Mayuyo^{1,2}, Oda Katsutoshi¹, Hirota Yasushi¹, Osuga Yutaka¹ *The University of Tokyo¹, Project for Cancer Epigenomics, The Cancer Institute Hospital of JFCR², Department of Integrative Genomics, The University of Tokyo³*

[Objective] The histone methyltransferase EHMT2 has been reported to be upregulated in many cancer types and is associated with tumor progression. Histone modification is involved in immune responses, including NFκB pathway activation and endogenous retrovirus (ERV) actions, which induce an interferon response. We investigated the function of EHMT2, focusing on its role in the immune system in ovarian endometrioid carcinoma (OEC). The frequency of ARID1A mutations is 30% in OEC. We also investigated the relationship between EHMT2 and ARID1A. **[Methods]** We examined the expression of EHMT2 in clinical tissues. Cell proliferation, apoptosis, and the change in immune system factors were examined under EHMT2 knock-down and inhibition in ARID1A-deficient mutant and wild-type OEC cell lines. Furthermore, we used an shRNA-mediated ARID1A knockdown cell line that was generated through long-term lentivirus infection. **[Results]** EHMT2 expression was significantly upregulated in OEC clinical tissues. In ARID1A-deficient cell lines, both knockdown and inhibition of EHMT2 resulted in a significant decrease in cell viability, increase in NFκB phosphorylation, and upregulation of ERV genes. In con-

trast, ARID1A wild-type cell line showed almost no change upon knockdown and inhibition. In addition, with ARID1A knockdown, cells showed an increase in sensitivity to EHMT2 inhibitors. **[Conclusion]** Our results provide the evidence for the synthetic lethality between ARID1A mutation and EHMT2 inhibition. NFκB and ERV may play an important role in mechanism of the synthetic lethality. This suggests that the EHMT2-ERV-NFκB pathway may be a potential therapeutic target in ARID1A-deficient OEC.

ISP-29-8

Establishment and characterization of reversibly immortalized ovarian epithelial cell lines using Sendai virus Okawa Masayo, Komatsu Hiroaki, Hikino Kouhei, Iida Yuki, Hosokawa Masayo, Sawada Mayumi, Kudoh Akiko, Sato Shinya, Taniguchi Fuminori *Tottori University*

[Objective] This study aimed to establish immortalized ovarian cell lines using Sendai virus (SeV) and to elucidate ovarian carcinogenesis mechanisms. **[Methods]** We collected normal ovary (Ov n), normal ovary with germline *BRCA1* or 2 mutation (Ov BRCA1 or 2), ovarian endometrioma (Ov endo) from each 4 patients. From another patient had rt. ovarian endometrioid borderline tumor and endometrioma, we collected rt. Ov endo, lt. Ov n, and rt./lt. FT from rt./lt. fallopian tubes. These cells were infected with SeV carried Bmi-1, hTERT, and SV40T. Immunoreactivity to the anti-EpCAM antibody was confirmed through flow cytometry. QH and multicolor FISH staining were performed for karyotyping of metaphase chromosomes. Some genes that showed significant expression in Human transcriptome sequencing analysis using total RNA were subjected to real-time PCR. **[Results]** SeV-infected cells could be long-term passages. Ov BRCA1/2 cells showed chromosome structural abnormalities than Ovn. Long-term passaged cells did not show response to anti-EpCAM antibodies. Ten genes were predominantly expressed in Ov BRCA1/2 compared to Ov n. Some of them were expressed in Ov endo too. Real-time PCR results also indicated higher expression of one gene in Ov BRCA1/2 and Ov endo. **[Conclusion]** We identified candidate genes that may be involved in ovarian carcinogenesis mechanisms.

ISP-29-9

The effect of neutrophil extracellular traps on tumor microenvironment of high-grade serous ovarian carcinoma Tamura Kohei, Saga Yasushi, Shinohara Miki, Takahashi Yoshifumi, Koyanagi Takahiro, Yoshida Takahiro, Takahashi Suzuyo, Taneichi Akiyo, Takei Yuji, Fujiwara Hiroyuki *Jichi Medical University*

[Objective] Recent studies have suggested that neutrophil extracellular traps (NETs) can promote cancer progression. It is well known that tumor-infiltrating lymphocytes (TILs) plays pivotal roles to regulate tumor cell behavior. However, how NETs affect TILs in tumor microenvironment (TME) and prognosis remains unknown. **[Methods]** The subjects were patients with high-grade serous ovarian carcinoma (HGSOC) who received primary debulking surgery between January 2006 and March 2018 in our hospital. Clinicopathological variables were obtained from the medical records. In addition, we performed multicolor immunohistochemistry to evaluate the density of NETs and TILs in tissues specimens or prognosis. **[Results]** A total of 138 patients were entered into this study. NETs was identified as CD66b (+) Cit-H3 (+) cells and their density was higher in advanced stage ($p < 0.05$). The densities of CD4 (+) and CD8 (+) T cells inversely correlated with that of NETs ($r = 0.5182$, $p < 0.01$; $r = -0.5684$, $p < 0.001$, respectively). Univariate analysis showed that progression free survival (PFS) was significantly worse in the NETs-high group ($p < 0.05$). However, neu-

trophils involving NETs did not correlate with PFS. Overall survival (OS) showed the same trend in the NETs-high group although the difference was not significant ($p = 0.18$). Poor prognostic factors were also CA125, stage, performance status and non-complete resection. Multivariate analysis revealed that NETs-high group (HR 5.08 95%CI : 1.15 to 19.4, $p = 0.021$) and non-complete resection (HR 2.64, 95%CI : 1.20 to 5.78, $p = 0.015$) were independent predictors of poor PFS. **[Conclusion]** : NETs in TME negatively regulate TILs which may assist progression of HGSOC. NETs in resected specimen can be used as a prognostic marker.

ISP-30-1

Clinical Implication of Biochemical Pregnancy Loss in Patients with Recurrent Pregnancy Loss : Insights from PGT-A Cases Shiraishi Tatsunori¹, Kuwabara Yoshimitsu¹, Kubota Yumene¹, Sakata Akiko¹, Matsuda Shigeru¹, Kasano Sayuri¹, Nakao Kimihiko¹, Yonezawa Mirei¹, Ichikawa Tomoko¹, Takeshita Toshiyuki², Suzuki Shunji¹ *Nippon Medical School Hospital¹, Takeshita Ladies Clinic²*

[Objective] Guidelines in Japan/US and Europe differ on whether to include BPL in the count of previous miscarriages. This study aimed to assess the clinical implications of biochemical pregnancy loss (BPL) in patients with recurrent pregnancy loss (RPL) while excluding embryonic factors. **[Methods]** We analyzed 52 cycles from 48 cases that underwent preimplantation genetic testing for aneuploidy (PGT-A) and received transfers of high-quality euploid embryos between April 2020 and Dec 2022. The cases were divided into three groups : those with prior unsuccessful assisted reproductive technology (ART) attempts (Group A), recurrent miscarriage following ART (Group B), and recurrent miscarriage without ART (Group C). The clinical backgrounds and outcomes were compared among the groups. **[Results]** Mean ages and human chorionic gonadotropin positivity rates did not significantly differ among the groups. However, BPL rates were notably different (Group A, 0% ; Group B, 25.0% ; Group C, 37.5%) that significantly impaired clinical pregnancy (CP) rates in patients with RPL ($p = 0.037$). Comparing pregnancy histories, past miscarriages and BPL showed significant differences between CP and BPL outcomes ($p < 0.05$). Including BPL in past miscarriage history improved the accuracy of predicting BPL risk (area under curve, 0.87). Although risk factors for RPL did not differ by outcome, lower K6 questionnaire scores before ART were observed in CP. **[Conclusion]** Patients with RPL possess an increased risk of BPL owing to maternal factors, possibly related to mild psychological stress. Consequently, BPL might be better regarded as a form of miscarriage, particularly after PGT-A.

ISP-30-2

Clinical presentation after Trachelectomy complicated by placental malposition Nakano Kota, Nakahara Kazushige, Sugiura Takako, Kiyokoba Ryo, Hachisuga Nobutaka, Sakai Atsuhiko, Fujita Yasuyuki, Kato Kiyoko *Kyushu University*

[Objective] Although trachelectomy is a fertility-sparing procedure for patients with early-stage cervical cancer, it is a high-risk pregnancy with a high incidence of premature delivery and abnormal bleeding during pregnancy. Placental malposition is also a high-risk pregnancy due to the high frequency of placental adhesions. However, there are few reports of cases of placental malposition complications after trachelectomy. In this study, we examined the clinical characteristics of pregnancies after trachelectomy experienced at our institution, dividing them into two groups according to the presence or absence of placental malposition. **[Methods]** Of the 39 cases and 48 pregnancies delivered by cesarean section after cervical trachelectomy per-

formed at our hospital from January 2008 to June 2023, we examined the amount of blood loss and the presence or absence of placental adhesions. **[Results]** Abnormal placental position was present in 10 cases (26.3%), with 7 cases of placenta previa, 3 cases of low placenta previa, and higher than the general frequency. Abnormal placental position significantly increased blood loss and operative time. The frequency of placenta accreta was higher in the placenta malposition group, but not significantly so, and there were no cases in the placenta malposition group that resulted in total hysterectomy due to bleeding or placenta accreta. **[Conclusion]** Cases of placental malposition complications in pregnancies after trachelectomy were considered to be at higher risk.

ISP-30-3

Perinatal and Postpartum Outcomes in Women with Delayed Diagnosis of Gestational Diabetes Sue Hideaki, Yamashita Hiroshi, Ogawa Masayuki, Koga Megumi, Isokawa Satoshi, Sugimi So, Suga Sachie, Fukuda Masashi, Yasuhi Ichiro *Nagasaki Medical Center*

[Objective] Gestational diabetes (GDM) is recommended to be screened and diagnosed between 24 to 32 weeks' gestation. The clinical significance of delayed diagnosis of GDM is not well documented. The aim of this study was to investigate the perinatal outcomes and the risk for early postpartum glucose intolerance. **[Methods]** We included singleton pregnant women with GDM and compared the adverse perinatal outcomes and the rate of early postpartum abnormal glucose tolerance (AGT) between women with GDM diagnosed at 33 weeks' gestation or later (delayed group) and those diagnosed between 24 and 32 weeks' gestation (appropriate group). **[Results]** We included 40 and 300 women in the delayed and the appropriate groups, respectively. Women in the delayed group were heavier at delivery (70.7 ± 14.7 vs. 65.8 ± 11.7 kg, $p < 0.05$) compared with the appropriate group. The rate of insulin therapy (48% vs 39%) was not different between the groups. Although the rate of heavy-for-dates (HFD) infants did not significantly differ between the groups (25% vs 14%, $p = 0.07$), birthweight SD was greater (0.68 ± 1.16 vs. 0.04 ± 1.04 , $p < 0.01$) and neonatal respiratory complication was more frequent (8% vs. 1%, $p < 0.05$) in the delayed group than the appropriate group. The rate of early postpartum AGT did not differ between the groups (23% vs. 28%). **[Conclusion]** Delayed diagnosis of GDM may affect the perinatal outcomes, probably due to delayed therapeutic interventions. The risk of postpartum AGT in women with delayed diagnosis was similar to that in women diagnosed appropriately.

ISP-30-4

The prevalence of estrogen replacement therapy after endometrial cancer surgery : Is estrogen therapy sufficiently performed? Inayama Yoshihide, Yamaguchi Ken, Egawa Miho, Koike Ayami, Higashiyama Nozomi, Kitamura Sachiko, Taki Mana, Yamanoi Koji, Murakami Ryusuke, Hamanishi Junzo, Mandai Masaki *Kyoto University*

[Objective] The prognosis of endometrial cancer (EC) is relatively good, and the quality of life (QOL) after EC treatment is important. Estrogen therapy (ET) is important in maintaining post-surgical QOL in patients with EC experiencing surgical menopause. We investigated the prevalence of ET after EC surgeries in Japan. **[Methods]** This study used the JMDC claims database. Women who underwent surgery for EC at 40-59 years from January 2006 to March 2021 were included. The cumulative ET prescriptions after EC surgeries was estimated using the Kaplan-Meier method. Women who had received chemotherapy or radiation therapy (adj-group) and those who did not (non-adj-group) were analyzed separately. The prescriptions were

also analyzed by hospital categories. **[Results]** In non-adj-group, of 958 women who underwent EC surgery, 85 women received ET. The cumulative proportions [95 confidence intervals (CIs)] of ET prescriptions at 24 months after surgery decreased with increasing age from 0.29 [0.21, 0.38] in the 40-44 years old to 0.009 [0.002, 0.034] in the 55-59 years old. In designated cancer care hospitals, the cumulative proportion was 0.36 [0.21, 0.57] and 0.052 [0.013, 0.19] in patients aged 40-44 and 45-49 years, respectively. In adj-group, ET was started in 30 of 517 women. The cumulative proportions of ET prescriptions at 24 months decreased from 0.17 [0.094, 0.31] in the 40-44 years old to 0 in the 55-59. **[Conclusion]** This study shows that ET after EC surgery may be underused in Japan, even in women who underwent surgery at 40-44 years without adjuvant therapy.

ISP-30-5

Single institutional retrospective study on ERT on surgical menopause Shima Kazuaki, Okamoto Mamiko, Kai Kentaro, Yamada Tomonori, Kodama Haruho, Yamamoto Shizuka, Obata Eri, Aso Saki, Aoyagi Yoko, Yano Mitsutake, Kobayashi Eiji *Oita University*

[Objective] Surgical menopause is associated with a quality of life due to acute symptoms of hormone deficiency and long term sequelae (osteoporosis, dyslipidemia, and atherosclerosis). We aimed to investigate the actual situation of surgical menopause patients after surgery for malignant diseases at our institution and to verify whether it is possible to improve the quality of life of young patients after surgery for malignant tumors. **[Methods]** This was an electronic health record-based retrospective study conducted at a university teaching hospital. We analyzed the cases of 112 patients with gynecologic malignant tumors who underwent definitive surgery and subsequently experienced surgical menopause at our institution between 2018 and 2022. **[Results]** The proportion of ERT among surgical menopausal patients was 18.9% (21/111). The distribution of prescribed each disease groups were cervical cancer in 11, endometrial cancer in 6 and ovarian cancer in 4. The mean age of the ERT group was 40.4 ± 11 years old, expect for one patient who discontinued due to side effects, the observation period has continued from the start of ERT to the present. In the ERT group, there were 2/21 (9.5%) recurrences, one in cervical cancer and another in ovarian cancer. On the other hand, no recurrence was observed in 10 cases of endometrial cancer. **[Conclusion]** Our retrospective study revealed that more surgical menopause patients may safely receive hormone therapy and the importance of awareness concerning ERT among obstetricians and gynecologists.

ISP-30-6

A case of ureterocele in duplicated kidney and ureter with vaginal cyst Koike Makoto, Kodama Michiko, Matsumoto Yuka, Kuruma Airi, Oi Yukako, Kakuda Mamoru, Endo Masayuki, Kimura Tadashi *Osaka University*

Ureteric ectopia with Gartner's duct cyst is caused by the failure of separation of ureteric bud from the mesonephric duct. We report a case of a dilated ectopic ureter with a vaginal cyst suspected to be a Gartner's duct cyst causing ureterocele. A 72-year-old woman, gravida 3 and para 3, visited her physician for vulvar discomfort and drooping. She was referred to our institution for an anterior vaginal wall prolapse. She neither had repeated urinary tract infections, nor had vaginal discharge previously. Prolapse was defined as POP-Q stage 3 (Aa +1, and Ba +2). Transvaginal ultrasonography revealed two cysts underneath the anterior vaginal wall. CT and MRI images showed left duplicated kidneys, ureters, and a vaginal cyst. The ureter leading from the upper atrophic kidney was markedly dilated to 4

cm in size, adjacent to the vaginal cyst. After a discussion with urologists, we concluded that the complete resolution of her symptoms would require the removal of the atrophic kidney, distended ureter, and vaginal cyst. The invasiveness of this procedure was too significant, therefore, we first offered conservative treatment to her. Needle aspiration of the vaginal cyst could not improve the prolapse, then ring pessary was attempted. The maximum size of pessary she could use without pain was 56 mm because of gh 3, and she self-managed it to be positioned near point Aa. After 5 months of pessary management, she decided to pursue surgery following the onset of cystitis. We plan laparoscopic nephrectomy, ureterectomy, and cystectomy of vaginal cyst.

ISP-30-7

Validation of IOTA ADNEX model among Japanese women by gynecology trainees and ultrasonic specialists : A retrospective diagnostic accuracy study Kadooka Mizuho¹, Suemitsu Tokumasa¹, Ashimoto Kensuke¹, Takesawa Ami¹, Otsuka Isao¹, Tajima Atsushi² *Kameda Medical Center¹, Kyorin University²*

[Objective] The ADNEX model is known as distinguishing between benign and malignant adnexal masses. We conducted this study to validate the accuracy of the ADNEX model in the Japanese population, whose distribution of the adnexal masses is significantly different from European. The learning point to improve gynecology trainees' performance were investigated. **[Methods]** This was a single-center, retrospective diagnostic accuracy study. 206 patients with an adnexal mass who underwent ultrasonography, checked CA-125, and had a postoperative histological diagnosis were included from January 2017 to March 2020. The diagnostic performance of the ADNEX model to differentiate malignant tumors was evaluated with AUC among two gynecology trainees and two ultrasonic specialists. **[Results]** Of 206 included Japanese women, 144 had benign, and 62 had malignant adnexal tumors. The AUC of the ADNEX model was 0.883 by Specialist-1, 0.898 by Specialist-2, 0.791 by Trainee-1, and 0.871 by Trainee-2. The sensitivity was 0.839, 0.839, 0.677 and 0.806. The specificity was 0.847, 0.861, 0.847 and 0.840. The accuracy of ADNEX was the highest on Specialist-2, the most experienced doctor, but Fleiss' Kappa was 0.586. The performance comparing trainees and specialists showed a significant difference in the evaluation of the proportion of solid tissue and the number of papillary projections. **[Conclusion]** The efficacy of the ADNEX model in Japanese women is suggested with a moderate degree of coincidence for four examiners. Better accuracy would be expected if focusing on training in the evaluation of the proportion of solid tissue and the number of papillary projections of the ADNEX model.

ISP-30-8

Association between Pre-existing Psychiatric Disorders and Less-aggressive Treatment in Patients with Gynecologic Cancer Yamada Tomonori, Kai Kentaro, Kodama Haruho, Shima Kazuaki, Yamamoto Shizuka, Obata Eri, Aso Saki, Aoyagi Yoko, Yano Mitsutake, Okamoto Mamiko, Kobayashi Eiji *Oita University*

[Objective] The prevalence of psychiatric disorders in the general population in Japan has been increasing annually, and its lifetime morbidity rate has reached >20%. The impact of psychiatric disorders on the treatment of gynecologic malignancies has been unknown. We investigated whether there is a correlation between pre-existing psychiatric disorders and the administration of less aggressive treatments in patients with gynecologic malignant tumors. **[Methods]** This was an electronic health record-based retrospective cohort study conducted at a

university teaching hospital with a psychiatric ward. We analyzed the cases of 514 patients with gynecologic malignant tumors who received their initial treatment at our department between 2018 and 2022. We divided the patients into groups based on the presence (n=34) or absence (n=480) of a psychiatric disorder and used the χ^2 -test to compare the incidence rates of less-aggressive treatments in each group. **[Results]** The incidence rate of less-aggressive treatment was 62% (13/34) in the group with psychiatric disorders and 22% (87/480) in the group without such disorders, revealing a significantly higher incidence rate of less-aggressive treatments in the group with psychiatric disorders compared to their counterparts ($p=0.004$). **[Conclusion]** Pre-existing psychiatric disorders in patients with gynecologic malignancy are associated with less aggressive treatments. Further investigations are necessary to determine the oncological outcomes of patients with both gynecologic cancer and a psychiatric disorder.

ISP-30-9

A case report : Hydronephrosis and unilateral lower limb swelling caused by pelvic actinomycosis mimicking adnexal malignancy disease Wang Wei-Jhu, Chen I-Hui *National Taiwan University Hospital Hsin-Chu Branch, Taiwan*

Pelvic actinomycosis, a rare infection caused by *Actinomyces* spp., often mimics gynecological malignancies. The clinical presentation of pelvic actinomycosis may mimic gynecological malignant disease by demonstrating an extending and infiltrating tumor mass without fever. The key elements of diagnosis include pathology and bacterial culture. Treatment of actinomycosis usually requires prolong high-dosage penicillin-based antibiotics. The treatment course could be shortened to 3 months if the patient underwent optimal surgical resection. We present the case of a 52-year-old woman gravida 3, para 2 with unilateral lower limb swelling initially suspected of ovarian cancer based on imaging findings. She had received IUD placement for more than 5 years and exchanged 2 years ago. Her tumor marker level, including CEA, CA-125, CA19-9 was within normal range. Exploratory laparotomy revealed retroperitoneal fibrotic tumor encasement of the left ureter and iliac vessels, prompting extensive surgical intervention including DBJ placement, total abdominal hysterectomy, bilateral salpingo-oophorectomy, tumor excision, peritoneal washing cytology, and sigmoid colon resection with anastomosis. The final diagnosis was pelvic actinomycosis related to prolonged intrauterine contraceptive device (IUD) use. This case highlights the importance of considering pelvic actinomycosis in patients with extended IUD use and suggestive symptoms, necessitating prompt diagnosis and a multidisciplinary approach for optimal management.

ISP-31-1

Development of ChatGPT4-used application on pregnancy consultation : attempt to solve the problem of pregnant women without prenatal checkup Akazawa Munetoshi¹, Hashimoto Kazunori¹, Matsuzawa Atsushi², Moriyama Makoto² *Adachi Medical Center, Tokyo Women's Medical University¹, Engineer, FIG Advanced Technology Inc.²*

[Objective] Pregnant women without prenatal checkup is an obstetrical problem, called as "Mijushin-Nimpu" in Japan. These women have many social problems such as poverty and isolation. Even though not visiting obstetricians, the women are aware of their pregnancy, seeking information about the unknown pregnancy and birth. Today, interactive artificial intelligence (AI) such as ChatGPT4 make it possible to obtain information as if having a chat conversation. Interactive AI could provide appropriate information through the chat anonymously, encouraging the women without prenatal checkup to visit obstetricians.

trician before 22 weeks of gestation or labor. **[Methods]** We developed a chatbot using ChatGPT4. Chatbot is an interactive application, responding to the questions which users write as if exchanging the e-mail or SNS messages. Having the medical staffs use it and answering the questionnaires, we evaluated (1) the accuracy of the pregnancy information, (2) the natural flow of the conversation, (3) the satisfaction of using the application, and (4) future improvements. **[Results]** The current model showed good performance on the point of the information accuracy, but the flow of the conversation remained a challenge, which leads to satisfaction of users. There are many improvement points, such as the creation of training data or improvement of natural language flow. **[Conclusion]** We demonstrated the potential of the chatbot application as an information tool, for the pregnant women who bear the problem alone without visiting obstetricians. The chat with interactive AI could give the first opportunity to discuss her pregnancy, which leads to the appropriate visit to obstetricians.

ISP-31-2

The risk factors of postnatal severe psychological status on working pregnant women Ando Hitomi, Takeda Jun, Namimatsu Kyoko, Kawasaki Yu, Kitamura Eri, Itakura Atsuo *Juntendo University*

[Objective] To date, the rate of working women in Japan is increasing. However, the information of their postnatal mental health is lacking. Hence, the study was conducted to clarify the risk factors of postnatal severe psychological status on working women during pregnancy. **[Methods]** A cross-sectional, multi-center questionnaire survey was undertaken for women who gave birth in seven institutions from March 2022 to December 2022. Questions related to basic characteristics, obstetrical clinical information, and socioeconomic characteristics were included in the questionnaire. Mental health status was also included in the questionnaire, and analyzed using Kessler 6 scale. Women who worked during pregnancy were selected, and among them, past history of mental disease and baby abnormality were excluded. We divided the participants into two groups: the high-risk group and the low-risk group with the cutoff value of 13 points with Kessler 6 scale. Both Univariate and multivariate logistic regression analysis were conducted to reveal the risk factors. **[Results]** A total of 963 women were answered completely, and 761 women were employed. Among them, data of 500 women were analyzed including 60 women of the high-risk group. The multivariate-adjusted odds ratio and 95% confidence interval of the risk factors of high Kessler 6 points were partners' unwanted pregnancy (1.93, 1.08-3.42), loss of love from parents (2.09, 1.34-3.16), harassment (3.62, 1.48-8.85), passive-smoking (2.78, 1.35-5.75). **[Conclusion]** Four risk factors of postnatal severe psychological status in working pregnant women were revealed with the study.

ISP-31-3

Maternity Care Access and Pregnancy Complications: Focusing on Cesarean Section and Dystocia Kang Soo Hyun¹, Seo Yeong Choi^{1,2}, Jeong Eon Kim¹, Jong Youn Moon² *Preventive Medicine, Gachon University College of Medicine, Korea¹, Artificial Intelligence and Big-Data Convergence Center, Gil Medical Center, Korea²*

[Objective] As South Korea grapples with a declining birthrate, maternity care accessibility has become challenging. This study examines their association with pregnancy complications, focusing on C-SEC and dystocia. Additionally, we will assess the impact of the maternity care desert support program on these areas. Data from the South Korean NHIS-NID was used to analyze 1,437,186 women with childbirths between 2010-2015. **[Meth-**

ods] The research defines 50 specific districts as maternity care deserts based on a list of maternity care underserved areas produced by the Ministry of Health and Welfare in 2011. Pregnancy complications were assessed through C-SEC using medical procedure and DRG codes, and dystocia was defined using ICD-10. Logistic regression analysis was used to examine the significance of the association. **[Results]** Among the population residing in underserved areas, 42,873 out of a total of 1,437,186 individuals were identified. For nationwide cases, the odds ratios (ORs) for C-SEC were 1.11 (95% CI: 1.08-1.13) and dystocia were 1.07 (95% CI: 1.05-1.09). In relatively accessible urban areas, the ORs for C-SEC and dystocia, based on whether they were maternity care deserts, were 1.16 (95% CI: 1.13-1.18) and 1.10 (95% CI: 1.08-1.19), respectively. **[Conclusion]** Poor accessibility to maternity care facilities is closely linked to high-risk pregnancies, including C-SEC and dystocia. Insufficient access to maternity care not only raises the risk of serious pregnancy complications but can also result in additional time and financial burdens for expectant mothers during both the prenatal and postnatal phases. Consequently, there is a pressing need for multi-faceted efforts to bridge this disparity.

ISP-31-4

Assessing the Efficacy of Simulation-Based Education for Paramedics in Extended Focused Assessment with Sonography for Trauma under Physician Guidance Nakato Hikari, Oohira Akiko, Maki Jota, Suemori Ayano, Ooba Hikaru, Mitoma Tomohiro, Mishima Sakurako, Kirino Satoe, Eto Eriko, Masuyama Hisashi *Okayama University*

[Objective] A high-quality educational program is essential to increase the number of Emergency Medical Technicians (EMTs) capable of performing procedures in vehicles under the direction of physicians. We investigated the effectiveness of simulation-based education in Focused Assessment with Sonography for Trauma (FAST), in which paramedics performed ultrasound examinations under the guidance of a physician. **[Methods]** The paramedics watched a 14-minute video on the features of the ultrasound system, its use, and the scanning method for each part of the body. The participants were then divided into four teams. Each participant performed four FAST examinations using a portable ultrasound device. The time required for visualizing each examination site and each FAST was assessed. Practical guidance for FAST was provided by an emergency physician or obstetrician/gynecologist with expertise in ultrasound examinations. The primary outcome was the time required for FAST performance. **[Results]** Twenty-eight EMTs participated. The mean time required for the first and fourth FAST was 144.6±52.4 s and 90.5±31.0 s, respectively. The time required for each test decreased with repeated testing ($p < 0.001$). The time to complete FAST was significantly shortened for the pericardial cavity (33.4±23.1/15.3±10.6 s, $p < 0.01$), right thoracic cavity (25.2±11.8/12.1±8.3s, $p < 0.01$), Morrison pouch (19.1±10.8/10.8±6.3s, $p < 0.05$), and left thoracic cavity (19.0±8.3/15.6±8.3 s, $p < 0.05$). **[Conclusion]** Hands-on seminar under the guidance of a physician significantly reduced the time required for FAST performance. Moreover, repeated practice enabled the EMTs to efficiently obtain accurate and clinically useful images.

ISP-31-5

Efficacy of Virtual Reality system on education of childbirth for medical students Nagata Hiroki, Komatsu Hiroaki, Miyamoto Keisuke, Harada Takashi, Taniguchi Fuminori *Totomi University*

[Objective] Medical students have fewer opportunities to experience childbirth due to declining birth rates and the spreading

of COVID-19. Virtual reality (VR) is a technology which simulates remote environments to provide a high level of immersion through computer-generated graphics. We have introduced a VR system to promote educational effectiveness. **[Methods]** We had obtained the patient's informed consent before recording the delivery scene. We used VR video recording systems in the delivery room and two distinct VR video playback devices. Five cameras can be used simultaneously, including two 360-degree visible cameras and three high-definition cameras for capturing enlarged views of patients and infants. We performed the education which mimics real experience related to childbirth to 66 clinical clerkship students using a combination of 4-screen projectors and head-mounted displays. After the lecture, we asked the questionnaires to the students. **[Results]** In the VR room with special equipment, medical students could experience immersive observations. In the absence of patients, these students asked the questions more freely than the in-person experience in the usual delivery room. The satisfaction rate in all medical students for the VR equipment was 95%. The scenes of delivery and suturing were impressive experiences in which the students expressed higher satisfaction. **[Conclusion]** Introducing a VR system with learning from the virtual field made medical students more satisfied with our educational course. VR technology would also be capable of improving the future education of residents and midwives.

ISP-31-6

Development of the Japanese Version of Pregnancy-Related Anxiety Questionnaire-Revised-2 : Measurement and Psychometric Properties Shirabe Ritsuko *Department of Health Communication, Graduate School of Medicine, The University of Tokyo*

[Objective] Tools to evaluate pregnancy-specific anxiety are lacking in Japan. This study aimed to develop a Japanese version of the Pregnancy-Related Anxiety Questionnaire-Revised-2, which can assess anxiety regarding child health, child loss, childbirth, and body image. **[Methods]** After scale translation and cognitive interviews, we conducted a cross-sectional study among 120 ≥18-year-old, singleton Japanese women before 15 weeks of pregnancy, recruited from four facilities. A total of 112 women completed the questionnaires. We tested the internal consistency, measurement error and reliability, structural validity, measurement invariance across nulliparous and parous women, construct validity by calculating omega, standard error of measurement (SEM), intraclass correlation coefficient (ICC), confirmatory factor analysis (CFA), multigroup CFA, multitrait-scaling analysis, correlational analyses with other measurements, and t-test to compare nulliparous and parous groups. **[Results]** Omega was 0.90 for the total score. SEM was 3.4 and ICC was 0.76. The CFA revealed an optimal fit for the three-factor model based on the original scale. Multigroup CFA supported measurement invariance across the nulliparous and parous groups, and multitrait-scaling analysis revealed 100% scaling success. The correlation coefficients with other scales of childbirth anxiety and general anxiety were 0.70 and 0.24. The mean total score of the nulliparous women was higher than that of the parous women (34.5 vs. 30.3, $p = 0.001$). **[Conclusion]** This developed scale is a reliable measure for the assessment of pregnancy-related anxiety in a Japanese population and can capture the intricacies of pregnancy-specific anxiety. (This abstract is based on the publication : Shirabe R et al. *Healthcare* 2023, 11 (13), 1935.)

ISP-31-7

Prevalence and Risk Factors of Postpartum Depression Rauf Sidra, Batool Mussarat, Javed Nosheela, Aftab Sadia, Nawaz

Farzana, Saeed Qurratulain, Sharafat Shirza, Jalil Mazhar, Shaikat Soha *Pakistan Institute of Medical Sciences, Pakistan*
[Objective] To find out the prevalence and risk factors of Postpartum Depression in the Pakistani population **[Methods]** This single-center cross-sectional study was used to examine women who gave birth within the past 12 months.. The primary outcome measure was the prevalence of PPD, as determined by the Edinburgh Postnatal Depression Scale (EPDS). Secondary outcome measures included demographic and obstetric characteristics, social support, stress levels, history of mental illness, and other risk factors associated with PPD. **[Results]** The prevalence of PPD was found to be 20.6% (95% CI : 16.7%-24.5%). Several risk factors were significantly associated with PPD, including low social support (OR : 2.34 ; 95% CI : 1.52-3.61), history of mental illness (OR : 2.15 ; 95% CI : 1.18-3.91), and high levels of stress (OR : 1.87 ; 95% CI : 1.20-2.92). In addition, the study found that women who had a Caesarean section were at higher risk of developing PPD than those who had a vaginal delivery (OR : 1.86 ; 95% CI : 1.12-3.10). However, women with higher education levels (Bachelor's degree or above) had a significantly lower prevalence of PPD (14.3%) compared to those with lower education levels (20.9% for high school or below and 25% for college) ($p=0.04$). We found a significant association between SES and PPD ($p=0.02$), with women in the lower SES category having the highest prevalence of PPD (24.6%). **[Conclusion]** Postpartum depression is a prevalent condition in our local setup. Women should be screened for known risk factors during antenatal visits so prompt support can be offered after the delivery of the baby.

ISP-31-8

Prevalence and Risk Factors of Peripartum Depression Among Women in the Prenatal and Postnatal Period in a Tertiary Hospital Gauce April Joy D, Barinaga Sigrid A *Davao Doctors Hospital, Philippines*

[Introduction] Postpartum Depression, is now recognized as "Major Depression, with Peripartum Onset" in the DSM-V, after observations that fifty percent of cases actually began antenatally. While postpartum depression is known to affect 10-20% of women globally, limited studies in the Philippines assessed the prevalence of antenatal depression. **[Objective]** This study was conducted to determine the prevalence and associated risk factors of Peripartum Depression among pregnant and postpartum women in a tertiary hospital in Davao City. **[Methods]** This cross-sectional study was conducted among pregnant women, in the second or third trimester, and postpartum women, who delivered within 2-6 weeks (N=138), utilizing a sociodemographic questionnaire and the Edinburgh Postnatal Depression Scale. **[Results]** Of the 138 participants, 24 scored 12 or higher in the EPDS, indicating a higher probability of depression. None of the participants scored a point on item number 10 regarding suicidal ideation. The post-partum group had a higher prevalence based on EPDS, at 23%, compared to the antepartum group with a prevalence of 12% ($P=0.036$). The significant risk factors noted in the postpartum group were being married for less than a year, having a planned pregnancy, and a history of pregnancy loss. The study was unable to determine which among the socio-demographic or clinical variables were significant risk factors in the pregnant group. **[Conclusion]** The results supported the findings of previous studies worldwide. This study urges health-care providers to identify depression early among pregnant and postpartum women through screening during their prenatal or postpartum visits and carry out necessary interventions.

ISP-32-1

Analysis of fertility preservation for childhood, adolescent

and young adult patients : a single-institution experience

Okaki Hiromu¹, Handa Mika¹, Goto Takeshi¹, Tsuji Saori¹, Honda Hidemine¹, Okada Aiko¹, Miyake Tatsuya¹, Kawano Mahiru¹, Takiuchi Tsuyoshi^{1,2}, Kimura Tadashi¹ *Osaka University¹, Clinical Genomics, Osaka University²*

[Objective] Advances in cancer treatment have dramatically improved the survival rate of young patients. In recent years, fertility preservation (FP) for childhood, adolescent and young adult (CAYA) patients with cancer and benign disease, including autoimmune disease and premature ovarian insufficiency has been attracted. **[Methods]** This retrospective cohort study was performed in a reproductive center from April 2018 to August 2023, involving 143 patients for FP counseling. We analyzed for patient's characteristics, FP decisions and outcomes. Our institution offers FP to female patients under the age of 43. **[Results]** Among 143 patients, 128 with malignancy and 15 with benign disease received FP counseling. Following the counseling, 83 patients (58%) expressed a desire for FP. The median age was 28 years (range : 7-42). The primary indications were gynecologic tumors (n=20, 24.1%), hematologic malignancy (n=19, 22.9%) and breast cancer (n=18, 21.7%). Twenty-one patients underwent embryo cryopreservation, while 46 patients underwent oocyte cryopreservation, and 15 patients underwent ovarian tissue preservation. Among 53 patients slated for chemotherapy and radiotherapy with an intermediate or high-risk of ovarian toxicity, 39 patients (73.6%) demonstrated a desire for FP. Among patients desiring pregnancy, 7 patients with gynecologic tumors or breast cancer who underwent embryo cryopreservation conceived after IVF-ET, whereas a patient with gastric cancer conceived spontaneously. In this cohort, one patient died due to a recurrence of breast cancer. **[Conclusion]** The individualized assessment of CAYA patients, incorporating their FP preferences and considering the potential risks associated with treatment-induced gonadal dysfunction, is imperative.

ISP-32-2

The Role of Genetic Counseling in Fertility Preservation for HBOC Taura Yumiko^{1,2}, Tomonobe Shoko², Hamada Norio², Kawamura Keiko², Yokota Natsuko², Kawamura Teruhiko², Isobe Akiko², Kato Kiyoko^{1,2} *Department of Clinical Genetics and Medicine, Kyushu University Hospital¹, Kyushu University Hospital²*

Patients with hereditary breast and ovarian cancer (HBOC) who consider fertility preservation (FP) have been reported to have conflicts and concerns about heredity. **[Objective]** To conduct a retrospective study on the implementation of FP in breast cancer (BC) with HBOC patients at our hospital, and to examine the involvement of GC. **[Methods]** The study period was from July 2019 to June 2023 and included BC patients aged < 43 years who were eligible for FP and presented to the Department of Clinical Genetics and Medicine. The number of GCs, age, marital status, parity, BRCA1/2 genetic testing results, stage, BC subtype, FP rate, and narrative at GC were examined. **[Results]** Of the 64 patients who underwent GC, 56 (87.5%) implemented BRCA1/2 genetic testing, while 11 of 56 (19.6%) were diagnosed with HBOC. BC subtype was predominantly triple-negative breast cancer (TNBC) in the HBOC group (BRCA1). FP was performed in 1 of 11 (9.1%) in the HBOC group and in 7 of 54 (15.6%) in the non-HBOC group. None of the HBOC group abandoned FP because of heredity. GC identified positive and negative narratives about heredity. **[Conclusion]** Rates of HBOC in BC patients aged < 43 years tend to be higher than rates in all BCs, making them more likely to be eligible for GC. Factors influencing decisions regarding FP in BC patients with HBOC were thought to include concerns about heredity in some cases. GC for BC patients with HBOC provides a variety of decision-making support and may contribute to adoption of FP.

ISP-32-3

The Efficacy of Progesterin-Primed Ovarian Stimulation for Fertility Preservation Therapy compared with GnRH Antagonist Protocol Matsuzawa Yuichi¹, Yamada Mitsutoshi¹, Miyazaki Kotaro¹, Saito Saki², Sakuma Moeko¹, Ooka Reina¹, Fukuoka Mio¹, Iwai Maki¹, Kamijo Shintaro¹, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Reproduction Clinic Tokyo, Reproduction Clinic Tokyo²*

[Objective] Improving survivorship in adolescents and young adults with cancer is challenging. Since the first guideline for fertility preservation (FP) was published in 2006, the indications for FP therapy have expanded. This prospective study aimed to examine the efficacy of different controlled ovarian stimulation protocols in FP therapy. **[Methods]** 55 patients with malignancies or autoimmune diseases were counselled between January 2018 and December 2022 and informed consent was obtained (approved by the Institutional Review Board of Keio University School of Medicine (approval number 20170019)). 37 patients who took FP therapy (Gonadotropin-releasing hormone antagonist (GnRH-ant) group 24 patients, 30 IVF cycles ; progesterin-primed ovarian stimulation (PPOS) group 13 patients, 15 cycles) before gonadotoxic treatment were included for analysis. **[Results]** Between the PPOS and GnRHant groups, the median age (32 [inter quartile range (IQR), 31-33.5] vs. 35 [30-38], P=0.245) and ovarian reserve parameters (AFC and AMH [14 [8-18] vs. 10 [2.95-15], P = 0.181 ; 1.96 [1.32-4.77] vs. 3.00 [1.52-4.84], P = 0.287)) were similar. The numbers of retrieved MII oocytes (10 [7-13] vs. 9 (8.8-15), P = 0.5020) were comparable. Similarly, the fertilization rate (91.7 [59.3-96.4] % vs. 62.8 [53.6-81.7] %, P = 0.497), and the number of frozen embryos (5 [2-6] vs. 4 [3-4], P = 0.601) were comparable. **[Conclusion]** The efficacy of PPOS in FP therapy was comparable to the GnRH-antagonist.

ISP-32-4

RNA sequencing analysis focusing on bacterial extracellular vesicles derived from genital microbiota Muraoka Ayako, Yokoi Akira, Yoshida Kosuke, Kitagawa Masami, Miyake Natsuki, Sonehara Reina, Nakamura Tomoko, Osuka Satoko, Kajiyama Hiroaki *Nagoya University*

[Objective] Numerous studies are focusing on the relationship between bacteria and disease. Vaginal *Lactobacillus* are well-known : "good" *Lactobacillus* produce lactic acid to prevent bacterial vaginosis, while "bad" *Lactobacillus* do not. Furthermore, several bacteria are known to be involved in female reproductive diseases, such as endometriosis. Bacteria actively produce and secrete extracellular vesicles (EVs) to communicate with the surrounding cells. Here we investigated RNAs in bacterial EVs (bEVs) that could reveal the functions of vaginal microflora, and further characterized them by comprehensive RNA sequencing. **[Methods]** Five types of *Lactobacillus* and two types of disease-causing bacteria [*Fusobacterium* and *Escherichia coli* (*E. coli*)] were cultured in an optimal medium. Bacterial bodies and bEVs were isolated from each of the seven bacterial species studied, and RNA-sequencing was performed. **[Results]** The isolated bEVs were characterized by nanoparticle tracking assays and cryo-electron microscopic analyses. RNA-sequencing ensured that each bacterial species was matched to the respective bacterial reference sequence. RNAs within bEVs showed distinctive patterns ; for example, *Lactobacillus iners* differed from the other *Lactobacillus* species. The RNA profiles of the bEVs produced by these seven bacterial strains were characteristic for each strain. **[Conclusion]** Our results demonstrate that RNAs in bEVs displayed characteristic profiles and could functionally influence the endometrial cells via bEVs through ascending infectious route. Further studies are required to examine the functional importance and mecha-

nisms of bEVs.

ISP-32-5

Temporal Trends in Syphilis and Chlamydia Infection Rates Among Couples Undergoing Fertility Treatment : A Retrospective Analysis in an Urban Reproductive Health Center Komiya Shinnosuke *HORAC Grand Front Osaka Clinic*

[Objective] Amidst the escalating prevalence of syphilis in Japan, there exists a paucity of comprehensive studies examining the infectious landscape among couples seeking fertility treatments. This study endeavors to delineate the trends in syphilis and chlamydia prevalence in an urban reproductive health center and to articulate recommendations for targeted infection prevention. **[Methods]** A retrospective analysis was performed on syphilis test results for couples undergoing fertility treatment at our institution from its inception in 2015 through March 2023. The incidence of syphilis and chlamydia was assessed using RPR-positive and TP-negative criteria for syphilis and Taqman PCR for chlamydia derived from cervical swabs. Ethical clearance was secured for retrospective data assimilation, and an opt-out provision was maintained. **[Results]** Our findings underscored a continuous ascent in syphilis prevalence among males from 2015 to 2023, climaxing at 1.4% in 2021. Conversely, female infection rates exhibited a plateau, capping at 0.5%. Chlamydia prevalence peaked at 3.5% in 2021 before showing a downward trajectory. **[Conclusion]** The data suggest that extramarital sexual encounters may underlie the uptick in syphilis prevalence among males seeking fertility treatment. While chlamydia incidence did not surge, it aligns with national epidemiological data, which indicates a stable-to-declining trend except within the 20-29 age demographic. These insights urgently necessitate heightened awareness and robust prevention strategies among couples in fertility treatment programs.

ISP-32-6

A retrospective analysis for acute and non-acute postoperative complications following transcervical resection Awano Sena, Kasahara Yuta, Hosoya Satoshi, Shinoda Akari, Katakura Wakako, Yokomizo Ryo, Hidaka Miwa, Sato Takuma, Shiraishi Eriko, Kishi Hiroshi, Okamoto Aikou *The Jikei University*

[Objective] We aimed to investigate the clinical features of acute and non-acute postoperative complications following transcervical resection (TCR). **[Methods]** In this retrospective analysis, patient characteristics and indications for surgery, surgical findings, and complications were investigated from medical records of TCR performed in our hospital between July 2018 and June 2022. Complications were classified into the following two categories : acute complications including uterine perforation and fluid intravasation, and non-acute ones including intrauterine adhesions and placental abnormalities. The difference in clinical features between the complication and non-complication groups was evaluated in each acute or non-acute complication category. The statistical analysis was performed using Mann-Whitney U test, or Fisher's exact test where appropriate. Exclusion criteria were pathological findings of malignancy and diagnostic hysteroscopic procedures. **[Results]** We analyzed data of 149 patients. Of the 149 cases, 70 (47.0%), 55 (36.9%) and 24 (16.1%) cases had endometrial polyps, submucosal myoma and other indications, respectively. Total complications following TCR occurred in 10 cases (6.8%). Uterine perforation and fluid intravasation as acute complications were 1.3% and 0.7%, respectively. Intrauterine adhesions and placental abnormalities as non-acute complications were 1.3% and 3.4%, respectively. In comparison of patient's clinical features, there were no significant differences between the complication and non-complication groups in each acute or non-acute complication category. **[Con-**

clusion] We showed the frequency of some acute and non-acute complications following TCR in our hospital. The featured backgrounds of cases with acute or non-acute complications were not clear. Further studies to lead to safer TCR procedure will be needed.

ISP-32-7

The detrimental effect of laparoscopic electrocoagulation on ovarian reserve in endometrioma attenuated in benign ovarian tumors : A systematic review and meta-analysis Lin Yu Hsuan^{1,2}, Lee Tsung-Hsien^{1,2,3}, Li-Hsin Hsia¹, Yun-Yao Huang¹, Hao-Jung Chang¹, Yung-Liang Liu¹ *Chung Shan Medical University Hospital, Taiwan¹, Institute of Medicine, Chung Shan Medical University, Taiwan², Division of Infertility, Lee Women's Hospital, Taiwan³*

[Objective] The detrimental effect of thermal injury on other types of benign ovarian tumors is unclear. We evaluated the impact of ovarian reserve using nonthermal hemostatic methods and compared it with bipolar electrocoagulation during laparoscopic cystectomy for endometriomas and benign ovarian tumors. **[Methods]** We searched the Cochrane Library, PubMed, EMBASE, and Web of Science databases, for the articles up to October 2022, and included RCTs that evaluate ovarian reserve using bipolar coagulation compared with nonthermal hemostasis methods during laparoscopic surgery. **[Results]** Thirteen RCTs were included. A total of 532 patients underwent laparoscopy with nonthermal hemostasis methods and 512 patients with bipolar electrocoagulation (total N=1043). In the endometrioma patients, the postoperative serum anti-Müllerian hormone was significantly higher in the nonthermal group than in the bipolar group at one month, three months, six months, and 12 months after surgery respectively. However, when comparing the patients with benign ovarian tumors, there is no significant difference between the two groups at 3-, 6-, and 12-month after surgery. A similar outcome is also observed in antral follicle count, while a statistically significant difference in decreased AFC was only observed in patients with endometrioma after surgery. **[Conclusion]** Nonthermal hemostasis method in laparoscopic surgery of ovarian tumors is more advanced in preserving ovarian reserve than bipolar hemostasis in patients with endometrioma. However, we found no significant effect of bipolar electrocoagulation on the ovarian reserve in other benign ovarian tumors.

ISP-33-1

CCM-C1, a curcumin analog, could be a potential therapeutic agent for preeclampsia as an autophagy activator Furuta Atsushi, Yamada Kiyotaka, Yoshida Mihoko, Shima Tomoko, Yoneda Satoshi, Nakashima Akitoshi *Toyama University Hospital*

[Objective] We clarified that the dysregulation of autophagy, an intracellular homeostasis mechanism, induced poor placentation and maternal hypertension, seen in women with preeclampsia (PE). Here we showed the role of autophagy relief oxidative stress (OS) in syncytiotrophoblasts (STB) via Hemoxygenase-1 (HO-1), antioxidative enzyme. **[Methods]** BeWo, primary human trophoblasts (PHT), and villous explant culture (VEC) were used as STB models. Bafilomycin A1 (BAF) was used as an autophagy inhibitor. Hydrogen peroxide (H₂O₂) was for OS induction. **[Results]** As BAF decreased HO-1 expressions in BeWo, PHT, and VEC, that express high HO-1, BAF augmented the inhibition of cell proliferation by H₂O₂ in STB. Moreover, BAF also increased the sFlt-1/PlGF ratio in VEC media. Next, we comprehensively screened the agents to induce HO-1 in VEC among autophagy modulators. We found curcumin (CCM) markedly increased HO-1 expressions in PE placental tissues, and subse-

quently, we focused on curcumin C1 analog (CCM-C1) as a less toxic reagent. CCM-C1 effectively induced HO-1 expression with autophagy activation at low concentrations, resulting in OS resistance in BeWo. Though hypoxia reduced HO-1 expressions in BeWo, CCM-C1 increased HO-1 expression in BeWo under hypoxia, a circumstance in PE placenta. **[Conclusion]** Suppression of autophagy enhanced the OS-mediated cytotoxicity in STB, which causes poor placentation. Though the decrease of HO-1 and hypoxia contribute to the increase of sFlt-1 secretion in STB, CCM-C1 effectively induced HO-1 expression and autophagy activation in STB under hypoxia, resulting in OS resistance. Thus, CCM-C1 could be a potential therapeutic agent for PE via HO-1 and autophagy.

ISP-33-2

External Validation of Prediction Model for Hypertensive Disorders of Pregnancy : Developing Two-way Communication Based Inter-conception Care Strategies Tano Sho^{1,2}, Kotani Tomomi¹, Matsuo Seiko¹, Ushida Takafumi¹, Imai Kenji¹, Kishigami Yasuyuki², Oguchi Hidenori², Kajiya Hiroaki¹ Nagoya University¹, Toyota Memorial Hospital²

[Objective] In inter-conception care (ICC), we have proposed the "annual body mass index (BMI) change" as a useful indicator for weight management to prevent hypertensive disorders of pregnancy (HDP). Ideal ICC is grounded in two-way communication between physician and patient. Based on this principle, we developed a prediction model. **[Methods]** We constructed a prediction model for HDP development using electronic data from 2 tertiary centers and 12 primary facilities collected between 2009 and 2019 (derivation cohort). This dataset comprised participants with two series of pregnancy records (index and subsequent pregnancy). In constructing the model, we aimed to minimize the number of variables used. This predictive model was subsequently validated using newly added data from 2 tertiary centers spanning 2020-2022 (validation cohort). **[Results]** The derivation and validation cohorts included 1,746 and 252 participants, respectively. The prediction model was developed using 5 parameters : maternal age, pre-pregnancy BMI, HDP history, pregnancy interval, and annual BMI change. The AUC values for the ROC and precision-recall curve analyses were 0.88 and 0.90, respectively, with a balanced accuracy of 0.83. The calibration curve analysis showed that the 95% confidence interval consistently overlaps with the ideal line, indicating a well-calibrated model. **[Conclusion]** Prediction models developed using minimal covariables demonstrated a high AUCs, indicating their potential for a user-friendly design. Furthermore, prediction model generated from the combined dataset of primary-facilities and tertiary-centers confers an enhanced generalizability. Such a predictive model can motivate patients toward ICC through visualizing efforts and results, and allows achieving ICC based on two-way communication.

ISP-33-3

Reducing Preeclampsia-Related Transports : Early Screening and Aspirin Intervention, Interrupted Time-Series Analysis Kotoku Rakan Kagoshima Prefectural Oshima Hospital

[Objective] Maternal and neonatal healthcare in remote islands presents unique challenges due to limited access to specialized perinatal care and transport constraints. Severe preeclampsia (PE) compounds these challenges, necessitating maternal transports over considerable distances. This study investigates the impact of early PE screenings and aspirin intervention on the incidence of severe PE-related transports in a remote island setting in Japan. **[Methods]** An observational cohort study was conducted from January 2018 to August 2023, utilizing medical records of a regional perinatal medical center. Pregnant women

undergoing prenatal check-ups constituted the study population. Interrupted time-series analyses assessed the intervention's effect on severe PE-related transports. **[Results]** The intervention demonstrated a reduction in transported cases by -1.47 (-0.386 to -2.46, 95% CI, $p=0.0316$). **[Conclusion]** The findings underscore the significance of early PE screenings and aspirin intervention in mitigating severe PE-related transports, particularly in resource-limited island settings. Strengths include a robust study design, while limitations include potential confounding and limited generalizability. Comparisons with global literature support the efficacy of these preventive measures. The observed reduction holds clear implications for clinicians and policymakers, emphasizing the adaptability of established strategies to unique healthcare landscapes. This study provides evidence supporting the implementation of early PE screenings and aspirin intervention to reduce severe PE-related transports in remote islands. The findings contribute to the evolving understanding of tailored perinatal care in geographically isolated settings, advocating for proactive preventive measures in similar contexts.

ISP-33-4

Performance of the sFlt-1/PIGF ratio as a predictive marker for preeclampsia Yamazaki Tomomi¹, Kawasaki Masaya², Nakagawa Hitoshi², Yorishima Makoto⁴, Tanaka Norifumi³, Date Kenjiro⁶, Nakanishi Yoshinobu⁷, Sakashita Tomohisa⁸, Mukai Yurika¹, Sugimoto Jun¹, Koh Iemasa¹, Kudo Yoshiki¹ Hiroshima University¹, Kawasaki Clinic², Nakagawa Clinic³, Yorishima Clinic⁴, Higashihiroshima Medical Center⁵, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital⁶, JA Hiroshima General Hospital⁷, Onomichi General Hospital⁸

[Objective] The measurement of the sFlt-1/PIGF ratio was covered by insurance to predict the onset of preeclampsia in July 2021. Currently the sFlt-1/PIGF ≤ 38 is used to rule out preeclampsia within 1 week and the sFlt-1/PIGF > 38 is used to rule in preeclampsia within 4 weeks. However, the reported positive predictive value for the sFlt-1/PIGF > 38 ruling in preeclampsia within 4 weeks is not so high, and several studies on the sFlt-1/PIGF ≥ 85 have been reported. Therefore, we evaluated the usefulness of a cutoff value of 85 in addition to confirming the practicality of the cutoff value of 38 at our institutions. **[Methods]** We enrolled Japanese pregnant women presenting with clinical suspicion of preeclampsia at 18 to 36 weeks' gestation at 1 tertiary care center, 4 secondary facilities, and 3 primary clinics. We measured the sFlt-1/PIGF ratio and collected clinical data over time. **[Results]** 66 (23.2%) of 284 enrolled pregnant women developed preeclampsia. The sFlt-1/PIGF ≤ 38 had a negative predictive value of 97.7% (95% CI, 95.6-98.9%) for ruling out preeclampsia within 1 week. The positive predictive value of the sFlt-1/PIGF ≥ 85 for ruling in preeclampsia within 4 weeks was 73.9% (95% CI, 55.4-86.9%), higher than 55.2% (95% CI, 45.9-62.6%) for the sFlt-1/PIGF > 38 . **[Conclusion]** We evaluated the performance of a cutoff value of 85 in addition to the cutoff value of 38 for the sFlt-1/PIGF. Combining the sFlt-1/PIGF ≥ 85 with the sFlt-1/PIGF ≤ 38 could improve the management of patient with suspected preeclampsia.

ISP-33-5

Association between hypertensive disorders of pregnancy and labor duration Isogami Hirotaka, Matsuoka Ryo, Okoshi Chihiro, Fukuda Toma, Yasuda Shun, Yamaguchi Akiko, Fujimori Keiya Fukushima Medical University

[Objective] Hypertensive disorders of pregnancy (HDP) are a serious obstetric complication affecting both pregnant women and fetus. As HDP pathogenesis involves an injury to the vascular endothelial cells due to inflammatory cytokine production,

women with HDP reportedly experience a shorter labor duration. However, little evidence supports this theory. Therefore, we assessed the association between HDP and labor duration. **[Methods]** Overall, 1,397 vaginal deliveries managed in our department from January 2018 to September 2023 were included in the study. We analyzed the delivery time separately for 745 primiparous (HDP cases : 31, 4.1%) and 652 multiparous women (HDP cases : 22 ; 3.3%). The analysis was also stratified based on the presence or absence of induction of labor. The Mann-Whitney's *U* test was used for statistical analysis. **[Results]** Among primiparous women, the duration of labor was significantly shorter in women with HDP ($p = 0.014$); however, no significant difference was observed in the need for induction of labor in women with and without HDP. Moreover, no significant difference was observed in the duration of labor among multiparous women with or without HDP ($p = 0.756$). **[Conclusion]** Our study suggested that the pathophysiology of HDP may result in a shortened delivery time among primiparous women. Furthermore, an association between HDP and labor duration was observed among primiparous women who were induced.

ISP-33-6

A case of systemic lupus erythematosus (SLE) pregnancy with severe thrombocytopenia Iio Kazuaki, Kondo Emi, Saito Yuma, Isoshima Yuka, Tajiri Ryosuke, Amimoto Shoko, Yoshino Kiyoshi *University of Occupational and Environmental Health, Japan*

The SLE pregnant woman was 30 years old, (gravida 1 para 0, spontaneous abortion at 8 weeks gestation at age 29) and had no history of thrombosis and had positive and high levels of three types of antiphospholipid antibodies (aPL). Before pregnancy, her platelet count was from 45,000 to 67,000/ μ l. First trimester, her blood pressure is within normal limit. At 19 weeks of gestation, fetal growth restriction (FGR) was observed. At 29 weeks and 3 days gestation, she was diagnosed with early-onset severe preeclampsia (severe hypertension, proteinuria, and FGR) and severe thrombocytopenia (platelet count was 17,000/ μ l). HELLP syndrome was excluded with normal liver function. She was diagnosed with antiphospholipid antibody syndrome (APS) due to both early-onset severe PE and high levels of three types of aPL. At 29 weeks and 4 days gestation, we performed emergency cesarean-section, because of slightly progressed hepatic and renal dysfunction and pleural and ascitic effusion. Postoperatively, the platelet count has been persistently decreased, despite the platelet transfusion. It was considered that thrombotic microangiopathy (TMA) with thrombocytopenia and low haptoglobin was occurred. It was excluded out thrombotic thrombocytopenic purpura (TTP) with under 10% of ADAMTS13 activity. Although platelet transfusions, anticoagulation, and antithrombotic therapy were administered as appropriate, her platelet count did not improve. Rituximab was administered for SLE, her platelet count recovered to 69,000/ μ l on postpartum day 25. This case was difficult to diagnose the cause of prolonged thrombocytopenia in pregnancy.

ISP-33-7

A case of pheochromocytoma detected incidentally in the fourth month of puerperium with hypertensive disorders of pregnancy Kondo Emi, Iio Kazuaki, Isoshima Yuka, Tajiri Ryosuke, Amimoto Shoko, Yoshino Kiyoshi *Hospital of the University of Occupational and Environmental Health*

Pheochromocytoma during pregnancy are diagnosed when severe hypertension (HT) is triggered. About 50% are diagnosed with gestational hypertension (GH) and about 60% present after 32 weeks of gestation. Elevated blood noradrenaline has been reported to decrease utero-placental blood flow and cause intra-

uterine fetal death (IUFD) caused fetal hypoxemia. The patient conceived spontaneously for the first time at the age of 34 and was diagnosed with GH due to mild HT at 24 weeks of pregnancy. Since then, her home BP readings was about 130/80 mmHg. At 38 weeks and 1 day of pregnancy, she was diagnosed with preeclampsia as urinary protein was 480 mg/day. Induction of labor was initiated, and her BP rose up to 180/110 mmHg or higher during labor, resulting in an emergency cesarean delivery. After delivery, BP remained within the mild range with the calcium channel blocker. She subsequently conceived spontaneously, however her pregnancy ended in IUFD at 11 weeks gestation and again six months later at 16 weeks gestation. During these pregnancies, the range of BP was mild. However, her home BP of readings sometimes was about 170/100 mmHg in the evening in the fourth month postpartum, and she was treated with an angiotensin receptor blocker, and her BP remained within the normal range. An abdominal ultrasound showed 6 cm left adrenal tumor. She was diagnosed with pheochromocytoma by urine metanephrines 0.61 mg/day and ¹²³I-MIBG scintigraphy. Even though the BP fluctuation did not change significantly for HDP, it is necessary to differentiate secondary HT.

ISP-34-1

Resolution of metabolic acidemia during recovery from acute and slowly evolving hypoxia Kasai Michi¹, Magawa Shoichi², Maeda Yoshiki³, Aoki Shigeru⁴, Ikeda Tomoaki², Ishikawa Hiroshi¹, Miyagi Etsuko⁵ *Kanagawa Children's Medical Center¹, Mie University², Kuwana City Medical Center³, Yokohama City University Medical Center⁴, Yokohama City University⁵*

[Objective] Hypoxia-ischaemia around the time of birth is associated with high risk of mortality or neurodevelopmental impairment. Measures of acidemia, including pH, lactate and base deficit remain key diagnostic and prognostic tools. The factors determining their evolution after severe hypoxic events are not fully understood. The aims of this study were to evaluate these parameters during and after both acute, severe hypoxia and repeated intermittent hypoxia. These two events broadly reflect sentinel events and evolving hypoxia as observed clinically. **[Methods]** Chronically instrumented fetal sheep at 0.85 gestational age were randomly assigned to receive repeated 1min umbilical cord occlusions (UCO) repeated every 2.5 or 5min ($n = 47$), or prolonged UCO for 15 or >15min ($n = 26$). A group with chronic hypoxic ($pO_2 < 17$ mmHg) was assigned to repeated UCO every 5min group. Fetal arterial blood was analysed before, during and during recovery for 72h after UCOs. **[Results]** Greater levels of lactate and base deficit were observed in the repeated UCO groups than in the prolonged UCO groups. Lactate and base deficit rapidly declined during recovery in the repeated UCO groups, but initially increased before showing a slower decline during recovery in the prolonged UCO groups. Acidemia resolved by 24 h recovery in all groups, except the severe prolonged UCO group. **[Conclusion]** Acidemia was greater after brief repeated UCO, than after a single prolonged episode of occlusion. Interestingly, in contrast, prolonged occlusion was associated with slower resolution of metabolic acidemia over the first 6 h of recovery and with persisting lactic acidemia at 24h.

ISP-34-2

Application of Machine Learning in Understanding the Time-Phase of Fetal Echocardiographic Images Onodera Yohei, Fujishima Akiko, Miura Hiroshi, Terada Yukihiko *Akita University*

[Objective] Most congenital heart diseases are diagnosed using fetal ultrasound. Prenatal diagnosis rates have increased with the advancement of ultrasound equipment and technology. To-

day, many technological innovations have been made using machine learning in fetal ultrasound; however, few technological studies have examined the heart, a dynamic organ. Thus, this study aimed to build a function for deciphering the time phase of the fetal heart using machine learning. **[Methods]** Spatio-temporal imaging correlation (STIC) data of fetal hearts from 20-30 weeks of gestation were used as the research material. The data collection comprised 240 datasets from 15 subjects. The datasets were divided into three categories: systolic, diastolic, and unclassifiable as training and test data. Machine learning was performed using Tensorflow to determine the learning effect. **[Results]** The 240 images were categorized into 91 systolic, 87 diastolic, and 62 unclassifiable images. The loss and accuracy in the neural network obtained by this study were 0.4009 and 0.8143, respectively. **[Conclusion]** Overall, this study demonstrated the usefulness of machine learning-based image analysis to determine the chronological phase of the heart. To improve the quality of the results, it is desirable to accumulate more cases and to set up detailed imaging conditions. Combining the proposed time-phase recognition system in this study with the region recognition of spatial structure, which is currently under development, will enable a four-dimensional understanding of the heart. Construction of a high-resolution imaging technology based on the abovementioned techniques is expected to improve the quality of perinatal care.

ISP-34-3

A new evaluation of fetal breathing movements using artificial intelligence Nagayasu Yoko, Sakaue Karen, Kawamura Rurimi, Maeda Anju, Nao Seiichiro, Matsumoto Tomoko, Daimon Atsushi, Nunode Misa, Sano Takumi, Fujita Daisuke, Ohmichi Masahide *Osaka Medical and Pharmaceutical University*

[Objective] Advances in ultrasound technology have made it possible to assess fetal activity. The typical "seesaw" breathing movements are a parameter of fetal well-being. However, there are no objective evaluation criteria. We aimed to establish a novel strategy for assessment of fetal well-being by creating a model that detects fetal breathing movements using segmentation. **[Methods]** We reviewed 103 ultrasonographic examinations of 62 women with singleton pregnancies at 25-40 weeks of gestation. We recorded the fetal breathing movements for approximately 30 s. The recorded data were divided into still images, and 1240 of them were used as training data. An ultrasound specialist annotated the diaphragms in the training data and built a model (using Efficient Net) to detect it. We verified the model's accuracy and mapped the diaphragm movements using an identified central point. Each week, the distance that the center point moved per second was evaluated. **[Results]** The average number of gestational weeks of the training data was 33.2 weeks. The diaphragm congruency in the evaluated data was 98.2%. We successfully mapped the breathing movements. The movements were small at 25 weeks and became more regular as the pregnancy progressed. Furthermore, the distance moved per second increased as the pregnancy progressed ($R^2 = 0.712$). **[Conclusion]** We developed a new method to evaluate the fetal breathing movements. This novel strategy evaluated the well-being in a shorter time and the same criteria was used for everyone. We believe that it will contribute to the development of fetal ultrasound in the future.

ISP-34-4

Prospective association between maternal serum insulin-like growth factor-1 and longitudinal change of fetal fractional thigh volume Akita Keisuke, Ikenoue Satoru, Tamai Junko, Hasegawa Keita, Kajikawa Kaoru, Takahashi Marina, Fukuma

Yuka, Tanaka Yuya, Otani Toshimitsu, Kasuga Yoshifumi, Yamagami Wataru, Tanaka Mamoru *Keio University*

[Objective] Insulin-like growth factor-1 (IGF-1) is one of the growth factors that promote protein and carbohydrate metabolism, and consequently affects birth weight. Although fetal fractional thigh volume is known to be a useful parameter for predicting fetal growth and quantifying fetal soft tissue development, the association between maternal serum IGF-1 and fetal fractional thigh volume remains unclear. This study aimed to investigate the association of maternal serum IGF-1 in mid gestation with longitudinal change of fetal fractional thigh volume in normal pregnancies. **[Methods]** A prospective study was conducted in a cohort of 34 singleton pregnancies. Maternal blood sample was obtained at 24 weeks' gestation, and fetal ultrasonography was performed at 24, 30, and 36 weeks' gestation. Fractional thigh volume was assessed as a cylindrical limb volume based on 50% of the fetal total diaphysis length using 3D ultrasonography. The association between maternal serum IGF-1 and fetal fractional thigh volume was examined using Pearson product moment correlations. **[Results]** Maternal serum IGF-1 at 24 weeks was 139.8 ± 31.7 ng/ml (mean \pm S.D.). Maternal IGF-1 wasn't associated with fetal fractional thigh volume at 24 weeks ($r = 0.24, p = 0.11$) and 30 weeks ($r = 0.29, p = 0.059$). Maternal IGF-1 significantly correlated with fetal fractional thigh volume at 36 weeks ($r = 0.43, p = 0.011$). **[Conclusion]** Maternal serum IGF-1 at 24 weeks significantly correlated with fetal fractional thigh volume in late gestation. Maternal serum IGF-1 in mid-gestation could be a useful marker for predicting fetal growth in late gestation.

ISP-34-5

Study on the association of CTG patterns, postnatal MRI findings, and types of Cerebral Palsy in a cohort with severe cerebral palsy Magawa Shoichi¹, Nakao Masahiro¹, Hasegawa Junichi², Toyokawa Satoshi³, Ichizuka Kiyotake⁴, Satoh Shoji⁵, Tamiya Nanako⁶, Nakai Akihito⁷, Fujimori Keiya⁸, Maeda Tsugio⁹, Iwashita Mitsutoshi¹⁰, Ikeda Tomoaki¹ *Mie University¹, St. Marianna University School of Medicine², Department of Nursing, Wayo Women's University³, Showa University Northern Yokohama Hospital⁴, Oita Prefectural Hospital⁵, Health Services Research Department, University of Tsukuba⁶, Nippon Medical School Tama Nagayama Hospital⁷, Fukushima Medical University⁸, Nishiyazu Frauenklinik⁹, Kugayama Hospital¹⁰*

[Objective] Cerebral palsy (CP) is defined as a permanent disorder of movement and posture, while there are many variations in the subtypes of CP, the causes and background information of those subtypes remain unknown. In this study, we used data from a cohort of severe CP cases to evaluate the association between subtypes of CP and maternal, neonatal background information. **[Methods]** We used the severe database of CP cases registered in The Japan Obstetric Compensation System for Cerebral Palsy, from 2009 to 2014. All CP cases were equivalent to levels three to five of the Gross Motor Function Classification System-Expanded and Revised. The 1069 cases with CTG data at delivery and postnatal MRI data and the subtype of CP were included. **[Results]** By subtypes of CP, 639 were Spastic, 55 were Hypotonic, 29 were Athetotic, and 346 were the others. The CTG patterns at delivery were similar between Spastic and Athetotic groups, while the Hypotonic group had a larger proportion of reasuring pattern during labor and delivery. In the postnatal MRI patterns, most of the Spastic and Athetotic groups showed a predominant damage in the basal ganglia-thalamus region, while a larger proportion of the Hypotonic group had normal or unclassified MRI patterns. **[Conclusion]** CTG patterns and MRI findings showed similar patterns between the Spastic and Athetotic groups, suggesting that pathogenesis between the two groups would be related. In contrast,

Hypotonic patterns showed both normal-like and severe hypoxic findings, suggesting there would be no single pathogenic mechanism.

ISP-34-6

Fetal growth restriction with Doppler abnormality predisposes postnatal intestinal disorder in preterm infants Ohtani Tomohiro, Ichinose Mari, Ariyoshi Yu, Toshimitsu Masatake, Sayama Seisuke, Seyama Takahiro, Kumasawa Keiichi, Iriyama Takayuki, Hirota Yasushi, Osuga Yutaka *The University of Tokyo*

[Objective] Intestinal disorders (ID) can be a severe burden for preterm infants after initial resuscitation, however existing reports are mostly about rare necrotizing enterocolitis (NEC) and are insufficient to elucidate the pathogenesis of ID. This study aimed to determine the obstetric risk factors for ID. **[Methods]** Singletons without congenital anomalies born between 22^{w0} and 28^{w6} weeks of gestation from January 2013 to December 2022 were investigated retrospectively. We compared the frequencies of the following obstetric factors between cases with ID (Group ID) and cases without ID (Group N). ID included meconium-related ileus (MRI), focal intestinal perforation (FIP), and NEC. The obstetric factors included maternal backgrounds, complications, fetal growth restriction (FGR : estimated body weight < -1.5 standard deviations), chorioamnionitis, Apgar score, and umbilical artery blood gas. **[Results]** Among 119 preterm cases, 22 cases (18.5%) had ID : including 14 MRI, 4 FIP, and 5 NEC, and 29 cases (24.4%) showed FGR. In comparison, FGR was the only factor which showed significant increase in Group ID than in Group N (9/22 40.9% vs 20/97 20.6% p=0.045 OR 2.67). Moreover, in FGR cases, Doppler abnormality was more common (7/9 77.8% vs 13/20 65.0%) and the median time from the onset of Doppler abnormality to delivery was longer in cases with ID (216 vs 60 hours). **[Conclusion]** Preterm FGR infants with prolonged exposure to Doppler abnormality are identified novelly at high-risk for ID. It implies chronic intrauterine environment may determine the postnatal vulnerability of the intestinal function.

ISP-34-7

A study of the characteristics of fetal cardiac output distribution to the placenta by birth weight and the effect of tocolysis Shimaoka Ryuichi, Ono Hitomi, Inuzuka Saki, Matsui Masako, Asai Kazuhiko, Iwagaki Shigenori, Takahashi Yuichiro *Gifu Prefectural General Medical Center*

[Objective] To clarify the characteristics of fetal cardiac output distribution to the placenta by birth weight and the effect of tocolysis **[Methods]** This single-center observational study included single fetuses without anomalies. The subjects were categorized into two groups based on their birth weight : appropriate-for-gestational-age (AGA) and small-for-gestational-age (SGA) groups. Additionally, each group was further divided based on the presence or absence of tocolysis during the ultrasound examination. Umbilical vein flow volume (UVFV) and combined cardiac output (CCO) were measured in all cases, defining the distribution as UVFV/CCO. A nomogram for distribution was established using fractional polynomial analysis, and the distribution was compared between groups using the Z-score. **[Results]** We analyzed a total of 268 patients, including 229 AGA and 39 SGA cases. The tocolysis group comprised 61 AGA and seven SGA cases. A nomogram was established from 168 AGA cases without tocolysis (AGA-control group). The Z-score of distribution was significantly higher in the AGA-tocolysis group than in the AGA-control group (0.47 ± 1.37, p=0.008). In contrast, the SGA group exhibited a significantly lower Z-score of distribution compared with the AGA-control

group (-0.88 ± 1.02, p<0.001). No significant difference was observed between the SGA-tocolysis and SGA-control groups (-1.03 ± 1.08 vs. -0.88 ± 1.02, p=0.742). **[Conclusion]** The distribution of cardiac output to the placenta was lower in the SGA group compared with that in the AGA group. Furthermore, tocolysis increased distribution in the AGA group but had no such effect in the SGA group.

ISP-35-1

Associations Between Short-term and Long-term Changes in BMI and Menstrual Cycle Characteristics Itoi Shiori^{1,2}, Sampei Makiko², Tatsumi Takayuki³, Izumi Gentaro¹, Osuga Yutaka¹, Koga Kaori^{1,4}, Morisaki Naho⁵ *The University of Tokyo¹, Department of Nursing and Social Epidemiology, Nippon Sport Science University², National Center for Child Health and Development³, Chiba University⁴, Department of Social Medicine, National Center for Child Health and Development⁵*

[Objective] To evaluate the association between short- and long-term changes in body mass index (BMI) and menstrual cycle characteristics using data retrieved from a smartphone app. **[Methods]** We analyzed data from 7,959 app users. Menstrual cycle characteristics (average of cycle length (CL) and standard deviation (SD) of CL) were retrieved. Changes in BMI were calculated based on the individual's reported height and weight at two points : for the short-term study, current reported weight at 2020/03-04 and 2020/05-06, and for the long-term study, recalled weight at age 18 and current reported weight. The association between changes in BMI and menstrual cycle characteristics was analyzed. **[Results]** In the short-term study, among women with BMI ≥ 23 in 2020/03-04, compared with those that had no changes in BMI, those with a decrease in BMI had a significant decrease in average CL [-0.68 (95%CI, -1.13-0.03)] and a decrease in SD of CL [-0.33 (95%CI, -0.66-0.01)]. In the long-term study, among women with BMI ≥ 23 at age 18, compared with those that had no changes in BMI, those with an increase in BMI had significantly higher average CL [1.15 (95%CI, 0.70-2.31)] and SD of CL [0.42 (95%CI, 0.18-0.66)]. In both studies, no significant association was observed for the underweight women. **[Conclusion]** Using a large dataset, we observed that for overweight/obese women, a short-term decrease in BMI leads to shorter cycles with less fluctuation, and a long-term increase in BMI leads to longer cycles with more fluctuation.

ISP-35-2

Successful Pull-through Vaginoplasty For Distal Vaginal Agenesis : A Case Report Cordova Mohanna M *Veterans Memorial Medical Center, Philippines*

Distal vaginal agenesis is a rare malformation of the vagina, resulting in genital outflow tract obstruction. Thorough history taking and physical examination, supplemented by diagnostic imaging are essential to arriving at an accurate diagnosis and appropriate management plan. We are presented with an amenorrheic, 13-year old patient who complained of pelvic pain. Perineal inspection revealed a pink dimple at the area of the introitus, with an intact hymenal fringe, and no vaginal opening. Magnetic Resonance Imaging (MRI) of the genitourinary tract and transrectal with transperineal ultrasound showed presence of hematometra and hematocolpos, consistent with distal vaginal agenesis. She underwent Pull-through vaginoplasty, excision of vaginal septum, with evacuation of hematocolpometa. An innovative vaginal stent, using a 10mL syringe barrel, pierced with holes was left in-situ to keep the vagina patent, while allowing drainage of blood. The patient tolerated the procedure well and was able to achieve regular menstrual flow following surgery.

ISP-35-3

Inferility and Associated abdominal Tuberculosis—A major cause in the developing country Gupta Bajrang L¹, Nigam Parul², Chaube Sanjay¹, Chaube Jyoti³ *Division of Minimally Invasive Surgery, St. Jude's Hospital, India¹, St. Jude's Hospital, India², Radiodiagnosis, St. Jude's Hospital, India³*

[Objective] As tuberculosis is a common disease in our part of country. Biochemical and imaging investigations are inconclusive to rule out abdominal tuberculosis. **[Methods]** Diagnostic laparoscopy, Hysteroscopy and methylene blue dye instillation was performed in 82 cases of infertility over a period of five years in our hospital to evaluate the cause of infertility in whom other imaging tests were normal. **[Results]** In Sixty two patients findings were suggestive of abdominal tuberculosis in form of adhesions, turbid colour fluid in the pelvis, and tubercles. Inten case endometriosis was present with small chocolate cyst and endometriotic deposits with adhesions in the POD. Tubal block was present in sixty six cases as there was no flow of M.blue when instilled P/V. **[Conclusion]** Abdominal Tuberculosis is a major cause of infertility in developing country in comparison to the developed countries where endometriosis is a major cause.

ISP-35-4

Exploring Uterus by Sonosalpingography : An Underutilized Diagnostic Modality Rizvi Suboohi *Mothers Clinic and Ultrasound Centre and FOGSI, India*

INTRODUCTION : Sonosalpingography (SSG) used to evaluate patency of fallopian tubes can also evaluate uterine cavity well. Selected patient taken up for hysteroscopic confirmation. **AIM :** Over the years with the onset of new modalities of investigations sonosalpingography is not used very often as a diagnostic modality in cases of subfertility. Here we present some cases which had come to our Mother's Clinic and Ultrasound Centre in whom sonosalpingography was done and was helpful in establishing a diagnosis. Also how after sonosalpingography a women of long standing subfertility could conceive in the same cycle. **METHOD :** Patients were given oral analgesics before the procedure done on the 6th day of menstrual cycle. The patient put in lithotomy position and number 8 Foley's catheter introduced in the uterine cavity. The Foleys balloon inflated by saline. The end of the foleys secured by artery forcep and 5-10cc normal saline pushed at a time upto 100cc. The flow through both the tubes seen and the uterine cavity visualized by ultrasound. Video clips taken during and also deflating balloon. Hysteroscopy in cases of positive finding helped in confirming the diagnosis and treatment. **CONCLUSION :** Sonosalpingography is a cost effective diagnostic test in patients of subfertility to see the patency of the uterine tube also and to visualize the uterine cavity well. A thickened endometrium on Ultrasound may actually be having polyps. Hysteroscopic confirmation of diagnosis and treatment done in selected cases. Sonosalpingography seems to help patients to conceive even if there is no apparent pathology in the uterus or tubes.

ISP-35-5

VAGINAL SYNECHIAE PRESENTING AS PRIMARY INFERTILITY : A CASE REPORT Asio Kimberly April M, Elauria-Manalastas Jean Aileen *Angeles University Foundation Medical Center, Philippines*

Problem statement : This is a case of a 29-year-old nulligravida who presented with primary infertility, complaints of intermenstrual spotting and dyspareunia. On transvaginal ultrasound, a hypoechoic band with a small opening was noted at the lower third of the vagina 1.3 cm away from the hymenal ring. This hypoechoic band was considered a vaginal synechia probably sec-

ondary to genital tract injury accrued from a vehicular accident. **Methods :** Ultrasound-guided lysis of the vaginal synechia was done to restore normal anatomy and postoperative insertion of vaginal dilators to prevent recurrence of synechia and maintain the caliber of the vagina. **Results :** Postoperatively, the patient was able to resume sexual activities with no complaints and had regular menses. She has then conceived ten months after the procedure. **Conclusion :** This case highlights the importance of careful evaluation of all primary infertile young couples, because an undocumented acquired, rare and asymptomatic reproductive tract defect could underlie the infertility necessitating surgical intervention.

ISP-35-6

Transcatheter arterial embolization for postpartum hemorrhage : a nationwide observational study Kamijo Kyosuke^{1,2}, Shigemi Daisuke³ *Nagano Municipal Hospital¹, Nagano Prefectural Shinshu Medical Center², Department of Clinical Epidemiology and Health Economics, School of Public Health, The University of Tokyo³*

[Objective] Transcatheter arterial embolization (TAE) is used for postpartum hemorrhage (PPH), a leading cause of maternal death globally. While TAE also preserves fertility in patients with PPH, its utility in obstetric settings remains unclear. The present study aimed to elucidate the demographics, clinical characteristics, and outcomes of patients with PPH who underwent TAE. **[Methods]** We conducted a retrospective observational study using the Japanese Diagnosis Procedure Combination inpatient database between April 2012 to March 2020. We identified the patients with PPH who underwent TAE and examined the patients' characteristics, interventions administered, and outcomes. **[Results]** We identified 2,705 patients with PPH who underwent TAE. The most common cause of PPH was uterine atony (68.7%), followed by disseminated intravascular coagulation (30.0%) and placenta accrete spectrum disorders (23.4%). Among patients who delivered at hospitals in which TAE was performed (n=1,212), 56.1% delivered via cesarean section. The proportion of patients who underwent a hysterectomy and repeat TAE was 7.0% and 2.4%, respectively. Among hysterectomies, 13.8% had the procedure performed before TAE, 38.8% underwent hysterectomy on the same day as TAE, and 47.4% had the procedure conducted after TAE. Of those who received a hysterectomy following TAE, 37.1% had the operation performed more or one week after the TAE procedure. Overall in-hospital mortality was 0.5%. **[Conclusion]** Despite the initial success in achieving hemostasis via TAE, vigilant patient monitoring remains imperative. These results could be helpful in clinical decision-making and providing patients with PPH additional treatment options to preserve the patient's fertility.

ISP-35-7

Effect of repeated pregnancies on lumbar and femoral bone mineral density in Japanese women Kurabayashi Takumi, Omomo Toshiyuki, Kitagami Haruka, Takahashi Kana, Shono Yuriko, Sugino Kentaro, Kamimura Naomi, Morikawa Kyoko, Tsuneki Ikunosuke, Tamura Masaki, Yanase Toru *Niigata City General Hospital*

[Objective] To determine the effect of repeated pregnancies on bone mineral density (BMD) of lumbar and femoral bone in parous women. **[Methods]** The BMD of the lumbar spine (LS) (L2-L4), femoral neck (FN), and total hip (TH) was measured using dual-energy X-ray absorptiometry in 1,547 healthy women. These measurements were performed within 2 to 30 days after delivery at our hospital between May 2010 and August 2023. In this longitudinal study, 145 women (mean age :

31.9±3.8 years at the first scan, 35.2±3.7 years at the second scan) had BMD measurements after their next delivery. We analyzed the change in BMD (Δ BMD%) between the first and second scans. The study was approved by the institutional review board of our hospital (No. 10-004). **[Results]** The mean BMD of the LS and TH after the next delivery was not significantly different from that after the initial delivery (LS : 0.968 ± 0.109 vs. 0.970 ± 0.108 g/cm², +0.2%, $p = 0.53$; TH : 0.822 ± 0.096 vs. 0.829 ± 0.099 g/cm², +0.9%, $p = 0.072$). However, the mean BMD of the FN after the next delivery was significantly lower than that after the initial delivery (0.716 ± 0.099 vs. 0.699 ± 0.091 g/cm², -2.4%, $p < 0.0001$). Age (old : ≥ 36 , young : < 36 years) and BMI (obesity, normal, and lean) at the first and second scans, and the length between the first and second scan did not effect Δ BMD% of the LS, FN, or TH. **[Conclusion]** Repeated pregnancies may reduce puerperal BMD of the FN, although they do not reduce BMD of the LS or TH.

ISP-35-8

Clinical characterization and long-term outcomes of HRT discontinuation Takahata Mioko¹, Yokota Megumi¹, Hiramatsu Makiko^{1,4}, Niki Akiko¹, Shiina Miki¹, Ohno Ayumi¹, Tanimoto Satoko^{1,3}, Nishio Hiroshi¹, Iwata Takashi¹, Deshimaru Ryota^{1,2}, Yamagami Wataru¹, Tanaka Mamoru¹ *Keio University¹, Tokyo Saiseikai Central Hospital², Shizuoka city Shimizu Hospital³, Japanese Red Cross Shizuoka Hospital⁴*

[Objective] Hormone replacement therapy (HRT) is used to relieve menopausal symptoms, but the criteria for termination of HRT is undetermined. The aim of this study was to determine the clinical characteristics and long-term outcomes of HRT discontinuation. **[Methods]** Fifty-three patients who underwent HRT at our hospital and completed HRT between January 2004 and September 2023 were retrospectively assessed. Reasons for HRT discontinuation, clinical symptoms, changes in bone mineral density (BMD) and low-density lipoprotein cholesterol (LDL-C) levels were evaluated. **[Results]** The mean duration of HRT was 4.9 ± 0.9 years. Reasons for discontinuation were disappearance of menopausal symptoms in 24 patients (45.3%), adverse events in 24 patients (45.3%, including 9 abnormal breast findings), and long-term administration in 3 patients (5.7%). 26 patients (49.0%) received alternative prescriptions after discontinuing HRT. 17 cases (32.0%) received Chinese herbal medicine. The mean observation periods for BMD and LDL-C after completion of HRT were 2.3 ± 1.7 and 2.7 ± 3.7 years, respectively, and there were neither significant changes in BMD nor in LDL-C during the observation period. **[Conclusion]** Approximately half of patients required alternative treatments for residual symptoms after discontinuation of HRT. No changes in lipid levels or bone mass were observed, suggesting that the protective effect of HRT may be maintained for several years after discontinuation.

ISP-35-9

Low-Level Laser Therapy in Alleviating Genitourinary Symptoms of Menopause and Stress Urinary Incontinence Wu Pei-Chi^{1,2}, Kuo Yih-Shing², Chen Chi-Hau¹, Lin Ho-Hsiung^{1,3} *National Taiwan University Hospital, Taiwan¹, National Taiwan University Hospital BeiHu Branch, Taiwan², Far Eastern Memorial Hospital, Taiwan³*

[Objective] Low-level laser therapy (LLLT) has been applied to improve wound healing and pain management. However, no data exist on its gynecological applications. We aimed to evaluate the effectiveness of LLLT in mitigating genitourinary symptoms of menopause (GSM) and stress urinary incontinence (SUI). **[Methods]** Between September 2022 and August 2023, we conducted a retrospective study involving women seeking treat-

ment for GSM and SUI at our clinic who received LLLT. Participants were categorized into GSM and SUI groups. We assessed the objective vaginal health index (VHI) and recorded subjective symptoms by questionnaires before and after the treatment course. **[Results]** A total of 41 women were included, with complete data available for 31 participants. Significant improvements were observed in all VHI domains, as well as in the total scores of questionnaires assessing lower urinary tract symptoms (LUTS) (ICIQ, UDI-6, IIQ-7, USS, and OABSS) in both groups. The GSM group exhibited substantial improvements in sexual function, including lubrication, pain, and total score, but not in the SUI group. Additionally, most domains in King's Health Questionnaire related to LUTS-affected life quality in the SUI group showed significant improvement. **[Conclusion]** This study represents the first attempt in the world to evaluate the effectiveness of LLLT in alleviating GSM and SUI. LLLT, being a cost-effective, non-invasive, and comfortable treatment, holds promise as a potential therapeutic option for managing GSM during menopause. Our pilot study yielded promising results, and ongoing prospective research aims to further explore its safety and efficacy for women experiencing GSM during menopause.

ISP-35-10

Perioperative complications and long-term outcomes of laparoscopic pectopexy for pelvic organ prolapse Nasu Hiroki, Shimoto Sayaka, Obata Mika, Shigekawa Kimiya, Murakami Fumihiro *Omuta City Hospital*

[Objective] In addition to laparoscopic sacrocolpopexy, laparoscopic pectopexy (LP) is emerging as a novel alternative treatment for pelvic organ prolapse (POP). The descended cervix or vaginal vault is suspended with a mesh by fixing the bilateral iliopectineal ligaments. We aimed to investigate the long-term effectiveness and safety of this procedure. **[Methods]** From October 2017 to July 2023, 76 patients who underwent LP diagnosed with POP in our department were included in the study. Patient characteristics such as age, POP-Quantification (POP-Q) stage, body mass index (BMI), and operative findings were collected and analyzed. Patient symptoms were assessed preoperatively using the International Consultation on Incontinence Questionnaire-Vaginal Symptoms (ICIQ-VS). Perioperative complications were specified using five grades of severity in accordance with the general rules of the Clavien-Dindo classification. Follow-up visits every three to six months assessed long-term effectiveness using the ICIQ-VS. **[Results]** Out of 76 patients with POP, 16 (21.1%), 41 (52.6%), and 20 (26.3%) were diagnosed with POP-Q II, III, and IV stages, respectively. The median age, BMI, and ICIQ-VS score were 71 years (range 36-92 years) and 22.8 kg/m² (range 17.4-35.3 kg/m²), 22.5 (range 4-52), respectively. Severe perioperative complications included bladder injury, iliac vein injury, and mesh-associated abscess, which comprises Clavien grade IIIb. During a median follow-up of 19 months, 13 (17.1%) patients had POP recurrence, 5 (6.6%) of which were cystocele and 8 (10.5%) of which were de novo rectocele. **[Conclusion]** LP presents a promising novel treatment for POP with long-term effectiveness, although rectocele and vein injury should be noted.

ISP-35-11

Prospective comparison of laparoscopic pectopexy and sacropexy with vaginal native tissue repair in treating pelvic organ prolapse in Taiwan Sheen Jiun-Yi¹, Wu Chin-Jui², Huang Kuan-Ju³, Li Ying-Xuan², Chang Wen-Chun¹, Wei Ling-Hung¹, Sheu Bor-Ching¹ *National Taiwan University Hospital, Taiwan¹, National Taiwan University Hospital, Hsinchu branch, Taiwan², National Taiwan University Hospital, Yunlin branch, Taiwan³*

[Objective] To compare the one-year outcome of laparoscopic pectopexy with sacropexy in treating pelvic organ prolapse (POP) **[Methods]** From May 2019 to July 2023, we prospectively enrolled 122 women who visited a regional hospital for POP stage II or higher and underwent laparoscopic pectopexy or sacropexy (IRB : 110-028-E). **[Results]** Eighty of 122 women were included in this study. Thirty-nine patients received laparoscopic pectopexy, and 41 patients received sacropexy. Patients receiving pectopexy (n=39) were significantly older (70.1 vs. 62.2, $p < 0.001$) and had higher parity (3.38 vs. 2.80, $p = 0.022$). The preoperative POP-Q stage and nine parameters were similar in both groups. Patients receiving pectopexy had significantly lower Aa, Ba, and Ap at postoperative three months compared with sacropexy (n=41). The operation time of pectopexy was markedly lower than sacropexy (146 vs. 170 min, $p=0.01$). In addition, the intraoperative blood loss was lower in the pectopexy group (27.69 vs. 57.56 ml, $p=0.048$). The complications of both pectopexy and sacropexy were few. The Kaplan-Meier analysis showed no significant recurrence rate in both groups in a mean follow-up of 12 months. **[Conclusion]** The pectopexy and sacropexy had similar successful rates in treating POP stage II or higher. The operation time and blood loss were favored in the pectopexy group. However, patients receiving pectopexy had significantly lower Aa, Ba, and Ap at postoperative three months compared with sacropexy. Further studies are required to clarify the difference.

ISP-35-12

A Randomized Controlled Trial : Preoperative Intra-Incisional Infiltration of Antibiotic at Pfannenstiel Site Versus Intravenous Prophylactic Antibiotic for Prevention of Surgical Wound Infection Khalil Arfa, Tabasum Shubana, Mushtaq Sumera, Rauf Sidra *Pakistan Institute of Medical Sciences, Pakistan*

[Objective] To check effectiveness of pre-operative intra-incisional antibiotic in comparison to prophylactic intravenous antibiotic use and also their effectiveness when combined at same antibiotic dose. **[Methods]** This study included 300 patients. Patients were allocated to equal 3 groups by computerized random number generator tool making 100 patients in each group. Group A received 1 gram of preoperative intravenous antibiotic, Group B received 1 gram of intra-incisional antibiotic preoperatively and Group C received 500mg intravenous antibiotic and 500mg intra-incisionally preoperatively. Wound site was examined post operatively. Data was recorded and entered in SPSS and analyzed. **[Results]** In our study among 300 patients surgical site infection was highest in Group A 13%, and lowest in Group B 6% while it was 10% in Group C on day 8 post surgery which proves our hypothesis to be correct and result findings are statistically significant. Age of patients ranged from 20-40 years while most of the patients were in between 26-30 years. Factors like old age, increased BMI, poor nutritional status, increased duration of surgery and late mobilization were associated with the high rate of surgical site infection in all study groups and no correlation was found between patient education, parity and timing of NPO break with SSI. **[Conclusion]** Pre Operative intra-incisional infiltration of antibiotic at pfannenstiel site has better efficacy in reducing SSI as compared to combined and intravenous group with same dose of antibiotic.

ISP-35-13

A review of 26 cases in which the MRI jelly method was performed and led to the diagnosis of colorectal endometriosis Takeuchi Shiori, Kitade Mari, Yanagihara Yasuho, Kobayashi Mutsumi, Ochiai Asako, Kawasaki Yu, Murakami Keisuke, Okada Yukiko, Kawamura Kazuhiro, Itakura Atsuo *Juntendo*

University

[Objective] The MRI jelly method is developed in our department as a diagnostic method for deep infiltrating endometriosis. This method is useful not only for the diagnosis of the degree of obstruction and nodules of the Douglas fossa, but also for the diagnosis of colorectal endometriosis (CRE). In this presentation, the effectiveness of the MRI jelly method for CRE was evaluated. **[Methods]** Patients with CRE who underwent MRI jelly method from January 2018 to December 2021 at our hospital were included. Patient background, characteristic MRI jelly findings and CRE outcomes were reviewed retrospectively. **[Results]** A total of 113 cases underwent the MRI jelly method during, of whom 26 (23%) had CRE. The mean age of the patients was 41.1 (23-48) years and 15 (55.2%) were heifers. The main complaints were gastrointestinal symptoms such as bloody stools and defaecation pain during menstruation in 16 cases (41%). MRI jelly findings showed nodule in 6 cases (22.2%) and the cord-like structures in 17 cases (62.9%). 21 cases (91.3%) of the lesions were in the Rs-Ra region. Only one patient was performed sigmoid colon resection, and 17 patients were well treated with hormonal therapy, except for five patients who wished to have a baby and whose symptoms improved after delivery. **[Conclusion]** The MRI jelly method is a minimally invasive technique that can diagnose CRE down to the site and morphology of the lesion and the presence of Douglas fossa obstruction. Thus it was considered useful for determining treatment strategy and preoperative diagnosis.

ISP-35-14

Spontaneous Bilateral Fallopian Tube Ectopic Pregnancy : A Case Report Manuel Marie Eleonor B, Faustino Karen M *Amang Rodriguez Memorial Medical Center, Philippines*

Bilateral tubal pregnancy (BTP) is estimated to occur at a rate of 1 : 200,000 pregnancies. It is the rarest form of extrauterine pregnancy in the absence of assisted reproductive techniques. A 25-year-old, G1P0, was admitted for hypogastric pain with vaginal spotting which started 19 days prior to consult. Transvaginal scan showed an impression of a bilateral adnexal mass, to consider bilateral tubal pregnancy. On admission, she had stable vital signs, hypogastric tenderness, cervical motion tenderness and bilateral adnexal motion tenderness. Pregnancy test was positive. She underwent emergency exploratory laparotomy with right salpingostomy and left salpingectomy. Intraoperatively, noted approximately 200 cc hemoperitoneum. The right fallopian tube, ampullary area, was dilated measuring approximately 4 x 3 cm with a 1 cm non-bleeding rupture site at the antimesenteric area. The left fallopian tube, ampullary area, was dilated measuring 5 x 3 cm with an actively bleeding 0.5 cm rupture at the antimesenteric area. Fallopian tubes had adhesions to the uterine fundus. Histopathology confirmed the final diagnosis of tubal pregnancy. It is difficult to pre-operatively diagnose BTP. Signs and symptoms are the same for unilateral and bilateral kind. The pre-admission ultrasound done in this case helped in the surgical management of the patient. Due to its rarity, guidelines for treatment of BTP is currently unavailable. In spontaneous BTP, salpingostomy is usually done if the fallopian tube looks benign. Salpingostomy is preferred over salpingectomy to preserve fertility. Proper inspection of both tubes intraoperatively is imperative to not miss the diagnosis of bilateral tubal pregnancy.

HS-1-1 更年期世代の日本人女性における血管運動神経症状が健康関連 QOL および労働生産性に及ぼす影響：横断的オンライン調査

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【目的】更年期世代の日本人女性における血管運動神経症状 (VMS) が健康関連 QOL と労働生産性に及ぼす影響を評価する。
【方法】1年以内に VMS を経験した 40~64 歳の女性を対象に, VMS が健康関連 QOL および労働生産性に及ぼす影響を, 更年期障害特有の QOL に関する質問票 (MENQOL), 睡眠障害/睡眠関連障害に関する質問票 (PROMIS SD SF8b/SI SF8a), 労働生産性および活動障害に関する質問票 (WPAI) を用いて横断的にオンライン調査した。VMS の重症度は, FDA 臨床評価ガイドラインに準拠し, 軽度:ホットフラッシュ (HF) はあるが汗は出ない, 中等度:汗を伴う HF はあるが日常生活は続けることができる, 重度:汗を伴う HF があり日常生活に支障をきたす, と定義した。【成績】調査対象者は, 1年以内の月経周期が不規則であった周閉経期女性 750 人 (平均年齢 49.5 歳), 1年以上無月経の閉経後女性 1438 人 (平均年齢 55.4 歳) の合計 2188 人であった。VMS 重症度別の割合は, 周閉経期女性で軽度 32.3%, 中等度 60.5%, 重度 7.2%, 閉経後女性で軽度 24.7%, 中等度 69.4%, 重度 5.9% であった。調査対象者において MENQOL の 4 つの尺度 (血管運動, 精神心理, 身体および性的機能) は, VMS 重症度が高くなると血管運動のみならず, 他の尺度に関する QOL も低くなる傾向にあった。調査対象者において睡眠障害が認められ, 睡眠関連障害の評価では VMS 重症度間で有意差が認められた。VMS の労働生産性への影響は, 欠勤より業務効率の低下による損失割合が高く, VMS 重症度が高くなることで労働生産性への影響も大きくなった。【結論】更年期世代の日本人女性において, VMS が健康関連 QOL と労働生産性に影響を及ぼすことが示された。

HS-1-2 血管運動神経症状 (ホットフラッシュ) を有する女性を対象とした fezolinetant 国内第 2 相試験結果: 副次および探索的有効性評価項目を中心とした報告

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【目的】閉経に伴う血管運動神経症状 (ホットフラッシュ [HF]) を有する 40~65 歳の日本人女性を対象に, 国内第 2 相ランダム化二重盲検プラセボ対照並行群間多施設共同試験を実施し, 選択的ニューロキニン 3 受容体拮抗薬である fezolinetant (以下, 本剤) の有効性, 安全性および忍容性を評価する。【方法】投与群は本剤 15mg, 30mg およびプラセボ群とし, それぞれ 1 日 1 回 12 週間投与した。有効性の副次評価項目は投与後 12 週までの HF 回数, 探索的評価項目は投与後 12 週までの HF 重症度, HF 回数が 50% 以上減少した被験者割合, 睡眠障害評価 (患者報告アウトカムである PROMIS SD SF8b), 健康関連 QOL (更年期障害関連 QOL 質問票である MENQOL) 等を設定した。【成績】計 147 例が本剤 15mg (53 例), 30mg (47 例) またはプラセボ群 (47 例) に割り付けられた。主要評価項目である投与後 8 週までの HF 回数は, プラセボ群と比較して本剤両投与群で有意に減少し, 安全性と忍容性プロファイルは先行した欧米での臨床試験の傾向と一致していた。副次評価項目の投与後 12 週までの HF 回数は, 1 週時にプラセボ群と比較して本剤投与群で有意に減少し, その後も減少が維持し, 12 週時でも有意な減少が認められた。探索的評価項目の HF 重症度は, 評価期間を通して本剤投与群でプラセボ群より高い改善傾向が認められた。HF 回数が 50% 以上減少した被験者割合は, 評価期間を通して本剤投与群でプラセボ群より有意に多かった。PROMIS SD SF8b および MENQOL の総スコアは, 12 週時に本剤投与群でプラセボ群より高い改善傾向が認められた。【結論】国内第 2 相試験において本剤の有効性, 安全性および忍容性を支持する結果が得られた。

HS-1-3 経膣 2D プローブによる骨盤底のスクリーニング評価—婦人科一般診療や健診において経会陰 US を活用するために—

三井記念病院

中田真木, 荷見よう子, 齊藤亜子, 小池 洋, 山本愛乃, 林 紘太, 上島千春

【目的】2 次元経会陰超音波画像 (2D-TPUS) による骨盤底支持の評価は, 目視よりも客観性が高く POP-Q よりも簡便である。ウロギネコロジー診療では主に 2D-TPUS に経膣プローブを用いるが, 経膣プローブを使用できる場面は限られている。婦人科一般診療や健診の場でも 2D-TPUS を活用するために, 経膣プローブによる 2D-TPUS を経膣プローブの場合と比較し, 後者による標準値を求めることを目指した。【方法】がん検診を希望する受診者のうち, 本研究への参加を承諾した人に経膣/経膣プローブによる 2D-TPUS を行い, 安静状態で恥骨結合, 膀胱頸部, 膀胱頸部, 直腸肛門角の 3 つの目印地点を含む骨盤出口の矢状断面像を画像ファイルに保存した (期間は 2022 年 11 月-2023 年 7 月)。3 点間の距離から肛門拳筋裂孔の前後径 (APDH) と拳筋裂孔から膀胱頸部までの距離 (BNH) を算出し, 年齢, ボディマス指数 (BMI), 経膣分娩回数との数量的関連を調べた。【成績】膣口を超える骨盤臓器脱がなければ, 経膣プローブで目印地点を含む矢状断面を描出できた。対象となった 327 例は, 年齢 23-88 歳, BMI 14.4-32.2kg/m², 経膣分娩回数 0-4 回だった。APDH と BNH の計測値は, それぞれ 4.76 ± 0.62cm と 2.21 ± 0.44cm (平均 ± SD) に分布し, 2 つの計測値には負の相関があった。APDH と BNH は経膣分娩回数や BMI と相関があり, 未産群においても BMI と APDH には弱い正の相関が認められた (cor=0.349)。【結論】経膣プローブによる 2D-TPUS は多くの受診者に実行可能である。この手法は, 膣や外陰部の違和感を自覚しているが有意な骨盤臓器脱とは見られない症例における除外診断や, 初期の骨盤臓器脱の経過観察などに真価を発揮することが期待される。

HS-1-4 医療上の事故等の発生防止のために産婦人科専攻医が修得すべき、知識・技術は何か～医療事故情報収集等事業のデータを用いて～

医科歯科大¹、獨協医大²
坂本里紗¹、鳥羽三佳代¹、尾林 聡²、宮坂尚幸¹

【目的】医療上の事故等の発生を防止するために、産婦人科専攻医が習得すべき知識・技術は何かを検討する。【方法】2010年1月から2021年12月までに、医療事故情報収集等事業に報告された事例のうち、当事者が医師歴2年以上の産婦人科医師であった1,089例を対象とした。医師歴2～4年の専攻医(117例)と5年以上の医師(972例)における、事故概要や発生要因の構成比の違い、および、知識・教育不足、未熟な技術が要因とされた事例の詳細を分析した。【成績】事故事例のうち、薬剤、処置のエラーに関する割合は、専攻医群で有意に多かった(13.7%vs.8.0%, 8.5%vs.3.7%, $p < 0.05$)。また事故の要因について、未熟な技術や知識・教育不足と評価された事例の割合は専攻医群が多かった(29.9%vs.22.2%, 17.1%vs.9.7%, 20.5%vs.11.6%)。そして専攻医における技術未熟や知識・教育不足のいずれかが要因と評価された54例(手術・処置の手技に関する事例25例、添付文書や院内ルール確認不足によるエラー18例、診断管理上の間違いによる事例11例)のうち、最も多かったのは帝王切開術に伴う母体の臓器損傷であった。また、事故発生後の対応や患者・家族等への説明などが問題となった事例が20.3%、指導体制の不備が指摘された事例が50.0%を占めた。【結論】専攻医の事故の発生防止と医療安全の向上のためには、専門領域の知識・技術の習得に加えて医療安全管理に関する知識も求められる。さらに、専門領域の指導体制の整備と、卒後医療安全教育の包括的プラットフォームの開発が望まれる。

HS-2-1 sFlt-1/PlGF比による早発型妊娠高血圧腎症の重症化予測

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【目的】soluble fms-like tyrosine kinaseとplacental growth factor (PlGF)の比(sFlt-1/PlGF比)は妊娠高血圧腎症(Preeclampsia: PE)の発症予測に有用であることが広く知られているが、PE発症例の周産期有害事象の予測能に関する一般的な見解はない。そこで早発型PE発症例において、その後の周産期有害事象の発症予測に関するsFlt-1/PlGF比の有用性を検討する。【方法】2015年4月から2023年8月までに67例の早発型PEの妊婦に、合計82回、PE診断後にsFlt-1/PlGF比の測定を行った。同一個体から複数回計測した症例では、分娩日に最も近い日に計測したsFlt-1/PlGF比を解析に利用した。sFlt-1/PlGF比とその後の1週間以内の周産期有害事象発症に対する予測能についてROC曲線を用いて検討し、そのカットオフ値を算出した。またsFlt-1/PlGF比と測定後の妊娠継続期間との相関性についてログランク検定を行った。【成績】早発型PEと診断後に40例(59.7%)が1週間以内に周産期有害事象を発症した(以下重複あり。胎児心音異常:15例、子癇発作・意識障害:2例、常位胎盤早期剥離:2例、治療抵抗性高血圧:3例、母体心機能悪化:7例、HELLP症候群:11例、重症凝固障害:1例)。ROC解析から1週間以内の周産期有害事象発症に対するsFlt-1/PlGF比の予測カットオフ値は224.7でAUC:0.76、感度:80.0%、特異度:70.4%であった。またsFlt-1/PlGF比と測定後の妊娠継続期間には有意差を認めた(224.7未満群:15.5日 vs 224.7以上群:5.4日, p 値<0.001)。【結論】sFlt-1/PlGF比は早発型PE発症例における、その後の周産期有害事象の発症予測に関して有用と考えられる。

HS-2-2 細胞融合抑制タンパク: サプレシンの発現は低酸素誘導因子 HIF により調整される

広島大
杉本 潤、工藤美樹

【目的】胎盤特異的な発現が特徴であるサプレシンは、細胞融合を抑制することにより胎盤トロホプラスト形成に関わると考えられる。このサプレシンの胎盤特異的な発現は、酸素濃度に依存することがこれまでの解析から確認されていた。今回我々は、サプレシンの酸素濃度依存的な発現メカニズムの検証を行うため、低酸素ストレスに対する細胞の適応応答で中心的役割を果たす転写因子: 低酸素誘導因子 HIF に着目し、分子生物学的解析を行った。【方法】まず、転写因子 HIF の直接的関与を検証するため、サプレシン 5'LTR (プロモーター) 配列の HIF 結合配列 (-cacgt-) を欠損させた pGL3 ルシフェラーゼコンストラクトを作成し、ルシフェラーゼ活性を確認した。次に、低酸素誘導因子 HIF (HIF1, HIF2) は ARNT (HIF-1 β) とのヘテロダイマー形成により遺伝子発現を誘導することから、HIF1 α , HIF2 α , ARNT 単独または HIF/ARNT 複合体を強制発現させた細胞でサプレシンプロモーター活性への影響を検証した。【成績】5'LTR に存在する HIF 結合配列の欠如は、プロモーター活性を低下させた。このことから、HIF タンパクの結合がサプレシン遺伝子の発現に直接関与することが予想された。さらに、HIF タンパクの強制発現解析によるプロモーター活性への影響を検証した結果、特に HIF2 α がサプレシンの発現誘導に強く関わっていることが明らかとなった。【結論】正常な胎盤形成、妊娠の維持にはサプレシンが深く関与しており、低酸素環境下での HIF タンパクによるサプレシン発現制御機構は、胎盤の低酸素状態との関係が示唆される各種周産期疾患(妊娠高血圧腎症、胎児発育不全など)の発症原因解明に重要な洞察をもたらす可能性がある。

HS-2-3 脳性麻痺モデルマウスにおけるヒト臍帯血移植治療が及ぼす神経系再構築とミクログリアに対する影響

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【目的】脳性麻痺に対する有望な治療法として、自己臍帯血細胞移植を用いた再生医療が期待されている。本研究では脳性麻痺モデルマウスとして新生仔脳虚血再灌流障害モデルマウスを作製し、脳スライス培養法を用いてヒト臍帯血による神経系再構築とミクログリアに対する影響を評価した。【方法】生後9日齢NOD/SCIDマウスの右総頸動脈の血流を一時遮断し、8% O₂による低酸素負荷後に再灌流させ、新生仔脳虚血再灌流障害モデルマウスを作製した。モデル作製より3週間後、脳障害を認めたマウスの脳スライスを作製し、ヒト臍帯血細胞と共培養した。共培養から3日後にスライスを固定し免疫染色を行い、神経系再構築及びミクログリアを形態学的に評価した。また同時に培養上清を採取し、ビーズアレイ法による上清成分の解析を行った。【成績】マウス脳スライスと臍帯血細胞を共培養したところ、doublecortin陽性神経前駆細胞の神経突起伸長及びミクログリアの形態学的変化が認められた。培養上清成分の発現解析では、臍帯血細胞と共培養した上清において、特定のサイトカインやケモカインの発現が上昇していた。【結論】本研究では、モデルマウスの脳スライスと臍帯血細胞を共培養することにより、神経系再構築とミクログリアの形態学的変化が認められ、特定のサイトカイン、ケモカインの産生により脳の微小環境を変化させていることが明らかとなった。今後は、シナプス小胞タンパクの発現などを評価し、神経系再構築に有効な因子の同定を行う予定である。

高得21日(日)
演題

HS-2-4 循環器疾患をもつ女性に対するプレコンセプションケアの有用性

国立循環器病研究センター

松吉 光、神谷千津子、小永井奈緒、小川範子、小川紋奈、手向麻衣、澤田雅美、中西篤史、柿ヶ野藍子、岩永直子、金川武司、吉松 淳

【目的】近年、生殖可能年齢の女性に対する妊娠前の健康管理“プレコンセプションケア”の重要性が高まりつつある。特に、基礎疾患を持つ女性が、プレコンセプションカウンセリング(PC)を受け、妊娠出産のリスクを十分に理解したうえで意思決定するプロセスは重要である。循環器疾患合併妊娠は、重症例では母児の生命にかかわるハイリスク妊娠である。循環器疾患をもつ女性に対するPCの有用性について検討した。【方法】2013年3月から2023年7月に当院PC外来を受診した循環器疾患をもつ女性を対象に、基礎循環器疾患、妊娠リスク重症度(modified WHO分類)とカウンセリング後の転帰を後方視的に抽出した。また同期間に当院で診療した循環器疾患合併妊娠のうち、PC外来受診の有無と妊娠転帰の関連について比較検討した。【成績】PC外来受診総数は470人(内訳:チアノーゼ性心疾患:84人、非チアノーゼ性心疾患:57人、心筋症:97人、不整脈:71人、弁膜症:61人、大動脈疾患:51人、虚血性心疾患:21人、肺高血圧症:15人、分類不可:13人)で、年々増加傾向であった。中でもチアノーゼ性心疾患術後患者の割合が増加していた。妊娠転帰のうち、母体循環器疾患適応による妊娠人工中絶は、PC外来を受診した女性では実施が無く、非受診の女性では49例実施されていた。一方で分娩症例におけるPC外来受診率に年時変化は無かった。【結論】PCの実施は、予定外の妊娠や人工妊娠中絶を減らすうえで有用と考えられた。PC外来受診者数は年々増加しているが、循環器疾患合併妊娠数も増加しているため、分娩症例におけるPC外来受診率は不変であり、さらなる受診率の向上が望まれる。

HS-3-1 再発子宮頸部非扁平上皮癌患者に対するS-1/オキサリプラチン(SOX療法)の第II相試験(TGCU206 study)

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【目的】再発子宮頸部非扁平上皮癌は治療抵抗性であり予後不良である。東北婦人科腫瘍研究会(TGCU)では、再発子宮頸部非扁平上皮癌患者におけるS-1/オキサリプラチン(SOX)療法の臨床第II相試験を実施した。【方法】2013年1月から2023年3月までに15人の患者が登録された。S-1は80~120 mg/body/日の用量で14日間経口投与し、オキサリプラチンは1日目に100 mg/m²の用量で静脈内投与した。治療サイクルは21日を1サイクルとし、疾患の進行または重篤な有害事象が発生するまで繰り返し投与した。抗腫瘍効果、有害事象、無増悪生存期間(PFS)、および全生存期間(OS)を調査した。【成績】患者の年齢中央値は54(41-73)歳、PSは0が11人、1が4人であった。化学療法の既往レジメン数の中央値は2(1-5)であった。組織型は通常型腺癌12人、類内膜癌、明細胞癌、未分類がそれぞれ1人であった。全奏効率は33.3%、病勢制御率は60%であった。グレード3以上の血液毒性は、白血球減少症、好中球減少症、貧血、血小板減少症がそれぞれ21.4%、35.7%、42.8%、28.5%に発生し、非血液毒性は嘔気7.1%に認められた。PFSとOSの中央値は、それぞれ6(95%CI:2-11)か月、22(95%CI:11-23)か月であった。なお治療関連死は認めなかった。【結論】登録症例は少なかったものの、SOX療法は一定の抗腫瘍効果を有し、かつ重篤な有害事象の発生頻度は少なかったことから、再発子宮頸部非扁平上皮癌に有用であることが示唆された。

HS-3-2 子宮体癌におけるセンチネルリンパ節の術中迅速診断に基づくナビゲーション手術の前方視的研究

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山田竜太郎, 鈴木裕太郎, 箕輪 郁, 嶋田知紗, 山村満恵, 青山聖美, 見延進一郎, 加藤秀則

【目的】子宮体癌におけるセンチネルリンパ節 (SLN) に関するマッピング研究の成果が集積され, SLN の同定率等概ね一致した報告が出てきた。当院では体癌症例に対し SLN 生検を行い, 術中迅速診断の結果により系統的郭清の適用を決めるナビゲーション手術の前方視的研究を施設内倫理委員会の承認を得て行っており, 現在までの進捗状況を報告する。【方法】対象はリンパ節転移スコア (Am J Obstet Gynecol 2003, Gynecol Oncol 2007, Gynecol Oncol 2013) で 0 または 1 点と診断された子宮体癌患者。SLN の同定には Tc99m フチン酸-ガンマブロープ, インドシアニングリーン-Photo dynamic eye を用いた。【成績】臨床試験登録 178 例のうち, SLN 同定不可であった 5 例を除いた 173 例における lymph node status の最終診断は macrometastasis (腫瘍径 2mm 以上) が 9 例, micrometastasis (腫瘍径 200 μ m 以上 2mm 未満) が 4 例, 孤立性腫瘍細胞 (腫瘍径 200 μ m 未満) が 9 例, 腫瘍細胞なしが 151 例であった。リンパ節同定は両側成功 152 例, 片側成功 21 例, 失敗 5 例であった。術中診断は 16 例が陽性, 157 例が陰性で, TRLBC 法の感度は 100% (13/13), 特異度は 97% (157/160) であり, 偽陰性例はなかった。現在のところリンパ節再発はなく, 特記すべき合併症も発生していない。【結論】子宮体癌でリンパ節転移スコア 0 または 1 点の症例に対して, SLN の術中迅速診断に基づくナビゲーション手術は安全に実施できる可能性がある。

HS-3-3 子宮筋腫における MED12 遺伝子変異と Cyclin-dependent kinase 8 (CDK8) 活性の関連

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【目的】子宮筋腫における最も高頻度な遺伝子異常は MED12 遺伝子変異であるが, MED12 野生型筋腫は変異型よりも腫瘍径が大きい傾向があり, 変異の有無により増殖機序が異なると考えられる。MED12 は CDK8 と複合体を形成し, RNA ポリメラーゼ II のリン酸化に関与し転写制御を担うが, 子宮筋腫の増殖機序との関連は明らかでない。今回 CDK8 のリン酸化活性に着目し, MED12 変異と CDK8 活性との関連を検討した。【方法】子宮筋腫の手術検体 44 例を用いてサンガーシーケンス法で MED12 変異の有無を同定し, 術前の GnRH アナログ使用の有無 (-/+) と MED12 変異の有無 (WT/MUT) で 4 群に分類した。検体からタンパク質を抽出し, 抗 MED12 抗体を用いて CDK8 を共免疫沈降した。in vitro でリン酸化反応を引き起こし, リン酸化した基質をウェスタンブロット法で測定し, CDK8 活性として定量評価した。また CDK8 や MED12 などのタンパク質発現をウェスタンブロット法で評価し, mRNA 発現を qRT-PCR 法で評価した。【成績】GnRH アナログ不使用例のうち, MED12 WT は 11 例, MUT は 15 例であり, GnRH アナログ使用例では MED12 WT と MUT が 9 例ずつであった。CDK8 のタンパク質や mRNA 発現は群間に有意な差を認めなかったが, MED12 WT/GnRH (-) 群は WT/GnRH (+), MED12 MUT/GnRH (-) 群と比較して CDK8 活性が有意に高かった ($P = 0.008$, $P = 0.004$: Kruskal-Wallis test)。【結論】MED12 野生型筋腫は CDK8 活性が高く, また GnRH アナログを使用後は CDK8 活性が低下しており, CDK8 が子宮筋腫の細胞増殖に関わっていると考えられた。CDK8 活性を抑制することで子宮筋腫の増大をコントロールできる可能性がある。

HS-3-4 パクリタキセルの末梢神経障害に対する牛車腎気丸の投与の効果—東北婦人科腫瘍研究会多施設共同前方視的研究—

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【目的】パクリタキセル (PTX) は膜貫通型受容体の transient receptor potential (TRP) V4 を増加させ, 四肢の疼痛閾値を低下させること, 牛車腎気丸の予防投与は, PTX の TRPV4 増加を抑え疼痛閾値を保つことができることを動物実験から証明した。今回我々は, TC 療法における牛車腎気丸の予防投与の有効性を前方視的に比較検討した。【方法】卵巣癌術後に TC 療法を 6 コース行う予定の患者を Grade (G) 2 以上のしびれ発現後に牛車腎気丸を服用する群 (A 群) 26 例と TC 療法 1 週間前から牛車腎気丸を服用する (B 群) 27 例にランダム化し, 全コース中のしびれ G の最高値, VAS によるしびれの強さ, 鎮痛補助薬の使用, TC 療法完遂率, 6 か月後のしびれの残存などを前方視的に比較した (UMIN000021361)。PTX は 175~180mg/m², カルボプラチンは AUC 5~6 を 21 日毎に施行した。牛車腎気丸エキス顆粒[®]7.5g/日分 3 で用いた。【成績】しびれの G 分布は両群間で差がなかった。A 群では用量依存性に G2 のしびれの累積発生率が増加した。一方, B 群では TC 療法 1 コース目の 1 週間目に 27 例中 8 例 (29.6%) が G2 のしびれを発症したがその後鎮痛補助薬なしで 8 例全員が治療を完遂した。TC 療法 6 コース終了時の VAS 値は B 群で有意に低値であった ($P < 0.05$)。鎮痛補助薬使用頻度は A 群で 66.7%, B 群では 27.3% であった ($P < 0.05$)。治療終了 6 か月後のしびれの残存は A 群で 55.6%, B 群で 18.2% であった ($P < 0.05$)。B 群ではしびれによる薬剤減量頻度は少ない傾向にあり, 中止例はなかった (A 群では 2 例中止)。【結論】TC 療法における牛車腎気丸の予防投与の有効性が明らかとなった。牛車腎気丸は, PTX による末梢神経障害の不可逆性変化を回避している可能性が示唆された。

HS-3-5 婦人科手術のインフォームドコンセントに伴う動画説明の有用性

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【目的】本研究は、婦人科良性手術に伴うインフォームドコンセント（Informed Consent；以下IC）の際に動画を用いることで、口頭説明が動画に代替可能かを明らかにする。【方法】良性手術を受ける患者を対象に、口頭による手術説明の際に、疾患と手術について説明した動画の視聴を依頼し、案内を配布した。術直前と術後の2回に分けて半構成的質問紙表を配布し、「病状」「術式」「合併症」の説明に対する口頭説明の必要性および理解度に関して、自記式調査を行った。【成績】32名の回答者のうち30名（93.8%）が視聴し、うち9名（28.1%）は手術内容を共有したいという理由から家人も動画を視聴していた。半数以上で「術式」「合併症」に関して「動画と手術説明書のみで口頭説明不要」と回答し、術前・術後ともに変化しなかった。しかしながら、「病状」の点では、「口頭説明不要」とした患者は術前18人（60%）で、術後は12人（40%）と減少した。特に50歳未満19人の内、術前は14人（73.7%）が「口頭説明不要」で十分と回答したものの、術後は9人（47.4%）と顕著に減少していた。手術を経験することで「病状」に対する口頭説明への需要が増加した。口頭でのIC時間が30分以上の患者では「病状」の理解度が有意に高かった（ $p=0.044$ ）が、「術式」「合併症」の理解度は差を認めなかった。【結論】「病状」の説明に関して十分な口頭説明が必要と考える。その一方、「術式」「合併症」の説明は動画で代替できる可能性が示唆された。動画を併用することでIC時間の分配を最適化することが患者理解度の増加に重要と考える。

P-1-1 卵巣粘液性境界悪性腫瘍発症後3年以内に進行粘液性癌として再発した2例

京都大

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【目的】卵巣粘液性境界腫瘍 (MBT) は再発しても予後良好であるが、まれに浸潤性粘液癌として再発する症例があり、その致死性の予後が問題となる。【方法】多発性腹膜播種を伴う浸潤癌として再発した MBT の2例のゲノムシーケンスを含め検討を行った。【成績】【症例1】30歳、左卵巣多房性腫瘍に対し腹腔鏡下囊腫核出術が施行された。病理診断は上皮内癌を伴う MBT であった。術後3か月、左卵巣に多房性腫瘍が再発し、左付属器摘出術が行われた。2回目の手術から19か月後、右卵巣に多房性囊胞性病変と多発腹膜播種が出現し、腫瘍縮小術が行われ、卵巣粘液性癌3B期と診断された。包括的ゲノムプロファイリング (CGP) により、MBT と癌腫の両方で頻繁に認められる KRAS G12D 変異が明らかになった。また、TMB 3 Muts/Mb を示し、TP53 変異はなかった。患者は再々発後10か月で死亡した。【症例2】76歳、卵巣腫瘍自然破裂の診断で両側付属器切除術を施行、MBT1C2期と診断された。術後30か月に多発腹膜播種および多量腹水、皮膚転移が出現した。試験腹腔鏡を施行し、粘液性癌4B期と診断された。腫瘍サンプルは Ki67 陽性が高い以外は前回の MBT (TP53 野生型) と同じ染色パターンを示した。再発1か月後に死亡した。【結論】MBT は時に早期に浸潤癌として再発する。一部の境界悪性腫瘍は急速に浸潤癌に進行する可能性があり、MBT と浸潤癌を分けるゲノムプロファイリングが早急に望まれている。

P-1-2 癌性胸膜炎を契機に卵管癌の診断に至った一例

小樽市立病院

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咳嗽、胸水貯留を契機に診断された卵管癌の1例を経験したので報告する。患者は60歳、1妊1産。2か月前より持続する咳嗽を主訴に近医受診し、右胸水貯留を認めたため当院呼吸器内科に紹介となった。PET-CTによる全身の画像検索では胸膜肥厚部位のみに異常集積を認め、腹腔内に異常集積は認めなかった。胸腔鏡検査にて、胸腔内に播種と考えられる多発結節が認められた。生検にて腺癌を認め、免疫染色ではCK7陽性、CK20陰性、TTF-1陰性であった。またPAX8、WT-1陽性であったことから卵巣あるいは卵管高悪性度漿液性癌 (HGSC) の胸膜転移が疑われ当科紹介となり、審査腹腔鏡ならびに両側付属器切除を施行した。腹腔内に肉眼的病変は認められなかった。腹水細胞診はClass Vであった。病理組織診では卵管采に1.5mm大のHGSCを認めた。同部位の免疫染色は胸膜病変と同様のパターンを示していたため、卵管癌が原発と考えられ、卵管癌IVB期 (FIGO) と診断した。漿液性卵管上皮内癌 (Serous tubal intraepithelial carcinoma: STIC) は卵巣・卵管HGSCおよび腹膜癌の初期病変に相当すると考えられており、原発巣が微小でも転移先で大型の腫瘍を形成することが稀ではないとされている。また、横隔膜には気孔様構造があり腹腔内から胸腔内へのリンパ液流出を可能にするため、STICは腹腔内のみならず胸腔内へ播種病変を生じる可能性がある。本症例は全身画像検索にて婦人科臓器由来悪性腫瘍を含め、原発巣を示唆する所見は認められず胸膜病変を認めるのみであったが、同部位の病理組織検査にてHGSCの可能性が疑われ、卵管癌の診断に至ることができた。現在、TC療法を施行中である。

P-1-3 術後早期に再発し急激な経過を呈した卵巣 mitotically active cellular fibroma 症例の一例

神戸医療センター

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【緒言】卵巣 mitotically active cellular fibroma (MACF) は、卵巣線維芽細胞性腫瘍の中で、細胞密度が高く核分裂像も多くみられるが、核異型は軽度でその多くは予後良好とされている。我々は術後早期に再発し急激な経過を呈した卵巣 MACF 症例を経験したので報告する。【症例】症例は72歳で腹部膨満感を主訴に受診した。充実性卵巣腫瘍の診断で両側付属器摘出術および子宮全摘術を施行した。腫瘍重量は約7000グラム、表面平滑で皮膜破綻や周辺臓器との癒着は認められなかった。術後の病理学的検索では、大部分は線維腫であったが、一部で細胞密度の上昇や核分裂像の増加が見られ MACF と診断した。術後経過は順調であったが、術後3か月以降受診なく、術後14か月後腹部膨満感にて再診となった。画像診断で初回受診時とはほぼ同じサイズの腫瘤を認めた。試験開腹術を行ったが、右外腸骨静脈・尿管および回腸を巻き込み不完全切除となった。摘出重量は約6000グラムであった。術後の組織学的検討では大部分が MACF であったが核分裂像が著明に増加していた。その後全身状態が徐々に悪化し、2回目の手術後8か月目に死亡した。免疫組織学的検討では、初回手術時の MACF では5%程度であった Ki-67 index は、再発時標本では12-15%と著明に増加していた。さらに、p16陽性率は初回手術時の線維腫部分では陽性であったが、MACF部分ではその陽性率は低下し、再発時の標本では陰転化していた。【考察】MACFは晩期再発が報告されているが、本症例のように術後短期間で巨大腫瘤を形成した報告はない。本症例における再発機序は不明であるが、何らかの原因で残存した p16 抑制腫瘍細胞集団が急激に増殖し腫瘤を形成した可能性がある。

P-1-4 リスク低減卵管卵巣摘出術時に漿液性卵管上皮内癌が判明し、経過観察中に発症した腹膜癌が急速に進行した1例

聖路加国際病院

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【緒言】BRCA 病的バリエント保持者がリスク低減卵管卵巣摘出術 (risk reducing salpingo-oophorectomy : RRSO) を施行した際に0.4~11%の頻度で漿液性卵管上皮内癌 (Serous Tubal Intraepithelial Carcinoma : STIC) が判明し、その後13%程度に腹膜癌が発症すると言われているが、そのサーベイランスの方法は確立していない。今回、BRCA2 病的バリエント保持者のRRSO時にSTICが判明し、その後発症した腹膜癌が急速に進行した1例を経験したので報告する。【症例】74歳2妊2産。36歳時に左乳癌で乳房全摘術と術後ホルモン療法を行い、71歳時に右乳癌を診断されBRCA2 病的バリエントを保持していることが判明した。乳癌加療に合わせてRRSOを施行しSTICが判明した。PET-CTなどの精査で転移を疑う所見はなく追加治療は行わなかった。術後は1-3か月おきに経過観察を行った。術後2年10か月目(X日)にCA125の上昇があり造影MRI検査を行ったところ、子宮漿膜面に造影される部位を認めたが、病変部位ははっきりしなかった。その後もCA125の上昇があり、X日から3週間後にPET-CT検査をしたところ、S状結腸レベルの骨盤底にFDG集積を認めた。診断のため審査腹腔鏡検査を行う予定としたが、Dダイマーの上昇がありX日から6週間後にCT検査を施行したところ、大網や腹膜に軟部影が多発し、顕在化していた。X日の7週間後に審査腹腔鏡検査を行い、ダグラス窩から大網、右横隔膜下まで病変を認めた。病理組織は高異度漿液性癌の診断であった。【考察】STIC判明後の経過観察やサーベイランスの方法は確立されていない。血液検査や画像検査を行い、異常を認めた際には腹膜癌などが急速に進行している可能性を考慮する必要がある。

P-1-5 再発卵巣癌として治療中、小腸癌が発見され、同一KRAS遺伝子変異により小腸癌の転移性卵巣腫瘍と判明した1例

大阪赤十字病院

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【症例】55歳4妊2産。下腹部痛を主訴に当科を受診し、小児頭大の左卵巣腫瘍を認めた。腹式子宮全摘+両側付属器摘出+大網部分切除を施行し、病理所見では大部分が粘液性境界悪性腫瘍であったが2×5mm大の腺癌を認め、卵巣癌IC2期と診断した。TC療法を6コース施行し、化学療法終了3か月後のCT検査にて腹膜播種像を認め卵巣癌の再発と判断した。Foundation One[®] CDxによるがん遺伝子パネル検査を実施し、KRAS^{G12C}遺伝子変異を検出したが当時標準治療以外に提案できる治療薬はなかった。他院での治療を希望され腹腔内化学療法を施行中、敗血症性ショックの状態で当院に搬送され消化管穿孔が判明した。回腸部分切除を施行し、穿孔部に4×2.5cmの陥凹型腫瘍を認め原発性小腸癌と診断され、RAS・BRAF遺伝子変異解析の結果、KRAS^{G12C}遺伝子変異が判明した。転移性卵巣腫瘍は境界悪性腫瘍～腺癌と様々な形相を示しうること、また卵巣、小腸病変ともに同一KRAS遺伝子変異を有することから小腸癌の転移性卵巣腫瘍と考えられた。敗血症性ショックは改善したが痛性腹膜炎が進行し再発診断後5か月で原病死した。【考察】小腸癌は全消化管癌の0.1~1.0%と稀で、早期発見が難しく標準治療も確立されていない。卵巣粘液性癌は転移性腫瘍との鑑別が重要で、再検証により77%が転移性であったとの報告もある。本症例では初回手術時に小腸腫瘍を指摘できず、KRAS変異の検出が原発診断に寄与した。卵巣粘液性癌は術前、術中、術後にも転移性の可能性について十分に検証すべきであり、またがん遺伝子パネル検査は原発診断と治療選択に寄与する可能性があると考えられた。

P-1-6 非細菌性血栓性心内膜炎の治療方針についての検討～非細菌性血栓性心内膜炎を伴う進行卵巣癌の症例経験より～

福岡徳洲会病院

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【目的】非細菌性血栓性心内膜炎 (NBTE : nonbacterial thrombotic endocarditis) は消耗性疾患や易凝固状態に合併することが多い無菌性的心内膜炎であり、担癌患者に合併することが多い。治療は原疾患の治療と抗凝固療法であり、急性心不全をきたす症例や再発する塞栓症例などでは心臓手術を考慮するとガイドラインにはあるが、原疾患の治療が行われなければ再発率は非常に高い。今回、繰り返す多発脳梗塞を契機に僧帽弁に可動性のある疣贅及び進行卵巣癌を認め、卵巣癌治療後に僧帽弁の疣贅が消失する一例を経験した。NBTEは稀少な症例であり治療方法について検討を行った。【症例】58歳、G0P0。頭痛・ふらつきを自覚し近医脳神経外科を受診し、多発性脳梗塞と診断された。めまい・嘔気自覚し、小脳梗塞を認め入院。精査目的にて当院循環器内科へ紹介、入院となった。経胸壁心エコーにて僧帽弁に8mmの疣贅を認めた。骨盤内腫瘍が見つかり進行卵巣癌・NBTEとして治療目的にて当科転科となった。腹式子宮全摘術及び両側付属器摘出術を施行し、リハビリを行った。術後56日目、僧帽弁の疣贅は消失、化学療法6クール終了後現在再発なく外来にて経過観察中である。【検討】医中誌より2003年~2022年でNBTEを検索し、うち婦人科癌合併は24症例が抽出された。心臓の手術を先行したものは10例、原疾患に対する治療が行われなかった5例は全て再発し、易凝固状態が続き全身状態は急速に悪化する。原疾患に対して二期的もしくは同時手術された場合は、易凝固状態が改善された。【結論】NBTEは進行癌に合併するため予後不良であるが、原疾患の治療を速やかに開始することで予後の改善が期待できると考える。

P-1-7 卵巣癌脳転移に対する維持療法としてPARP 阻害薬を使用し長期奏効が得られた2例

大阪赤十字病院

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【背景】卵巣癌脳転移は稀だが発症後の予後は不良である。最も奏効率が高い放射線治療, 手術, 化学療法の併用であっても生存期間の中央値は2年に満たない。卵巣癌脳転移に対し維持療法としてPARP 阻害薬を使用し長期奏効が得られた2例を経験したため, 報告する。【症例】【症例1】51歳, 卵巣癌IVB期, 高異型度漿液性癌。術前TC療法後にinterval debulking surgery (IDS)を行い, 術後TC+Bevacizumab (Bev)療法, Bev維持療法を施行した。27か月後, 多発脳転移に対し開頭腫瘍摘出, 術後全脳照射+TC療法を行った後Olaparibによる維持療法を開始した。20か月後多発脳転移が再発したためOlaparibを中止し, 放射線治療を施行した。その後, 多発脳転移再発に対し放射線治療, 手術を施行したが, 以後24か月無再発生存中である。【症例2】86歳, 卵巣癌IIIB期, 高異型度漿液性癌。術前TC療法後にIDSを行い, 術後TC+Bev療法を施行した。腎不全のため維持療法は省略した。38か月後, 左小脳転移, 脾転移が判明し, 脳転移に対しては放射線治療, 脾転移に対してはTC療法+姑息照射を行った後Olaparibによる維持療法を開始した。以降15か月無再発治療継続中である。【考察】卵巣癌脳転移治療後のPARP 阻害薬投与により, 1例目は20か月, 2例目は15か月の無増悪生存期間を得ることができた。一般に, 低分子量で正電荷を持つ脂溶性分子のみが血液脳関門を通過できるとされる。PARP 阻害薬は分子量が小さく血液脳関門通過性があり, 脳転移治療後長期の奏効期間が得られた可能性がある。【結語】卵巣癌脳転移の予後は不良であるが, PARP 阻害薬での維持療法により長期の無増悪生存期間が得られる可能性があり更なる検討が必要である。

P-1-8 GOPC-ROS1 融合遺伝子を認めた卵巣高異型度漿液性癌の一例

近畿大

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【緒言】卵巣高異型度漿液性癌(HGSOC)では, TP53変異やBRCA1/2などのHRDといった遺伝子構造異常が主であるが, ドライバー遺伝子を有する症例は稀である。当院で治療ターゲットとなりうるROS1融合遺伝子を検出した卵巣高異型度漿液性癌の症例を経験したため, 報告する。【症例】50歳女性, 既往歴は特になく, 家族歴は詳細不明である。腹腔鏡下腫瘍生検術を施行し, HGSOCIVB期(肝転移)と診断した。術前化学療法(TC3コース, TC+Bev1コース)を行った。腹式単純子宮全摘術+両側付属器切除術+骨盤リンパ節郭清+傍大動脈リンパ節郭清+腹膜切除術を施行し, Complete surgeryを達成した。術後補助化学療法としてddTCを2コース行い, その後ニラパリブ維持療法を開始した。維持療法中の術後2年後にCA125が上昇したため, 遺伝子パネル検査を行った。術前化学療法後に摘出した卵巣検体から, GOPC-ROS1融合遺伝子を認めた。タレトリクチニブの治験に適合していることが判明し現在治験に参加中である。【考察】ROS1融合遺伝子により生成される蛋白質は, 細胞増殖活性化シグナル経路を恒常的に活性化することで癌の増殖に関与しており, 主に肺癌で見られる。GOPC-ROS1融合遺伝子を有するHGSOCに対してROS1阻害薬のクリゾチニブを投与し, 奏功したという報告が1例ある。本症例はそれに次いで2例目の報告であり, タレトリクチニブの治験に参加できた症例の報告としては1例目である。【結語】本症例において, がん遺伝子パネル検査の施行により, 治験に繋がる有意な所見を得ることができた。今後のprecision medicineの進展が期待される。

P-1-9 骨盤内再発を認めた成熟嚢胞性奇形腫の悪性転化に対して術後化学療法後にbevacizumab維持療法を行った一例

東京女子医大

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【緒言】成熟嚢胞性奇形腫の悪性転化は卵巣悪性腫瘍の1.5%と稀な腫瘍であり, 化学療法のレジメンに関しては確立されていない。今回, 我々は成熟嚢胞性奇形腫の悪性転化に対する妊孕性温存手術後3か月で骨盤内再発を認め, 術後化学療法後にbevacizumab維持療法を行った一例を経験したので報告する。【症例】27歳, 0妊0産, 未婚, 子宮内膜症を認めた。右卵巣成熟嚢胞性奇形腫の悪性転化を疑われ, 当科紹介となり, 腹式右付属器切除+左卵巣嚢腫摘出+傍大動脈リンパ節生検を施行した。術後診断は成熟嚢胞性奇形腫からの扁平上皮癌および腺癌であり, TNM分類はpT1aN0M0であった。術後補助化学療法は行わず経過観察の方針としたが, 術後3か月でSCC上昇とCTで骨盤内腫瘍を認め, 腹式回腸部分切除+腸間膜リンパ節生検を施行した。術後診断は扁平上皮癌であり, リンパ節転移は認めなかった。術後補助化学療法としてtri-weekly TC療法を2コース目からbevacizumabを加えて6コース行い, 維持療法としてbevacizumabを2年間, 35コース投与した。現在, 再発診断時から3年1か月経過し, 再々発兆候なく経過している。【結語】骨盤内再発を認めた成熟嚢胞性奇形腫の悪性転化の一例に対してbevacizumab維持療法を行うことで予後改善に寄与した可能性があると思われた。

P-1-10 骨転移を契機に診断された腺癌への悪性転化を伴う卵巣成熟奇形腫の一例

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【緒言】卵巣成熟奇形腫の悪性転化は組織型として約80%が扁平上皮癌であり、腺癌は約7%と稀である。今回骨転移を契機に腺癌への悪性転化を伴う卵巣成熟奇形腫と診断された症例を経験したため報告する。【症例】66歳 G1P1。腰痛、左下腿知覚異常を自覚し、その1週間後より歩行困難となり近医を受診した。精査目的にCT・MRIを撮影しTh3-4, L2-3の転移性骨腫瘍および骨盤内腫瘍、骨盤底のS状結腸の拡散低下、腹腔内播種を認めた。画像所見から卵巣癌の悪性転化や、大腸癌が考えられた。食思不振等の臨床症状を認めていたことから、手術加療の方針とした。卵巣腫瘍に対し片側付属器摘出術を施行し、術中所見で腹膜および大網に播種病変を多数認め、大網部分切除術、腫瘍生検、人工肛門造設術を行なった。前医で卵巣粘液性癌と診断され、精査加療目的に当院に紹介となった。組織型から大腸癌からの転移性卵巣腫瘍が疑われ上下部内視鏡検査を施行したが、胃癌や大腸癌を疑う所見は認めなかった。当院で病理組織検体を再検討し、腺癌への悪性転化を伴う卵巣成熟奇形腫と診断した。転移性骨腫瘍による脊髄圧迫で対麻痺となり、PS4と全身状態不良であった。骨病変に対する緩和的放射線治療とテノスマブ投与を行なったが、全身状態や組織型を鑑み積極的治療は行わず、BSCの方針とした。【考察】悪性転化を伴う卵巣成熟奇形腫の組織型のほとんどは扁平上皮であるが、腺型も約7%の頻度で存在する。また粘液性腺癌において、原発性卵巣癌と転移性癌の区別はしばしば困難であり、卵巣癌に対する治療が遅れる可能性がある。【結語】成熟奇形腫の治療にあたる際は、腺癌への悪性転化の可能性も念頭におく必要がある。

P-1-11 骨盤腹膜内腺症を背景とした大細胞性神経内分泌癌成分を伴う類内腺癌の一例

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症例は47歳, 0妊0産, 未閉経で, 2型糖尿病の内服治療中だが悪性腫瘍はない。家族歴は祖母に胃癌の既往のみ、数年前より不正出血を認め、前医を受診し、子宮内腺組織診で類内腺癌が疑われ、当院紹介受診となった。MRIで子宮内腺は正常内腺よりT2強調像で軽度低信号、拡散強調像で軽度拡散制限を認め、筋層に比べて造影効果は乏しかった。両側卵巣にT1強調像で高信号の嚢胞性病変を認めた。CTでリンパ節転移・遠隔転移の指摘なし。子宮内腺組織診の結果は類内腺癌G1であった。子宮体癌cStageIA期、類内腺癌G1の診断で腹腔鏡下子宮全摘術とリンパ節生検を予定したが、内腺症でダグラス窩は閉鎖しており、直腸Lsに径3.5cm大の結節性病変を認め、同部の術中迅速診断で腺癌が認められ、最終的に腹式単純子宮全摘+両側付属器切除+直腸低位前方切除術+リンパ節生検を実施した。組織学的には、子宮・両側卵巣・卵管周囲・直腸Rsに、各々EIN/AEHや内腺症を伴った類内腺癌G1を多巣性に認めた。直腸Rsでは類内腺癌に接して神経内分泌癌成分(約60%)を認め、背景の内腺症/類内腺癌/神経内分泌癌成分では免疫染色でPAX2(+/-), RB1(+/-, focal/-)を呈し、内腺症由来の類内腺癌及び神経内分泌癌への分化が示唆された。子宮及び卵巣の類内腺癌にも広く非浸潤性病変を伴い、免疫形質も異なり、骨盤内腺症由来の腹膜癌(類内腺癌G1+大細胞神経内分泌癌)及び、子宮体癌・卵巣癌の重複癌と解釈した。ただし、同時性子宮体部卵巣類内腺癌の多くはclonalな病変とされ、原発巣の解釈には議論があり得る。希少例であり文献的考察を加えて供覧する。

P-1-12 進行卵巣癌・卵管癌・腹膜癌症例において良質なHRD検査検体を得るため腫瘍生検時に術中迅速病理診断を応用する試み

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【緒言】進行卵巣癌・卵管癌・腹膜癌症例においてPARP阻害薬が応用されるにあたり、コンパニオン診断として腫瘍検体を用いてHRD検査が行われるようになった。進行期決定開腹手術や一次的腫瘍減量手術が施行困難な症例においては、chemotherapy-naiveな腫瘍をいかに確実にサンプリングするかが非常に重要になる。われわれは検体の質的評価に術中迅速病理診断を応用し始めたため現状を報告する。【方法】症例は2021年以降当院で治療を行った4例で、年齢は68-78歳であった。3例が審査腹腔鏡、1例が試験開腹であった。播種病巣の選択は十分な体積が得られ術中合併症が発生しにくい部位を選択した。日本病理学会ゲノム研究用病理組織検体取扱い規定に準じ摘出された検体は、その一部が速やかに迅速病理診断され腺癌であること、強い炎症所見がないこと、腫瘍細胞が最低20%存在すること、検体量が永久標本での診断に加えHRD検査および将来の遺伝子学的検査に十分な体積があることを確認した。【結果】診断は卵巣癌2例、卵管癌2例でいずれも臨床進行期はIIIC期であった。組織型は3例が高悪性度漿液性癌、1例が癌肉腫であった。HRD statusは2例が陽性、2例が陰性であった。試験開腹を行った1例は当初高悪性度漿液性癌の診断であったが、腫瘍減量手術時の病理診断で癌肉腫と診断されたため腫瘍減量手術時の検体からHRD検査を提出、BRCA1変異が検出された。他の3例は審査腹腔鏡時の検体からHRD検査を提出可能であった。【結語】迅速病理診断の併用により確実にHRD検査用検体が採取できることは進行卵巣癌・卵管癌・腹膜癌治療戦略策定において重要であると思われ、今後も症例数を増やし検討を重ねていく。

P-1-13 手術困難な再発顆粒膜細胞腫に対して GnRH 作動薬とアロマターゼ阻害薬の併用療法が奏功した 2 例の報告と文献的考察

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卵巣顆粒膜細胞腫は悪性卵巣腫瘍の約 5% を占めるまれな病態である。手術療法が主流だが 1/3 は再発し、再発例の 50~80% は原病死となる。また再発例への手術、化学療法、放射線治療には限界があり、最適な治療法は確立していない。今回、手術困難な再発顆粒膜細胞腫に対して、アロマターゼ阻害薬と GnRH 作動薬の併用療法が奏功した 2 例を経験した。本治療は倫理委員会の承認と患者の同意を得て行った。症例 1 は 56 歳で、再発顆粒膜細胞腫に対して 2 回の手術を行ったが、強い腹腔内癒着のため腸管損傷をきたした。その後の再発にアロマターゼ阻害薬単剤によるホルモン療法を行うも奏効しなかった。TC + ベパシズマブ投与も奏効せず、長期的な腫瘍のコントロールを目指して再度ホルモン療法としてアロマターゼ阻害薬と GnRH 作動薬の併用を行ったところ奏功 (complete response) した。症例 2 は 84 歳で、再発顆粒膜細胞腫に対して、2 回の手術と化学療法を施行し、最終の手術では腹腔内の強い癒着を認めた。その後再発したためアロマターゼ阻害薬単剤投与、weekly TC 療法を行うも奏効せず、再度ホルモン療法として、アロマターゼ阻害薬と GnRH 作動薬の併用を行ったところ、奏効 (partial response) した。2 例とも 2 剤による化学療法を継続中である。上記 2 例の経験に文献的考察を加えて報告する。

P-1-14 HBOC に対する RRSO で偶発的に high-grade serous の診断となった症例

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【背景】遺伝性乳癌卵巣癌症候群 (Hereditary Breast and Ovarian Cancer Syndrome: HBOC) は、BRCA の生殖細胞系列バリエーションに起因する乳癌/卵巣癌をはじめとするがんの易罹患性症候群である。わが国では 2020 年 4 月 1 日以降、乳癌または卵巣癌既発症、かつ BRCA 病的バリエーション保持者の場合に限りリスク低減卵管卵巣摘出術 (Risk Reducing Salpingo-Oophorectomy: RRSO) が保険診療となった。今回、当院で経験した RRSO 後に high-grade serous の診断となった症例を経験したため報告する。【症例】47 歳 2 経妊 2 経産 20XX 年 6 月に左乳癌 stage2 に対して、左乳房全摘術+センチネルリンパ節生検施行後、術後補助療法後、再発なく経過していた。20XX+3 年 6 月 HBOC 診断目的に BRCA 検査を施行し、BRCA1 病的変化を認めた。家族歴として、乳癌、前立腺癌、膵臓癌、腹膜癌があった。リスク低減手術の希望あり、当院乳癌外科と合同で RRSO+右乳房全摘術 (Contralateral Risk Reducing Mastectomy: CRRM) を行った。手術時間 3 時間 32 分、術中出血量 10ml。術後病理にて、右卵管に High-grade serous carcinoma with serous tubal intraepithelial carcinoma (STIC), pT1a, 1.1* 0.7mm。左付属器: 漿液性腺線維腫。右卵巣/子宮内膜/右乳房は悪性所見なし。の診断であった。卵巣癌 IA 期として、開腹単純子宮全摘術+大網切除術+骨盤リンパ節郭清+傍大動脈リンパ節生検を施行した。術後、パクリタキセル+カルボプラチン療法 6 コースまで施行する。【結論】本邦では RRSO が保険適応となり、対象例において積極的に施行されるようになった。本症例のように、RRSO 施行後に癌の診断となる症例も増える予想される。RRSO であっても慎重な手術/管理が必要と考えらる。

P-1-15 虫垂炎を合併した卵管卵巣膿瘍に対して腹腔鏡手術を施行した 2 例

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【緒言】卵管卵巣膿瘍 (tubo-ovarian abscess: TOA) は性感染症、子宮内感染、経腔的な手術操作等が原因の上行性感染が主である。下行性感染として虫垂炎や腹膜炎からの波及も考えられるが頻度は稀である。今回、虫垂炎を合併した TOA に対して腹腔鏡手術を施行した 2 例を経験したので報告する。【症例】①43 歳、3 妊 3 産。TOA の疑いで当科入院管理のもと抗菌薬投与を 12 日間行い退院した。退院 2 週間後に 38℃ 台の高熱と下腹部痛を自覚したため当院救急外来を受診した。血液検査で炎症反応は高値であったが CT で熱源は判然とせず、TOA 再燃の可能性があるので当科で入院管理を行い、診断と治療目的で腹腔鏡手術を施行した。右卵管と虫垂は腫大し、癒着により一体化していた部分に膿瘍腔を認め、周囲を剝離後に右卵管切除術を施行した。虫垂腫大は虫垂炎の可能性が高く、外科で虫垂切除術を施行した。②85 歳、1 妊 1 産。右下腹部痛を主訴に前医を受診し、CT で腸管穿孔疑いを指摘され当院救急外来へ搬送となった。穿孔性虫垂炎の診断で当院外科へ紹介となり、同日腹腔鏡下虫垂切除術を施行した。虫垂切除後の所見で右卵管腫大および右卵管周囲に膿瘍を認め、TOA が疑われ当科へ術中紹介となった。腹腔内の癒着は高度で膿瘍破綻をきたしたが、膿瘍除去後に右付属器切除術を施行した。【考察】TOA と虫垂炎を同時に発症することは稀であり、画像診断では診断が困難な場合も多く、早期の腹腔鏡手術が診断に有用である。また保存的加療が困難な場合、外科的治療が重要となり、腹腔鏡手術は治療においても有用である。【結論】虫垂炎を合併した TOA に対して腹腔鏡手術は治療と診断において有用である。

P-2-1 子宮内膜癌進行期分類 (FIGO2023) の検証

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【目的】国際産婦人科連合 (FIGO) は 2023 年に子宮内膜癌の病期分類を改訂した (FIGO2023)。本研究の目的は現行の FIGO 2008 からのステージ移行と FIGO2023 に再分類した場合の予後を検討することである。【方法】対象は 2014 年 1 月から 2019 年 3 月までに当院で手術を受け、プロジェクト HOPE コホート研究として次世代シーケンサーにより分子プロファイリングが行われた子宮内膜癌 83 例。FIGO2008 および FIGO2023 に沿って病期分類を行い、ステージ移行と各病期の疾病特異的生存率 (DSS) を算出した。【成績】FIGO2008: I 期 62 例, II 期 5 例, III 期 11 例, IV 期 5 例。FIGO2023: I 期 48 例, II 期 19 例, III 期 12 例, IV 期 4 例。WHO 分子遺伝学的分類: POLE-ultramutated 11 例, MMR-deficient 22 例, p53-mutant 13 例, no specific molecular profile (NSMP) 37 例。ステージ移行: 15 例 (アップステージ 14 例, ダウンステージ 1 例)。5 年 DSS (FIGO2008): I 期 96.4% (95%CI 86.3-99.1), II 期 50.0% (95%CI 5.8-84.5), III 期 100% (95%CI NA-NA), IV 期 40% (95%CI 5.2-75.3)。5 年 DSS (FIGO2023): I 期 97.6% (95%CI 83.9-99.7), II 期 83.3% (95%CI 56.8-94.3), III 期 100% (95%CI NA-NA), IV 期 25.0% (95%CI 0.9-66.5)。【結論】今回の検討では、FIGO2023 は子宮内膜癌の病態と予後を FIGO2008 より反映した分類だった。

P-2-2 分子分類を組み込んだ子宮体癌 FIGO2023 (FIGO2023m) の有用性

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【目的】FIGO2008 から FIGO2023 の改訂に伴い分子分類が新たな staging に組み込まれた。早期癌において分子分類が可能な場合、POLE 変異症例は stageIA_mへ、筋層浸潤を伴う p53 変異症例は stageIIC_mへと変更になった。本研究では、FIGO2008, 分子分類を組み込まない FIGO2023 (FIGO2023), 分子分類を取り入れた FIGO2023 (FIGO2023_m) の 3 つの FIGO 分類による予後識別能の違いを検討することを目的とした。【方法】当院 IRB の承認 (2015-278, 2017-331) のもと、1997-2019 年に当院で初回手術を施行した子宮体癌のうち、POLE 変異の target sequencing, MMR 蛋白および p53 蛋白に対する免疫染色を施行した 265 例を対象とした。各々の FIGO 分類を Harrell's concordance index (C-index), Akaike information criterion (AIC), time-dependent receiver operation characteristics (ROC) 曲線で比較した。【成績】FIGO2023 と FIGO2023_mを比較すると 19 例が stageIA_mへ downstage し、4 例が stageIIC_mへと upstage した。3 つの FIGO 分類のうち、FIGO2023_mは最も低い AIC 値、最も高い C-index 値を示した。また、time-dependent ROC 曲線においても他 2 つの FIGO 分類と比較して術後 1 年以降全期間で良好な分別能を示した。さらに、stageIIIC において、p53 変異症例は p53 wild-type と比較して 5 年生存率が有意に予後不良であった (24.3% vs 83.7%, p=0.0005)。【結論】FIGO2023_mは 3 つの評価方法全てで最も良好な識別能を示した。本研究では進行癌 (stageIIIC) においても p53 変異の有無は予後因子であり、可能な限り全 stage において分子分類を取り入れることが良好な予後予測につながる事が示唆された。

P-2-3 当院で経験した子宮体癌 1190 例の組織型別の臨床的特徴についての解析

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【目的】子宮体癌の組織型別の臨床学的特徴を明らかにすること。【方法】2000 年-2022 年に当院で初回治療を行った子宮体癌 1190 例を組織型別に年齢、進行期、予後について後方視的に解析した。【成績】類内膜癌 924 例 (78%), 明細胞癌 52 例 (4%), 漿液性癌 80 例 (7%), 混合癌 41 例 (3%), 癌肉腫 (6%), その他の組織型 29 例 (2%) であった。各群の年齢中央値はそれぞれ 58 歳, 69 歳, 65 歳, 65 歳, 66 歳, 69 歳, III/IV 期は 15%, 42%, 43%, 39%, 30%, 59%, 5 年生存率は 91%, 81%, 61%, 65%, 59%, 46% であり、非類内膜癌は高齢で、進行症例が多く、5 年生存率も低かった。Cox 回帰分析では 60 歳以上 (HR 2.8, 95%CI 2.0-3.7), III 期 (HR 3.0, 95%CI 2.2-4.1), IV 期 (HR 11.9, 95%CI 8.4-16.8), 漿液性癌 (HR 1.7, 95%CI 1.1-2.5), 癌肉腫 (HR 3.9, 95%CI 2.6-5.8), その他の組織型 (HR 3.7, 95%CI 2.2-6.3) が全生存期間に関する独立した予後不良因子であった。その他の組織型の中でも神経内分泌癌 (4 例) は極めて予後不良であった。2000-2006 年受診症例の非類内膜癌の割合は 16% であったが、2007-2014 年は 19%, 2015-2022 年は 28% と増加していた (p<0.001, Cochran-Armitage test)。特に漿液性癌と混合癌の増加が顕著であった (2000-2006 年症例 2%, 2015-2022 年症例 15%)。5 年生存率は 2007-2014 年症例 88% に比べて、2015 年-2022 年症例 84% と低下していた (p=0.019, Log-rank test)。【結論】非類内膜癌は予後不良であった。近年非類内膜癌の割合が増加し、子宮体癌の予後が悪化している可能性がある。

P-2-4 子宮体癌に対するロボット支援傍大動脈リンパ節郭清について

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【目的】子宮体癌再発中・高リスク症例に対する傍大動脈リンパ節 (PAN) 郭清術は婦人科腫瘍学的に重要な手技である。開腹術では、剣状突起から恥骨までの非常に大きな創部となり、身体的侵襲が非常に大きい。ロボット手術では創部が小さく、術後早期社会復帰可能であり、メリットが高い術式であるが、現在保険適応ではない。当院では院内倫理委員会承認の上、2021年4月よりロボット支援下傍大動脈リンパ節郭清術を開始し、現在までに13例を経験しており、今回後方視的に検討した。【方法】子宮体癌1A特殊型、1B、2期を対象とし、患者年齢は中央値で56歳、BMIは23であった。対象症例13例に対して、ダヴィンチXiを用いて当該術式を行った。トロッカー配置は臍下2cmにカメラポート、左右2か所ずつポート配置し、サイドドッキング施行した。経腹膜アプローチで腹膜を吊り上げ視野確保し、PAN郭清を施行した。単一術者による手術で、婦人科腫瘍専門医、産婦人科内視鏡技術認定医の資格とロボット手術のプロクター資格を持つ術者が施行した。【成績】総手術時間は中央値280(235-326)分、PAN部分は150(120-160)分、出血量は少量、輸血症例はなかった。摘出したPAN個数は中央値14(7-22)個、術中合併症は認めなかった。術後に3例乳糜腹水を認め、経過観察にて改善した。平均入院期間は6日間で、術後1日目にドレーン抜去、2日目にシャワー可能、4日目には退院可能であった。【結論】子宮体癌に対するロボット支援下PAN郭清術は安全に施行することが可能であった。今後症例をさらに経験し、より安全に手術できるように、また先進医療や保険収載に向けて備えたいと考える。

P-2-5 子宮体癌新 FIGO2023 病期分類の妥当性と当院の課題

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【目的】2023年子宮体癌のFIGO病期分類が改訂された。本研究では、2023FIGO分類と2009FIGO分類を比較し、その臨床的妥当性と当院の課題について検討した。【方法】2018-2022年までに当院で初回治療を行った子宮体癌355例を対象とし、2009FIGO分類および2023FIGO分類に従って層別化した。病期移行を分析し、病期別の5年無増悪生存期間(PFS)と全生存期間(OS)を比較した。【成績】当院の子宮体癌の治療件数は2018年から2022年までに12.1%から29.6%へ(APC24.2, 95%CI10.2-39.9, P=0.01)増加した。2009FIGO分類ではI期249例(70.1%), II期21例(5.9%), III期52例(14.6%), IV期33例(9.3%)に対して、2023FIGO分類ではI期210例(29.2%)と39例がII期へUp stageした(表2)。また、III期は56例と4例がIV期よりDown stageした。2023FIGO分類では、2009FIGO分類と比較して5年PFS, OSがI期で高くなった(PFS 93.7% vs 88.0%; OS 98.7% vs 94.3%)。特にII期の5年PFS, OSに差が認められた(PFS 73.1% vs 88.2%; OS 82.9% vs 100%)。III期では、2023FIGO分類と2009FIGO分類のPFS, OSは同等であった(III期PFS 71.5% vs 71.0%; OS 76.8% vs 74.8%)。IV期では、2023FIGO分類は2009FIGO分類と比べ、より予後不良な結果となった(PFS 4.5% vs 13.2%; OS 19.9% vs 31.7%)。2023FIGO分類ではPFS, OSの予測がより正確であることが示唆された(図1)。分子生物学的分類は、MIS検査22例(5.9%), p53免疫染色検査107例(30.2%)で施行した。【結論】新しい2023FIGO分類は11.8%の患者でステージの変化を認め、予後診断の精度が向上していた。当院の分子生物学的分類は十分とはいえず、今後さらなる拡充が必要と考える。

P-2-6 子宮悪性腫瘍におけるセンチネルリンパ節の同定：当院の2年間の臨床実績

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【目的】センチネルリンパ節(SLN)理論とは、がんが最初に転移するリンパ節(LN)に転移がなければ系統的リンパ節郭清を省略できるという概念である。インドシアニングリーン(ICG)を子宮頸部より注入する蛍光法のみを用いたSLN同定の2年間の臨床実績を報告する。【方法】子宮頸癌11例(全例開腹)、子宮体癌40例(開腹22例, ロボット16例, 腹腔鏡2例)に対して、全身麻酔直後にICGを子宮頸部4か所に計5mg注入した。SLN同定には近赤外線蛍光造影カメラを使用し骨盤リンパ節(PeN)のみを確認した。SLNは2mm幅でスライスして迅速病理組織診(迅速)を行い、転移の有無によらず全例PeNのgold standardとした。【成績】51例中48例(頸癌10例, 体癌38例)でSLN同定ができた。LN転移は9例に認め、9例中1例はSLN自体が同定できなかった。SLNが同定された8例中、6例は迅速でSLN転移ありと診断できた。2例は永久ではSLN転移を認めたが迅速で診断できなかった(偽陰性)。micro転移とMELF型浸潤の各1例ずつで、前者は迅速検体に腫瘍を認めず、後者は腫瘍細胞を組織球との判断した。また迅速でSLN転移と診断されたが、永久でendosalpingiosisと診断され転移陰性と判断された偽陽性例が1例あった。SLNが同定された患者における成績は感度75%、特異度98%、陽性的中率85%、陰性的中率95%であった。SLN生検に起因する合併症はなかった【結論】SLNが同定されたLN転移例の全例でSLN転移を認めたことから蛍光色素法のみでSLN同定は可能であるが、術中にSLN転移を正確に診断することが今後の課題と思われた。

P-2-7 レンパチニブ・ペムプロリズマブ併用療法を施行した再発子宮体部癌肉腫3症例の後方視的検討

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【目的】がん化学療法後に増悪した切除不能な進行・再発の子宮体がんに対して、レンパチニブ (Len)・ペムプロリズマブ (Pem)併用療法の有用性が確認され、2021年12月から保険収載されたが、子宮体部癌肉腫に対しての効果は明らかになっていない。そこで当科における使用経験を報告する。【方法】当院で2022年4月から2023年9月までにLen・Pem併用療法を施行した再発・進行子宮体がん症例のうち、組織型が癌肉腫であった3例について、後方視的に検討した。【成績】症例1は60歳で、腹膜播種を伴うIVB期に対し、手術での肉眼的完全切除およびドキシソルビシン・シスプラチン療法5コース後3か月で多発腹膜播種および多発リンパ節転移再発を認めた。MSI検査陰性でありLen・Pem療法を開始した。Grade3の膀胱炎と疲労がありPemの休薬とLenの減量を要したものの、4コース終了後には縮小率73%の部分奏功と判定し、以後13コースまで再燃なく継続している。症例2は53歳で、手術での肉眼的完全切除およびパクリタキセル・カルボプラチン療法3コース後7か月で骨盤内に再発を認めた。MSI検査陰性でありLen・Pem療法を開始したが、3コース後に34%の病変増大と新規病変の出現を認め、進行と判定した。症例3は54歳、手術での肉眼的完全切除およびパクリタキセル・カルボプラチン療法6コース直後の画像評価で新規に肝転移巣を認めた。MSI検査は未施行であり、Len・Pem療法を開始し3コースまで施行し、継続中である。【結論】少数例での検討であるが、化学療法抵抗性の極めて予後不良な症例で奏功しており、子宮体部癌肉腫症例に対してもLen・Pem併用療法は治療選択肢となり得ると考えられた。

P-2-8 当院における進行・再発子宮体癌に対するレンパチニブ+ペムプロリズマブ併用療法の使用経験と有害事象に関する検討

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【目的】レンパチニブ (Len)+ペムプロリズマブ (Pem)併用療法 (LP療法)は、免疫関連有害事象 (irAE)を始め、多岐にわたる有害事象 (AE)の管理に苦慮することが少なくない。今回当院でのLP療法の使用経験やAEについて報告する。【方法】2022年1月から2023年9月に当院で再発・進行子宮体癌に対してLP療法を施行した18例について後方視的に検討した。【成績】平均年齢59歳、進行2例、再発16例、MSI-high3例、MS stable9例であった。組織型は類内膜癌G1:5例、G2:2例、G3:1例、漿液性癌4例、混合癌3例、その他3例であった。前治療は17例でDCまたはTC療法を施行していた。irAEはPem投与後中央値76日目で見られ、Grade1の甲状腺機能低下症13例はレボチロキシン内服で改善した。Grade3の腸炎3例、関節炎・急性膀胱炎・脳炎・胆管炎を1例ずつ認め、4例 (腸炎3例、脳炎1例)でステロイド投与を要し、中央値2.5日で改善した。他は対症療法により中央値22.5日で改善し、治療後経過は良好であった。irAE以外のAEは全例で見られ、Grade3以上は尿蛋白4例、倦怠感3例、悪心3例、リパーゼ上昇2例、顎骨壊死・貧血・血小板低下1例ずつで、Len開始から中央値17日で発症した。中央値8日間の休薬を要し、再開後もGrade3以上のAEを中央値23日で認め、再休薬を要した。14例はAEによりLenを減量し、1例は減量してもAEが再燃し中止した。最良治療効果はCR1例、PR1例、SD6例、PD10例であり、総治療回数は中央値4.5コースであった。【結論】LP療法は奏効している例もある一方で、Gradeの高いAEも散見され治療継続に難渋する例も多い。特にirAE出現時は関連診療科と密に連携を取り、副作用管理と治療を並行して行うことが重要である。

P-2-9 PET/CT所見を用いた子宮体癌リンパ節転移低リスク群の設定

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【目的】子宮体癌でのリンパ節郭清は合併症等の理由からその省略基準の設定が求められている。子宮体がん治療ガイドライン (GL)では低リスク群 (類内膜癌 Grade 1,2で筋層浸潤1/2未満)ではリンパ節郭清の省略を提案するとしているが、組織型が術前生検と摘出子宮で異なることは少なくない。われわれはFDG-PET/CT検査を行うことで、リンパ節転移低リスク群の設定が可能かについて検討を行った。【方法】2006年6月から2017年6月までに当院でのPET-CT検査後に手術 (リンパ節摘出省略を含む)を受けた子宮体癌症例のうち、卵巣癌合併例、子宮内腔に異常集積のなかった例を除く250例を対象とした。なお、術後療法はリンパ節摘出後に転移のなかった類内膜癌症例では省略した。【成績】250例中28例 (11%)にリンパ節転移・再発 (LNMR)を認めた。組織型が術前組織診で類内膜癌 Grade 1,2であった症例のうち、摘出子宮で高リスク (類内膜癌 Grade 3,漿液性,明細胞癌等)となったのは14% (20/139)であった。摘出後の病理検査結果でGL低リスク群となった124例中、LNMRは6例 (4.8%)にみられた。原発巣のSUVmaxの平均は非LNMR例では12.22 (95% CI, 11.32-13.12)で、LNMR例の16.22 (95% CI, 13.70-18.76)に比べ有意に低かった ($p=0.004$)。原発巣のSUVmax 13.5未満で筋層浸潤1/2未満の121例ではLNMRは6例 (5.0%)に生じ、5例は骨盤内、1例は傍大動脈であった。6例中、転移リンパ節に異常集積がなかったのは4例 (3.3%)であった。【結論】子宮体癌でのリンパ節転移低リスク群の設定において、術前PET/CTでのSUVmaxと筋層浸潤の組み合わせは、摘出子宮での組織型と筋層浸潤の組み合わせと同等に有用と考えられる。

P-2-10 早期子宮体癌に対する FIGO 子宮体癌病期分類 (2023) の検証

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【目的】2023年、国際産婦人科学会 (FIGO) による子宮体がん進行期分類が改訂された。全国調査研究データを使用し、早期子宮体癌における 2023FIGO 病期分類 (新 FIGO) の妥当性について検証を行った。【方法】2015年から2017年に、低侵襲手術で治療された子宮体がん患者のデータを収集し、後ろ向きコホート研究とした (n=3633)。【成績】2009年 FIGO 分類 (旧 FIGO) に基づく I 期は新 FIGO では IA1 期 (30.9%), IA2 期 (55.7%), IIB 期 (7.6%), IIC 期 (5.7%) に再分類され、同様に旧 FIGO の IB 期は新 FIGO の IB 期 (56.4%), IIB 期 (29.8%), IIC 期 (13.7%) に再分類された。旧 FIGO の II 期は新 FIGO の IIA 期 (63.6%), IIB 期 (18.7%), IIC 期 (17.8%) に再分類され、IIIA 期は新 FIGO の IA3 期 (100%) に再分類された。全生存率は、IA1 期 (98.4%), IA2 期 (98.3%), IA3 期 (86.1%), IB 期 (95.1%), IIA 期 (98.4%), IIB 期 (92.9%), IIC 期 (82.4%) であった。I 期 (n=2937) において、IA2 期は IA1 期と比較して死亡リスクに有意な差は見られなかった (aHR 1.04; 95% CI, 0.55-1.96; P=0.902)。しかし、IA3 期および IB 期は、IA1 期と比較して有意に死亡率が増加した (aHR 3.80; 95% CI, 1.01-14.30; P=0.048 および aHR, 2.39; 95% CI, 1.04-5.48; P=0.039)。II 期 (n=696) では、IIB 期は IIA 期と比較して生存率が悪化していたが、有意差は見られなかった (aHR 5.35; 95% CI, 0.74-39.34; P=0.099)。一方、IIC 期は有意に死亡率が増加した (aHR 14.86; 95% CI, 2.02-106.8; P=0.008)。【結論】子宮体がんの新しい進行期分類 (FIGO 2023) は、IA 3, IB, IIA, IIB, および IIC のステージ間で生存率の差を区別する可能性を示唆した。

P-2-11 進行・再発子宮体癌に対するレンパチニブ・ペンプロリズマブ併用療法の使用経験

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【目的】2021年12月、がん化学療法後に増悪した切除不能な進行・再発子宮体癌に対してレンパチニブ・ペンプロリズマブ (LP) 療法が保険取載された。当院で施行した LP 療法の使用経験について報告する。【方法】2022年2月から2023年8月までに LP 療法を施行した子宮体癌 12 例において、有効性および安全性について後方視的に検討した。【成績】年齢の中央値は 58 歳 (範囲: 34-66)、類内膜癌が 9 例、中腎腺癌が 1 例、混合癌が 1 例、癌肉腫が 1 例だった。PS は 0 が 11 例、2 が 1 例だった。先行レジメン数の中央値は 2 (1-7)、PFI が 6 か月未満は 7 例 (不応性 5 例を含む)、6 か月以上 12 か月未満が 4 例、12 か月以上が 1 例だった。12 例中 9 例は MSI 検査陰性で、残り 3 例は未実施だった。観察期間の中央値は 24 週 (10-67) であり、最良総合効果は PR が 7 例 (58%)、SD が 5 例 (42%)、奏効期間の中央値は 15 週 (1-21) だった。有害事象は全症例で認められ、頻度順に高血圧 10 例 (83%)、甲状腺機能低下 9 例 (75%)、倦怠感 8 例 (67%)、口腔粘膜炎 8 例 (67%)、発熱 6 例 (50%)、蛋白尿 6 例 (50%) 等だった。Grade3 以上の有害事象は高血圧 4 例、菌内感染 2 例、発熱・口腔粘膜炎・気胸・下痢・関節痛・尿路感染の 1 例ずつだった。有害事象のためレンパチニブを減量したのは 7 例 (58%) だった。LP 療法を中止したのは 5 例で、4 例は病勢増悪、1 例は経済的理由によるものだった。【結論】LP 療法は、がん化学療法後に増悪した子宮体癌に対して高い疾患制御を期待できる一方で、様々な副作用の管理を要する。

P-2-12 当院で治療した子宮体癌術前 I A 期の治療および予後の検討

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【目的】早期子宮体癌に対して鏡視下手術が急速に普及し、術前診断の重要性がより一層高まっている。当院の術前 T1aN0 M0 症例について後方視的に検討した。【方法】2010年から2021年に当院で治療した子宮体癌術前 T1aN0M0 の 253 例について、術前・術後の組織診断一致率、進行期分類一致率、治療方法、再発の有無について後方視的に解析した。【成績】pT1aN0M0 だったのは 223 例で進行期分類一致率は 88% だった。pT1aN0M0 症例のうち類内膜癌 G1/G2 は 171 例であり、術前からの組織診断一致率は 99% だった。再発は 7 例で 5 例は術後化学療法なし、うち 3 例は類内膜癌 G2、2 例は漿液性癌の症例だった。pT1aN0M0 に対して術後化学療法は 27 例に実施し、そのうち再発は漿液性癌の 2 例でどちらも筋層浸潤は Imm 以下だった。pT1bN0M0 は 25 例で類内膜癌 G1/G2 は 64%、組織診断一致率は 76% だった。pT2N0M0 は類内膜癌 G2 の 1 例、pN1, pM1 はそれぞれ 1 例ずつで両方とも漿液性癌だった。傍大動脈リンパ節郭清を実施したのは 11 例で、pN2 はいなかった。pT3a は 3 例あり、うち 2 例は漿液性癌、1 例は類内膜癌 G2 で組織診断一致率は 33% だった。術後アップステージした 30 例中 23 例に術後化学療法を実施し、そのうち漿液性癌 2 例に再発し、原病死した。一方で本人希望もしくは全身状態不良で化学療法を実施しなかった 7 例中、原病死は未分化間質肉腫の 1 例のみだった。【結論】特に漿液性癌は術前の組織診断および画像診断が難しい。組織診断率が下がる原因として生検量の不足や免疫染色の省略が考えられる。傍大動脈リンパ節郭清術の必要性についてバイオマーカーの開発など更なる研究結果が待たれる。

P-2-13 子宮体癌におけるロボット手術、腹腔鏡手術と開腹手術の再発パターンの検討

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【目的】子宮体癌罹患患者数は年々増加し、鏡視下手術は増加している。鏡視下手術において、気腹による腹膜播種再発の増加が危惧されるが、再発パターンについての報告は少ない。今回、鏡視下手術と開腹手術の再発パターンを明らかにすることを目的とした。【方法】2015年1月～2022年12月の期間に、初回治療でロボット手術、腹腔鏡手術または開腹手術を施行した子宮体癌497例において、臨床情報、再発パターンにつき検討した。【成績】症例は、ロボットは189例、腹腔鏡は126例、開腹は182例であった。進行期はIA期304例、IB期86例、II期28例、IIIA期18例、IIIB期7例、IIIC期53例、IVB期1例であった。組織型は類内膜癌G1、G2:389例、G3:33例、漿液性癌34例、明細胞癌6例、粘液性癌3例、癌肉腫28例、その他4例であった。再発症例は46例で、組織型は類内膜癌G1、G2:18例、G3:4例、漿液性癌11例、明細胞癌2例、癌肉腫9例、その他2例であった。進行期はI期20例、II期1例、III期25例で、ロボットは所属リンパ節転移1例、遠隔転移2例、腹膜播種1例、腹腔鏡は腔断端再発2例、腹膜播種1例、遠隔転移1例、開腹は腔断端再発5例、所属リンパ節転移4例、腹膜播種11例、遠隔転移18例であった。開腹はロボット、腹腔鏡より腹膜播種、遠隔転移再発が多かった(p<0.05)。ロボット、腹腔鏡の再発例はすべてI、II期で、開腹手術のI、II期再発例は、腔断端再発3例、所属リンパ節転移1例、腹膜播種2例、遠隔転移7例であった。I、II期再発例においては、開腹手術がロボット、腹腔鏡に比較して遠隔転移が多かった(p<0.05)。【結論】ロボット、腹腔鏡手術は開腹手術と比較し、特有の再発形態はとらなかった。

P-2-14 当科における初期子宮体癌に対する腹腔鏡およびロボット支援下手術成績の中間報告

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【目的】当科において、2018年より初期子宮体癌に対する内視鏡下手術を施行している。その安全性と成績を報告する。【方法】2023年8月までに、内視鏡下手術を施行し最終病理診断が子宮体癌となった症例を対象に、手術アウトカム、治療成績を後ろ向きに検討した。【成績】対象症例は136例であり、ロボット支援下手術は91例(骨盤リンパ節郭清あり74例、なし17例)、腹腔鏡下手術は45例(郭清あり16例、なし29例)であった。各因子の中央値(範囲)は、郭清あり/なしで、手術時間は302.5(190-500)分/178.5(81-290)分、出血量は17(0-240)ml/0(0-137)ml、術後在院日数は4(3-10)/4(3-8)日であった。リンパ節郭清施行例の摘出リンパ節個数は21(7-50)個であった。Clavien-Dindo分類III度の合併症を1例(リンパ浮腫)認めたが、輸血、conversion、他臓器損傷等の術中合併症は認めなかった。術後追加治療を要するup-stageは18例(13.2%)、up-gradeは10例(7.3%)に認め、追加療法は31例(22.8%)に施行した。観察期間は31(2-79)か月で、再発は1例に認め、手術進行期II期、類内膜癌G2の症例であり、術後1年で多発肺転移を認めた。現病死はなかったが、乳がんによる死亡を1例認めた。よって、DFS、OSとも99%であった。【結論】当科において、内視鏡下子宮体癌手術を導入し5年が経過するが、安全に施行し、現時点で治療成績は良好である。長期予後は今後の経過観察を要する。

P-3-1 早期子宮体癌術後4か月後に新たに卵巣癌を発症した一例と当院で経験した子宮体癌卵巣癌重複癌の後方視的検討

岡山大

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子宮体癌と卵巣癌は約5～10%重複すると報告されている。早期子宮体癌の術後4か月後新たに卵巣癌を発症した一例と、2009年1月から2023年9月で後方視的に検討した子宮体癌卵巣癌重複癌16例を報告する。症例は41歳で、子宮体癌IA期類内膜癌Grade1相当と診断し、子宮全摘出術、両側卵管摘出術を施行した。術後4か月後にCA19-9、CA125の上昇、画像検査で右付属器の腫大を認めた。卵巣癌または子宮体癌卵巣再発の疑いで右付属器摘出術を施行した。術中迅速病理診断は子宮内膜症成分背景の卵巣原発類内膜癌で、左側卵巣摘出術、骨盤内及び傍大動脈リンパ節郭清術、大網切除術を追加した。確定診断は卵巣癌IA期類内膜癌Grade1で、後療法は行わず経過観察の方針となった。当院で経験した子宮体癌卵巣癌重複癌16例の発症年齢中央値は53(39-67)歳。子宮体癌は全例I期、卵巣癌は14例がI期であった。組織型は、子宮体癌は1例を除き類内膜癌、卵巣癌は14例が類内膜癌、Gradeの一致は10例で認めた。13例は一期的に手術を施行し偶発的に子宮体癌卵巣癌重複癌と診断された。3例は子宮体癌治療後4か月、2年3か月、2年11か月後に新規卵巣癌と診断された。早期子宮体癌術後4か月後、新たに卵巣癌の診断に至った1例を経験した。本症例のように子宮体癌卵巣癌重複癌は必ずしも同時期に発症するわけではない。同じ組織型の子宮体癌卵巣癌重複癌において子宮体癌、卵巣癌の各々の分子生物学的共同性が報告されているが、実臨床で重複癌の予測は困難である。適切な治療を行えば予後良好であるが、低悪性度子宮体癌の中には時間において卵巣癌を重複する群が一定数含まれるため卵巣温存を選択する際には慎重な経過観察が重要である。

P-3-2 子宮頸管ポリープにCIN3を認め、超音波で外子宮口より2cm以上奥に茎の遺残を同定し、腹腔鏡下子宮全摘術を行った1例—異型子宮頸管ポリープに対する治療指針の文献学的考察—

愛仁会千船病院

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【緒言】子宮頸部に発生するCIN3以上の異型に対する治療指針は確立しているが、子宮頸管ポリープ(以下ポリープ)がCIN3以上の異型を伴う場合の治療方針は未だ明確でない。摘出後にCIN3と診断されたポリープ茎の遺残を外子宮口から2cm以上離れた所に超音波・MRIで確認し腹腔鏡下子宮全摘術後の病理診断で残存病変を認めなかった1例の経験を踏まえ、治療方針に関する文献学的考察を行った。【症例】50歳、3妊2産。前医でポリープを捻除により摘出し、その後の病理診断でCIN3のため当院へ紹介された。カラードップラー法を併用した経腔超音波およびMRI検査で基底部分外子宮口より24mmの位置にあるポリープの遺残茎を認めた。外子宮口から2cm以上の距離があり、円錐切除術は困難と判断した。妊孕性温存の希望は無く、診断・根治目的で腹腔鏡下子宮全摘術を実施した。摘出標本で13mmの遺残ポリープ茎の基底部分は外子宮口から28mmの位置にあり、病理診断でポリープの遺残茎に異形成の残存は認めず、ポリープ原発のCIN3と診断した。【考察】ポリープは殆どが良性だが0.1%に悪性、0.5%に異形成を認める。ポリープは外来で捻除する例が多いが、基底部分が子宮頸管の奥にある場合は捻除のみでは茎が遺残する可能性がある。CIN3以上の病変が出る可能性を踏まえ、まず経腔超音波検査のカラードップラー法でポリープの基底部分の位置を確認し、外子宮口より2cm以上離れている場合は子宮鏡を併用し基底部分の切除が望ましい。CIN3以上で茎の断端が陰性でも子宮側に残存病変を認める例の報告があり、子宮全摘術または妊孕性温存希望の場合は円錐切除術および子宮頸管キュレットが望ましいと考えられた。

P-3-3 選択的静脈血ホルモンサンプリングにより局在診断し腹腔鏡手術を施行した卵巣ステロイド細胞腫瘍の一例

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【緒言】ステロイド細胞腫瘍は非常に稀な腫瘍で、画像検査で診断できない症例も多く選択的静脈血ホルモンサンプリングが有効とされている。今回、両側卵巣腫瘍に対して選択的卵巣静脈血サンプリングにより局在診断し腹腔鏡手術を施行した卵巣ステロイド細胞腫瘍の一例を経験したので報告する。【症例】37歳。G0P0。無月経を主訴に前医受診し、高テストステロン血症が指摘され当院に紹介となる。前頭部の脱毛、顔面ざ瘡、陰核肥大等、男性化徴候を認め、血液検査ではテストステロン値7.01ng/mLと高値であった。経腔超音波と骨盤内MRIで、右卵巣に23mmの充実性腫瘍、左卵巣に60mmの単房性嚢腫が指摘された。頭部MRI・腹部CTで副腎・下垂体等に腫瘍は認めず多嚢胞性卵巣症候群も否定的で、卵巣アンドロゲン産生腫瘍が疑われたが左右の局在は不明であった。アンドロゲン産生腫瘍の局在を同定目的に左右副腎静脈、下大静脈右卵巣静脈合流部、左右卵巣静脈末梢の選択的静脈血ホルモンサンプリングを施行した。右側卵巣静脈末梢側のテストステロン値は550ng/mLと他部位に比べて異常高値を示したことから右卵巣アンドロゲン産生腫瘍と診断し、腹腔鏡下右側付属器摘出術、左側卵巣嚢腫摘出術を施行した。病理組織検査で右はステロイド細胞腫瘍、左は粘液性嚢胞腺腫と診断した。術後4日目はテストステロン値は正常範囲となり、術後3か月で脱毛など男性化徴候は軽快傾向を示した。【考察】選択的静脈血ホルモンサンプリングはホルモン産生腫瘍の局在を同定に有用と考えられた。

P-3-4 診断、治療に難重した尿管子宮内膜症より晩期発生したと考えられたSerous Cystadenofibroma-like Tumorの1例

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【目的】尿管子宮内膜症は全子宮内膜症の0.1%程度の発生率とされる。薬物療法、外科的治療を基本とするが、進展した場合、腎機能廃絶も危惧される。一方で漿液性嚢胞腺線維腫は上皮性および線維性間質成分を含む卵巣上皮腫瘍の比較的まれな良性の変異体である。画像上悪性腫瘍と酷似するため不必要な侵襲を避ける必要がある。今回尿管子宮内膜症に対して右腎尿管を摘出後、10年間の偽閉経療法、黄体ホルモン療法を経て同部位から発生したSerous Cystadenofibroma-like Tumorを経験したため報告する。【方法】症例は37歳時に右腎盂尿管移行部に尿管周囲の腫瘍進展による狭窄を認め、外科的に右腎尿管を摘出した。腫瘍病変は病理結果でEndometriosisと診断し、術後から偽閉経療法、黄体ホルモン療法を継続した。術後10年目に確認した精査で同手術部位から発生する悪性を示唆する腫瘍進展を認め、子宮内膜症より発生した悪性腫瘍と考え、組織学的探索のため試験開腹術の方針となった。【成績】腫瘍は右総腸骨から内外腸骨血管領域を巻き込むように発生しており、慎重な操作で腫瘍生検を行った。肉眼的には播種性病変はなく、腫瘍表面は平滑で異型血管も認めず、3箇所を生検を施行し術式終了とした。迅速病理は悪性所見を認めず、術後病理診断はSerous Cystadenofibroma-like Tumorであった。以後は黄体ホルモン療法を継続し、術後より現在までの腫瘍増悪は認めていない。【結論】Cystadenofibroma-like Tumorは画像上悪性腫瘍との鑑別が困難であるため、術中の肉眼的所見及び迅速病理所見での手術侵襲の程度を判断すること、永久標本確認後の二期的な外科的切除を考慮することが重要であると考えられた。

P-3-5 右付属器領域に発生した虫垂粘液性腫瘍の2例

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虫垂粘液性腫瘍は右卵巣腫瘍との鑑別が困難な場合がある。なかでも低異型度虫垂粘液性腫瘍 (Low-grade Appendiceal Mucinous Neoplasm, LAMN) は病理組織学的には腺腫だが浸潤性に虫垂外へ進展し、腹膜偽粘液腫の原因となるため慎重な取り扱いを要する。今回、右付属器と癒着があり、術前に卵巣腫瘍との鑑別が困難であった虫垂粘液性腫瘍の2症例を報告する。症例1は45歳女性。右下腹部痛があり、近医産婦人科、内科を受診したが卵巣腫瘍か虫垂炎か鑑別が困難で当科紹介。MRIで右付属器領域に5cm大の多房性嚢胞と腫大した虫垂が接して認められた。卵巣腫瘍としては典型的ではなく、右付属器膿瘍の虫垂癒着を疑い、腹腔鏡下手術を施行。術中、右卵巣に腫瘤を認め、虫垂腫瘍と癒着しており右付属器切除術、回盲部切除術を施行。病理組織検査ではLAMNの診断で、卵巣内にLAMNと同様の粘液貯留が認められた。症例2は74歳女性。右下腹部痛があり内科受診。虫垂炎の疑いでCT撮影したところ、右卵巣腫瘍が疑われ当科紹介。CTで6cm大の多房性嚢胞が認められ、虫垂は嚢胞内腔に連続し、右卵巣と一塊となっていると考えられた。虫垂炎の膿瘍形成、右卵巣へ波及の疑いで、腹腔鏡下手術を施行。右付属器から虫垂、盲腸まで強固に癒着した腫瘤病変が認められ、同部を一塊にして摘除。病理組織検査ではLAMNを背景に一部に高異型度成分を認め、虫垂粘液腫の診断となった。付属器浸潤はなかった。症例1, 2共に術前診断は困難であった。卵巣腫瘍として典型的な所見が認められず、正常な虫垂構造が見られない場合、虫垂粘液性腫瘍に留意し診療を行う必要があると考えられた。

P-3-6 両側水腎症とAGCを契機に胃癌子宮転移の診断に至った1例

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胃低分化型腺癌は若年女性に多く、高率にリンパ節転移や腹膜播種をきたし、遠隔転移を認める場合の5年生存率は7%未満と予後不良である。胃癌は卵巣、子宮へ転移することが知られている。今回両側水腎症のため婦人科受診し、AGCを契機に胃癌子宮転移の診断に至った症例を経験したため報告する。症例は57歳、2妊2産、既往歴、家族歴に特記事項なし。嘔気症状を主訴に近医内科受診され、腹部CT検査にて両側水腎症および腎機能障害 (BUN: 20.7mg/dl, Cr: 2.36mg/dl) を認めたため、原因検索目的に当院消化器内科、泌尿器科および産婦人科紹介受診となった。経膈超音波検査上、子宮内腔に子宮内膜ポリープを疑う腫瘤病変は認めしたが、子宮、卵巣ともに明らかな悪性を疑う病変は認めなかった。MRI検査にても子宮、卵巣に悪性を疑う所見は認めなかった。ダグラス窩に腹水を認め穿刺にて採取、細胞診はClassIであった。子宮頸部細胞診はAGC、コルボスコピーでは明確な病巣は認めなかったが、生検にて malignant neoplasm の診断であった。子宮体部細胞診はClassIII、子宮内膜組織検査では子宮頸部と同様の異型細胞を認めた。上部消化管内視鏡検査で胃癌を認め、審査腹腔鏡を行った。壁側腹膜全体に白色小結節病変を認め、左右卵管根部が硬く、尿管を巻き込んでいた。免疫組織学検査で子宮頸部の異型細胞および腹膜病変は胃癌と類似した異型細胞であり、胃癌の子宮転移との診断に至った。現在化学療法中である。水腎症を来す原因として婦人科悪性腫瘍を疑うが、本症例のように転移性腫瘍も念頭におくことが重要である。またAGCで明らかな病変が断定できない場合でも生検をしておくことで診断の一助となることを認識した。

P-3-7 ステロイド治療により子宮腫瘍が縮小し子宮サルコイドーシスと推定された一例

磐田市立総合病院

寺本麻友子, 趙 現, 川岡大才, 甲木哲也, 小田木秋人, 深田せり乃, 勝又佳菜, 徳永直樹

【緒言】サルコイドーシスは非乾酪性類上皮細胞肉芽腫を形成する原因不明の全身疾患であり、あらゆる臓器に病変を認める。主に肺、眼、心臓、皮膚、リンパ節などで病変を認めることが多く、女性生殖器のサルコイドーシスは稀である。今回腎臓や耳下腺とともに子宮に病変を認め、治療により縮小、子宮サルコイドーシスと推定された症例を経験したため報告する。【症例】51歳女性、1妊1産、既往歴特記事項なし。耳下腺腫脹精査のため当院耳鼻科を紹介受診。血液検査にてクレアチニンの上昇がみられたため、腎臓内科に紹介となった。血液検査で血清Cre 2.4mg/dL、可溶性インターロイキン2レセプターの上昇、アンジオテンシンI転換酵素の上昇あり、ガリウムシンチグラフィで耳下腺、両側腎臓、子宮腫瘍への集積を認めた。骨盤部MRI検査にて子宮筋層の肥厚及び腫瘤を認めた。腎生検にて類上皮細胞肉芽腫を伴う尿管管間質炎の病理所見を認め、以上によりサルコイドーシスの診断となった。腎障害のためサルコイドーシスの全身治療を優先し、プレドニゾン40mg内服を開始したところ、耳下腺腫大の縮小、腎機能障害の改善とともに子宮腫瘍も縮小した。病状の推移に合わせプレドニゾンは漸減、継続中であり、現在は7mg内服で安定している。更年期障害のためホルモン補充療法を施行しているが子宮腫瘍の増大はみられていない。【結論】全身治療により子宮腫瘍が縮小し、子宮サルコイドーシスと推定された症例を経験した。子宮病変がサルコイドーシスである確定はできなかったが組織診断がなされなくても、治療による臨床診断に至れば、手術を回避できる可能性が示唆された。

P-3-8 婦人科悪性腫瘍に対する当院での重粒子線治療の経験

山形大

榎 宏論, 佐野詩織, 郷内雄太, 堀川翔太, 奥井陽介, 清野 学, 太田 剛, 永瀬 智

【目的】当院には東北・北海道地区で初の重粒子線治療が2021年3月より稼働している。2023年4月には切除不能な子宮頸部腺癌が保険診療の、切除不能な子宮頸部扁平上皮癌や外陰部悪性黒色腫が先進医療の適応となり数例を経験した。加えて、転移性リンパ節腫瘍への適応として卵巣癌のリンパ節再発の治療例も経験した。今回は当院の重粒子線治療例に文献的考察を加え報告する。【方法】症例は子宮頸部腺癌が1例、子宮頸部扁平上皮癌が1例、卵巣癌の腹腔内リンパ節再発例が2例だった。現在、子宮頸部腺癌1例が治療中である。子宮頸部腺癌および扁平上皮癌では週1回のシスプラチン(40mg/m²)を併用した。【成績】1例が治療中にせん妄が増悪したため治療中止となった。治療を完遂した3例中2例では治療後半年以上経過も再発を認めていない。卵巣癌腹腔内リンパ節再発に対する治療の1例は、照射野内再発はないが、他のリンパ節に再発を生じ、現在化学療法中である。いずれの症例においても治療中Grade3以上の有害事象は認めなかった。【結論】既存の報告で、局所進行子宮頸部腺癌への同時化学重粒子線治療は、2年無増悪生存率84%と良好な治療成績が報告されている。また転移性リンパ節への治療成績は治療後2年の局所制御率、全生存率がそれぞれ85%、63%と良好な成績が報告されている。特にこれまで放射線治療抵抗性と言われた非扁平上皮癌や30mm以上の腫瘍径の症例でも良好な成績が報告されている。当院での治療例でも局所制御率は現在まで100%(3/3例)であり、良好な治療成績が得られている。以上より、局所進行子宮頸癌、さらに婦人科癌のリンパ節転移再発例に対しては重粒子線治療が選択肢として考慮されうる。

P-3-9 卵巣腫瘍茎捻転を発症したチトクローム P450 オキシドレダクターゼ異常症の11歳女児の一例

宮崎大

永井昌美, 後藤裕磨, 安永夏穂, 東真理恵, 吉本 望, 藤崎 碧, 平田 徹, 山口昌俊, 桂木真司

【背景】チトクローム P450 オキシドレダクターゼ異常症 (Cytochrome P450 Oxidoreductase Deficiency : PORD) はステロイド産生障害やアロマトラーゼ活性低下を伴う常染色体性遺伝疾患である。この疾患の女性ではゴナドトロピン過剰産生により若年で卵巣腫瘍を発症することがある。今回 PORD の11歳女児が卵巣腫瘍茎捻転を発症した症例を経験したので報告する。【症例】母体の本児妊娠中の男性化などの症状から1歳頃に PORD を疑われ、遺伝子検査で確定診断し、当院小児科で経過観察されていた。約3週間前に7cm大の右卵巣腫瘍を近医で指摘され、当科紹介となった。明らかな悪性所見なく緊急性は乏しいと判断され、画像精査の方針としていた。待機期間の夜間に腹痛を主訴に受診し、当初は便秘と診断され下剤を投与された。翌日排便後も症状が残存していたため、夜間再診した。造影CTで右卵巣腫瘍茎捻転・左卵巣腫瘍が疑われ、緊急腹腔鏡手術の方針とした。右付属器は8cm大に腫大して約180度捻転し、暗紫色の色調変化を認めた。捻転を解除後も血流が戻らないことを確認し、温存は困難と判断した。左卵巣に5cm大の左卵巣腫瘍を認めた。右付属器切除術・左卵巣腫瘍摘出術を施行した。病理組織診断では壊死のため正確な組織型は判明しなかったが、悪性所見は認めなかった。術後経過は良好であり、当科および小児科で経過観察中である。【結論】PORDの女性では、下腹部痛があれば低年齢でも積極的に卵巣腫瘍茎捻転を疑い、画像精査を行う必要があった。今回は付属器切除術を施行せざるを得なかったが、温存困難と考えられる卵巣であっても早期診断・治療介入で卵巣機能を維持できる可能性が示唆されている。

P-3-10 当科で経験した腔原発小細胞癌の一例

岐阜大

神田明日香, 早崎 容, 菊野享子, 坊本佳優, 桑山太郎, 村瀬紗姫, 古井辰郎, 磯部真倫

原発性腔癌は女性生殖器癌の1-3%程度と非常に稀な疾患であるが、中でも腔原発小細胞癌は極めて稀な疾患である。今回、腔原発小細胞癌と診断した1例を経験したので報告する。症例は、41歳3経妊2経産女性で、不正性器出血を主訴に近医を受診。子宮頸部に60mm大の腫瘍を認め、生検にてcarcinomaの診断で当科紹介となった。当院での生検では小細胞癌と診断された。造影MRIでは後腔円蓋に充満する60mm大のT2強調像で高信号腫瘍を認め、後唇発生の子宮頸癌との診断であった。明らかな傍組織浸潤は認めず、造影CTでも明らかな転移なく子宮頸癌IB3期として広汎子宮全摘、両側付属器摘出、骨盤内リンパ節郭清術を施行した。標本は肉眼的に子宮頸部と腫瘍の連続なく、術後病理結果にて腔原発小細胞癌I期と診断された。現在術後補助療法としてEP(エトポシド+シスプラチン)療法を行っている。極めて稀な疾患であり、報告数も少なく文献的考察を加えて発表する。

P-3-11 ライディッヒ細胞腫の1例

加古川中央市民病院

清水香陽子, 房 正規, 熊谷美咲, 中筋由紀子, 佐藤沙貴, 市橋さなえ, 西田友美, 宮本岳雄, 太田岳人

性索間質性腫瘍は卵巣腫瘍の約5%を占める。中でもセルトリ細胞腫は間質への分化のみを示す純粋型性索腫瘍であり、卵巣腫瘍の0.1%以下と非常にまれな腫瘍である。閉経後に発症することが多く、95%が片側性であり、ラインケ結晶を持つライディッヒ細胞が優勢な増生を示す良性腫瘍である。今回、我々はライディッヒ細胞腫の1例を経験したため、文献的考察を踏まえて報告する。症例は67歳、1経妊1経産。高血圧、高脂血症にて近医内科へ通院中であった。多毛、頭髮脱毛などの男性化徴候を認め、テストステロン5.88ng/mLと上昇を認めたため、当科紹介となった。経陰超音波では両側卵巣に明らかな腫大はなく、胸腹部CTにて両側卵巣に腫瘍は認めなかった。また、異所性を含め男性化副腎腫瘍を疑う所見は認めなかった。明らかな卵巣腫大を認めない場合にもホルモン産生腫瘍の可能性があることを説明したが、手術加療は希望されなかった。紹介元の内科にて経過観察としていたが、その後もテストステロンは上昇傾向が持続し、8.49ng/mLまで上昇を認め、70歳時に再度当科紹介となった。骨盤MRIにて拡散制限および早期濃染像を示す2cm大の結節を右卵巣に認め、副腎シンチグラフィでは明らかな病変は指摘できなかった。ホルモン産生卵巣腫瘍を疑い、腹腔鏡下両側付属器切除術を施行した。病理組織学的に右卵巣にライディッヒ細胞腫を認め、術後テストステロンは0.27ng/mLまで低下した。ライディッヒ細胞腫は小さな腫瘍として見つかることが多く、明らかな卵巣腫大を伴わない場合もライディッヒ細胞腫を鑑別に挙げるのが重要である。

P-3-12 Pagetoid spread を呈した外陰部腺癌の1例

九州労災病院

梶尾 悠, 西村和朗, 和田 環, 土岐尚之, 鏡 誠治

【緒言】Pagetoid spread は、皮膚に隣接する臓器の癌が上皮内を移動して表皮に進展し、Paget 病様の組織像を呈する稀な病態である。直腸や肛門管の腺癌が由来になることが報告されているが、外陰部原発の報告はほとんどない。今回外陰部原発と診断した Pagetoid spread を呈した外陰部腺癌を経験したので報告する。【症例】84歳女性、3妊3産。既往歴としてアルツハイマー型認知症、高血圧、2型糖尿病、骨粗鬆症がある。家族が右外陰部腫瘍に気づき、当科を受診した。右外陰部に5cm大の隆起性腫瘍があり、病理結果は Paget 細胞がシート状に集塊し、一部非腫瘍性扁平上皮内にも小胞巣状に散在性に進展する所見を認めた。免疫組織化学染色ではCK20、CK7は陽性、CDX2は陰性であることから、乳房外 Paget 病ではなく、Pagetoid spread を示唆する所見だった。腫瘍マーカーは、CEA 2.6 ng/ml、SCC 3.2 ng/ml だった。造影CT検査では右外陰部腫瘍、右鼠径および腹部大動脈周囲のリンパ節腫大を認めた。肛門や直腸、尿路に病変は認めず、外陰部原発腺癌のリンパ節転移と診断した。年齢、認知機能から治療は困難であると判断し、緩和ケアの方針となった。【結語】Pagetoid spread を呈した外陰部腺癌は極めて稀であり、ほとんど報告がない。文献的考察を含めて報告する。

P-3-13 経過観察中に自然軽快した広汎性卵巣浮腫の2症例

札幌医大

馬場 剛, 遠藤俊明, 新開翔太, 真里谷葵, 染谷真行, 森下美幸, 岩崎雅宏, 石岡伸一, 齋藤 豪

【緒言】広汎性卵巣浮腫 (Massive Ovarian Edema: MOE) は間質浮腫により卵巣腫大をきたす稀な非腫瘍性疾患である。多くの症例は腹痛と腫大した卵巣を契機に発見され、卵巣茎捻転や組織学的診断のため付属器摘出術か卵巣部分切除術が行われている。一方、ごく一部の症例は手術による腹腔内観察と対症療法で管理されている。今回我々は、待機的な経過観察のみで自然に卵巣腫大が改善した MOE と考えられる2症例を経験したので報告する。【症例1】48歳、2妊2産。過多月経のため LNG-IUS を使用中。経陰超音波断層法で、6か月前の定期健診では異常を指摘されていなかった右卵巣に51×41mmの多房性のう胞性病変を認めた。なお、疼痛等の症状はなかった。MRIでの精査でも同様の所見だが悪性を示唆する所見に乏しく経過観察の方針とした。3か月後には卵巣腫大が40×30mmに縮小、4か月後には正常大に復した。【症例2】35歳、1妊1産。右下腹部痛が出現し受診。翌日時点で右卵巣が79×41mmに腫大していた。非ステロイド性抗炎症薬で疼痛が軽減したため経過観察の方針とし、1か月後の時点で56×46mm、3か月後には22×22mm、6か月後の時点で卵巣腫大の消失が確認された。【考察】MOEの成因は部分的・間欠的な卵巣茎捻転により静脈・リンパ還流が阻害されることが最も有力な仮説とされるが不明な点が多い。そのため標準的な治療法は確立されておらず、若年者に多い疾患であることも考慮するとより低侵襲的で妊孕性への影響が小さい治療法が望まれる。【結論】MOEの診療においては、腹痛などの随伴症状の程度によっては保存的経過観察も選択肢となり得る。

P-3-14 子宮腺筋症より発生した未分化子宮肉腫の1例：子宮腺筋症の悪性化リスクの考察

諏訪赤十字病院

長井友邦, 吉池奏人, 高野宏太, 森川めぐみ, 高木 緑, 戸田文香, 高木 靖

子宮腺筋症を起源として発生した子宮内膜間質肉腫 (ESS) の報告は非常に少ない。今回、腺筋症を背景に未分化子宮肉腫 (UUS) を発症し全身多発転移をきたした1例を経験した。症例は62歳, 4妊4産, 閉経54歳。腹部膨満感, 腹痛, 排尿障害を主訴に前医を受診し当科紹介となった。MRIではT2強調像で不均一な高信号, T1強調像にて低信号主体で淡い高信号を有する子宮腫瘍を認め, PET-CTでは同腫瘍と後腹膜リンパ節, 両側副腎, 左肺, 胸郭, 骨盤骨に異常集積が認められた。子宮内膜細胞診はATEC-US (class 3), 子宮内膜組織診では肉腫への分化を示す悪性腫瘍の所見を認め, LDHは816 U/Lであった。診断目的で単純子宮全摘術, 両側付属器摘出術, 大網部分切除術, 骨盤リンパ節生検を施行した。病理組織検査ではUUSの背景に腺筋症を認め, 腺筋症の間質と腫瘍とに連続性があったことから, 腺筋症を母地として発生したUUSと考えられた。術後はドキソルビシン療法を施行するもPDで, その後がん遺伝子パネル検査でTMB-Highが判明しペムプロリズマブ療法を施行したがPDとなり, 術後9か月で原病死した。ESSは子宮内膜症との関連が示唆されているが, 腺筋症由来の高異型度子宮内膜間質肉腫 (HG-ESS) およびUUSの報告例は極めて希少である。HG-ESS/UUSは閉経後に多く, 不正性器出血や下腹部痛を示す。一方で, 腺筋症の悪性化 (子宮体痛なども含む) は不正出血が少なく早期診断が難しい。腺筋症は閉経を期にフォローを終了することも多いが, 稀に悪性化することを念頭に置く必要がある。特に, 不正性器出血がなくても下腹部痛や腫瘍マーカーの上昇を認める症例には注意を要する。

P-4-1 正常妊婦における腔内細菌叢の日内変動についての研究

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【目的】周産期疾患に関連する16S rRNA 遺伝子配列解析を用いた妊婦の腔内細菌叢の研究が多く行われている。近年、腸管や口腔内の細菌叢に日内変動があることが報告されているが、妊婦の腔内細菌叢の日内変動についての研究はまだ行われていない。我々は正常な妊娠経過の妊婦における腔内細菌叢とその日内変動について調べた。【方法】本研究は、本学の倫理委員会の承認を得た(UOEHCRB21-087)。妊娠経過に異常を認めない妊婦から1日3回、昼間、就寝前、起床後に腔分泌物を採取した。2名については3日間連続で検体を採取した。腔分泌物1gあたりの総細菌数、グラム染色によるNugentスコアの評価およびクローンライブラリ法による16S rRNA 遺伝子配列を用いた細菌叢解析を行った。【成績】16名の妊婦から計60検体を採取した。検体採取時と分娩時の妊娠週数中央値はともに妊娠38週であった。腔分泌物中の細菌数は日中、就寝前、起床後で有意差はなかった。Nugentスコアで正常であった妊婦では腔内細菌叢の日内変動はみられなかったが、Nugentスコア中間群以上では日内変動を認めた。変動のある細菌叢においては一貫して就寝前に早産に関連すると報告されている嫌気性菌の割合が低下していた。菌叢の変動に主に関連していた嫌気性菌は *Atopobium vaginae* と *Sneathia sanguinegens* であった。【結論】Lactobacillus 種優勢の多様性の低い腔内細菌叢では日内変動は認めないが、多様性の高い菌叢においては日内変動を認めた。1日以内の短時間で菌叢が変動することは異常な腔内細菌叢の指標となる可能性があり、今回の研究に加えて異常妊娠経過の妊婦における腔内細菌叢の日内変動についても調査する必要がある。

P-4-2 胎盤オルガノイド (ミニ胎盤) を用いた糖代謝異常のメタボローム解析

大分大

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【目的】生体内組織や臓器にきわめて似ている3D培養システムは分化した組織の複雑な空間的パターンを再現でき、生理学的機能の解析に有用である。これまで他臓器の開発に比べて胎盤の組織モデルが存在しなかった。われわれは胎盤オルガノイド (ミニ胎盤) の樹立を行い、モデルとしての有用性について検討した。【方法】当院で中絶もしくは出産時の胎盤組織を対象とした。独自の手法によりマトリゲル内で単一多機能幹細胞より細胞性栄養膜細胞、合胞体栄養膜細胞構造を再構築できる条件を開発 (特願2023-67387, 特願2023-67391) し、免疫組織学的に再構築を確認した。グルコース負荷 (0~40μM) の糖代謝を時間依存的に網羅的メタボローム解析にてその変動を統計学的に検討した (本学倫理委員会承認研究)。【成績】3D-免疫組織学的検討により胎盤オルガノイドをITGA6 (細胞性栄養膜細胞), Syndecan (合胞体栄養膜細胞) のマーカー抗体でオリジナルの絨毛組織と比較して2層構造が反転して再構築されることが確認された。グルコース負荷で代謝産物のメタボローム解析 (多変量解析) を行ったところ濃度ごとに時間依存性に同一のクラスター化 (n=3) を示すことを確認した。さらにMetaboAnalystによる解析でグルコース濃度による糖代謝経路の変動を同定した。【結論】今回、3D培養システムとしてのミニ胎盤の樹立に成功した。われわれの知る限り国内での報告はなく、英国グループ (Turco et al.Nature.2018) の報告のみである。また代謝産物の解析により組織的な機能を保持することを初めて報告した。このミニ胎盤を活用することによりこれまでの細胞レベルの研究から組織レベルでの胎盤研究が可能となることが十分期待できる。

P-4-3 妊娠による母体の体重変化が次回以降の妊娠分娩転帰に与える影響の検討

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【目的】日本人女性を対象に、妊娠による母体の体重変化が次回以降の妊娠分娩転帰に与える影響を検討する。【方法】2000年から2022年に当院で分娩した女性のうち、初回と2回目の妊娠がともに単胎妊娠であった2861例を対象とした。初回の妊娠前body mass index (BMI)と2回目の妊娠前BMIが1単位以上低下した女性または1単位以上増加した女性の2回目の妊娠における妊娠分娩転帰をBMIの変化が1~1単位であった女性の妊娠分娩転帰と比較した。【成績】初回の妊娠から2回目の妊娠までにBMIが1単位以上増加した女性では、2回目の妊娠における妊娠糖尿病(GDM)の発症リスクの上昇(調整オッズ比[aOR] 1.51, 95%信頼区間[CI] 1.18-1.95)およびlarge for gestational age (LGA)児の出産リスクの上昇(aOR 1.67, 95%CI 1.15-2.42)を認めたが、妊娠37週以前の早産のリスクは低下した(aOR 0.66, 95%CI 0.46-0.95)。初回の妊娠から2回目の妊娠までにBMIが1単位以上減少した女性では、2回目の妊娠におけるGDMの発症リスクの低下を認めた(aOR 0.51, 95%CI 0.31-0.85)。また、初回の妊娠前BMIによって3群に分けたサブグループ解析では、初回の妊娠前BMIが25以上の肥満女性においては、初回の妊娠から2回目の妊娠までにBMIを1単位以上減少することで、2回目の妊娠におけるGDMの発症リスクが著明に低下していた(aOR 0.33, 95%CI 0.12-0.88)。【結論】上記の結果は、プレコンセプションケアの一環として初回の妊娠から2回目の妊娠の間の体重管理が重要であることを示している。従って、初回の分娩を終えた女性が今後も妊娠を考えている場合には、健康的な体重を維持することの重要性を伝える必要がある。

P-4-4 切迫早産患者に maintenance tocolysis は必要か?

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【目的】本邦では長年、切迫早産に対し、子宮収縮抑制剤投与による初期治療(acute tocolysis: AT)開始後48時間以降に子宮収縮が治まっても薬剤投与を継続する maintenance tocolysis (MT)が広く用いられてきたが、近年、不要なMTを回避しようとする風潮がある。当科でも2022年6月以降、AT開始48時間以降に切迫早産徴候が改善しない症例のみMTを行う targeted maintenance tocolysis (tMT)を導入した。tMT導入前後で分娩結等に差があるかを検討した。【方法】2021年3月から2023年8月に、切迫早産と診断されて入院し、子宮収縮抑制剤を48時間以上点滴投与した患者のうち、当院で分娩した単胎症例60例を対象とした。前置・低置胎盤、常位胎盤早期剝離、胎児機能不全、妊娠高血圧症候群は除外した。universalにMTを行っていたuMT群(〜2022年5月)、tMT導入後(2022年6月〜)のtMT群の2群に分け、分娩転帰等について後方視的に比較検討した。【成績】uMT群34例、tMT群26例であった。入院時週数は2群間で差を認めなかったが(uMT群 vs tMT群: 28.1 [22.6-34.3] 週 vs 26.6 [22.0-35.0] 週, p=0.7)、子宮収縮抑制剤点滴期間は、uMT群に比しtMT群で有意に短かった(32.0 [3-92] H vs 15.5 [4-68] H, p<0.01)。一方、分娩週数(35.8 [24.4-40.3] 週 vs 35.4 [25.9-39.7] 週, p=0.4)、ならびに、37週未満早産率(55.9% vs 65.7%, p=0.6)について2群間に差を認めなかった。また、tMT群において初回治療後に再入院または点滴再開を要した再発症例は2例(7.7%)であった。【結論】tMT導入により子宮収縮抑制剤点滴期間は有意に短縮したが、早産率は増加しなかった。切迫早産全例に対するMTは不要であると考えられた。

P-4-5 重症妊娠悪阻における Helicobacter pylori 感染による入院長期化予測の検討

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【目的】重症妊娠悪阻は、その発症と *Helicobacter pylori* (*H.pylori*) 感染との関連の報告が散見されるが、明確なエビデンスはまだ得られていない。重症妊娠悪阻で入院を要した症例において、抗 *H.pylori* IgG 陽性が重症妊娠悪阻の症状の遷延・重症化に与える影響を明らかにすることを目的とした。【方法】2011年1月から2023年6月に当施設(多施設)で重症妊娠悪阻のため入院し、抗 *H.pylori* IgG を測定した単胎妊娠の164例を対象とした。診療録を用いて後方視的に検討し、解析を行った。統計学的解析は、Mann-Whitney U 検定、Fisher の正確検定、ロジスティック回帰分析を用い、p<0.05 を有意差有りとした。本研究は倫理委員会の承認を得て行った。【成績】164症例のうち、抗 *H.pylori* IgG 陽性は23例、陰性は141例であった。2群間で年齢、経産、生殖補助医療、BMI、甲状腺機能、血清hCG値、尿ケトン定性、入院時および退院時の Emesis Index に差は認めなかった。抗 *H.pylori* IgG 陽性群は陰性群と比較して入院日数が有意に延長した(p=0.0318)。また、21日間以上の入院を要した症例では、リスク因子としてがFT4(p=0.0276)、尿ケトン定性(p=0.0178)、抗 *H.pylori* IgG 陽性(p=0.0251)であり、多変量解析でも抗 *H.pylori* IgG 陽性が独立したリスク因子であった(p=0.004)。【結論】抗 *H.pylori* IgG 陽性が重症妊娠悪阻の症状遷延、21日以上入院期間延長のリスク因子となることが示唆された。

P-4-6 双胎間輸血症候群を発生した双胎妊娠における母体循環動態の検討

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【目的】双胎妊娠は周産期心筋症のリスク因子であり、子宮の増大は下大静脈の圧迫による静脈還流量の低下に繋がる。双胎間輸血症候群(TTTS)の羊水過多による子宮の著明な増大やTTTS自体の母体循環への影響に関しては明らかにされていない。今回、TTTS発症時の母体循環の変化を検討した。【方法】2022年10月から2023年3月までに当院に通院した妊婦54例を対象とした。単胎妊娠群(単胎群)、合併症のない絨毛膜二羊膜(MD)双胎妊娠(nMD群)、TTTS発症例(TTTS群)の3群に分け、母体心臓超音波検査を施行し、左室情報、左室収縮能・拡張能及び下大静脈径を評価した。本研究は当院の倫理委員会の承認の下、同意を得て行なった。【成績】単胎群は28例、nMD群は12例、TTTS群は12例であった。TTTS群・単胎群はnMD群と比較し、左室収縮率(ejection fraction: EF)及び左室内径短縮率(fractional shortening: FS)が有意に上昇した(EF: nMD vs TTTS: $p=0.015$, 単体 vs nMD: $p=0.005$, FS: nMD vs TTTS: $p=0.026$, 単体 vs nMD: $p=0.013$)。TTTS群はnMD群と比較し、左室収縮末期容積(end-systolic volume: ESV)が有意に小さかった($p=0.047$)。TTTS群と単胎群は全項目で有意差を認めなかった。一回心拍出量(stroke volume: SV)や心拍出量(cardiac output: CO)、心拍数(heart rate: HR)は3群間に有意差を認めなかった。【結論】MD双胎妊娠では単胎妊娠よりも循環血液量が増加しているため、SVを一定に保つために、合併症のないMD双胎妊娠でも単胎妊娠よりもEFやFSが低下していた可能性が考えられた。一方、TTTSを発生したMD双胎妊娠では、血管透過性の上昇などを伴うため、合併症のないMD双胎妊娠と比較しEFやFSが上昇していた可能性が考えられた。

P-4-7 前置胎盤における子宮内遺残物(RPOC)の危険因子や産褥出血との関連に関する検討

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【目的】子宮内遺残物(retained products of conception: RPOC)は、しばしば分娩後の大量出血(severe postpartum hemorrhage: severe PPH)を引き起こすことがあるが、前置胎盤症例におけるRPOCの臨床的特徴については不明な点が多い。今回当院の前置胎盤症例におけるRPOC発生の危険因子およびRPOCとsevere PPHとの関係について解析を行った。【方法】2004年1月から2021年12月の間に、当院で前置胎盤に対し帝王切開術を行い、胎盤が剝離された単胎妊婦を対象とし、後方視的に検討した。RPOCは、分娩後に子宮内に遺残した絨毛由来組織と定義されており、超音波・造影CTまたは造影MRIで診断した。【成績】対象者は335人で、RPOCを発生した症例(RPOC群)は24例(7.2%)で、既往帝王切開後妊娠(Odds ratio (OR) 5.98, $p<0.01$)、major previa(全前置胎盤および部分前置胎盤)(OR 3.15, $p<0.01$)、癒着胎盤(PAS)(OR 92.70, $p<0.01$)の頻度が高かった。また、多変量解析の結果、既往帝王切開後妊娠(OR 10.70, $p<0.01$)とPAS(OR 140.32, $p<0.01$)がRPOCの独立危険因子であった。Severe PPH発生群は、RPOCを合併した症例(58.3% vs 4.5%; $p<0.01$)、既往帝王切開後妊娠(OR 9.23, $p<0.01$)、major previa(OR 11.35, $p<0.01$)、胎盤前壁付着(OR 3.44, $p=0.01$)、PAS(OR 16.47, $p<0.01$)の症例が有意に多かった。Severe PPH発症に対する多変量解析では、既往帝王切開後妊娠(OR 4.71, $p=0.02$)、major previa(OR 7.50, $p<0.01$)に加えてRPOC(OR 13.26, $p<0.01$)が独立危険因子であった。【結論】前置胎盤におけるRPOCの危険因子として、既往帝王切開術とPASが同定された。また、RPOCはsevere PPHと関連性があり、前置胎盤におけるRPOCに対する新たな戦略が必要である。

P-4-8 小型モバイル分娩監視装置での在宅モニタリングを併用したハイリスク妊娠管理の実現可能性調査

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【目的】切迫早産か胎児発育不全の診断を受けた妊婦において、在宅で妊婦が小型モバイルCTGを装着し医師がデータを評価するシステムの実現可能性調査を実施した。【方法】研究は、日本産婦人科医会情報技術部会のプロジェクトとして、メロディ・インターナショナル社の小型モバイルCTG(iCTG)を用い、大学病院10施設で実施した。28週以降の単胎妊婦で、切迫早産(頸管長25mm未満か性器出血のあった症例)か胎児発育不全(推定児体重-1.5SD以下)の診断例を対象とした。iCTGを対象者に貸与し、週1回以上40分以上の装着を指示した。データは担当医がリアルタイムに確認し、医学的対応が必要と判断した際には対象者へ電話連絡した。対象者には、研究終了時に質問紙でアンケート調査を実施した。【成績】33例(切迫早産20例、胎児発育不全15例、重複2例)が対象となった。研究開始時週数は、切迫早産 31.5 ± 2.3 週と胎児発育不全 31.1 ± 3.0 週で、データ取得期間はそれぞれ 25.8 ± 17.9 日、 38.0 ± 21.9 日であった。2例(2/33: 6.6%)で電話対応を行ったが、受診は要さなかった。切迫早産の6例(30%)はデータ取得期間に入院し2例が自然早産となり、他14例は満期産であった。胎児発育不全の3例(20%)はデータ取得期間に入院し、1例がNRFSで30週に、1例が常位胎盤早期剝離で33週に緊急帝王切開を要した。アンケート回答率は97.0%(32/33)で、27例(84.3%)が入院管理よりCTG在宅モニタリングを併用した外来通院を希望した。【結論】CTG在宅モニタリングを併用したハイリスク妊娠管理は、対象の適切な選択下で安全に実施でき、妊婦のニーズが高いと考える。本研究を継続し、システム構築の基礎データを収集予定である。

P-4-9 当院における PGT-A 後妊娠の周産期合併症発症についての検討

杏林大

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【目的】本邦では反復着床不全、習慣流産症例に対して着床前胚染色体異数性検査 (PGT-A) が生殖補助医療 (ART) における選択肢の一つとして行われており、出産例も増加している。PGT-A 後妊娠については早産、妊娠高血圧症候群 (HDP)、臍帯の附着部異常の頻度が高くなるという報告があるが、これらの妊娠合併症は ART による妊娠、母体年齢の上昇に伴って頻度が高くなるとされており、症例の蓄積が必要とされている。今回、当院で管理した PGT-A 後妊娠例 (PGT-A 群) の周産期合併症発症について、同時期に当院で管理した凍結胚盤胞移植後の妊娠例 (ART 群) と比較し検討した。【方法】2021 年 1 月から 2023 年 6 月までの 30 か月間に当院で管理した妊娠症例を対象とし、診療録から後方視的に検討した。検定には Mann-Whitney U 検定、Fisher の正確検定を用いた。【成績】期間内の PGT-A 群は 15 例 (A 判定 14 例, B 判定 1 例)、ART 群は 170 例であった。母体年齢中央値はそれぞれ 41 (37-46) 歳, 38 (28-45) 歳で有意差を認めた ($p < 0.05$)。早産数 (オッズ比 1.30 : 95% 信頼区間 0.13-6.49)、妊娠高血圧症候群 (1.65 : 0.03-14.53)、妊娠糖尿病 (1.51 : 0.26-6.22)、前置胎盤 (0 : 0.7-0.2)、臍帯附着部異常 (1.67 : 0.36-6.14) でいずれも両群間に有意差は認めなかった。【結論】今回の検討では母体年齢のみに有意差を認めたが周産期合併症の発症に関しては差を認めず、従来からの凍結胚細胞移植後の妊娠として管理する事で問題ないと思われた。しかし凍結胚細胞移植後の妊娠がハイリスク妊娠に相当し、嚴重な周産期管理は必要であると思われた。更なる症例の蓄積が必要と考える。

P-4-10 REMS 法を用いた超音波骨密度測定装置で測定した妊娠初期骨密度に影響を与える因子の検討

慶應義塾大

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【目的】妊娠中は胎児骨形成のためカルシウム需要が増加し、骨密度は低下する。妊娠初期に骨密度が低い場合はさらに低下するため、妊娠中や産後の骨粗鬆症や脆弱性骨折のリスクが増大する。今回我々は Radiofrequency Echographic Multi Spectrometry (REMS 法) を用いた新たな超音波骨密度測定装置 (EchoS システム) を用いて測定した妊娠初期骨密度に影響を与える因子について検討した。【方法】対象は 2023 年 1 月 1 日から 9 月 13 日に当院を受診した妊娠 9~16 週の妊婦 47 人である。EchoS システムを用いて右大腿骨頸部の骨密度推定値 (eBMD) を測定後、積率相関係数および重回帰分析を用いて母体年齢、分娩回数、妊娠週数、身長、非妊娠時 BMI、乳製品摂取量から算出した摂取カルシウム量と eBMD との関連を解析した。【成績】対象者の年齢は 34.68 ± 4.58 歳 (平均 \pm 標準偏差)、測定時妊娠週数は 13.77 ± 1.32 週、eBMD は $0.68 \pm 0.06 \text{g/cm}^2$ であった。eBMD と各項目の相関関係を解析したところ、年齢 ($r = -0.29$, $p = 0.04$)、身長 ($r = 0.32$, $p = 0.03$)、非妊娠時 BMI ($r = 0.83$, $p < 0.01$)、摂取カルシウム量 ($r = 0.32$, $p = 0.03$) が eBMD と有意に相関した。また、重回帰分析でも同様に、年齢 (標準偏回帰係数 $\beta = -0.39$, $p < 0.01$)、身長 ($\beta = 0.34$, $p < 0.01$)、非妊娠時 BMI ($\beta = 0.84$, $p < 0.01$)、摂取カルシウム量 ($\beta = 0.09$, $p = 0.03$) と有意な関連を認めた。また、 β 値より非妊娠時 BMI が eBMD に最も影響を与えることが判明した。【結論】妊娠初期骨密度に関連する因子を検討したところ、妊娠前の低 BMI や乳製品摂取不足は妊娠初期の低骨密度と関連することが明らかとなった。

P-4-11 母体眼窩血流評価における Maternal Orbital Vascular Sonobiopsy (MOVS) の再現性に関する検討三宅医院¹, 三宅医院間屋町テラス², 三宅おおふくクリニック³, 香川大⁴高吉理子^{1,4}, 秦 利之^{1,4}, 佐野力哉³, 伊藤 綾¹, 酒本あい¹, 清川麻知子¹, 小田隆司¹, 小國信嗣², 橋本 雅¹, 宮木康成³, 三宅貴仁^{1,2,3,4}, 金西賢治⁴

【目的】超音波 3D パワードブラを用いた Placental Vascular Sonobiopsy は、胎盤の血液灌流の評価に用いられている。今回我々は、新しく母体眼窩血流計測のための maternal Orbital Vascular Sonobiopsy (MOVS) を考案した。本研究では、MOVS の再現性を検討することを目的とした。【方法】妊娠 25~40 週の正常妊婦 9 例 18 眼, GDM 妊婦 10 例 20 眼を対象とし、3D パワードブラによる VOCAL histogram analysis を用いて、vascularization index (VI), flow index (FI), vascularization flow index (VFI) を計測し、その検者内、検者間の再現性について、Bland-Altman test と correlation coefficient を用いて検討した。Pulse repetition frequency : 0.9 kHz, wall motion filter : low, Thermal Index : 0.3 or 0.4, Mechanical Index : 0.8-1.1 の設定で検査を行い、検査時間は 1 分以内であった (一つの volume の acquisition time は 5 秒)。【成績】VI, FI, VFI の検者間及び検者内の平均差と 95% 一致率は、それぞれ 0.0803 (7.3417, -7.1810) % と -0.6823 (10.8095, -12.1742) %, -0.4816 (6.0624, -7.0256) % と 0 (9.0746, -8.8384) %, 0.0058 (2.6937, -2.6821) % と -0.2892 (3.8910, -4.4694) % であった。検者内の VI, FI, VFI の相関係数は、0.9749, 0.8882, 0.9704 であり、良好な相関を示した。検者間の VI, FI, VFI の相関係数も、0.9364, 0.7832, 0.9214 と、良好な相関を示した。【結論】MOVS は再現性が良好であり、母体眼窩血流を評価する新しいパラメーターとなり得る可能性が示された。今後、妊娠高血圧症候群、白衣高血圧における母体循環に及ぼす影響などについて検討を行ってきたい。

P-4-12 COVID19 陽性妊婦の罹患後症状調査

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【目的】新型コロナウイルス（以下、COVID19）の世界的パンデミックが始り、4年が経過した。当初は知識経験も乏しくその対応に苦慮したが、現在その特徴や治療法については様々な知見が得られてきた。妊娠についても国内外から多数の情報が揃いつつあり、日常診療へと活かされてきている。しかしながら、そういった状況下においても妊産婦の罹患後症状については殆ど情報がない。咳・痰などの感冒症状のみならず、抑うつ、睡眠障害、疲労、倦怠感など症状は多岐にわたるが、肉体的精神的にも負荷が強い産後育児への影響はどうだろう。この度我々はこの点に着目し、アンケート調査を行う事とした。福井県における陽性妊婦の罹患後症状について、明らかになった事を報告する。【方法】当院で入院管理を行った COVID19 陽性妊婦 94 名に対し調査票を郵送しアンケートとして回答いただいた。主な調査項目として、感染した時期、感染した妊娠週数、ワクチン接種の有無、罹患後症状の有無、授乳方法、EPDS 点数（電子カルテより）、について集計し、統計学的解析を試みた。【成績】アンケート回収数は 43 名、回収率は 45% だった。2.3 か月以上症状が持続した場合罹患後症状ありとしたところ、6 名が該当した。ワクチン接種による罹患後症状の影響、授乳状況の変化については明らかな影響は確認できなかった。EPDS 値の変化も有意差は認めないもののある程度の傾向はうかがえた。【結論】過去に情報の無い妊婦の罹患後症状について調査を行った。リミテーションも多く、いずれにおいても有意といえるものにはならなかった。正確な知識を得るために、より広範で精細な情報が得られるよう求めたい。

P-4-13 新生児腎体積に影響する周産期因子について

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【目的】近年、慢性腎疾患の罹患率が上昇しているが、その背景に低出生体重児など周産期からの関連が指摘されている。本研究では解剖学的変化としての新生児腎体積を調査し、妊娠中の母体の栄養状態・生活習慣などの周産期因子との関連について検討した。【方法】2023 年 4 月から 2023 年 9 月に当院で出産した産婦のうち同意のあった妊婦 31 例を対象とした。早産例、先天性疾患例を除外した。妊娠 12 週から 16 週にフィブロスキャン (CAP, E 値), in body 測定, 尿中バイオピリンの測定を行った。分娩後に超音波断層像を用いて新生児腎体積測定を行った。妊娠期間中の母体情報 (年齢, BMI, 不妊治療の有無, GDM の有無, 飲酒・喫煙の有無, 葉酸摂取の有無, CAP, E 値, 産科合併症の有無, 妊娠期間中の体重増加, 妊娠第 1 三半期の筋肉率, 筋肉量, 体脂肪率, 体脂肪量), 新生児情報 (分娩週数, 出生体重, 出生身長, 性別) を集積し, 新生児腎体積との関連を調査した。【成績】対象は合計 31 例のうち 5 例を除外した 26 例で検討を行った。母体年齢, BMI, 産科合併症の有無, 筋肉率, 体脂肪率, CAP, E 値と新生児腎体積との関連で有意なものも認めなかったが, 妊娠期間中の体重増加率が大きいほど新生児腎体積が大きい傾向にあった。【結論】新生児腎体積と母の妊娠期間中の体重増加率の関連について有意な関連は認められなかったが, 本研究では症例数が少なく, 今後さらに検討を重ねることで明らかな関連となる可能性が示唆された。今後は更なる症例の集積と再検討を行っていく。

P-4-14 当院における TOLAC 症例の検討

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【目的】当院では、医学的条件を満たした既往 1 回帝王切開後妊婦に対し、患者の同意を得た場合に TOLAC を施行しておりこれまで多数例を扱ってきた。今回、成功率や安全性などについて検討した。【方法】2013 年 1 月から 2022 年 12 月に当院で分娩管理を行なった既往 1 回帝王切開妊娠例のうち、TOLAC 症例を対象とした。なお、早産、多胎、胎児異常、死産、2 回以上の子宮手術既往については除外した。TOLAC 成功 (VBAC) 群と TOLAC 不成功で緊急帝王切開に至った (emCS) 群の 2 群に分け、母体年齢、在胎週数、出血量、児の出生体重、Apgar score、臍帯血 pH、VBAC 歴の有無について診療録を用いて後方視的に検討した。【成績】TOLAC 例は 2033 例、VBAC 群は 1583 例 (77.9%)、emCS 群は 437 例 (22.1%) であった。緊急帝王切開術を行った場合の手術適応の内訳は、微弱陣痛 200 例 (45.8%)、胎児機能不全 72 例 (16.5%)、前期破水 41 例 (9.4%)、その他は妊娠高血圧症、回旋異常などであった。子宮破裂は 5 例で全 TOLAC のうち 0.2% で認めたが、母体死亡、子宮全摘、新生児死亡に至った例はなかった。VBAC 群と emCS 群における分娩時の年齢 (歳) は 34.9 vs 35.5、在胎週数 (週) は 38.7 vs 39.0、出血量 (ml) は 476 vs 452、児の出生体重 (g) は 3028 vs 3144、Apgar score1 分値は 8.7 vs 8.0、5 分値は 9.7 vs 9.1、臍帯血 pH は 7.29 vs 7.28 だった。VBAC 歴を有する 292 例のうち 277 例 (94.9%) が再度 VBAC に至った。【結論】VBAC 群と emCS 群で分娩転帰に有意な差はなく、子宮破裂例を少数認めたが母児の重篤な合併症の発生はなかった。緊急時に迅速に対応できる体制のもとであれば安全に施行できると考えられる。TOLAC 成功因子として VBAC 歴が挙げられる。

P-5-1 妊娠および女性ホルモン剤関連静脈血栓塞栓症患者における候補遺伝子パネルを用いた解析結果の検討

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【目的】妊娠および女性ホルモン剤と関連して発症する静脈血栓塞栓症 (VTE) の誘因の一つに、血液凝固制御因子であるアンチトロンビン (AT), プロテイン C (PC), プロテイン S (PS) の先天的欠乏が挙げられる。通常これらの遺伝性血栓性素因は活性値と抗原量から診断されるが、妊娠、女性ホルモン剤や抗凝固薬などの影響を受け、診断に苦慮することも多い。我々は VTE 候補遺伝子パネルを作成している。このパネルによる解析結果と臨床情報を照合し、診断精度について検討することを目的とした。【方法】対象は、妊娠および女性ホルモン剤内服と関連して発症した VTE 患者で、遺伝性血栓性素因を疑った 9 症例である。試料は、血液から抽出した DNA を用いた。AT, PC, PS, プロトロンビン, FV などの遺伝子を 29 含む VTE 候補遺伝子パネルで解析し、臨床情報と照合し検討した。【成績】9 症例中 4 例に合計 5 個の病的バリエントを同定した。内訳は、AT (*SERPINC1* 遺伝子) にナンセンスバリエント, PC (*PROC* 遺伝子) にナンセンスおよびミスセンスバリエント, PS (*PROSI* 遺伝子) にミスセンスバリエント 2 個である。1 例は *PROC* と *PROSI* のダブルヘテロを同定した。しかし、活性値等から遺伝性血栓性素因が強く疑われるも、バリエント非検出となった症例を 2 例認めた。【結論】今回の解析では、VTE 候補遺伝子パネルでの同定率は 44% (4/9) であった。ダブルヘテロも 1 例に認め、候補遺伝子を一度に解析できるメリットがある。しかし、本法でも検出不可能なバリエントもあると考えられるため、さらなる解析方法の検討が必要である。

P-5-2 当院の妊娠糖尿病 (gestational diabetes mellitus ; GDM) 患者の分娩前 (妊娠後期) の血清を用いた miRNA 解析

防衛医大

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【目的】miRNA は多くの遺伝子や蛋白質の発現制御に関与している non-coding RNA の一種である。近年悪性腫瘍患者と健康者との間に特定の血清中 miRNA に発現量の違いがみられ、診断用バイオマーカーとして期待されている。妊娠合併症の発症にも miRNA の関与が示唆されており、本研究では当院における妊娠糖尿病合併妊婦 (GDM 群) および合併症のない妊婦 (非 GDM 群) に発現した血清中 miRNA を比較し、今までの報告されていない miRNA があるのかを検討した。【方法】2017 年 9 月から 2022 年 12 月の間に当院で分娩した 32 例から分娩前 (妊娠後期) に血清中 miRNA を次世代シーケンサーを用いて網羅的な解析を行った。Wilcoxon 検定を用いて解析を行い、 $p < 0.05$ を有意差ありとし miRNA を抽出した。そのうち miRNA の発現量で有意となるものを $\log_2(\text{fold change (FC)} = (\text{GDM 群の miRNA 発現量の median} / \text{control 群の miRNA 発現量の median})) > 2$ と定義し、ROC 曲線を用いて評価した。【成績】GDM 群 12 例, 非 GDM 群 20 例を対象とした。GDM 群は非 GDM 群と比べて糖尿病の家歴歴を有する症例が有意に多かった (25% vs 5%; $p = 0.02$) が、年齢, 分娩回数, 非妊娠時 BMI, 早産の有無では有意差はなかった。125 種類の miRNA が 2 群間で有意差を示し、さらに GDM 群で発現量に有意差を示したのは、miR-4732-5p, miR-183-5p, miR-4732-3p, miR-486-5p の 4 種類の miRNA であり、その中で miR-4732-5p および miR-183-5p が最も AUC が高かった (AUC=0.87)。この内 miR-183-5p については過去に GDM との関連性の報告はあるが、その他の 3 種類の miRNA について関連は明らかになっていない。【結論】今回は新たな GDM と関連する miRNA が同定された。今後これらの機能解析を実施して関連性をより検討して行く必要があると考える。

P-5-3 産後に新生児マススクリーニング異常で判明した悪性貧血の 1 例

倉敷中央病院

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【緒言】妊娠中の貧血のほとんどは鉄欠乏性貧血であるが、ビタミン B12 (VB12) 欠乏などその他の原因も念頭にあげる必要がある。今回、産後に新生児マススクリーニング異常で判明した悪性貧血の 1 例を経験したため報告する。【症例】36 歳初産婦。体外受精で妊娠成立し、当科で妊娠管理を行っていた。妊娠 19 週で小球性貧血を認め、鉄剤内服を行い改善した。妊娠 41 週 1 日に胎児機能不全の適応で緊急帝王切開術を施行した。同日の血液検査で大球性貧血を認めていた。産後 1 か月時点で貧血は改善していたが MCV は高値であった。新生児マススクリーニングでメチルマロン酸血症もしくはプロピオン酸血症が疑われたため、児の精査を行ったところ VB12 欠乏の診断に至った。その後母体の血液検査にて VB12 欠乏、抗内因子抗体を認め、母体上部消化管内視鏡検査を施行したところ自己免疫性胃炎と診断された。今回の VB12 欠乏は悪性貧血による VB12 吸収障害と考えられた。悪性貧血はまれではあるが、胃癌発症リスクがあるため今後も定期的な内視鏡検査が必要である。【結語】新生児マススクリーニング異常で判明した悪性貧血の 1 例を経験した。妊娠中の貧血は鉄欠乏性貧血のみならず、VB12 や亜鉛、葉酸欠乏などの可能性も考え、適切な診断、治療介入が必要である。

P-5-4 肥満妊婦における妊娠初期からの妊娠糖尿病に対する治療介入の有用性

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【目的】肥満妊婦を対象として、妊娠初期に診断された妊娠糖尿病 (GDM) の治療の有効性を検証すること【方法】研究に参加した5施設で妊娠20週までにGDMと診断された肥満 (非妊時 BMI \geq 25kg/m²) 妊婦を対象とした。初期介入群は全例妊娠初期からGDMとして治療介入した。初期非介入群は妊娠中期に再度75gOGTTを行うまで無治療とし、中期75g OGTTでもGDMパターンを呈した場合 (True GDM) のみ治療介入した。一方で、中期75gOGTTで正常だった妊婦は治療介入しなかった。初期GDMと診断されたもののうち、肥満症例 (n=194) において初期介入群 (n=88) と初期非介入群 (n=86) の分娩転帰について後方視的に検討した。【成績】非妊時BMIは初期介入群で29.7kg/m²、初期非介入群で28.8kg/m²であり有意差は認めず、インスリン治療率を含む母体背景には有意差は認めなかった。肥満妊婦では初期非介入群の65%がTrue GDMだった。出生体重は初期介入群2993g、初期非介入群で3080gであり有意差は認めなかった。(p=0.32)初期介入群では初期非介入群に比べて、SGA率には差は認めなかった (6.8%vs3.5%, p=0.50) もの、有意にLGAが少なかった。(6.8%vs19%, p=0.023) LGA以外の母児の有害事象については両群間で有意差を認めなかった。【結論】妊娠初期にGDMと診断された肥満妊婦への妊娠初期からの積極的な治療介入は、SGAを増加させる事なくLGAを減らした。肥満妊婦では、GDMに対する妊娠初期からの介入が有効な事が示唆された。

P-5-5 随時血糖値からHbA1c値に指標を変更した妊娠初期糖代謝異常スクリーニング法プロトコルの有用性

山梨大

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【目的】妊娠初期の糖代謝異常スクリーニングは随時血糖値が推奨されているが、妊娠初期は妊娠糖尿病 (GDM) の診断が主眼ではなく、妊娠中の明らかな糖尿病 (overt DM) を見逃さないことが肝要であり、初期75gOGTTにおける診断基準の妥当性や初期に診断されたGDMへの治療介入には議論の余地がある。そこで妊娠初期からの過剰な治療介入を抑制すべく、当院では初期スクリーニング法を随時血糖値からHbA1c値に変更したプロトコルを作成しその有用性を変更前後で比較し検討した。【方法】2020年10月から2023年9月までの期間に、当院もしくは同様のプロトコルを採用したセミオープン施設で妊娠初期から分娩まで管理した糖代謝異常合併妊婦を対象とした。2021年4月より初期スクリーニング指標を随時血糖値 (カットオフ \geq 100mg/dL) からHbA1c値 (カットオフ \geq 6.0%) に変更し、変更前後で妊娠初期に診断されたGDM, overt DM症例数とその治療内容を後方視的に比較検討した。【成績】糖代謝異常合併妊婦症例は、随時血糖値群 (A群, 2020年3月から2021年3月に初期採血施行), HbA1c値群 (B群, 2021年4月から2023年4月に初期採血施行) でそれぞれ63/688例 (9.2%), 86/1205例 (7.1%) であった。カットオフ以上はA群15例 (2.2%) /B群11例 (0.9%) であり、初期75gOGTTは12例/7例で施行されていた。診断の内訳はGDM15例/8例, overt DM0例/0例であり、75gOGTT正常が0例/3例であった。インスリン使用を要した症例はA群の20% (3/15例) に対してB群は73% (8/11例) と高率であった。【結論】HbA1c値による妊娠初期糖代謝異常スクリーニング法は、初期75gOGTT施行症例を減らし、またインスリン使用を要するハイリスクGDM抽出に有用である可能性がある。

P-5-6 当院における子宮筋腫合併妊娠の検討

JCHO 大阪病院

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【目的】子宮筋腫合併妊娠は全妊娠の4%といわれており、頻度が高い。子宮筋腫合併妊娠では、帝王切開、胎位異常、分娩後出血などの分娩時合併症が増加するといわれている。当院における子宮筋腫合併妊娠における帝王切開、胎位異常、分娩後出血量、子宮筋腫サイズと筋腫の位置と分娩時合併症に関して報告する。【方法】当院において2018年1月から2023年6月までに分娩となった子宮筋腫合併妊娠について診療録を用いて後方視的に分娩転帰等を検討した。【成績】2018年1月から2023年6月までに子宮筋腫合併妊娠は、61例 (全分娩例 (2640例) の2.3%)。既往帝王切開を除いた57例中経陰分娩は、47例 (82.4%)、帝王切開は10例 (17.6%)。帝王切開の適応は、胎児心拍異常1例、分娩停止1例、骨盤位が8例。分娩障害となりえる子宮体下部、頸部に子宮筋腫がある症例は15例で、骨盤位の4例は帝王切開を行ったが、残りの頭位の11例では、1例のみ分娩停止で帝王切開となった以外は経陰分娩が可能であった。全61例中での骨盤位などの胎位異常は、7例 (11.4%) であった。経陰分娩47例中、800ml以上の分娩時出血例は、14例 (29.7%)、帝王切開14例中1600ml以上の分娩時出血例は、4例 (28.5%) であった。経陰分娩例で、子宮筋腫サイズが8cm以上11例の平均出血量は、722ml、子宮筋腫が子宮体下部、粘膜下または頸部にある10例では、526ml、体部もしくは底部にある37例では、755mlであった。【結論】子宮筋腫のサイズおよび部位によらず胎位異常例以外では、経陰分娩が高い確率で可能であった。筋腫合併例では分娩時出血量の多い症例が多かったが、筋腫の部位や大きさとは直接関係が示唆されなかった。

P-5-7 妊娠中期の糖代謝異常スクリーニング法の検討

神戸大

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【目的】妊娠中期の糖代謝異常スクリーニング法として50g糖負荷試験(50gGCT)法と随時血糖(CBG)測定法がある。前向きコホート研究により両検査の糖代謝異常検出精度を比較する。【方法】2022年6月～2023年6月に当院で妊娠中期に50gGCTによる糖代謝異常スクリーニングを受けた全妊婦を対象とした。負荷前血糖値をCBG値とみなし、 $CBG \geq 100$ mg/dLをCBG陽性、負荷後1時間血糖値 ≥ 140 mg/dLをGCT陽性として、75gOGTTを実施し、糖代謝異常を診断した。CBGとGCTの糖代謝異常診断精度を比較した。【成績】全対象268人中、33人(12.3%)が糖代謝異常(overt DM 1人, 妊娠糖尿病(GDM)32人)と診断された。糖代謝異常の有無の別による糖尿病家族歴、初産婦、ART妊娠に有意差は認めなかった。CBG陽性50人中、糖代謝異常13人(26.0%)(overt DM 1人, GDM 12人)だった。一方、GCT陽性70人中、糖代謝異常29人(41.4%)(overt DM 1人, GDM 28人)だった。糖代謝異常診断におけるGCT法の感度39.4%、特異度84.3%、Youden index (YI) 0.2、GCT法の感度87.9%、特異度82.6%、YI 0.7だった。一方、CBGのみ陽性32人中、4人(12.5%)が糖代謝異常と診断され、GCT陽性であった糖代謝異常29人中、20人(69.0%)はCBG陰性であった。【結論】妊娠中期糖代謝異常スクリーニングには、CBG法より50gGCT法の方が有効である。

P-5-8 周産期心筋症既往をもつ女性の次回妊娠の予後

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【目的】周産期心筋症(PPCM)は妊娠出産が病態に関与しているため、次回妊娠は再発リスクを伴う。海外では、左室駆出率(LVEF)が50%以上に回復した症例のPPCM再発率は1-3割、LVEFが50%以上に回復しなかった症例の再発率は5割と報告されている。そのため、LVEFが50%未満の症例では、次回妊娠は推奨されない。一方、日本ではPPCM既往をもつ女性の次回妊娠についての報告はあまりない。そこで、心機能が回復したPPCM既往をもつ女性において次回妊娠時の再発率を明らかにすることを目的とした。【方法】単施設後方視的コホート研究で、対象は2009年1月から2023年6月に分娩管理を行った、PPCM既往をもちLVEF $\geq 50\%$ に回復した妊婦である。分娩後6か月以上の経過観察をされなかった症例は除外した。主要転帰はPPCMの再発とし、再発率を検討した。PPCM再発の定義は、妊娠中から分娩後6か月以内に新たに左室収縮能低下(LVEF $\leq 45\%$)もしくは心不全を発症したものとした。また、次回妊娠時の周産期転帰を検討した。【成績】解析対象は11人で、PPCM診断から次回妊娠までの期間は中央値3年2か月[1年0か月-8年3か月]、妊娠前のLVEFは中央値59%[53-64]であった。PPCM再発は2人(18.2%)に認めた。1人は分娩後に血圧上昇を認め内服薬を調整した。再発した2人の心機能低下は軽度で、早期に回復した。分娩週数の中央値は37週4日[36週0日-38週3日]で、7人(63.6%)が帝王切開であったが全て産科適応であった。産科合併症は胎児発育不全1人(9.1%)、分娩後血圧上昇4人(36.4%)であった。分娩後は11人全て授乳を行っていた。【結論】心機能が回復しているPPCM既往をもつ女性の次回妊娠での再発率は18.2%で、海外と同様であった。

P-5-9 どのような子宮筋腫を妊娠前に治療介入するべきか?～筋腫合併妊娠の後方視的検討～

杏林大

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【目的】子宮筋腫合併妊娠では周産期合併症の頻度が増加するが、筋腫の特徴によってどのような合併症と関連するかは明らかではない。筋腫の手術歴がない妊娠期の周産期予後から、リスクになりうる筋腫の特徴を明らかにすることを目的とした。【方法】2012年1月～2023年1月に当院で管理を行った筋腫合併妊娠207例を対象とし、筋腫の特徴(最大径, 個数, 位置)と周産期予後について検討した。妊娠前に筋腫に対する手術歴のある症例は除外し、筋腫の所見は妊娠14週までに経陰超音波断層法で評価したものとした。解析はMann-Whitney U検定, カイ二乗検定, 二項ロジスティック解析, 重回帰分析を用い、 $p < 0.05$ を有意とした。【成績】母体年齢の中央値は37歳、筋腫の最大径の中央値は6cmであった。入院を要する切迫流早産は最大径10cm以上で有意に多くなったが、早産を増加させる筋腫の特徴(最径大や位置)は見出だせなかった。最大径7cm以上で胎位異常が有意に上昇し、帝王切開を必要とした。経陰分娩では筋腫の特徴と分娩時出血量、陣痛促進、器械分娩、分娩停止との相関は認めなかったが、帝王切開分娩では最大径5cm以上または複数個の筋腫で出血量が多くなった。年齢、経産回数、子宮筋腫の最大径, 位置, 個数の項目で多変量解析を行うと、入院を要する切迫流早産例, 胎位異常, 帝王切開分娩の出血量いずれに関しても、子宮筋腫の最大径のみが影響を与える独立した因子になった。【結論】早産予防を目的とした妊娠前介入は、筋腫の特徴のみでは判断し得ない。帝王切開時の出血量が筋腫最大径と相関し、胎位異常による帝王切開への移行を考慮すると、不妊症の直接原因となる粘膜下筋腫以外では、7cm以上の筋腫は妊娠前の治療介入が検討されると思われる。

P-5-10 当院におけるSLE合併妊娠の周産期予後の検討

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【目的】全身性エリテマトーデス(以下SLE)合併妊娠における母体背景や周産期合併症、分娩転帰から、周産期管理における留意点について明らかにする。【方法】2013年4月から2023年3月までに妊娠12週以降に分娩したSLE合併妊娠33例について後方視的に検討した。【成績】周産期合併症を17例(51.5%)に認め、早産10例(30.3%)、妊娠高血圧症候群8例(24.2%)、新生児集中治療室(NICU)入室12例(37.5%)、light for dates児(出生時体格基準値の10%tile未満)7例(21.9%)、新生児ループスを1例(3.1%)に認めた。妊娠中にSLEが増悪した6例(18.1%)では、非増悪群に比し妊娠28週未満の早産率が有意に高かった(33.3% vs. 0%, $p < 0.05$)。しかし、合併症発症やSLE増悪に特徴的な母体背景は見出せなかった。24例(72.7%)は内科医より妊娠許可を得てから妊娠したが、周産期合併症発症率に有意差はなかった。副腎皮質ステロイドやヒドロキシクロロキンの内服の有無により分娩転帰に有意差は認めなかったが、妊娠中の副腎皮質ステロイド内服量の理想とされるプレドニゾン換算5mg/日以下の内服量に抑えられていた群では分娩週数が有意に延長され(妊娠39週0日 vs. 妊娠37週1日, $p < 0.05$)、NICU入室率も低かった(19.0% vs. 72.7%, $p < 0.05$)。【結論】周産期合併症発症や妊娠中のSLE増悪は母体背景から予測困難であり、妊娠許可が得られていてもSLE合併妊娠は慎重な周産期管理が必要であることを再認識した。妊娠前の副腎皮質ステロイド内服量を抑えることで周産期合併症の発生率を低下させる可能性が示唆され、妊娠前のSLEの病勢コントロール及び内服薬の調整が周産期予後の改善に寄与すると考えられた。

P-5-11 妊娠中に発症した悪性腫瘍と妊産婦の予後に関する研究

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【目的】妊娠中に発症した悪性腫瘍が妊娠に与えた影響、妊娠が悪性腫瘍に与えた影響を検討する。【方法】2013年1月から2022年12月までの10年間で1県内における1三次施設と1二次施設において、妊娠中に悪性腫瘍を発症した19症例を検討した。診断・病期、診断週数、妊娠中の悪性腫瘍の経過・治療、分娩週数、分娩後の悪性腫瘍の経過・治療に関して、診療録をもとに後方視的に検討した。【成績】診断は子宮頸癌9例、乳癌4例、舌癌1例、気管腫瘍1例、甲状腺癌1例、膀胱癌1例、消化管間質腫瘍1例、白血病1例だった。症例の進行期はI期7例、II期4例、III期3例、IV期3例だった。16例は妊娠中に診断され、残り3例は分娩後1か月以内に診断された。症状の自覚から診断までに2か月以上かかった症例が5例あった。8例は妊娠22週以前に診断され、うち1例は診断後に稽留流産となり、2例は妊娠延長を行わず、5例は妊娠延長した。妊娠中に悪性腫瘍に対して手術を施行したのは7例だった。妊娠中に化学療法を施行したのは4例だった。悪性腫瘍の治療のため、早産期に分娩したのは4例だった。分娩後に手術を施行したのは7例、分娩後に化学療法を施行したのは13例だった。診断後1年以内に死亡した症例は3例だった。【結論】妊娠中の発生による悪性腫瘍で3名が死亡し、6例が治療目的に流早産となった。症状の自覚から診断まで2か月以上かかった症例が5例あり、妊娠中の精査が遅れている可能性が示唆された。

P-5-12 当院における妊娠糖尿病既往女性の再発リスク及びスクリーニング施行時期の検討

弘前大

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【目的】2014年より当院で行っている妊娠糖尿病(GDM)フォローアップ外来におけるGDM既往女性の中で、フォロー中に新たな妊娠をしたGDM既往女性のGDM再発率やリスク因子、スクリーニング施行時期について検討すること。【方法】当院でフォローしているGDM既往女性288名のうち、新たな妊娠をした32名を対象とした。32名を再発GDM群(再発群)と正常耐糖能群(非再発群)に分け、先行妊娠および新たな妊娠時の患者背景や75g糖負荷試験(OGTT)、妊娠間隔や妊娠間の体重増加、新たな妊娠時の初期血糖、OGTT施行週数等を比較検討した。【成績】再発群19名(再発率56.4%)、非再発群13名であった。この2群の比較では、再発群において先行妊娠の最大インスリン使用量(中央値で再発群18単位 vs 非再発群3単位)、先行妊娠の産褥OGTT2時間値(平均130.1mg/dl vs 114.2mg/dL)が有意に高かった。再発群では初期の随時血糖高値は5名(26.3%)でその中央値は86mg/dL、全例で初期(中央値12週)にOGTTを行っており、17名(89.5%)がGDMの診断となった。一方、非再発群の初期随時血糖は中央値87mg/dLで、再発群との比較では有意差はなかった。【結論】再発率は既存報告同様に高く、最大インスリン使用量及び産褥OGTT2時間値が再発のリスク因子となる可能性が示された。また、再発群と非再発群で初期随時血糖には有意差がないことより、GDM診断には妊娠初期のOGTTが必要である可能性が示唆された。

P-5-13 妊娠糖尿病と正常妊婦の産褥早期の骨格筋量の比較検討

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【目的】最近の研究で骨格筋量の低下と2型糖尿病リスクとの関連性が報告されている。妊娠糖尿病 (GDM) は将来の2型糖尿病の強いリスク因子であるが、骨格筋量に関する報告はない。今回 GDM 既往女性の産褥早期の骨格筋量について検討した。【方法】前方視的観察試験である「妊婦筋肉量測定プロジェクト」に登録された妊娠 35 週以降の単胎分娩症例を対象とした。産褥早期 (1 か月) に体組成測定装置 (タニタ MC780A-N) を用いて四肢骨格筋量 (ASM) と脂肪量を測定し、ASM/体重 (BW) 比および ASM/body mass index (BMI) 比を算出した。プロジェクト登録対象のうち、GDM と診断された妊婦 (GDM 群) の分娩後の ASM/BW および ASM/BMI を、耐糖能正常妊婦 (対照群) と比較した。【成績】GDM 群は 154 例、正常群は 381 例で、GDM 群は産褥 BMI (24.3 ± 4.4 vs 22.9 ± 3.6 , $p < 0.001$)、体脂肪率 (35.1 ± 7.6 vs 33.1 ± 6.7 , $p < 0.001$) とともに対照群より有意に高値であった。産後 1 か月の絶対骨格筋量は両群間で差はないものの (16.8 ± 2.1 vs 16.4 ± 2.0 , $p = 0.06$)、ASM/BW (0.28 ± 0.03 vs 0.29 ± 0.03 , $p < 0.01$) および ASM/BMI (0.71 ± 0.10 vs 0.74 ± 0.10 , $p < 0.01$) は GDM 群が有意に低下していた。【結論】本研究は GDM 既往女性の産褥早期の骨格筋量を正常耐糖能女性と比較した初めての報告である。GDM の発症には、肥満とともに骨格筋量の低下が関与している可能性が示唆された。【結論】本研究は GDM 既往女性の産褥早期の骨格筋量を正常耐糖能女性と比較した初めての報告である。GDM の発症には、肥満とともに骨格筋量の低下が関与している可能性が示唆された。

P-5-14 本邦の妊産婦の悪性腫瘍による死亡症例の分娩経緯に関する検討

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【目的】我が国における悪性腫瘍に関連する妊産婦死亡症例を再評価し、分娩方法と娩出理由について検討を行う。【方法】日本産婦人科医会に報告され妊産婦死亡症例検討委員会で検討された 2010-2022 年における妊産婦死亡例のうち悪性腫瘍が原因で死亡した症例を抽出し、後方視的に分娩経緯の特徴を解析した。【成績】対象者 26 名の悪性腫瘍の内訳は多い順に白血病 7 例、胃癌 5 例、脳腫瘍 3 例、乳癌 3 例、尿管癌 2 例、悪性黒色腫 2 例、悪性リンパ腫、肺癌、子宮頸癌、肝臓癌は各 1 例であった。初発症状から診断までの中央値 (範囲) は 5 週間 (0-15) で、診断時の臨床ステージは評価可能 14 例で III-IV 期 13 例、IIb 期 1 例であった。分娩転帰は未分娩、流産、早産、満期産が順に 6, 3, 15, 2 例で、分娩時期は妊娠 30 週 (25-40) であった。未分娩 6 例 (9-24 週) のうち 1 例は分娩同意が得られず、残り 5 例 (白血病 4, 乳がん 1) は急性増悪であった。流産例は 2 例 (白血病 2) が化学療法による自然流産、1 例 (悪性黒色腫) は加療目的の人工妊娠中絶であった。早産例では尿管癌の 1 例が自然早産、残り 10 例 (固形がん 10 例) が全身状態悪化のため、4 例 (胃がん 1, 白血病 1, 悪性リンパ腫 1, 乳がん 1) が加療目的で帝王切開となった。早産症例は全て生児を出産した。【結論】悪性腫瘍による妊産婦死亡例では母体状態の悪化の為に早産が全体の 58% を占め、帝王切開がそのうちの 93% を占めていたが、生児獲得に繋がっていた。未分娩、流産は全体の 35% を占め、母体の急性増悪、加療による胎児死亡が主な原因であった。

P-6-1 胎盤特異的 miRNA の胎盤-母体細胞コミュニケーションを担う細胞間輸送体は細胞外小胞でなく細胞外ナノ粒子である

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【目的】絨毛栄養膜細胞から分泌される細胞外小胞 (EV: extracellular vesicle) は胎盤特異的 miRNA の主な細胞間輸送体であり、母体細胞に取り込まれ、妊娠維持に影響を与えている。近年、いくつかの癌細胞株から EV よりも小さな非小胞の細胞間輸送体として細胞外ナノ粒子 (EP: extracellular nanoparticle) である exomere および supermere が報告された。今回、絨毛栄養膜細胞から分泌される EP を初めて同定したので報告する。【方法】倫理委員会の承認を得て満期胎盤を採取し、絨毛栄養膜細胞を分離培養した。多段階超遠心分離法により、培養上清から順次回収し、異なる 4 つの細胞間輸送体 (P1, P2, P3, P4) を分離し、構造解析 (ナノ粒子トラッキング解析, 電子顕微鏡解析) および EP マーカー (AGO2, ENO2), EV マーカー (ANXA1, CD63) の Western blot 解析, さらに胎盤特異的 miRNA (*miR-517a-3p* など) の PCR 解析を行った。【成績】P3 [ANXA1 (-), CD63 (-), AGO2 (+), ENO2 (-); 毛玉状微粒子; 粒径 ~ 30 nm] は exomere (EP), P4 [ANXA1 (-), CD63 (-), AGO2 (+), ENO2 (+); 毛玉状微粒子; 粒径 ~ 20 nm] は supermere (EP) であった。一方, P1 [ANXA1 (+), CD63 (-), AGO2 (-), ENO2 (-); カップ状小胞; 粒径 ~ 180 nm] は ectosome (EV), P2 [ANXA1 (-), CD63 (+), AGO2 (-), ENO2 (-); 球状小胞; 粒径 ~ 90 nm] は exosome (EV) であった。また、胎盤特異的 miRNA は EV (P1, P2) よりも、EP (P3, P4) に ~ 70 倍濃縮されていた。【結論】絨毛栄養膜細胞から分泌される EP を初めて同定した。胎盤特異的 miRNA の主要な細胞間輸送体は EV でなく EP であり、胎盤-母体細胞コミュニケーションを担っていることが示唆された。

P-6-2 癒着胎盤の病態形成における TGF- β /UCHL5/Smad シグナリングの役割

帝京大

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【目的】癒着胎盤は産科危機的出血を来し得るハイリスクな病態であるが、その分子メカニズムは明らかとなっていない。TGF- β /UCHL5/Smad シグナル伝達経路はがん浸潤能および血管新生能において重要な役割を担っていることが知られている。そこで本研究では、TGF- β -Smads シグナルの癒着胎盤での生物学的役割とメカニズムについて検討を行い、絨毛細胞の浸潤性と血管新生能に寄与する因子を同定することを目的とした。【方法】絨毛がん細胞株 JEG-3 および絨毛細胞株 HTR-8/SVneo を用いて、TGF- β 添加刺激後に脱ユビキチン化酵素阻害剤 bAP15 によって時間・用量依存的に UCHL5 を阻害した。ウェスタンブロット法、蛍光免疫染色法、ELISA 法による血管内皮増殖因子 (VEGF) 濃度測定、血管内皮ネットワーク形成アッセイ、および浸潤アッセイを行い、TGF- β -Smad シグナルと浸潤能・血管新生能との関係を検討した。【成績】UCHL5 の阻害は、TGF- β 誘導性の Smad2 の活性化を抑制し、絨毛細胞の浸潤性を低下させた。Smad1/5/9 と細胞外シグナル制御キナーゼ (ERK) は同時に活性化され、培地中の VEGF 濃度上昇を認めた。しかし、培養上清を用いた血管内皮ネットワーク形成アッセイでは、ヒト臍帯静脈内皮細胞の血管新生能は著しく阻害された。これらの結果は、下流の ERK 経路と Smad1/5/9 が絨毛細胞における TGF- β 1-Smad 経路の血管新生能を潜在的に制御していることを示しており、一方 Smad2 はその浸潤性に寄与していると考えられた。【結論】絨毛細胞の浸潤能および血管新生能の異常は TGF- β 1-Smad 経路と ERK 経路の相互作用によって引き起こされ、それらは癒着胎盤のメカニズムの一つであると考えられた。

P-6-3 胎児発育不全、羊水過少を伴う切迫早産症例の胎盤病理組織学的検討

産業医大

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29歳2妊0産、妊娠26週時点から胎児推定体重が1~-1.5SD 相当の胎児発育不全を指摘されていた。妊娠28週より切迫早産の診断でリトドリン塩酸塩内服、妊娠31週よりリトドリン塩酸塩点滴を開始された。妊娠32週0日に胎児発育不全、および羊水最大深度3cm未満の羊水過少を認めたため、妊娠分娩管理目的に当科へ搬送となった。前医での入院時の血液検査でWBC10100/ μ l、CRP2.48mg/dlと炎症反応の上昇を認めていた。当院搬送時の血液検査はWBC7400/ μ l、CRP1.33mg/dlと軽度の炎症反応の上昇を認めた。胎児心拍陣痛図では胎児心拍数基線は170bpm、基線細変動は減少しており、明らかな一過性徐脈は認めなかった。胎児超音波検査で胎児推定体重は1337g(-2.1SD)、羊水最大深度は17mm、胎児血流異常は認めなかった。胎児の体幹運動、四肢の屈曲、呼吸様運動は認められた。胎児頻脈のためリトドリン塩酸塩を中止して硫酸マグネシウム製剤の投与を開始した。また、早産が予知されたためリネデロン12mgの筋注を実施した。入院翌日に胎動減少を認め、NRFSの診断で妊娠32週1日に緊急帝王切開術で児を娩出した。胎盤の病理組織検査で、亜急性絨毛羊膜炎、および壊死性臍帯炎を認め、胎盤表面の血管は一部閉塞、再開通の所見を認め、一部胎児血管灌流障害を示唆する絨毛のミネラル化を認めた。炎症菌については培養検査でも不明であった。今回の原因不明の胎児発育不全の病態として、切迫早産以外に症状を伴わない絨毛羊膜炎に長期罹患したことで胎盤の炎症に伴い胎児血管灌流障害を生じ、結果的に胎児発育不全やNRFSの原因となっている可能性を疑った。

P-6-4 Cytotrophoblast の合体化の過程における形態学的変化

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【目的】Cytotrophoblast (以下CTB) がSyncytiotrophoblast (以下STB) へ合体化する際の形態学的変化を、細胞膜に着目し、画像的検証することを目的とした。【方法】妊娠6-10週に妊娠を中断し、研究参加に同意した女性を対象に、手術検体(子宮内容物)から絨毛組織を採取した。検体は樹脂ブロック化し、電子顕微鏡で観察した。また、一部は200枚の連続切片化し、走査電子顕微鏡の反射電子検出器を用いて観察した。取得データはPhotoshopとDragon Flyで画像解析を行った。【成績】妊娠6-10週のいずれ(n=12)においても中胚葉性間質とその基底膜に隣接して存在するCTBを認めた。CTBは全て基底膜に接して存在していた。切れ込みのある単核を有し、細胞質内にはミトコンドリアや粗面小胞体などのオルガネラが豊富であった。細胞膜は2重構造で接着斑も認められた。CTBに隣接して多核の巨細胞の存在も確認され、STBを観察しているものと思われた。この巨細胞の細胞質内には複数の類円状の核のほかにも多数の小空胞やホルモン様物質が観察されたが、オルガネラは認めなかった。複数の核のうちCTBの近傍に存在するものの一部では、核およびその周囲の細胞質を断続的に取り囲む線状構造が確認され、断片化した細胞膜と考えられた。線状構造には二重構造や接着斑を認め、また連続切片を作成し立体構築して観察すると、線状構造は連続性を持ち、紡錘形様の構造をしていた。【結論】STBの核周囲で確認された線状構造は、CTBがSTBへ合体化する過程における細胞融合を観察したものと推察される。CTBの細胞融合の過程を示唆する細胞膜の電子顕微鏡所見を初めて確認した。

P-6-5 妊娠37週以降にSARS-CoV-2感染した胎盤の組織学的特徴

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【目的】妊婦がウイルスに感染すると胎盤を通じて児へ感染するが、ウイルスの種類、感染時期により胎盤や児へ及ぼす影響が様々であり、SARS-CoV-2感染による胎盤・児への影響は充分明らかにはされていない。今回妊娠期間中にSARS-CoV-2に感染した妊婦の胎盤を用いてウイルス感染による胎盤の組織学的障害につき検討した。【方法】2021年10月から2023年7月までの期間、SARS-CoV-2に感染した症例について分娩後胎盤を回収し、ホルマリン固定後HE染色及び免疫染色を用いて、妊娠37週以降に感染した症例について胎盤の病理組織学的変化を観察した。【成績】対象期間中に妊娠期間中にSARS-CoV-2に感染した妊婦は76例、うち妊娠37週以降に感染した症例は7例であった。対象症例中観察期間後分娩した症例は3例でいずれも帝王切開分娩であったが、2例は陣痛発来しSARS-CoV-2感染の適応、1例は産科適応であった。病理所見では7例中3例に母体血管還流障害、4例に胎児血管還流障害を認め、2例に多発絨毛炎を認めた。抗SARS-CoV-2抗体による免疫染色では絨毛炎の有無にかかわらず陽性診断から3日以内に分娩となった2例においてsyncytiotrophoblast及び絨毛内血管内に陽性細胞を認めた。いずれの症例も児への感染は認められなかった。【結論】SARS-CoV-2感染による胎盤の変化は特異的な所見はないという報告がなされているが、今回の検討では感染後3日以内で分娩となった症例で児への感染は認められないものの慢性絨毛炎や抗SARS-CoV-2抗体陽性細胞を絨毛組織内に認めた。今後症例を蓄積し分析する必要がある。

P-6-6 MRI画像での前置胎盤の胎盤付着部血管拡張と術中出血量の関連についての検討

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【目的】前置胎盤のMRI画像では、胎盤付着部の子宮筋層内に著明に拡張した複数の血管を認める症例があるが、その臨床的意義は不明である。今回、MRI画像での前置胎盤の胎盤付着部の血管拡張と術中出血量の関連について検討した。【方法】当院で2008年～2023年に超音波で前置胎盤と診断し、妊娠中にMRIを撮影した116症例を対象とした。放射線科医を含む3名で胎盤と内子宮口との位置関係、胎盤付着部の子宮筋層内の血管拡張の有無と血管拡張部分の筋層の厚みを計測し、術中出血量との相関を後方視的に検討した。統計解析にはEZR(Ver.1.74)を用いた。【成績】MRI撮影時の妊娠週数の中央値は32週(IQR:30週-34週)で、MRIで前置胎盤と判断した症例は99症例(85.3%)であった。そのうち胎盤付着部の子宮筋層内の血管拡張陽性は47症例(40.5%)で血管拡張部分の厚さの中央値は13.0mm(IQR:9.0mm-19.0mm)であった。血管拡張の有無と術中出血量に有意差はなく($p=0.42$)、同部の厚さと術中出血量にも相関はなかった(相関係数=0.05)。一方、17例(14.7%)で、経膈超音波断層像では血管拡張部を胎盤の一部とみて前置胎盤と診断していたが、MRIで子宮筋層内の血管拡張と判明し、低置胎盤や常位胎盤に診断が修正された。【結論】MRI画像での前置胎盤の胎盤付着部の血管拡張と術中出血量の関連はなかった。拡張した血管の存在により、経膈超音波断層像では胎盤付着範囲が広く評価され、前置胎盤と誤認される可能性があり、注意が必要と思われる。

P-6-7 一過性骨髄異常増殖症症例の胎盤病理所見と周産期経過の検討

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【目的】一過性骨髄異常増殖症(Transient abnormal myelopoiesis; TAM)は21トリソミーの新生児の約10%に発症するとされる。一部は胎児期に発症し、胎児超音波検査で肝腫大や胎児水腫を認め、胎児機能不全や子宮内胎児死亡といった重篤な経過をたどることもある。胎盤にも変化が認められる事があるが、胎児状態との関連については不明な点も多い。当院で経験したTAM症例の胎盤病理所見と、周産期の経過について検討する。【方法】2009年1月から2023年8月までに当院で出生し、生後(剖検も含む)にTAMと診断された10例について、胎児超音波所見、臨床経過、胎盤病理結果について診療録より後方視的に検討した。【成績】10例は全例21トリソミーであった。胎盤病理検査が提出されていたのは6例であった。このうち胎児水腫を認めたのは5例で、うち1例は胎内で胎児水腫が軽快した。胎児期に肝腫大を指摘されていたのは3例、胎児発育不全を認めたのは3例であった。胎児機能不全で緊急帝王切開となったのは4例、子宮内胎児死亡が1例であった。胎盤病理所見では、芽球を認めたものが6例(100%)、胎盤重量が妊娠週数の95%tileを超えるものが3例(50%)、血栓形成を認めたものが5例(83%)、fetal vascular malperfusion(FVM)を認めたものが3例(50%)であった。【結論】胎児期発症のTAMでは胎児機能不全や子宮内胎児死亡など胎児状態の悪化が認められることがある。TAM症例の胎盤では重量の増加や胎盤内血栓、FVMを高率に認めた。胎盤の変化と胎児状態悪化の関連も示唆される。今後さらに症例数を蓄積していきたい。

P-6-8 当院の Retained products of conception (RPOC) 75 例の検討

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【目的】RPOC の治療方針として血管内塞栓や子宮全摘などの侵襲的な外科的治療がある一方、経過観察も突然の出血のリスクがあり判断が難しい。出血リスクの時期、適切な治療介入やその治療期間について明らかにするため、当院の RPOC 症例について解析した。【方法】2015 年 1 月 1 日から 2022 年 12 月 31 日までに当院で RPOC と診断された症例 78 例から、治療転帰の確認できなかった 3 例を除外した 75 例について診療録から後方視的に検討した。【成績】対象症例の年齢の平均値は 35.1 歳 (±4.8 SD)、初産婦 46 例 (61.3%)、経産婦 29 例 (38.7%) であり、初期流産後 29 例 (38.7%)、中期流産後 9 例 (12.0%)、妊娠 22 週以降の分娩後 37 例 (49.3%) であった。診断は胎盤遺残 49 例、胎盤ポリープ 22 例、仮性動脈瘤 3 例、子宮動脈静脈瘻 1 例であった。経過観察のみで腫瘍消失した経過観察群は 43 例 (57.3%)、外科的切除や血管内塞栓など積極的加療を実施した介入群は 32 例 (42.7%) でバルーンタンポナーデ 6 例、胎盤用手剥離 3 例、子宮内容除去 14 例、子宮鏡下手術 10 例、血管内塞栓 9 例、腹式胎盤除去 1 例、単純子宮全摘 1 例であった。RPOC 診断から腫瘍消失までの日数を治療期間とし、平均値は経過観察群で 110.8 日 (±115.5 SD)、介入群で 94.5 日 (±129.0 SD) であり、有意差は認めなかった ($p=0.61$)。介入群のうち、待機的に治療を行った症例は 14 例 (43.8%)、緊急で治療を行った症例は 18 例 (56.2%) であった。緊急治療は全例で RPOC 診断から 2 か月以内に行われていた。【結論】経過観察群と介入群の治療期間に有意差は認めなかった。緊急治療を要する症例は RPOC 診断から 2 か月以内にリスクが高い可能性が示唆された。

P-6-9 Fetal Vascular Malperfusion の血管障害部位と臨床所見との関係

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【目的】Fetal Vascular Malperfusion (FVM) は胎児血管灌流障害であるが上流の臍帯血管から下流の無血管絨毛まで所見は多岐にわたる。臨床症状との関連は絨毛膜羊膜炎や血液凝固異常に伴うものから子宮内胎児発育不全 (FGR) 胎児機能不全 (NRFS) さらには子宮内胎児死亡 (IUFD) と様々である。今回当院で胎盤病理検査に提出し FVM と診断された症例において障害部位と臨床所見の関係について検討したので報告する。【方法】2021 年 1 月から 2023 年 8 月までに当院で胎盤病理検査に提出され FVM の診断となった 22 週以降の単胎症例を抽出し胎盤肉眼所見・血管障害部位と妊娠経過・分娩時所見・新生児所見等の臨床所見を比較検討した。【成績】2021 年 1 月から 2023 年 8 月までに提出された胎盤のうち FVM と診断された症例は 71 例であった。臍帯卵膜付着は 4 例・フォーク状付着は 5 例・単一臍帯動脈 3 例であった。血管障害部位は臍帯血管 1 例・絨毛外血管 1 例・絨毛膜板血管 23 例・幹絨毛血管 42 例・絨毛血管 (無血管絨毛) 4 例であった。臨床経過は 37 例で胎児心拍異常を認めた。FGR は 12 例・NRFS は 6 例・IUFD は 6 例であった。新生児所見では正期産 40 例中 28 例は呼吸障害で入院となった。IUFD の症例は臍帯血管から絨毛膜板といった上流の病変を認めた。大半を占めた幹絨毛血管に病変がある症例の臨床所見は多岐にわたった。無血管絨毛のみの症例でも 3 例は胎児心拍異常を認めそのうち 1 例は FGR の症例であった。【結論】FVM の症例において上流の病変の存在は IUFD 等臨床所見が重篤であるが無血管絨毛のみの症例でも臨床所見との関連を認めたため臨床的に異常のあった症例の原因検索として胎盤病理検査を行うことは重要であると考えられた。

P-6-10 胎児発育不全 (FGR) と胎盤病理所見の検討

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【目的】胎児発育不全 (FGR) の原因として、①母体因子、②胎児因子、③胎児付属物 (胎盤や臍帯) 因子など様々な要因があるが、原因が不明であることも多い。特に胎盤や臍帯因子の診断には、病理学的検索が必要であり、またその病理組織学所見についても議論がある。炎症を伴わない慢性絨毛間膜炎や MPFD (massive perivillous fibrin deposition) は、死産や FGR の原因となる病理組織学所見とされ次回妊娠での再発も多い。今回、当院で FGR と診断した症例のうち、胎盤病理検査を行った症例について、胎盤・臍帯因子の関与について後方視的に検討したので報告する。【方法】2017 年 1 月～2023 年 9 月までの 5 年間、FGR の診断で胎盤病理を提出した 34 例のうち、絨毛膜羊膜炎 (CAM) の 3 例を除いた 31 例について、産科歴、FGR の程度、病理所見について検討した。【成績】母体年齢の中央値は 33 歳、初産が 21 例、経産婦が 10 例であった。臍帯因子が 3 例、感染兆候がなくフィブリン沈着を伴うものが 13 例、14 例では明らかな原因を認めなかった。胎盤にフィブリン沈着を認めるもののうち HDP が 6 例、23 週の超早産が 1 例、双胎が 2 例であり、胎盤因子と考えられる症例は 4 例 (30%) であった。胎盤に異常所見を伴わないもののうち、HDP が 3 例、臍帯過捻転が 1 例、双胎が 2 例であり臨床的にも病理学的にも原因不明のものが 8 例 (57%) あった。MPFD として矛盾しない所見であるものは 1 例認め、母体合併症に混合性組織球症を認めた。【結論】臨床的に原因が明らかでない FGR 症例にはについては、胎盤因子の可能性を考慮し、病理検査を提出し原因検索に努めることが重要であると考えられる。

P-6-11 早産症例における重症組織学的絨毛膜羊膜炎に対する臨床的絨毛膜羊膜炎の診断基準の診断能

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【目的】臨床的絨毛膜羊膜炎 (cCAM) の診断に使用されている母体体温, 白血球およびCRPの早産症例における重症組織学的絨毛膜羊膜炎 (hCAM) の診断能を検討する【方法】2018年から5年間に当院で妊娠22週から35週に自然早産となった単胎妊婦を対象とした横断研究である。胎児死亡, 胎児構造異常と染色体異常, 胎盤病理のデータ欠損例は除外した。評価項目はBlanc stage IIIの重症hCAMの頻度, 検討因子は分娩前24時間以内の母体体温・白血球数・CRPとした。カットオフ値は母体体温38.0℃, 白血球数15000/μLとし, CRPはROC曲線から最適値を求めた【成績】38例を除外した解析対象は197例で, 分娩週数の中央値は妊娠32週3日(22週0日-35週6日)であった。重症hCAMは61例(31.0%)で, うち35例は妊娠28週未満の分娩であった。CRPの最適カットオフ値は3.12mg/dLであった。母体体温, 白血球数, CRPの重症hCAMに対する陽性尤度比・陰性尤度比は, それぞれ4.29・0.75, 3.40・0.41, 6.60・0.36であった。また母体体温 \geq 38.0℃かつ白血球数 \geq 15000/μLをcCAMとした場合の陽性尤度比・陰性尤度比は, 5.54・0.75であった【結論】cCAMの診断に広く用いられる母体体温と白血球数, またCRPによる重症hCAMの診断能は低い。したがって, 従来のcCAMの診断基準以外の新規の指標の開発が求められる。

P-6-12 前置胎盤に対する予防的子宮腔内バルーンの有用性の検討～出血量の軽減を目指して～

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【目的】前置胎盤は子宮下部の子宮収縮が不十分なため, 術中のみだけでなく産褥期にも大量出血を起こす。当院では2017年9月より前置胎盤の全症例で術中に予防的に子宮腔内バルーンを挿入するプロトコルを導入した。今回, 導入前後で術中・術後の出血量や追加治療の有無を検討した。【方法】当院で分娩となった前置胎盤症例を対象とし, 2014年1月から2017年3月までを導入前群, 2017年4月から2023年4月までを導入後群とした。前置胎盤の種類, 手術時間, 術中出血量, 術後24時間出血量, 大量輸血(濃厚赤血球輸血を10単位以上使用), 追加治療の有無などを後方視的に検討した。【成績】今回の検討の対象となる前置胎盤症例は全てで73例あり, 導入前群が30例で, 導入後群が43例であった。全前置胎盤・部分もしくは辺縁前置胎盤は導入前群が16・14例で導入後群が24・19例であった。手術時間・術中出血量・術後出血量・大量輸血症例・追加治療は, 導入前群が73.5 \pm 5.9分・1329 \pm 167ml・227 \pm 112ml・6.7%(2/30)・6.7%(2/30), 導入後群が83.0 \pm 33分・1439 \pm 88ml・117 \pm 12ml・2.3%(1/43)・0%(0/43)で有意差はなかった。子宮腔内バルーン挿入による明らかな有害事象は認めなかった。【結論】今回, 前置胎盤症例に対する予防的子宮腔内バルーン挿入の有用性は示すことが出来なかった。今後症例を蓄積し, 予防的子宮腔内バルーンの挿入の有用性を再検討する。

P-6-13 妊娠中に性器出血が持続した症例の後方視的検討 (CAOSと非CAOS群)

静岡県立こども病院

加茂亜希, 平林 慧, 増井好穂, 竹原 啓, 新谷光央, 河村隆一

【目的】慢性早剥羊水過少症候群 (chronic abruption-oligohydramnios sequence : CAOS) は, ①分娩前7日以上続く性器出血②羊水量が正常な時期がある③破水の証拠がなく羊水過少となる, の3つの基準を満たすものだが, 一方で同様に出血を認めながら羊水過少を来さない症例もある。分娩前7日以上出血のあった症例でCAOSとそれ以外の症例について後方視的に検討した。【方法】2011年~2023年の間, 分娩前7日以上出血し, 新生児治療を受けた症例を対象とした。羊水過少の有無によりCAOS群(10例)と非CAOS群(21例, うち1例双胎)に分け, 臨床経過, 胎盤病理, 児の合併症について調査した。【成績】出血開始時期はCAOS群, 非CAOS群とも中央値13週であった。分娩時期・児の出生時体重はCAOS群で中央値24週4日600g, 非CAOS群は26週3日855gであった。胎児発育不全はCAOS群1例(10%), 非CAOS群は5例(22.7%)で合併していた。絨毛膜下血腫(以下SCH)はCAOS群9例(90%), 非CAOS群17例(77.3%)に見られた。帝王切開分娩はCAOS群8例(80%), 非CAOS群19例(90.5%)であった。分娩契機が子宮収縮抑制不可であったのはCAOS群6例(60%), 非CAOS群12例(57.1%)あり, 胎盤病理で絨毛膜羊膜炎(Blanc分類2・3度)はCAOS群4例(40%), 非CAOS群6例(28.6%), ヘモジデリン沈着はCAOS群6例(60%), 非CAOS群19例(90.5%)に見られた。児の予後は, CAOS群では死亡1例(10%), 慢性肺疾患(以下CLD)7例(70%)で, 非CAOS群では死亡3例(13.6%), CLD3例(13.6%)であった。【結論】長期間SCHや出血が見られると早産リスクが極めて高い。特にCAOSを発症するとより早期に分娩となり, 児はCLDを高率に発症するため, 厳重な管理に加え羊水量の評価も肝要と思われる。

P-6-14 閉塞性単一臍帯動脈の症例の臨床経過

大阪母子医療センター

山田拓馬, 川口晴菜, 和形麻衣子, 山本 亮, 石井桂介

【目的】単一臍帯動脈 (SUA) は一本の臍帯動脈が無形成である先天性 SUA と、二次的な閉塞による閉塞性 SUA に分類される。閉塞性 SUA の妊娠経過に関する検討は限られているため、今回自験例の経過を報告する。【方法】2013年1月から2022年12月の期間に、当院で閉塞性 SUA と診断して分娩まで管理した単胎症例を対象としたケースレビューである。産婦人科専門医がカラードプラ法を併用した超音波断層法を行い、胎児の膀胱脇および臍帯フリーループの2カ所で臍帯動脈の血流が1本のみである場合に SUA とした。SUA と診断された症例のうち、病理学的検査で2本の臍帯動脈の存在が確認された場合に閉塞性 SUA とした。【成績】対象は12例で、SUA は中央値妊娠 27 (24-40) 週に診断された。診断時に羊水過少を7例で認めたが、うち5例では経過観察の後に羊水量が正常化した。6例は胎児発育不全であったが、妊娠高血圧症候群は合併していなかった。分娩週数の中央値は妊娠 36 (24-40) 週で、胎児機能不全を適応とした帝王切開は3例であった。胎児死亡が1例で、新生児死亡は認めなかった。出生体重の中央値は 2280 (392-3072) g であり、Small for gestational age は2例であった。先天異常や染色体異常の症例は無かった。病理学的検査で4例に臍帯動脈血栓、2例に臍帯過捻転を認めた。【結論】今回経験した閉塞性 SUA の症例では、羊水過少等のなんらかの周産期有害事象を合併したものが過半数であったが、先天異常と診断された症例は無かった。閉塞性 SUA は先天性 SUA とは異なる臨床的特徴を持つ可能性がある。

P-7-1 帝王切開子宮癒痕症における疼痛や出血症状に対する腹腔鏡下子宮癒痕部修復術の効果

滋賀医大

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【目的】帝王切開癒痕症候群と称されていた病態は現在国際的に帝王切開子宮癒痕症 (Cesarean scar disorder : CSDi) として認知されるようになってきた。本邦においても、帝王切開癒痕部に起因する月経困難症や過長月経に対して腹腔鏡下子宮癒痕部修復術が保険収載された。しかし、本術式の月経時疼痛や出血に対する効果の報告は少ない。そこで、これらの症状に対する本術式の効果について検討した。【方法】本検討は当院の倫理委員会の承認を得て、診療録をもとに後方視的に行った。対象期間は2021年3月から2023年3月までとし、当院で腹腔鏡下子宮癒痕部修復術を行った症例を対象とした。当院では全例子宮鏡を併用し、子宮峡部の側面および後面を焼灼し、陥凹部の頸部側をループ電極で切削し、子宮鏡を用いて切除範囲を同定している。また癒痕部を切除した後の子宮筋層は2層単結節縫合(1層目は modified Gambee 縫合)を行っている。さらに、腹腔鏡下に両側円靭帯の縫縮を施行している。【成績】当該期間における症例数は27例であった。全例合併症は認めず、全ての症例が術後3日以内に退院可能であった。手術時間は平均209分であり、半数以上の症例で出血量は計測できないほど少量であった。1周期あたりの出血期間の中央値は術前14日(四分位範囲:11-14)が術後7日(四分位範囲:5-8)に有意に短縮され ($p < 0.0001$)、月経時疼痛の Numerical Rating Scale の中央値は術前5(四分位範囲:2-7)から術後1(四分位範囲:0-3)に有意に低下していた ($p < 0.0001$)。【結論】腹腔鏡下子宮癒痕部修復術は、帝王切開子宮癒痕症の疼痛や出血症状に対しても有効な術式であると考えられた。

P-7-2 婦人科腹腔鏡下手術後の悪心嘔吐におけるオンダンセトロン予防的投与の検討

岐阜県立多治見病院

榎植志織

【目的】2022年にセロトニン受容体拮抗薬であるオンダンセトロンが術後悪心嘔吐 (PONV) に適応となった。PONV は手術患者の20-30%に発症すると言われている術後合併症であり、そのリスクファクターには女性、腹腔鏡下手術があげられる。また月経周期や低用量ピルとの関連も報告されている。そのため、産婦人科では特にPONVへの対応が必要である。本研究では、オンダンセトロンを予防投与した症例を後方視的に解析し有用性を検討した。【方法】対象は2023年1月から7月までに当科で行った腹腔鏡下手術患者に対しオンダンセトロン投与を行った84例とオンダンセトロン導入前の2022年の同時期に手術を行った対照症例84例における患者背景、PONVの頻度と発生時期、レルゴリクスの使用の有無を診療録より抽出し、比較検討を行った。【成績】PONVの発症率は、オンダンセトロン投与群では6%、オンダンセトロン非投与群では25%とオンダンセトロン投与群で有意にPONVの発症が減少した。オンダンセトロン投与群ではレルゴリクス使用群に、オンダンセトロン非投与群ではレルゴリクス不使用群にPONVの発症が多い傾向を認めた。【結論】婦人科腹腔鏡手術症例では、オンダンセトロン投与によりPONVを有意に減少することが可能であった。

P-7-3 経腔分娩歴のない症例における経腔的内視鏡手術 (vNOTES) の導入

徳島市民病院

立花綾香, 山本哲史, 柳原里江, 福井理仁, 古本博孝

【目的】経腔的内視鏡手術 (vNOTES) は、整容性に優れ術後疼痛の軽減も期待できる術式として近年注目されている。経腔操作が必要なため経腔分娩歴のある症例が良い適応とされるが、当院では経腔分娩歴のない症例にも、積極的にvNOTESを施行している。今回、現在までに経験した未経腔分娩症例におけるvNOTESの手術成績について報告する。【方法】2021年12月から2023年7月までに当院でvNOTESを施行した未経腔分娩症例を対象とし、評価した。【成績】対象症例は25例であり、子宮全摘術11例、卵巣嚢腫摘出術10例、付属器摘出術4例であった。子宮全摘術11例のうち10例はvNOTESを完遂し、平均手術時間・出血量・子宮重量は、132分(68-192)・141ml(20-270)・254g(95-700)であった。1例は強固なダグラス窩癒着のため経腹的腹腔鏡手術に移行した。卵巣嚢腫摘出術症例の手術時間・出血量・嚢腫径は、90分(49-148)・69ml(10-250)、7cm(4-18)で、全例vNOTESを完遂した。付属器摘出術症例4例のうち1例はダグラス窩癒着のため経腹的腹腔鏡手術に移行し、残る3例の手術時間・出血量・嚢腫径は53分(49-60)・10ml(10-10)・7cm(5-10)であった。同時期に経腹的腹腔鏡手術を選択した未経腔分娩症例は、子宮全摘術1例、卵巣嚢腫手術2例のみであり、子宮頸部下降不良症例と強固な骨盤内癒着症例であった。今回、未経腔分娩での腹腔鏡手術のうち、子宮全摘術の92%(11/12例)、卵巣嚢腫手術の88%(14/16例)でvNOTESの適応とし、92%(23/25例)でvNOTESを完遂した。【結論】経腔分娩歴のない症例においても、vNOTESは積極的に選択可能な術式であると思われる。

P-7-4 当院におけるMEA施行症例に関する検討

稲城市立病院

黒田由香, 櫻井信行, 高橋 董, 坂巻智美, 中里紀彦, 菅裕佳子, 増田 充, 伊東正昭

【目的】過多月経に対する根治治療は子宮摘出であるが、手術リスクが高い場合や子宮摘出を希望しない患者においては、マイクロ波子宮内膜アブレーション(Microwave endometrial ablation; MEA)は治療選択肢の一つとなる。今回、当院で実施したMEAの有用性に関して検討した。【方法】2017年1月以降、2022年12月までに過多月経に対しMEAを施行した27例を後方視的に検討した。【成績】MEA施行時の年齢中央値は46(37-56)歳、BMIは23.2(18.9-36.0)kg/m²、術前Hb値は10.1(4.5-13.1)g/dLであった。機能性過多月経は6例(22.2%)、器質性過多月経の要因としては子宮筋腫が16例(59.3%)、子宮腺筋症が8例(29.6%)、子宮内膜ポリープが5例(18.5%)に認められた(重複あり)。手術合併症は認めず全例が手術翌日に退院した。MEA施行後に子宮摘出に至った症例は5例(18.5%)であり、MEA施行から根治術までの期間は中央値571日(186-1490日)であった。適応は過多月経の再燃ではなく、子宮筋腫の増大や腺筋症の疼痛増悪であった。【結論】挙児希望がない年齢であっても子宮の温存を希望する患者は多く、MEAは子宮摘出を回避したい過多月経患者に対し有効な選択肢であった。一方、MEA施行後に根治術を要した症例も5例あり、過多月経以外による理由で子宮摘出に至った。子宮筋腫や腺筋症を合併しているような症例では器質性疾患により術後も長期のフォローや子宮摘出が必要になることがあり、MEAを適応する場合の症例選択は慎重に行う必要があると考えられた。

P-7-5 妊婦・術前の自己血貯血の有用性の検討

聖マリアンナ医大横浜市西部病院¹, 聖マリアンナ医大²

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【目的】産婦人科、特に産科では常に大量出血の可能性があるが、時に輸血を要する。同種血輸血による感染リスクは低下しているが、生殖年齢の女性の場合、輸血による不規則抗体陽性の増加、不規則抗体保有妊婦から出生した児の溶血・黄疸の増加が知られている。同種血輸血を回避する対策として当院では産科危機的出血への対応指針などを踏まえ、婦人科疾患も含め大量出血が予測される場合、自己血貯血を行っている。臨床的な自己血の有用性を自院例で検討した。【方法】2013年4月-2023年3月の10年間、当院で自己血貯血を行った産科婦人科患者について、病歴からデータを抽出・解析した。【成績】非妊娠群21例、妊娠群105例に貯血を施行し、貯血量平均は975mLであった。適応は非妊娠群では子宮筋腫術前81%、悪性腫瘍手術14.3%で、妊娠群では前置胎盤・低置胎盤75.2%で貯血量平均1139mL、筋腫合併妊娠11.4%で貯血量662mL、癒着胎盤疑い6.7%で貯血量971mLだった。追加で同種血輸血を要した例は婦人科では0、産科で7例あった。さらに、産科危機的出血の代表である前置癒着胎盤のため帝王切開後子宮全摘を余儀なくされた9症例について(自己血貯血あり5例、なし4例)検討した。妊娠週数は28-37週、MRIで癒着が疑われた例は4例、子宮摘出決定からの時間は24-132分、出血量は1602-11880mL。近年手術時間も短縮傾向があり、自己血貯血群の2例では、4600mLを超える出血量でも輸血追加なく対応できた。【結論】輸血による有害事象回避のため、自己血貯血は、特に産科危機的出血の予測される症例では有用なことが示唆された。

P-7-6 坐骨神経痛を契機に診断された子宮内膜症性嚢胞に対し腹腔鏡下手術を行い症状改善を認めた一例

大阪府済生会吹田病院

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子宮内膜症は疼痛を主訴とし、月経痛をはじめ月経時以外の骨盤痛、腰痛、性交痛、排便痛などの頻度が高いが坐骨神経痛などの下肢痛を訴えることは意外に知られていない。今回、腰痛と坐骨神経痛を主訴に整形外科を受診したところ卵巣チョコレート嚢胞を指摘され、手術後症状が消失した一例を経験したので報告する。症例は46歳2妊2産。月経困難症あり、性交痛、排便痛なし。ほか特記事項はない。下肢疼痛を主訴に整形外科を受診したが理学所見、腰部レントゲン検査で異常を認めず原因不明の坐骨神経痛と診断され鎮痛剤で経過観察となっていた。しかし症状改善せず腰部MRI画像検査を施行したところ骨盤内腫瘍を認めた。近医産婦人科を受診し両側チョコレート嚢胞の診断で手術目的に当院紹介となった。超音波では子宮は正常大、右骨盤内に8cm大、左に2.5cm大の嚢胞を認め、内診所見はダグラス窩に硬結、圧痛はなかったが子宮の可動性は不良で挙上痛を認めた。上記疾患に対して腹腔鏡下手術を施行した。腹腔内所見ではダグラス窩は完全閉鎖していた。右広間膜内で卵巣が腫大していたため、右卵管は反時計回りに内側へ捻れ、骨盤漏斗靱帯は子宮側に強く牽引されていた。癒着を剝離し右付属器摘出術、左卵巣囊腫摘出術を行った。摘出標本の病理診断はendometriotic cystであった。術後、腰痛および坐骨神経痛は消失した。整形外科領域では坐骨神経痛の原因として子宮内膜症を含めた婦人科疾患は鑑別のひとつである。一方、我々も含めて婦人科では子宮内膜症との関連があまり認知されていないため、下肢痛の有無を問うことはほぼないと思われる。子宮内膜症と坐骨神経痛の関連を文献的考察を加えて報告する。

P-7-7 ダグラス窩に穿孔したLNG-IUSを腹腔鏡下に摘除した一例

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【緒言】レボノルゲストレル放出子宮内システム (LNG-IUS) は月経困難や過多月経に悩む女性にとって、副作用が少なく、避妊効果にも優れている。一方で、少ないが子宮穿孔の合併症がある。今回、ダグラス窩にLNG-IUSが穿孔し腹腔鏡下に摘除した症例を経験したので、経過とこれまでの報告をまとめ発表する。【症例】46歳、3妊2産、前医でLNG-IUSの交換をした。その後腹痛が続き、経腔超音波でLNG-IUSが確認できず、腹腔内迷入の可能性を考えられ紹介となった。腹部レントゲンで下腹部にLNG-IUSが映り、その後単純CT検査で子宮の後方にLNG-IUSが存在する事を確認した。腸管穿孔や腹膜炎の原因となるリスクを説明の上、翌週腹腔鏡下に回収を試みた。麻酔導入後に腹部レントゲンで骨盤内にLNG-IUSが存在する事を確認し、手術を開始した。頭低位で大網を少しずつ頭側に牽引していったところ、先端が子宮後壁の穿孔部に癒着していた。その付近の大網内にLNG-IUSが捕捉されていた。これを摘除し、子宮後壁の穿孔痕を縫合して終了した。【考察】過去の症例報告では、LNG-IUSは子宮および両側付属器に癒着しているか、大網に補足されている事が多い。本症例でも大網内から発見された。報告によると時代と共に開腹への移行は減っており、腹腔鏡下に安全に摘除できている。しかし、膀胱内や腸管への穿孔も度々報告があり、同時に膀胱鏡や外科医の協力が必要となるため、事前にCTでLNG-IUSの位置を正確に診断して準備しておく必要がある。

P-7-8 ロボット支援下仙骨腔固定術後に乳び腹水を来した一例

杏嶺会一宮西病院

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【緒言】当院では2021年6月よりロボット支援下手術を開始し、2023年7月までに297例施行している。そのうちロボット支援下仙骨腔固定術 (RSC) は同年9月より開始し53例行っている。術後に乳び腹水を来した症例を経験したため若干の文献的考察をふまえ報告する。【症例】70歳、4経産。既往：糖尿病。子宮脱2度の診断にてRSCを施行し術後経過は問題なく術後4日目に退院となった。1月後の定期診察時に腹満感の訴えあり経腔超音波にて腹水貯留あり、経腔的穿刺にて乳び腹水認めた。絶食、高カロリー輸液補液、オクトヌクレオチド皮下注にて入院治療開始とし、入院3日目に腹満感消失、7日目のCTにて腹水消失確認、8日目に食事開始、その後常食とし入院後12日目に退院となった。以後再発は認めていない。【考察】手術動画を見返し、岬角前面の露出の際のリンパ管損傷による乳び腹水と診断した。RSCにおいてリンパ節を操作する状況もあるが剝離する層の改善やリンパ管を念入りに焼灼するなど工夫していきたい。

P-7-9 直腸脱, 子宮脱に対する腹腔鏡下同時手術導入における初期経験

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【はじめに】直腸脱は人口の約0.5%で発症するとされ、高齢や女性でより頻繁に発生する。直腸脱に対する腹腔鏡下直腸固定術および骨盤臓器脱に対する腹腔鏡下仙骨腔固定術は増加している。我々は直腸脱, 子宮脱合併症例に対し外科と合同で腹腔鏡下同時手術を導入したので報告する。【手技】ポートは臍部および左右の上下腹部, 下腹部正中の計6ポートとし, 臍部, 下腹部正中には12mmポートを使用している。ポート配置や, デバイスのセッティングは円滑な手術操作に重要であり, 手術開始時には互いにポート配置を確認している。外科医による全周性の直腸剝離から開始し, 次に婦人科医による両側付属器切除および子宮上部切除を施行する。膀胱腔間隙を十分に剝離し, 3.5cm幅のメッシュを腔前壁に縫合固定する。肛門挙筋下端外縁を両下端とし腔後壁を覆うように頸部後壁までカバーするように縫合する。再び外科医に交代し, 直腸前面にメッシュを縫合固定し, 仙骨前面にそれぞれのメッシュを重ねてタッキングし, メッシュを被覆するように腹膜を連続縫合で閉鎖して手術を終了する。【結果】現在までに5例経験した。平均手術時間は328分, 1例に術後腸管麻痺を認めたが, その他の合併症は認めなかった。【考察】高齢化社会に伴い直腸脱, 子宮脱の合併症例は今後増加すると思われる。しかし, 直腸脱は受診時に認めないこともあり, 直腸脱の合併の有無について確認することが必須である。また, 同術式は両科の術前マネージメントならびに術中コミュニケーションが肝要であり, 互いの連携を高めることで手術時間の短縮を図り, 症例蓄積による術式の定型化を目指している。

P-7-10 TAEによる止血術が奏功した非産科的外傷性外陰部血腫の1例

秋田赤十字病院

並木竜介, 富樫嘉津恵, 大山則昭, 佐藤宏和, 千葉和宏, 高須賀緑, 今野めぐみ, 佐藤 朗

【緒言】非産科的な外陰部外傷のうち血腫形成に至る例は0.6%とまれである。今回TAE(Transcatheter Arterial Embolization: 経カテーテル的動脈塞栓術)による止血術が奏功した外傷性外陰部血腫の1例を経験し報告する。【症例】24歳0妊。作業中に受傷し, 30分後より歩行困難が生じ, 車椅子で救急外来を受診した。初診時, 受傷より4時間経過し, 疼痛を伴い, 左大陰唇が腫脹し, 造影CT検査では左会陰部に72×45×上下52mmの血腫, 左内陰部動脈からのわずかな出血を認めた。排尿障害に対し膀胱留置カテーテル挿入を試みた所で自壊し, 血腫を排泄したが, 持続出血を認めず, 疼痛が軽減し, 圧迫止血による保存的治療の方針とした。しかし翌日, 血腫再増大, 貧血の進行を認め, TAEにより左内陰部動脈塞栓後, 外科的左外陰血腫除去術の方針に切り替えた。【治療】左小陰唇～腔前庭に開口した瘻孔部より血腫直上を腔口に平行な4cmの皮膚切開において, 血腫を除去し, 出血点を検索した。左球海綿体筋表層で後陰唇動脈の枝が損傷し, 緩徐な持続出血あり結紮止血した。腔壁左側の間質組織より静脈性出血が散在し, 結紮及び電気メス焼却により止血し, 閉創した。ドレーンは留置しなかった。血腫再形成予防のため腔内へガーゼ充填した。手術中出血量は除去した血腫を含め210gだった。術後1日目に腔内ガーゼによる圧迫を解除し, 血腫の再増大傾向なし。術後2日目に膀胱留置カテーテルを抜きし排尿障害ないことを確認し, 術後3日目に退院した。【考察】外陰部血腫は疼痛を伴わなければ保存的治療が可能だが, 血腫が増大すると疼痛を伴い, 血腫除去術が必要となる。本症例では術前にTAEによる左内陰部動脈の止血を行い, 手術中の視野確保や, 出血量を減少させたと推測される。

P-7-11 レボノルゲストレル放出子宮内システム(LNG-IUS)の腹腔内迷入を1年1か月後の検診で偶然発見した1例

愛媛県立今治病院

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レボノルゲストレル放出子宮内システム(LNG-IUS)は, 2014年から月経困難症及び過多月経に対して保険適応となり, 使用頻度が増加してきている。しかし稀ではあるが重大な合併症として子宮穿孔を来すことがあり, その約半数は無症状という報告もある。今回我々が経験した症例は, 30歳, 2妊2産, 経産分娩後8週間でLNG-IUSが挿入され, その際授乳中であった。挿入後1年1か月後の検診の際自覚症状はなかったものの, 内診・経腔超音波断層法でLNG-IUSを確認できず, 腹部X線写真・腹部CT検査で腹腔内迷入と診断した。後日腹腔鏡下手術で大綱に埋もれたLNG-IUSを回収したが, 子宮に明らかな穿孔部位は認めなかった。他施設からの報告に本症例を加えた27症例を比較・検討したところ, それぞれ中央値で, 診断年齢は33歳, 分娩回数は2回, 分娩からLNG-IUS挿入までの期間は10週, 発見までの期間は5か月であった。挿入直前の分娩方法は経産分娩が11例, 帝王切開が8例, 残りは不明であった。授乳の有無については有が8例, 無が1例, 残りは不明であった。無症状は13例, 有症状は12例, 残りは不明であった。子宮穿孔の種類は完全穿孔が17例, 部分穿孔が7例, 残りは不明であった。治療方法は腹腔鏡が25例, 経腔的除去が2例であった。添付文章では分娩後6週以前のLNG-IUS挿入は禁忌とされているが, 授乳中の挿入は禁忌ではない(注意が必要とはある)。産褥期や授乳期の子宮筋層は菲薄化・軟化し脆弱で, 授乳によって子宮収縮が起こるため子宮穿孔のリスクが高まる。そのリスクを下げるため, 添付文書の挿入可能時期や授乳の有無に関する記載は見直せる可能性がある。

P-7-12 原因の特定できない骨盤痛に対して腹腔鏡手術を行い症状改善を得た一例

姫路赤十字病院

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下腹部痛および骨盤痛はしばしば遭遇する主訴の一つであり、原因として子宮内膜症や卵巣腫瘍などが特定されることが多いが、時に診察や画像検索では原因が特定できない症例に遭遇することがある。今回我々は、非ステロイド性鎮痛剤やホルモン療法で改善を認めない原因不明の骨盤痛患者に対して、原因検索と治療のため腹腔鏡下手術を施行し、改善を得た症例を経験したため報告する。症例は23歳、性交経験なし。3年前に左の骨盤痛を訴え試験開腹術となった既往がある。今回は数日続く下腹部痛と下痢を主訴に近位内科を受診され、細菌性腸炎の診断で抗生剤を処方された。数日後に下痢は改善したが左下腹部痛は改善せず、精査目的に当科紹介となった。診察では内診で左付属器領域に圧痛を認めたが、超音波検査では異常を指摘できなかった。非ステロイド性鎮痛剤、オピオイド鎮痛剤、ホルモン療法は効果を認めず、疼痛のため度々救急外来を受診、入退院を繰り返したため、原因検索目的に腹腔鏡下手術を施行した。術中所見では左付属器と大網に前回手術の影響が疑われる癒着を認め、癒着剥離を行った。その他に特記すべき異常は認めなかった。術後疼痛は完全に消失し、現在外来フォロー中であるが再燃は認めていない。本症例では、左付属器周囲の癒着を認め、同部位を剥離することにより疼痛の改善を認めたため、癒着が疼痛の原因であった可能性が考えられた。また一部の報告では術中に所見がない患者でも腹腔鏡手術による改善が報告されている。上記より術前に原因が特定できない骨盤痛を認める患者に対して、診断目的に腹腔鏡手術を行うことは、疼痛を改善する可能性があると考えられた。

P-7-13 OHVIRA 症候群の一亜型と考えられた尿路生殖器奇形に対する子宮鏡手術の臨床経験

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【緒言】中隔子宮、腔中隔、重複尿管といった尿路生殖器奇形を伴う不妊女性に対して、子宮鏡手術を行った症例を経験した。患者に同意を得た上で報告する【症例】44歳、女性。1妊1産（筋腫核出術後による帝王切開）。36歳時に子宮粘膜下筋腫にて、腹腔鏡下子宮筋腫核出術の既往がある。続発性不妊にて、他院にて治療中であり、中隔子宮、左側の子宮に粘膜下筋腫を認めたため、X年8月に、筋腫核出の依頼にて紹介。前医で子宮鏡ファイバー検査を行うも内腔へのファイバー挿入が困難であったとされる。子宮鏡ファイバー検査を実施したところ、ファイバーは問題なく挿入することができ、中隔子宮および左側の子宮内腔に13mm大の粘膜下筋腫を認めた。子宮鏡手術が可能と判断し、X年9月に全身麻酔下に、子宮鏡手術の方針とした。術前頸管拡張は実施しなかった。術中の頸管拡張が困難であり苦慮した。術中に初めて腔中隔の存在、右腔に認めた頸管より、中隔と粘膜下筋腫があることが判明。さらに頸管拡張を試みていたのは、左腔側の頸管内であり、内腔が盲端になっていることに気づいた。さらに尿路異常として、重複尿管の手術既往があったことが術後に判明した。精査のための骨盤CT検査で、左腎細胞がんが診断され、X+1年1月に他院にて、ロボット支援下左腎部分切除が行われ、淡明細胞癌G2(pT1aN0M0)であった。【考察】OHVIRA 症候群の亜型と思しき症例に対する子宮鏡手術の一例を経験した。中隔子宮などの生殖器奇形を認める症例では、腔中隔などの有無を丁寧に確認するほか、尿路のチェックや既往歴の確認を十分に行う必要があると再認識した。

P-7-14 腹腔鏡下手術におけるポートサイトヘルニア発症予防について

近畿大

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腹腔鏡手術は、低侵襲で術後の回復も早く、婦人科手術においても需要が高く、適応が広がっている。それに伴い合併症の報告も増えている。術後のトロッカー創部に関する合併症の一つにポートサイトヘルニアがある。発症した場合、緊急手術が必要となる場合が多く、場合によっては腸管切除が必要となることもあるため、臨床的に重要な合併症である。当科での発症部位は、12mmの創部が全例で、縫合が不十分であることが主な原因であった。当科で、2013年から2022年の2819例の婦人科腹腔鏡手術のうち、5例のポートサイトヘルニアを発症した。発症する度に問題点を振り返り対策を変更してきた。個々の症例を振り返るとともに、文献的考察と予防法について検討した。

P-8-1 卵巣明細胞癌における血栓性イベントと免疫染色の検討

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【目的】卵巣明細胞癌 (OCCC) は血栓性イベント (TEEs) 発症の危険因子といわれている。今回, OCCC における TEEs 発症の危険因子や TEEs が予後に与える影響および TEEs と血栓関連タンパク質との関連を調査した。【方法】2000 年から 2019 年に当院で OCCC と診断され, 治療を受けた患者 101 例を対象とした。治療期間中にいずれかで TEEs を発症した患者を TEEs 群とそれ以外の患者を非 TEEs 群に分けて, TEEs の血栓因子や予後について後方視的に検討した。また, tissue microarray (TMA) を作成して, TF (Tissue factor), IL-6, JAK2, STAT3 について免疫染色で評価を行い, TEEs との関連を調査した。【成績】TEEs 群は 20 例 (19.8%) であり, 初回治療前に TEEs と診断されたのは 12 例 (11.9%)。初回治療後に診断されたのは 8 例 (7.9%) であった。TEEs 群において有意に再発が多く ($p=0.048$), プラチナ抵抗性再発が多かった ($p=0.025$)。TEEs 群の無増悪生存期間 (PFS) および全生存期間 (OS) は, 非 TEEs 群に比べて不良であり (PFS; $p<0.01$, OS; $p<0.01$), PFS および OS に対する多変量解析において, TEEs 発症が予後不良因子として描出された。 (PFS; $p=0.013$, OS; $p<0.01$)。TEEs を発症した患者において TF 陽性もしくは JAK2 陽性が有意に多かった (いずれも $p=0.030$)。【結論】TEEs を合併した OCCC の予後は不良であり, TF および JAK2 が TEEs の発症と関連している。TEEs を合併した OCCC に対する新たな治療標的として TF および JAK2 が候補になる可能性がある。

P-8-2 卵巣未熟奇形腫の診断の再現性に影響する因子の検討

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【目的】卵巣未熟奇形腫は 3 胚葉由来の様々な未熟組織と成熟組織で構成される奇形腫である。未熟神経上皮成分の割合により grade1-3 に分類され, 予後推定の指標とされる。一方で成熟奇形腫内に微量の未熟な神経成分の病巣を認める場合は, 予後良好でこれは未熟奇形腫とは診断しない。しかしこの微量についての明確な基準はない。多施設から集積した未熟奇形腫症例に対して中央病理判定を行い, その診断結果について検討した。【方法】2000 年 1 月から 2020 年 12 月に手術を行った 19 施設 159 症例に対して, 中央病理判定を行った。中央病理判定の結果, 臨床情報ならびに病理学的特徴を後方視的に検討した。【成績】中央病理判定の結果, 未熟奇形腫と診断された症例 (未熟群) は 108 例で成熟奇形腫と診断された症例 (成熟群) は 51 例であった。両者を比較したところ年齢中央値は未熟群 23 歳, 成熟群 28 歳 ($p=0.017$) であり未熟群で有意に低く, 腫瘍の最大径の中央値は未熟群が 151mm で成熟群が 115mm ($p<0.01$) であり未熟群で有意に大きかった。未熟群では卵巣腫瘍摘出術 (Cys) 12 例, 付属器切除術 (SO) 96 例に対し, 成熟群は Cys29 例, SO22 例であった ($p<0.01$)。次に未熟群 108 例に対して SALL4 ならびに Oct4 の免疫染色を行なったところ, 特に grade2, 3 の症例で胎芽性癌や卵黄嚢腫瘍の混在が疑われた症例が 33 例あった。【結論】未熟奇形腫の診断は難しく, 特に grade1 と成熟奇形腫の鑑別は治療方針にも影響するため明確な診断基準が必要である。

P-8-3 卵巣癌に対する PARP 阻害薬維持療法の治療強度に関連する因子の検討

藤田医大

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【目的】進行・再発卵巣癌に対してプラチナ化学療法奏効後に PARP 阻害薬維持療法が選択されるが, 有害事象による薬剤の休薬減量を要することは少なくない。本研究では卵巣癌に対する PARP 阻害薬維持療法につき治療強度の実際とそれに関連する臨床的因子につき検討を行った【方法】当院で 2018 年 1 月~2023 年 8 月に初回・再発化学療法後のオラパリブ・ニラパリブ維持療法が開始された卵巣癌 (卵管癌, 腹膜癌を含む)64 例を対象とした。臨床情報を診療録より後方視的に収集し, 休薬・減量の時期, 相対用量強度 (RDI), 背景因子, 予後につき解析を行った【成績】対象症例の年齢中央値は 60 (37-84) 歳, 投与期間中央値は 8.5 か月 (0.5-58), 初回治療が 37 例, 再発治療が 27 例, オラパリブ投与が 39 例, ニラパリブ投与が 25 例であった。休薬を要した症例の割合, 休薬開始時期の中央値, 減量を要した症例の割合, 減量開始時期の中央値, RDI 平均値 \pm SD はそれぞれオラパリブで 38.5%, 12 週目 (1-11), 30.8%, 20 週目 (0-14), $83.6 \pm 27.3\%$, ニラパリブで 60.0%, 4 週目 (2-16), 56%, 8 週目 (0-8), $75 \pm 23.7\%$ であった。休薬減量開始時期, RDI, 年齢, 進行期, 初回再発別, BRCA 遺伝子変異, 前化学療法での骨髄抑制といった臨床的背景との相関は認めなかった。RDI 平均値以上と未満の PFS 中央値は, オラパリブで初回例が 20.5 か月, 13.5 か月, 再発例が 20.5 か月, 10.5 か月, ニラパリブで初回例が 10.5 か月, 5.5 か月, 再発例が 4 か月, 3 か月でありいずれも有意差を認めなかった【結論】今回の検討からは PARP 阻害薬維持療法の治療強度と関連する背景因子や予後との相関は示されなかった。規定された用量で開始し有害事象の発現に応じた適正な休薬や減量を行う限りは治療効果への影響は乏しいと考えられた。

P-8-4 進行卵巣明細胞癌に対するペバシズマブを併用した初回化学療法はプラチナ抵抗性再発の割合を低下させる (TGCU-RS001A 試験)

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【目的】卵巣明細胞癌は化学療法抵抗性であり予後不良とされる。これまで多くの臨床試験が行われてきたがTC療法を上回る治療成績を示すことはできなかった。我々はペバシズマブ (BEV) を併用したプラチナベースの初回化学療法の有用性を後方視的に検討した。【方法】2013年11月から2023年3月までの期間に東北婦人科腫瘍研究会の7施設において、進行卵巣明細胞癌と診断され、プラチナベースの初回化学療法を受けた73例を対象とした。これらをBEV併用群23例と非併用群50例に分け、プラチナ抵抗性再発の割合、奏効割合、無増悪生存期間 (PFS)、全生存期間 (OS)、有害事象を比較検討した。抗腫瘍効果はRECISTVer1.1, 有害事象はCTCAEver5.0-JCOGを用いた。【成績】BEV併用群と非併用群の観察期間中央値は27.5か月 (8-89), 18.5か月 (2-106) であった。再発はBEV併用群で14例, 非併用群では45例に認め、プラチナ抵抗性再発の割合はそれぞれ17.3%, 68.0%であった (P=0.002)。測定可能病変を有する症例の奏効割合はそれぞれ100%, 35.1%であった (P<0.001)。またPFS, OS中央値はそれぞれ28か月, 7か月 (P<0.001), 47か月, 19か月 (P=0.007) であった。BEV併用群ではgrade3の高血圧, 尿蛋白, 血栓症がそれぞれ1例, grade4の消化管穿孔が1例に認めた。なお治療関連死は認めなかった。【結論】進行卵巣明細胞癌に対するペバシズマブを併用したプラチナベースの初回化学療法は、プラチナ抵抗性再発の割合を低下させ、PFSおよびOSも延長する可能性が示された。

P-8-5 PARP 阻害薬投与後のプラチナ感受性再発卵巣がんに対するペバシズマブの効果

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【目的】近年、PARP 阻害薬投与後のプラチナ感受性再発卵巣がんに対して、再度 BEV を併用しない多剤化学療法をおこなっても奏効率は低く、PFS も短いという報告が散見される。このような症例に BEV を併用した場合の有用性を後方視的に調査した。【方法】2019年4月1日から2023年8月31日までに PARP 阻害薬投与後にプラチナ感受性再発と診断された卵巣がん・卵管がん・原発性腹膜がんで、多剤化学療法を行った49例を対象とした。これらを BEV 併用群30例と非併用群19例に分け、有効性と安全性を比較検討した。抗腫瘍効果は RECISTver1.1, 有害事象は CTCAEver5.0-JCOG を用いて評価した。【成績】PS は全例0または1であった。組織型は BEV 併用群は漿液性癌26例, 明細胞癌4例であり, 非併用群では漿液性癌17例, 明細胞癌, 類内膜癌がそれぞれ1例であった。BEV 併用群, 非併用群の PFS 中央値はそれぞれ9か月 (95%CI: 7-13), 5か月 (95%CI: 3-11) (P=0.00832), OS 中央値はそれぞれ29か月 (95%CI: 16-NA), 5か月 (95%CI: 14-NA) (P=0.524) であった。また奏効割合と病勢制御率はそれぞれ86.7%, 26.3% (P=0.00003), 93.3%, 42.1% (P=0.00013) であった。BEV 併用群における有害事象は grade3 の高血圧, 蛋白尿がそれぞれ23.3%, 6.6% に認められたが, それ以外は各群間でほぼ同程度の有害事象の発症率であった。なお, 治療関連死は認めなかった。【結論】PARP 阻害薬投与後のプラチナ感受性再発に対する BEV を併用した多剤化学療法は, PFS の延長効果が得られる可能性が示された。

P-8-6 卵巣癌 IV 期の術前化学療法後の手術介入の意義に関するアンケート調査

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【目的】卵巣癌 IV 期に対する治療として術前化学療法 (NAC) 後に可及的腫瘍減量術 (IDS) を行うことが推奨されているが, 特に NAC 後遠隔転移が残存している症例について IDS が予後改善に寄与するかを調べた報告は少ない。日本での卵巣癌 IV 期の治療の実情を把握するためにアンケート調査を行った。【方法】「卵巣癌 IV 期症例に対して NAC-IDS を行う意義があるのか」に関して, JCOG 参加施設に計4大項目で構成されるアンケート調査を行った。主目的は NAC を行い遠隔転移病巣が PR/SD 症例の治療方針の調査とし, 比較対象として遠隔転移病巣が CR 症例の治療方針に関しても調査した。回答が得られた39施設の結果を解析した。【成績】NAC を行い遠隔転移が PR/SD の症例について, 44% の施設が IDS を行うと回答した。IDS を行う施設の中で R0 resection を目標に他臓器合併切除を含めた手術を行う施設は40% だった。遠隔転移病巣が多岐にわたる場合でも摘出可能であれば摘出すると答えた施設は15%, 転移の組み合わせで方針を変更する施設は49%, 手術をしないと回答した施設は36% だった。「IV 期で NAC を行い遠隔転移が PR/SD の症例」で IDS が必要とする施設は23%, 迷いながらも実施している施設は51%, 必要ないとする施設が26% だった。「遠隔転移が CR の症例」で IDS が必要とする施設は82%, 迷いながらも実施している施設は18% であり, 必要ないと思っている施設はなかった。【結論】本研究結果から, 卵巣癌 IV 期に対する治療方針は施設間でばらつきがあり, 特に遠隔転移の状況によっても差異があった。IDS の治療意義検証のため, まず後方視的研究が必要と考える。

P-8-7 進行卵巣癌・卵管癌・原発性腹膜癌における相同組換え修復機構への化学療法の影響

愛媛大

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【目的】当院で経験した進行卵巣癌・卵管癌・原発性腹膜癌において、化学療法による HRD status の変化を検討する。【方法】当院において2020年11月から2023年4月に治療を開始した進行卵巣癌・卵管癌・原発性腹膜癌のうち、初回化学療法前と化学療法後のIDS時と両方の組織でHRD検査を実施可能であった12例を対象とした。初回化学療法前の組織と、術前化学療法後の腫瘍減量術(IDS)時に採取した組織において、myChoice™診断システムを用いたHRD検査を施行し、HR status・GISの変化を比較検討した。【成績】組織型は全て高異型度漿液性癌であった。化学療法前のHRD statusは、HRD 6例/HRP 6例で、化学療法後のHRD statusはHRD 4例/HRP 8例であった。化学療法前後でHRDがHRPとなった2例はいずれもtBRCAwt症例であり、GISがそれぞれ51→34, 49→41と低下していた。また、化学療法前にBRCA体細胞バリエントを有していた3例において、化学療法後にも同じバリエントが認められた。さらに、化学療法前にHRPの症例は、化学療法後でも全例HRPと診断された。【結論】化学療法の前後で、12例中2例(16.7%)でHR statusが変化した。その2例はいずれも化学療法前はHRD症例であった。進行卵巣癌・卵管癌・原発性腹膜癌治療において、化学療法によりHR statusが変化してHRPとなる症例が存在するため、化学療法開始前の組織を用いてHRD検査を実施することが治療選択のために重要である。

P-8-8 進行卵巣癌における術前化学療法に対するKELIMスコアの検証

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【目的】進行卵巣癌治療では初回腫瘍減量術(PDS)もしくは術前化学療法(NAC)後の腫瘍減量術(IDS)において手術完遂度が重要である。近年提唱された化学療法感受性マーカーであるThe modeled CA-125 elimination rate constant K (KELIM)とIDS完遂度の関連について検討した。【方法】2019年1月~2023年7月までに当科でNAC後にIDSを行い、当院で継続して経過フォローした24例を対象とした。【成績】KELIM ≥ 1 群: 9例, KELIM < 1 群: 15例であり年齢・観察期間の中央値に有意差はなかった。組織型はKELIM ≥ 1 群の1例(endometrial carcinoma, G1)を除き全てhigh grade serous carcinomaであった。optimal surgeryの可否を判定するpredictive indexはそれぞれ中央値9 [0-14]と8 [2-14] (p=0.54)であった。optimal surgery以上が達成されたのはKELIM ≥ 1 群は9例, KELIM < 1 群は13例 (P=0.38), complete surgery達成は5例と2例 (P=0.04)であった。再発は1例と7例 (P=0.08)であった。PFSの中央値は16か月 [6-54]と18か月 [8-45]で有意差はなかった。【結論】KELIM ≥ 1 であれば化学療法の感受性が高いため、IDSでcomplete surgeryできる可能性が高いと考えられた。

P-8-9 Niraparib投与を行った30例の血小板減少の検討

鹿児島大

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【目的】Niraparib (NIRA)は国内で保険収載されているPARP阻害薬の一つで、1日1回の服用であり、プラチナ製剤に奏功すればコンパニオン診断に関係なく使用可能である。国内の第2相試験において、約6割前後の血小板減少が報告されているが、日常診療においても、この副作用がNIRA継続投与の律速段階となっていると考えられる【方法】当院のNIRA30例の血液毒性について調査し、血小板減少の頻度、時期、および影響を与える因子について検討を行った。【成績】初回治療の維持療法10例、再発20例(早期癌再発4例含む)。年齢中央値59 (39-75)歳、体重中央値52.0 (36.3-80)kg。NIRA投与までの化学療法レジメン数中央値2.5 (1-5)であった。投与期間中央値は20 (2-141)週。休薬や減量を行った症例18例(60%)。特に、血小板減少によるものが16例(50%)で、内3例が中止となった。最低血小板数は中央値5.7 (0.1 - 9.1) $\times 10^4$ /mm³であり、NIRA開始後2-5週間が最も多く全体の約8割を占めた。また休薬後2-4週後に最低値を示す症例もみられた。血小板減少による休薬・減量あり群となし群の患者背景に、年齢、体重、前治療レジメン数などに群間差はみられなかったが、前治療中の最低血小板数およびNIRA投与直前の血小板数に有意な差をみとめた (p<0.001)。また回帰分析によるNIRA投与後の血小板数に影響を与える因子の検討でも、前治療中の最低血小板数の関与が示唆された (p=0.034)。【結論】NIRA投与後の血小板減少による休薬・減量が半数に認められ、これには、前治療中の血小板数減少が関与していることが示唆された。重症例も認められ、既出の通り、投与後2か月は特に注意する必要があると考えられた。

P-8-10 HRD陽性は重複癌との関連性があるか

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【目的】HBOCは卵巣癌および乳癌をはじめとする癌易罹患性症候群であり、BRCA1/2遺伝子の病的バリエーションはHRDを引き起こすとされているが、それ以外にもHRDは様々な原因で生じるとされている。HRD陽性症例に癌易罹患性の傾向があるかを後方視的に検討した。【方法】当院で初回加療したStageIII/IV期の進行卵巣癌および腹膜癌の21症例を対象とした。治療前手術検体でHRD検査を行い、陽性率(tBRCAの有無)、ゲノムの不安定スコア、重複癌の有無について検討した。【成績】HRD検査を行った21例のうち陽性(HRD群)を11例(tBRCA陽性2例)、陰性(HRp群)を8例、解析不可を2例認め、年齢およびPSに差は認めず、19例(90%)が維持療法投与となった。組織型は漿液性癌14例、類内膜癌1例、明細胞癌2例、粘液性癌2例、卵巣癌肉腫2例で、解析不可は2例とも粘液性癌であった。全症例のうち重複癌を5例(HRD群4例、HRp群1例)認め、うち2例は維持療法中に新規病変として確認された。重複癌はすべて外科的切除を行われ、病理診断で卵巣癌および腹膜癌再発ではないことを確認した。tBRCA陰性のHRD群においても重複癌を3例(膀胱癌、膀胱癌、腎癌)認め、ゲノム不安定スコアは重複癌症例で高い傾向にあった(53±19 vs 42±21)。【結論】当院でHRD検査を施行した進行卵巣癌および腹膜癌症例の検討を行い、HRD群で重複癌を伴いやすい傾向にあることが示唆された。HRD群では重複癌の存在を踏まえて、慎重に管理する必要がある。

P-8-11 進行初発卵巣がん患者に対するdose-denseTC療法後のニラパリブ維持療法の検討

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【目的】進行初発卵巣がん患者に対するニラパリブの有効性と安全性はPRIMA試験で報告されているが、dose-denseTC(ddTC)療法後の有効性と安全性については明らかになっていない。今回、ddTC療法後のニラパリブ維持療法の有効性と安全性を評価することを目的とした。【方法】2021年4月から2023年4月に当院でddTC療法後にニラパリブを投与した患者の診療録を後方視的に検討した。有効性については無増悪生存期間(PFS)と全生存期間(OS)を Kaplan-Meier法に従って評価した。安全性についてはCTCAE v5.0を用いて有害事象を評価した。【成績】症例は36例で、観察期間の中央値は12.9か月、年齢の中央値は57(41-79)歳であった。高異型度漿液性癌が33例(92%)、相同組織型修復異常は陽性(HRD)が27例(75%)、陰性(HRp)が7例(19%)に認められた。FIGO StageはIIICが16例(44%)、IVが16例(44%)で、ddTC療法の最良効果は完全奏効が0例(0%)、部分奏効が26例(72%)、不変が4例(11%)、評価不能が6例(17%)であった。PFSとOSの中央値はそれぞれ未達(観察期間:1.4-29か月)、未達(観察期間:1.4-29か月)であった。Grade3以上の有害事象は14例(39%)に観察された。Grade1-4の血小板減少は22例(61%)で、grade3以上は8例(22%)に認められた。ニラパリブの減量を要した症例は18例(50%)で、毒性によるニラパリブの中止は2例(6%)に認められた。【結論】進行初発卵巣がん患者に対するddTC療法後のニラパリブ維持療法の有効性は、観察期間が短く、患者背景も異なるためPRIMA試験との比較は困難であった。一方で、安全性は、長期間の成績は不明であるものの、骨髄抑制に代表される短期間の成績はPRIMA試験と同程度であった。

P-8-12 進行卵巣がんにおける腫瘍減量術後化学療法開始までの期間と予後

千葉大
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【目的】進行卵巣がんの最大の予後因子は、腫瘍減量術で残存腫瘍なしを達成することであり、播種が著明な場合は腹腔内の広範囲な切除を必要とすることが多い。しかし、広範囲な切除により術後合併症が発症し、化学療法の開始が遅れることがある。今回われわれは、腫瘍減量術後化学療法開始までの期間と予後について検討した。【方法】2008年から2020年に当科で初回治療を行ったFIGOIII/IV期卵巣・卵管・腹膜癌のうち、腫瘍減量術後に化学療法をおこなった354例を対象とした。腫瘍減量術後から化学療法を開始した期間と予後について検討した。【成績】対象症例のperitoneal cancer indexは中央値15点(四分位点6-21)で、surgical complexity scoreは中央値12点(四分位点8-15)であった。腫瘍減量術後化学療法開始までの期間の中央値は27日(四分位点21-34日)であった。無病生存期間(PFS)および全生存期間(OS)は、27日以内に化学療法を始めた群と28日以降に始めた群に有意な差はなかった(PFS中央値35か月 vs 34か月, p=0.85, OS中央値106か月 vs 101か月, p=0.85)。Cox比例ハザードモデルでPFSに関連する因子を検討したところ、腫瘍減量術後残存腫瘍なしのみが独立した予後因子(p<0.01)で、28日以降に化学療法投与開始、performance status 2以上、FIGO IV期、Surgical complexity score 8点以上、Primary debulking surgery、は予後因子とならなかった。【結論】腫瘍減量術後化学療法開始までの期間は予後因子とはならず、残存腫瘍なしを達成することが予後因子であった。術後合併症等により腫瘍減量術後の化学療法開始が遅れたとしても、完全切除を達成することが予後に寄与することが示唆された。

P-8-13 オラパリブ+ベバシズマブ維持療法における Genomic instability score の意義

千葉大

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【目的】 Genomic instability score (GIS) はゲノム不安定性の状態を示すスコアであり, 進行卵巣がん患者の維持療法においてオラパリブ+ベバシズマブ (PAOLA-1) 維持療法の biomarker となっている。しかし, GIS が予後因子になるかは明らかになっていない。PAOLA-1 維持療法の患者において GIS の予後因子としての意義を検討した。【方法】 2021年4月から2023年8月までに, Homologous recombination deficiency 陽性の進行卵巣がん症例に対して PAOLA-1 維持療法をおこなった56例を対象とした。再発の有無を目的変数として GIS を用いて ROC 曲線を作成し, GIS の cut-off 値の設定をおこなった。高 GIS 群と低 GIS 群の無増悪生存期間 (PFS) の生存解析をおこない, 他の臨床的因子と多変量解析をおこなった。【成績】 56例の年齢の中央値は59歳で, 進行期はIII期31例, IV期25例であった。完全切除された症例は53例 (95%) であった。維持療法開始時の CA125 中央値は9.8 IU/ml (4分位点: 6.9-15.7) であった。経過観察期間の中央値は15.8か月であった。56例中7例で再発し, 3例が癌死した。2年無増悪生存割合 (2yPFS%) は89.5%, 2年全生存割合が92.7%であった。ROC 曲線を用いて, GIS の cut off 値を69点と設定した (AUCは0.646, 感度100%, 特異度49%)。高 GIS 群 (n=24) と低 GIS 群 (n=32) の2yPFS%の比較をおこなったところ, 高 GIS 群: 100%, 低 GIS 群: 80.9% であり, 高 GIS 群は有意に高かった (log rank test p=0.029, Wilcoxon test p=0.038)。多変量解析では, GIS (p=0.008), BRCA 変異 (p=0.089), 完全切除 (p=0.112) となり, GIS が有意な独立した予後因子であった。【結論】 PAOLA-1 維持療法の患者において GIS が独立した予後因子となることが示唆された。

P-8-14 PARP 阻害剤の有害事象予測における栄養評価指標の有用性

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【目的】 PARP 阻害剤は, その高い有害事象発症率により, 治療を中止せざるを得ない患者が多く存在する。近年, 宿主関連因子の1つである栄養状態の指標が, 卵巣癌患者において予後を予測するバイオマーカーとなりうることが報告されている。本研究の目的は, 栄養状態の評価と, PARP 阻害剤がもたらす有害事象との関連を明らかにする事である。【方法】 2018年9月から2022年9月までの4年間に当院で卵巣癌初回または再発維持療法として PARP 阻害剤を使用した42症例について検討した。年齢, BMI, 進行期, 既往レジメン数, 減量の有無に加え, 治療開始時の栄養評価指標 (CONUT・mGPS・PNI) と有害事象の関連を後方視的に検討した。エンドポイントは有害事象による治療の中止とした。【成績】 維持療法として42例中29例がオラパリブ, 13例がニラパリブを使用した。G3以上の有害事象は40.5%で認められ, その内訳は, 貧血が19%, 好中球減少が16.7%, 血小板減少が7.1%であった。有害事象により内服が中止となった症例は8例認められ, その内訳は, 腎機能障害が2例, 全身そう痒が1例, 血小板減少が1例, 倦怠感と関節痛が1例, 高血圧が1例, 貧血が1例, 急性骨髄性白血病が1例であった。それぞれの臨床所見ならびに栄養評価指標と有害事象による治療の中止について解析した結果, 単変量解析において, PNI が有意な予測因子として抽出された (HR=0.093, P=0.004)。【結論】 PARP 阻害剤開始前の栄養状態の評価, 特にPNIは, 有害事象による治療の中止を予測するバイオマーカーとなる可能性が示唆された。

P-9-1 診断に DWIBS を利用した子宮体癌の一例

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【緒言】 DWIBS は2004年に開発された新しい広範囲の拡散強調の撮影技術である。癌の診断, 治療効果判定, 再発の早期発見などの臨床応用が期待されている。PET に比べ撮影時間が短く低コストであり, 薬剤を使用しないというメリットもある。今回 DWIBS を利用して診断した子宮体癌の症例を経験したので報告する。【症例】 67歳の未産婦, 4年前から帯下異常を認めていた。息苦しさを主訴に当院へ救急搬送された際, 異常子宮出血 (AUB) を認め婦人科疾患を疑ったが診察に対する強い拒否があり診察できなかった。それから3か月後, ふらつきと AUB を主訴に再び当院へ救急搬送された。脳梗塞の診断となり内科で治療が開始されたが, AUB も持続しており婦人科疾患も疑われた。過去に婦人科診察を強く拒否していたため, 先に骨盤 MRI を撮影した。MRI では子宮内を充満する腫瘍を認め子宮体癌が疑われた。画像を提示しながら病状説明を行うことで理解が得られ, 診察が可能となった。子宮内膜組織診で類内膜癌 G1 の診断となり, 造影 CT では PAN に10mm以下のリンパ節の描出がみられた。PET を検討したが当院にその設備はなく, 脳梗塞治療中であるため他院で撮影することも困難であった。そこで, 当院でも撮影可能で全身の病変を評価することのできる DWIBS を撮影した。DWIBS では PAN にも拡散制限のあるリンパ節を認め, 手術で PAN の摘出まで行うこととした。本症例は結果的に PET を撮影することができたため, DWIBS 画像と PET 画像を比較し, また最終病理診断とも比較して検討した。【結論】 DWIBS の画像は視覚的に分かりやすく, 患者への病状説明にも役立つ。また画像の特徴を理解して利用すれば婦人科腫瘍の診断にも有益である。

P-9-2 当院における低悪性度子宮内膜間質肉腫 (Low-grade endometrial stromal sarcoma) の検討

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【緒言】低悪性度子宮内膜間質肉腫 (LG-ESS) は子宮間質肉腫の10%未満と稀な腫瘍である。晩期再発の可能性があり慎重な経過観察が必要とされる。当院で2010年から2023年の間に経験した5症例について報告する。【結果】平均年齢は47歳(21-68)、臨床病期は4例がIB期、1例がIVB期で、IVB期を含む3例が再発した。平均観察期間91(2-199)か月、無増悪生存期間は47か月(4-163)で全例が生存している。再発の3例について、症例①は21歳IB期で、筋腫核切除後LG-ESSと診断され、追加でTAH、BS、両側卵巣生検、骨盤リンパ節生検を施行した。術後48か月で右卵巣と腹直筋内、163か月で後腹膜、187か月で右閉鎖リンパ節に再発し、それぞれ腫瘍切除とMPA療法を行い現在199か月生存中である。症例②は44歳IV期で、TAH、BSされ術後補助療法としてMPA療法を開始し、64か月で腹膜と小腸に再発した。再発病変切除と両側卵巣を切除しMPA療法を開始し現在72か月生存中である。症例③は61歳IB期で、TAH、BSO、骨盤リンパ節生検、大網部分切除術を施行した。術後15か月で肺門部リンパ節に再発しMPA療法開始し現在19か月生存中である。無再発の2例について、症例④は40歳IB期でTAH、BSOを施行し、症例⑤は68歳IB期でTAH、BSO、大網部分切除術、骨盤及び傍大動脈リンパ節廓清術を施行し、ともにMPA療法は施行せずにそれぞれ163か月、2か月生存中である。【結論】LG-ESS臨床病期が初期でも晩期再発する可能性は十分にあり、治療終了後長期に経過観察する必要がある。今後症例を蓄積し術式や術後補助療法を検討していく。

P-9-3 VEGF 阻害剤投与後に急性大動脈解離を起こした2例

信州大

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ベバシズマブ (BV) やレンパチニブ (LEN) などの血管内皮細胞増殖因子 (VEGF) 阻害作用を有する薬剤では、VEGF による血管内皮細胞保護作用が阻害されることによる高血圧症、血栓塞栓症、蛋白尿などの副作用が知られているが、動脈解離についての情報は乏しい。我々は VEGF 阻害剤投与後に急性大動脈解離 (AAD) を起こした2例を経験したので報告する。症例1は65歳の女性で、59歳時に子宮頸癌 (扁平上皮癌) IVB期 (単径リンパ節転移) に対し同時化学放射線療法が施行された。62歳時に第一腰椎棘突起の骨転移に対し放射線療法が施行され、今回、同部位への再々発に対しパクリタキセル・カルボプラチン・BV療法が施行された。2コース目のDay 20に突然の胸部絞扼感、呼吸困難が出現し、造影CTにてStanford A型AADと診断され、人工血管置換術が施行された。症例2は74歳の女性で、子宮体癌 (漿液性癌) IVB期 (大網転移) に対し、術後化学療法6コース施行後のCTで腹膜播種再発を指摘されLEN・ベンプロリズマブ療法の方針となった。治療開始後のDay 35に突然の胸骨部痛がみられ、造影CTにてStanford A型AADと診断され、人工血管置換術が施行された。なお、これら2症例において、AAD発症前に血圧上昇は認めなかった。我が国において、VEGF阻害剤と動脈解離の関連性についての積極的な注意喚起はなされておらず、本2症例においても、AAD発症にBVやLENが関与したかは不明である。一方で、Health Canadaのレビューでは、VEGF受容体チロシンキナーゼ阻害薬の使用は動脈解離に関連する可能性が指摘されている。発症頻度は低いものの、VEGF阻害薬使用時には動脈解離の発症に注意を要すると考えられた。

P-9-4 子宮体癌に対する準広汎子宮全摘、両側付属器切除および、骨盤・傍大動脈リンパ節廓清術後にコレステロール塞栓症を発症し足趾壊死に至った1例

八尾市立病院

藤井健太, 永井 景, 植田陽子, 松浦美幸, 重光愛子, 佐々木高綱, 山田嘉彦

コレステロール塞栓症は血管内カテーテル操作や抗凝固療法等を契機に、大動脈内の粥腫が破綻し、コレステロール結晶が全身の末梢動脈を閉塞することにより発症する。症状としては皮膚症状および腎機能障害を来することが多いと言われている。今回、傍大動脈リンパ節廓清を伴う子宮体癌術後にコレステロール塞栓症を来した1例を経験したので報告する。【症例】73歳女性、3妊2産、X年12月、前医より子宮筋腫経過観察中に不正出血が持続し、悪性腫瘍の可能性を考慮され当院に紹介受診となった。子宮内膜生検および画像検査から術前診断、子宮体癌 (類内膜癌G1) IA期と診断した。翌年1月、腹腔鏡下準広汎子宮全摘と両側付属器切除術を施行し、術中に摘出標本を確認した所、肉眼的に1/2以上の筋層浸潤認めため、開腹し、骨盤・傍大動脈リンパ節廓清を追加した。術後病理で類内膜癌G1 (pT1bN1M0、傍大動脈リンパ節転移のみ陽性) IIIC期と診断した。術直後より右母趾に疼痛の訴えがあり、経時的に疼痛範囲の拡大および色調の変化を認めた。末梢動脈塞栓症を疑い、下肢エコー検査を施行した所、患部に明らかな血栓を伴わない血流異常を認め、コレステロール塞栓症と診断された。術前CTで認められた大動脈内の粥腫が術後CTでは縮小していた。壊死患部は本人希望もあり経過観察し自然脱落となった。【結語】リンパ節廓清等血管周囲の手術操作を想定する場合には、術前評価時に血管内腔の評価も行い、粥腫等認める場合は手術操作による破綻および塞栓の可能性を考慮した手術説明や術後評価を念頭に置く必要性が示唆された。

P-9-5 両側卵巣転移を認めた子宮体部に発生した中腎様腺癌 (mesonephric-like adenocarcinoma) の1例

滋賀県立総合病院

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子宮体部原発の中腎様腺癌は子宮体癌取り扱い規約第5版より新たに項目に加わり, 国内では数例の報告があるのみである。希少な疾患であり, その治療方針や予後に定まったものはない。今回, 子宮体部原発の中腎様腺癌を経験したので報告する。症例は53歳G3P2。1か月前からの下腹痛を主訴に近医を受診し, 精査目的に紹介となった。造影MRIで子宮内腔の腫瘍及び両側卵巣腫瘍を認めた。右卵巣は充実部を伴う多房性囊胞性腫瘍で, 左卵巣は出血性囊胞が疑われた。子宮内膜搔把組織診では異形内膜増殖症を認め, 重複癌の可能性も考えられた。造影CT, PET-CTでは他に転移はなかった。腹式単純子宮全摘術+両側付属器切除術を施行した。右卵巣腫瘍の術中迅速組織診は境界悪性以上の診断であり, リンパ節郭清は行わずに手術を終了した。腹腔内に播種を疑う病変はなかった。摘出標本の病理所見では子宮体部と右卵巣腫瘍ともに異型細胞の乳頭状・篩状増殖を認めた。免疫染色ではER陰性, GATA3およびTTF-1部分陽性であり, 中腎様腺癌に合致する所見であった。また, 左卵巣内の線線維腫状の変化のある部分で右卵巣・子宮と同様の免疫染色パターンを認めた。これら全ての腫瘍は同一起源であると考え, 最も腫瘍量の多い子宮体部を原発とし, 子宮体部中腎様腺癌 IIIA 期と診断した。文献的に中腎様腺癌では肺転移など遠隔転移をきたす症例が多く再発高リスクであると考え, 現在術後補助化学療法を施行中である。子宮体部原発の中腎様腺癌はHE染色のみでは診断が難しく, 免疫組織学的検査が有用である。また, 予後不良との報告もあり術後治療に関して慎重な選択が必要と考える。

P-9-6 当科での再発子宮体癌に対するレンパチニブ・ペムプロリズマブ療法6例の検討

高知大

氏原悠介, 牛若昂志, 松浦拓也, 樋口やよい, 前田長正

【緒言】プラチナ製剤を含む化学療法歴のある再発子宮体癌に対してレンパチニブ・ペムプロリズマブ療法 (LP 療法) が推奨されている。当科でLP療法を行った症例に関して, 有害事象も含め後方視的にまとめたので報告する。【症例】計6例の子宮体癌再発に対してLP療法を行った。初回再発が3例, 2回目の再発2例, 6回目の再発が1例であった。年齢の中央値は55歳であった。組織型は, 類内膜癌が5例, 明細胞癌が1例であった。MSI statusはMSI-Hが3例, MSSが2例, 未測定1例, 自費ゲノム検査でMTB-Highが1例であった。初回治療は5例が手術と化学療法, 1例がCCRTであった。全例で前治療にプラチナ製剤を含むレジメンが投与されていた。最良治療評価はCRが1例, PRが2例, SDが1例, 評価不能が2例であった。投与終了・中止が3例 (PD中止1例, 有害事象で中止1例, 本人希望の終了が1例) で, 3例が継続中である。有害事象中止を除く5例で減量を要していた。CRの1例は本人希望により5か月で終了したが, その後半年間再発は認めていない。PRの2例中1例で19か月と長期に投与を継続している。全例にG2以上の有害事象を認め, 1例でG4の消化管出血を認めた。【考察】難治性の子宮体癌再発に対して有効な病勢コントロールであった。G2以上の有害事象はほぼ全例に認めたが, 多くはレンパチニブの減量で対処可能であった。G4の消化管出血症例は放射線治療既往があり, 放射線性腸炎からの出血を増悪させた可能性が考えられた。【結語】再発子宮体癌に対するLP療法は, 有害事象のコントロールが可能であれば有効な治療である。

P-9-7 腫瘍圧迫により大腿神経麻痺を来し術後早期にリハビリ介入した脱分化型子宮内膜癌の一例

香川大

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【緒言】子宮体部脱分化癌は, 分化型内膜癌に未分化癌が混在する組織型であり, 子宮体がんの0.25%と稀な腫瘍である。今回, 不正性器出血と共に急激な体重減少と大腿神経麻痺を来し歩行困難となった子宮体部脱分化型癌症例を経験したため報告する。【症例】52歳, 0妊0産。近医受診3か月前より性器出血を自覚していた。心窩部痛を主訴に近医を受診した際の血液検査で重度の貧血 (Hb5.0g/dl) を認めた。CT検査にて下腹部巨大腫瘍を認め前医紹介となった。前医ではMRI検査が施行され, 子宮悪性腫瘍が疑われ当院紹介となった。当院受診時の血液検査では, Hb7.1g/dl, 補正Ca15.5mmol/lと重度貧血と高Ca血症を認め, PTHrP8.3pmol/Lと高値であった。また, 急激な体重減少を認めていたのに加え, 腫瘍の圧迫による大腿神経麻痺を来し自立歩行困難であった。受診日に緊急入院とし, 貧血と電解質補正を行った上で1週間後に開腹拡大子宮全摘術+両側付属器切除+大網切除術を施行した。病理組織診断は, 脱分化型子宮内膜癌であった。術後, 高Ca血症は改善したが, 左大腿神経麻痺は残存しており, 術後3日目より早期にリハビリ介入を開始した。術後1週間後の画像診断で肝/肺転移を認め, 速やかに化学療法を開始した。並行して約1.5か月間リハビリを継続し自立歩行可能となった。【考察】巨大腹腔内腫瘍摘出術を施行し, 術後大腿神経麻痺を認めた報告は散見されるが, 本症例の様に術前より腫瘍圧迫等により大腿神経麻痺を来す症例は稀である。また, 脱分化型子宮内膜癌は悪性度が高く, 進行も速く予後不良とされる一方, MSI-Hの率が高いとされる。これらを中心に若干の文献学的考察を加え, 治療経過も含めて報告する。

P-9-8 子宮内膜由来の中腎様癌 (Mesonephric-Like Carcinoma) と診断された2例

防衛医大

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【緒言】子宮内膜由来の中腎様癌 (mesonephric-like adenocarcinoma: MLA) は全子宮体癌の1%程度と稀な疾患である。今回子宮内膜由来の MLA と診断された2例を経験したので報告する。【症例】症例1は58歳, 3妊3産。不正出血を主訴に当院を受診した。子宮内膜細胞診は Class IV, 子宮内膜組織診では、腫瘍細胞が大小不規則な管状, 乳頭状, 樹枝状に増殖していた。免疫組織学的検査では TTF1, CD10, GATA3 が陽性で, MLA を疑う腺癌であった。MRI 検査では子宮体部由来の腫瘍性病変が頸部間質へ浸潤し, 子宮体癌 II 期相当として広汎子宮全摘術, 両側付属器切除術, 大網部分切除術, 傍大動脈リンパ節郭清を実施した。最終診断は MLA, 病期は II 期だった。補助療法として TC 療法6コースを実施し, 再発なく経過している。症例2は74歳, 3妊2産。不正出血を主訴に当院を受診した。腔の狭小化が強く経腔的診察はできなかった。MRI 検査では子宮内腔に腫瘍性病変があり, T2 強調画像で高信号と低信号が混在, 拡散低下も示し悪性が示唆された。子宮体癌を疑い手術をする方針とした。術中迅速病理検査で類内膜癌 (Grade1) であり, 単純子宮全摘術, 両側付属器切除術, 骨盤リンパ節郭清を実施した。摘出検体では, 腫瘍細胞が小型管状, 乳頭状に浸潤, 増殖しており, 腺腔内に好酸性の硝子様分泌物が散見された。免疫組織学的検査で CD10, GATA3, Calretinin が陽性, TTF1 が陰性で, 最終診断は MLA, 病期は IA 期だった。補助療法を推奨したが本人希望で実施せず, 再発所見なく術後4か月経過している。【結語】子宮内膜由来の MLA は臨床経過や病理学的特徴などについて不明確な点が多く, 今後症例を蓄積, 検討していく必要がある。

P-9-9 重症貧血を繰り返し診断・治療に苦しんだ子宮腺肉腫の1例

社会保険田川病院

光山丈彦, 宗 邦夫, 藤井 毅, 蜂須賀徹, 黒松 肇

【緒言】子宮腺肉腫は稀な良性腺上皮と肉腫成分からなる混合腫瘍である。今回約10年間継続した性器出血の後子宮腺肉腫の診断に至った症例を経験したので報告する。【症例】当科入院10年前から不正性器出血があり, 前医にて定期的に子宮内膜細胞診を受けていたが陰性で経過観察されていた。3年前不正性器出血を主訴に前医を救急受診。ヘモグロビンが1.8g/dL であり輸血施行。超音波検査では子宮内膜が4cmと肥厚。CA125は110U/mLと高値のため子宮体癌を疑い子宮内膜生検を行ったが良性の診断であった。さらなる検査は希望されず退院。その後医療機関の受診はなく経過していた。1か月前より不正出血が多くなり, 当科に救急搬送。ヘモグロビンは4.0g/dL であり入院後輸血を行った。MRでは筋層浸潤を伴う子宮体癌。CTでは傍大動脈領域, 右腸骨動脈領域にリンパ節転移を伴う子宮体癌と診断された。CA125は40.9U/mLであった。子宮内膜細胞診は疑陽性。子宮内膜生検は非活動性子宮内膜であり, 画像診断と病理診断が一致しなかった。開腹術を勧めたが, 本人に手術希望なく肉親を含め再度病状を説明。腹式子宮全摘術を行い術中病理迅速診断で悪性であれば, 骨盤リンパ節生検のみを追加することで了解された。病理組織診断では, 広範囲な子宮腺筋症をベースに子宮腺肉腫と異型子宮内膜増殖症を認めた。右内腸骨動脈リンパ節に転移は認めなかった。進行期はIA期であった。術後の追加手術, 化学療法の希望はなく経過観察となった。【結語】子宮腺肉腫発生の時期は不明であるが広範な子宮腺筋症を背景に異型子宮内膜増殖症とは独立して発症したと推測された。

P-9-10 当院における進行・再発子宮体癌7例に対するレンパチニブ+ペムプロリズマブ療法の治療成績

JCHO 徳山中央病院

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【緒言】がん化学療法後に増悪した切除不能な進行・再発の子宮体癌に対する新たな治療法として, レンパチニブ+ペムプロリズマブの併用療法 (LP 療法) が2021年12月に薬事承認された。婦人科癌治療では初めてのマルチキナーゼ阻害剤と免疫チェックポイント阻害剤の併用療法であり, 効果に期待する一方で, これまでに経験されることがなかったirAEを含む様々な有害事象に適切に対応する必要がある。今回当院でLP療法を施行した7例の有効性および安全性について検討したので報告する。【対象】2022年2月から2023年10月までに当院でLP療法を施行した進行・再発子宮体癌7例を対象とした。【結果】年齢は中央値65歳 (57-76歳)。進行期は1B期1例, 2期2例, 3C期2例, 4B期2例であった。組織型は類内膜癌G2が4例, 類内膜癌G3が1例, 明細胞癌が1例, 粘液性癌が1例であった。MSIhighの症例は1例, MSSの症例は4例, 未検例が2例であった。PFIは6か月未満が3例, 6か月以上12か月未満が2例, 12か月以上が2例であった。治療期間は中央値4か月 (1-16か月) で, 最良治療効果はCRが1例, PRが4例, SDが1例, PDが1例であり, 現在4例が治療継続中である。主な有害事象としては血小板低下, 甲状腺機能低下症, 倦怠感があり, 4例でレンパチニブの減量を行った。また1例はirAEとしての髄膜炎を認め, 治療の中止が必要であった。【考察】LP療法はMSSの症例でも奏効が得られた症例もあり, これまで有効な治療法がなかった進行・再発子宮体癌に対する有効な治療法であると考えられた。従来の治療法とは異なった有害事象を呈するため, 有害事象の的確な評価と薬剤の適切な休薬・減量, また他科との連携も重要であると考えられた。

P-9-11 レンパチニブ・ペムプロリズマブ療法で高度な手足症候群を認めた進行子宮体癌の1例

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【緒言】切除不能な進行・再発子宮体癌に対するレンパチニブ・ペムプロリズマブ療法が2021年12月保険収載され、使用頻度が増加している。今回我々は、レンパチニブにより手足症候群を来した症例を経験したので報告する。【症例】32歳、未妊。子宮体癌 IIIA, 癌肉腫。5回にわたる再発治療を経て、初回治療から4年3か月、腹膜播種、肺転移、肝転移、骨転移に対しレンパチニブ・ペムプロリズマブ療法を開始した。2サイクル目 day5 に手指の紅斑・疼痛が出現した。レンパチニブによるG2の手足症候群と診断し、ステロイド軟膏塗布を開始した。皮膚洗浄や保護などを継続し、増悪なく経過した。下痢や肝障害のためレンパチニブを減量、休業しつつ治療を継続した。3サイクル後のCTで骨盤内腫瘍、腹膜播種、リンパ節転移、肺転移の縮小を認めた。4サイクル目 day3 より両手背に著明な発赤と浸出液の流出を認め、強い疼痛のため、日常動作が困難となった。手足症候群 G3 と判断し、レンパチニブ・ペムプロリズマブの投与を中止した。最増悪時には、手掌、手背、足底、足背、腹部に病変を認めた。疼痛コントロールのため麻薬性鎮痛薬を使用し、皮膚洗浄、ステロイド軟膏・皮膚保護剤での処置を継続した。day17 より徐々に疼痛の改善を認め、壊死組織のデブリードマンを行った。day34 より上皮化を認め、day55 にはわずかにびらんが残存する程度となった。治療再開が可能な状況となったが、病勢進行による全身状態の増悪のため困難と判断し、Best supportive care の方針となった。【結語】有害事象が発生した際には適切に減量・休業を行い、治療が継続できるようにマネジメントすることが重要である。

P-9-12 MSI-high の再発子宮体癌に対してレンパチニブ・ペムプロリズマブ併用療法中に irAE 睪炎を発症した症例

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【緒言】高頻度マイクロサテライト不安定性 (MSI-high) の再発子宮体癌に対して、レンパチニブ (Len)・ペムプロリズマブ (Pem) 療法を施行し、免疫関連有害事象 (irAE) として睪炎を発症した症例を経験した。【症例】症例は 50 代、既往歴は特記なし。MSI-high の子宮体癌 IIIC2 期 (類内臓癌、粘液性癌の混合癌) に対して根治術施行後に多発骨転移を認め、TC (パクリタキセル、カルボプラチン) 療法を施行したが増悪し、Len/Pem 療法へ変更した。Pem6 コース後に Grade2 の睪酵素上昇と PET-CT で睪尾部に集積を認めたが、MRI では腫瘍性病変はなく、無症候性であったため経過観察とし、睪酵素は自然に低下した。Pem7 コース後に Gr2 の間質性肺炎、腸炎を認め、irAE としてプレドニゾロン (PSL) を投与し症状が改善したため、Pem8 コース目を投与した。投与後 Day7 より irAE による腸炎を再発し PSL を投与し改善したが、Day62 に再度下痢、発熱を認めた。血液検査では、アミラーゼ 767U/L、リパーゼ 1446U/mL と上昇を認め、CT 検査では軽度の睪腫大があり、Grade3 の急性睪炎の診断となった。絶食、細胞外液負荷、ウリナスタチンの投与に加え、PSL 1mg/kg/day の投与を開始した。治療 3 日目は睪酵素は著明に低下し食事を開始し、PSL を減量している。【考察】Pem 投与中に無症候性の睪酵素上昇をきたす報告はあり、睪酵素の値にも注意して管理を行う必要がある。また、irAE としての急性睪炎の報告は稀であるが、本症例のように早期にステロイド投与を行うことで症状改善が期待できる。【結語】Pem 投与中は睪酵素上昇や急性睪炎を発症する可能性があることを念頭において診療を行うことが重要である。

P-9-13 免疫関連有害事象により Pembrolizumab の投与が1回で中止となったが、Lenvatinib 単剤内服で奏功した再発子宮体癌の一例

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【緒言】再発子宮体癌に対して Lenvatinib と Pembrolizumab の併用療法 (LP 療法) を開始したが、免疫関連有害事象により Pembrolizumab を投与 1 回で中止、Lenvatinib 単剤内服を継続して奏功した症例を経験した。【症例】61 歳、未妊未産。59 歳時に子宮体癌 IA 期 (類内臓癌 Grade2) および左卵巢粘液性境界悪性腫瘍 IC1 期に対してロボット支援腹腔鏡下子宮全摘出術+両側付属器摘出術+大網部分切除術+虫垂切除術を行った。術後 1 年 1 か月、腔断端再発および骨盤内リンパ節、骨盤骨、頸椎 C3、胸椎 Th3、多発肝転移を認めた。腫瘍マーカーは CA19-9: 12,860U/ml、CA125: 745U/ml と上昇していた。腔断端腫瘍の生検から子宮体癌の再発と判断した。weekly TC 療法を行ったが、PD となり、レジメンを変更し、LP 療法を開始した。1 コース目 Day22 で Grade3 の肝逸脱酵素上昇を認め Pembrolizumab による免疫関連有害事象が考えられたため、以降 Pembrolizumab を中止、Lenvatinib のみ継続した。Lenvatinib により血小板数低下、高血圧、甲状腺機能低下、鼻出血といった有害事象を認めたため休業・減量を行い、現在 10mg/日を内服している。LP 療法開始後 5 か月で CA19-9 および CA125 は正常化し、5 か月目に CT で CR と判断した。【考察】Lenvatinib はマルチキナーゼ阻害薬であり、腫瘍血管新生を抑制する。腫瘍免疫を促進する作用もある。免疫チェックポイント阻害剤である Pembrolizumab と併用した際の抗腫瘍効果には劣るが、Lenvatinib 単剤でも子宮体癌に対する抗腫瘍効果を認める。一方で Pembrolizumab は 1 回でも投与すれば長期的な抗腫瘍効果が望めるといふ報告があり、今回の抗腫瘍効果が Lenvatinib 単剤内服によるものであったかは断定できない。

P-9-14 Leiomyoma with bizarre nuclei (LBN) の子宮全摘術後に、傍椎体部と胸壁に平滑筋肉腫転移を来した一例

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【緒言】奇怪核を伴う平滑筋腫 Leiomyoma with bizarre nuclei (LBN) は、病理学的に Leiomyosarcoma (LMS) との鑑別を要するが、良性子宮平滑筋腫に分類される。近年では、分子生物学的に LMS との共通点が示唆されており、LMS へと悪性転化する可能性も議論されているが詳細は不詳である。今回、LBN の子宮全摘術の 19 年後に LMS の転移を来した一例を経験したので報告する。【症例】84 歳、3 妊 3 産。X 年に変性筋腫疑いの診断にて腹式単純子宮全摘術+両側付属器切除術を行い、病理所見より LBN と診断され終診となった。X +19 年に胸部レントゲンにて偶発的に肺腫瘍を指摘され、呼吸器外科にて摘出術を施行、Benign metastasizing leiomyoma と診断された。精査にて他に転移を認めなかった。X +20 年に他科で撮影された CT にて径 3cm の左傍椎体部腫瘍と左胸膜外腫瘍 2ヶ所を認め、子宮筋腫転移再発の疑いにて当科に紹介された。外科的検査による侵襲を考慮し画像検査での経過観察としたが、その 4 か月後に腰背部痛による体動困難のため緊急入院した。左傍椎体部腫瘍は径 5cm に増大しており、症状の原因と考えられた。胸腔鏡にて胸膜播種病変を生検し、Leiomyosarcoma と診断された。高齢のため化学療法を希望されず Best Supportive Care の方針とした。腰背部痛に対して放射線緩和照射を施行し、症状は改善傾向で自宅退院となった。【結論】LBN の管理において、非常に稀ではあるが、再発とその後 LMS へと悪性転化する可能性を念頭に置く必要があると示唆された。

P-10-1 HIV 母子感染におけるリスク因子に関する検討

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【目的】HIV 母子感染は高率に予防可能となってきたが、現在も散発的に発生し続けている。今回、現在とはほぼ同様の母子感染予防対策が可能となった 2000 年以降の分娩例を対象に、母子感染のリスク因子を検討した。【方法】われわれ研究班が集積した 2000 年以降分娩に至った例のうち、未確定 62 例を除く児の感染・非感染が確定した 590 例を対象に、感染例・非感染例を比較検討した。【成績】母子感染例は 22 例、非感染例は 568 例で、母体の感染判明時期は母子感染例では分娩後が 18 例 (81.9%)、妊娠前 1 例 (4.5%)、妊娠中 3 例 (13.6%)、非感染例では妊娠前が 341 例 (60.0%) と最多で、分娩後は 2 例 (0.4%) であった。また妊娠中に母体の感染が判明した 219 例のうち妊娠後期での判明は 26 例で、母子感染の 3 例が含まれていた。一方非感染例では 484 例 (85.2%) が妊娠初期・中期に判明していた。抗ウイルス薬療法は母子感染例では 3 例 (13.6%) のみに施行され、非感染例では 524 例 (92.3%) で施行されていた。非感染例で妊娠後期に初めて感染が判明した 23 例のうち、母体への抗ウイルス療法未施行例は 4 例で、その他は妊娠後期から抗 HIV 療法もしくは分娩時の AZT 点滴が施行されていた。【結論】HIV 母子感染は予防可能になりつつあると言われるが、母子感染率は予防対策不十分例を含めた実臨床上では 3.8% と無視できる数字ではない。しかし母子感染例の多くは妊娠中に HIV 感染が判明していない例であり、薬剤の発展により妊娠後期に判明した場合も予防可能になりつつある。感染判明時期の遅れが母子感染における最大のリスク因子であり、今後いかにして分娩前に感染を検出するかということが、母子感染予防の鍵になると考えられる。

P-10-2 臨床的絨毛膜羊膜炎の新たな診断基準の検討

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【目的】絨毛膜羊膜炎 (CAM) は新生児後に影響を与えるため、早期診断や娩出が必要である。Lencki の基準などの臨床診断基準が頻用されるが、子宮圧痛、腔分泌物や羊水の悪臭は主観的指標であり、判別し難い症例が数多くある。今回客観的指標のみを用いた臨床診断基準作成を目的に研究を行った。【方法】2003 年から 2022 年までに当院で胎盤病理検査を行った患者を対象として、Blanc 分類 StageII 以上の CAMII/III 群 (疾患群) と、StageI の CAMI 群 (対照群) に分類した。両群間で母体データ (年齢、分娩歴、分娩週数、BMI、妊娠糖尿病など) や分娩直前データ (WBC、CRP、体温、母体脈拍数、破水後時間、分娩時間など) を比較し、抽出した因子で新基準を作成した。また両群間で新生児予後、産褥入院日数を比較した。【成績】対象症例は CAMII/III 群 538 例、CAMI 群 324 例の計 862 例であり、WBC、CRP、体温、初産婦率の 4 項目が CAMII/III 群で有意に高値 ($p < 0.05$) となった。各因子のカットオフ値を求め、ロジスティック回帰分析の β 値でスコアリングしたところ、WBC12000/ μ L、CRP1mg/dL、体温 38.5°C がカットオフ値となり、基準値以上で各々 1, 2, 2 点、基準値未満でいずれも 0 点、初産婦は 1 点追加、総スコア 4 点以上で臨床的 CAM という診断モデルを作成できた。ホールアウト検証で、Lencki の基準と新基準の AUC を比較すると、各々 0.621, 0.741 となり、有意な改善 ($p < 0.001$) を認めた。両群間の予後比較では、CAMII/III 群で新生児臍帯動脈 pH7.2 未満、産褥 10 日以上入院の症例数がそれぞれ有意に増加 ($p < 0.05$) した。【結論】臨床的 CAM の診断における新基準の有用性が示された。基準を満たす症例には早期のターミネーションが推奨される。

P-10-3 サイトメガロウイルス (CMV) 未感染妊婦における次回妊娠初期 CMV 抗体スクリーニング結果の検討

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【目的】CMV 未感染妊婦が妊娠中に初感染する率は1-2% であると知られている。また、経産婦は妊娠中のサイトメガロウイルス (CMV) 初感染のリスクファクターの一つである。妊娠中に CMV 未感染のままであった妊婦について、次回妊娠初期までの CMV の感染の有無を検討する。【方法】倫理承認およびオプトアウトでの後方視的研究を行った。県下で行っている 2013 年～2022 年の妊婦 CMV 抗体スクリーニングコホートの中から、妊娠初期に CMV 抗体未保有で後期に抗体が陽転しなかった妊婦の、次回妊娠の CMV 抗体スクリーニング結果を検討した。【成績】妊娠初期 CMV 抗体スクリーニングを受けた妊婦は 4 万 405 例であった。このうち 1 万 8539 例が CMV IgG 陰性であり未感染と診断された。1 万 614 例が妊娠後期に IgG 再検を受け、陽転したのは 69 例であった。尚、このうち 20 例に新生児の CMV 先天感染を認めた。IgG 陽転しなかった 1 万 545 例の妊婦のうち、次回妊娠で初期に CMV 抗体スクリーニングを受け IgG 陽転していたのは 110 例であり、妊娠中に陽転した 69 例よりも多かった。【結論】CMV 未感染妊婦は、出産後も次回妊娠初期までに CMV に感染するリスクがある。特に次回妊娠を希望している女性にとっては、妊娠初期の CMV 初感染リスクとなる可能性がある。

P-10-4 待機管理を行った超早産期の cCAM 症例の母児の短期予後

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【目的】臨床的絨毛膜羊膜炎 (cCAM) では娩出が考慮されるが、超早産期の場合に児の未熟性を考慮して待機管理をすべきか、直ちに娩出すべきか検討されていない。本研究は超早産期に発症した cCAM 症例の待機管理における母児の予後を明らかにする。【方法】2016 年からの 7 年間に、妊娠 22 週 0 日から妊娠 28 週 0 日未満に cCAM と診断され、待機管理を行った単胎症例を対象としたケースシリーズ研究である。診断から 24 時間以内の分娩症例、積極的 newborn 蘇生希望がない症例は除外した。cCAM は Lencki の基準で診断し、抗菌薬 (アンピシリン, ゲンタマイシン) および必要時の子宮収縮抑制薬の投与を行った。感染の改善は 38 度未満に解熱かつ cCAM の診断基準から全て外れたものと定義した。診療録から母体背景、診断時情報、分娩転帰に関する情報を抽出し、母児の短期予後について調べた。【成績】対象 11 例の診断週数の中央値は 23 (22-25) 週であった。11 例中 5 例が感染改善を認め、妊娠継続日数の中央値は 20 (13-37) 日、非改善群 6 例は 3 (2-6) 日であった。娩出の適応は感染改善群では陣痛 2 例、感染増悪 2 例 (母体敗血症 1 例を含む)、臍帯脱出 1 例で、非改善群は陣痛 3 例、感染増悪 3 例であった。母体敗血症は両群ともに 1 例ずつ認めたが、分娩後速やかに改善した。Blanc 分類 Stage3 の組織学的 CAM は 6 例、臍帯炎は 8 例に認めた。非改善群で児の敗血症を 1 例、死亡退院を 2 例に認めたが、改善群には認めなかった。生存退院のうち 8 例が III 度または III 型の CLD を認め、6 例が HOT を導入した。【結論】抗菌薬開始後に感染改善を認めた cCAM は妊娠期間を延長できる可能性があるが、母体敗血症例もあり慎重な管理を要する。

P-10-5 県内における新生児サイトメガロウイルススクリーニング

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【目的】我々はこれまで県内において妊婦サイトメガロウイルス (CMV) 抗体スクリーニングにより CMV 初感染母体を抽出し、先天性 CMV 感染児の同定につなげてきた。しかしながら最近になって、母体の初感染の有無に関係なく先天性 CMV 感染児を同定することができる新生児 CMV スクリーニングも行っている。今回、県内における新生児 CMV スクリーニングの中間結果について報告する。【方法】県内 6 施設において、2022 年より希望症例に対し行われた、新鮮尿または濾紙尿を使用した CMV 核酸増幅検査による新生児 CMV スクリーニング結果を解析した。また、先天性 CMV 感染児の母体の CMV 感染状態について可及的に確認した。【成績】2022 年 7 月～2023 年 7 月までに、10 組の双胎を含む 494 例の新生児 CMV スクリーニングが行われていた。先天性 CMV 感染児は 1 組の双胎を含む計 4 例 (0.81%) であった。4 例のうち、症候性感染児は 2 例であった。先天性 CMV 感染児の母体 3 例のうち、1 例は妊婦 CMV 抗体スクリーニングを受けており CMV IgG (+) IgM (+) の結果であった。残りの 2 例は妊婦 CMV 抗体スクリーニングを受けておらず、産後の CMV 抗体検査では CMV IgG (+) IgM (-) の結果であった。【結論】県内において、母体の初感染の有無に関係なく新生児 CMV スクリーニングによる先天性 CMV 感染児の同定が可能になったと考えられる。

P-10-6 当院における新型コロナウイルス感染妊婦の母児同室管理について

自衛隊中央病院

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【目的】新型コロナウイルス感染症蔓延により感染妊婦や出生した児の管理は施設ごとで多様である。当院における新型コロナウイルス感染妊婦、母児同室管理について文献的考察を加えて報告することを目的とする。【方法】2020年4月(緊急事態宣言発令)から2023年9月までの間に当院で分娩に至った妊婦を対象とした。当院において入院時の新型コロナウイルス検査はリアルタイムPCRで行った。陽性となったものを陽性例、発熱があり検査で陰性が確認された症例を疑似症として管理した。分娩方法は経膈分娩を基本とし、帝王切開を含む急速遂娩は産科適応で決定した。新型コロナウイルス陽性妊婦に対応するスタッフは感染防護衣を着用して対応した。【成績】総分娩数は1250例、そのうち新型コロナウイルス感染妊婦は9例、疑似症は2例だった。分娩様式は自然経膈分娩が7例、吸引分娩が1例、選択的帝王切開術が1例であった。また、分娩を契機に感染症症状が増悪した症例はなかった。平均入院日数は8.4日だった。2022年12月以降の新生児については、日齢1, 2に等温核酸増幅法(NEAR法)で陰性を確認し、希望のあった症例は母児同室を許可した。母児同室とした6例において、新型コロナウイルスの母児感染はなかった。退院後も新型コロナウイルスの母児感染は確認されていない。【結論】新型コロナウイルス感染妊婦は周産期で症状増悪は確認されず、分娩転帰にも影響はなかった。母児同室でも新生児への感染は確認されなかったため、母体やスタッフの感染防護を徹底すれば通常の産後管理が可能である可能性がある。今後症例の蓄積が求められる。

P-10-7 自作AIプログラムを用いたトキソプラズマIgM抗体陽性妊婦2,400例の先天感染発生の予測モデルの開発と重要因子の抽出—アビディティだけで診断できるのか?—

ミュージレディスクリニク

小島俊行

【目的】AI(人工知能)を用いて機械学習を行い、先天感染発生の妊婦の特徴量を抽出し、トキソプラズマ(以下Tと略す)先天感染発生の有無を予測し、重要因子を抽出する。【方法】1998年6月~2016年3月の間の自験例T-IgM抗体陽性妊婦2,400例を対象とした。妊婦の(1)外注T-IgG抗体(ELISA法)(上限値=240)、(2)T-IgM抗体(ELISA法)測定値、演者が全て測定した(3)T-IgG抗体(ELISA法、希釈し最終値を求めた)とT-IgG抗体のアビディティ値((4)OD=0.7[自施設の方法]及び(5)OD=cut-off値[Hedman原法])と、母体治療の有無((6)アセチルスピラマイシン、(7)ピリメタミン+スルファジアジン、(8)スピラマイシン)、(9)出生児の先天感染の有無の9項目を指標とした。AIコードの作成には、プログラミング言語にPython3を使用し、学習モデルに決定木及びサポートベクトルマシン(以下SVMと略す)を実装し、目的関数に各々交差エントロピー、ヒンジ損失を用いた。モデルの検証には、擬似乱数ジェネレータを用い正解率を検討した。【成績】(1)正解率(正診率)は、決定木で学習用データセットが100%、テスト用データセットが99.6%、SVMで各々99.6%、99.8%で、汎化性能の高いモデルが作成された。(2)決定木の重要度は、アビディティが46.8%、T-IgGが24.7%、自施設測定T-IgGが14.6%、T-IgMが8.4%であった。【結論】AIプログラムを作成し、出生児の胎内感染を予測可能なことが示唆された。従来臨床的に重要と考えられていたハイリスク因子が、AIモデルで数量化された。しかし、アビディティ単独で胎内感染を予測するのではなく、その他の抗体値の多次元の数値の組合せで診断することで精度が上昇することが示された。

P-10-8 妊婦HTLV-1スクリーニング検査における1次抗体検査の偽陰性率に関する検討

長崎大

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【目的】妊婦のHTLV-1スクリーニング検査では、1次抗体検査の陽性例にはラインプロット法(Line Immunoassay; LIA法)で確認検査を行っている。一方、1次抗体検査の陰性例は、原則として、その時点でHTLV-1非感染と判定されるが、前回のスクリーニング検査の結果から1次抗体検査の結果に疑義が生じた例を経験した。そこで、本研究では、HTLV-1スクリーニング検査における偽陰性率を明らかにすることを目的とした。【方法】2011年1月から2023年8月までに長崎県でHTLV-1スクリーニング検査を施行された、のべ113813例の妊婦を対象として、検査結果ならびに偽陰性例の臨床所見について後方視的に調査した。【成績】妊婦113,813例のうち、1次抗体検査陽性は980例(0.86%)、陰性は112,753例(99.07%)であった。カットオフ値付近で陰性と判定されたのは80例(0.07%)存在し、うち確認検査陽性は2例で、1次抗体検査の偽陰性率は0.0018%(2/113,813例)であった。この偽陰性2例のうち1例は、前回妊娠時の1次抗体検査が陽性、確認検査で陰性と判定されていた。残る1例は前回HTLV-1キャリアと判定されていたが、今回の妊娠では1次抗体検査陰性であり疑義が生じたため、確認検査が施行された。偽陰性2例の検査法はいずれも1次抗体検査はゼラチン粒子凝集反応(Particle agglutination; PA法)、確認検査はLIA法であった。【結論】1次抗体検査で偽陰性を呈したHTLV-1キャリア妊婦を2例経験した。妊婦のHTLV-1検査では、1次抗体検査で陰性と判定されても、HTLV-1スクリーニング検査の既往歴からHTLV-1感染が疑われるときには、1次抗体検査の結果が偽陰性である可能性を考慮した確認検査が必要である。

P-10-9 既往梅毒と診断された妊婦から先天梅毒児が出生した1例

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【緒言】先天梅毒は年間20名程度発症し、妊娠初期に陰性と判断された母体からも出生している。今回妊娠初期より梅毒に感染していたが既往と判断され、先天梅毒児の出生で再感染と診断された症例を報告する。【症例】28歳、2妊1産。4年前に27週で先天梅毒により死産となり、産褥期に抗生剤を内服して治療と判断された(最終RPR値2.7倍)。前回と異なるパートナーとの間で妊娠が成立し、初期のRPRは8倍であったため、梅毒既往と判断された。経過に異常は無かったが、妊娠35週5日に胎児機能不全の診断で当院へ母体搬送となり、搬入時のRPR11倍、TP327倍であった。経腹超音波断層法でBPS2点(羊水のみ)だが胎児や胎盤に異常はなく、胎児心拍数陣痛図で胎児頻脈と一過性頻脈の消失、基線細変動の減少を認め、胎児機能不全と診断した。緊急帝王切開術を施行し、児は2213gの男児でApgarスコア1分後8点、5分後9点、臍動脈血pH7.365であった。児は肝腫大、四肢の紅色丘疹・水疱などの身体的特徴と血液検査のRPR51倍、TP177倍、Xpでの四肢の骨幹端の破壊像および透見像認め、先天梅毒と診断した。10日間のPCG静脈内投与で治癒し、外来で経過観察中である。母体も再感染の診断でAMPC1500mgを8週間内服し、現在RPR値をフォローしている。【結語】RPRが低値のため再感染の診断に至らず、児は先天梅毒を来した。RPR・TPの陽性者は妊娠中に再検査を行い、治療を要する妊婦の検出を図ることが先天梅毒の予防に必要である。今回、当院管理の梅毒妊婦の経過と文献的考察も加えて提示する。

P-10-10 帝王切開術後の *Mycoplasma hominis* による感染で治療に難渋した1例

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【緒言】*Mycoplasma* 属は泌尿・生殖器官に存在する常在菌であり、細胞壁を持たないため通常のグラム染色では検出されず、細胞壁合成阻害作用を有する抗生剤に感受性がないため治療に難渋することが報告されている。本邦における *Mycoplasma hominis* (以下 *M. hominis*) の妊婦での保菌率は11.2%と報告されており、産褥熱や帝王切開後の創部感染、早産などに関与すると言われている。今回我々は帝王切開後、子宮筋層に *M. hominis* による膿瘍形成をきたし治療に難渋した症例を経験したため報告する。【症例】37歳、1妊0産の既往歴のない女性。顕微授精にて双胎妊娠成立し、妊婦健診を受診していた。妊娠36週0日に陣痛発来のため緊急帝王切開で分娩となった。術後より炎症反応高値でありCMZ1g×3回/日の投与を行ったが改善が乏しかったため造影CTを撮像し、子宮筋縫合部前面に膿瘍形成を指摘されたためABPC/SBT3g×4回/日に変更し、術後13日目に膿瘍穿刺を実施した。臨床経過から *Mycoplasma* 属による感染も疑われたためCLDM600mg×3回/日を追加したところ、ドレナージ効果と併せて炎症反応の改善が認められ、術後22日目で退院となった。ドレーン培養からは *M. hominis* が検出された。【考察】本症例では発熱、炎症反応高値であり腹腔内感染を念頭にCMZやABPC/SBTを選択して投与していたが改善は乏しかった。ドレナージ排液を *Mycoplasma* 専用の培地で培養した事で正しく診断し、適切な抗生剤の使用により治癒に至ることができた。【結語】産褥熱患者においてβラクタム系抗生剤を使用しているにも関わらず治療効果が乏しい場合は、*Mycoplasma* 感染症も念頭に置き専用培地での培養や適切な抗生剤選択を行うことが重要である。

P-10-11 母体 *Listeria monocytogenes* 菌血症により絨毛膜羊膜炎を引き起こし早産に至った2例

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【緒言】*Listeria* 属は嫌気性で芽胞を形成しないグラム陽性桿菌の食肉共通の食品媒介性感染症である。妊婦は非妊婦と比較して感染の頻度が高く、経胎盤的に児に感染すると流産・早産や新生児敗血症の原因となる。今回、我々は母体 *Listeria monocytogenes* 感染症から絨毛膜羊膜炎となり早産に至った2例を経験したため報告する。【症例】132歳、経産歴なし。妊娠22週4日に前医で切迫早産のため子宮収縮抑制剤が開始されたが妊娠22日5日に破水し当院へ搬送となった。妊娠22週6日に陣痛発来し経陰分娩に至った。母体腔培養、児の胃液培養から *Listeria monocytogenes* が検出され *Listeria monocytogenes* 感染症による絨毛膜羊膜炎であったと診断した。230歳、経産歴なし。妊娠33週3日に切迫早産の診断で前医に入院となった。妊娠33週4日で発熱、胎児頻脈あり当院へ搬送となった。臨床的絨毛膜羊膜炎の診断で子宮収縮抑制剤を中止し経陰分娩に至った。母体の血液培養、児の咽頭粘液培養、胃液培養から *Listeria monocytogenes* が検出された。【考察】本症例2例では母体抗生剤を投与していたが児の咽頭、胃液培養からは *Listeria monocytogenes* が検出された。*Listeria* 感染が疑われる妊婦に対して高容量抗生剤を投与することで児への感染を防止できたとの報告もあるが、2例共に娩出までの時間が短く、抗生剤投与の効果は限定的であったと考えられる。【結語】*Listeria monocytogenes* による感染症は母児共に予後不良の経過をたどることもあり、母体へ感染してから抗生剤投与が児への感染予防となると報告もあるが、母体が有症状となった際には経胎盤感染している可能性が高く、母体感染予防の啓発が重要である。

P-10-12 当院における梅毒感染妊婦の症例の検討と今後の課題

昭和会音羽病院
野溝万吏

【緒言】梅毒は *Treponema pallidum* が皮膚や粘膜の傷から体内に侵入し、血行性に散布され全身に症状を引き起こす性感染症であり本邦では近年増加傾向を示している。それに合わせて梅毒感染妊婦も増加しており、当院でも2015年から2023年に3例を経験した。【症例1】23歳初産婦。妊娠初期検査で梅毒陽性となり、1期梅毒の診断となり内服治療を行った。経膈分娩となり、母児感染は認めなかった。【症例2】22歳2経産婦。妊娠初期検査では梅毒は陰性であり、妊娠後期に性器ヘルペス治療を行った。産褥に外陰部腫瘍が改善しないため梅毒検査を施行したところ陽性となり、2期梅毒と診断した。出生児は新生児梅毒として入院管理での点滴治療を行った。【症例3】22歳初産婦。妊婦健診は未受診で自宅死産となり、当院に救急搬送された際に梅毒の診断となった。また児は剖検の結果、梅毒感染による死産と診断された。パートナーや家族の支援が得られない状態であり、それが妊婦健診の未受診の原因になったと考えられる。【考察】梅毒は適切な治療で胎児が先天性梅毒に罹患する確率はかなり抑えられるため、初期スクリーニングの重要性を再認識する必要がある。しかし、症例2では初期検査で異常はなく、妊娠後期に感染成立して診断が遅れた。また、症例3ではそもそも未受診であるために感染の診断や治療に至る前に死産という転帰をたどった。【結論】生殖年齢女性での梅毒感染が増えることで、周産期関連疾患として母児感染、新生児感染も増加する。母児感染を防ぐためには、妊婦を含めた一般社会への啓蒙が必要である。

P-10-13 繰り返す発熱を契機に *Campylobacter jejuni* 菌血症の診断に至った妊婦の一例

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【緒言】*Campylobacter* 感染症は細菌性食中毒の中でも報告が多く、*Campylobacter jejuni* (*C. jejuni*) は最も多く分離検出される。腸炎の他、晩期にギランバレー症候群を発症することでも知られ、妊娠中の感染は流産や新生児感染の原因となるとの報告も散見されるが、菌血症まで至る例は0.1-1%と少ない。【症例】31歳、1妊0産。2週間前からの発熱で前医を受診し、セフトリオンを内服し加療するも解熱せず、炎症反応高値が持続したため、妊娠32週5日に当院を紹介受診した。軽度の細菌尿を認め尿路感染を疑ったが、明らかな感染源が不明であったことから各種培養も採取しセフトリアキソンで加療を開始した。第2病日に血液培養2セットからグラム陰性小桿菌が検出され、*Campylobacter* 感染症の可能性が高いと判断。抗菌薬をメロペネムに変更したところ炎症は改善し血液培養で *C. jejuni* が検出されたため、*C. jejuni* 菌血症の診断に至った。加療後症状再燃や胎児の異常は認めず、妊娠38週2日に経膈分娩に至り、現在まで母児ともに異常なく経過している。【結語】腸炎での発熱が知られる本疾患であるが、発熱のみで不明熱のような臨床像を呈することもあり、本症例のように診断に苦慮する場合がある。また *C. jejuni* による新生児早期感染症は敗血症や髄膜炎をきたし予後不良であるといった報告もあり、抗菌薬による加療後も母体の晩期合併症もさることながら、出生児の慎重な経過観察を行う必要がある。

P-10-14 子宮内感染を疑う胎児機能不全を契機に診断に至った母体感染性心内膜炎の一例

長浜赤十字病院
山野和紀、若園依未、北野 照、林真麻子、濱口史香、倉倉道和、中島正敬

【緒言】胎児機能不全の一因として子宮内感染があり、その多くは膈からの上行性だが、一部は血行性である。今回、子宮内感染を疑う胎児機能不全を契機に、血行性感染としての母体感染性心内膜炎の診断に至った症例を経験した。【症例】30歳代の初産婦。既往歴にアトピー性皮膚炎があり、家族歴に特記はなかった。前医で自然妊娠成立と診断され、妊娠中の菌科治療を含む観血的治療歴はなかった。妊娠39週6日に39℃台の発熱を主訴に前医を受診し、CTGモニターで数分間隔の子宮収縮と胎児頻脈・高度遅発一過性徐脈を認め、胎児機能不全として当院に搬送された。未破水での子宮内感染を疑う胎児機能不全と診断され、緊急帝王切開術が施行された。搬送時の母体血液培養、帝王切開中の子宮内容物の培養と新生児血液培養の全てで感受性良好な *Staphylococcus aureus* が検出され、母体の経胸壁心臓超音波検査で大動脈弁に疣贅を認め、母体感染性心内膜炎と診断された。【結語】未破水での発熱を伴う胎児機能不全は血行性の子宮内感染が鑑別である。感染性心内膜炎を含む血行性感染診断のために血液培養が考慮される。

P-10-15 帝王切開患者の絨毛膜羊膜炎・産褥子宮内膜炎管理において偽膜性腸炎の合併が疑われた一症例

董仙会恵寿総合病院

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【背景】今回我々は、帝王切開(CS)を行った周産期感染症患者の管理においてCDIが疑われた症例を経験したので報告する。
【症例】40歳G1P0。妊娠39週2日に前期破水のため入院。破水11時間後からCEZ8時間毎投与を開始。陣痛誘発を行ったが、妊娠39週4日に臨床的絨毛膜炎(CCAM)を疑いABPC/SBT投与を開始した。分娩進行が認められなかったためCSを試行。術後発熱が増悪し、術後2日目から子宮の圧痛を認めたため産褥子宮内膜炎(PEM)が疑われた。また、同時に水様便頻回となり、便培養にてCDAg(+)であったためCDIが鑑別に挙げられた。CCAMが疑われ加療を行っていたこと、新生児感染症が認められ加療を要していたことから本感染症重症化の主体はPEMであると考えられた。妊娠34週4日の陰分泌培養結果(E.Coli, Citrobacter youngae, Klebsiella pneumoniae)、新生児感染症がABPCで軽快傾向であったこと、当院アンチバイオグラムスペクトルからこれらの起炎菌に対してCTRXの効果が高いとの判断し、CTRX12時間毎投与を開始した。また、CDI予防のためメトロニダゾールとプロバイオティクス剤内服投与を開始した。結果PEMは軽快し、下痢症状は治療5日目から改善傾向となった。その後の検査においてCTTox陰性であったが、NAAT検査は陽性と判明しCDIを発症していたことが疑われた。しかし、下痢症状は再発することなく経過し術後9日目に母児共に退院した。前期破水時培養結果E.Coli陽性、羊水培養陰性、胎盤病理検査において絨毛膜羊膜炎が認められ、絨毛膜炎内および臍帯静脈内に化膿性血栓が認められた。
【結語】CSはCDI発症率を高めるとの報告がある、CS患者または術後感染症を発症した患者が下痢症状を発症した場合にはCDIに留意を要する。

P-11-1 当院の妊娠高血圧症候群(hypertensive disorders of pregnancy:HDP)患者における血清中micro RNAの網羅的解析

防衛医大

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【目的】micro RNA(miRNA)は21-25塩基長の一本鎖RNA分子であり、細胞増殖・分化・代謝などで重要な役割を果たし、妊娠高血圧症候群(HDP)発症に関連すると言われている。本研究はHDP合併妊婦(HDP群)と産科合併症の無い妊婦(非HDP群)のmiRNA発現量の違いを明らかにし、現在までに報告されていないmiRNAがあるか検討した。【方法】2017年1月から2022年12月の間、HDP群(18名)と非HDP群(20名)の計38名を対象に、分娩前の妊娠第3期の血清を用い、次世代シーケンスによるmiRNAの網羅的解析を行った。関連性の強いmiRNAを同定するため $p < 0.001$, $q < 0.001$ および $|\log_2 \text{fold change}| > 2$ で解析を追加し、ROC曲線で評価した。【成績】HDP群は非HDP群と比べて早産($p=0.002$)、高血圧の家族歴($p=0.024$)が多かった。発現量に有意差を認めたmiRNAはmiR-145-5p, miR-23a-3p, miR-24-3p, miR-548ad-5p, miR-22-3p, miR-30b-5p, miR-27a-3p, miR-505-3p, miR-130b-3p, miR-223-3pの10種類であり、その中でmiR-145-5p, miR-27a-3pが最もAUCが高かった($AUC=0.93$)。これまでの研究でmiR-145-5p, miR-29b-3p, miR-30b-5pはHDPとの関連が報告されているが、残りの7種類のmiRNAはHDPとの関連は報告されていない。【結論】従来報告されているHDP関連miRNAに加えて、さらに7種類の新たなmiRNAを同定した。今後、追加で同定できたmiRNAの機能を解析することで病態解明やHDP発症のバイオマーカーの同定に繋がる可能性がある。

P-11-2 妊娠高血圧腎症既往患者における低用量アスピリン療法と臨床・胎盤所見の検討宮崎大¹, 宮崎大病理²魏 馨予¹, 佐藤勇一郎², 永井昌美¹, 石井隆徳¹, 菅野知佳¹, 中山徹男¹, 松澤聡史¹, 山田直史¹, 土井宏太郎¹, 児玉由紀¹, 桂木真司¹

【目的】妊娠高血圧症候群の原因として妊娠初期における胎盤形成異常が推定されており、発症予防として低用量アスピリン療法が広く使用されている。しかし、低用量アスピリン療法の発症予防機序については不明な部分が多く、さらに胎盤病理に基づいた検討はほぼなされていない。本研究では、アスピリン療法の予防機序を臨床病理学的に明らかにすることを目的とした。【方法】当施設の分娩症例(2053症例, 2011-2021年)より、妊娠高血圧腎症既往を有する患者を後ろ視的に抽出し、予防的アスピリン内服が行われた9症例(Low-dose aspirin, LDA群)、アスピリン内服が行われなかった17症例(non-LDA群)を対象とした。胎盤病理については、decidual arteriopathy, 梗塞の頻度を検討した。免疫組織化学的検討にはCD31, CD39, smooth muscle actin, CD3抗体を用いて、局在ならびに発現の程度(Allred score)を評価した。また、今回2021年以降に新たに追加されたアスピリン使用3症例についても検討する。【成績】検討終了の範囲内では、LDA群ではnon-LDA群に比して、妊娠週数が延長し(32.3 ± 6.2 週 vs 36.7 ± 2.7 週, $p < 0.05$)、妊娠高血圧腎症の再発頻度が低くなった(59% vs 11% , $p < 0.05$)。組織所見としては、decidual arteriopathyが減少していた(88% vs. 44% , $p < 0.05$)。免疫組織化学的検討では、血管内皮細胞マーカー(CD31, CD39)の発現が増加し(5.6 ± 0.9 vs. 7.5 ± 0.5 , 5.8 ± 1.7 vs. 7.2 ± 0.8 , $p < 0.05$)、血管平滑筋マーカーの発現が低下(2.8 ± 3.0 vs. 0.9 ± 1.4 , $p < 0.05$)していた。【結論】低用量アスピリン療法は胎盤形成と母体血管内皮細胞機能を改善することで周産期予後の改善に寄与していると考えられた。

P-11-3 妊娠高血圧腎症において MgSO₄ が母体血液中 Syndecan1 に与える影響についての検討

近畿大

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【目的】我々は妊娠高血圧腎症 (PE) に対する MgSO₄ 長期投与が血管内皮障害マーカー血中アンチトロンビン (AT) の減少を阻止することを報告した。Syndecan1 (SDC1) は血管内皮グリコカリックス構成成分の一つであり、AT と結合し抗血栓性に関与する。SDC1 は絨毛膜栄養膜細胞に発現し、PE では胎盤形成不全に伴い SDC1 の発現が低下する。本研究では PE における MgSO₄ 投与後の SDC1 と AT の推移を評価した。【方法】PE 3 例の血中 SDC1 を ELIZA 法にて測定し、MgSO₄ 投与後の AT 活性との関連を評価した。【成績】【症例 1】妊娠 27 週加重型 PE、MgSO₄ 開始後 AT、SDC1 値の上昇を認めた (77→83%、17.8→20.5ng/ml) が、嘔気のため中止した。中止後も血圧重症域を認め MgSO₄ を再開すると、AT、SDC1 値は上昇した (77→87%、13.2→15.9ng/ml)。妊娠 29 週母体胸腹水貯留にて緊急帝王切開となった。【症例 2】妊娠 32 週加重型 PE、MgSO₄ 開始後 AT、SDC1 の低下を認めたがその後上昇した (111→109→120%、20→6.6→19.6ng/ml)。妊娠 36 週腎機能悪化のため分娩誘発を行った。【症例 3】妊娠 31 週 PE、MgSO₄ 開始後 AT、SDC1 値の上昇を認めた (69→78%、15.6→18.3ng/ml)。妊娠 32 週胎児機能不全のため緊急帝王切開となった。【結論】血中 SDC1 は MgSO₄ 投与後 AT と同様に増減した。PE における SDC1 の発現推移を評価することにより、MgSO₄ が血管内皮障害の改善をもたらす機序を解明できる可能性がある。

P-11-4 新生児の安静時磁気共鳴機能画像法 (rs-fMRI) を用いた、妊娠高血圧症候群が胎児に与える脳障害の評価

名古屋大

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【目的】妊娠高血圧症候群 (HDP) を発症した母から生まれた児は、将来の神経発達障害や精神疾患へのリスクが高いことが知られている。今回我々は、在胎 34 週未満の早産児の修正在胎 40 週前後 (37~43 週) の頭部 MRI 画像をもとに、先進的ニューロイメージング技術を用いて、HDP による児の脳障害への影響を検討した。【方法】2014~2020 年に当院で出生した 34 週未満の早産児 236 例から、多胎、胎児奇形、明らかな脳障害症例、撮影条件不良症例を除外した 57 症例を対象とした (HDP 群: n=8, 非 HDP 群: n=49)。鎮静下の安静時磁気共鳴機能画像法 (rs-fMRI) を用いて脳全体に 90 個の領域 (region of interest: ROI) を設定し、各々の領域全ての組み合わせ間の MRI 信号変化を機能的結合性 (functional connectivity; FC) として、2 標本 t 検定、network based statistic 法を用いて 2 群間で有意に異なる成分を検索した。【成績】対象症例は分娩週数 (HDP 群: 31.1±2.3 週, 非 HDP 群: 29.9±2.8 週; p>0.05)、出生体重 (HDP 群: 1235±382g, 非 HDP 群: 1380±504g; p>0.05) には有意差を認めなかった。また、rs-fMRI では 90 個の ROI 間の FC のうち、2 群間に有意差があるものは認めなかった。【結論】今回 rs-fMRI を用いて、HDP による早産児の脳への影響を検討した。修正満期時点での脳領域間のネットワーク結合性は、2 群間では有意差を認めなかったが、HDP は新生児の自閉症スペクトラム障害や注意欠如多動性障害などの発達障害のリスクと考えられ、1.5 歳や 3 歳など長期的な評価が必要である。

P-11-5 妊娠高血圧症候群による児の脳容積への影響: 先進的ニューロイメージング技術を用いた検討

名古屋大

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【目的】妊娠高血圧症候群 (HDP) を発症した母から生まれた児は、神経発達障害や精神疾患のリスクが高いことが知られている。今回我々は、在胎 34 週未満の早産児の修正満期頭部 MRI 画像をもとに先進的ニューロイメージング技術を用いて、HDP による児の脳容積への影響を検討した。【方法】2012~2022 年に当院で出生した 22 週から 34 週未満の早産児から、双胎、胎児奇形、明らかな脳障害、MRI 未撮影、画質不良などの症例を除外した 113 症例 (HDP 群 [n=29] と非 HDP 群 [n=84]) を対象とした。SPM12 および Infant FreeSurfer を用いて HDP による深部灰白質 (左右視床、尾状核、被殻、淡蒼球、海馬、扁桃核、側坐核) における脳容積を評価した。HDP による局所脳容積の変化を多変量解析 (共変量: 性別、在胎週数、MRI 撮影週数、MRI 機器) にて評価した。【成績】在胎週数は HDP 群 29.4±3.0 週, 非 HDP 群 30.5±2.8 週 (p=0.08) であった。多変量解析では、すべての部位において HDP 群と非 HDP 群では脳容積に有意差は認めなかった。【結論】今回先進的ニューロイメージング技術を用いて、HDP による早産児の脳への影響を検討した。本検討では HDP により深部灰白質における各領域での脳容積の変化は認めなかった。今後も、HDP による将来的な神経発達障害や精神疾患のリスク上昇の原因を検討していく必要がある。

P-11-6 妊娠高血圧腎症における血中エクソソーム量変化

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【目的】妊娠高血圧腎症 (PE) の発症予知因子について確立しているとは言い難い。絨毛細胞からも放出される小型小胞体エクソソーム (Exo) 量が PE 予知因子になり得るかどうかを検討している。【方法】血漿中 Exo を超遠心法で精製し, 粒子数を Exo マーカーの CD9 で測定 (ELISA 法) した。①発症後比較: PE 発症なし (N) 群 vs. PE 群。②発症前比較: 妊娠初期段階で採血し, 後に PE 発症なし (NC) 群 vs. PE 発症 (PO) 群。PE 群は早発型 (EO-PE), 遅発型 (LO-PE) に細分化して検討した。N 群: 26~29 週 14 例, 35~36 週 24 例, PE 群: EO-PE 11 例, LO-PE 11 例, NC 群: 24 例, PO 群: 2 例。統計学的手法は Mann-Whitney U 検定を用いた。【成績】①発症後比較: Exo 粒子数 (中央値 [四分位]) は, N 群より EO-PE 群で有意に高値 ($12.0 \times 10^{10} / \text{mL}$ [$10.0 \times 10^{10} - 15.0 \times 10^{10}$] vs. $34.0 \times 10^{10} / \text{mL}$ [$22.4 \times 10^{10} - 49.0 \times 10^{10}$], $p=0.003$) で, LO-PE 群でも同様の傾向を認めた ($14.0 \times 10^{10} / \text{mL}$ [$10.5 \times 10^{10} - 18.0 \times 10^{10}$] vs. $21.5 \times 10^{10} / \text{mL}$ [$15.3 \times 10^{10} - 23.8 \times 10^{10}$], $p=0.07$)。②発症前比較: Exo 粒子数は, NC 群と PO 群とでは差を認めなかった ($15.0 \times 10^{10} / \text{mL}$ [$12.5 \times 10^{10} - 16.5 \times 10^{10}$] vs. $13.8 \times 10^{10} / \text{mL}$ [$11.6 \times 10^{10} - 15.9 \times 10^{10}$], $p=0.92$)。【結論】血中 Exo 量は EO-PE 群で増加した。一方, 妊娠初期では PO 群の 2 例では増加していなかったが, 症例を増やして検討中である。

P-11-7 早発型妊娠高血圧腎症の重症化予測における sFlt-1/PlGF 比の有用性の検討

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【目的】soluble fms-like tyrosine kinase 1 (sFlt-1) / proangiogenic placental growthfactor (PlGF) 比は妊娠高血圧腎症 (Preeclampsia; PE) の発症予測に有用であるが, PE 診断後の重症化予測に関する報告は少ない。今回我々は sFlt-1/PlGF 比の早発型 PE 診断後の重症化予測の有用性を検討した。【方法】2016 年 6 月から 2022 年 12 月までの期間に早発型 PE 発症後に sFlt-1/PlGF 比を測定した 48 例を対象とし, 測定時から 1 週間以内の Termination を主要評価項目として後方視的に検討を行った。【成績】測定週数の中央値は 30 週 6 日, 計測時の妊婦の平均年齢は 34.4 歳, sFlt-1/PlGF 比の平均値は 387.2 であった。出生した児の週数の中央値は 33 週 2 日, 出生体重の平均値は 1,461 g であった。Termination の基準は全て産科的適応に基づくものであった。sFlt-1/PlGF 比測定から 1 週間以内の Termination の必要の有無に関して, sFlt-1/PlGF の crude Odds Ratio (cOR) は 1.003 (95% 信頼区間 1.000-1.004) で, ROC 曲線の AUC は 0.689, 感度特異度が最大となる Cut Off 値は 164.7 であった。sFlt-1/PlGF ≥ 165 であった 31 例のうち 16 例 (51.6%), sFlt-1/PlGF < 165 であった 17 例のうち 2 例 (11.8%) で 1 週間以内の Termination が必要となった。sFlt-1/PlGF ≥ 165 である症例の 1 週間以内の Termination の有無に関して cOR は 11.1 (95% 信頼区間 1.1-107.1) であった。【結論】sFlt-1/PlGF 比を計測し, Cut off 値を 164.7 とした場合, 早発型 PE における 1 週間以内の Termination の可能性を予測できる。早発型 PE と診断した後に sFlt-1/PlGF 比を測定することで, 高次医療機関への搬送やステロイド投与時期を決定する際に有用となりうる。

P-11-8 胎児発育不全症例に対する sFlt-1/PlGF 比測定の有用性の検討

新潟大

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【目的】sFlt-1/PlGF 比測定は妊娠高血圧腎症 (PE) の短期発症予測マーカーとして用いられている。本検討は胎児発育不全 (FGR) 症例に対する同比測定の有用性を明らかにすることを目的とした。【方法】当院で 2022 年 4 月から 2023 年 7 月の間に, 妊娠 18~35 週で推定体重 (JSUM) -1.5SD 未満の FGR に対して sFlt-1/PlGF 比を測定した 20 例の臨床的背景, 同比と子宮動脈 PI (UtA-PI) 値との相関, 妊娠経過について, 診療録を元に後方視的に検討した。なお, sFlt-1/PlGF 比 > 38 を陽性, 両側 UtA-PI 値の平均値が 95%tile 以上を高値と定義した。【成績】20 例の sFlt-1/PlGF 比測定時の妊娠週数中央値は 28 週 (22-33), sFlt-1/PlGF 比は 8 (0.5-662), UtA-PI 値は 0.87 (0.53-2.04) であった。分娩時週数は 36 週 (27-40), 出生体重は 1570 g (190-2566) であった。sFlt-1/PlGF 比陽性は 20 例中 7 例であり, うち PE を発症したのは 1 例のみであった。他, 子宮内胎児死亡 2 例, 胎児機能不全 2 例, 常位胎盤早期剝離 1 例であり, 同比が陽性であった 7 例中 6 例が妊娠転帰不良であった。sFlt-1/PlGF 比と UtA-PI 値に有意な正の相関を認め ($r=0.55, p=0.01$), 同比が陽性かつ UtA-PI 高値の 4 例全例が妊娠転帰不良であった。一方, sFlt-1/PlGF 比陰性であった 13 例中 11 例が 36 週以降まで妊娠延長が図れていた。【結論】FGR に対する sFlt-1/PlGF 比計測は, 陽性であっても PE 発症はわずかであった。一方, UtA-PI 値測定と併用することにより周産期予後を推定しうる可能性が示唆された。

P-11-9 妊娠高血圧症候群発症リスクと考えられる頸動脈内膜中膜複合体のカットオフ値

愛知医大

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【目的】高齢妊娠の定義は1992年に30歳以上から35歳以上に改定された。近年、高齢妊娠の増加によりハイリスクとして扱われる割合は上昇傾向にある。ハイリスクの中の1つに妊娠高血圧症候群(HDP)があり、年齢の上昇とともに低下する血管内皮機能が、HDPリスクを上昇させると考えられている。我々は、器質的血管障害の指標である頸動脈内膜中膜複合体厚(IMT)に注目し、母体IMTの肥厚はHDP発症に影響することを報告してきた。今回、妊婦のIMTを計測し、HDP発症リスクとの関連性を検討した。【方法】2020年4月～2022年1月までに当院で分娩となった331名の妊婦を対象とした。HDPと診断された妊婦は331名中49名であった。対象者の右頸動脈のIMTを計測し、以下の3項目を検討した。①年齢とIMTの相関を検討した。②HDPの発症率が上昇するIMTのカットオフ値を、ROC曲線を用いて検討した。【成績】①年齢とIMTは、正の相関を示した($R=0.402, P<0.001$)。②HDP発症率が上昇するIMTのカットオフ値は、0.38mmであり、感度60.0%、特異度85.0%であった($AUC=0.75, 95\%CI=0.68-0.83$)。【結論】器質的血管機能の視点からHDPリスクを評価したところ、IMT:0.38mmがHDP発症リスクを上昇させる最適なカットオフ値と考えられた。

P-11-10 妊娠高血圧症候群と診断された症例のうち、頭部MRI&MRA検査で可逆性脳血管攣縮を指摘された症例のリスク因子の検討

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【目的】妊娠高血圧症、妊娠高血圧腎症、高血圧合併妊娠、加重型妊娠高血圧腎症と診断され、頭部MRI&MRA検査で可逆性脳血管攣縮を指摘された症例の背景因子と合併疾患を検討する。【方法】2022年1月から2022年7月に妊娠高血圧症候群として診断され、当院外来もしくは入院管理を行った症例を対象とした後方視的研究である。一過性に血圧上昇を認めその後妊娠高血圧症候群が否定された症例、分娩時初診の未受診妊婦のため妊娠経過が不明であった症例は除外した。主要評価項目を頭部MRA検査での脳血管攣縮の頻度、副次評価項目を妊娠高血圧症候群の発症に起因する疾患としてHELLP症候群、常位胎盤早期剝離、脳出血、PRES、胎児発育不全、羊水過少とした。また主要評価項目の有無による母体背景を比較した。統計学的検定はカイ二乗検定、Fisher正確確率検定、Mann-Whitney U検定を用い、有意水準は $P<0.05$ とした。【成績】対象期間中に妊娠高血圧症候群と診断された症例196例のうち、19例に脳血管攣縮を認めた。5% (3例)にHELLP症候群、26% (5例)に胎児発育不全、5% (3例)に羊水過少を認めた。撮像前に頭痛や視野症状を含む神経症状を認めた症例は63% (12例)であった。可逆性脳血管攣縮を認めた群では認めなかった群に比べて、収縮期血圧の最高値($P=0.000695$)、拡張期血圧の最高値($P=0.042$)が有意に高く、胸腹水や肺水腫を認めた症例が有意に多かった($P=0.00187$)。【結論】分娩時を含めた妊娠中、分娩後に収縮期血圧もしくは拡張期血圧で重症高血圧を認めた症例、胎児発育不全や羊水過少を認めていた症例では、脳出血や脳梗塞の原因となる可逆性脳血管攣縮を起こす可能性が高い可能性がある。

P-11-11 子癇発症と妊娠高血圧症候群の不一致：23症例による後方視的解析

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【目的】妊娠高血圧症候群(Hypertensive Disorders of Pregnancy: HDP)は子癇発症の主要リスク因子であるが、血圧や検査所見に異常がなくても子癇を発症する症例を稀に経験することがある。さらに、子癇は母児に重篤な転帰を生じる可能性があるが、その発症予測は困難である。今回我々は子癇症例の発症直前の臨床所見やHDP合併の有無について多施設の情報を収集し、後方視的検討を行った。【方法】当院および周産母子センターを有する協力施設で2007年5月から2021年9月において子癇を発症し詳細な医療情報の入手が可能だった23例を対象とした。子癇発症前の臨床所見を記録より収集し、HDP合併や血圧上昇など子癇発症のリスク因子の有無を症例毎に明らかにした。【成績】子癇を発症した23例の平均年齢は31歳で、初産は17例(73.9%)だった。発症した時期は妊娠中5例(21.7%)、分娩中7例(30.4%)、分娩後が11例(47.8%)だった。発症前にHDPと診断されたのは16例(69.5%)であり、うち妊娠高血圧腎症が7例(30.4%)と最も多かった。発症直前に著明な血圧上昇を呈していたのは9例(39.1%)だった。血圧上昇症例の中で最も高い血圧値の中央値は収縮期血圧185mmHg、拡張期血圧102mmHgだった。なお、7例(30.4%)は発症前に血圧上昇や検査所見の異常がなく突然子癇を発症していた。【結論】今回検討した子癇症例の30.4%が血圧上昇やHDPの発症がないにもかかわらず発症していた。このことから、子癇の病態とは必ずしもHDP発症とは一致していない可能性が示唆された。今後さらに対象者を拡大して子癇発症のリスク因子の解析を行う予定である。

P-11-12 妊娠高血圧症候群に対する降圧薬導入時期と妊娠アウトカムとの関連

北海道大

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【目的】妊娠高血圧症候群 (HDP) は、そのコントロール不良により母体の子癇や脳出血、胎盤機能不全、胎児発育不全など様々な異常を来し、周産期において母体および胎児の予後に大きな影響を与える。かつては、胎盤血流量低下による胎児発育の阻害を懸念し、軽度とされる収縮期血圧 160mmHg/拡張期血圧 110mmHg 未満であれば降圧薬の導入に関しては慎重な姿勢がとられる傾向にあったが、近年では妊娠初期～中期の間できるだけ早期から降圧薬による介入を行い収縮期血圧 140 mmHg/拡張期血圧 90mmHg 以下に保つことで早産や新生児および母体における重篤な合併症のリスクが低減することが報告されている。当院でも早期からの循環動態の安定化に取り組んでおり、治療開始時期によって妊娠アウトカムに差異がでるか検討することとした。【方法】HDP 患者に対し降圧薬が導入された週数を調べ、介入が 20 週未満の群と 20 週以降の群とを比較し、早産率や出生体重、胎盤重量との関係を解析した。【成績】2013 年から 2023 年に当院で分娩した妊婦について検討し、妊娠 36 週以前の早産率は、妊娠 20 週未満に降圧薬による介入を行った群 (n=21) で 19.0% であったのに対し、妊娠 20 週以降の介入群 (n=60) では 56.7% と高かった (p=0.0013)。低出生体重児および出生体重が 2SD を下回る確率は、同様に 20 週以降の介入群で増加する傾向にあった。【結論】妊娠高血圧症候群に対する早期の降圧薬導入は早産や胎児の低体重を有意に抑制し、母体および胎児の良好な妊娠経過に寄与する。

P-11-13 妊娠中のヘマトクリット値と妊娠高血圧腎症発症の関連

長崎医療センター

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【目的】妊娠中のヘマトクリット (Ht) 値は、正常の妊娠経過では循環血漿量の増加に伴い希釈性に低下することが知られているが、PE においてはそれらの増加制限が生じることで Ht 値は通常より高値を示すという報告があり、妊娠中の Ht 値が PE 発症の予測因子となる可能性が示唆されている。今回我々は妊娠中の Ht 値と PE 発症との関連を検討した。【方法】2022 年 1 月 1 日から 1 年間の当科における全分娩産例を対象とし、主要転帰を PE として、妊婦初期 (12 週前後)、中期 (30 週前後)、および後期 (36 週前後) の Ht 値が PE 発症と関連するか否かについて後方視的に検討した。また、Ht 値に関連する他の因子についても併せて検討した。【成績】対象は 625 例であり、HDP は 66 例 (10.6%)、PE は 26 例 (4.1%) に発症した。妊娠中期の Ht 値は PE 発症と正の相関を認めた (p<0.05) が、初期および後期の Ht 値は有意な関連を認めなかった。ROC 曲線から求めた妊娠中期の Ht 値のカットオフ値は 35.4 であり、35.4 以上の症例の PE 発症オッズ比は 3.8 (95% 信頼区間 1.5-9.7) であった。また、妊娠中期の Ht 値は、初産 (p<0.05) および肥満群 (非妊時 BMI25kg/m² 以上) (p<0.001) で高値であり、35 歳以上の高齢産婦で高い傾向があった (p=0.066)。これらの交絡因子を調整すると Ht 値と PE 発症の関連は有意ではなかった。【結論】肥満、初産、高齢は PE 発症の古典的リスク因子である。今回の検討では統計的パワー不足のために、Ht 値と PE 発症の独立関連性についての検討には至らなかったが、これらの古典的リスク因子と妊娠中の血液希釈動態の関連は必ずしも明らかではない。臨床的には、妊娠 30 週前後の Ht 値高値の症例は PE 発症を考慮した管理が必要である。

P-11-14 産後蛋白尿が残存する妊娠高血圧腎症における尿細管障害の検討

愛知医大

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【目的】妊娠高血圧腎症 (PE) では妊娠中急速に蛋白尿が増悪し、多くは産後すみやかに改善するが一部において蛋白尿が残存する。我々はこれまで蛋白尿を呈する PE 妊婦において妊娠中に尿細管障害が起きていることを報告してきたが、PE における尿細管障害が産後どの程度持続するかは明らかになっていない。今回、PE 妊婦を産褥 3 か月まで追跡し、産後長期にわたり蛋白尿が持続する PE 妊婦の尿細管障害について考察した。【方法】2019 年 1 月から 2022 年 12 月までに当院で分娩した PE 妊婦 20 例を、産褥 3 か月に尿蛋白 0.15 g/gCr 未満であった 14 例 (尿蛋白消失群) と、0.15 g/gCr 以上であった 6 例 (尿蛋白残存群) に分別し、PE の診断時における尿蛋白/クレアチニン比を比較した。尿細管障害の指標として、PE の診断時と産褥 3 か月における尿中 N-acetyl- β -D-glucosaminidase (NAG)/クレアチニン比、尿中 liver-type fatty acid-binding protein (L-FABP)/クレアチニン比を両群間で比較検討した。【成績】PE の診断時において、尿蛋白残存群は消失群よりも尿蛋白 (g/gCr) が有意に高く (p<0.05)、尿中 NAG (U/gCr) が有意に高く (p<0.05)、尿中 L-FABP (μ g/gCr) が有意に高かった (p<0.05)。産褥 3 か月において、尿蛋白残存群は消失群よりも尿中 NAG (U/gCr) が有意に高く (p<0.05)、尿中 L-FABP (μ g/gCr) が有意に高かった (p<0.05)。【結論】尿蛋白残存群は消失群よりも産褥 3 か月の尿中 NAG と尿中 L-FABP が有意に高値であり、産後長期にわたり蛋白尿が持続する PE 妊婦は尿細管障害が残存している可能性が明らかとなった。

P-12-1 当院における新生児薬物離脱症候群の傾向

佐賀大

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【目的】新生児薬物離脱症候群は妊娠中に内服した薬剤や嗜好品が胎盤を通過することによって児に移行し、分娩により供給が中断することで中枢神経系、自律神経系、消化器系症状を呈する疾患である。今回は当院における向精神薬を2剤以上内服している妊婦から出生した児の新生児薬物離脱症候群の症状や発症する症例の傾向を検討した。【方法】2018年4月1日から2023年8月31日までに当院にて出生し、新生児科管理となった新生児を電子カルテから後方視的に検討した。新生児薬物離脱症候群と診断された児の評価は電子カルテの記載内容を参考に磯部スコアで算出した。【成績】当院で出生し新生児管理となった新生児は431人であった。その中で、新生児薬物離脱症候群の診断で新生児科管理となった症例は23人であった。23人中新生児薬物離脱症候群の症状を呈したのは7人(30.4%)で、内服薬剤数の中央値は5(3-7)剤であった。てんかんで3剤内服した母体から出生した2例の児はともに傾眠傾向を呈した。7例中5例が眠剤を内服し、4例が眠剤を2種類以上内服した。症状では振戦が3例(42%)で最も多かった。治療介入を要した症例はなかった。磯部スコアの中央値は2.5点(1-5)であった。向精神薬の内服数で症状の出現に有意差はなかった。【結論】新生児薬物離脱症候群のリスクとなる可能性と考えられるのは複数の抗てんかん薬、眠剤の内服であった。向精神薬の新生児薬物離脱症候群の発症は内服数に依存せず、内服する薬剤の種類に依存することが示唆された。

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P-12-2 当院で経験した梅毒合併妊娠21例の周産期予後の検討

愛染橋病院

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【目的】近年全国的に、特に都市部で梅毒感染者数が急増している。当院は大阪市内の総合周産期母子医療センターであり、周産期管理を行った梅毒感染妊婦において、周産期管理と新生児転帰の関連について検討した。【方法】2018年10月から2023年7月までに当院で周産期管理を行った梅毒感染妊婦症例を対象とし、後方視的に検討を行った。【成績】4651例のうち梅毒感染妊婦は21例(4.5%)認めた(紹介患者13例)。患者の年齢の中央値は23(18-40)歳、初産婦は15例(71%)、診断時週数の中央値は23(8-37)週、無症候性症例が20例(95%)、早期梅毒症例は21例(100%)であった。また、未受診妊婦は8例(38%)、性産業従事者は4例(19%)であった。治療は経口ペニシリン薬が19例(90%)、ペニシリン筋注が2例(10%)であった。妊娠中に治癒と判定された症例は38%(8例)であった。分娩週数の中央値は39週(28-41週)、児の出生体重の中央値は2822g(1222-3558g)であった。先天梅毒の児は3例(14%)で、うち1例は出生前診断で先天梅毒の所見を認めた。3例中1例は妊娠32週で死産、2例は妊娠28、妊娠30週での分娩となり、治療開始後4週以内での分娩であった。【結論】本研究で梅毒合併妊婦は若年、未受診妊婦などの社会リスクが高い症例が多く、診断・治療開始が遅れる症例が多いことが分かった。梅毒合併妊婦は、胎児診断のついていない症例や早産期に分娩となる症例も多いことから、周産期センターでの管理が望ましい。

P-12-3 下垂体機能低下症合併妊娠の周産期予後の検討

千葉大

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【目的】下垂体機能低下症合併妊娠は、妊娠中の生理的な変化に即してホルモン補充量を変更する必要があること、産科合併症の増加、下垂体後葉ホルモンであるオキシトシン分泌不全が原因と思われる帝王切開率の上昇や分娩時出血の増加等が指摘されている。当院で経験した下垂体機能低下症合併妊娠の周産期予後について検討したので報告する。【方法】2014年4月から2023年3月に当院で管理した下垂体機能低下症合併妊娠11症例15妊娠について、妊娠中のホルモン補充、産科合併症、分娩誘発の有無、分娩方法、分娩時出血量、児の予後等を後方視的に検討した。【成績】妊娠前からホルモン補充を行っていた症例は14妊娠、このうち後葉ホルモンであるバソプレシン(VP)を使用していたのは10妊娠であった。14例中7妊娠で薬剤の増量が必要であった。分娩方法は、予定帝王切開が2妊娠(骨盤位・既往帝王切後妊娠)、経陰分娩試行が13妊娠であった。自然陣痛発来は5妊娠(この内1妊娠で分娩促進)で全て経陰分娩、分娩誘発は8妊娠で、経陰分娩に至ったものが3妊娠、緊急帝王切開が5妊娠であった。緊急帝王切開の原因は、分娩停止が3妊娠、胎児機能不全と児頭骨盤不均衡がそれぞれ1妊娠であった。経陰分娩試行13妊娠中の経陰分娩率は8妊娠(61.5%)であった。また、このうちVPを使用していた10妊娠中経陰分娩となったのは、5妊娠(50%)であった。輸血を要した分娩時大量出血症例はなかった。早産・不当軽量児はそれぞれ1妊娠であった。【結論】下垂体機能不全症合併妊娠は、経過中にホルモン補充量の調整を考慮する必要がある。帝王切開率は高いが、適切な管理で経陰分娩も可能である。

P-12-4 脳卒中ハイリスク妊婦に対する頭部MRIスクリーニング検査の検証

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【目的】脳卒中のハイリスク妊婦に対して、頭部MRIスクリーニングによる脳動脈瘤の指摘の有無、その後の経過を明らかにする。【方法】2010年1月から2022年12月までに、当院で下記の基準に該当し頭部MRIを撮像した妊婦を対象とした後方視的検討である。撮像基準は①慢性高血圧②脳血管疾患の既往を主項目とし、①40歳以上②父親または母親の脳血管疾患の既往③慢性頭痛④妊娠高血圧症候群(HDP)の既往⑤BMI $\geq 25\text{kg/m}^2$ を副項目とし、主項目1つ以上かつ副項目2つ以上該当とした。既知の脳血管疾患のある妊婦は除外した。頭部MRIでの脳動脈瘤の有無、また脳動脈瘤が指摘された場合はその後の経過を検討した。【成績】対象は28例で既知の脳血管疾患のある6例を除外した22例が解析対象となった。脳動脈瘤が指摘されたのは2例であった。1例はHDPの既往のある43歳1経産婦。高血圧合併妊娠のため妊娠26週に頭部MRIを撮像され、右内頸動脈傍突起部に7mmの脳動脈瘤が指摘された。妊娠35週に加重型妊娠高血圧腎症の診断で緊急帝王切開術が行われた。以降、定期的にMRI撮像され瘤径は変化なく、以後6年くも膜下出血なく経過している。もう1例は、父親の脳出血の家族歴のある36歳1経産婦。非妊娠時のBMI: 41.0kg/m^2 。妊娠16週に頭部MRI撮像され前交通動脈に5-6mm大の脳動脈瘤を指摘された。血圧上昇のため妊娠37週に既往帝王切開術に対して選択的帝王切開術が行われた。38歳時に予防的にコイル塞栓術が行われた。以後11年くも膜下出血なく経過している。【結論】22例中2例に脳動脈瘤を認めた。指摘された脳動脈瘤の2例に破裂はなかった。本検討は症例数が限られているため、さらなる症例の積み重ねにより頭部MRI撮像基準の検証が引き続き必要である。

P-12-5 妊娠中の子宮頸管ポリープ切除に関する後方視的検討

倉敷中央病院

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【目的】妊娠中の子宮頸管ポリープは流早産のリスク因子と考えられ、後期流産を含む流早産率は16~31%と報告されている。またポリープ切除による流早産予防効果は不明である。当院ではポリープが比較的大きなものや出血を伴う場合、吸引による結紮切除またはケリー鉗子による捻除を行っており、今回その成績について検討した。【方法】過去5年間に妊娠14週以前に診断した子宮頸管ポリープを有する単胎妊娠例について、ポリープ切除の有無や方法、その他の診療情報および分娩経過について後方視的に検討した。【成績】ポリープ切除例は34例(結紮切除: L群13例, 捻除: T群21例)、保存的管理群(C群)14例だった。性器出血があったのは、L, T, C群それぞれ10, 8, 9例で、子宮口から突出している部分の長径(平均)は、19, 13, 2mmだった。切除週数(平均)はL群12.3週, T群10.2週で、病理所見は全体でdecidual polyp21例, cervical polyp11例, necrotic polyp2例だった。切除以外の治療として、腔洗浄, プロバイオティクス製剤投与, 黄体ホルモン投与が切除群(L+T群)で5, 6, 5例, C群で0, 4, 3例に施行されていた。切除群5例, C群3例に頸管短縮(25mm未満)を認め、それぞれ3例, 0例に治療的頸管縫縮術を施行していた。14週以降の流早産例は切除群で3例(8.8%), C群で4例(29%)だった。【結論】当院では切除群の流早産が少ない傾向を認めたが、追加治療を要する症例もあり、有効性は不明だった。治療方針の決定には更なる検討が必要と考えられた。

P-12-6 妊娠後期の胎盤機能低下に伴うインスリン使用量に関する検討

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【目的】胎盤からの抗インスリン物質は妊娠後期まで産生され、それに伴いインスリン需要量は増加するが、中には胎盤機能低下に伴いインスリン需要量が減少する症例もみられる。そこで妊娠中にインスリン治療を受けた糖代謝異常合併妊娠の患者を検討し、インスリン使用量に関し検討した。【方法】2022年4月から2023年3月までに当院で分娩となった952例のうち、妊娠中にインスリンを使用した2型糖尿病合併妊娠8例、妊娠中の明らかな糖尿病1例、妊娠糖尿病33例の計42例について、妊娠中の最大インスリン使用量、分娩直前のインスリン使用量、分娩方法、陣痛発来の有無、出生児体重などについて後方視的に検討した。【成績】分娩直前のインスリン使用量は減少する傾向にあり、特に妊娠糖尿病と診断されインスリンを使用していた33例では、分娩直前のインスリン使用量は最大使用量と比べ有意に減少していた(中央値4単位 $P=0.013$)。2型糖尿病合併妊娠・妊娠中の明らかな糖尿病をあわせた9例では、症例数が少なく有意差を認めなかったが($p=0.203$)、分娩直前のインスリン使用量は最大使用量と比べ減少する傾向にあった。出生児がAFD (appropriate for date)・LFD (light for date)であった33例では、HFD (heavy for date)児と比べて分娩直前のインスリン使用量は有意に減少していた(中央値4単位 $p=0.023$)。【結論】妊娠16週頃からインスリン抵抗性が高まり、妊娠37週頃までインスリン必要量は増加するとの報告があるが、分娩が近づき胎盤機能と共にインスリン抵抗性が低下すると、追加に必要なインスリン使用量が減少する可能性に十分留意し管理することが重要と考えられる。

P-12-7 妊婦の脳出血—症状と対策, 4症例からの検討—

岐阜県総合医療センター

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【目的】我が国の妊産婦死亡の原因の15%は脳出血・脳梗塞でありその早期発見は臨床上的重要なテーマの一つである。当院で経験した脳出血4症例について症状と対応について報告する。【方法】当センターにおいて2010年1月より2023年7月までの間に経験した、妊娠中に脳出血を来した4例。【成績】発症年齢は28~37歳、発症時期は全例妊娠後期であった。特記すべき既往症や妊娠合併症を持つ症例はなかった。初発症状は1)起床時の嘔気と今までに経験のない後頭部痛2)分娩中の嘔気・頭痛および突然の意識レベル低下3)突然の回転性眩暈、側頭部痛、嘔気4)突然の意識消失・25分間続く意識障害、であった。脳動脈瘤破裂によるくも膜下出血(SAH)が3例と脳幹部出血が1例あった。3例に母体適応の緊急帝王切開(eCS)、1例に胎児適応のeCSを施行した。SAHに対しては2例が開頭クリッピング術をeCS後に施行し、1例がコイル塞栓術をeCS前に施行した。周産期予後は母体死亡が2例であった。1例は脳幹部出血により呼吸停止に至っており脳外科治療の適応なく看取りとなった。1例はコイル塞栓術により状態改善していたが脳血管攣縮を起こし、脳虚血により死亡した。他2例は神経学的後遺症がまったくなく、または軽度残存のみで退院となった。【結論】今回の4症例もさることながら妊娠中の脳出血は脳血管疾患からの出血が半数以上を占め、なかでも脳動脈瘤破裂によるSAHは2大原因の一つである。脳血管疾患を疑うためには初発症状を知り、そして速やかに脳外科治療につなげることが非常に重要である。また、脳動脈瘤のスクリーニングは未だ一般的ではないが、機会があれば施行することで救命可能な症例の増加を期待したい。

P-12-8 妊娠初期耐糖能異常検査についての検討

近江八幡市立総合医療センター

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【目的】産婦人科ガイドライン産科編2020において、妊娠初期のスクリーニングの目的は妊娠中の明らかな糖尿病を見出すことを主目的とするのも一案であると記載され、産婦人科ガイドライン産科編2023においても同様の記載が認められる。本研究の目的は、その方針の妥当性について検討することである。【方法】妊娠初期に75gOGTTを受けた82症例を対象とし、A群:75gOGTT陰性、B群:75gOGTT陽性かつHbA1c<6.5%、C群:HbA1c6.5%≤の3群に分類し、母体・新生児予後について検討を行う。【成績】C群は1症例のみであった。A群52症例、B群29症例について検討を行った。帝王切開率、HDP合併率、NICU入室率、人工呼吸管理率、分娩週数、出生体重(g)、出生体重(SD値)、Apgarスコア1分値・5分値に有意差を認めなかった。インスリン使用の有無について、A群では0症例に対してB群で17症例(58.6%)と有意に高値であった。【結論】妊娠中の明らかな糖尿病を見出すことを主目的とすることにより、治療対象症例を大幅に減少させることができる(30症例→1症例:3.3%)。A群とB群とで母体予後・新生児予後について有意差を認めず、妊娠中の明らかな糖尿病を見出すことを主目的とすることが妥当であるとも言えるが、B群ではインスリンを用いて治療されている症例が有意に多く、治療介入により予後に差がなくなった可能性も十分にある。妊娠中の諸検査の主目的は、妊娠・分娩予後の改善であり、妊娠中の明らかな糖尿病を見出すこともその手段の一つである。診断基準の変更、特に緩和には慎重な検討が必要であると考えられる。

P-12-9 トレプロスト吸入を使用し分娩管理した肺高血圧合併妊娠の一例

国立循環器病研究センター

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【背景】肺高血圧合併妊娠は分娩直後の静脈還流量急増による急変リスクが高い。エボプロステノール注射は強力な肺血管拡張作用を有するが、抗血小板作用による出血合併症が報告されている。一方、最近日本でも使用可能となったトレプロスト吸入は局所に作用するため出血合併症が少ないことが期待される。【目的】肺高血圧合併妊娠におけるトレプロスト吸入の有効性を調べる。【症例】症例は心室中隔欠損閉鎖術後の40歳初産婦。肺動脈圧(PAP)61/27(41)mmHg、肺血管抵抗(PVR)12.6WU、心拍出係数(CI)2.2L/min/m²の肺動脈性肺高血圧が残存していたが、挙児希望が強く妊娠に至った。妊娠28週時点でPAP57/25(40)mmHg、PVR6.2WU、CI3.2L/min/m²の肺動脈圧高値が持続していた。分娩時の血行動態変動に備え、妊娠33週よりエボプロステノールを開始した。低置胎盤であり易出血性を極力抑えるため、トレプロスト吸入併用でエボプロステノール必要量の軽減を図った。エボプロステノール0.4ng/kg/min、トレプロスト54μg、ベラプロスト360μg、タダラフィル40mg投与下に、妊娠34週3日脊髄くも膜下硬膜外併用麻酔下に、低置胎盤のため帝王切開で女児を分娩した(出生体重1877g[-0.6SD]、Apgarスコア1分8点/5分9点)。術中出血量は1550mlで、血行動態の破綻はなかった。産褥にトレプロストを162μgへ増量しエボプロステノールを終了した。産褥3週、PAP58/24(38)mmHg、PVR10.6WU、CI2.2L/min/m²で、妊娠前と同等の血行動態であった。【結論】低置胎盤、肺高血圧合併妊娠に対して、帝王切開前にエボプロステノール持続静注とトレプロスト吸入を併用し、合併症なく手術を終え生児を得た。

P-12-10 妊娠初期のスタチン曝露と児の先天異常リスク評価：妊娠と薬情報センター 65 例のケースシリーズ

国立成育医療研究センター妊娠と薬情報センター
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【目的】 高脂血症治療の第一選択薬である HMG-CoA 還元酵素阻害薬 (スタチン) は、動物実験における催奇形性、及び児の神経発達に対する潜在的なリスクを理由として、日本では妊婦が添付文書上「禁忌」に設定されている。本邦の成人家族性高コレステロール血症診療ガイドライン 2022 では、妊娠する少なくとも 3 か月前の本剤中止が推奨されている。一方で冠動脈疾患など重篤な合併症リスクの高い患者においては妊娠中でも必要な場合があることから、妊娠中のスタチン使用について安全性情報のニーズがあるが情報は不足している。本研究の目的は、スタチンの妊娠初期曝露による児の先天異常リスクを評価することである。【方法】 国立成育医療研究センター妊娠と薬情報センターにおいて、2005 年 10 月から 2017 年 12 月までに妊娠中の薬の安全性情報に関するカウンセリングを 13,599 人の女性に行った。質問紙法による分娩転帰の追跡調査について同意が得られた 5,840 人のうち、妊娠初期に本剤を使用した 65 例について、出生後 1 か月時点での児の先天異常の有無とその内容を調査した。【成績】 妊娠初期にスタチンを使用した 65 例のうち、児の先天異常は 4 例 (6.2%) に見られた。4 例の内訳は、大奇形 1 例 (先天性心疾患)、小奇形 3 例 (停留精巣、卵円孔閉存、副耳) であった。【結論】 妊娠初期曝露による先天大奇形は 65 例中 1 例であった。更なる症例の集積によりスタチンの妊娠初期曝露による先天異常リスクの評価を行うことで、妊娠中もスタチンによる治療が不可避である女性患者にとって有益な情報になることが期待される。

P-12-11 弁膜症術後妊娠中に感染性心内膜炎を発症し、心不全増悪をきたし最終的に開心術を要した一例

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【緒言】 妊娠中は循環血漿量の増加により、心疾患合併妊婦では症状が増悪することがある。今回我々は大動脈弁置換術後の妊婦において、感染性心内膜炎 (IE) による心不全増悪のため帝王切開術を行い、開心術を要した一例を経験したため報告する。【症例】 33 歳、2 妊 1 産。既往歴：先天性大動脈弁狭窄 (AS) に対して 26 歳時自己心膜を用いた大動脈弁再建術施行。僧帽弁逆流 (MR) および狭窄 (MS) は経過観察中。29 歳時帝王切開にて第一子分娩。現病歴：妊娠 14 週から微熱、咳嗽、倦怠感あり、数回の抗菌薬治療後も改善しなかった。妊娠 16 週心エコーでは疣贅はなく弁膜症の増悪なし。妊娠 24 週時倦怠感、咳嗽を主訴に当院小児科受診。白血球数、CRP、BNP の上昇と経過から IE が疑われ入院した。入院時心エコーで疣贅はなく、重度 AS と軽度大動脈閉鎖不全 (AR)、MS、MR を認めた。入院後はバンコマイシンとセフトリアキソンを投与し、利尿薬も併用。一時的に症状は改善したが白血球増多や CRP 上昇は持続し、妊娠 26 週頃より咳嗽が再増悪した。妊娠 27 週 1 日 BNP、トロポニン I が上昇し、心エコーで重度 AR が見られ、感染による形成弁の破壊が示唆された。母体心不全治療のため同日全身麻酔下に緊急帝王切開術を行った。術後は内科的管理を試みたが全身状態不良であり、術後 5 日目に外科治療のため高次施設に搬送された。翌日、大動脈弁および僧帽弁の二弁置換、上行大動脈グラフト置換、冠動脈縫合術が行われた。術後経過は良好で、術後 2 か月に退院した。【結語】 妊娠中は循環血漿量の増加により心血管系への負担が増すため、心疾患合併妊婦においては易疲労感や息苦しさ等の症状を見逃さず積極的に評価を行っていくことが重要である。

P-12-12 当院で周産期管理を行った卵子提供妊娠の 5 例

東海大

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【目的】 近年の晩婚化に伴い、40 歳代半ばから閉経後の卵子提供妊娠が増加している。卵子提供妊娠は高齢妊娠に伴う合併症に加え、卵子提供特有の合併症として妊娠高血圧腎症 (HDP) や産後出血など母体リスクを伴う。今回、卵子提供後に当院で周産期管理した 5 例を報告する。【症例】 症例 1 は 45 歳 G3P1、41 歳時双胎妊娠で C/S。マレーシアで 2 回目の卵子提供で妊娠。妊娠 33 週に HDP で管理入院。切迫子宮破裂で妊娠 36 週 5 日緊急 C/S。症例 2 は 47 歳 G2P0、46 歳時米国で卵子提供妊娠も 13trisomy で 18 週に中絶。再度卵子提供で二絨毛膜二羊膜双胎 (DD 双胎) 妊娠。妊娠 30 週に管理入院。妊娠 34 週 5 日 HDP で緊急 C/S。症例 3 は 45 歳 G1P0、ハワイで卵子提供にて DD 双胎妊娠。妊娠 29 週に部分前置胎盤で管理入院。HDP で妊娠 36 週 4 日緊急 C/S。産後出血にて子宮動脈塞栓術 (IVR) 及び大量輸血 (自己血 4 単位、赤血球濃厚液 (RBC) 26 単位、新鮮凍結血漿 (FFP) 30 単位、血小板濃厚液 (PC) 50 単位) を要した。症例 4 は 53 歳 G1P0、パートナー不在で米国にて卵子・精子提供妊娠。辺縁前置胎盤で妊娠 32 週に管理入院。妊娠 36 週 1 日 C/S。癒着胎盤による術中大量出血にて IVR、腹式単純子宮全摘術、輸血 (自己血 6 単位、RBC6 単位、FFP6 単位、A T-III 製剤 3000 単位) を要した。児は社会的適応で乳児院へ退院。症例 5 は 39 歳 G1P0、急性リンパ性白血病で骨髄移植後不妊にて米国で卵子提供妊娠。HDP で妊娠 39 週 6 日緊急 C/S。産後出血で輸血 (RBC4 単位、A T-III 製剤 3000 単位) を要した。【結論】 当院の卵子提供妊娠はほぼ全例で濃厚な周産期管理を要した。卵子提供妊娠は極めてリスクの高い妊娠であり、IVR や輸血など緊急対応が可能な高度医療機関での管理が必要である。

P-12-13 右骨盤半裁術後に妊娠し生児を得た1例

安城更生病院

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【緒言】骨盤半裁術後妊娠では、子宮の支持組織が半側のみとなるため、妊娠中の子宮脱等に注意が必要である。また子宮の増大に伴い腹部で固定する義足の装着が不可能となり日常生活が困難となるため、生活環境の調整を含めた周産期管理が必要である。今回幼少期に右骨盤半裁術をうけ、妊娠37週で分娩した症例を経験した。【症例】30歳、G1P0。転居に伴い妊娠9週で当院へ紹介となった。患者は2歳の時に横紋筋肉腫のため右骨盤半裁術をうけていた。前医で妊娠前に撮影されたCT画像では右骨盤より足側は完全に欠損しており、子宮は右骨盤腹膜に沿って偏位していたが大きさは正常大であった。切迫早産や子宮脱に注意して周産期管理を継続した。妊娠23週に子宮頸管長が14mmへ短縮し管理入院とした。外子宮口は前唇がやや下垂していたが、子宮脱はなかった。その後一時退院したが、妊娠30週で妊娠高血圧症候群を発症したため入院管理とし、妊娠37週で全身麻酔下にて予定帝王切開を行った。右卵巣動脈および右卵巣は萎縮し、右側の脂肪組織や腹直筋は菲薄化し腹壁は左右で厚さが大きく異なっていた。術後経過は良好で術後7日目に退院となった。【結語】右骨盤半裁術後妊娠の1例を経験した。本症例では右付属器の萎縮を伴っており、子宮への血流低下に伴う切迫早産や子宮支持組織の欠損に伴う子宮脱に注意しながら周産期管理を行うことが必要であると考えられた。帝王切開時には腹腔内の癒着や臓器の偏位の可能性にも留意が必要である。子宮増大に伴う生活環境変化への整備も必要であり、妊娠に向けたプレコンセプションケアが重要であると考えられた。

P-12-14 重症血管病変に妊娠前インターベンションを行い、周産期管理した3症例

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【背景】未修復の大動脈縮窄や重症の腎動脈狭窄における妊娠出産は、重篤な母児の合併症を生じる可能性があり勧められない。今回妊娠前のインターベンションにより、母児に重篤な合併症なく管理できた大動脈縮窄1例と腎動脈狭窄2例を経験したので報告する。【症例】【症例1】31歳、2妊1産。第一子妊娠初期に高血圧を認めたが、介入される事なく、妊娠41週で経腔分娩した。産後に高血圧が持続し、精査で大動脈縮窄と診断された。当院受診時の大動脈圧較差は96mmHgで、妊娠は勧められない状態であった。全弓部置換術を施行後、自然妊娠し、経過は順調で、妊娠37週に経腔分娩に至った。【症例2】39歳、2妊0産。36歳時に健診で高血圧を指摘された。精査で腎動脈狭窄による高血圧と診断され、妊娠は勧められない状態だった。経皮的腎動脈形成術(PTRA)を行い、高血圧は改善した。39歳で自然妊娠し、経過は順調で、妊娠39週に経腔分娩に至った。【症例3】38歳、2妊1産。20歳頃より健診で高血圧を指摘され、原発性高血圧と診断されていた。34歳で自然妊娠し、慢性高血圧合併妊娠として管理された。妊娠23週より子宮内胎児発育不全と血圧上昇があり、加重型高血圧腎症と診断された。妊娠25週に緊急帝王切開で分娩したが、児は循環不全のため生後42日で死亡した。35歳時に再度児希望があり当院を受診したが、腎動脈狭窄を認め、妊娠は勧められない状態だった。PTRAを行い高血圧は改善した。38歳で自然妊娠し経過は順調で、妊娠38週に選択的帝王切開術で分娩に至った。【結論】妊娠を勧められない様な重症大動脈縮窄や腎動脈狭窄も、妊娠前にインターベンションを行うことで安全に周産期管理できることが示唆された。

P-13-1 産科異常出血におけるフィブリノゲン濃縮製剤の安全性に関する介入研究

群馬大

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【目的】産科異常出血でのフィブリノゲン濃縮製剤の使用における有効性と副作用の発生頻度を明らかにする。【方法】本研究は前方視的介入研究として、当院倫理審査委員会の承認のもと行った。当院で管理した、分娩中・分娩後に産科危機的出血やショックになった妊婦・褥婦を対象とした。対象者もしくはその家族に本研究への同意を取得し、フィブリノゲン濃縮製剤3gを経静脈投与した。投与前から投与後14日までを観察期間とした。本研究は2017年～2023年の7年間、19例に対して行った。プライマリーエンドポイントは輸血関連循環過負荷(TACO)の発症頻度、セカンダリーエンドポイントはその他の合併症の発生率、被験薬1g投与による血清フィブリノゲン増加値(投与開始から終了までの時間も記録)とした。【成績】年齢中央値は33歳(19-40歳)であった。症例の内訳は、分娩時異常出血(羊水塞栓症を含む)が12例、常位胎盤早期剝離が5例、敗血症性ショック1例、前置胎盤1例であった。他院から搬送された症例が11例であった。全例でTACOの発症は見られなかった。そのほかの合併症として、血栓塞栓症を2例、肺水腫を1例認めた。いずれも症状は軽度であり、生存退院された。フィブリノゲン濃縮製剤投与前と投与後の比較検討で、フィブリノゲン1gあたり34mg/dL(15-66)の上昇がみられた。【結論】産科異常出血の際の、低フィブリノゲン血症に対するフィブリノゲン濃縮製剤の使用に際して、合併症はみられたものの重症化はせず、血中フィブリノゲンの的確な上昇が確認できた。

P-13-2 経腔分娩における癒着胎盤の検討

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【目的】癒着胎盤は、基底脱着膜欠損部位から絨毛が子宮筋層に侵入し、分娩後胎盤が自然脱落困難となった状態である。前置胎盤や既往帝王切開例では、分娩前に確定診断し、術前準備が可能であることも多い。一方、経腔分娩時に遭遇する癒着胎盤は、分娩前の診断が困難、かつ状況も多岐に渡るため、対応に苦慮する。今回我々は、当院での経腔分娩時の癒着胎盤症例について検討し、報告する。【方法】2020年4月～2023年9月に当院で分娩に至った1460例の内、帝王切開510例を除く経腔分娩950例において、経腔分娩時に胎盤用手剥離を要し、癒着胎盤と診断された21例(2.2%)を対象とし、母体年齢、既往歴等の母体背景、出血量、輸血の有無、その後の経過等に関し後方的に検討を行った。【成績】癒着胎盤21例の出産平均年齢は35.9歳(26歳～43歳)、平均分娩週数は39週6日(38週0日～41週5日)、不妊治療を12例(57.1%)に施行し、9例は凍結胚移植妊娠であった。流産手術、筋腫のTCRなど子宮内操作既往は11例、前期破水9例、陣痛促進・強化を要したのは11例で、吸引分娩3例、クリステレル圧出法を5例に施行した。第3期所要時間は平均61.7分(13分～285分)、分娩時出血量は1847.8g(630g～4740g)であり、輸血を9例(42.9%)に施行し、子宮内バルーンを3例に留置した。病理学的にFIGO grade2は5例であり、胎盤ポリープを5例で形成した。凍結胚移植後妊娠、粘膜下筋腫のTCR既往は、有意に経腔分娩時の癒着胎盤と関連を認めた。【結論】経腔分娩時の癒着胎盤の21例を報告した。分娩前の診断は容易ではないが、凍結胚移植後妊娠、TCR既往はリスク因子であり、癒着胎盤の存在を念頭に置いた分娩管理を要すると思われる。

P-13-3 産科出血における分娩後動脈性子宮出血(PRACE)の臨床像の解析

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【目的】弛緩出血のうちdynamic CTの早期相で子宮腔内へ造影剤の漏出像を認める症例は、PRACEと定義され、通常の場合と異なる対応を要する可能性がある。本研究では、PRACEの評価方法ならびに臨床像を明らかにする。【方法】日本産科婦人科学会周産期委員会の事業として、2021年1月から12月までに産科出血のため周産母子センターへ搬送された症例のうち、前置胎盤、胎盤早期剥離、産道裂傷、子宮内反症などを除外し、dynamic CT画像を解析した。3名の検者(産科医、放射線科医)で個別にPRACEの有無を評価し、最後に3名同時に再評価し画像診断を統一した。臨床情報は、Mann-Whitney検定ならびにカイ二乗検定にて評価した。【成績】29施設のdynamic CT101例のうち、撮影条件不良の5例と産道裂傷と診断した4例を除いた92例を解析した。PRACEの検者間一致率は77%(71/92)で、評価の不一致の要因は、遺残胎盤や拡張子宮動脈を血管外漏出像と診断したことであった。10例(11%)は子宮内の胎盤が造影されていた。PRACE群34例(37%)と非PRACE群48例(52%)の臨床情報の中央値を比較した。PRACE群では、血清フィブリノゲン値(142 vs 210 mg/dL)が有意に低値であり、総出血量(3,487 vs 2,735 ml)や輸血量(FFP/RBC 8/10 vs 5.5/8単位)は有意に多かった。治療では、子宮動脈塞栓術(76 vs 21%)を有意に要した。【結論】分娩後出血に対するdynamic CTの評価において、撮影条件を最適化し出血の原因に対応した画像所見の特徴を共有することで、診断率が向上する可能性がある。搬送を要する産科出血のうち、PRACEは約4割を占め臨床的に重症であり、治療の際には子宮動脈塞栓術を要することを念頭に置く必要がある。

P-13-4 V字縫合(VUS)：前置胎盤の術中止血に非常に有効な新しい非圧迫縫合法

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【目的】前置胎盤の術中止血法は種々報告されているが一長一短がある。今回我々は新しい非圧迫縫合法であるV字縫合(V-shape uterine suture: VUS)を開発し良好な成績を得たので報告する。【方法】2018年1月から2023年6月に、前置胎盤と診断された24例のうち、以下の基準を満たした19例に対してV字縫合を実施した。内子宮口付近からの湧き出る出血で、一旦出血を除去した後、子宮切開部より下部を再充填するまでの時間(refilling time)が5秒以内。V字縫合では、超鋭針付きモノディオックス^R(針長8cm, 直・2号モノフィラメント糸)を使用し、縫合法は胎盤付着部側の子宮壁(後壁ないし前壁のどちらか)に対し、内子宮口を頂点とするV字型に貫通縫合した。【成績】19例中癒着胎盤は2例であった。術中出血量の平均は1191±471mlであり、これは既存の報告と比べても少なかった。V字縫合後の追加止血処置は、ガーゼ充填と子宮内バルーン挿入の各1例のみであった。術後経過は特に問題はなく、このうち3例でその後に妊娠し帝王切開にて問題なく出産した。【結論】従来の子宮下部圧迫縫合では子宮下部前後壁の阻血範囲が広く、また子宮下部内腔の状況が把握できず追加の止血処置も難しくなる。一方、V字縫合は阻血範囲が小さく簡便に行え、止血効果も直視下で確認できる。またネラトン絞扼術との組み合わせや、子宮内バルーン留置、ガーゼ充填、compression sutureなどの追加が容易な利点もある。V字縫合は前置胎盤の止血にfirst lineとして非常に有効と思われる。

P-13-5 当院におけるRPOCに対する子宮動脈塞栓術の奏効率と妊娠予後の検討

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【目的】RPOC (retained products of conception) は、流産または児娩出後の子宮内妊娠組織遺残物の総称であり、産褥出血の原因となる。その治療法は、待機療法、子宮鏡下手術、子宮動脈塞栓術(UAE)、子宮全摘術など臨床症状により選択が異なる。今回我々は、RPOCに対するUAEの奏効率と妊娠予後の検討を行ったので報告する。【方法】2016年1月～2022年12月に当院でRPOCと診断しUAEを行った症例を対象とした。対象について、再UAEの必要性、その他の止血処置の必要性を検討した。また、その後に妊娠した症例の経過について検討を行った。【成績】対象は15例であり、初回妊娠は8例(53.3%)であった。妊娠週数の内訳は、妊娠37週以降の分娩後9例(60%)、妊娠22未満の死産または中絶後5例(33.3%)、妊娠初期の中絶後1例であった。RPOCの診断後、予防的にUAEを行ったものは3例、治療的に行ったものが12例であり、UAEは、1例を除く(コイル塞栓)全例でゼラチンスポンジで塞栓を施行した。退院日の平均(範囲)はUAE後10.6日(4-24日)でありUAEの合併症は認めなかった。また、再出血のため再UAEを行った例は1例、パクリバルーンを挿入した例が1例でありどちらもその後寛解となった。UAE後の妊娠例は5例、全てがゼラチンスポンジで塞栓を施行した例であり、うち1例が流産、4例が正常産で分娩となった。【結論】ゼラチンスポンジを用いたUAEは効果的で安全な治療法であり、妊孕性温存を希望する女性にとって良い選択肢となると考えられた。今後、更なる安全性と妊孕性の検討が望まれる。

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P-13-6 分娩後異常出血の当院搬送症例における緊急IVRの有用性

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【目的】『産科危機的出血への対応指針』では、産科危機的出血の治療選択としてInterventional radiology (IVR)が明記されている。我々は、分娩後異常出血の搬送症例を解析し、当院での緊急IVRの有用性を明らかにすることを目的とした。【方法】2005年4月1日から2023年8月1日までの期間に、産後24時間以内の分娩後異常出血で当院に搬送された96症例をIVR施行有無でIVR群と非IVR群に分類し母体背景、原因疾患、治療、総出血量につき比較した。なお当院のIVRはUterine Artery Embolization (UAE), Resuscitative endovascular balloon occlusion of the aorta (REBOA)を含み、患者の全身状態や院内対応可否を踏まえた現場判断で実施されていた。【成績】IVR群は12例、非IVR群は84例で、IVR群にはREBOA7例、UAE5例、REBOAとUAEの併用1例を認めた。両群間で母体年齢、分娩週数に有意差はなく、原因疾患として弛緩出血・胎盤遺残がIVR群で各50.0%・16.7%、非IVR群で67.9%・21.4%と頻度に有意差はなかった。しかし、IVR群は非IVR群に比べ前医の搬送前 shock index は高い傾向があり(中央値1.3 vs 0.8, p=0.06)、止血までの総出血量も多量であった(中央値5300ml vs 3000ml, p=0.0012)。また、IVR群、非IVR群で各33.3%、79.8%に外科的治療を要した(p=0.034)。両群の子宮摘出例は各2例で有意差を認めず、死亡例は非IVR群にのみ2例認めた。【結論】分娩時異常出血搬送における緊急IVRは、搬送時点で全身状態のより重篤な症例に施行され、結果的に総出血量も多量であった。しかしIVR群では外科的治療は有意に少なく、非IVR群と同等に子宮が温存され、IVRの有用性が示された。

P-13-7 当院で子宮動脈塞栓術(UAE)を施行したRetained products of conception (RPOC)症例の検討

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【目的】RPOCとは分娩や流産後に子宮内に残留した胎児胎盤付属物の総称で、治療は待機療法から子宮全摘まで多岐にわたり選択に苦慮する。当院では、大量出血や出血継続を伴うRPOCの治療の第1選択としてUAEとRPOC除去術を併用しており、今回その治療の有用性を検討した。【方法】対象は2013年4月1日から2022年3月31日の期間に当院でUAEとRPOC除去術を施行し、病理学的にRPOCの確定診断を得た14例について、症例の背景、検査所見、治療、臨床経過を後方視的に検討した。【成績】症例の年齢は中央値35歳で、経産婦13例(92.9%)、ART妊娠2例(14.3%)、今回の妊娠帰結は、満期の経陰分娩7例(50.0%)、早産期の経陰分娩1例(7.1%)、帝王切開1例(7.1%)、流産5例(35.8%)で、流産でのD&C施行は2例(14.3%)であった。全例が出血を契機に診断され、分娩・流産後からRPOC診断までの期間は中央値14.5日、UAE実施までの期間は中央値28日であった。UAE前の超音波検査でのRPOC長軸は中央値19mm(8-65mm)であった。UAE後のRPOC除去方法は、子宮内容除去術11例(78.6%)、胎盤用手剥離2例(14.3%)で、1例はRPOCの自然排出のため除去術を試行しなかった。13例(92.9%)は、UAEまたはRPOC除去術後に速やかな止血を得たが、UAE後に胎盤用手剥離を行った1例のみ止血せず、開腹下に子宮圧迫縫合術を要した。なお輸血例は4例(28.6%)で、臨床的診断までの期間の中央値が0.5日、長軸40mm以上のRPOCを3例(75.0%)に認めたが、輸血不要例は10例(71.4%)で、同期間の中央値が21日、長軸40mm以上は1例(10.0%)のみであった。【結論】RPOCに対するUAEとRPOC除去術の併用は良好な治療結果を得た。しかし、分娩後早期の診断例でRPOC長軸が40mm以上の場合は、大量出血の危険が高い可能性がある。

P-13-8 前置胎盤にOB-balloon!その治療成績と使用上の勘どころ

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金井貴弘¹, 田中政彰², 横田貴子², 荒木皓光², 榎本咲子², 高橋 仁², 小林寛人², 堀 芳秋², 加藤じゅん², 田嶋公久³, 干場 勉⁴, 齋藤 滋⁵

【目的】前置低置胎盤帝王切開では、胎盤剝離面からの止血に難渋する。多量出血による子宮摘出が3%と報告されている。前置低置胎盤止血を目的に新規開発され、2023年5月に販売開始となったOB balloonの治療成績を報告する。使用経験上の要点も紹介する。【方法】OB balloonとは、長さ30cmのダブルバルーンである。子宮内のバルーンは陰側のバルーンに牽引され子宮下部を強く圧迫し、胎盤剝離面からの出血を重点的に止血する。バルーン拡張の注入口は子宮側に存在し、帝切時子宮側から両バルーンを拡張できる。臨床試験は倫理委員会の承認を得て2015年4月より開始されている。対象疾患は、帝切時胎盤剝離面より持続する出血を認める前置或いは低置胎盤で、癒着胎盤は除外した。【成績】多施設共同(研究参加施設数:4)で、2018年7月までに55症例に使用した。術中操作は容易であり、挿入が困難であった症例は無く、バルーン滑脱は2例(3.6%)だった。術中出血量の平均は1306gであり、OB balloon挿入から翌日抜去までの子宮内出血の平均は70gであった。自己血輸血を行った症例は30例(65%)で、同種間輸血を要した症例は2例(3.6%)であった。【結論】前置低置胎盤帝王切開時のOB balloon使用に関し、安全性が確認され、出血低減に寄与する可能性が示唆された。

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P-13-9 分娩後異常出血において血尿を認めた凝固障害例の凝固線溶系検査値の特徴

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【目的】分娩後異常出血で血尿を認めた症例において凝固線溶系検査値の分娩後の推移を非血尿例と比較すること。【方法】多施設共同前向き研究データのうち過去3年間の分娩時出血量2000g以上の119例を対象とした。血尿例と非血尿例とで血小板数、PT-INR、フィブリノゲン(Fbg), FDP, Dダイマー, トロロンビン・アンチトロロンビン複合体, プラスミン・ α 2プラスミンインヒビター複合体(PIC), FDP/Dダイマー, ヘモグロビン/Fbgの推移を比較した。【成績】血尿例は2例あり、共に帝王切開分娩で、症例1では癒着胎盤を認め症例2では多胎以外に特記事項はなかった。共に初回採血時(分娩後1.5;4時間)の出血量(2215;1300g)に見合わないFbg値の低下(62;38mg/dL)を認めた。血尿例(n=2)と非血尿例(n=117)とで明らかに異なる動態を示した項目の分娩後4時間以内の測定値の中央値(97%ile値), ならびに血尿例の初回測定値[症例1;2]:FDP 28.9(499)[960;960] μ g/mL, Dダイマー 10.5(126)[425;491] μ g/mL, PIC 2.2(21.6)[68.3;28.4] μ g/mL, ヘモグロビン \times 100/Fbg 3.1(10.4)[16.3;19.7]であった。FDPは分娩後10時間後まで696 μ g/mL以上の異常高値を示した。【結論】血尿例における出血量に見合わないFbg値の低下は、プラスミンの異常活性化に伴う一次線溶の亢進によるものであることが、PICおよびFDP動態から説明でき、これは線溶亢進型DICの病態に一致する。DICの臨床診断に血尿は重要項目と考えられ、今後も症例の蓄積が望まれる。

P-13-10 産科DICにおけるアンチトロロンビン活性とアンチトロロンビン製剤投与の関係:単施設ならびに多施設後方視的検討

関西医大
森川 守

【目的】産科DICとアンチトロロンビン(AT)活性/AT製剤投与との関係を実証すること。【方法】単施設研究(研究1):2016年から2021年に分娩した4,264名のうち、経陰分娩で2,000mL以上または帝王切開で2,500mL以上の出血量を認めた症例を対象とした。多施設研究(研究2):7施設で2018年に分娩した7,524名のうち、経陰分娩で1,000mL以上または帝王切開で2,000mL以上の出血量を認めた症例を対象とした。AT製剤投与を決定するパラメータ候補をAT活性値, 出血量, ショック指数, 産科DICスコアとした。【成績】産科DICの発症率は、研究1で0.23%, 研究2で0.49%だった。研究1に73名(産科DIC10名, 非産科DIC63名), 研究2に167名(産科DIC23名, 非産科DIC144名)が含まれた。産科DICと非産科DICの比較におけるAT製剤投与のオッズ比は、研究1では9.00だったが、研究2ではカットオフ値を認めなかった。多変量解析によって研究1のAT活性値 \leq 49%, 研究2のAT活性値 \leq 52.3%および出血量 \geq 2,141mLは、各々AT製剤投与と有意な正の相関を示した。産科DICにおいてAT製剤投与を決定するためのAT活性値のカットオフ値は、研究1では \leq 45%だったが、研究2ではカットオフ値を認めなかった。【結論】AT活性は産科DICにおけるAT製剤投与を決定する要因である可能性が高いが、施設間である程度の選択バイアスも存在する。

P-13-11 当院における、産科危機的出血に対するフィブリノゲン製剤使用経験の検討

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倉崎昭子¹、植村育子¹、勝手恵理子¹、松井尚彦¹、佐野陽子¹、眞鍋静恵²、吉井紀子²、原 澄子¹

【目的】2021年9月より、産科危機的出血に伴う後天性低フィブリノゲン血症に対するフィブリノゲンの補充が保険適応となった。当院は年間約1700例の分娩を擁する産科一次施設である。いわゆる搬送前施設において発生した産科危機的出血に対するフィブリノゲン製剤使用の有用性を明らかにすることが本研究の目的である。【方法】2021年9月から2023年7月までに、当院で産後にフィブリノゲン製剤を投与した8例のうち、分娩後24時間までに大量出血をきたした5例を対象とし、フィブリノゲン投与前の血中フィブリノゲン値、分娩からフィブリノゲン投与までの時間、フィブリノゲン投与までの出血量、フィブリノゲン投与後の出血量を調べた。【成績】症例の内訳は、弛緩出血1例、子宮型羊水塞栓症1例、癒着胎盤1例、常位胎盤早期剝離1例、低置胎盤1例であった。うち帝王切開は低置胎盤の1例のみであった。母体搬送となったのは子宮型羊水塞栓症の1例であった。投与前フィブリノゲン値の中央値は104mg/dL、分娩からフィブリノゲン投与までの時間の中央値は113分、分娩からフィブリノゲン投与までの出血量の中央値は1800ml、投与後出血の中央値は440mlであった。【結論】フィブリノゲン投与後、出血量は劇的に減少する傾向にあった。このことから、フィブリノゲン製剤の使用により、産褥搬送件数や他の輸血製剤の投与量を減らすことができる可能性が示唆された。輸血製剤のストックが無く、取り寄せに時間がかかる産科一次施設においても、フィブリノゲン製剤の使用によって出血量を減らすことができると考えられた。

P-13-12 後産期大量出血に対するスポンジ鉗子を併用した子宮腔内バルーンタンポナーデの有用性

トヨタ記念病院

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【目的】子宮腔内バルーンタンポナーデは後産期大量出血に対して簡便で低侵襲な止血法であるが、腔内への脱落が課題である。【方法】我々は後産期大量出血に対して、全身麻酔下に子宮腔内バルーンを留置後、スポンジ鉗子で子宮腔部を挟鉗した止血方法を実施してきた。全身麻酔を維持しながら輸血等のDIC治療を行い、DICを脱した後に翌日バルーンを抜去している。2020年1月から2023年8月までに経験した22例について後方視的に検討した。【成績】平均年齢は35歳(21-42歳)、分娩後出血量の中央値は2,000 mL (530-3,500 mL)であった。治療前のショックインデックスの中央値は1.01 (0.48-2.00)で、産科DICスコアは5-32点であった。血液検査所見はHb 3.3-9.0 g/dL、血小板 $6.4-23.0 \times 10^4 / \mu\text{L}$ 、フィブリノゲン 20-307 mg/dLであった。9症例において前医で子宮腔内バルーンが留置されていたが、病着時には5例(55.6%)が腔内に脱落していた。全身麻酔下に子宮内に子宮腔内バルーンを留置し、スポンジ鉗子で子宮腔部を挟鉗し、輸血を含めたDIC治療を行った。輸血量はRBCが4-50単位、FFPが0-40単位、血小板濃厚液が0-40単位であった。フィブリノゲン製剤の投与例は7例(31.8%)であった。21例(95.5%)で出血がコントロールでき、DIC臨床効果判定スコアは3-20点減少し有効であった。1例(4.5%)は心肺虚脱型の羊水塞栓症で出血コントロールができず子宮全摘出術を施行したが母体救命ができなかった。【結論】スポンジ鉗子を併用した子宮腔内バルーンタンポナーデは、後産期大量出血の初期治療として有用であった。

P-13-13 突然の悪心で発症し母児ともに救命し得た臨床的羊水塞栓症の1例

日立総合病院

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【緒言】羊水塞栓症の頻度は2-3万分娩に1例と稀で、破水や陣痛発来時、帝王切開分娩時に発症することが多い。今回我々は、未破水・未陣発にも関わらず羊水塞栓症を発症した1例を経験したため報告する。【症例】31歳、2妊1産。自然妊娠。妊娠20週0日でCOVID-19感染があった他、経過は特記事項なし。妊娠32週3日に突然発症の悪心を主訴に受診。嘔吐、SpO2低下、意識障害、眼瞼や口唇の腫脹、四肢末梢冷感、腹部板状硬、尿失禁を認めた。未破水・未陣発、性器出血なし。胎児超音波検査では胎児心拍数100回/分、胎盤肥厚や胎盤後血腫など常位胎盤早期剝離を疑う所見はないものの羊水腔にdebris様の貯留を認めた。胎児心拍陣痛図では基線細変動減少、1-2分毎の周期的な遅発一過性徐脈を認め、胎児機能不全を適応に全身麻酔下の緊急帝王切開術を行った。児は1591g、女児、Apgar score 1/2点、臍帯動脈pH 6.823。早産と重症新生児仮死のため新生児搬送となった。母体は術中よりDICを呈しRBC8単位、PC40単位、FFP28単位輸血、ICUに挿管帰室となった。DICは速やかに改善し術後1日目に抜管、肺高血圧症を発症したが経過観察のみで改善し術後7日目に退院となった。手術中の血液検査でSTN 370.0 U/mL (基準値 45.0 U/mL以下)、亜鉛コプロポルフィリン-1 2.9 pmol/mL (基準値 1.6 pmol/mL未満)と羊水塞栓症に矛盾しない所見であった。【結語】妊娠後期に未破水・未陣発でも、母児同時に急激な状態変化を来す羊水塞栓症またはそれに類似した病態が起こりうる。

P-13-14 発症早期より集学的治療を開始し、CIインヒビター投与により救命しえた臨床的羊水塞栓症の一例

岐阜県立多治見病院

篠根早苗, 足立健敏, 柘植志織, 松川 哲, 中村浩美

羊水塞栓症は、劇的に発症し集学的治療を要するが、発症予測は困難であり、また急速に悪化する全身管理を行いつつ他疾患との鑑別を要する非常に緊急性の高い疾患である。今回妊娠高血圧症候群に対する分娩誘発中に心肺虚脱型羊水塞栓症の一例を経験したため報告する。患者は43歳の自然妊娠の1経産婦。妊娠35週より血圧上昇を認め妊娠36週5日に当院へ紹介受診となった。翌日より分娩誘発行うも、有効陣痛とならず、妊娠37週4日オキシトシン点滴開始後、11:54意識低下(JCSIII-300)、胎児心拍60pmまでの低下あり、超緊急帝王切開施行。12:13児娩出(APS2/4)。術中に徐脈となり蘇生処置しながら循環器内科医より肺塞栓症との診断で速やかに止血処置および閉腹としECMO導入とした。術後施行したCTでは肺血管に血栓を認めず、また膀胱子宮窩に留置いたドレーンより大量出血認め、著しいDICも認めたため臨床的羊水塞栓の診断にて、大量輸血、抗DIC治療、CIインヒビター投与を行った。翌日にはDIC傾向に改善認め、循環動態安定したことからECMO離脱、開眼確認できるも腹腔内微小出血持続あり、腹部膨満著明なため呼吸状態不安定となり腹水排液、輸血しつつ全身状態の安定化を図り、術後15日目に抜管となった。翌日には一般病棟に転棟し、廃用症候群に対しリハビリテーション継続中である。なお、児は現時点にて頭部MRI、脳波検査にて異常みとめず、術後22日目に自宅退院となった。また発症直後の採血にて施行したZn-CPI及びSTN値については基準値以内であったが、CIインヒビター活性が31%（基準値42%以上）と低値であり、今回のCIインヒビター投与が有効であったこととの関連が示唆された。

P-14-1 子宮内膜症の初期発生部位を検討するための微小骨盤腹膜病変 mapping

富山県立中央病院

草開 妙, 谷村 悟, 山本健太, 松田美智子, 山口彩華, 本多真澄, 草開友理, 小幡武司, 炭谷崇義, 吉越信一, 南 里恵, 飴谷由佳

【目的】子宮内膜症では卵巣子宮内膜症やダグラス窩閉鎖などの粗大病変が目されやすい。近年、腹腔鏡技術の進歩により腹腔内の詳細な観察が可能となった。そこで、子宮内膜症と診断された既往のない症例において骨盤腹膜の微小病変の有無を観察しその部位をmappingすることによって、子宮内膜症の発生部位を検討することを目的とした。【方法】2022年4月から2023年4月までに腹腔鏡手術またはロボット支援化下手術を行った20代～40代の症例のうち、術前の画像検査や術中所見で卵巣子宮内膜症性嚢胞・子宮腺筋症・ダグラス窩閉鎖と診断された症例は除外し、微小骨盤腹膜病変の有無を観察した45例を対象とした。病変部位の分布を評価するために骨盤腹膜を7区画に分類しマップを作成した。卵巣窩はさらに3区画に細分化した。【成績】微小骨盤腹膜病変の有無を観察した45例の平均年齢は40.6歳(SD 5.8)であった。骨盤腹膜病変を認めたのは31例(68.9%)であった。腹膜病変を認めた31例のうち20例(64.5%)で、月経困難、過長月経、過多月経のいずれかの症状を有した。また、29/31例(93.5%)は卵巣窩に病変を認めた。次いでダグラス窩、仙骨子宮靭帯にそれぞれ13/31例(41.9%)、12/31例(38.7%)ずつ病変を認めた。9/31例(29.0%)で卵巣窩単独に病変を認めた。卵巣窩に病変を認めた29例のうち27例(93.1%)は、尿管の子宮動脈交叉部付近に病変を認めた。【結論】卵巣子宮内膜症性嚢胞・子宮腺筋症・ダグラス窩閉鎖を認めない症例であっても、68.9%で子宮内膜症の微小骨盤腹膜病変を認めた。また、29.0%では卵巣窩単独に病変を有した。卵巣窩微小腹膜病変が、他の子宮内膜症病変に先行して発生する可能性が示唆された。

P-14-2 当院における胸腔内子宮内膜症の治療についての検討

日本赤十字社愛知医療センター名古屋第一病院

福原伸彦, 安藤智子, 正橋佳樹, 鈴木美帆, 伊藤由美子, 手塚敦子, 坂堂美央子, 齋藤 愛, 廣村勝彦, 津田弘之, 水野公雄

【目的】胸腔子宮内膜症とは稀少部位子宮内膜症のひとつで月経随伴性気胸、月経随伴性咯血などに分類される。2018年10月に発刊された稀少部位子宮内膜症診療ガイドラインでは部位別の治療法について推奨レベルが示されたが、胸腔子宮内膜症の薬物療法についてはエビデンスが乏しく弱い推奨にとどまっている。当院での胸腔子宮内膜症の治療経過をまとめて考察する。【方法】2009年1月から2023年6月までに当院で診療を受けた稀少部位子宮内膜症の患者65例のうち胸腔子宮内膜症の症例15例を抽出し、年齢、治療、再発の有無などについて後方視的に検討した。【成績】15例中咯血の症例が2例、気胸の症例が13例であり、発症時の平均年齢は34.9歳であった。咯血の2症例はどちらも20歳代でLEPによりコントロール良好であった。気胸の症例は初回治療として手術療法を行った症例が3例で、いずれも術後薬物療法を行ったが、1例で気胸の再発を認めた。初回治療として薬物療法を選択した10例のうち、5例は薬物療法単独で既ねコントロール良好であったが、5例は気胸の再発により胸腔鏡下手術を要し、うち1例は術後の薬物療法中に再度気胸を認めた。薬剤別ではLEP、GnRHアナログ、ジエノゲストのいずれの使用においても気胸の再発を経験した。【結論】咯血症例では薬物療法が効果的であるが、気胸症例では薬物療法単独での効果は限定的であった。ガイドラインでも気胸に対しての手術療法は薬物療法より推奨度が高く、気胸の程度によってはより積極的な手術療法も推奨できると考えられた。薬物療法の選択や投与方法については、今後さらなる症例を重ねた検討が必要である。

P-14-3 全腹腔鏡下腔式子宮全摘術 (TLH) 後の inclusion cyst による急性腹症に対して緊急手術を施行したものの術後に再発を認め、治療に難渋した症例

JA 長門総合病院
中島博予

Peritoneal inclusion cyst (PIC) は腹腔内の炎症や手術が原因で生じた骨盤内癒着により、腹膜の液体吸収機能が低下した結果、閉鎖腔へ限局性に液体貯留を生じた状態を指す。今回、全腹腔鏡下腔式子宮全摘術 (TLH) 後に PIC による急性腹症をきたし、手術を行うも再発を認めて治療に難渋した症例を経験したため、文献的考察を併せて報告する。症例は 39 歳、2 妊 2 産。20XX 年 3 月に月経痛の増悪を主訴に当科を受診した。3 cm 大の右チョコレート嚢胞と 6 cm 大の筋腫を認め、手術の方針となった。同年 4 月に TLH+右付属器摘出術を施行した。術後、Low dose Estrogen Progestin (LEP) またはジェノゲストの内服も提案したが希望されず、定期検診の方針とした。同年 7 月、急激な下腹部痛を認めたため当科を受診した。経腔エコーでは左付属器領域に 8 cm 大の多房性嚢胞性腫瘤あり、捻転の可能性を考慮して緊急手術の方針となった。腹腔内を確認したところ左付属器領域に腸管の癒着と、それに包まれた嚢胞を認めた。癒着を剝離していったところ正常卵巣を認め、PIC であると判断した。可及的に 8 cm 大の嚢胞壁を切除して手術を終了した。術後 1 か月後には再発は認めなかったが、2 か月後に左卵巣の周囲に嚢胞性の病変を認め、PIC の再発を疑った。治療目的に LEP 内服を開始したところ、徐々に嚢胞性病変は縮小傾向を認め、以後増大は認めず経過している。ジェノゲストや LEP による排卵抑制により卵胞液の貯留を抑制することで、PIC の保存的加療に有効性が高いと考えられた。

P-14-4 当院にて月経随伴性気胸が疑われた 19 症例の後方視的検討

帝京大
渡邊さや、平野茉来、宮川恒介、小野寺貴子、竹原洗平、高崎和樹、高橋ゆう子、西田晴香、一瀬隆行、平池春子、長阪一憲

【目的】月経随伴性気胸 (Catamenial Pneumothrax, 以下 CP) の病態や治療法は明らかでない。当院にて CP が疑われた症例について、後方視的に検討をしたので報告する。【方法】2017 年 1 月 1 日~2023 年 8 月 31 日の間、CP の疑いで当院紹介となった 19 症例を対象とした。年齢、body mass index (BMI)、既往歴、妊娠歴、喫煙歴、気胸部位と発症回数、骨盤内子宮内膜症の有無、治療前の血清 CA125 値、治療介入の内容、切除病巣の病理組織学的所見、再発の有無、再発後の治療内容などについて検討を行った。【成績】患者の発症年齢中央値 37 歳 (14-50 歳)、BMI 中央値 20、初経年齢中央値 12.5 歳、月経異常あり 2 例 (10.5%)、7 例 (36.8) が経産婦、6 例 (31.5%) に喫煙歴があった。14 例 (73.7%) が右側発症であり、発症回数の中央値は 1 回であった。3 人 (15%) に骨盤内子宮内膜症 (卵巣子宮内膜症性嚢胞 3 例、子宮腺筋症 0 例) を認めた。治療前の血清 CA125 値中央値は 19.55、治療内容は 8 例で胸腔鏡下病巣切除術、2 例で胸膜癒着術 (重複あり) を行っていた。術中所見や病理診断で確定診断を得たのは 7 例 (36.8%) であった。低用量エストロゲン・プロゲステン剤 (LEP) 内服が 3 例、黄体ホルモン剤内服が 7 例、GnRH アンタゴニスト剤内服が 1 例であった。初回治療後の再発は 2 例であったが、全て LEP 周期投与による維持療法中であった。一方、GnRH アンタゴニスト剤と黄体ホルモン剤内服併用維持療法を行った 9 症例では、2 回目の再発を認めなかった。【結論】初経の低年齢化や少子化による月経回数の増加により、CP を疑われる患者の増加が予想される。GnRH アンタゴニスト剤と黄体ホルモン剤内服を併用維持療法は、再発予防に有用である可能性がある。

P-14-5 婦人科がん手術前後の生活の質、感情、更年期症状に関する 1 年間の縦断的観察研究

鹿児島大
唐木田智子、松川仁登美、新原有一朗、内田那津子、崎濱ミカ、薬詔伸太郎、小林裕明

【目的】婦人科がん手術前後の生活の質 (Quality of life: QOL)、感情、外科的閉経に伴う更年期症状の 1 年間の変化を調査し、どの時期にどのような影響があるかを明らかにして診療に活かすことを目的とした。【方法】2017 年 10 月から 22 年 9 月に当科で婦人科がん手術を受け文書調査すべてに適切な回答が得られた 164 例を対象とした。QOL および更年期症状を Functional Assessment of Cancer Therapy-General, Endocrine symptoms subscale-19 (FACT-G, ESS-19)、感情を The Center for Epidemiologic Studies Depression Scale (CES-D) を用い、術前、6 か月後、12 か月後で評価した。【成績】背景は、年齢中央値 49 歳、子宮体癌 94 人、子宮頸癌 48 人、卵巣癌 17 人、重複癌 5 人であった。FACT-G は術前 76.6±15.8、6 か月後 82.1±15.1、12 か月後 82.7±15.3 で、術前が低く 6 か月後で有意に改善し 12 か月後でも維持された。CES-D がカットオフ値以上で抑うつが疑われた人は、術前 65 人 (39.6%)、6 か月後 34 人 (20.7%)、12 か月後 37 人 (22.5%) で、術前が最も多く 6 か月後で半減したが 12 か月後でも抑うつが 2 割程度で持続していた。外科的閉経患者 70 人について ESS-19 を用いて更年期症状を調査し、術前 60.8±9.7、6 か月後 62.9±8.7、12 か月後 63.1±8.4 と術前が低く 6 か月後で改善し 12 か月後でも維持された。ホルモン補充療法は 70 人中 36 人で行われた。【結論】婦人科がんサバイバーは術前から抑うつ感情が QOL に強く影響し 6 か月程度で改善した。外科的閉経では更年期症状が強く現れやすいことが良性婦人科腫瘍手術を対象とした報告で指摘されているが、外科的閉経に伴う婦人科がんサバイバーの更年期症状および QOL の悪化は認めなかった。

P-14-6 月経前症候群 (PMS) の症状は低血糖エピソードと関連するののか香川大健康科学¹, 香川大²
塩田敦子¹, 金西賢治²

【目的】月経前症候群 (PMS: Premenstrual Syndrome) に悩む若年女性は多く、情緒不安定、イライラなどの精神的な症状に困ることが多い。しかしその原因については未だに詳しく解明されていない。月経前には黄体ホルモンの影響で血糖調節が不安定になることが考えられ、低血糖症状とPMSの症状が似ていることから、低血糖とPMS症状の出現が関連している可能性について検討したいと考えた。【方法】対象は本学医療系女子大学院生で月経周期のずれが9日以内のもので糖尿病の家族歴のないもの7名である。月経5-7日前から、皮下間質液中のグルコース値を連続的に2週間測定、記録できるグルコースモニタリングシステムを上腕に装着し計測、食事や間食の状況および心身の症状について適宜記録してもらった。月経前、月経中、月経終了後に分けて血糖変動を解析した。【成績】7名の平均年齢は22.6歳。月経をはさむ2週間の血糖値がTIR (Time in range) と呼ばれる70-180mg/dlの範囲内であった割合は平均98(95-100)%であった。70mg/dl以下となる低血糖エピソードを6名で複数回認め、月経前に多かった。情緒不安定、倦怠感、空腹感、眠気などPMS症状のあったものが4名で、低血糖エピソードとのタイミングは一致していることが多かったがずれていることもあった。【結論】月経前から月経中にかけては血糖調節が不安定になっており、その影響で過食、情緒不安定、倦怠感などが起こっている可能性が示唆された。今後は症例を集積して統計的解析を行い、PMSに悩む女性への食事指導に役立てたい。プレコンセプションケアとして女性の健康維持、社会参加に役立つばかりでなく、医療費の削減にもつながると考える。

P-14-7 本邦初の経口妊娠中絶薬の市販後調査東壽会東峯婦人クリニック¹, 対馬ルリ子女性ライフクリニック銀座²
松峯美貴¹, 対馬ルリ子², 松峯寿美¹

【目的】経口妊娠中絶薬が2023年5月より有床施設限定で処方可能になった。本研究では経口妊娠中絶薬による人工妊娠中絶の有効性と安全性について検討した。【方法】2023年5~8月の間、年齢16~45歳まで、人工妊娠中絶術の適応と判断された子宮内妊娠63日以下の妊婦46症例を対象とした。1錠目ミフェプリストン200mgを単回投与し、その36~48時間後に2錠目ミソプロストール800 μ gを単回投与し、中絶完了まで院内待機した。院内待機中は、2時間毎に患者を観察し、経腔超音波検査による胎嚢排出が確認された時点で人工妊娠中絶完了と定義した。下腹痛の程度は、鎮痛剤投与にて対処可能なものを軽中等度と定義した。【成績】全例で人工妊娠中絶が完了した。中絶が完了したもののうち54%が2錠目投与後2時間以内、93%が6時間以内、10時間以内に100%人工妊娠中絶が完了した。2錠目投与後、軽中等度の子宮出血を除く副作用の出現割合は、中等度の下腹痛が50%で最多であり、次に下痢/排便26%、嘔気13%であったが、ほとんどのケースで軽症であった。一方で、多量出血により外科的処置が必要になったもの1例、脱水と下腹痛のため点滴入院が必要になったもの1例、パニック発作と過換気症候群を発症し、連続モニター管理をしたもの1例と、医療介入が必要になった例が6.5%あった。【結論】経口妊娠中絶薬による中絶法は、成功率が高く、副作用は概ね軽度であり、外科手術と並ぶ有力な選択肢となることが示唆された。しかし、医療介入が必要なケースが、6.5%存在したことから、処方可能な医療機関は、有床施設であることが望ましいが、頻回の状態観察や副作用への対応ができれば、無床施設での処方も可能と考えられた。

P-14-8 都心部における中期中絶の社会的背景に関する研究小畑会浜田病院¹, 国立スポーツ科学センター², 帝京大³
合阪幸三¹, 土屋富士子¹, 板橋香奈¹, 森嶋かほる¹, 長谷川亜希子¹, 秋山純子¹, 木村好秀¹, 山村菜実¹, 能瀬さやか², 平池春子³, 長阪一憲³

【目的】都心部に位置する当院における、過去6年間の中期中絶の社会的背景を調査した。【方法】2017年1月より2022年12月までの当院における中期中絶128例において、年齢別の症例数および各症例の社会的背景につき、retrospectiveな検討を行った。研究開始に当たり、プロトコルをすべて公開した後、当院の倫理委員会に諮って許可を得た。対象となった症例に対しては、個別にカウンセリングを行い、研究協力についてのインフォームドコンセントも十分に行って同意を得た。【成績】中期中絶の総数は、2017年から2022年までの6年間でそれぞれ、27, 16, 26, 21, 19, 19例と、合計128例であった。年齢別にみると、10, 20歳台の症例数は年に0.3例と少数であったが、30歳以上ではそれぞれ、24, 15, 24, 21, 18, 18例と高齢の症例が多くを占めていた。またそれらの多くは、児の染色体異常もしくは多発奇形を合併していた。ARTによる妊娠率は73.9%であった。【結論】当院の出産例のうち43.9%が35歳以上であり、初婚年齢の上昇は高齢初産を増加させる因子となる。またNIPTをはじめとする出生前診断の技術進歩は有用であるが、一方で中期中絶の増加などの倫理的問題と妊婦の心理的葛藤を派生させる。さらにこれらの出生前診断は実費診療となり、費用も高額であることから実施を断念するケースも存在し、医療における経済的格差の問題も孕んでいる。このように妊婦の高齢化は母児の周産期リスクに加えて、出生前診断の技術進歩に伴う倫理的、社会的な課題にも直結する状況となりつつある。

P-14-9 産褥・授乳期のカルシウム補充が骨密度・骨微細構造に与える影響

長崎大

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【目的】妊娠・授乳期の母体は骨吸収を亢進させて胎児・新生児へカルシウムを供給する。その結果、母体の骨密度は低下するが、授乳を終了すると妊娠前の骨密度へ戻る。今回、産褥授乳期6か月間の骨密度・骨微細構造にカルシウム補充が与える影響について検討した。【方法】分娩後に本研究に同意した褥婦17人を対象とした。無作為に2群に分け、カルシウム(カルシウム600mg, ビタミンD5.0 μ g)を内服するカルシウム群(Ca群:9人)とコントロール群(non-Ca群:8人)を比較した。DXA法による骨密度、HR-pQCTによる骨微細構造を測定し、分娩後1か月目を基準とし、6か月目の変化を検討した。【成績】初診時の平均年齢はCa群30.0 \pm 2.1歳, non-Ca群31.4 \pm 4.6歳だった。全例、正期産で分娩し登録時から6か月目まで授乳していた。腰椎骨密度の6か月の変化率は、Ca群で(中央値(最小-最大)) -1.37(-8.40-3.88)%, non-Ca群で-3.40(-6.73-1.12)%であり、大腿骨骨密度はCa群で-2.93(-5.82-1.25)%, non-Ca群で-5.6(-10.42--4.19)%だった(P=0.01)。骨微細構造の変化率は、脛骨皮質骨多孔性がCa群で中央値6.6%, non-Ca群で18.35%と有意差を認めた(P=0.04)。また、脛骨海綿骨vBMDがCa群で-2.3%, non-Ca群で-6.0%と有意差を認めた(P=0.03)。【結論】産褥授乳期の骨密度は6か月目に低下を認めたが、産褥授乳期のカルシウム補充は骨密度・骨微細構造の低下を緩和させる可能性が示唆された。

P-14-10 若年婦人科がん治療後の骨量変化と治療効果の検討

徳島大

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【目的】婦人科がん患者の30~40%は50歳未満の女性であり、患者の多くは両側卵巣摘出術を含む手術や化学療法、放射線療法などを受け、これらの治療により卵巣機能の廃絶を伴っている。長期的なエストロゲン欠乏は骨粗鬆症のリスクファクターであり、がん治療後早期からの骨量管理が望まれる。当院で婦人科がん治療により閉経をきたした症例の骨量変化と治療効果について検討した。【方法】当院で婦人科がん治療後に閉経となった55例を対象に、がんの治療方法、骨量変化、骨粗鬆症に対する治療効果について後方視的に検討した。【成績】診断の内訳は、子宮頸癌28例、子宮体癌13例、卵巣癌14例で、年齢中央値は47歳(33~56歳)、閉経年齢は40歳(20~51歳)であった。子宮頸癌、子宮体癌、卵巣癌症例のBMI中央値はそれぞれ20.1kg/m², 28.2kg/m², 19.2kg/m²、がん治療後初回の平均腰椎骨密度(BMD)はそれぞれ、0.902g/cm², 0.998g/cm², 0.897g/cm²であった。56例中6例(10.7%)は骨粗鬆症、15例(26.7%)は骨量減少と診断され、経過観察中に1例に腰椎圧迫骨折を認めた。癌の治療法別にみると、両側卵巣摘出を含む手術のみ31例、手術+化学療法10例、CCRT12例、CCRT+化学療法2例で、治療群間で骨密度に有意差は認めなかった。骨代謝に対する治療としてはHRT単独22例、活性型ビタミンD36例、HRT+活性型ビタミンD3併用7例、SERMやビスホスホネートなど8例で、HRT+活性型ビタミンD3併用例で有意に骨密度上昇効果を認めた。【結論】がん治療後に閉経を来した患者においては、将来の骨折予防とQOLの維持という観点から、十分な説明の上積極的にHRTを導入することが必要である。

P-14-11 妊娠後骨粗鬆症に対してロモソズマブを使用した症例

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【目的】妊娠後骨粗鬆症は、主に妊娠後期または分娩後から授乳期に発生する閉経前の骨粗鬆症である。病態は明らかになっていない部分も多く、治療に関して明らかな指針が決まっていない。当院で妊娠後骨粗鬆症に対し、ロモソズマブを第一選択薬として使用した2症例を経験したので報告する。【症例】症例1)38歳, 3妊1産, 身長162cm, 体重50.0kg, BMI19.5kg/m²。分娩後4か月での多発圧迫骨折のため当院紹介受診となった。Dual-energy X-ray Absorptiometry(DXA)で、腰椎Bone Marrow Density(BMD)が0.714, Young Adult Mean(YAM)62%, 大腿BMD0.758, YAM81%であった。アルファカルシドール、メナテレンオンカプセルを併用し、ロモソズマブを開始した。治療中の新たな骨折はなく、12か月の治療後、DXA結果は、腰椎BMD0.781, YAM79%, 大腿BMD0.626, YAM79%であった。その後、妊娠希望がないためゾレドロン酸を使用している。症例2)34歳, 2妊2産, 身長152cm, 体重38.0kg, BMI16.4kg/m²。圧迫骨折の既往あり、分娩後DXA施行したところ、腰椎BMD0.635, YAM64%, 大腿BMD0.521, YAM66%であった。3か月の授乳後に断乳し、ルファカルシドール、ロモソズマブで治療介入となった。現在11か月治療しているが、新規骨折なく経過安定している。【結論】ロモソズマブは骨形成促進剤であり、重度の妊娠後骨粗鬆症においても第一選択薬になる可能性が示唆された。

P-14-12 胎生期低栄養環境による脂肪組織の炎症関連遺伝子発現変化の検討: Developmental Origins of Metaflammationの観点から

浜松医大

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【目的】胎生期低栄養(Under Nutrition: UN)環境に引き続き授乳期にCatch-up growthを経験するとメタボリックシンドローム(MS)を発症するリハイスク群となる。近年、MS発症における脂肪の慢性炎症が注目されMetaflammation(MF)という概念が提唱されている。今回、マウス脂肪組織のマイクロアレ解析を行った。【方法】UN/catch-up growth促進マウスモデルの産生仔に高脂肪餌を与え、Vehicle(Veh)または二次胆汁酸(Tauroursodeoxycholic acid: TU)を投与した。16週齢の精巣周囲脂肪組織のマイクロアレ解析を行った。【成績】16週齢産生仔の体重・脂肪重量ともに、UNでは有意に増加し、TU投与により有意に改善した($p<0.05$)。Mφ数はUN群で増加しTU投与により減少した。UNの有無およびUNにおけるTU投与の有無による発現変動遺伝子群のエンリッチメント解析では、共通して変化する4つの炎症に関連するGene Ontology(GO)を同定した。4GOに含まれる遺伝子群の発現量は、UN環境とTU投与により相反する増減を認めた。また、両比較群で共通する2番目に発現変化率の高い遺伝子としてOrphan receptor X(ORX)が認められ、UNおよび高脂肪餌投与により、内臓脂肪特異的に発現が増加することが明らかとなった。【結論】UN環境およびcatch-up growthによる慢性炎症が、DOM(Developmental Origins of MF)における遺伝子発現変化の一端となることが明らかとなり、現在解析を続けている。

P-14-13 小児AYA(adolescent and young adult)スクリーニングシートからみえてきたもの: 性腺毒性中リスク以上の治療をうけたがんサバイバーの妊孕能のフォローの重要性名古屋医療センター¹, 藤田医大ばんだね病院²吉田沙矢子¹, 熊澤詔子¹, 稲葉智子¹, 中西 豊¹, 菅沼信彦²

【目的】当院では2019年より0歳~39歳まで(小児AYA世代)の癌を疑う症例に、身体的なつらさ、治療内容や性機能に関する疑問点、周囲の人との関係性、経済面などを含めた状況確認(スクリーニング)を行っておりAYAサポートチームによる包括的な医療を目指している。【方法】2019年7月~2023年3月までに登録されたスクリーニングシート1242シート(重複含む)のうち妊娠や性に関心があるものは72例であり、そのうち良疾患を除外しASCOのガイドライン性腺毒性中リスク以上の治療を施行した、もしくは治療中の19例について、原疾患、記入時年齢、治療前妊孕性温存療法施行の有無、治療後の性腺機能につき後方視的に検討した。【成績】原疾患の内訳は急性リンパ性白血病6例、骨肉腫3例、悪性リンパ腫3例、精巣癌1例などであった。記入時年齢は中央値(四分位範囲)が26(24.5~29)歳であった。19例中妊孕性温存療法を施行できた例は5例(卵巣凍結1例、精子凍結4例)であった。原疾患が寛解となり性腺機能フォローが継続されている例は15例(性腺機能正常5例、カウフマン療法5例、精子凍結後経過観察2例<うち1例は結婚し生児を獲得>、無精子症1例、他院でフォロー2例)、治療中が3例、フォローなしが1例だった。治療中や詳細不明を除いた高リスク10例中7例、中リスク2例中0例(それぞれ70%、0%)が妊孕性を喪失していた。【結論】当院での妊孕能のフォローについては19例中18例(97.4%)でされていた。原疾患治療時と妊孕性を考える時期が異なるため複数回のスクリーニングシートを用いる意義は大きい。治療後のがんサバイバーの妊孕性につき卵子凍結の提案やカウフマン療法での卵巣機能温存など細やかな配慮が必要である。

P-15-1 当院で行った子宮体がん手術症例に対するミスマッチ修復タンパク免疫染色の調査

浜松医大

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【目的】ミスマッチ修復タンパク免疫染色(MMRp-IHC)検査の意義は、新規治療薬の適応判断とリンチ症候群スクリーニングの2面を持つが、同一症例内でMSI検査を併用できないことや、リンチ症候群のユニバーサルスクリーニングとしては大腸癌しか適用がないことなど、子宮体がん患者では実臨床で知見を集積しにくい。当院では2022年10月より、新規子宮体がん症例に対してMMRp-IHC検査を研究で行っており、研究開始から1年間の研究結果を報告する。【方法】当院で子宮体がん手術を施行する全患者を対象、術前に同意が得られた患者を登録し、2022年10月~2023年9月までの1年間の登録症例について検討した。【成績】対象症例は52例で、登録症例は39例であった。そのうち、MMRp-IHC判定陽性者は9例(23.1%)で、MLH1とPMS2の同時低下が7例(77.8%)、MSH2とMSH6の同時低下が2例(22.2%)であった。判定陽性者の背景(括弧内は陰性者背景)は、年齢中央値が53歳(60歳)で、50歳未満が22.2%(30.0%)、病期はI期33.3%(76.7%)、II期22.2%(13.3%)、III期44.4%(10.0%)、IV期0%(0%)であった。組織型はすべて類内膜癌で、Gradel/2が66.7%(63.3%)、Grade3が33.3%(6.7%)であった。家族歴でリンチ症候群関連がんの罹患者がいた症例は、33.3%(30.0%)であった。【結論】子宮体がんのMMRp-IHC判定陽性率は、既報と同様であった。今後、本研究を継続し、MSI検査との比較や子宮体がんにおけるリンチ症候群拾い上げ体制の構築などを検討していく予定である。

P-15-2 当院における遺伝性乳癌卵巣癌症候群に対するリスク低減卵管卵巣摘出術の現状

徳島大

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【目的】BRCA 病的バリエーションをもつ乳癌既発症者に対して、卵巣癌発症リスク低減を目的としたリスク低減卵管卵巣摘出術 (RRSO) が保険取裁された。当院での初期成績をもとにRRSOの現状と課題について検討した。【方法】2020年4月~2023年5月に当院でRRSOを施行した症例の患者背景と術後経過について診療録をもとに後方視的に検討した。【成績】対象症例は17例、gBRCA1変異5例、gBRCA2変異12例であった。平均年齢は48(37-67)歳で11例でRRSOの施行推奨年齢を超過していた。9例はRRSOのみを施行、8例は子宮筋腫などの良性病変を認め、かつ子宮悪性腫瘍予防などのメリットとデメリットを相談のうえ単純子宮全摘術を併施した。全例腹腔鏡下手術で実施しており、平均在院日数6.5(5-8)日、周術期合併症は認めなかった。病理組織診断ではsectioning and extensively examining the fimbriated end (SEE-FIM) プロトコルに準じて標本を作成している。結果、漿液性卵管上皮内癌 (serous tubal intraepithelial carcinoma : STIC) 2例、浸潤がん2例 (高異形度漿液性癌) と17例中4例 (23.5%) に病変を認めた。STICの2例は単純子宮全摘術を併施しており慎重に経過観察中である。悪性であった2例では単純子宮全摘出+大網切除+骨盤リンパ節郭清術を追加で施行、それぞれ左外腸骨リンパ節、子宮漿膜・大網への転移を認めstageIIIの診断となり化学療法中(TC+bev)である。【結論】全例で合併症なく安全にRRSOを施行できたが、当科の初期成績では、RRSOの推奨年齢を超過した症例が多く、オカルトがんの発見率が高かった。適正とされる時期にRRSOを実施できるよう、関係診療科などとの連携を深めていくことが重要であると思われる。

P-15-3 腹腔鏡下リスク低減卵管卵巣摘出術を施行した遺伝性乳癌卵巣癌の臨床病理学的検討

熊本大

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【目的】遺伝性乳癌卵巣癌 (Hereditary breast and ovarian cancer : HBOC) は、BRCAの生殖細胞系列の病的変異に起因する癌の易罹患性症候群である。今回われわれは、HBOC症例に対して腹腔鏡下リスク低減卵管卵巣摘出術 (Risk reducing salpingo-oophorectomy : RRSO) を施行した症例について、臨床病理学的検討を行った。【方法】2021年4月から2023年10月までに、当科にて腹腔鏡下にRRSOを施行したHBOC症例における遺伝学的背景や手術所見、摘出組織の病理学的所見などについて後方視的な解析を行なった。【成績】対象となった16症例 (BRCA1遺伝子変異9例、BRCA2遺伝子変異7例) におけるRRSO手術時の年齢の中央値は49歳 (38-67歳) であり、各種ガイドラインで推奨されている35-40歳での施行は1例のみであった。乳癌の既往が14例でみられ、それ以外の2例に対しては自費診療としてRRSOを施行した。また、16症例中3例に対しては、対側リスク低減乳房切除術を同時に施行した。手術所見に関しては、手術時間は76-193分 (中央値117分)、出血量は0-25g (中央値0g) であった。術後入院日数は、3-6日 (中央値4日) であり、全例で周術期合併症はみられなかった。摘出検体の病理診断では、SCOUTが2例、STILが2例みられたが、STICを含む悪性所見は1例も認められなかった。【結論】今の一連の解析の結果から、40歳未満でRRSOを施行した割合が低いことが明らかにされ、今後は乳癌外科との密接な連携を推進していく必要があると考えられた。各症例における遺伝学的背景の理解や腹腔鏡下RRSOの適切な手術手技、そして正確な病理組織学的診断は、HBOC症例の生涯における最適なマネジメントに繋がることが期待される。

P-15-4 当院における遺伝性乳癌卵巣癌症候群 155 症例の診療経験

都立駒込病院

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【目的】当院は都道府県がん診療拠点病院として、2011年よりBRCA1/2 遺伝学的検査を導入し、遺伝性乳癌卵巣癌症候群 (HBOC) 診療を開始している。当院で診療したHBOC患者の臨床背景や診療フローを後方視的に検討し、遺伝医療連携体制の構築と、適切な予防医療やサーベイランスの提供を目指すことを目的とした。【方法】2011年4月~2023年9月に当院で診療を行ったHBOC患者155名 (女性: 151名, 男性: 4名) について、診療録を後方視的に検討した。【成績】卵巣癌既発症者29名、乳癌既発症者107名 (男性1名)、乳癌及び卵巣癌既発症者12名、膀胱癌既発症者2名、未発症者が29名であった。他院での診断された紹介例が36名であった。これまでにリスク低減卵管卵巣摘出術が40名、リスク低減乳房切除術が30名に施行された。リスク低減卵管卵巣摘出術施行症例の年齢の中央値は48歳 (36-63歳)、3例 (45-60歳) でオカルト癌が見つかった。当院で診療を継続した症例のうち、一部既発症のHBOC関連癌の病状により行われていない場合もあるが、ほぼ全例で乳癌・卵巣癌に関するサーベイランスは実施されている。しかし、乳癌卵巣癌以外の関連癌に関するサーベイランスが行われている症例は3例にとどまった。【結論】当院は都道府県がん診療拠点病院として、他施設との連携により多くのHBOC患者の受け入れを行っている。院内では乳癌外科、遺伝診療科との円滑な連携のもとリスク低減手術及びサーベイランスを適切に行なっている。一方で、その他のHBOC関連癌を扱う診療科との連携や系統的サーベイランス体制の構築、血縁者への遺伝診療の拡充は今後の課題である。

P-15-5 RRSO (risk reducing salpingo-oophorectomy) を希望し当科を受診した HBOC 患者の動向

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【目的】RRSO を希望し当産婦人科を受診した HBOC 患者の動向について検討し、当院 HBOC 患者診療についての課題を抽出する【方法】2020年4月～2023年6月に RRSO 希望され当産婦人科を受診した HBOC 患者を対象とした。対象患者の年齢・出産歴・受診経路・家族歴・遺伝子検査・遺伝カウンセリングの有無等の各項目について診療記録をもとに抽出した。またリスク低減手術の選択等について検討した。【成績】対象は38例で、発症者(乳癌)28例、未発症者10例であった。<発症者>初診時平均年齢は49歳。他院からの紹介が12例で最多であった。1例を除いて BRCA Analysis が実施され、病的バリエーションは BRCA1 10例、BRCA2 18例であった。RRSO を実施したのは23例。RRSO を希望しなかった5例では、30代3例のうち2例で妊孕性温存を実施していた。<未発症者>初診時平均年齢は39歳。診断の契機となった発症者は母親が4例と最多、次いで同胞が3例であった。病的バリエーションは BRCA1 7例、BRCA2 3例であった。RRSO が実施されたのは4例で実施時年齢は30代1例、40代2例、50代1例であった。全て BRCA1 の病的バリエーション保持者で、うち3例に卵巣癌の家族歴があった。また1例で初期卵巣癌が見つかった。RRSO を希望しなかったのは6例で、挙児希望者が3例、自費のため希望しなかったものが1例あった。2例は実施タイミングを考慮中である。【結論】今後も変化するであろう HBOC 診療体制において、患者背景を考慮し適切な遺伝カウンセリングを提供すること、リスク低減手術やサーベイランスに対する正確な情報提供が重要であると考えられる。また将来的には未発症者に対しても適切な診療環境が整えられることが望ましいと考える。

P-15-6 当院における遺伝性乳癌卵巣癌 (HBOC) に対するリスク低減卵管卵巣摘出術 (RRSO) の後方視的検討

福島県立医大

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【緒言】遺伝性乳癌卵巣癌 (HBOC) は BRCA1/2 生殖系列病的バリエーション (PV) による遺伝性腫瘍であり、卵巣・卵管・腹膜癌の発症リスクが高いことから、リスク低減卵管卵巣摘出術 (RRSO) が推奨されている。当院で保険収載後に施行された症例について後方視的に検討し報告する。【方法・結果】2020年4月から2023年9月末まで、25例の患者に対して RRSO を施行した。患者年齢の中央値は 49.0 ± 9.7 歳であり、BRCA1PV は12例、BRCA2PV は13例であった。二度近親者までに HBOC 関連癌発症者を認めたのは20例で、乳癌・卵巣癌の両方を認めたのは5例、乳癌のみ14例、卵巣癌のみ1例であった。また、乳癌既発症が23例、癌未発症が2例であり、後者は自費診療にて施行し、全例が腹腔鏡下手術で完遂された。手術時間の中央値は 72.0 ± 26.6 分であり、出血量は全例で10ml未滿であった。RRSO 単独施行が21例、リスク低減乳房切除術 (RRM) を同時に施行したのは4例であった。病理検査は SEE-FIM プロトコールに則り評価を行い、漿液性卵管上皮内癌 (STIC) やオカルト癌を認めなかった。術後入院日数の中央値は RRSO 単独施行例で 4.0 ± 0.9 日、RRM 同時施行例では 11.0 ± 2.0 日であり、自費診療での施行例では入院日数が短かった。術後合併症や RRSO 後の腹膜癌発症、更年期障害や骨粗鬆症を生じた症例は認めなかった。【考察・結語】卵巣癌の生涯累積危険度は、BRCA1PV 保持者で36-63%、BRCA2PV 保持者は10-27%とされている。HBOC の診療において、乳癌外科、遺伝診療部、病理診断部と連携し、適切な遺伝カウンセリングや症例検討を行うことが肝要である。今後は腹膜癌の発症や外科的閉経による健康障害について長期のフォローアップが必要である。

P-15-7 家族歴・組織型から遺伝性乳癌卵巣癌症候群 (HBOC) を疑い、遺伝カウンセリングを経て診断に至った卵巣癌 II 期患者の一例

九州がんセンター

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初回治療が奏功した FIGO 分類 III 期以上の進行卵巣癌症例に対し、相同組換え修復欠損を評価する検査が維持療法のコンパニオン診断として行われ、結果として HBOC が診断されることが少なくない。しかし、II 期以下の卵巣癌症例に対しては積極的に HBOC を疑い、診断していく必要がある。2020年4月より乳癌および卵巣癌症例に対する BRCA 遺伝学的検査が保険収載され、II 期以下の卵巣癌症例にも積極的に BRCA 遺伝学的検査を提供する必要がある。本演題では初回治療が奏功した卵巣癌 II 期症例に対し、家族歴・組織型から HBOC を疑い、診断に至った自験例をもとに、婦人科診療における HBOC 診断の課題について考察する。症例は63歳女性。G2P2。家族歴で妹と長女に乳癌あり。骨盤内腫瘍を主訴に当科紹介受診した。悪性を疑う右卵巣腫瘍を認め開腹術を施行した。右付属器は充実部を伴う5cmの腫瘍で子宮に浸潤していた。右付属器の迅速組織診は腺癌であった。Staging laparotomy を肉眼的残存病変なく終了した。術後組織診は卵巣癌 IIA 期(高異型度漿液性癌)であった。術後補助療法として TC 療法を6コース施行し初回治療終了した。家族歴・組織型から HBOC を疑い、当院がん遺伝外来に診察依頼した。BRCA PRO™ は60%と高く、BRCA 遺伝学的検査が提供された。BRCA1 病的バリエーションが見出され、HBOC の診断となった。今回、卵巣癌 II 期症例について家族歴・組織型から積極的に HBOC を疑うことで診断確定に至った。婦人科医が HBOC に注意を払うことで、患者はリスク低減手術が適応となり、血縁者には適切なサーベイランスが提供される。婦人科医が臨床遺伝学に精通することは、血縁者を含めて適切な情報提供・診療が可能になると考えられる。

P-15-8 miRNA sequencingによる絨毛癌における疾患特異的 miRNA 解析

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【目的】miRNAは、20-25塩基対のnon coding-RNAであり、標的遺伝子の転写後発現の制御に関わっている。さまざまな癌腫でmiRNAの役割が研究されているが、絨毛癌における病因や進行における役割に関する情報は不足している。本研究の目的は絨毛癌におけるmiRNA発現プロファイルとその役割を明らかにすることである。【方法】当院で診療を行った絨毛癌11症例、全胎状奇胎(侵入奇胎を続発しなかったもの)5症例を解析対象とした。FFPE検体からlaser microdissectionを用いて栄養膜細胞のみから選択的にRNAを抽出し、miRNA Sequencingによる網羅的解析を行った。Volcano plotを用いて絨毛癌と全胎状奇胎を比較し、絨毛癌に特徴的なmiRNAを同定した。次に絨毛癌細胞株を用いて発現変動miRNAの機能解析を行った。【成績】全胎状奇胎に比べて絨毛癌で2倍以上有意に発現が上昇したmiRNAは87個、低下したmiRNAは28個であった。発現が低下した28個のmiRNAのうち、13個がCromosome19 miRNA cluster (C19MC)に属するmiRNAであった。本研究では、C19MCの中でも特に発現量の多かったmiR-516b-5pに注目し、絨毛癌細胞株であるJAR, JEG-3を用いて機能解析を行った。その結果、miR-516b-5pを過剰発現させたJEG-3においてControlと比べて遊走能・浸潤能が有意に低下した(P<0.05)。また、JARにおいても同様の傾向がみられた。【結論】絨毛癌では全胎状奇胎に比べてmiR-516b-5pの発現が低下しており、そのことが絨毛癌細胞の悪性度を高めている可能性がある。またmiR-516b-5p以外のC19MCも全胎状奇胎に比べて絨毛癌で低下しており、絨毛癌の発生にC19MCが関与していることが示唆され、更なる研究開発が求められる。

P-15-9 ホモシステインによるアポトーシスに着目した難治性絨毛癌に対する新規治療法の検討

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【目的】化学療法抵抗性絨毛癌の治療成績の向上を目指すため、メトトレキサート(MTX)の既知の抗腫瘍効果である葉酸代謝経路阻害とは別の、細胞内ホモシステイン濃度上昇作用に注目し、ホモシステインが絨毛癌細胞のアポトーシスを誘導し、化学療法抵抗性絨毛癌治療に応用できないか検討した。【方法】①ホモシステイン添加による絨毛癌細胞のアポトーシス誘導の検討。絨毛癌細胞株Jarにホモシステインを添加し、細胞増殖が抑制されるか検討した。さらにその細胞増殖がアポトーシスによるものかをAnnexin V/PIを用いたフローサイトメトリーを用いて検討した。②MTX添加によるホモシステイン濃度上昇の検討。JarにMTXを添加し、ホモシステイン濃度上昇がみられるかをホモシステイン測定ELISA kitを用いて検討した。さらにMTX抵抗性Jarを用いて比較検討した。【成績】①ホモシステインをそれぞれ、0, 1, 2, 5mM, メディウムに添加し、48時間培養したところ、ホモシステイン濃度依存性に細胞増殖が抑制された。また、ホモシステイン5mM, メディウムに添加し、24時間培養したところ、初期アポトーシス、後期アポトーシスのいずれにおいても増加が認められた。②MTXをそれぞれ、1nM, 10nM, 100nM, メディウムに添加し、24時間培養したところ、MTX濃度依存性に細胞培養上清中のホモシステイン濃度上昇が認められた。また、MTX抵抗性Jarではその上昇が認められなかった。【結論】MTXの絨毛癌細胞への作用として、細胞内ホモシステイン濃度の上昇がアポトーシスを引き起こし、細胞増殖抑制につながっており、この作用が化学療法抵抗性絨毛癌治療に応用できる可能性が示唆された。

P-15-10 腹腔鏡下手術にて診断された腹膜妊娠が術後病理診断にて絨毛癌と診断された1例

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【緒言】絨毛癌は全胎状奇胎の1~2%に続発するとともに、分娩・産後などあらゆる妊娠に続発し得る。今回、腹腔鏡下手術によって診断された原発性腹膜妊娠が、術後病理診断によって絨毛癌と診断された症例を経験したので報告する。【症例】38歳、妊娠歴:3経妊2経産。これまでの妊娠は満期産、胎状奇胎既往はなし。急性腹症を主訴に受診された。妊娠反応陽性、最終月経より妊娠6週であり血中hCG値:28834mIU/mlであったが、子宮内に胎嚢を認めず腹腔内出血を認めた。異所性妊娠を疑い緊急腹腔鏡手術を施行した。腹腔内所見では子宮、両側付属器に異常は認めず、回盲部付近の腹膜に20mm大の凝血塊とその近傍からの活動性の出血を認め、腹膜妊娠と判断し、周囲の腹膜と共に同部位を摘出した。術中出血量は1450ml。病理診断では他の絨毛性疾患との鑑別において、合胞体栄養膜細胞様、中間型栄養膜細胞様の異型細胞の増殖を認め、絨毛構造を認めておらず、絨毛癌と診断された。免疫染色にてKi67, HCGがびまん性陽性、p63が一部陽性であった。子宮内膜検体には増殖期相当の内膜がみられ、絨毛構造は認めていない。これらの経過から今回の腹膜妊娠が先行妊娠と考えられた。化学療法施行前に当院で施行したPET-MRI検査で右肺に肺転移を疑う高集積を示す結節を認めた。当院で絨毛癌に対しMEA療法4コースを施行中である。【結語】絨毛性癌には病理組織学的診断が望ましいが、実際には組織学的確定診断が得られない場合が多い。異所性妊娠を疑う症例でも、病理学的診断は重要であり、絨毛癌の可能性も考え対応する必要があると考えられた。

P-15-11 黄体化過剰反応による卵巣茎捻転をきたした臨床的侵入奇胎の1例

秋田大

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黄体化過剰反応 (HL) は妊娠や絨毛性疾患による高 hCG 血症が原因となり、莢膜黄体化嚢胞を形成し卵巣腫大を呈する。今回、臨床的侵入奇胎の治療中に HL を発症し卵巣茎捻転をきたした症例を経験したので報告する。症例は 35 歳、2 妊 0 産 (自然流産、今回妊娠)。前々医にて妊娠 8 週に稽留流産の診断で子宮内容除去術 (Day0) を施行し、病理診断では胎状奇胎成分は認めなかった。性器出血が持続するため Day 7、14 に同医を受診し、子宮内血液貯留と右卵巣腫大を認めていた。Day 26 に症状改善なく、血中 hCG 950,000 mIU/mL 以上と絨毛性疾患を疑われた。Day 32 に前医へ紹介され、MRI 検査で子宮は 20 cm 大に腫大し内部には嚢胞状病変を認め、両側卵巣は 8cm 大で多房性に腫大していた。造影 CT 検査で他臓器病変は認めなかった。翌日に当科紹介、同日に子宮内容除去術を施行し全胎状奇胎と診断された。前々医での病理検体を当院で免疫染色を追加して再評価した結果、全胎状奇胎 (絨毛癌診断スコア 1 点、FIGO Scoring 6 点) の診断であった。適切な処置がされていない経過非順調型であり臨床的侵入奇胎と診断し、1 週間後に 2 回目の子宮内容除去術を施行した。両側卵巣は 13cm 大に腫大していた。Day 44 より methotrexate (MTX) 療法を開始した。Day 52 に左下腹部痛があり当院救急外来を受診し、左卵巣茎捻転疑いで緊急腹腔鏡手術を施行した。左卵巣は 360° 捻転していたが、内溶液を吸引した後に捻転を解除し卵巣は温存できた。Day 56 に 3 回目の子宮内容除去術を施行し、その後も MTX 療法を継続し、2 コース終了時点で β hCG 値は 816 mIU/mL まで低下した。絨毛性疾患では HL による卵巣腫大をきたす可能性を念頭においた管理を行うべきである。

P-15-12 化学療法抵抗性侵入奇胎の一例

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侵入奇胎は単剤化学療法で 9 割は治癒に至るが、時に治療抵抗性となり症例数が少ないことから治療方法の選択に難渋することがある。今回単剤化学療法では治癒に至らなかった侵入奇胎の一例を経験したため報告する。症例は 30 歳、0 妊 0 産。近医の超音波断層法で胎状奇胎を疑われ当科紹介となった。血中 hCG は 723,312 mIU/ml と高値であった。子宮内容除去術を 2 回施行し摘出標本病理組織診断で全胎状奇胎と診断した。2 次管理に移行したが経過非順調型となり、MTX 筋注療法を 4 コース施行したが血中 hCG 値の上昇を認めた。全身造影 CT 検査で肺転移と子宮内病巣を認め侵入奇胎と診断した。ActD 療法へ変更し 3 コース投与後に血中 hCG 値の再上昇を認めた。子宮摘出とその後の多剤併用療法、または、多剤併用療法でのみの治療を提示し後者を選択された。血中 hCG 低値が持続したが 3 コース後に血中 hCG が陰転化し、追加で 3 コース施行した。2022 年の NCCN ガイドラインによると、化学療法抵抗性の high risk GTN については絨毛癌に準じて加療をすることが提案されている。本症例では、孤在性の肺転移については単剤療法後も増大を認めなかったため多剤併用療法で治療効果がなかった場合は摘出を検討し、子宮病変については子宮摘出後の多剤併用療法を検討した。妊孕性の温存を考え、子宮摘出を行わずに多剤併用療法を行う提案も行い、ご本人の希望に沿い治療を施行した。

P-16-1 子宮平滑筋腫瘍の増殖能、転移能、再発能に相関する分子学的分類の検討

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【目的】子宮平滑筋を起源とする子宮平滑筋腫瘍は、良性的平滑筋腫 (富細胞性平滑筋腫、異型平滑筋腫を含む)、悪性度不明な平滑筋腫瘍 Smooth muscle tumor of uncertain malignant potential (STUMP)、悪性の平滑筋肉腫に分類される。この分類は核分裂数、核異型度、凝固壊死などの病理学的所見に基づくが、実際には境界的特性を示す腫瘍も存在し、臨床特性と乖離する。本研究では増殖、転移、再発などの悪性特性を特徴付ける因子を同定し、臨床所見と相関する分子学的分類を試みた。【方法】倫理承認および患者同意に基づき、当院で外科的切除された子宮平滑筋腫瘍 26 症例を対象に、凍結組織 26 検体、FFPE 組織 32 検体を用いて DNA メチル化アレイ、コピー数変異、ゲノム変異の解析を行った。組織内訳は、原発巣 30 検体、再発巣 28 検体であり、同一腫瘍内に異なる病理所見を含む 3 症例については multiple sampling を実施した。【成績】解析実施組織の病理診断結果は子宮平滑筋肉腫 41 検体、STUMP 2 検体、子宮平滑筋腫 15 検体であった。異時性再発症例では原発巣と再発巣の DNA メチル化パターンは症例ごとに類似性を示した。また臨床的には肉腫様の特性を示しながらも病理学的所見では平滑筋肉腫の診断基準を満たさない症例でも、分子学的には子宮肉腫類似パターンを示すことを明らかにした。【結論】DNA メチル化プロファイルは、子宮平滑筋腫瘍における増殖、転移、再発という臨床的特性との相関が明らかになった。これらの解析を進めることで、より臨床特性と相関する分子学的分類の可能性が示唆された。

P-16-2 免疫チェックポイント阻害剤投与に伴う免疫関連有害事象の発症率と傾向

聖マリアンナ医大

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【目的】婦人科悪性腫瘍領域において、免疫チェックポイント阻害剤 (ICI) の単剤/多剤併用療法が近年主流となってきた。そこで免疫関連有害事象 (irAE) の発症予測因子を調査することを目的とした。【方法】当院で2019-2023年にICIの投与を行った症例の臨床データや患者背景とirAE発症との関連を後方視的に解析した。【成績】子宮体癌及び子宮頸癌症例のうち、19例にICIの投与が行われた。内訳は、MSI-high再発子宮体癌または再発子宮頸癌に対するペムプロリズマブ (pem) 療法が5例、再発子宮体癌に対するレンパチニブ+pem併用療法が8例、進行再発子宮頸癌に対する化学療法±ペバシズマブ+pem併用療法が6例であった。irAEの診断は9例、そのうちGrade2以上は7例であった。そのうちICI投与中止となった症例は2例、ステロイド併用で治療継続となった症例は3例であった。irAEの発症リスクについて、原疾患、年齢、BMI、前治療数、治療開始時のPS、単剤/多剤併用、レンパチニブまたはペバシズマブ併用の有無、治療開始時のリンパ球数、好中球/リンパ球比 (NLR) について検討した。irAE発症率は、レンパチニブまたはペバシズマブ併用例において有意に高く ($p=0.036$)、多剤併用療病例において高い傾向にあった ($p=0.140$)。また、治療開始時のPSが悪い症例の方が重篤なirAEの発症が多い傾向にあった ($p=0.078$)。【結論】レンパチニブまたはペバシズマブ併用、多剤併用、PS不良がリスクとなる可能性が示唆された。今後さらなる研究と症例の蓄積が必要である。

P-16-3 アソシエーションルールを用いた、超高齢者化学療法の重篤な有害事象発現因子の組み合わせに関する検討

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【目的】超高齢者の化学療法では重篤な有害事象により治療自体が患者の不利益になることがあり、実施前のリスク評価は重要な課題である。本研究は超高齢者への化学療法の実施可能性を予測する患者背景の組み合わせの抽出を目的とした。【方法】2018年から2020年に実施した75歳以上の婦人科がん化学療法54治療 (44人) を対象とした。GNP-based Rule Mining Methodを利用した機械学習プログラムを用いて、治療の中止または入院を要した重症の有害事象 (Severe Adverse Effect: SAE) の発生と初回がん化学療法または再発治療前の患者背景 (治療前の病状、合併症、併用薬剤数、血液検査異常、社会的状況など) の組み合わせについてアソシエーション分析を行った。【成績】全体のSAE発生率は38% (20/54件) であった。SAE発生率が100%となった因子の組み合わせは2つあり、いずれも原疾患の予後不良因子 (III期以上、補助療法以外の治療実施) と社会活動制限および要支援・介護認定の有無の組み合わせを有していた。年齢、合併症、ポリファーマシー、血液検査異常などの影響は軽微であった。【結論】超高齢者化学療法のSAE発生リスクとしては生活自立性の制限が強く影響していることが示唆された。暦年齢や合併症の有無だけで治療の差し控えを判断せず、患者の生活状況も十分評価する必要がある。問題となるリスク因子への積極的介入がSAEの発生を抑制できる可能性があり、今後の課題である。

P-16-4 地域がん登録データを用いたHPV関連がんの動向の解析 (1977-2019年): 子宮頸がんの年齢調整罹患率の増加トレンドの横ばい化についての検討

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【目的】HPVワクチンによる予防が期待されるHPV関連がんの動向把握を目的とした。【方法】1977~2019年に地域がん登録に登録された子宮頸がん・膣がん・外陰がん (女)、陰茎がん (男)、肛門がん・中咽頭がん (男女) について解析した (上皮内がんを含めない)。統計解析にはStata MP 17を用いた。年齢調整罹患率 (人口10万対) は、1985年の日本のモデル人口を用いJoinpoint Regression Modelで動向解析した。【成績】子宮頸がんは1977~1981年は横ばい (1.8)、1981~1998年で減少 (-5.8*)、1998~2015年において増加 (4.1*)、2015年以降は横ばいに転じていた (-1.5)。膣がんは期間を通して横ばいであった (-0.4)。外陰がんは1977~1997年で減少 (-3.0*)、1997年以降は増加に転じていた (同=3.7*)。陰茎がんは1977~1995年で減少 (-5.1*)、1995年以降は増加に転じていた (同=2.0*)。肛門がんは男女とも一貫して増加していた (1.8*, 1.3*)。中咽頭がんは男性において一貫して増加していた (4.2*)。女性においては横ばいであったが (1.75)、1997年以降は増加に転じていた (6.7*)。 (括弧内は年平均変化率。*は有意を示す。 $p<0.05$) 【結論】多くのHPV関連がんは増加傾向にあったがトレンドは一致していなかった。これは、HPVの寄与度が異なることが原因の一つと考えられる。子宮頸がんは増加から近年横ばいに転じていた。横ばいに転じたのはHPVワクチンの薬事承認からわずか3年後であり、また接種率が高い生まれ年度はまだ25歳以下と頸がん罹患率が低い年齢であるため、HPVワクチンの導入が罹患率のトレンド変化に影響した主要な要因とは考えにくい。今後の動向を注視する必要がある。

P-16-5 婦人科悪性腫瘍における MSI-high 腫瘍についての多施設共同研究

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【目的】本研究はマイクロサテライト不安定性 (MSI) -high の婦人科悪性腫瘍を臨床病理学的に解析することを目的とした。【方法】関西臨床腫瘍研究会 (KCOG) に所属する 11 施設で、2018 年 12 月から 2020 年 12 月に MSI 検査を実施した婦人科悪性腫瘍症例について、ペムプロリズマブの効果、中央病理判定による病理組織型、ミスマッチ修復分子 (MMR) の欠損、さらにリンチ症候群の遺伝カウンセリングや遺伝学的検査の有無、予後について調べた。【成績】MSI 検査は 529 例に施行され、MSI-high は 11% (56 例)、うちペムプロリズマブは 23 例で投与され奏効率は 50% であった。MSI-high の比率は子宮体癌 23% (51/223)、子宮体癌と卵巣癌の重複癌 50% (2/4)、子宮癌肉腫 3% (1/32)、子宮頸癌 1% (1/109)、卵巣癌 1% (1/152)、外陰癌 (0/3)、陰癌 (0/4)、その他 (0/5) であった。子宮頸癌と卵巣癌の組織型は類内膜癌 G1、子宮癌肉腫の上皮成分の組織型も類内膜癌 G1 であった。MMR 分子の欠損あるいは発現減弱はすべての症例で認められた。MSI-high 腫瘍のうち遺伝カウンセリングは 14 例 (25%)、遺伝学的検査は 6 例 (11%) で実施され、うち 4 例がリンチ症候群であった。またペムプロリズマブ投与後の 5 年無増悪生存期間は約 50%、5 年全生存期間は約 55% であった。【結論】MSI-high となる婦人科悪性腫瘍はほとんどが子宮体癌であり、子宮頸癌や卵巣癌であっても異所性子宮内膜と関連の深い組織型である。遺伝カウンセリングや遺伝学的検査を実施された症例は極めて少ない。既報よりも本研究では予後は良い結果であった。

P-16-6 当院における婦人科がん患者に対するがん遺伝子パネル検査の現況と課題

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【目的】当院は 2019 年 9 月にがん医療拠点病院に指定されており、連携病院以外の症例への対応や臓器横断的な治験情報の共有等によるがんゲノム医療提供体制の強化に取り組んできた。当院における婦人科がん患者に対するがん遺伝子パネル検査の現状について報告する。【方法】2019 年 10 月～2023 年 8 月の期間に当院でがん遺伝子パネル検査を行った婦人科がん 159 例を対象に、臨床的背景と検査結果について後方視的に検討した。【成績】がん種の内訳は、卵巣がん 68 例 (43%)、子宮体がん 50 例 (31%)、子宮頸がん 39 例 (25%)、外陰がん 2 例 (1%) であった。検査種別では F1CDx 142 例 (89.3%)、Gardant 360 CDx 10 例 (6.3%)、NCC オンコパネル 6 例 (3.8%)、F1CDx Liquid 1 例 (0.6%) であり、145 例 (92%) で適切な解析結果が得られた。出検からエキスパートパネル開催までの期間の中央値は 29 日であった。Actionable な遺伝子変異は 60 例 (38%) で同定され、MSI-H、TMB-H のいずれかが検出された症例は 9 例 (5.7%) であった。生殖細胞系列バリエーションは 19 例 (12%) で同定された。63 例 (40%) で何らかの推奨薬剤が提示され、3 例 (1.9%) で保険診療での治療が施行された。20 例 (13%) で臨床試験・治験が提示され、10 例 (6.3%) が治験に組み入れとなった。全 159 例のうち、がん遺伝子パネル検査の結果に基づき治療が施行されたのは 13 例 (8.2%) であった。【結論】がん種や組織型毎の臨床試験・治験情報等の実施状況や候補遺伝子異常の頻度を把握しつつ、検査期間や全身状態等も考慮したうえで機会損失とならぬような検査提案をしていくことが重要と考えられた。

P-16-7 婦人科がん治療患者の休暇取得は最も職場復帰に影響する

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【目的】婦人科がんは就労世代に多い悪性腫瘍の 1 つである。婦人科がん患者は健常群と比べて離職や失業率が高く、本邦でもがん治療後の復職率を向上させるため、2016 年にがん対策基本法が改正され、がんになっても雇用継続できるよう、事業主に対してがん患者就労に関する啓発・知識の配慮がなされた。しかし未だ法改正前後の状況を比較した報告はなく、婦人科がん治療後患者の離職状況を明らかにすることを目的に検討を行った。【方法】当病院で婦人科がんの治療を受けた女性 194 名 (がん治療後 1 年以上、65 歳未満) を対象に就労復帰アンケート作成し、調査を実施。解析はロジスティック回帰分析を用いた。【成績】がん診断時の年齢中央値は 49 歳、がん治療からアンケート開始までの期間の中央値は 3.8 年だった。2015 年に当病院で施行した職場復帰に関する調査と比較し、どの職種も職場復帰率は向上しており、復職率が 71.2% から 82% に向上していた。離職率 (転職も含む) が高い因子として、単変量解析では非正規雇用者 (P=0.018)、1 日 5 時間以内勤務 (P=0.023)、個人低所得 (p=0.004)、休暇未取得 (p<0.001)、進行癌 (p=0.018)、3 か月以上治療期間 (P=0.032) が関連し、多変量解析にて非正規雇用者 (P=0.049)、休暇未取得 (p<0.001) と進行癌 (p=0.041) が関係性を認めた。今回の結果で、最も休暇未取得が職場離職と関連していた。【結論】婦人科がん治療後患者の復職において、休暇の取得が重要であることが判明した。復職率向上のために本邦でも休暇制度が求められ、どのような休暇が望ましいか今後の検討が期待される。

P-16-8 婦人科疾患と鑑別が困難だった他臓器原発腫瘍の検討

弘前大

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【目的】婦人科疾患と診断された症例が他臓器原発であることはしばしば経験する。正しい診断ができていれば治療方針が異なる症例もある。正しい診断をするためには何が重要なのか、過去の症例から学ぶことを目的とした。【方法】2010年1月から2023年8月までに当科に入院した症例のうち最終診断が他臓器原発であった16例から炎症性疾患2例を除外した14例について、検査項目や臨床の特徴などを診療録をもとに後方視的に検討した。【成績】14例の内訳は、術前診断が骨盤内腫瘍10例(術後診断が消化器癌6例, 低異型度虫垂粘液性腫瘍2例, GIST1例, 横紋筋肉腫1例), 子宮腫瘍2例(他臓器癌の転移2例), 陰・外陰部腫瘍2例(他臓器癌の転移1例, GIST1例)であった。術前に鑑別できていた症例は9例(そのうち腹水・腫瘍穿刺や組織診で診断がついていた症例は4例), 鑑別できなかった症例は5例(横紋筋肉腫, 胃GIST, 粘膜病変のない大腸癌, 虫垂癌, スキルス胃痛)であった。【結論】CEA, CA19-9の異常高値や術前の腹水・腫瘍細胞診が診断の一助になる。しかし, 稀少癌やGISTは診断が困難であり, また消化管内視鏡検査で異常がないと診断されても, 消化器癌のことがあるため留意する必要がある。

P-16-9 当院における遺伝子パネル検査の現状と課題

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【目的】当院における遺伝子パネル検査の現状を明らかにし, 問題点や課題を検討することを目的とした。【方法】2020年1月より2023年6月に遺伝子パネル検査を施行した54例の婦人科がん症例について, actionableな遺伝子変異を有した症例, 治療提案された症例, 実際の治療到達症例の割合や, 治療不達の原因等を, 後方視的に検討した。【成績】1, 遺伝子パネル検査を行った症例は, 子宮頸がん10例, 子宮体部悪性腫瘍16例(うち肉腫8例), 卵巣がん・卵管がん26例, 外陰がん2例であった。2, 바이오マーカーを有した症例は, MSI-H1例, TMB-H(10Muts/Mb以上)6例(1例MSI-Hと重複), NTRK融合遺伝子2例, 卵巣がん・卵管がんのLOH-H(16%以上)7例の15例(28%)。3, actionableな遺伝子変異は53例あり, そのうち治療提案されたのは27例(50%), 実際に治療を行った症例は保険治療3例, 治験参加4例の合計7例(13.0%)であった。4, 推奨治療なくその後死亡された症例の予後は, エキスパートパネル開催日より0-18か月(中央値4か月)と非常に悪かった。5, 治療薬推奨されてもできない理由は, 保険適応がないため, すでにプラチナ耐性であるため, すでに使用して無効であったため, 本人の全身状態の悪化, であった。【結論】遺伝子パネル検査によって50%の症例が治療提案されたが, 実際に治療を行った症例は13.0%であった。治療不達の原因としてパネル検査を行うタイミングの課題が示された。

P-16-10 当科における免疫チェックポイント阻害薬(ICI)の使用経験

神戸大

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【目的】近年, 婦人科悪性腫瘍でも免疫チェックポイント阻害薬(ICI)が使用されているが, ICI使用には特有の副作用管理が必要と考えられる。当科ではICI導入において腫瘍内科等と連携をとることで副作用対策を行ってきた。当科での使用経験を報告する。【方法】2018年4月~2023年10月までに当科でICI使用をおこなった症例を対象とし, その患者背景および副作用について検討した。【成績】これまで, 当科では子宮頸癌; cemiplimab: 3例, 子宮頸癌; TC+Pembrolizumab(PEM): 3例, 子宮体癌; Lenvatinib(LEM)+PEM: 7例, 子宮体癌; PEM: 3例の16例にICIを使用した。投与期間中央値は122日(23-719)であった。MSI検査は9例(MSI high: 3例, MSI陰性: 6例)で行った。MSI high: 3例は子宮体癌でありPEM単剤療法おこなった。自己中断の1例を除く2例は平均711日のPFSを得ている。MSI陰性6例の投与期間中央値は108日(78-202)で, 3か月以上の投与継続症例は6例中5例であった。副作用は甲状腺機能障害が最も多く6例(43%)であり, 投薬を必要とするG2が4例(29%)であった。副作用により治療薬の休薬および減量を必要とした4症例あり, いずれもLEM+PEM症例であったが, 投与中止に至った症例はなかった。また, 全症例を通じてG3を超える重篤な副作用に至った症例はない。【結論】ICIは特有の副作用管理を行いつつ, 投与継続することが重要と考えられる。他科との連携は, ICI導入に対して有効と考えられる。

P-16-11 当科におけるペムプロリズマブ単剤療法の治療成績

琉球大

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がん化学療法後に増悪した進行・再発の高頻度マイクロサテライト不安定性 (MSI-High) または高い腫瘍遺伝子変異量 (TMB-High) を有する進行・再発の固形癌に対するペムプロリズマブ単剤療法が保険適用となり, 婦人科悪性腫瘍にも適応拡大が進んだが, 長期投与における有効性や有害事象など, 本邦でもリアルワールドデータの集積が望まれる。【目的】当科のペムプロリズマブ単剤療法症例の長期予後や安全性について報告する。【方法】2018年12月から2023年9月までに当科でペムプロリズマブ単剤療法を施行した MSI-High または TMB-High 症例を診療録から後方視的に抽出し, 患者背景や治療期間, 治療効果, 有害事象について検討した。【成績】対象は12症例, 年齢と観察期間の中央値は51歳と51.5か月, 原疾患は子宮体癌が7例, 卵巣癌が3例, 子宮頸癌が2例であった。適応は MSI-High が10例, TMB-High が2例であり, 前治療としての化学療法レジメンの中央値は1, 前治療からのペムプロリズマブ投与までの期間の中央値は1.5か月であった。ペムプロリズマブの投与サイクル数と投与期間の中央値は17.5サイクルと14.5か月であり, 治療効果は完全寛解が9例(75.0%), 部分奏効が1例(8.3%), 病勢進行が2症例(16.7%)であり, 予後は無病生存が10例(83.3%), 担癌生存が1例(8.3%), 原病死が1例(8.3%)であった。コントロール不可能な免疫チェックポイント阻害薬関連有害事象は見られなかった。【結論】MSI-High や TMB-High はペムプロリズマブ単剤療法の有用なバイオマーカーであり, 早期に把握するメリットがある。ペムプロリズマブ単剤療法は有害事象のマネジメントにより安全に長期投与が可能と思われる。

P-16-12 当院骨盤外科カンファレンスの取り組みが婦人科悪性腫瘍手術にもたらす影響について

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【目的】婦人科悪性腫瘍手術で他臓器浸潤を認めた場合, 消化器外科をはじめ関連他科の応援を要する。当院では2020年以降, 消化器外科・産婦人科・泌尿器科で骨盤外科カンファレンス(以下:骨盤カンファ)を定期開催し, 術前画像や術式, 術後管理について事前検討を行なっている。この取り組みで, 手術成績や術後経過にどのような影響がみられたかを検証した。【方法】2020年4月-2023年7月の婦人科悪性腫瘍手術190例のうち, 外科合同手術となった30例を対象とし, 術式, 完全切除率, 術後合併症, 予定外の合同手術割合などについて検証した。【成績】年齢中央値は57.5(35-83)歳, 全例開腹手術で行われ, 腸管合併切除13例, 肝部分切除3例, 横隔膜切除2例, 骨盤内臓全摘2例(鏡視下手術併用), 人工肛門造設1例であった。完全切除率は60%(18/30例), うち3例で他臓器合併切除を行っていた。術後合併症は14例, Clavien-Dindo分類GradeIII以上では, 骨盤内臓全摘後に腸管吻合不全とコンパートメント症候群を1例ずつ認めた。その他はGradeI以下(イレウス7例その他5例)で, いずれも軽快した。予定外の合同手術となった症例は20%(6/30例)であった。【結論】骨盤内臓全摘2例を除くと, 再手術を要した症例もなく遅滞ない術後療法へつながっていた。予定外の合同手術がなくなることは難しいが, 対象症例を見極める力も養いつつある。婦人科医の立場からは, 腸管剝離や授動などを学べる機会となり, 他の婦人科手術の安全性も高まっている。さらに想定される術式への理解が深まることで, 確度の高い術前説明が可能となり, 患者の安心感につながることも期待される。当院骨盤カンファでの取り組みの詳細について報告する。

P-17-1 胎動減少と周産期予後の関連についての研究—FMAM recorderによる胎動計測—

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【目的】胎動が胎児 well-being を反映しているが, 胎動減少がどの周産期異常と関連しているかは不明である。今回, 我々は客観的に長時間の胎動計測ができる FMAM recorder を用いて, 胎動減少と周産期異常との関連について検討をした。【方法】当院で妊婦健診, 分娩を行った妊婦470例を対象とした。妊娠28~39週までに週1回, 妊婦自身が FMAM recorder を装着し胎動を記録した。4時間以上の胎動計測ができたデータ(390例2,145データ, 約14,000時間)を対象とした。正常経過の妊婦64例から作成した FMAM recorder 胎動標準曲線を用いて, 1回以上10%tile未満を示した例(胎動減少群)と control 群の2群に分けて, 周産期異常(早産, 帝王切開, 鉗子・吸引分娩(胎児機能不全, 分娩停止), 骨盤位分娩, 前期破水, 妊娠高血圧症候群, 胎児機能不全, 在胎不当過小(過大), Apgar 7点以下(1分値, 5分値), 臍動脈 pH 7.15未満)の発生頻度を比較検討した。解析は χ^2 乗検定および多変量解析を用いた。【成績】胎動減少群は122例, 522データ, 約5,000時間, control 群は269例, 1,392データ, 約9,000時間であった。胎動減少群では早産の発症が23例19.0%であり, control 群(27例10.0%)と比べ, 頻度が高かった。妊娠高血圧症候群は14例11.6%(14例5.2%), 在胎不当過小は13例10.7%(13例4.8%), 1分値 Apgar 7未満は9例7.4%(7例2.6%)で有意に頻度が高かった。多変量解析では, 1分値 Apgar 7未満 (p=0.09) が胎動減少群と最も関連する項目として抽出された。【結論】胎動減少は胎盤機能や胎児 well-being 悪化と深く関連しており, FMAM recorder で胎動が10%tile未満の場合はこれら周産期異常に注意する必要がある。

P-17-2 先天性股関節脱臼・臼蓋形成不全と診断された乳幼児4例のFMAMレコーダーを用いた胎動測定の臨床的意義について

帝京大

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【目的】長時間の胎動計測ができるFMAM (Fetal Movement acceleration measurement) recorderは胎児の粗大な動きとなる足の動きなどを検出できる装置である。今回我々は、乳幼児期に先天性股関節脱臼(先股脱), 臼蓋形成不全と診断された4症例のFMAM recorderによる胎動記録を後方視的に検討した。【方法】4例は乳幼児期に整形外科医によって先股脱, 臼蓋形成不全と診断された。妊娠28週以降のFMAM recorderによる胎動測定されており、一晚で4時間以上の記録があるもののみ採用した。胎動記録を10秒毎のエポックに分割し、胎動ありエポックの占有割合を算出した。正常妊娠経過の64例から作成した胎動占有割合の基準曲線をコントロールとし、対象となる4例の胎動占有割合について解析した。【成績】症例1は妊娠20週より切迫流産で入院し早産管理されていた。胎動は妊娠28, 29, 31, 34, 35, 36週にて、それぞれ75.7, 53.9, 7.3, 32.3, 66.3, 6.3% tileとなった。症例2の妊娠経過は順調であり、胎動は妊娠32週で46.9% tileであった。症例3は妊娠期間中に抗精神病薬を内服しており、妊娠30週から早産管理されていた。胎動は妊娠33週で97.0% tile以上だった。症例4の妊娠経過は概ね順調であったが、胎動は妊娠29, 30, 34週にて、それぞれ11.0, 9.5, 5.4% tileであり、32週には3.0% tile未満と減少となった。【結果】4例中2例(計測12回中5回)で胎動減少(10% tile以下)を示した。胎動増加(90% tile以上)を示したのが1例あったが、抗精神病薬の影響が考えられた。FMAM recorderによる胎動計測は、出生前の筋骨格異常診断にも有用である可能性がある。

P-17-3 胎動低下を示した脳性麻痺症例の検討：産科医療補償制度データベースから

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【目的】胎動低下は胎児well-being悪化の一徴候で、脳性麻痺となった児の一部に胎動低下がみられた例が存在する。しかし、胎動低下を示した例の詳細な検討はなされていない。【方法】2009年1月1日から2021年3月26日にわが国の産科医療補償制度で認定された脳性麻痺児のうち、出生前に母体が胎動低下または消失を訴えた症例の原因分析報告書を調査した。【成績】225症例が解析対象となった。明らかな原疾患は特定できないが「低酸素・酸血症」と判断されたのは117例(52%)と最も多く、常位胎盤早期剥離(早剥)45例(20%), 母児間輸血症候群(母児間輸血)32例(14%)と続いた。正期産が112例(50%)であった。低酸素・酸血症、早剥、母児間輸血の3群で比較(Steel-Dwass検定)したところ、臍帯動脈血pHは低酸素・酸血症群、母児間輸血症群、早剥群の順に有意に低下した。低酸素・酸血症群においては臍帯卵膜・辺縁付着が有意に高率(22/106:21%)に観察された。胎動低下から娩出まで6時間以内で娩出された症例は早剥群32例(32/44:73%), 低酸素・酸血症群15例(15/104:14%), 母児間輸血症群が1例(1/28:4%)で、早剥群が有意に高率であった(P<0.0001)。【結論】母児間輸血症候群は胎動低下から娩出まで時間を要する疾患であることが分かった。臍帯卵膜・辺縁付着を合併すると胎動低下後、脳性麻痺を惹起することがあるため、妊娠中の付着部位スクリーニングおよび、妊婦への胎動指導が重要であることが示唆された。

P-17-4 新生児聴覚検査の精度管理：10年5675例の検討

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【目的】新生児聴覚検査は、早期に聴覚障害の診断を行うことで、適切な治療や支援につなげることを目的に、全国的に行われている。年間分娩数101件以上の産科施設では、ほぼ全てで実施され、公費負担を行う自治体も多い。当センターで10年間に行った新生児聴覚検査を解析した。【方法】日齢3~4に第1次スクリーニングを自動聴性脳幹反応(AABR)で行い、異常(Refer)の場合は1か月健診までに再検査をAABRで行う。再検査でも異常の場合、もしくは1次検査で明らかに異常を疑う症例は精密検査を行う。2013~2022年に当センターで1次検査より行った新生児聴覚検査について、小児科管理の有無別のRefer率、精密検査児の特徴、正常化率等について解析した。【成績】10年5675例中、産科管理(O群)3209例、小児科管理(N群)2466例について解析した。再検査数はO群26例(0.8%)N群36例(1.5%)、精密検査数はO群16例(0.05%)N群35例(1.4%)であった。精密検査で異常であったもの考える原因としては、原因不明が22例、染色体異常10例、奇形症候群9例、遺伝素因7例、CMV感染2例、器質性1例であった。このうち6例が生後8か月までに正常化し、改善傾向が見られたものも6例認めた。器質性の例は発育後手術で改善が見込まれており、計13例で改善傾向、もしくは正常化していることがわかった。原因不明の22例中8例(36%)で正常化もしくは改善していた。【結論】新生児聴覚検査では、片耳Refer児の方が両耳Refer児より多かった。小児科管理となった児の再検査率、精密検査率が産科管理群より高かった。精密検査で原因不明例のうち36%は聴力正常化もしくは改善しており、出生児の検査精度にも限界があることが推察された。

P-17-5 人工知能と自由エネルギー原理による胎児意識の存在の発見

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【目的】胎児の脳活動は胎児表情と関連するとされているので、人工知能（AI）を利用して胎児表情から算出したカオス的次元を介して、胎児の意識の存在を自由エネルギー原理にて説明すること。【方法】観察研究として、まず2020年1月から9月までの妊娠19週から38週の93例の胎児から4次元超音波技術を用いて922枚の胎児表情画像を収集し、表情認識AIを開発した。次にこのAIを2021年2月から12月までの妊娠27週から37週の33例の胎児からの37本の表情ビデオに適用し、各表情カテゴリの信頼度スコアから構成された7次元時系列データを生成した。ついでカオスの次元を計算し、次元から胎児脳活動を解釈するための自由エネルギー原理の数理モデルを作成した。統計解析には、マン・ホイットニー検定、共分散分析を用いた。【成績】表情認識AIの正診率は0.996だった。時系列データから密と疎の状態の存在とその変動とを発見した。カオス的次元値の平均±SD値は密と疎のそれぞれで 1.19 ± 0.22 , 1.33 ± 0.27 ($P < 0.05$)で、妊娠週数との関連性はなかった。カオス的次元と変分自由エネルギーには関連性があるとして、Kullback-Leibler divergence, generative density, recognition densityの概念などを用いて胎児表情から胎児脳活動を解釈できる数理モデルを作成できた。【結論】AIによって計算された脳活動に関連するカオス的次元値は自由エネルギー原理に関連していると考えられ、得られた定量的脳活動状態には密と疎の状態があり変動していたことから、変分自由エネルギーが変化する過程が検出されたことは能動的推論の存在が考えられた。したがって少なくとも妊娠27週以降の胎児には意識が存在することを示唆している。

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P-17-6 高度な胎児水頭症をきたした原因不明のMirror症候群の一例

尾道総合病院

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【緒言】Mirror症候群は胎児水腫、胎盤肥大、母体の全身浮腫を呈する疾患であるが、病態は明らかではない。高度な胎児水頭症をきたしたが原因を特定できなかったMirror症候群の一例を報告する。【症例】34歳1妊0産。妊娠20週まで前医の胎児超音波所見に異常はなかった。22週頃に感冒様症状が出現し、23週の超音波で胎児の脳実質が確認できず、頭蓋内は液体で置換されていた。同時期から母体の浮腫と乏尿が出現し、24週に肝機能障害、腎機能障害が出現し当科を紹介受診した。母体の浮腫と乏尿は発症から約2週間で自然軽快し、肝・腎機能障害も徐々に改善した。また胎児MRIでは頭蓋内は液体で満たされており、脳実質はわずかに確認できたが構造は不明瞭であった。胎児には心嚢水、腹水があり、胎盤肥大と母体の β -hCG異常高値、低蛋白血症も認めた。以上からMirror症候群と診断した。母体の大球性貧血があり、肝・腎機能障害は自然軽快したことから、何らかのウイルス感染が示唆されたが特定には至らず、胎児の脳所見の変化も説明できなかった。胎内死亡の可能性があるため慎重に経過観察の方針とした。BPDは+5~7SDで推移したがAC、FLは週数相当の発育であった。経過中CTGはreassuringであった。42週0日に4704gの男児を経陰分娩した。Apgar score 7/7点であり啼泣・自発呼吸を認めた。生後のCTで高度な水頭症と診断し、日齢8に脳室ドレナージを行なった。髄液の色調はキサントクロミーであり蛋白濃度が高いことから胎中の頭蓋内出血が示唆された。水頭症の原因精査中であるが、TORCH症候群、パルボウイルスB19はいずれも胎内感染を疑う結果ではなく、原因の特定には至っていない。

P-17-7 FGRに対するタダラフィル投与の有効性に関する考察

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【目的】子宮内胎児発育不全（FGR）の胎内治療を目的としてホスホジエステラーゼ5阻害薬であるタダラフィルを用いた臨床試験を行っている。タダラフィルは胎児胎盤循環改善、内皮障害改善作用が期待されているが、実際の作用機序は解明されていない。欧州を中心にFGRへの治療効果の検討が行われたシルデナフィルとの違いも含めて、これまでのデータを再考する。【方法】FGR（胎児推定体重 $\leq -1.5SD$ ）に対してタダラフィルの経母体投与を行った症例における、①超音波ドプラ法における胎児-胎盤循環への影響の検討、②angiogenic factorの検討、③胎児発育に関する検討を行い、タダラフィルの有効性について検証した。【成績】①多施設共同ランダム化比較試験（TADAFERII）の結果から、タダラフィル治療群で臍動脈PIの有意な低下を認めたが従来型治療群では逆に上昇していた。②NO合成酵素阻害薬を用いたマウスの研究で、タダラフィル投与群で胎盤のPIGF上昇を認めた。③単施設での後方視的検討では、HCの増加とHC/AC ratioの低下を認めた。シルデナフィルは胎盤を通過し胎児へ直接作用するのに対し、タダラフィルは母体血中濃度の1/3-1/4程度の臍帯血濃度であり、胎盤移行性が少ないと考えられた。【結論】タダラフィルは胎児-胎盤循環を改善させる可能性があり、さらなる知見の集積が必要である。現在行われているプラセボ対照ランダム化比較試験の結果が待たれる。

P-17-8 正期産 SGA 児に関わる周産期因子の検討

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【目的】在胎不当過小児 (small for gestational age : SGA) は肥満, 低身長, 成人期の高血圧や糖尿病などの発症リスクの他, 精神運動発達, 神経発達にも影響を及ぼすため長期的なフォローアップが重要である。正期産 SGA 児に関する周産期因子を検討した報告は少なく, 当院で在胎 37 週以降に出生した SGA 児の母体及び新生児の背景因子について検討した。【方法】2018 年から 2022 年の間に当院で分娩に至った単胎妊娠 1365 例のうち, 外国人及び先天異常症例を除く 1280 例について, SGA 児と非 SGA 児に関連する周産期因子について診療録を用いて後方視的に検討した。SGA の定義は出生体重 10 パーセントイル未満とした。母体背景として初産/経産, 年齢, 身長, 非妊娠時体重, 妊娠中体重増加, 飲酒・喫煙歴, 初経年齢, GDM/HDP 発症率を, 新生児背景として在胎週数, 性別, 出生時体重, Apgar score, 体格 SD (身長, 頭囲, 体重) について両群間で比較検討した。有意差検定に Fisher の正確検定と t 検定を用い, 5% を優位水準とした。【成績】1280 名のうち SGA 児は 112 名, 非 SGA 児は 1168 名であった。SGA 児と非 SGA 児の比較では, 不妊治療歴 (7.1% vs 21.2%; $p < 0.01$), 母体身長 (156cm vs 158cm; $p = 0.011$), 妊娠前及び分娩時 BMI (妊娠前 BMI : 19.6 vs 20.9; $p < 0.01$, 分娩時 BMI : 23.6 vs 25.1; $p < 0.01$), 胎盤重量 (445g vs 550g; $p < 0.01$) に両群間で有意差を認めた。【結論】妊娠前の母体プロポーシオン (身長, 妊娠・出産前母体の痩せ) が胎児発育に強く影響すると推察された。プレコンセプションケアとして健全な生活習慣・体重の維持についての啓蒙活動が必要である。

P-17-9 FGR 児の推定胎児体重の正確性についての検討: 自施設後方視的調査

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【目的】胎児発育不全 (Fetal Growth Restriction : FGR) は, 米国では推定胎児体重 (Estimated Fetal Weight : EFW) または腹囲が 10%ile か 3%ile 未満, 日本では EFW-1.5SD 未満と定義される。しかし, 重度 FGR や妊娠高血圧腎症 (Preeclampsia : PE) 症例では EFW を過大評価していることをしばしば経験する。自験例の FGR や PE 症例を対象に, 後方視的に EFW の正確性を評価した。【方法】2020 年 6 月~2022 年 11 月に当院を受診した単胎妊娠のうち, 妊娠 20 週以降で EFW 10%ile 未満を 2 回以上記録した症例を抽出した。胎児異常や転帰不明症例は除外した。対象を FGR の程度により群別し, 各群で娩出直近の EFW と出生体重の誤差を算出して, $\pm 10\%$ 以内におさまる頻度, 過大評価した割合について比較した。PE 合併症例についても同様に検討した。【成績】対象は 175 例で, 10%ile (-1.28SD 相当) 未満~1.5SD 群 (45 例), -1.5SD 未満~3%ile (-1.88SD 相当) 群 (57 例), 3%ile 未満~2.0SD 群 (17 例), -2.0SD 未満~-2.5SD 群 (35 例), -2.5SD 未満~-3.0SD 群 (12 例), -3.0SD 未満群 (9 例) に群別した。娩出直近の EFW と出生体重の誤差が 10% 未満だったのはそれぞれ 82.2%, 78.9%, 82.4%, 75.7%, 36.8%, 44.4% であった。また, EFW を過大評価していた割合はそれぞれ 46.7%, 50.9%, 52.9%, 40.5%, 25%, 88.9% であった。PE 症例 (30 例) に限り検討すると, 誤差が 10% 未満だったのは 70% で, 過大評価していたのは 80% だった。【結論】FGR の程度が 2.5SD 未満の時 EFW と出生体重との誤差が大きく, 特に 3.0SD 未満や PE 合併例で EFW を高率に過大評価していた。この原因特定は困難だが, 検者が測定誤差のしやすい腹囲等で過大評価している可能性があり, 計測にはより留意する必要がある。

P-17-10 推定胎児体重が -1.5 より大きいが -1.3SD 以下の児と SGA および周産期有害事象との関連

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【目的】英国や米国では推定胎児体重 (EFBW) $< 10\%$ tile (約 -1.3SD 以下) を胎児発育不全 (FGR) とするが, 本邦の基準 -1.5SD 以下と異なる。-1.5SD $<$ EFBW $<$ -1.3SD の胎児の特徴に関する検討はない。今回, 妊娠 28 週頃の -1.5SD $<$ EFBW \leq -1.3SD と Small for gestational age (SGA) 及び周産期有害事象との関連を検討した。【方法】妊娠 14 週未満に当院を初診し, 妊娠 27-30 週に EFBW を計測され, 2015 年 5 月~2021 年 12 月に分娩した単胎を対象とした後方視的コホート研究である。胎児構造異常や染色体異常は除外した。評価項目は SGA の割合と周産期有害事象 (周産期死亡, 陣痛前の胎児機能不全による緊急帝王切開, 臍帯動脈血ガス pH $<$ 7.1, Apgar スコア 5 分値 $<$ 7, RDS, 挿管 5 日以上の NICU 入院) の割合とした。-1.3SD $<$ EFBW (A 群), -1.5SD $<$ EFBW $<$ -1.3SD (B 群), EFBW $<$ -1.5SD (C 群) で, A 群を対照に B 群, C 群の評価に対する調整オッズ比 (aOR) をロジスティック回帰分析で算出し, -1.5SD より大きい胎児における B 群の診断精度を算出した。【成績】対象 4132 例のうち 255 例を除外した 3877 例で A 群, B 群, C 群は 3757 例 (96.9%), 63 例 (1.6%), 57 例 (1.5%) であった。SGA, 周産期有害事象に対する B 群の aOR は 15.7 (95%CI : 7.40-33.3, $P < 0.01$), 2.07 (95%CI : 0.96-4.50, $P = 0.06$) で, C 群の aOR は 28.9 (95%CI : 14.6-57.3, $P < 0.01$), 3.20 (95%CI : 1.57-6.52, $P < 0.01$) であった。SGA に対する B 群の感度, 特異度, 陽性的中率, 陰性的中率, 陽性尤度比, 陰性尤度比は 17.5%, 98.6%, 15.9%, 98.7%, 12.5, 0.84 であった。【結論】 -1.5SD $<$ EFBW $<$ -1.3SD の胎児は SGA のハイリスクである。

P-17-11 胎児発育不全と腹水を呈した同種免疫性胎児肝障害の1例

宮崎大

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【緒言】同種免疫性胎児肝障害は胎児の肝細胞に対する母体感作により母体のIgG抗体が産生され、胎児、新生児期に肝不全を引き起こす予後不良な疾患である。肝及び脾などの多臓器への鉄沈着を特徴とする新生児ヘモクロマトーシスの原因として確立されてきた。【症例】母体は26歳、1妊0産、自然妊娠。妊娠19週5日に推定体重170g (-2.8SD)と胎児発育不全を認めた。原因検索で母体因子、先天奇形及び染色体異常はなかった。妊娠24週5日から少量の腹水貯留を認めていた。臍帯動脈の血流異常はなく、中大脳動脈血流速度は正常上限であった(60.10cm/s)。妊娠29週1日に発育停止のため緊急帝王切開術を行った。男児、出生体重702g (SFD, -3.5SD), Apgarスコア(1分)3点、(5分)5点、臍帯動脈血pH7.292であった。出生時にHt 19.9%、Hb 6.5g/dLの著明な貧血を呈し、赤血球輸血を要した。出生時の肝逸脱酵素は基準範囲内であったが、日齢5から上昇し始め、日齢46にAST 71U/L ALT49 U/L、直接ビリルビン12.4mg/Lとなった。腹水は出生時少量であったが、日齢21頃から増悪し、穿刺した腹水検査から漏出性と判断した。日齢29のフェリチン値は3,057ng/mLであった。日齢49に肝不全及び呼吸不全で死亡した。病理解剖で肝門部優位に肝全体が高度な線維化を呈し、肝臓及び甲状腺、心筋、膵臓、脾臓、リンパ節の肝外臓器に鉄沈着を認めた。King's collegeの診断基準と併せて同種免疫性胎児肝障害と診断し、臨床経過及び検査結果から胎児期発症を疑った。【結語】次回妊娠時の免疫グロブリン母体治療による次子の新生児ヘモクロマトーシス再発予防が可能となるため、本疾患を診断することは重要である。

P-18-1 PCOSに対する腹腔鏡下卵巣多孔術の治療成績の検討

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【目的】多嚢胞性卵巣症候群(PCOS)は、月経異常や多嚢胞性卵巣、LH高値やアンドロゲン高値、インスリン抵抗性、肥満といった内分泌学的特徴を有する疾患である。排卵障害のためPCOS女性の約40%が不妊を呈するとされ、排卵までの誘発が難しく多胎やOHSSなど重篤な病態を引き起こすことから不妊治療において慎重かつ厳密な管理が必要となる。クロミフェン療法・ゴナドトロピン療法が無効、もしくは妊娠しない場合腹腔鏡検査に進むが、PCOに対する腹腔鏡下卵巣多孔術(LOD)の有効性を検討した。【方法】当院にて2020年1月から2022年12月の間にPCOSと診断され、HSG後のタイミング療法で妊娠成立なくLODを施行した237例を対象とした。年齢、BMI、基礎ホルモン値、手術前後のAMH値、妊娠の有無などについて後方視的に検討した。【成績】LODを施行した237例のうち、術中所見により内膜症焼灼術を行ったのは153名、前医でのリビオドール残存あり洗浄を行ったのは3名。AMH値は術前6.67、術後3か月2.96、術後6か月3.26であった。術後採血・治療成績を得られた190例のうち妊娠は自然排卵41症例、HMG-timing 22例、IVF妊娠72例の137例。自然排卵での妊娠は25例(60%)が手術直後の周期であった。【結論】PCOSに対してLODを施行し、術中に初めて子宮内膜症と診断されて焼灼術を追加した症例は少なくなかった。当院が不妊専門クリニックであることから、PCOS患者に偏りがある可能性はあるものの適切な時期に腹腔鏡検査を行うことの意義が示唆された。また術後の自然排卵による妊娠成立は多くみられた。一方で半年後AMH値が再上昇を認めたことから、術後の適切なタイミングでのステップアップも重要と考える。

P-18-2 腹腔鏡補助下卵巣のう腫摘出法の新手順は卵巣成熟奇形腫の内容物漏出が少ない

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【目的】卵巣成熟奇形腫(以下、奇形腫)は術中の、のう腫内容物漏出で化学腹膜炎が起きる懸念がある。我々は卵巣のう腫に対してのう腫下方上転と腹壁直下の表面把持固定を特徴とする腹腔鏡補助下卵巣のう腫摘出術(LAC)の新手順を考案し実践している。今回、この新手順LACを、従来法LAC/腹腔鏡下卵巣のう腫摘出術(LC)と比較したので報告する。【方法】新手順LACでは皮膚切開はダイヤモンド式とした。卵巣固有靭帯または骨盤漏斗帯を有窓鉗子で把持して180度ひねり、他の鉗子でのう腫を下から支え、のう腫を腹壁側に反転挙上させ、子宮操作鉗子で子宮ごとのう腫を押し上げる。のう腫は卵巣固有靭帯/骨盤漏斗帯よりの表面に直視下でヒダを確認でき、2本のペアン鉗子で短時間の把持固定が可能になる。その間で表面を切開し、太い吸引管2本で内容を吸引除去してから従来同様のLACを行う。術式はのう腫の大きさ、固形内容の有無などを考慮し、術者判断により選択された。2021年5月-2023年9月に当院の奇形腫手術、新手順LAC9例/従来LAC9例/LC9例に関して術中破綻・内容物漏出の有無、手術時間について比較検討した。統計はそれぞれFisher検定、Steel検定を用いた。【成績】新手順LAC/従来LAC/LCそれぞれののう腫径の中央値は5/9/6cmであった。術中破綻例は0/2/4例、内容物漏出も1/6/6例と破綻も内容物漏出も新手順で有意に少なかった(p=0.05)。手術時間は125(113-138)/147(136-166)/89(82-119)分とLCで有意に短かった(p=0.06)。【結論】新手順LACは従来法LACやLCと比較して、有意に奇形腫の内容物漏出を少なくできる確実な新手順と判断された。

P-18-3 当院における帝王切開癒痕症候群外来設立に向けての取り組み

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【目的】帝王切開癒痕症候群は、帝王切開術後の創部陥凹に月経血が貯留し過長月経や月経困難症および続発性不妊症の原因となる疾患として知られており、排卵日周囲に観察される茶褐色の帯下が特徴である。2022年4月から本疾患に対する腹腔鏡下子宮癒痕部修復術が保険収載され、症例数の増加が見込まれる。病診連携・適切な診断と治療法の選択、術前評価、患者への情報提供のために「帝王切開癒痕症候群外来」を設立した。【方法】症例を紹介していただける連携の構築や患者説明パンフレットの作成やホームページ上での情報提供を行った。また、診療内容の統一化のために来院された患者への問診項目・検査項目について統一した。検査は月経周期に合わせた専門検査(子宮鏡検査・超音波検査・慢性子宮内膜炎の検査など)のための外来枠を設定し、より綿密な治療前評価を可能にした。院内で診断基準・手術施行基準を統一させるためにカンファレンスを行った。【成績】現在までに本疾患に対する手術を25例(子宮鏡手術13例、腹腔鏡下手術12例)施行した。【結論】本疾患は不妊治療と並行して検査・治療を行う症例が多く、患者への情報提供や迅速な検査・診断によりスムーズに治療に移行できると考えられた。今後、更なる症例の集積を通じて改善を図っていきたいと考えている。

P-18-4 当科における良性疾患に対するロボット支援下子宮全摘出術と腹腔鏡下子宮全摘出術の比較検討

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【目的】2018年4月より婦人科良性疾患に対するロボット支援下子宮全摘出術(Robot assisted hysterectomy: RH)が保険収載され、全国的に症例数が増加しつつある。当科では2020年4月よりRHを導入し、2023年9月までに85例を経験した。一方で腹腔鏡下子宮全摘出術(TLH)に対するRHの位置付けおよび症例の選択に関しては議論の余地がある。【方法】2020年4月から2023年9月までに行った婦人科良性疾患および前癌病変(CIN, AEH)に対するTLH 309例, RH 85例を対象とし、患者背景(年齢・BMI)および手術時間、出血量、摘出標本重量を後方視的に比較検討した。検定はMann-Whitney-U検定を用い、P値<0.05の場合に統計学的に有意と判定した。また、合併症についても調査した。【成績】RH群, TLH群を比較し手術時間はRH群で有意に長く、出血量はRH群で有意に少なかった。BMI25以上の肥満症例および、摘出子宮重量300g以上の症例においては、RH, TLH両群の手術時間に有意差を認めなかったが、出血量はRH群で有意に少なかった。合併症として、TLH群では6例に術中出血量500ml以上の症例を認め、また1例に膀胱損傷を認めた。RH群ではポートサイトヘルニアを1例認めた。【結論】ロボット支援下手術においては、腹腔鏡下手術と比較し出血量が少ない。一般市中病院において、子宮の大きい症例や肥満症例においてはロボット支援下手術を選択することで安全性を確保できる可能性がある。

P-18-5 帝王切開癒痕症候群に対して、子宮鏡観察下に腹腔内から穿刺した針先をメルクマールにして癒痕部切除を行った癒痕修復術12例の検討

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【目的】帝王切開癒痕症候群は、帝王切開術後に子宮創部筋層に陥没性癒痕を生じ、過長月経や不正性器出血、不妊症の原因となる症候群とされている。腹腔内から癒痕部修復術を行う際、その切除範囲の同定が困難である場合もある。その点に注目し、当院での手術手技とその治療成績を検討した。【方法】2015年2月から2023年12月の期間に手術を行った12例を対象とした。手術時平均年齢は36.3±3.8歳、全例不妊症例であり、9例に過長月経を認めた。子宮前屈は4例、後屈は8例であった。手術方法は、7例で子宮鏡併用開腹術、5例で子宮鏡併用腹腔鏡下手術であった。【成績】腹腔鏡(あるいは開腹術)と子宮鏡を同時に行った。子宮に針糸をかけて頭側に牽引し、癒痕部の空間が広がるようにした。癒痕部を同定するため、腹腔内から針を穿刺し、子宮鏡で針先の位置を見て、癒痕部の切開端を確認した。癒痕部切除の際には、断端の筋層が十分厚くなるように切除した。両側断端の縫合では、吸収糸0号を両側の筋層の全層が合うように連針して、4か所単結紮縫合し、さらに減張縫合を2か所かけた。術後、全例で子宮癒痕部所見は消失した。過長月経は、9例中7例で改善した。子宮後屈8例は、全例前屈になったが、その後3例は後に後屈にもどっていた。術後、7例に妊娠が成立した。妊娠の契機は、自然妊娠2例、ART5例であった。妊娠後は、3例は満期産、3例は経過観察中、1例は流産であった。【結論】子宮鏡観察下に腹腔内から針を穿刺して子宮鏡観察下に癒痕部切除部位を同定する方法は有効な手技であると思われた。本術式は、過長月経や不正性器出血の症状改善、また、妊孕性改善にも寄与すると思われた。

P-18-6 当院における広汎性子宮頸部摘出術後の体外受精成績に因する因子の検討

慶應義塾大

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【目的】広汎性子宮頸部摘出術 (radical trachelectomy: RT) は早期子宮頸がんに対する妊孕性温存手術であり, RT 後の妊娠は現実的な選択肢となっている。開腹 RT 後の妊娠率は他のアプローチに比べて有意に低いことが報告されているものの, その原因は明らかでない。そこで本研究は RT 後の体外受精成績を評価し, 臨床的特徴の解明を目的とした。【方法】早期子宮頸がんに対して当院で RT を行い, その後当院にて体外受精を施行した 41 人の研究参加者を対象に, 初回採卵時年齢, BMI, 血清 AMH 値, 頸管狭窄, 頸管開口術, 胚移植 (ET) 決定時の子宮内膜厚, 臨床的妊娠率・出生率に関するデータを収集し, 妊娠成立の有無による差を統計解析した。【成績】出生群 (24 人) の初回採卵時年齢は非出生群 (17 人) と比較して有意に若かった (34.8 歳 vs 38.6 歳, $p=0.002$)。BMI は両群間で同等だったが, 血清 AMH 値はわずかに有意差を認めた (3.7ng/ml vs 1.7ng/ml, $p=0.045$)。頸管狭窄は出生群では 8 人 (33.3%), 非出生群では 11 人 (64.7%) でありわずかに有意差を認めた ($p=0.047$)。頸管開口術は出生群で 5 人, 非出生群で 7 人に行われた ($p=0.157$)。出生群では ET 決定時の子宮内膜厚が有意に厚かった (10.2 mm vs 9.0mm, $p=0.006$)。【結論】RT 後の体外受精は, 初回採卵時年齢が若く ET 決定時の子宮内膜厚が厚いほど治療成績が良好だった。出生に至るためには適切なタイミングで不妊治療のステップアップをはかるとともに, 子宮内膜厚が重要である可能性が示唆された。

P-18-7 双頸双角子宮の帝王切開癒痕症候群に対して腹腔鏡下子宮癒痕部修復術を行った一例

医科歯科大

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帝王切開子宮癒痕症 (CSDi) の子宮癒痕部修復術では, 非薄化した部位を確実に切除し縫合することが重要である。双頸双角子宮は正常な子宮と構造が異なるため, 癒痕部修復の際には特別な注意を要する。自験例をもとに双頸双角子宮に対する腹腔鏡下子宮癒痕部修復術の注意点と工夫を報告する。症例は, 挙児を希望する双頸双角子宮の 35 歳女性。前医で子宮卵管造影検査 (HSG) での帝王切開癒痕部から腹腔内への造影剤流出を指摘され, 当院を紹介受診した。MRI で子宮前壁筋層の非薄化を認め, 左右の頸管が欠損部で交通していた。手術の際には, 左右の子宮内にマニピレーターないし HSG チューブを留置し, 頸管の走行を容易に視認できるようにした。ポートより術野へ挿入可能な腹腔鏡下手術用の超音波プローブを用いて, これらが適切に留置されていること, また頸部の構造を術中に確認しつつ癒痕部を切除した。子宮頸管の閉塞予防と縫合手技の容易化のために頸管をあらかじめ十分に拡張し, 頸管拡張鉗子で内腔を都度確認しながら縫合した。縫合後には子宮鏡で左右子宮頸管の開通と前壁の欠損部がないことを確認した。以上の操作により, 腹腔鏡下に双頸双角子宮の帝王切開癒痕部を修復し得た。双頸双角子宮の CSDi に対して腹腔鏡下に癒痕部を修復する際は, その解剖学的特異性を考慮して事前に十分な準備をすること, 縫合後に左右の子宮頸管がともに開通していることを十分に確認することが重要である。

P-18-8 凍結胚移植後の早期流産による子宮内遺残物 (RPOC) に対し子宮鏡下切除術を行った 1 例新生会総合病院高の原中央病院¹, 中部産婦人科医院²曾山浩明¹, 鈴木聡一郎¹, 奥口聡美¹, 吉田剛祥¹, 中部 健², 谷口文章¹

【目的】凍結胚移植は retained products of conception (RPOC) のリスク因子と近年報告されている。今回凍結胚移植後に流産となり, 子宮内容除去術を施行したが RPOC となり, その後子宮鏡手術により安全に切除をできた症例を経験したので報告する。【症例】35 歳, 未経産。凍結胚移植で妊娠成立するも妊娠 6 週で流産となった。子宮内容除去術目的で前医受診し子宮内容除去術を実施した。病理検査では異常は無く, 術後の異常出血も無かった。その後 3 か月経過するも月経来せず, 経陰超音波検査で子宮腔内に 2.5cm 大の腫瘍性病変を認め当院へ紹介となった。当院初診時の β -hCG は 3.5 mIU/mL であり, 造影 MRI では活動性の血流は認めなかった。RPOC と診断し, 子宮鏡下切除術を実施した。子宮腔内には暗赤色の腫瘍性病変を認めたが, 全て鈍的に剝離でき出血もごく少量だった。病理検査では変性した絨毛組織を認めた。術後 4 日目に月経も開始し, 術後 1 か月目には β -hCG の陰性化も確認した。【結論】RPOC は大量出血を来す可能性があり, 慎重な管理を要し子宮動脈塞栓術のようなより侵襲的な治療が必要なこともある。しかしながら術前に血流の評価が出来れば, 子宮鏡を用いて必要最小限の切除のみで安全に対処できると考えられた。血流が無ければ保存的治療も可能だが, 早期の妊娠を望む不妊治療患者には子宮鏡下の切除も選択肢の 1 つとなり得る。

P-18-9 異なる症状を呈する帝王切開癒痕部症候群に対し、子宮鏡併用腹腔鏡下子宮癒痕部修復術を実施した2症例

JCHO 大阪病院

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【緒言】帝王切開癒痕部症候群は多彩な症状を認める。今回、過長月経・月経困難症、及び非排卵期子宮頸管粘液の分泌過多、との異なる症状を呈した帝王切開癒痕部症候群2症例を経験したので、報告する。【症例1】45歳、G3P3、帝王切開の既往3回。過長月経、月経困難症、帝王切開術後の血液の貯留にて当科を紹介受診。超音波検査、骨盤単純MRI検査を実施し、子宮体下部筋層の厚みが1mmと菲薄化を認めた。子宮鏡検査にて、子宮体下部前壁の憩室様腔の内面から出血の流出を認める小孔を認め、帝王切開癒痕部症候群と診断した。腹腔鏡・子宮鏡併用にて、帝王切開癒痕部修復術、子宮円靭帯短縮術を実施した。術後、過長月経と月経困難症は消失した。【症例2】39歳、体外受精・凍結融解胚盤胞移植にて妊娠成立。X年6月に、骨盤位妊娠の適応にて当院で妊娠38週2日に選択的帝王切開術を実施。X+2年6月、第2子希望あり不妊治療を開始。凍結融解胚移植時<卵胞期>の頸管粘液が多量で胚移植が困難と指摘され、当科を紹介受診。超音波検査、骨盤単純MRI検査を実施し、子宮体下部筋層に楔型欠損部を認めるも子宮筋層の厚みは6mm程度に保たれていた。子宮鏡検査にて、子宮体下部前壁の憩室様腔の内面に多数の毛細血管を認め、帝王切開癒痕部症候群と診断した。腹腔鏡・子宮鏡併用にて、帝王切開癒痕部修復術を実施した。術後、多量の非排卵期子宮頸管粘液の分泌は、消失した。【結語】帝王切開癒痕部症候群はその病態や管理方針などまだ不明な点が多く、治療法の選択に苦慮することも多い。文献的考察を加えて報告する。

P-18-10 子宮腺筋症合併不妊・不育症患者に対して、腺筋症核出術を行い生児を得た1例

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【緒言】子宮腺筋症（以下、腺筋症）合併不妊・不育症患者に対して腺筋症核出術を行い、生児を得た1例を経験したので報告する。【症例】39歳G0P0、原発性不妊、腺筋症合併のため当院を紹介受診した。MRI検査では前壁直径85mm、子宮内膜から連続する腺筋症を認めた。早期に体外受精の方針とし、6個の良好胚盤胞を凍結保存した。融解胚移植を施行したが1回目妊娠せず、2回目妊娠6週で流産、3回目妊娠せず、4回目（2個胚移植）妊娠7週で流産した。腺筋症が不育症原因と考えられ、病巣の増大も認めたことから腺筋症核出術を施行、術後4か月に5回目の胚移植で妊娠成立した。妊娠28週1日で性器出血、子宮収縮を認め入院管理とし、リトドリン塩酸塩の投与を開始した。MRI検査ではわずかに病巣が残存する子宮前壁に胎盤が付着しており、一部で胎盤が漿膜側に向かって楔状に突出する部分を認め、この周囲には漿膜側から血管が侵入している所見を認めた。陥入胎盤以上の術前診断で、分娩時は尿管ステント留置、帝王切開、子宮動脈塞栓術、子宮摘出を行う方針とした。35週4日予定術式を施行、手術時間4時間17分、出血量1130g、児は女児、2089gであった。病理所見では、絨毛組織と子宮筋層が接する多くの部分で脱落膜を欠き、絨毛が筋層内に入り込む部分を認めたことから陥入胎盤と診断した。母児ともに大きな合併症なく退院された。【結語】腺筋症合併不妊・不育症患者に対しての治療法は統一されていないが、腺筋症核出術が有用な治療となる可能性がある。術後に妊娠した場合は、癒着胎盤に注意して周産期管理を行う必要がある。

P-18-11 Cesarean scar disorder (CSDi) に対する手術療法についての検討

長崎大

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【緒言】本邦における帝王切開分娩の割合は年々増加傾向にあり、帝王切開術後に不正性器出血、月経困難症、不妊症などの症状を呈するCesarean scar disorder (CSDi)の増加が問題になっている。2022年4月に腹腔鏡下子宮癒痕部修復術が保険取載され、今後手術症例数の増加が見込まれる。これまで当科で行ってきた手術療法について報告する。【対象および方法】当科ではこれまで、4例のCesarean scar disorder (CSDi)に対する手術療法を行った。既往帝王切開回数は、1例は4回、3例は1回であった。3例は今後の挙児希望を有していた。MRI検査にて術前の癒痕部および残存子宮筋層の評価を行った。腹腔鏡下の観察では、いずれの症例も子宮漿膜側からの癒痕部同定は困難であった。子宮鏡下観察では子宮前壁の頸部直上にドーム状に拡張したスペースがあり、褐色の液体貯留が認められ、癒痕部と考えられた。癒痕部には樹枝状血管の発達も認められ、子宮内膜ポリープが多発していた。子宮鏡と腹腔鏡を併用し、子宮鏡の光源が透見できる範囲を確認しながら癒痕部の境界を同定し、膀胱の剝離を行った。癒痕部を切除後、吸引糸で縫合して筋層を修復した。【結果】全例で手術後に症状の改善が認められ、1例が自然妊娠した。【結語】腹腔鏡下子宮癒痕部修復術は、症状の再発予防及び妊娠性の改善に配慮した手技の工夫が必要である。これまでの経験より、本術式の要点は以下の3点と考える。1) 腹腔鏡下の切除の前に、子宮鏡下に癒痕部を可及的に切除しておく。2) 子宮に頭側方向のテンションをかけながら、膀胱を十分に剝離する。3) 腹腔鏡と子宮鏡を同時に用いて、子宮鏡の光源を指標として、癒痕部の範囲を確認する。

P-19-1 一卵性二絨毛膜二羊膜双胎における臨床的検討

杏林大

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【目的】二絨毛膜二羊膜双胎(以下DD)は、双胎妊娠のなかでは比較的予後良好と考えられているが、一卵性DDの予後を検討した報告はないため、その臨床的予後を明らかにすることを目的とした。【方法】母体背景因子をそろえるため、妊娠方法は生殖補助医療(ART)の症例に限定し、2018年1月から2022年12月に当施設で分娩したDD54組108児を対象とした。ホルモン補充周期の単一胚移植で妊娠成立した6組を一卵性DDと想定しA群とし、自然周期の単一胚移植と二個胚移植で妊娠成立した48組をB群とした。検討項目は臍帯付着部位置異常、早産、出生体重、胎盤総重量、母体合併症(HDP・GDM)の発症とし、A群とB群を比較検討した(検討1)。さらに一卵性DDと二卵性DDの臨床的予後を比較するため、児の性別が異なる22組を確実な二卵性DDと想定しC群とし、検討1と同項目についてA群とC群を比較検討した(検討2)。統計学的検討にはカイ2乗検定・Fisher検定・マンホイットニーのU検定を用いた。【成績】結果1:A群はB群間では臍帯付着部異常(OR 8.1; 95% CI 2.25-29.1), HDP(OR 7.0; 95% CI 1.94-25.2)の発症率が有意に高かった。結果2:A群はC群と比較し臍帯付着部異常(OR 6.3; 95% CI 1.59-25.0)の発症率が有意に高かった。その他の項目では有意差を認めなかった。【結論】二絨毛膜二羊膜双胎は、双胎妊娠のなかでは比較的予後良好と考えられているが、今回の検討により一卵性DDは臍帯付着部異常を念頭においた管理が必要であり、さらに検討1よりHDPのリスクも考慮しなければいけないことが示唆された。これらより、DD双胎の中でも一卵性DDはより一層厳重な管理が求められると考えられた。

P-19-2 胎児治療施行例および未施行例の一絨毛膜二羊膜双胎の羊水中NT-proBNPと血中NT-proBNPの相関について

東邦大

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【目的】胎児治療施行例および未施行例の一絨毛膜二羊膜双胎(MD)双胎において、心不全バイオマーカーであるNT-proBNPの羊水中濃度が、どの程度血中濃度を反映するのかを検討した。【方法】2015年から2021年に当院で管理したMD双胎を対象とした。分娩時の羊水と臍帯血試料を用いてNT-proBNPを測定した。本研究は当院倫理委員会の承認の下、患者より書面による同意を得て行った。【成績】胎児治療後のMD双胎において、羊水と臍帯血が同時に測定できたものは44例(受血児・大児23例, 供血児・小児21例)であった。羊水NT-proBNPは臍帯血濃度と有意な正の相関を示した($r=0.654, p<0.001$)。また、羊水総蛋白濃度(TP)を考慮した羊水NT-proBNP/TPも臍帯血NT-proBNPと有意な正の相関を示した($r=0.601, p<0.001$)。臍帯血NT-proBNPに対する重回帰分析では、羊水NT-proBNP/TPが有意な項目として抽出された。胎児治療未施行のMD双胎は84例であり、羊水NT-proBNP, NT-prpBNP/TPは臍帯血濃度と有意な正の相関を示し($p<0.001$)、臍帯血NT-prpBNPに対する重回帰分析では、分娩週数, 出生時体重差, 羊水NT-prpBNP/TPが有意な項目として抽出された。【結論】MD双胎では、胎児治療の有無, つまり吻合血管の有無に関わらず羊水NT-proBNP, NT-proBNP/TPは臍帯血濃度を反映した。吻合血管を有する場合は児の体重差も羊水NT-proBNPと関連しており、吻合血管に起因する病態の考察に有用となる可能性がある。

P-19-3 妊娠16週から18週における胎児鏡下胎盤吻合血管レーザー凝固術後の経過と予後

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【目的】一絨毛膜性双胎妊娠の管理が向上し、胎児鏡下胎盤吻合血管レーザー凝固術(FLP)の適応となる双胎間輸血症候群(TTTS)や一児発育不全を伴う一絨毛膜性双胎(sIUGR)が早期に紹介される機会が増加した。一方、早い週数でのFLPにおいては羊膜剝離(CMS)の合併が多いことが知られており、CMSに伴う破水、早産、新生児生存率の低下、羊膜索症候群などの合併が報告されている。当院における妊娠16週から18週で施行されたFLP症例の経過と予後について検討した。【方法】2015年10月から2023年9月の間に当院でFLPを行った妊娠19週未満に施行した症例を対象とし、術前のQuintero stage, 経産回数, 頸管長, CMSの有無, 前期破水, 分娩週数, 生産数, 羊膜索症候群の有無について診療録より後方視的に検討した。【成績】対象期間に行われたFLP311例中、妊娠19週未満の症例が96例(31%)であった。術前のQuintero stageはStage1 13例, Stage2 20例, Stage3 46例, Stage4 3例, sIUGR 14例で、経産回数の中央値は0回(range 0-2)、術前の頸管長の中央値は40mm(range 25-59mm)であった。術後のCMSは35例(36%)に認めた。術後2週間以内の破水が9例(9%)あり、このうち2例が流産に至った。分娩転帰の判明している93例の分娩週数の中央値は34.2週(range 18-40)で、28週未満の早産は8例(8.6%)であった。出生時両児生存が57例(62%)、一児生存が31例(33%)、二児死亡が5例(5%)で、少なくとも一児生存の割合は95%であった。CMSに伴う羊膜索症候群を生児145人中6人(4%)で認めた。【結論】妊娠19週未満のFLPにおいてはCMSの割合が多く、CMSに伴う羊膜索症候群の合併を認めた。分娩週数や生産率は過去の報告と差がみられなかった。

P-19-4 当施設における胎児鏡下胎盤吻合血管レーザー凝固術後の一絨毛膜二羊膜双胎の短期予後の検討

宮崎大

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【目的】胎児鏡下胎盤吻合血管レーザー凝固術 (fetoscopic laser photocoagulation : FLP) は、妊娠 26 週までの双胎間輸血症候群 (twin-twin transfusion syndrome : TTTS) の生存率と神経学的後遺症の予後を改善すると報告されている。今回、当施設での FLP 後の一絨毛膜二羊膜双胎 (monochorionic diamniotic twin : MD twin) の短期予後を検討した。【方法】2009 年 1 月から 2023 年 6 月までの期間に、当施設で周産期管理を行なった MD twin を対象とし、FLP を施行した症例の短期予後を検討した。なお、当院は FLP 導入施設ではないため、全例他院にて FLP を施行されている。【成績】検討期間中の MD twin 124 組中 9 組に FLP が施行された。適応は全て TTTS で、FLP 施行時の Quintero 分類は stage I 2 例、stage II 2 例、stage III 3 例、stage IV 2 例であった。FLP 施行週数の中央値は 21 週、分娩週数の中央値は 29 週であった。分娩時期は 8 例が早産となり、それぞれの分娩契機としては、前期破水 4 例、陣痛発来 3 例、Mirror 症候群による母体適応 1 例であった。また正期産での選択的帝王切開術を 1 例に行った。9 組の児 18 例の周産期予後は子宮内胎児死亡 (供血児) 1 例、新生児死亡 (受血児の胎児水腫) 1 例、乳児死亡 (供血児の肝不全) 1 例であった。生存児 15 例の退院前頭部 MRI 検査は脳室内出血後が 1 例、脳室周囲白質軟化症が 3 例あり、11 例には異常所見は認めなかった。【結論】FLP 施行後であっても、9 組中 5 組に死亡や頭部画像所見異常が認められる症例があり、その後の循環動態や神経学的異常に注意し、厳重な管理を要する。

P-19-5 当院の双胎妊娠における分娩様式の検討

愛仁会高槻病院

伊藤弘樹, 柴田貴司, 森本 始, 小島祥文, 宇田菜都, 加藤大樹, 中後 聡

【目的】双胎妊娠では、経陰分娩のリスクを懸念して帝王切開を希望する例が少ない。経陰分娩の成功に関わる因子を検討した。【方法】2012 年 4 月から 2022 年 3 月に当院で妊娠 32 週以降に分娩を行った双胎妊娠を対象とした。経陰分娩成功例と不成功例の間で、母体因子 (年齢, 身長, BMI, 初経産, 妊娠方法, 母体合併症, 陣痛誘発の有無) および胎児因子 (FGR, 胎位, 膜性, 両児の体重差) を比較し、後方視的に検討した。【成績】経陰分娩を試みた 133 例を解析対象とした。115 例 (86%) が両児ともに経陰分娩に至り、18 例 (14%) が帝王切開となった。分類回帰樹木法 (CART : Classification and Regression Trees) による解析で、経陰分娩の成功因子として経産婦 ($p < 0.01$), 29 歳以下の初産婦 ($p = 0.02$) が抽出された。【結論】経産婦, 29 歳以下の初産婦は双胎の経陰分娩の成功率と関連しており、分娩様式選択の有用な情報となり得る。

P-19-6 当院で管理した一絨毛膜一羊膜双胎妊娠 7 例の検討

市立札幌病院

川端公輔, 安藤里沙, 渡邊 碧, 今泉 翠, 橋本大樹, 山口正博, 箱山聖子, 早貸幸辰, 奥山和彦, 首藤聡子, 平山恵美

【目的】一絨毛膜一羊膜 (MM) 双胎は、臍帯相互巻絡による胎児死亡や双胎間輸血症候群 (TTTS) による胎児機能不全の危険はあるが、近年は十分な管理を行うことで周産期死亡率は 20% 前後と以前より改善しているとされる。当院では MM 双胎妊娠の分娩を 32 週以降と設定してきたが、母児の予後向上を目指し従来の管理内容と周産期転帰を検討し今後の課題を明らかにする。【方法】2013-2022 年までの 10 年間に当院で分娩管理を行った MM 双胎 7 例 (21 週未満の両児死亡 3 例を除く) の患者背景, 分娩週数, 周産期有害事象などについて後方視的に検討した。【成績】IVF が 1 例でほかは自然妊娠。胎児死亡は 2 例で 24 週の紹介初診時に両児死亡が 1 例, もう 1 例は 22 週 1 児死亡かつ生児も繰り返す高度徐脈や羊水過少などの胎児機能不全があり予後は極めて厳しいことが想定され十分な IC のうえで外来管理とし 28 週胎児死亡となった。いずれも強い臍帯相互巻絡を認めた。生児を獲得した 5 例に胎児心拍数異常はなく、分娩は全て選択帝王切開で分娩の中央値は 34 (32-34) 週であった。臍帯相互巻絡を 85.7% (6/7) に認めた。出生体重の中央値は 1690g で全例 NICU を生存退院した。出生まで血流異常を含めて TTTS 所見はなかったが新生児診察で受血側と判断される児に下大静脈の虚脱と腎動脈血流途絶を認め、血液量低下のため循環作動を要した児がいた。妊娠高血圧症候群や分娩後異常出血を来したものはなかった。【結論】臍帯相互巻絡による胎児死亡はあるものの周産期有害事象は既報と同程度に低かった。臍帯相互巻絡があっても胎児機能不全や胎児死亡を来さなければ 32 週以降の分娩は妥当で、現在の超音波と胎児心拍数陣痛図を中心とした管理は有効である。

P-19-7 子宮頸管長短縮を伴う症例に対する胎児鏡下レーザー手術時の子宮頸管縫縮術の有用性

東邦大医療センター大森病院

神谷美緒, 鷹野真由実, 立原茉優, 小瀧 曜, 島袋麻希子, 長崎澄人, 中田雅彦

【目的】双胎間輸血症候群(TTTS)は胎児鏡下レーザー手術(FLP)により予後の改善が見込まれるが、手術の侵襲性により、術後に子宮収縮や流産・早産といった合併症が問題となる。子宮頸管長短縮を認める症例では術後に流産・早産となるリスクが高いため手術を差し控える場合もある。当院ではそのような症例に対しFLP施行時に子宮頸管縫縮術(cervical cerclage:CC)を施行しており、合併症や周産期予後の検討を行ったので報告する。【方法】2015年から2023年にTTTSに対してFLPを施行した患者を対象とし、術前に子宮頸管長短縮を認め縫縮術を施行した患者の周産期情報を後方視的に検討した。CCはFLP施行時に脊髄くも膜下麻酔下にマクドナルド法にて二重に縫縮した。本研究は当院倫理委員会の承認の元、患者本人より書面による同意を得た上で行った。【成績】対象数は197例でCCは8例(4.1%)に施行した。FLP施行週数の中央値は24.1週(17.1-25.9週)だった。術前の子宮頸管長の中央値は13mm(0-18mm)だった。2例に術前の破水も合併していた。全例(8例,100%)でCCは施行可能であり、CC後にFLPの完遂が可能だった。術中、術直後に重篤な合併症を認めなかった。分娩週数の中央値は30.0週(26.3-34.3週)で、治療から分娩までの期間の中央値は51日(12-75日)だった。一児の胎児死亡を認めたが(6%)全例で少なくとも一児の生存が得られた(100%)。【結論】TTTSにおいて、頸管長短縮症例においてもCCを施行することにより、FLPは施行可能だった。妊娠期間を約50日延長でき、児の生存率も悪化させなかったことから、有効な治療戦略の一つと考えられた。

P-19-8 一絨毛膜一羊膜双胎に類した胎盤を有した一絨毛膜二羊膜双胎の2例

四国こどもとおとなの医療センター

長尾亜紀, 森根幹生, 杉本達朗, 前田崇彰, 米谷直人, 檜尾健二, 前田和寿

【緒言】MD双胎では1つの絨毛膜を共有するため、大半の症例で児間の血管吻合を有する。今回、MM双胎に類した胎盤を有したMD双胎の2例を報告する。【症例1】29歳、1妊0産。妊娠21週に両児の体重差(discordant rate:33.7%)、大児に羊水過多、小児の羊水量は正常であるも貧血所見(MCA-PSV 45.31cm/sec(1.69MoM))と臍帯動脈の周期的な途絶・逆流を認め、selective IUGR type3と診断した。妊娠27週より大児に高拍出性心不全を認めた。妊娠31週には両児の羊水量とMCA-PSVは正常化し、小児の臍帯動脈波形も正常化した。大児の左心機能の増悪のため、帝王切開術を施行した。胎盤は臍帯付着部が非常に近接し、臍帯付着間に太い動脈-動脈吻合を認めた。また、胎盤小葉を共有するように数本の動脈-静脈吻合を認めた。【症例2】33歳、1妊0産。妊娠22週にMD双胎一児死亡を確認した。死児には皮下浮腫と少量胸水貯留を認めた。生存児には腹水貯留と貧血所見(MCA PSV 56.15cm/sec(2.0MOM))を認め、feto-fetal hemorrhageが疑われた。妊娠24週に生存児の腹水は消失した。その後、妊娠30週に胎胞突出、骨盤位のため帝王切開術を施行した。胎盤は全体が生存児の血管で栄養されており、死亡児の占有部は同定できなかった。臍帯付着部は非常に近接し、臍帯付着間に太い動脈-動脈吻合を認めた。【結語】MD双胎にも関わらず、臍帯付着間の太い動脈-動脈吻合や近接する臍帯付着部を有する症例においては、血行力学的変化に関連した様々な合併症が生じる可能性があると考えられた。

P-19-9 減胎手術に関する倫理的課題の解決へ向けて～当院における減胎手術の実例を踏まえた、臨床研究の必要性とその展望～

大阪大

涌井菜央, 三宅達也, 川西陽子, 岡田愛子, 中村幸司, 平松宏祐, 河野まひる, 味村和哉, 木村敏啓, 遠藤誠之, 木村 正

多胎妊娠は様々な母児に関する合併症のリスク因子である。当院ではループス腎炎を基礎疾患に持つ女性が品胎妊娠となり、当該症例に対して減胎手術を行ったため報告する。症例は29歳、2妊胎0経産の女性である。SLE及びループス腎炎IV型の治療開始時に妊孕性温存目的で当科を受診され、受精卵凍結を行った。原疾患寛解後に自然妊娠が成立し、妊娠6週時点で品胎(2絨毛膜性3胎)の診断に至った。原疾患を考慮すると品胎妊娠の継続は母体の生命を脅かす可能性があるが、本人は妊娠継続を希望しており、院内の多職種で構成された診療・看護倫理委員会での審議を経て、当該女性に①品胎妊娠の継続②人工妊娠中絶③減胎術の3つの選択肢があることを提示した。患者は減胎術を希望され、膜性、物理的な児の位置及び原疾患の重篤性を踏まえ、妊娠11週に1絨毛膜内に存在する2胎の心腔内に塩化カリウム溶液を注入し、減胎手術が完遂された。その後は単胎として妊娠を継続し、妊娠38週に自然陣発、経陰分娩に至った。減胎手術のあり方については厚生科学審議会でも議論がなされ実際に一部の医療現場では実施されている一方で、母体保護法や墮胎罪との関連性が曖昧であることや胎児の選別等の観点から、減胎手術を議論すること自体がタブー視され、手技や予後の評価は全くなされていない。こうした状況のなかで医学的に減胎術が必要な女性は罪悪感や社会的孤立を感じながら短期間に非常に苦痛な意思決定を迫られ、適切な支援体制が得られていないのが現状である。当院では減胎手術の安全性及び患者の心理的負担を評価するため、臨床心理士も含めたチームを構成し、倫理審査委員会へ臨床研究計画を申請している。

P-20-1 胎児心拍数記録装置アイリス®を用いた胎児心電図によるQT時間の計測

国立循環器病研究センター

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【目的】胎児不整脈の診断に、胎児心電図記録装置アイリス®を用いて診断する方法が試みられているが、生データは波形の各セグメントは困難である。そこで、生データの多数の波形を加算平均できる新しいアルゴリズムが開発された。しかし、それにより各セグメントを認識できるか、QT時間を計測できるかはわかっていない。そこで、新アルゴリズムを用いて、胎児QT時間を計測できるかを明らかにする。【方法】2019年1月から2022年4月に当院で管理したQT延長症候群(LQT)合併妊婦について、アイリス®で記録された胎児心電図波形を対象とした後方視的観察研究である。母体LQTの胎児心電図を用いて加算平均した心電図のうち、各セグメントが認識できた割合を出した。次に、各セグメントが認識できた波形について、胎児心電図QTc時間を算出し、新生児心電図(日齢1)のQTc時間との一致性についてBland-Altman分析を用いて確認した。【成績】解析対象は14波形だった。各セグメントが認識できたのは14波形中6波形(43%)であった。胎児心電図と新生児心電図のQTc時間の計測に誤差はなく、ほぼ一致した。(p=0.5625)。【結論】新アルゴリズムにより、約半数で各セグメントが認識でき、QT時間を計測することができた。また、胎児心電図と新生児心電図のQTc時間はほぼ一致していた。しかし、症例数が少ないため、症例の更なる集積により新アルゴリズムの妥当性を検証する必要がある。

P-20-2 母体腹壁誘導胎児心電図アイリスモニタ®による胎児の上室性期外収縮と心室性期外収縮の判別

国立循環器病研究センター

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【目的】胎児不整脈の診断に、母体腹壁誘導胎児心電図(アイリス®)を用いる試みがある。加算平均することにより生データのノイズの低減が見込める。従来のアルゴリズムでは特定の波形を選択し加算平均することができたが、選択する波形の数に限りがあり、臨床応用は困難であった。最近、RR間隔を指定することで、指定する波形を無限に選択し加算平均できる新たなアルゴリズムが開発された。そこで、この新アルゴリズムを用いて、胎児上室性期外収縮(PAC)と心室性期外収縮(PVC)が判別できるかを明らかにする。【方法】2019年1月~2023年4月に当院で、PACもしくはPVCと診断された胎児の心電図波形を対象とし、後方視的に検討した。まず、P波が認識可能か検証するため、PACと診断された胎児の心電図波形を新アルゴリズムと生データに分け、10人の産科・循環器専門医によりP波の視認率を算出した。次に、PACとPVCを判別可能か検証するため、PACもしくはPVCと診断された胎児の心電図波形を新アルゴリズムと生データに分け、同様の方法で正診率を算出し比較した。【成績】解析対象は18症例、31区画であった。PACと診断された胎児の心電図では、新アルゴリズム(n=23)で23%、生データ(n=23)で8%とP波の視認率に有意な差を認めた(P=0.005)。PACもしくはPVCと診断された胎児の心電図では、新アルゴリズム(n=8)と生データ(n=8)でPACの正診率は63% vs. 46%(P=0.18)、PVCの正診率は28% vs. 47%で有意差はなかった(P=0.07)。【結論】新アルゴリズムはアイリス®での胎児不整脈の判別を向上させうる。臨床応用に向けて、RR間隔を指定する方法の工夫とアルゴリズムの改良が必要である。

P-20-3 当院で経験したTurner症候群の検討

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【目的】Turner症候群はX染色体モノソミーを代表とする性染色体異常で、低身長や性腺機能不全などの特徴を持つ。胎児期に超音波検査でNT肥厚やcystic hygromaなどを指摘されたことから診断に至る症例もあるが、胎児期の正確な予後予測は難しいとされている。今回我々は、胎児期に診断されたTurner症候群の特徴を明らかにするため、後方視的検討を行った。【方法】当院にて2017年5月~2023年5月までの6年間で診断に至ったTurner症候群の14例について検討した。【成績】妊婦の平均年齢は31.7歳、初産婦9例(64.3%)、自然妊娠11例(78.6%)であった。当院初診時の超音波検査においてNT肥厚を2例(14.3%)、cystic hygromaを12例(85.7%)に認めた。胸水貯留が11例(78.6%)、先天性心疾患は3例(21.3%)に見られた。経過観察中にIUFDに至った症例が6例(42.9%)、中期中絶を選択した症例が6例(42.9%)、妊娠継続を希望して生児を得た症例は2例(14.2%)であった。全症例で児の染色体核型が判明しており、45,Xが11例(78.6%)、45,X/46,XXのモザイクが3例(21.3%)であった。【結論】生児を得た症例ではNT肥厚やcystic hygromaの増悪が見られなかった。今回の検討では、胸水貯留例が多く見られたことから、cystic hygromaかつ胸水貯留はTurner症候群の特徴的所見と考えられた。出生後のTurner症候群の核型は、45,Xとモザイクが半々程度とされているが、今回の症例では45,Xが多く、胎児期に診断され、浮腫が増悪していく症例が多かった可能性がある。また、経過観察中にIUFDとなる症例も多く、出生前検査の時期と種類については、ご夫婦とよく話し合うことが重要である。

P-20-4 当院で周産期管理を行った胎児先天性右横隔膜ヘルニアの9例

兵庫県立こども病院

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【目的】先天性横隔膜ヘルニア (CDH) は近年の周産期管理の進歩により予後が向上した。しかし、先天性右 CDH は欠損孔が広く、肝臓の圧迫による肺低形成の程度が強いため重症になるとされているが、軽症例の報告もあり予後も様々である。今回当院で経験した先天性右 CDH 9 例について、実際の臨床経過や予後について検討した。【方法】2008 年から 2023 年の間に当院で周産期管理を行った先天性右 CDH 9 例について LHR, o/eLHR, 臨床経過, 児の予後等について後方視的に検討した。【成績】先天性右 CDH の診断妊娠週数は中央値 28 週 2 日 (24 週 2 日-31 週 4 日), LHR 中央値 1.51 (範囲 0.59-2.70), o/eLHR 中央値 47.94 (範囲 25.0-92.13) であった。経過中 4 例に羊水過多を認め、分娩週数の中央値は 37 週 3 日 (31 週 3 日-39 週 0 日) であり、分娩方法は帝王切開 7 例, 経陰分娩 2 例であった。9 症例すべてに胸腔内への肝脱出を認めたが、胃の脱出を認めた症例はなかった。合併奇形のない先天性右 CDH 単独症例は 6 例であった。出生後の経過として、2 例は高度な肺低形成により早期新生児死亡となった。1 例は横隔膜弛緩症の診断となった。治療として新生児遷延性肺高血圧症 (PPHN) に対し NO 療法施行した症例が 6 例, 体外式膜型人工肺 (ECMO) 導入例はなかった。手術介入した症例は 5 例だった。生後の入院期間の中央値は 101 日 (範囲 1-404 日) だった。現時点での自宅退院は 4 例, うち 1 例は在宅酸素療法を要した。【結論】検討した 9 例は、胎児診断で軽症と診断した症例が多く、自宅退院し外来を通院している症例もあり一概に予後不良とはいえない結果であった。ただし、先天性右 CDH は症例数が少なく、今後も長期予後を含め検討が必要であると考えられる。

P-20-5 非認証医療機関での NIPT を受けた結果、陽性とされた妊婦について当院で行った確定検査結果

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【目的】非認証施設における NIPT 実施の問題点を探る【方法】2019 年 1 月から 2023 年 9 月までの間に、非認証医療機関で受けた NIPT の結果、陽性と判定され、当院に相談に来られた 23 例について、NIPT の結果と、当院で行った確定検査の結果を比較した。また、妊娠の転帰についても調査した。【成績】23 例の陽性結果の内訳は、21 トリソミーが 7 例, 18 トリソミー 1 例, 13 トリソミー 1 例, この他の常染色体トリソミー 6 例 (3 番, 5 番, 15 番, 22 番がそれぞれ 1 例, 8 番が 2 例), X モノソミー 6 例, XXY 2 例であった。23 例中、超音波所見が明らかな 6 例は絨毛採取で、残り 17 例は羊水穿刺による染色体検査を行った。このうち、21 トリソミー陽性の 7 例および 18 トリソミー例では全て染色体検査で診断が確定されたが、13 トリソミー, 15 トリソミー, 5 トリソミー陽性例と 8 トリソミー陽性例のうちの 1 例は偽陽性であった。また、8 トリソミー陽性例の 1 例と 22 トリソミー陽性例では FISH 法, G 分染法共にモザイクが認められたが、3 トリソミー陽性例では FISH 法ではモザイクが見られたものの、G 分染法では調べたすべての細胞が正常核型であった。15 トリソミー陽性例では UPD15 についても調べたが、UPD は認められなかった。X モノソミー陽性例では、4 例がさまざまな種類のモザイクで、1 例は 46,XX, 残り 1 例は調べた 100 細胞すべてが 47,XXX であった。XXY の 2 例はいずれも羊水穿刺で 47,XXY であった。【結論】21, 18, 13 以外の常染色体トリソミー陽性例でも、X, Y 染色体の異数性陽性例でも、胎児にモザイクが認められることが多く、その説明および妊娠管理・周産期管理に様々な注意を必要とする。

P-20-6 当院で meso/dextrocardia と胎内診断した症例に関する検討

慶應義塾大

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【目的】心軸異常である meso/dextrocardia には様々な合併症を伴う予後不良なものもある一方で、meso/dextrocardia と胎内診断された症例に関する知見は少なく、管理法などに関する一定の見解はない。今回我々は当院で meso/dextrocardia と胎内診断した症例について検討した。【方法】対象は 2014 年から 2023 年に当院で周産期管理を行い、胎児期に meso/dextrocardia と診断した 27 症例である。診断は正常心軸より正中向きの場合に mesocardia (8 例), 心臓が右胸腔に存在する場合に dextrocardia とした (19 例)。さらに、dextrocardia は心臓位が右に存在する dextroposition (15 例) と心軸が右向きの dextroversion (4 例) の 2 種類に分類した。【成績】Mesocardia のうち、右肺低形成が 3 例 (3q トリソミー, 食道気管支瘻, 左肺動脈スリング), 左上大静脈遺残 (PLSVC) が 5 例 (単独 2 例, VACTERL 連合 1 例, 13 トリソミー 2 例) であった。Dextroposition のうち、先天性肺気道奇形が 7 例, 肺分画症が 1 例, 先天性横隔膜ヘルニアが 6 例, 右肺無形成+食道閉鎖+VACTERL 連合 1 例であった。Dextroversion のうち、無脾症候群が 2 例, 単心室症が 1 例, PLSVC+両側肺動脈低形成症+テンブル症候群が 1 例であった。【結論】今回我々は meso/dextrocardia と胎内診断した症例について検討した。PLSVC 単独などの予後良好例を認めた一方で、染色体異常や出生後集学的管理を要する疾患を合併した予後不良例も散見された。胎児期に meso/dextrocardia と診断した際には高次医療機関での慎重な周産期管理が望ましく、超音波断層法などによる肺・気管支評価と大血管を中心とした胎児構造異常精査が重要であると考えられた。

P-20-7 胎児期に消化管拡張を認めた14例における消化管閉鎖の診断に有用な因子の検討

四国こどもとおとなの医療センター

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【目的】胎児消化管閉鎖の特徴的な超音波所見として腸管拡張が挙げられるが、腸管の所見は蠕動運動により経時的に変化する。そのため胎児期に腸管拡張所見を認めていても出生児に異常を認めない症例もあり、胎児消化管閉鎖の診断に有用な因子を明らかにすることとした。【方法】2013年1月から2023年10月に胎児期に消化管拡張所見を認めた14例について、指摘時週数、超音波所見（腸管壁肥厚、羊水過多、胎便性腹膜炎など）、胎児心拍異常の有無などを検討した。【成績】胎児期に腸管拡張を認めた14例のうち出生児に消化管疾患を認めたのは7例で、小腸閉鎖3例、腸重積2例、消化管出血（アレルギー性）1例、消化管穿孔1例であった。腸管拡張所見に加え、腸管壁肥厚を認めた7例のうち小腸閉鎖3例、腸重積2例、消化管穿孔1例であった。腸管壁肥厚を認めなかった6例は正常であった。腹水を認めた5例のうち小腸閉鎖1例、腸重積2例、消化管出血1例であった。腹水を認めなかった9例のうち小腸閉鎖2例、消化管出血1例であった。羊水過多を認めた2例のうち1例は消化管穿孔であった。嚢胞やwhirlpool signを認めた例はなかった。胎児心拍異常を認めたのは3例で、消化管出血1例、腸重積1例、消化管穿孔1例であった。また妊娠34週以降に指摘された6例中5例が正常であった。【結論】腸管拡張所見を認めた週数と超音波所見（腸管壁肥厚、羊水過多、胎便性腹膜炎など）、胎児心拍異常は消化管閉鎖などの消化管疾患を示唆する有用な因子となり得る。

P-20-8 先天性肺嚢胞性疾患に対して経母体ステロイド投与を施行した5例の検討

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【目的】先天性嚢胞性肺疾患（以下CCLD：congenital cystic lung diseases）は胎児期に胸腔内占拠性病変を認める疾患群であり、腫瘍が大きいと胎児水腫を伴い周産期死亡となることがある。当科では、CVR 1.6を超える腫瘍では1週間以内に再検し急性増悪もしくは胎児水腫出現した際に経母体ステロイド投与を行い、投与後約4週間で効果が低ければ追加投与を施行している。本研究は当院で経母体ステロイド投与を施行した胎児CCLD症例の特徴を明らかにすることを目的として行った。【方法】2004年1月から2023年9月までに当院で分娩したCCLD47例中、経母体ステロイド投与をした5例を後ろ視的に検討した。【成績】胎児水腫合併は4例であった。初回投与時期は中央値妊娠21週（19-26週）、CVRは中央値2.7（1.79-3.33）であった。全例投与直後に腫瘍増大速度は低下した。1-2週間後に再増悪し追加投与を2例施行した。妊娠転帰は、子宮内胎児死亡1例（初回投与2日後）、妊娠23週での人工早産（母体ミラー症候群発症）1例、正期産3例であった。新生児予後は早期新生児死亡1例、正期産児3例のうち2例に対して生後3か月時に肺葉切除術施行、1例対しては生後1日目にECMO管理下肺葉切除が施行された。周産期死亡となった2例はCPAM（congenital pulmonary airway malformation）type IIIであった。【結論】CCLDに対する経母体ステロイド投与は、腫瘍増大速度を低下させるが、1-2週間後に再度増悪する症例もある。少なくとも縮小傾向に入るまで慎重な経過観察が必要である。

P-20-9 胎児の疾患を理由とした妊娠中期の人工妊娠中絶を検討する人々に対する情報提供のあり方に関する考察

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【目的】胎児の疾患を理由に妊娠中期の人工妊娠中絶（以下、中絶）を検討している人々への支援の充実を目指し、その際の情報提供のあり方について検討した。【方法】診療録を振り返り、妊婦・家族からの質問、情報提供が役立ったことを抽出、個人的なことを除き、一般的事項をまとめて考察した。【成績】質問が多かった事項は、中絶の方法、費用、入院期間、受診回数、初回受診から入院、火葬、退院後の診察までの流れ、中絶のリスク、処置の痛みとその対策（硬膜外麻酔の有無）、身体の回復経過、次の妊娠はいつから可能か、などであった。また、質問がなくても次子再発率や着床前診断の選択肢、次回妊娠時の胎児検査の選択肢などの情報を伝えると「それは知りたい情報だった」と言う人が多かった。中絶のタイミングは、妊娠週数だけでなく、誕生日や結婚記念日などを避けたり仕事や家族の用事の都合を考慮して決めることを希望している人が多かった。当院から中絶施設に紹介する際には、家族の立ち合いの可否を考慮したり、あえて自宅から遠いところを選んだり、過去に出産した施設や将来出産を考えている場所とは違うところで中絶を希望する人も少なからずいた。娩出児に会って写真を撮ったり呼び名をつけたりすることの意義の話し合いや、仕事をしている妊婦に対する職場への伝え方や中絶後に産後休が発生すること、上の子の育児休暇が終了する可能性があることについての情報提供も重要と思われた。【結論】胎児理由による中期中絶は、実質的に選択可能であるが、中絶するかどうか決断する過程の支援と並行して、中絶をめぐる具体的な情報提供のあり方について議論が進むことが望まれる。

P-20-10 当院で2020年～2022年の3年間で診断された胎児心臓病について

榊原記念病院

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【目的】胎児心臓病は、その発生頻度が1.0%と高く、染色体異常を合併することも多く、出生後早期より加療の必要な疾患の為、臨床上出生前診断が期待されている。2006年に胎児心エコー検査ガイドラインが発行され胎児心エコー検査をスクリーニング(レベルI)と精査(レベルII)に分類し、各レベルで行うべき検査範囲が明示された。このガイドライン発行後、全国で行われている胎児心エコー検査(レベルII)は年々増加し、2010年には胎児心エコー検査の健康保険収載され、2021年に胎児心エコー検査ガイドラインの第2版が改定された。当院産婦人科は2014年に循環器専門病院に産婦人科が新設。小児循環器内科、小児心臓外科がある当院は、産婦人科開設前は、近隣より新生児搬送で先天性心疾患の治療を行っていたが、産婦人科が開設後は妊娠中の胎児心臓病の診断に産婦人科・小児循環器内科、臨床遺伝科医師とともに力をいれてきた。妊娠中に胎児心臓病を診断することで出生後早急に適切な治療を開始することができ治療成績が良くなっている。【方法】今回2020年1月～2022年12月までの3年間、当院で診断された胎児心臓病の週数、紹介された疑い病名・主訴、胎児心臓病名、出生後の染色体異常の有無、妊娠の転帰につき後方的に解析を行う。【成績】超音波機器の進歩やスクリーニング技術の向上により早い妊娠週数、疑い病名・主訴で紹介され診断される胎児心臓病が増えている。ここ3年間、当院で診断される胎児心臓病は年間約70-80人です。【結論】妊娠中より胎児心臓病を診断することで妊娠中の胎児の状態・出生後の治療につき情報提供を行い、母児分離することなく出生後の治療を開始することができる。

P-20-11 当院の出生前診断における検査の実施状況と課題についての検討

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【目的】当院では2021年9月に出生前診断を開始し、2022年10月にNIPTを導入した。十分な出生前遺伝カウンセリング(GC)の上で、羊水染色体検査(AC)、超音波初期スクリーニング(US)、クアトロ検査(QT)、NIPTを選択する。NIPT導入前後で受検した検査を比較し、各検査の実施状況と課題について検討した。【方法】2021年9月から2023年8月に出生前診断目的で妊娠13週までに当院を来談し、GC・検査を完了した55例を対象とした。NIPT導入前(2021年9月～2022年9月)14例、導入後(2022年10月～2023年8月)41例に分けて、受検した検査および初診時に診療時間外まで対応した割合を後方的に確認した。【成績】導入前は全例でUSを受検し、8例(61.5%)はUSのみで終了した。1例(7.1%)が他院でNIPTを行い、4例(30%)がQT、1例(7.1%)がACを併用した(重複あり)。導入後、NIPT受検率は41例中22例(53.6%)と有意に増加し、US受検率は41例中35例(85.4%)と有意に減少した。US受検者の12例(29.3%)はUS単独で、19例(46.3%)がNIPT、2例(4.9%)がQT、5例(12.2%)がACを併用した。US未施行の6例中3例(7.3%)はGCのみで終了し、3例(7.3%)はNIPTのみ実施した。また、出生前診断枠を設けている外来診療日のうち初診時の診療終了時間が診療時間外となった割合は、導入前10.2%に対し導入後37.0%と有意に増加した。【結論】NIPT導入後、出生前診断の来談者数は増加しNIPTの実施数も増加した。受検後の意思決定にも多大な影響を及ぼしうるUSの受検率はNIPT導入後に減少したが、依然として高かった。一方で十分なGCやUSは時間を要し時間外診療の増加につながった。限られた時間や医療資源の中で満足度の高い診療ができる体制を構築する必要がある。

P-21-1 16srRNA 遺伝子解析を用いた腔マイクロバイーム検査と腔細菌培養検査の一致率に関する検討

琉球大

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【目的】腔細菌培養検査で異常がなくとも絨毛羊膜炎により早産となる症例は存在し、腔細菌培養検査で検出できない菌の存在が疑われる。16srRNA 遺伝子解析を用いた腔マイクロバイーム(腔MB)検査により、腔細菌培養検査で検出できない菌の検出が可能となるかどうか、および両者で検出力に差がある菌の細菌学的特徴について検討する。【方法】2019年4月から2021年8月の間に当院で妊娠初期に腔MB検査と腔細菌培養検査の検体を同時に採取し検査を行った19例について、診療録を後方的に検討した。【成績】対象者の平均年齢は33.7歳で検体採取時期の平均は妊娠12.6週であった。検出された菌種は腔MB検査で16種類、腔細菌培養検査で6種類であった。19例中15例(78.9%)では両検査での優勢菌が一致したが、4症例(21.1%)は一致しなかった。腔MB検査においてLactobacillusが90%以上を占めるLDM(Lactobacillus-dominant microbiota)が7例(36.8%)、90%未満であるNLDM(Non-LDM)が12例(63.2%)であったのに対し、Nugent scoreが0-3点は16例(84.2%)、4-6点は2例(10.5%)、7点以上の細菌性腔症は1例(5.2%)であった。腔MB検査では検出されているが腔細菌培養検査では検出されていない症例が多い菌には、流早産の原因となるUreaplasmaやGardnerellaなどが挙げられ、分離・培養が困難な細菌学的特徴としては細胞壁を持たずPCR法での検出を要すること、偏性嫌気性菌であること、コロニーが小さいことが挙げられた。【結論】腔MB検査により腔細菌培養検査では検出されない菌が検出され、それらは細菌性腔症や流早産の原因となりうる菌であった。腔MB検査を導入することにより流早産への治療介入の選択肢が増える可能性がある。

P-21-2 分泌物鏡検での大型桿菌像による細菌性陰症除外の有用性

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【目的】細菌性陰症は帯下異常の原因として頻度が高い病態である。診断のゴールドスタンダードは Nugent score だが、検査を外注している場合当日中に結果が得られない難点がある。今回、日常外来のセッティングにおいて分泌物鏡検像から細菌性陰症の有無を推定できないか、検討した。【方法】対象は2022年4月から2023年8月まで当院で Nugent score を調べた症例とした。カルテからデータを抽出し、分泌物鏡検が実施されていない症例を除外した。鏡検像1視野で大型桿菌を30個以上認める場合を大型桿菌あり、下回る場合をなしとした。大型桿菌の有無と Nugent score との一致率を調べた。【成績】対象症例は67症例だった。15症例は分泌物鏡検が実施されておらず除外し、52症例が解析対象となった。平均年齢38.1歳(SD13.9)、閉経前45症例、閉経後7症例だった。大型桿菌有るかつ Nugent score 陰性は18症例、大型桿菌なしかつ Nugent score 陽性は26症例、一致率は83.0%だった。一致しなかった症例のうち大型桿菌ありかつ Nugent score 陽性は1症例であり、大型桿菌ありの症例に絞って解析すると一致率は94.7%だった【結論】分泌物鏡検での大型桿菌陽性と Nugent score 陰性の一致率は94.7%だった。分泌物鏡検での大型桿菌像は細菌性陰症の否定に有用と思われた。より精度を上げるためには、複数視野での観察や他所見を合わせて考慮することが必要と考えられる。

P-21-3 卵巣卵管膿瘍に対して臀部からの経皮的穿刺ドレナージが有効であった2症例

大津赤十字病院
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【緒言】卵巣卵管膿瘍(tubo-ovarian abscess: TOA)は主に腔内からの上行性感染に伴う感染症であり、生殖可能年齢の女性に多く見られる。骨盤内炎症性疾患(Pelvic inflammatory disease: PID)の診断基準を満たした患者のうち、15-34%にTOAが認められるとされている。今回、TOAと診断された症例に対して抗菌薬治療や膿瘍穿刺が奏功せず臀部からの経皮的穿刺ドレナージ術が有効であった2症例を報告する。【症例1】43歳0妊0産。内膜症性嚢胞に対して3回の開腹手術歴あり。左内膜症性嚢胞に感染を起こした8cm大のTOAは腹腔内高度癒着のため、手術加療は困難と思われた。抗菌薬治療と経腔超音波下ダグラス窩穿刺にて排膿を行ったが治療抵抗性であった。放射線科との協議の末、CT・超音波ガイド下に左臀部仙骨左縁から穿刺ドレナージを施行し症状改善、退院に至った。【症例2】51歳0妊0産。コントロール不良な緑内障の既往あり。13cm大の左TOAに対して手術加療は本人の抵抗があったため抗菌薬治療を行ったが奏功しなかった。放射線科にて、CT・超音波ガイド下に左臀部仙骨左縁から穿刺ドレナージを施行し症状改善、退院となった。フォローのMRI検査でもTOAは消失していた。【結語】抗菌薬治療に難渋したTOAに対して、臀部からの経皮的穿刺ドレナージ術によって治療が奏功した2例を経験した。TOAでは、腹腔内の炎症や癒着が高度で手術が困難となることも多く、他臓器損傷のリスクも高い。安全に最小限の侵襲に抑えることができる経皮的穿刺ドレナージ術はTOA治療において十分有用な方法であり、治療選択肢として考慮されるべき治療法の1つであると考えられる。

P-21-4 悪性腫瘍との鑑別が困難であったクレブシエラ子宮膿瘍の一例

島根県立中央病院
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【緒言】Klebsiella pneumoniae(以下K.pneumoniae)のうち過粘稠性を示すものは病原性が高く、血行性に全身へ移行し多発膿瘍をきたす。症状は肝膿瘍、眼内炎、髄膜炎、脳膿瘍、腸腰筋膿瘍など多彩であるが、婦人科臓器での報告例はまれである。今回は子宮膿瘍をきたした症例を経験したので報告する。【症例】70歳代女性。高熱を契機に当院を受診し、尿培養・血液培養からK.pneumoniaeが検出された。腎盂腎炎としてSBT/ABPC点滴を開始されたが、感受性良好な抗菌剤にもかかわらず治療効果に乏しかった。熱源検索のCTで子宮腫大をみとめたものの、下腹痛や子宮圧痛などの症状に乏しかったこと、帯下が膿汁ではなかったことから子宮感染症としては非典型的であった。悪性リンパ腫既往で定期的な画像検査があり、半年前に正常所見であった子宮が急速に増大したこと、頸部が著しく変形していることより当初は悪性腫瘍を疑ったが、組織生検では悪性所見を認めず、炎症を示唆する好中球浸潤のみであった。骨盤MRIでも子宮膿瘍が疑われ、第12病日からドレナージ目的で子宮内洗浄をおこなった。洗浄開始後に炎症所見が改善し、外科治療を要することなく自宅退院した。帯下培養から分離されたK.pneumoniaeはstring test陽性で過粘稠性が確認された。【結論】過粘稠性K.pneumoniaeは侵襲性の全身感染症として他科で治療開始されることが多いが、血行性に播種性病変をきたすため、子宮に膿瘍形成することがある。子宮筋層が破壊されるような侵襲性病変で悪性腫瘍との鑑別に苦慮したが、培養でK.pneumoniaeを認めた場合は本症例のようにドレナージが有効であることに留意すべきである。

P-21-5 腔瘍を疑ったが子宮腔部ヘルペス感染症と考えられた一例

岡崎市民病院

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【緒言】性器単純ヘルペスウイルス感染症は多彩な所見を呈することがある。今回、腔粘膜に不整な肥厚を呈し、悪性腫瘍と鑑別が困難であった症例を経験したので報告する。【症例】47歳。3妊3産。職業セクシャルワーカー。下腹部痛にて受診。内診で腔全体に壊死を伴う不整な壁肥厚を認めた。造影MRI検査にて腔粘膜に不整な造影不良域があり、造影CT検査では、両側鼠径部、腸骨領域、傍大動脈のリンパ節腫大を認めた。子宮、付属器には特記すべき所見を認めなかった。腫瘍マーカーはCEA, SCCともに正常であった。上記検査から腔瘍を疑い、腔壁組織を病理検査へ提出したが、重層扁平上皮の得られた部位では明らかな異型を認めなかった。血液検査では炎症反応高値(WBC14500, CRP10.69)であり、腫瘍性または感染性の上昇を考慮し、入院にて抗生剤治療開始とした。身体所見では口唇、四肢、陰部に皮疹や潰瘍を認め、HSV定性検査陽性であったため、バラシクロビル内服開始とした。梅毒、淋菌、クラミジア、HIV検査は陰性で、各種培養検査では有意菌の発育を認めなかった。入院後、炎症反応は改善し、入院6日目に退院した。初診から3週間後の診察で、腔粘膜の病変は消失し、造影CTでは腫大していたリンパ節の縮小を認めた。以上の経過から、悪性腫瘍は否定的であり、感染に伴う病態であったと考えた。【結語】感染に伴い腔粘膜が不整に肥厚する症例を経験し、悪性腫瘍と鑑別を要した。生殖器の不整な病変を診察する際には病理検査に加え、感染症を念頭に培養検査や性感染症スクリーニングを行うことが有用である。

P-21-6 慢性骨盤痛を伴う骨盤うっ血症候群に対して血管塞栓術が有効であった一例

大阪警察病院

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【はじめに】骨盤うっ血症候群とは卵巣静脈が逆流することで骨盤内にうっ血と静脈瘤を形成し、慢性骨盤痛を呈する症候群である。その多くは20~45歳に発症し、多胎妊娠歴がある。発症頻度がまれであり、明確な診断基準がないため医師の認知度は低く、対症療法のみで経過観察される患者が数多くいると考えられる。今回、骨盤うっ血症候群に対して血管塞栓術が有効であった症例を経験したため報告する。【症例】45歳、2妊2産。3か月前から持続する月経とは無関係の左下腹部痛を主訴に前医を受診した。CTで左卵巣静脈の拡張を認め、骨盤うっ血症候群の疑いで当科紹介受診となった。経腔エコーにて、子宮、付属器に器質的異常を認めなかったが、左付属器圧排による痛みを認めた。骨盤うっ血症候群と診断し、内服加療やホルモン剤による治療を提案するも、血管内治療を希望されたため、卵巣静脈塞栓術の方針となった。両側大腿アプローチで左卵巣静脈を選択し血管造影を行うと、逆行性血流によって骨盤内静脈が拡張しており、左内腸骨静脈への排血を確認できたため、同静脈コイル塞栓を施行した。術後経過は良好で、術翌日に退院した。術翌日より左下腹部痛は消失し、再増悪を認めていない。【まとめ】骨盤うっ血症候群に対して血管塞栓術が有効であった一例を経験した。原因不明の慢性骨盤痛に対しては、画像検査で卵巣静脈の拡張を確認し、骨盤うっ血症候群を疑う症例に対しては積極的な診断と治療を考慮するべきである。

P-21-7 S状結腸を用いた性別適合手術により形成した腔にタンポンが迷入し、大腸内視鏡で抜去し得た一例

藤田医大ばんだね病院

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性同一性障害とは、近年では医学的診断名を性別不合同もいい、身体の性と心の性が一致しない状態である。2003年に性同一性障害に関する法律が制定され性別適合手術(SRS)が認められ、2018年には保険適用も開始された。またLGBT法の制定など社会でも性の多様性が広く知られるようになってきている。しかし日常診療において我々産婦人科医がトランス女性(MTF: Male to Female)を診療する機会は未だ少ない。今回S状結腸を用いた性別適合手術を受けたMTFにおいてタンポン抜去が困難となった症例を経験したため報告する。【症例】26歳MTF、20歳時にタイでS状結腸を用いた造腔術による性別適合手術を受けた(陰茎・精巣摘出・陰核・会陰形成を含む)。普段よりS状結腸粘液による帯下が多く、時々タンポンを使用していた。前日挿入したタンポンの糸が腔内に迷入し抜去困難となり近医受診。はっきり確認できず当院紹介された。外陰部はSRSのため女性型を呈し腔はSS腔鏡が入る程のサイズであった。腔鏡で観察できる範囲に異物はみられなかったがCTを撮影したところ腔のさらに奥にタンポンを疑う異物を認めた。疼痛が強くなり、静脈麻酔下で自由鉤や筋鉤を使用し抜去を試みたがS状結腸による腔が細長く、タンポンの視認は困難であった。穿孔のリスクを懸念し一旦終了した。翌日のMRIでは蠕動の影響によりタンポンはさらに頭側に移動していた。大腸内視鏡で抜去を試みたところ、比較的容易に抜去できた。【考察】SRS後の腔内異物を経験した。通常的女性と解剖学的構造が異なり、抜去に難渋した。今後LGBTを囲む社会状況の変化により一般の産婦人科医もMTFの診療に携わる機会が増えると考えられSRSにも精通していく必要がある。

P-21-8 身体所見が乏しく診断に難渋した卵巣動脈瘤破裂

防衛医大

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【目的】産褥期以外の卵巣動脈瘤破裂はまれである。今回身体所見が乏しく診断に難渋した症例を経験したので報告する。〔方法・成績〕症例は63歳, 4妊4産, 既往歴, 家族歴に特記事項はなかった。右側腹部痛, 肩背部痛を主訴に前医を受診し, 胸腹骨盤単純CTで右付属器周囲に出血が疑われ当院救急搬送された。来院時バイタルサインは血圧140/90mmHg 心拍数96回/分であった。身体所見は右側腹部に軽度圧痛があるのみで, 反跳痛, 熱感はなく背部叩打痛もなかった。経陰超音波検査では腹水, 卵巣腫大, 子宮内膜肥厚は明らかではなく, 経腹超音波検査では腎盂拡大はなかった。胸腹骨盤造影CTでは, 骨盤底から後腹膜にかけての血腫, 脾動脈瘤, 右卵巣動脈拡張がみられた。Dynamic CTでは, 右卵巣動脈は拡張し, 一部瘤化がみられたが明らかな造影剤の血管外漏出はみられなかった。骨盤造影MRIを撮影すると動脈瘤血腫内部に右卵巣動脈の瘤状の拡張がみられた。これらの所見より, 卵巣動脈瘤破裂が考えられ, IVR治療を行った。Interventional Radiology (IVR) 時の透視造影で右卵巣動脈に2か所の動脈瘤があり, コイル塞栓を行った。術後経過は良好であり10日後に退院となった。1か月後の骨盤造影CTでは右卵巣動脈瘤は消失し, 後腹膜血腫も消滅傾向であった。その後は経過観察のため定期的に造影CTを撮影しており, 術後3年経過しているが再発はみられていない。【結論】本症例では身体所見が乏しく, 好発年代ではなかったため診断に難渋した。卵巣動脈瘤破裂は珍しく, 診断が困難な腹痛では鑑別に入れ, CTによる検査も考慮する必要がある。

P-21-9 利用可能エネルギー不足による続発性無月経について～女性アスリート外来症例より～

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女性アスリートの健康問題として, エネルギー不足, 無月経, 骨粗鬆症が三主徴として挙げられる。女性が活躍し注目される一方でその重要性は知られていない。当県では国民スポーツ大会の開催にあたり, 数年前から長期的な目標を持ち, 医師会, 栄養士会, スポーツ協会など多方面から女性アスリートの支援体制を構築, その一環として当院婦人科に女性アスリート外来を開設した。婦人科医師と栄養士が中心となり, 適応は主に月経にまつわる問題とした。2022年8月末までに初診30名, 平均年齢18歳(13—42歳)。競技は陸上, 水泳, 各種球技。アスリートのレベルは中高生の部活動(全国大会出場も含む), 大学生, 社会人, アマチュア, トップアスリートまで幅広い。その中で内科的問題からアスリート外来に紹介された症例を経験した。症例は40歳代, アマチュアで長距離走。就業先の健診で肝機能異常を指摘され肝臓内科受診。腹部エコーで右心系拡大の疑いあり, 循環器内科へコンサルト。精査にて軽度甲状腺機能低下のため内分泌内科にも併診。結果, るいそうによる肝機能障害, 心負荷, 甲状腺機能異常の診断であった。1年前から続発性無月経を来しており, 当外来へ紹介。1900Kcal/日の食事にも関わらず, BMI15, 月200kmのランニングから, 利用可能エネルギー不足による無月経と診断。骨密度は腰椎YAM66%と低下。栄養指導を行い経過観察中である。女性アスリート外来として, 無月経だけではなく全身の影響を及ぼす状態になり得るという知識を広め, またパフォーマンスを下げない解決法を確立し女性アスリート, 指導者などに受け入れられる様, 啓蒙していくことの重要性を認識した。

P-21-10 当科におけるTurner症候群の検討

琉球大

知念籽子, 大石杉子, 仲村理恵, 宮城真帆, 平敷千晶, 銘苅桂子, 関根正幸

【目的】当科において治療歴のあるTurner症候群の臨床像と臨床経過を明らかにすること。【対象・方法】1986年10月～2023年5月までの期間, 当科において治療を行ったTurner症候群16例を対象とし, 診療録を後方視的に検討した。Turner症候群の合併症検索として, 原則, 心疾患や甲状腺疾患, 肝機能異常の有無と骨塩定量を精査している。【結果】診断時の年齢中央値は11歳(1-36)であった。小児科で診断された症例が11例, 婦人科で診断された症例が5例であった。婦人科初回受診時の年齢中央値は19.5歳(14-39)。現在も通院中の8例の年齢中央値は30.5歳であった。平均身長は142.9cm(133-154)であった。12例で原発性無月経, 3例で続発性無月経を認めた。当科で診断された5例はいずれも遺伝カウンセリングが施行されたが, 小児科からの移行例については施行されていない。13例(81.3%)に合併症を認め, 最多は骨塩量低下(9例), 次いで甲状腺機能低下(8例), 肝機能異常(7例), 聴力低下(4例)であった。循環器系合併症では, 両大血管右室起始症, 心室中隔欠損症, 肺高血圧を同時に合併した症例が1例, 僧帽弁逆流1例, 三尖弁逆流1例, 心電図異常を3例に認めた(重複あり)。妊娠出産を経験した症例や妊孕性温存を行った症例はなかった。合併症精査に関して, 肝機能検査は全例で行われており, 骨塩定量, 甲状腺疾患, 心疾患の検査施行率は87.5%であった。全例において致命的な合併症はなく経過している。【結論】Turner症候群の合併症の頻度は高く, 婦人科で診断する症例に対する合併症検索を抜けなく行う必要がある。また, 小児期に診断され婦人科へ移行した症例に対する遺伝カウンセリングの実施を検討する必要がある。

P-21-11 本邦における更年期障害女性の治療実態に関する後ろ向き観察研究

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【目的】更年期世代の日本人女性での更年期障害による受診、薬剤処方状況について検討した。【方法】JMDC社のレセプトデータを用い、2017年1月から2021年12月までに更年期障害と診断された40~65歳の女性を対象に、患者背景、薬物治療パターン等を解析した。【成績】調査期間において126,443人が更年期障害と診断され、そのうち108,828人(平均年齢±標準偏差: 50.3±5.1歳)が新規に診断された女性、17,615人(52.0±5.1歳)が調査期間以前に診断されており受診を継続している女性であった。更年期障害の初回診断年齢は、既報の平均閉経年齢と類似していた。新規の更年期障害女性において、婦人科領域の既往疾患として多かったのは子宮筋腫25.8%、子宮内膜症7.7%であり、ホルモン補充療法(HRT)の禁忌、慎重投与となる既往疾患として肝疾患11.4%、片頭痛6.5%が認められた。初回治療が行われた診療科は、婦人科50.1%、一般内科35.9%、その他14.0%であった。薬剤使用割合は漢方薬54.4%、抗うつ薬や睡眠薬等の中樞神経系(CNS)薬27.8%、HRT14.6%(経口薬12.8%、貼付剤4.7%、ゲル剤2.4%)であった。漢方薬とHRTよりも、漢方薬とCNS薬の併用割合が高かった。薬剤処方頻度の中央値はCNS薬5.0回/年、HRT4.0回/年、漢方薬3.0回/年であった。治療継続期間の中央値はCNS薬217.0日、HRT(貼付剤)212.0日、HRT(経口薬)167.0日、漢方薬107.0日であった。【結論】本研究において示された更年期障害を有する女性の初回診断年齢は、平均閉経年齢と類似していた。漢方薬、CNS薬はHRTよりも高い割合で処方されており、更年期障害の治療継続期間はこれまでに報告されている更年期症状の持続期間に比べ顕著に短かった。

P-22-1 当院における初回進行卵巣癌のダグラス窩針生検の現状

愛媛大

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【目的】進行卵巣癌・卵管癌・原発性腹膜癌(以下、卵巣癌)において、初回手術にてoptimal surgeryに至ることが困難な症例は、化学療法を先行することが考慮される。その場合、化学療法開始前に腫瘍組織を採取することは、正確な病理診断のために必要なだけでなく、HRD検査を含めた遺伝学的検査を行う上でも非常に重要である。当院では腫瘍組織の採取方法として、試験開腹や審査腹腔鏡に加え、症例によってはダグラス窩針生検も選択肢としている。今回、当院におけるダグラス窩針生検の現状について報告する。【方法】2022年1月~2023年7月、進行卵巣癌に対して術前化学療法の開始前にダグラス窩針生検を施行した10例について、後方視的に検討した。【結果】年齢の中央値は68.5歳、病期はIIC期:5例、IVA期:2例、IVB期:3例であった。ダグラス窩針生検の適応の条件は、①経腔超音波検査を施行し、ダグラス窩に腫瘍性病変があること、②組織採取可能な大きさであること、③穿刺部位に腸管や血管の妨げがないこと、などである。全例において入院の上、針生検を行っており、経腔超音波ガイド下にPRIME CUT IIを用いて穿刺した。穿刺回数はそれぞれ4~6回、全ての症例で組織が採取され、組織型の確定が可能であった。特記すべき合併症もなく、初回化学療法を円滑に導入できていた。【結論】進行卵巣癌の初回治療として、化学療法開始前にダグラス窩針生検が10例に実施された。症例の経過に加え、HRD検査における結果などを中心に、文献的考察も加えて報告する。

P-22-2 原発性左卵巣癌疑いとして手術を施行し、病理検査にて神経内分泌乳癌卵巣転移の診断に至った1例

弘前総合医療センター

國井基忠, 横山美奈子, 門ノ沢結花, 當麻絢子, 丹藤伴江

【緒言】転移性卵巣癌は卵巣腫瘍全体の1~2%、卵巣悪性腫瘍全体の10~25%を占め、乳癌原発は14%と報告されている。一方、神経内分泌乳癌は神経内分泌腫瘍の1%未満と稀である。今回、原発性左卵巣癌疑いとして手術を施行し、病理検査にて神経内分泌乳癌卵巣転移の診断に至った1例を経験したので報告する。【症例】48歳、0妊0産。3年前に乳癌の診断のため前医にて術前化学療法後に右乳房部分切除、右腋窩リンパ節郭清術を施行し、病理検査で浸潤性乳癌pT3N2M0pStageIIIAの診断となった。術後放射線治療、ホルモン療法を行っていたが、1年前に右腋窩リンパ節再発の診断で右腋窩リンパ節摘出術を行った。その後、再発なく経過していたが、定期フォローのPET-CTで骨盤内にSUV max 10.0の集積を伴う6×4cmの腫瘤を認め、左卵巣腫瘍疑いとして当科紹介となった。原発性左卵巣癌の疑いで手術の方針となり、腹式での左付属器切除術を行い、術中迅速病理検査で上皮性悪性腫瘍の診断となり、腹式単純子宮全摘、右付属器切除、骨盤リンパ節生検を施行した。術後の病理検査では核異型の強い腫瘍細胞の増生があり、免疫染色ではPAX8は陰性、GATA3、ER、Synaptophysinが陽性となり神経内分泌乳癌による卵巣転移の診断となった。1年前に右腋窩リンパ節再発で手術した際の病理標本を再評価したところ、組織像が類似しており、追加した免疫染色でも同様の所見であった。最終的に浸潤性乳癌から神経内分泌乳癌の診断に変更となり、今回の卵巣腫瘍はその転移と診断に至り、乳腺外科にて化学療法開始となった。【結語】転移性卵巣癌の中で神経内分泌乳癌転移は非常に稀であり、本症例に関して文献的考察を交え報告する。

P-22-3 腎移植後腹膜癌患者に対する、PARP 阻害薬（ニラパリブ）の使用経験

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症例は71歳女性、慢性糸球体腎炎に対して15年前に生体腎移植を受け、シクロスポリン (CyA) およびプレドニゾロンを内服している。また、後遺症はないが脳梗塞の既往がありアビキサパンを内服している。CT・MRI・腫瘍マーカー検査から腹膜癌が疑われ、診断的腹腔鏡下手術での大網および腹膜生検から高異型度漿液性癌が検出され腹膜癌 Stage IIIC 期と診断された。HRD 検査は陽性で腫瘍からは BRCA1 病的変異が検出された。大網や腸管表面・横隔膜下など広範に播種病巣があり、Predictive index が8点であったため、手術療法ではなくパクリタキセル (PTX) ・カルボプラチン (CBDCA) 併用療法を行った。CyA と PTX の代謝拮抗が考慮され PTX を 20% 減量して 164mg/m² で治療を行ったが、骨髄抑制や下痢に伴う電解質異常等の副作用が強く、第3コースは CBDCA の AUC を 6 から 4 に減量した。しかし第4コース終了2週間後に重急性心筋梗塞に伴う心不全を発症し、第5コースは PTX をさらに 20% 減量して治療を行ったが血小板数が 2.3 万/μl まで低下した。腫瘍完全切除には腸管切除を要するため全身状態を考慮するとリスクが高く、化学療法の継続も副作用の面から困難であった。第5コース終了時点の治療効果は PR であり、HRD 検査陽性、特に BRCA 病的変異を有することから PARP 阻害薬での維持療法が考慮された。オラパリブとシクロスポリンは代謝酵素として CYP3A4 を共有するため両者の血中濃度が不安定になりやすいことが想定されたため、代謝経路の異なるニラパリブでの維持療法を開始した。腎移植既往のある患者に PARP 阻害薬を使用した既報は我々が検索した限りではなく、相互作用などを含めた留意点や臨床経過について報告する。

P-22-4 卵巣腫瘍術後に虫垂 Goblet cell adenocarcinoma の両側卵巣転移と判明した1例

伊勢赤十字病院

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【緒言】転移性卵巣腫瘍の頻度は悪性卵巣腫瘍のうち 8.4~31.1% 程度である。虫垂癌は大腸癌全体の 1% を占める、比較的稀な疾患である。今回卵巣腫瘍術後に病理組織診断で虫垂 Goblet cell adenocarcinoma および両側付属器転移と判明した一例を経験したので報告する。【症例】46歳、4妊3産の女性。健康診断で貧血を指摘され、前医を受診した。子宮筋腫と診断され経過観察されていたが腫瘍が増大し、精査加療目的に当院に紹介された。当院初診時、CEA6.3ng/ml, CA125 43.3U/ml と腫瘍マーカーの軽度上昇を認め、造影 MRI で両側卵巣由来と考えられる充実性腫瘍を認めた。造影 CT で多発リンパ節腫大および腹膜肥厚があり、PET-CT では充実性腫瘍部分に軽度集積を認め転移性卵巣腫瘍を疑い、上部下部消化管内視鏡検査を行ったが原発病巣は特定されなかった。転移性卵巣腫瘍を強く疑い試験開腹術を行った。両側付属器は術中迅速組織診断で印環細胞癌と診断された。腹腔内には多数の播種病変を認めたが原発巣は特定できず、正常外観ではあったが追加で回盲部切除を行った。術後病理結果は虫垂 Goblet cell adenocarcinoma StageIVC, 両側卵巣転移であった。現在、残存腫瘍に対し化学療法中である。【結語】虫垂 Goblet cell adenocarcinoma は比較的稀であり、虫垂や十二指腸に好発し、卵巣転移が多いとされる。虫垂 Goblet cell adenocarcinoma は粘膜下腫瘍の形態をとる粘膜内に病変を認めないことも多いため、術前診断が困難であるが、転移性卵巣腫瘍を疑う症例では虫垂 Goblet cell adenocarcinoma を含む虫垂腫瘍を鑑別診断の1つとして検討し、虫垂の同時切除も考慮すべきである。

P-22-5 Gliomatosis Peritonei を発症した卵巣未熟奇形腫の一例

岡崎市民病院

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【緒言】未熟奇形腫は gliomatosis peritonei (GP) と呼ばれる播種病変を伴うことがあるが予後良好とされている。今回、未熟奇形腫 grade1 と診断後、経過観察中にポートサイト再発、腹膜播種をきたし GP と診断した症例を経験したので報告する。【症例】29歳、0妊。X年急激な腹痛を主訴に当院を受診し、経腹超音波検査と MRI 検査で右成熟嚢胞性奇形腫を疑う腫瘍を認めた。同部位に圧痛を認め、卵巣腫瘍茎捻転を疑った。CA19-9, SCC, AFP は高値であった。腹腔鏡下手術を施行し、右卵巣に不整形な充実性腫瘍を認め、360度捻転していた。正常卵巣は温存可能と判断し腹腔鏡下右卵巣腫瘍摘出術を施行した。摘出検体の病理検査で未熟奇形腫 grade1 の診断であり、術後経過観察の方針とした。腫瘍マーカーは陰転化し、CT 検査で再発の所見なく経過していた。X+2年 CT 検査で左下腹壁に増大する腫瘍の出現を認めた。他に腫瘍性病変は認めず、腫瘍マーカーは SCC が微増していた。未熟奇形腫のポートサイト再発を疑い、腹壁腫瘍切除術の方針とした。術中所見では、腹壁腫瘍が腹膜に覆われたまま腹腔内に突出していた。さらに腹壁、大網、子宮、両側付属器に多数の粟粒状播種病変を認めた。診断のため腹壁腫瘍の切除と播種病変の一部生検を施行した。病理検査では腹壁腫瘍、播種病変のどちらも GP の診断で、経過観察の方針とした。【結語】GP は画像検査で指摘できないことがあり、診断には病理学的評価が必要不可欠である。未熟奇形腫はしばしば GP で再発することがあり、未熟奇形腫の再発を疑う症例においては再発病変の生検を行い、十分な病理検査により診断を行う。

P-22-6 深部子宮内膜症から発生した類内膜腺癌の一例

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【目的】異所性子宮内膜症の悪性化はまれであり、発生部位によってその病態は多岐に渡る。今回、深部子宮内膜症から発生して後腹膜腔に進展した類内膜腺癌の一例を経験したので報告する。【症例提示】症例は44歳、未妊未産。40歳から月経困難症に対して低用量エストロゲン・プロゲステロン配合剤（LEP）を使用していた。卵巣腫瘍と腫瘍マーカー（CA125, CEA）の高値を指摘され、当科紹介となった。子宮頸部背側を中心に腫瘤を認め、内診では2/3以上の左子宮傍組織浸潤を認めた。子宮頸部、子宮内膜細胞診は異常を認めず、子宮腔部に肉眼的に病変は認めず生検でも悪性所見は認めなかった。臨床経過の中で後陰門蓋に腫瘍が出現し、同部位の生検より endometrioid carcinoma の診断を得た。最終的に深部子宮内膜症から発生した類内膜腺癌とした。試験開腹術（子宮全摘術+両側付属器切除+低位前方切除+大網切除）を行った。腫瘍は腹腔内には認めず、膀胱子宮間、基韧带、直腸に浸潤しており、腫瘍は固く輪郭が不明瞭で、左側基韧带は骨盤壁深くまで浸潤していたため完全切除することはできなかった。組織型は endometrioid carcinoma, G3 で、子宮外～子宮壁深部を中心とした病変の広がりを示すことから子宮内膜症由来と考えられた。また両側卵巣は子宮内膜症性嚢胞を認め、境界悪性相当の上皮を認めた。画像診断から骨盤外に腫瘍の転移はないと考えられたため、術後に放射線同時化学療法（CCRT）を施行した。PET-CTで腫瘍の消失を確認し、現在も再発なく経過している。【考察】深部子宮内膜症から発生し、後腹膜腔に進展した悪性腫瘍はまれである。本症例は可及的な腫瘍減量術と放射線治療で良好な局所制御が得られた。

P-22-7 術中迅速検査が有効であった卵巣中腎様癌の1例

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【緒言】近年、中腎様構造を模倣した腫瘍が子宮や卵巣に発生することが報告され、中腎様癌として2020年にWHO分類に新たに追加された。今回、術中迅速病理で診断可能であった卵巣中腎様癌の症例を報告する。【症例】56歳女性、0妊0産婦、44歳時に子宮筋腫に対し子宮全摘術施行した。下腹部痛を主訴に前医受診し経腔エコー及び骨盤造影MRIで左卵管癌が疑われ紹介となった。腫瘍マーカーはCA125 29.8U/ml, CA19-9 0.4以下U/ml, CEA 4.1ng/ml, SCC 0.9ng/ml, 骨盤造影MRIでは左卵巣に長径約5cm, 充実成分主体で一部嚢胞構造を持つ腫瘍性病変あり、左卵管や一部嚢胞に出血成分を有し、内膜症を背景とした卵巣悪性腫瘍が疑われた。胸腹骨盤造影CTで明らかな転移性病変はなかった。以上より術中迅速病理併用の上、手術が施行された。左卵巣腫瘍の術中迅速病理所見は、クロマチンの増量、大小不同の類円形腫大核と好酸性円柱状から不整形胞体を有するN/C比の高い腫瘍細胞が線維性間質を背景に癒合管状、小管状、充実性パターンを呈しつつ結節状に増殖しており、腺管内には好酸性分泌物が散見され、中腎様癌または性索間質性腫瘍の診断であった。両側付属器切除、骨盤リンパ節生検、大網生検を施行し手術を終了した。組織学的所見は迅速病理と同様で、免疫組織化学的所見はPAX8陽性、calretinin部分的に陽性、GATA3わずかに弱陽性、CD10一部の腺管内に陽性、ER, PGR, WT1, TTF1陰性であり、卵巣中腎様癌FIGO IAの診断となった。再発高リスク群として、術後補助化学療法を施行されている。【結語】卵巣に発生し、術中迅速検査で診断可能であった卵巣中腎様癌の症例を経験した。中腎様癌に対する術中迅速検査に関しても今後更なる症例の蓄積が望まれる。

P-22-8 CTガイド下生検で診断に至った卵巣原発悪性リンパ腫の1例

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【緒言】悪性リンパ腫の20%~40%は節外性であり、卵巣原発悪性リンパ腫は卵巣悪性腫瘍の0.08%~0.3%程度と極めて稀な疾患である。診断には病理組織の採取が必須であり、これまで手術による生検の報告がいくつかなされている。今回我々は、画像検査にて悪性リンパ腫を疑い、CTガイド下生検で卵巣原発悪性リンパ腫の確定診断に至り、早期に治療開始し得た症例を経験したので報告する。【症例】40歳、乳癌術後タモキシフェン内服中。近医での経腔超音波検査にて右卵巣59mm大、左卵巣37mm大の腫大を認め、精査加療目的で当院紹介受診した。当科受診後の骨盤単純MRIでは、両側卵巣の充実性腫大を認めたが、卵巣腫瘍を示唆する所見が乏しく、経過観察となった。その後も定期的にMRI検査と腫瘍マーカー測定にて経過フォローしていた。初診から4か月後の骨盤単純MRIで、両側卵巣サイズが増大傾向にあり、辺縁に残存卵胞を有する腫瘤を認めた。画像所見から卵巣原発悪性リンパ腫を疑い、IL-2Rを測定したところ、621.0U/mlと高値を認めたため、血液内科にコンサルトし、病理学的確定診断目的でCTガイド下生検を施行した。病理標本の免疫染色の結果、diffuse large B-cell lymphomaの診断に至った。診断後23日目からDA-EPOCH-R療法開始となった。【結論】卵巣原発悪性リンパ腫は、外科的治療後、病理組織検査で診断されることが多く、主治療である化学療法の開始が遅れる傾向がある。手術より低侵襲的な生検で診断を行うことで、早期に治療開始することができる。

P-22-9 再発卵巣癌治療中に中枢性塩類喪失症候群を来した髄膜癌腫症の一例

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【緒言】中枢性塩類喪失症候群 (cerebral salt wasting syndrome : CSWS) は中枢神経疾患に伴う著明な低 Na 血症と脱水をきたす疾患であり、頭部外傷やくも膜下出血で発症する報告は多いが、卵巣癌など悪性腫瘍での報告は少ない。再発卵巣癌治療中に髄膜播種をきたし、CSWSによる低 Na 血症を発症した症例を経験したため報告する。【症例】53 歳、既往歴特記なし。卵巣癌 IV 期高異型度漿液性癌に対し手術、化学療法を施行後、1 年 3 か月で再発し、化学療法を繰り返していた。初回治療から 7 年 5 か月後に頭部 CT で脳表の髄膜播種を指摘され、全脳照射を施行し播種は消失していた。以後 TC 療法を施行中、放射線治療から 6 か月後に低 Na 血症に伴う意識障害のため入院し、脱水による低 Na 血症と診断し、補液にて軽快し退院した。退院から 3 日後に頭痛と嘔気、低 Na 血症を認め、再入院した。再入院時に神経学的な異常は認めなかった。血液検査にて低 Na 血症と尿中 Na 高値、血症浸透圧低値を認め、SIADH や腎性塩類喪失症候群、CSWS を鑑別とした。補液にて血中 Na 値は改善したが、頭痛や嘔気の改善が乏しく、下肢のしびれ感が出現したため、脊椎造影 MRI 検査を施行した。脊髄表面に播種を疑う所見があり、髄液中から腺癌細胞を認め、髄膜播種と診断した。低 Na 血症について生理食塩水の補液により改善を認めたことと脱水の所見、尿中ミクログロブリン正常値であったことから髄膜播種による CSWS の診断とした。現在 PS の低下に伴い緩和療法中である。【結語】卵巣癌の化学療法中に生じた低 Na 血症では、下痢などの Na 喪失や SIADH であることが多いが、髄膜癌腫症から CSWS を生じることもあり、頭痛、嘔気などの症状に注意が必要である。

P-22-10 TMB-High の原発不明な明細胞癌に Pembrolizumab が奏効した 1 例

市立広島市民病院

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【緒言】Pembrolizumab は、化学療法歴のある高い腫瘍遺伝子変異量 (TMB-High) を有する固形癌患者に対して保険適応となっている。今回、TMB-High の原発不明な明細胞癌の症例に対して、Pembrolizumab を投与し、奏効が得られた症例を経験したため報告する。【症例】47 歳女性。子宮内膜症に対して治療をされていた。発熱、右下腹部痛のため右付属器炎疑いのため当科紹介となった。抗生剤投与するも発熱の改善なく、画像検査にて右外腸骨リンパ節領域に 3cm 大の腫瘍を認め、周囲の右総腸骨領域、傍大動脈リンパ節の腫大もあり、悪性リンパ腫を疑い、腹腔下に右街腸骨リンパ節の生検を行ったが、病理組織検査では明細胞癌の診断であった。PETCT 検査では腫大したリンパ節に集積を認めたが、その他集積は認めず、原発巣は不明であったが、背景に内膜症があること、CA125 が高値であること、明細胞癌であることから卵巣癌に準じた治療を開始した。TC 療法施行後、HRD 陽性であり PAOLA レジメンによる維持療法を行ったが、TC 療法終了後 9 か月で再増大を認めた。癌ゲノム検査にて TMB-High であり、Pembrolizumab の投与を開始した。投与後 4 時間後から spike fever を認め入院管理を要し、infusion reaction と診断しステロイドを投与し改善を認めた。その後 PSL 内服しながら現在 5 コース投与しているが、腫瘍の縮小を認めている。【結論】TMB-High の原発不明がんまたは卵巣癌は稀であるが、Pembrolizumab で治療効果を認めた症例を経験した。今後のさらなる症例の蓄積が望まれる。

P-22-11 卵巣癌肝転移との鑑別が困難であったベバシズマブ投与後の肝類洞拡張症の 1 例

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【緒言】肝類洞拡張症 (hepatic sinusoidal dilation) は、肝静脈の流出障害に伴う肝毛細血管の拡張を意味し、さらに肝実質のうっ滞が起こるとされている。原因として、心不全や Budd-Chiari 症候群、類動脈閉塞症などがあるが、ベバシズマブ (Bev) が原因となった報告は認めない。今回我々は、卵巣癌肝転移との鑑別が困難であった Bev 投与後の肝類洞拡張症の 1 例を経験したので報告する。【症例】症例は 44 歳、卵巣癌 IIIC 期、高異型度漿液性癌と診断し、NAC-IDS 後にオラパリブ、Bev による維持療法を行っていた。維持療法開始後約 1 年半の CT 検査で新たに肝外側区に乏血性の約 10mm の結節を認めたが、同部位に PET/CT 検査で FDG の集積は認めなかった。EOB-MRI 検査の肝細胞相で取り込みが低下しており転移が疑われた。孤発性の肝転移を疑い、肝部分切除術を行った。病理学的に悪性所見はなく、中心静脈周囲を主体に類洞の拡張とその周囲のうっ血や肝細胞の脱落を認め、肝類洞拡張症と診断された。その後は 2 年間のオラパリブの内服を継続し、現在再発なく経過している。【考察】EOB-MRI 検査で肝転移と肝類洞拡張症ともに肝細胞相で取り込みの低下が認められるが、後者では辺縁が不明瞭との報告がある。本症例でも境界は不明瞭であり、術前に鑑別にあげることができた可能性がある。病理学的には、中心静脈の内皮細胞障害や壁の線維化、内腔狭窄に加えて中心静脈域周囲の肝細胞障害なども認め、これらは微小循環障害を示す所見であり、Bev が原因となった可能性が考えられた。【結語】Bev 投与中もしくは投与後に出現した肝臓の乏血性結節の場合、肝類洞拡張症を鑑別にあげる必要があると考えられた。

P-22-12 子宮内膜症性嚢胞に対する両側付属器摘出の3年後に発症した原発性腹膜癌

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【症例】54歳 未経妊【現病歴】X年に子宮筋腫に対し腹式単純子宮全摘出術, X+7年に両側卵巣嚢腫に対し腹腔鏡下両側付属器摘出術を施行した。病理診断は子宮内膜症性嚢胞で、悪性所見を認めなかった。X+10年に下腹部痛を主訴に前医を受診し、骨盤内に7cm大の充実性腫瘤を指摘され当科紹介となった。骨盤造影MR検査で骨盤内に内部に増強される充実部を伴う7cm大の腫瘤を認め、chronic expanding hematomaが疑われ、腫瘤の由来は不明であった。造影CT検査で腫瘤の直腸浸潤を疑う所見を認め、遠隔転移やリンパ節腫大を認めなかった。上下部消化管内視鏡検査で病変を認めなかったが、注腸でS状結腸に腸管浸潤の可能性を指摘された。骨盤内腫瘍の診断目的で開腹術予定とした。外来精査中に、発熱、腹痛が出現し腹膜炎の診断で入院、絶食の上抗菌薬加療を施行し軽快した。経腔的に腫瘍の穿刺吸引細胞診と培養検査を施行し、細胞診は陰性で細菌の検出を認めなかったが経腔的腫瘍生検で漿液性癌の診断であった。開腹術を行い、腔断端近傍に鶏卵大の腫瘤を認め直腸Ra~Rsに浸潤していた。腹膜に多数の1cm未満の播種を認め大綱に粗大な病変はなかった。直腸高位前方切除術、腫瘍切除、腹膜生検を施行した。腹腔内には多数の1cm未満の播種が残存した。病理診断は高異型度漿液性癌で腫瘍は直腸の漿膜側から固有筋層へ浸潤し、直腸近傍のリンパ節に転移を認めた。腹膜播種生検標本にも最大5mmの転移を認めた。原発性腹膜癌IIIB期(pT3bN1M0)の診断で、現在術後補助化学療法(パクリタキセル・カルボプラチン療法)を施行中である。

P-22-13 相同組換え修復欠損を伴う卵巣成熟嚢胞性奇形腫から発生した扁平上皮癌の一例

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卵巣成熟嚢胞性奇形腫(MCTO)の悪性転化は0.17~2%に認められ、様々な組織型を呈するが、その80%は扁平上皮癌(SCC)である。進行例における予後は非常に不良であるが、その稀少性から標準的治療は確立されていない。今回当院で手術進行期分類IIIC期の、相同組換え修復欠損(HRD)を伴うMCTOから発生したSCCを経験したため報告する。症例は40歳代、3妊2産。他院より右側MCTO疑いに対する加療目的で当院紹介となり、定時手術を予定していた。待機期間中に急性腹症を呈し緊急腹腔鏡手術の方針となり、術中所見で右卵巣腫瘍破裂と診断し、腹腔鏡下右付属器摘出術を施行した。その際、腫瘍破裂部と接していた膀胱子宮窩腹膜に不整な腫瘤を認めた。術後病理診断は右側MCTOから発生したSCCであり、後日、進行期決定開腹手術を施行した。追加手術では膀胱子宮窩および回腸一部に播種性病変を認め、手術進行期分類IIIC期相当であった。子宮・左側付属器摘出術、膀胱子宮窩腹膜ストリッピング・膀胱部分切除・再建術、回腸部分切除・再建術、傍大動脈および骨盤リンパ節郭清術、大綱重切除術にて完全切除を達成した。術後病理検査でMCTOから発生したSCCの膀胱子宮窩腹膜播種、回腸腸間膜播種および筋層浸潤の診断で、pT3cN0M0、手術進行期分類IIIC期の確定診断だった。術後化学療法としてTC療法を開始し、並行して腫瘍のHRD statusを確認したところGIS:78と陽性であったため、TC+Bevacizumab療法からPAOLAレジメン(Olaparib+Bevacizumab)による維持療法を開始した。現在まで明らかな再発所見なく、維持療法として16サイクルのBevacizumab投与を終了し、Olaparib単剤での維持療法を計2年となるまで継続予定である。

P-22-14 卵巣粘液性境界悪性腫瘍術後約1年で多発肺転移をきたした1例

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【緒言】卵巣境界悪性腫瘍では粘液性腫瘍が最多で、非常に予後良好な疾患であるため再発の報告例は少ない。今回我々は術後約1年で多発肺転移をきたした1例を経験したので報告する。【症例】症例は57歳、5妊3産、閉経53歳で、既往歴に特記事項はなかった。2-3週間前からの心窩部痛・腹部膨満感を主訴に近医を受診し、経腹超音波検査で骨盤内腫瘍を認めたため当院へ紹介となった。MRI検査で長径20cmに及ぶ多房性嚢胞性腫瘤を認め、内部に造影効果を示す充実部分はなく、粘液性境界悪性腫瘍を疑う所見であった。開腹手術を施行したところ右卵巣に腫瘍を認め、術中迅速組織診は粘液性境界悪性腫瘍の結果であった。腹腔内精査を行い肉眼的に明らかな転移巣は認めなかったため、腹式単純子宮全摘+両側付属器切除+大綱部分切除を施行した。術後の永久病理組織診ではごく一部で間質浸潤を認めるものの5mm未満で卵巣粘液性境界悪性腫瘍IA期と診断した。術後追加治療は行わず外来で経過観察としていたが、術後1年目に撮影したCTで多発肺腫瘍を認めた。また下部消化管内視鏡検査では5mm大の隆起性病変を認め、生検結果は神経内分泌腫瘍(NET)G1との結果であった。多発肺腫瘍の生検結果は粘液性腺癌でNETの転移は否定的であり、肺腫瘍が多発であることとTTF-1(-)であることから肺原発の可能性は低いことが考えられ、粘液性境界悪性腫瘍の悪性転化と診断した。【結論】卵巣境界悪性腫瘍術後に悪性転化をきたし再発した症例報告は少なく非常に稀な症例を経験した。文献的考察を踏まえ報告する。

P-22-15 進行卵巣癌の初回治療におけるニラバリブ維持療法についての検討

三重大

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【目的】進行卵巣癌におけるニラバリブ維持療法が保険収載されおおよそ3年になる。PRIME試験の結果から個別化容量に対するニラバリブ維持療法の成績が報告されている。当院におけるニラバリブの実臨床データから治療効果や副作用について、後方視的に検討し報告する。【方法】2020年9月から2023年4月に進行卵巣癌でニラバリブを維持療法で用いた18例について、症例背景(年齢, 病期, 組織型, BRCAバリエント, HRステータス, HRDスコア, 手術方法, 手術完遂度)ニラバリブ継続期間, 副作用, 再発の有無, PFSについて検討した。【成績】全症例でニラバリブ開始容量は200mg/日であった。組織型: 高異形度漿液性癌が12例, 低異形度漿液性癌が2例, 明細胞癌が1例, 粘液性癌が2例, 類内膜癌が1例であった。HRDステータス: HRDは2例, HRPは9例, 未施行は7例であった。有害事象: 血小板減少は5例, 好中球減少は3例, 貧血は5例, 悪心は5例であった。減量を要した症例は7例あったが有害事象による投与中止はなかった。再発症例は8例あり, 継続期間中央値は7か月(2-19か月)であった。PFSは中央値17か月であった。【結論】当院の治療成績は既報と大きな差はないが明細胞癌, 粘液性癌では効果が乏しい可能性がある。個別化容量での有害事象は許容可能で有害事象による中止はなかった。実臨床における効果, 安全性についてさらなる症例の蓄積が必要である。

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P-23-1 子宮頸癌 IB2 期を含むトラケクトミーの治療成績と周産期予後に関する検討: 不妊治療としての頸管拡張術の有用性

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【目的】子宮頸癌に対する妊孕性温存手術である腹式広汎および準広汎子宮頸部摘出術(以下, Trachelectomy)を施行した例では10-15%に術後頸管狭窄が起こる。本研究ではTrachelectomy後の頸管狭窄に対する頸管拡張術の有用性を検討した。【方法】当科でTrachelectomyを施行した63例(IA1-2期11例, IB1-2期52例)を対象として後方視的な観察研究を行った。当科ではIB2(腫瘍径3cm以下)までをTrachelectomyの適応とした。術後頸管狭窄例を伴う不妊患者に対し, 不妊治療の一環として頸管拡張術を行った。治療成績, 治療後経過, 周産期成績について検討した。Trachelectomy63例の予後は5年無増悪生存(5yPFS), 全生存(5yOS)を Kaplan-Meier 曲線と Log-rank test で調べた。【成績】5yOSは100%であった。5yPFSは同じ進行期の広汎子宮全摘例で97%, Trachelectomy例で94%であり, 治療成績は同等であった(p=0.7)。挙児希望のある27例中19例(70.4%)が妊娠し, 累計26回の妊娠があった。不妊治療として頸管拡張術が2018-2023年に9例(33.3%)で施行され, 9例中5例(55.6%)が術後に妊娠に至った。一方, 頸管拡張が不要であった18例中14例(77.8%)が妊娠に至った。人工中絶1例を除き, 18症例では全例妊娠30週前に管理入院を行っているが, 8例(47.1%)は36週未満の早産であった。【結論】IB2期を含むトラケクトミーの治療成績は子宮全摘と同等であった。妊娠率70%, 早産率47%は良好な周産期予後であった。術後頸管狭窄は不妊として顕在化することが多い。頸管拡張後の妊娠例が多いことから, 不妊治療としての頸管拡張は考慮されるべきである。

P-23-2 子宮頸部上皮内腫瘍に対するタラボルフィンナトリウムを用いた光線力学的療法の医師主導治験

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【目的】円錐切除術は確実な診断と高い治療率を得られる子宮頸部上皮内病変(CIN)の標準治療法であるが, 早産率上昇が懸念される。一方, CIN治療オプションの一つとして光線力学的療法(PDT)は早産率上昇を伴わず高い治療率を得られるものの長期間に及ぶ光線過敏症を伴うため普及はしなかった。本邦で開発された第二世代光増感剤のタラボルフィンナトリウムは光過敏を伴う期間が短く, 2003年早期肺がんに対し保険適用となりその後再発食道がん及び悪性脳腫瘍に対し適用拡大をしてきた。今回, CINに対するタラボルフィンナトリウムPDT(T-PDT)の有効性及び安全性について第II相多施設医師主導治験により検討したので報告する。【方法】選択基準を満たしたCIN2及びCIN3症例に対しタラボルフィンナトリウム40mg/m²を静注し, 投与後4時間経過後に子宮頸部病変ヘリレーザー照射を行った。治療12週以降で病理診断により治療効果判定を行った。治療効果判定後は定期的なコルポスコピー及び病理診断を行い追跡した。有害事象はCTCAE ver.5.0を用いて評価した。【成績】同意が得られたCIN2及びCIN3の77例に対しT-PDTを施行した。中央判定委員会により2例が除外され75例を有効性評価の対象とした。75例全例でCR判定となり追跡期間中に再発を認めた症例は1例であった。T-PDTを施行した77例においてSAEは認めず, Grade3の有害事象が4件のみで他はGrade2以下であった。【結論】高い有効性及び安全性が確認できたため, T-PDTはCIN治療の選択肢となりうる可能性が示唆された。

P-23-3 当院における CIN2/3 に対する子宮頸部蒸散術に関する検討

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【目的】CIN2/3 に対する子宮頸部蒸散術の治療成績、妊娠への影響について検討した。【方法】当院において CIN の蒸散術の適応は、①最大病変が CIN3 までであること、②腺系病変がないこと、③コルポスコピー上可視病変であること、④蒸散術の希望があることなどである。2010 年 1 月から 2022 年 12 月までの間に 40 歳以下で下平式高周波手術器を用いて蒸散術を行った 137 例と同時期に下平式高周波手術器を用いて円錐切除術を行った 279 例を比較対象として術前診断、患者背景、6 か月以上追跡した症例の再発の有無、妊娠例の流早産率について比較検討した。【成績】蒸散術群 (A 群) は平均年齢 32.2 歳、円錐切除術群 (B 群) は 33.8 歳、未産率は各々 56.9%、29.4% であった。術前診断は A 群は CIN2 が 59 例、CIN3 が 78 例、B 群では CIN2 が 14 例、CIN3 が 257 例、SCC・腺系異常が 8 例であった。追跡症例は、A 群は 117 例、B 群は 239 例であった。A 群で術後細胞診・組織診異常がみられた症例は 6 例で、ASC-US: 1 例、LSIL: 2 例、CIN1: 1 例、CIN2: 1 例、CIN3: 1 例であった。B 群で術後細胞診・組織診異常がみられた症例は 3 例で、LSIL: 1 例、CIN3: 2 例であった。術後妊娠例は A 群ではのべ 54 例 (双胎 1 例、IUFD 1 例、妊娠経過中 8 例)、B 群ではのべ 59 例妊娠 (無脳児 1 例、妊娠経過中 3 例) であった。双胎・IUFD・無脳児症例を除外した流早産率は、A 群 9.1%、B 群 21.8% であった。A 群では妊娠 34 週未満の流早産例は認めなかった。【結論】下平式高周波手術器による蒸散術は流早産のリスクが低く、CIN3 までの症例であれば再発率も高いことが推察された。症例の選別が的確であれば、妊孕性温存希望症例に対して子宮頸部蒸散術は有用であると思われる。

P-23-4 HPV ワクチンの子宮頸がん予防効果：我が国初のエビデンス

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【目的】我が国では HPV (ヒトパピローマウイルス) ワクチンの接種率が高い 1994-1999 年生まれの世代 (ワクチン世代) が子宮頸がん検診の対象となる 20 代に到達し、これまで子宮頸部前癌病変に対するワクチン効果が報告されてきた。本研究では、子宮頸癌に対する予防効果について検討した。【方法】子宮頸癌罹患の年齢層別動向を検討するために、一般公開されている国立がん研究センターがん情報サービス (全国がん登録、1975-2019 年) と本学会腫瘍委員会 (患者年報 2003-2020 年) のがん登録データをポアソン回帰分析にて解析した。さらに HPV ワクチン特異的な予防効果を検証するために、多施設共同疫学研究 (MINT スタディ) に登録された子宮頸癌患者において HPV ワクチンが予防できる HPV16/18 型の陽性率の推移を年齢層別に解析した。【成績】20 代でのみ、子宮頸癌の罹患がそれまでの増加傾向から一転して、2011 年以降は有意に減少していた ($p < 0.0001$)。全国がん登録では 2016 年以降は登録形式が変更されたが 2016 年以降のデータに限っても 20 代でのみ子宮頸がん罹患率が有意に減少していた ($p < 0.01$)。一方、MINT スタディに登録された子宮頸癌患者の HPV16/18 陽性率は、20 代でのみ 2017 年以降で低下した ($p=0.05$)。【結論】2 つのがん登録データは HPV ワクチン接種歴と結びつけられていないため、20 代での子宮頸癌罹患の減少は検診効果や性行動の変化など別の要因であることも考えられるが、ワクチン世代を含む 20 代でのみ HPV16/18 陽性率が低下していることから、HPV ワクチンが一定の効果を示したと考えられる。これらの結果はわが国における HPV ワクチンの子宮頸癌予防効果を示唆する初めての報告である。

P-23-5 再発子宮頸癌に対するセミプリマブの治療効果・有害事象に関する前向き観察研究 (中間報告)

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【目的】化学療法歴のある進行又は再発子宮頸癌患者に対してセミプリマブが 2023 年 3 月に保険承認された。本邦における治療経験はまだ少数であるため、治療効果・安全性に関して更なるデータの集積が必要と考え、単施設での前向き観察研究を実施することとした。【方法】初回のプラチナ製剤を含む化学療法を投与後に再発・進行した子宮頸癌患者を対象とし、過去に抗 PD-1 抗体・抗 PD-L1 抗体等の免疫関連治療を受けた症例は除外した。現在症例集積中であるが、今回 2023 年 4 月~2023 年 9 月までに登録された 9 症例について、治療成績・安全性を検討し報告する。【成績】全 9 症例のうち組織型は扁平上皮癌が 5 例、腺癌が 2 例、神経内分泌腫瘍が 1 例、神経内分泌腫瘍を含む腺癌が 1 例であった。前治療レジメン数の中央値は 2 (1-6) であった。最大治療効果は PR が 2 例、SD が 3 例、PD が 4 例で、奏効割合は 22% であった。免疫関連副作用は grade 3 以上の重篤な副作用は認めなかった。薬物治療を要したものは、掻痒感を伴う皮膚障害 grade2 と口腔粘膜炎症 grade2 を併発した 1 例とリウマチ性多発筋痛症が 1 例であった。【結論】今回の検討では EMPOWER-Cervical1 試験と比較し前治療レジメン数 2 以上の割合が多い患者集団であったが、比較的高い奏効率を認めた。安全性に関しては grade3 以上の副作用は認められなかった。本邦においてもセミプリマブが進行再発子宮頸癌に対して安全に使用でき、一定の効果を期待できる可能性がある。今後さらなるデータの集積・検討を行い、報告する予定である。

P-23-6 子宮頸部多発嚢胞病変での生検診断の有効性の検討

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【目的】子宮頸部多発嚢胞病変 (CMCL) では、胃型病変である分葉状頸管腺過形成 (LEGH) と胃型腺癌 (GAS) との鑑別が特に重要だが、術前診断はしばしば困難である。今回、CMCL での生検診断の有効性の検討を行った。【方法】2005 年から 2023 年に当院にて CMCL を有し子宮摘出を行った 33 症例を対象とし、生検や円錐切除術と摘出子宮の病理診断の一致率を後方視的に検討した。【成績】術前に子宮腔部生検または頸管内搔爬が施行された症例 (生検群) は 31 例 (術後病理診断: 腺癌 14 例 (GAS 12 例), 異型 LEGH 8 例, LEGH 9 例), 円錐切除術が行われた症例 (円切群) は 11 例 (術後病理診断: GAS 2 例, 異型 LEGH 5 例, LEGH 4 例) であった。生検群では、摘出子宮の GAS 12 例の生検診断は、腺癌 10 例 (10/12, 83%), うち 8 例が GAS (8/12, 67%) であり、上皮内腺癌 (AIS) 1 例, 診断困難 1 例であった。異型 LEGH 8 例の生検診断は異型 LEGH 1 例 (13%), LEGH 2 例 (25%), 病変無し 4 例 (50%), CIN3 1 例であった。LEGH 9 例の生検診断は LEGH 4 例 (44%), 胃型病変 4 例 (44%), 病変無し 1 例 (11%) であった。一方、円切群では、摘出子宮での GAS 2 例の円切診断は、GAS 1 例, AIS 1 例であり、異型 LEGH 5 例での円切診断は異型 LEGH 4 例 (80%), LEGH 1 例 (20%) で、LEGH 4 例は全例 LEGH (100%) であった。胃型形質の検出には AB-PAS 染色, 免疫染色 (HIK1083, Claudin18 など) の併用が有用であった。【結論】GAS 症例では、生検でも高率に診断可能であるが、異型 LEGH の生検での診断率は低く、円錐切除術が有効であると思われる。また、胃型病変の診断には AB-PAS 染色や免疫染色の併用により診断率が向上すると考えられた。

P-23-7 進行再発子宮頸癌に対して Pembrolizumab 併用化学療法を施行した 12 症例の検討

四国がんセンター

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【目的】進行再発子宮頸癌の予後は極めて不良である。2022 年 10 月, 子宮頸癌に対して初めて免疫チェックポイント阻害剤を併用した化学療法が保険収載され, 治療効果を期待する一方, 多様な症例に適応され, 適切な症例選択の基準が定まっていないのが現状である。【方法】2022 年 10 月~2023 年 9 月に, 当院で Pembrolizumab 併用化学療法を施行した進行再発子宮頸癌 12 例を対象に, 後方視的に検討した。【成績】年齢の中央値は 55.5 歳 (44-71)。進行期は I 期 1 例, II 期 2 例, III 期 3 例, IV 期 6 例。組織型は SCC7 例, Adeno1 例, 特殊型 4 例。初発 1 例, 再発 11 例であり, 本治療前の化学療法ありは 3 例, 放射線治療歴ありは 8 例であった。CPS < 1 1 例, CPS ≥ 1 11 例。Bevacizumab は 8 例で併用していた。最良効果判定は PR 7 例, SD 4 例, PD 1 例であり, 奏効率 58.3% であった。現在化学療法中 5 例, 維持療法中 3 例, 中止 4 例であった。irAE を 5 例に認め, その内 1 例は免疫性血小板減少症を発症し, 治療中止となった。その他, 重大な副作用として認めた。【結論】Keynote 826 試験よりも奏効率は低い, 特殊型や前治療歴を有する症例にも効果を認めた。今後, 本邦での realworld data を蓄積し, 治療のタイミングや症例の選択において検討する必要がある。

P-23-8 進行・再発子宮頸癌におけるペムプロリズマブ併用化学療法の検討

鹿児島大

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【目的】KEYNOTE-826 試験により化学療法単独群に対するペムプロリズマブ (Pem) 併用の予後改善効果が明らかとなった。自験例での検討を行った。【方法】2022 年 10 月から 2023 年 4 月末までに進行・再発子宮頸癌で TC+Pem (±) ベバシズマブ (Bev) 療法を開始した 16 名において, 後方視的に電子カルテより抽出・解析した。全例に治療開始前及びコース毎に免疫関連有害事象 (irAE) に関する血液検査が行われた。【成績】対象者は初回治療 4 例 (FIGO2018stageIIIC1: 1, IVB: 3), 再発 12 例 (遠隔のみ: 5, 局所+遠隔: 5, 骨盤内のみ: 2) であり初回再発 8 例, 2 回目再発 2 例, 3-4 回目 2 例であった。8 例は全身加療歴無しであった。年齢中央値 (範囲): 49 (37-74) 歳, 観察期間中央値 (範囲): 6 (4-9) M であった。治療は Pem に加えて全例に TC+Bev が併用された。投与回数中央値 (範囲): 6 (3-8) 回であり, そのうち 9 例が Pem のみの維持療法に移行している。TC 療法における投与遅延は認めなかったが 2 例 (1 例: FN, 1 例: 末梢神経障害) により 1 段階減量した。Pem 及び Bev の投与遅延, 減量, 休業はなかった。有害事象は末梢神経障害 G1 以上: 5 例, 骨髄抑制 G3 以上: 5 例, 悪心嘔吐 G2 以上: 4 例, 倦怠感 G1: 4 例, 高血圧 G3 以上: 2 例, FN: 1 例, 多形紅斑: 1 例, 味覚障害: 1 例, 耳閉感: 1 例であり, 内分泌関連の有害事象は認めなかった。最良治療効果 (16 例で解析) は CR: 6 例, PR: 7, SD: 1, PD: 2 であった。転帰は 1 例が現病死であり 10 例は治療継続中である。【結論】Pem 併用化学療法は重篤な有害事象は認めず, 進行・再発頸癌における有効な治療選択肢と思われる。

P-23-9 当科における進行・再発子宮頸癌に対する Pembrolizumab 併用化学療法への検討

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【目的】2022年9月に進行・再発子宮頸癌に対する Pembrolizumab 併用化学療法が保険承認された。当科での Pembrolizumab 併用化学療法の現状を把握することを目的とした。【方法】2022年10月から2023年9月にかけて、進行・再発子宮頸癌に対して Pembrolizumab 併用化学療法を施行した12例を対象とした。年齢、進行期や組織型、併用レジメンや治療効果・副作用について、診療録を用いて後方視的に検討した。【成績】年齢は中央値56歳(45-67歳)、12例すべてが再発症例で組織型は扁平上皮癌8例、通常型腺癌3例、胃型腺癌1例、腺扁平上皮癌1例であった。11例で放射線治療歴があり、うち1例は重粒子線治療を受けていた。再発部位は照射外再発が6例、照射内再発を有する症例が7例であった。10例は6コース終了時点でPRが得られ、9例は維持療法に移行した。治療中断は2例で、1例はgrade4の重症薬疹のため投与中止、1例が3コース後にPDで中止となった。維持療法中の再発は2例で、胃型腺癌1例、腺扁平上皮癌1例であった。それぞれPFS2か月、4か月と早期の再発だった。5例にgrade3以上の有害事象を認め、1例にgrade4の重症薬疹、2例にgrade4の消化管穿孔、1例は非閉塞性腸間膜虚血症疑いで死亡した。【結論】12例中10例でPRが得られており、うち7例は再発なく維持療法を継続できている。維持療法後に早期再発の2例は胃型腺癌と腺扁平上皮癌の特殊組織型かつ、MSSであった。grade3以上の有害事象は5例、1例で死亡例を認めており、適切な有害事象マネジメントが重要と思われる。

P-23-10 子宮頸部神経内分泌癌に対する初回治療の検討—60例の後方視的検討から—

兵庫県立がんセンター
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【目的】子宮頸部神経内分泌癌(NEC: neuroendocrine carcinoma)は子宮頸癌の中で稀なサブタイプである。その症例数の少なさから他臓器のNEC治療に基づいて治療が選択されており、前向き研究も困難である。治療法を探るために単一施設の後方視的調査を行った。【方法】1996年から2023年の間に兵庫県立がんセンターで診断されたNECの患者60例を対象とした。臨床的、病理学的特徴、および生存データを含む情報を臨床記録から収集した。統計解析はKaplan-Meier法およびlog-rank検定を用いて評価した。ハザード比に関してはCox比例ハザード回帰分析を用いて評価した。【成績】症例数は60例で年齢の中央値は42歳(26-82歳)であった。術前診断で早期(FIGO2019 I期またはII期)の症例が48例(80%)で、進行期(FIGO2019 III期またはIV期)症例が12例(20%)であった。手術施行群は49例で手術非施行群は11例であった。手術施行群は非施行群と比して生存期間が有意に延長していた(HR, 0.3269; 95%CI, 0.1459-0.7328, P値=0.004)。術後全身化学療法を行った症例が32例、術後同時化学放射線療法(CCRT)を行った症例が8例であった。全身化学療法群はCCRT群と比して生存期間が有意に延長していた(HR, 0.344; 95%CI, 0.1342-0.8821, P値=0.0193)。【結論】子宮頸部神経内分泌癌に対する初回治療として手術加療は有用であり、術後補助療法として全身化学療法の方がCCRTよりも生存期間を延長させる可能性が示唆された。本発表は兵庫県立がんセンター倫理審査委員会の承認を得ている。

P-23-11 子宮頸癌 IIB 期 (旧 FOGO 分類) の予後検討

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石川光也、三浦穂乃果、小川史子、瀧川 若、川野さりあ、中原万里子、小澤梨紗子、夏目貴史、藤井えりさ、加藤真弓、棚瀬康仁、宇野雅哉

【目的】本邦では2B期に対して手術も選択されているが、手術を行った場合には術後追加治療が行われる可能性が高い。この群の予後を後方視的に解析し、予後の検証と治療法の比較を行った。【方法】2004年から2021年に当院にて治療を行った子宮頸癌の中から治療開始時点の進行期2B期(FIGO2008)の症例を抽出し、後方視的観察研究を行った。特殊組織型、術前化学療法実施例、傍大動脈リンパ節腫大例は除外した。当科では手術が可能と判断された場合は、両治療法を提示して治療方針を決定している。手術では広汎子宮全摘出術および術後高リスク群に対して術後放射線照射を行う。放射線療法は同時化学放射線療法である。【成績】対象117名。年齢中央値55歳。扁平上皮癌95例、腺癌22例。治療前評価での腫瘍径4cm以上72例、腔進展52例、骨盤リンパ節腫大50例であった。全対象において観察期間中央値63.8月での5年DFS63.3%、5年OS86.0%であった。治療前因子のうち予後に関連する因子はなかったが、扁平上皮癌の5年DFS/OSは71.0%/90.1%であるのに対し腺癌は30.7%/67.7%で、予後の有意な差が認められた。手術は60例で行われ、そのうち41例で術後補助療法が行われていた。放射線治療は57例であった。扁平上皮癌では41例で手術が行われ、腫瘍径4cm以上では放射線療法が選択される比率が高かった。扁平上皮癌において治療前因子の調整を行い治療法による予後の比較を行ったが、有意な差は認められなかった。一方腺癌では19例(86.4%)で手術が選択されていた。【結論】2B期扁平上皮癌では治療法による予後の差は認めなかったが、腫瘍径が大きくなると放射線治療が選択される傾向にあった。腺癌は手術の比率が高いが予後は不良であり、治療法の改善が望まれる。

P-23-12 子宮頸癌に対する CCRT (concurrent chemoradiotherapy) 後の骨折について

琉球大

新垣精久, 赤嶺日菜, 玉那覇育子, 玉城夏季, 宮城美紀, 渡部俊陽, 下地裕子, 平良祐介, 仲本朋子, 久高 亘

【目的】放射線療法後の骨折リスク因子を見つけること。【方法】診療録を後方視的に検討。2014年～2023年に当科でCCRTを完遂した子宮頸癌症例で、治療後に照射野内の骨折と診断された症例を対象とした。除外基準として、IVB期症例、腺癌、NAC-CCRT、再発治療、治療前に骨折を認めた症例とした。統計解析はカイ二乗検定、名義ロジスティック解析を使用した。【成績】対象症例は226例であり、20例に骨折を認めた。骨折部位としては第5腰椎5例、恥骨8例、仙骨13例、坐骨1例、腸骨2例であった。単変量解析では、年齢、閉経の有無、CT値で有意差があり、それぞれ $p=0.0029$, 0.0045 , 0.0003 であった。BMI、治療期間、CDDP投与量については有意差を認めなかった。多変量解析においては、CT値のみが $p=0.0377$ と有意であった。骨折症例、非骨折症例において、治療期間やCDDP投与量には差がなかったことから、治療強度が骨折に影響したわけではないと考えられた($p=0.9798$, $p=0.4523$)。Ishikawaらは、治療前の椎骨、骨盤骨のCT値が骨粗鬆症を反映し、それが骨折リスクにつながるのではないかと考察した。Uezonoらはそのcut off値を35HUとしたが、Sakaguchiら、Nardoneらの報告と比較しても、cut off値については一定の見解がなく、HUが低いことがリスクと考えられる。【結論】CCRT後の骨折リスクについて、第5腰椎のHUが低いことが分かった。ただし、cut off値についてはさらに検討を要する。

P-24-1 小児卵巣捻転の2症例に関する検討

JCHO 大阪病院

光田 紘, 原 知史, 一宮汐里, 久原ゆい, 花澤綾香, 田中稔恵, 繁田直哉, 清原裕美子, 井上貴史, 筒井建紀

【緒言】卵巣捻転は小児の腹痛の原因としては比較的稀な疾患である。卵巣機能温存のためには早期の診断と治療が不可欠だが、受診科が産婦人科に限らないことや、経膈超音波・CT・MRIなど診断補助に有用な検査に対するハードルが成人よりも高いことから、しばしば診断に難渋する。当院で経験した2症例をもとに、小児の卵巣捻転に対する診断、治療法、予後などに関して検討する。【症例1】11歳、月経発来は未。当院受診3日前より右側腹部痛と嘔吐が出現し、近医小児科を受診し急性胃腸炎と診断された。受診前日の23時頃より腹痛が増悪し、翌日の早朝に当院救急搬送となった。炎症反応上昇を認め、急性虫垂炎を疑い腹部CTを撮像したところ、右卵巣捻転疑いを指摘された。術中所見では右付属器は2回捻転し、壊死が進行しており付属器温存は困難と考えられ、腹腔鏡下右付属器切除術を実施した。術後の経過は良好であり、術後5日目に退院。摘出した検体は壊死組織が主であり、組織型の判定は困難であった。【症例2】13歳、月経発来後。左下腹部痛を主訴に近医内科を受診し、経膈超音波では明らかな異常はなく、便秘疑いで経過観察となった。腹痛が持続するため近医産婦人科を受診し、骨盤MRIで左卵巣に腫瘍は見られなかったが、卵巣浮腫と卵巣門周囲の捻れを疑う所見を認め、捻転が疑われたため、緊急手術の方針とした。術中所見では左卵巣は3回捻転しており、浮腫状で軽度腫大していたが阻血所見や腫瘍性病変はなく、捻転を解除し手術を終了した。術後4日目に退院。

P-24-2 婦人科腫瘍に合併した骨盤臓器脱に対する腔断端仙骨子宮靭帯固定術 (Shull法) の有用性について

和歌山県立医大

八幡 環, 武田真一郎, 藤野めぐみ, 岩橋尚幸, 堀内優子, 馬淵泰士, 南佐和子, 井篁一彦

【目的】近年の高齢化社会に伴い、骨盤臓器脱 (POP) は増加傾向にあり、腹腔鏡 (ロボット支援) 下仙骨腔断端固定術が広く行われるようになってきている。一方で、前がん病変、または悪性腫瘍が疑われる婦人科腫瘍にPOPを合併する場合、両者を適切に治療することが望ましい。婦人科腫瘍を合併する場合、症例によっては、現在主流となっているmeshを用いた手術を行うべきか議論の余地がある。我々は、婦人科腫瘍手術と同時に、前後腔断端を仙骨子宮靭帯に吊り上げるshull法を実施し、その有効性について検討した。【方法】2022年3月から2023年8月までに婦人科腫瘍に合併したPOPの5例を対象とした。手術時間、出血量、合併症の有無、術前後のPOP-Q systemのスコア、および再発の有無について検討した。【成績】婦人科腫瘍 (術前診断) の内訳は、腹膜偽粘液腫疑い、卵巣境界悪性腫瘍疑い、子宮内膜増殖症既往、子宮内膜増殖症疑い、子宮体癌 (頸内膜癌 G1) 推定 IA 期であり、婦人科腫瘍に対する手術に加えて、全症例でDeLancey Level I 損傷を伴うstage II~IV のPOPを認めたため、前者2例は腹式、後者3例は腹腔鏡下腔断端仙骨子宮靭帯固定術を実施した。中央値として、年齢60 (50-64) 歳、手術時間286 (207~379) 分、出血量20 (15~355) mLであった。1例で、術後の神経因性膀胱を認めたが、18日目に改善した。POP-Qスコアの術前/術後の中央値は、Aa: +1/-2cm, Ba: +1/-2cm, C: -1/-5cm (各々 $P<0.05$) であり、手術によりスコアは有意に改善した。また、追跡期間の中央値は116 (29-433) 日であり、現在、再発例は認めていない。【結論】婦人科腫瘍に合併したPOPの手術において、メッシュを用いないShull法も有効な術式のひとつとなり得ると考える。

P-24-3 当院 HPV ワクチン副反応支援センターを受診した症例の後方視的検討

北海道大

櫻井愛美, 松宮寛子, 山崎博之, 黒須博之, 井平 圭, 遠藤大介, 三田村卓, 金野陽輔, 渡利英道

【目的】2022年4月からヒトパピローマウイルス (HPV) ワクチンの積極的勧奨が再開となったが、未だ接種に対する不安を抱いている人も少なくない。当院では、2014年にHPVワクチン副反応支援センター(当センター)を設立し、多科が連携して診療する体制を整え、副反応が疑われる症例への対応を行ってきた。当センターを受診した症例に対する対応や転機等について情報を提供することで、HPVワクチン接種の普及や拡充へとつながることを目的とする。【方法】2014年10月から2023年3月の間に、当センターを受診した全24症例を后方視的に検討した。【成績】接種時期は、2013年の初回の積極的勧奨中が16例、2022年4月以降が3例、その間が3例、時期不明が2例であった。初回接種年齢の中央値は14.5(12~20)歳、症状発現年齢の中央値は15.5(12~20)歳であった。初回接種から発症までの期間の中央値は11(-12~71)か月であった。認められた症状は、頭痛が12例(50%)で最多で、次いで局在性疼痛が11例(46%)、めまいが7例(29%)であった。受診診療科数の平均は2.9(1~7)であった。その後、当院フォローアップとなったのが13例で、全て軽快や治癒に至った。【結論】ほとんどの症例が適切な診療科への受診、診断や対応により症状の軽快や治癒に至っている。クリニック等で接種することも多く、接種医療機関のみで副反応が疑われる症例に対応するには限界がある。副反応支援センターの存在は、医療従事者や接種者へのより安心して接種へつながるのではと考えられる。HPVワクチン接種の拡充に向け、当センターに関して今後も情報提供を行っていく。

20日(土)
日本語ポスター**P-24-4** A自治体におけるHPVワクチン接種の現状と普及への取り組み宮崎県立看護大専門基礎分野¹, 宮崎大²川越靖之¹, 藤崎 碧², 魏 馨予², 平田 徹², 土井宏太郎², 桂木真司²

【目的】A県の子宮頸がんの罹患率は高く、がん検診率の向上に加え一次予防であるヒトパピローマウイルス (HPV) ワクチン(以下、ワクチン)の普及が急がれている。A県B市において接種率の向上を目的とし2023年度から中学校での保護者を含めた個別の説明会を開始した。【方法】ワクチン接種率向上のためB市においては全27の中学校で1年生を中心とした生徒およびその保護者を対象とし、医師によるワクチン説明会を実施している。2023年の6~9月に15校で説明会を行い、会の終了後にアンケート調査を実施し説明会に出席した中学生2015人、保護者324人から回答があり分析を行った。【成績】ワクチンを接種済であったのは受講した生徒のうち4.1%(84/2015)であった。接種済の生徒(n=84)を除き以下検討した。説明前からワクチンの存在を知っていたのは生徒のうち43.7%(882/1931)、保護者は89.5%(273/305)であり生徒自身への周知がより必要と思われた。説明会で理解が深まった~やや深まったと答えたのは生徒93.7%(1811/1931)、保護者96.7%(295/305)であった。一方で説明の後に接種したいと思うと答えた生徒は50.5%(976/1931)、させたいと思う保護者は68.2%(208/305)に留まり、理解は深まったものの接種行動に繋がらない可能性が示唆された。約7割の保護者が長期休暇期間での接種を希望し、接種しやすい環境の整備を求めている。【結論】医師から生徒および保護者へワクチンに関し説明することで理解は深まるものの接種を希望するかどうか迷う傾向を認め、継続的な情報提供が必要と考えられた。また長期休暇前の接種に関するプロモーション活動がより有効な可能性がある。

P-24-5 医学部新入生女子のHPVワクチン接種状況の13年間の経年的変化国家公務員共済組合連合会横浜南共済病院¹, 横浜市立大²古野敦子¹, 助川明子², 水島大一², 鈴木幸雄², 宮城悦子²

【目的】2009年12月にHPV2価ワクチンが日本で発売され10年以上が経過し、この間、ワクチンを取り巻く社会情勢は大きく変化した。HPVワクチン接種率の変化を明らかにすることを目的に経年的にアンケート調査を行った。【方法】2011年度から2023年度にY大学医学部医学科・看護学科の女子学生を対象としHPVワクチン認知度や性教育の内容などについて無記名でのアンケート調査を行った。また2022年4月のHPVワクチン接種積極的勧奨再開とキャッチアップ接種導入前後である2021-2023年度を詳細に検討した。【成績】研究に参加した医学部新入生女子は102-143人で、年齢中央値は18歳であった。2011-2023年度のHPVワクチン接種率はワクチン発売直後の自費接種のみであった2011、2012年に比べ、緊急促進事業で公費助成が使用できるようになった2013年以降は上昇した。2014年が69.8%と最も高率であるが、その後やや減少していた。定期接種になったものの2か月後の2013年6月には積極的勧奨中止となり、接種率は急激に減少し、2021年は5.4%であった。2022年の接種率は7.5%とやや上昇にとどまったが2023年の接種率は35.3%と急激に上昇した。HPVワクチン接種率は2021-2023年度のカイ二乗検定を用いたトレンド解析において $p<0.001$ と有意差をもって上昇した。ワクチン認知度も2021年44.6%、2022年65.8%、2023年81.3%と同様に有意差をもって上昇した。 $(p<0.001)$ 【結論】HPVワクチンキャッチアップ接種導入となって1年が経過し、徐々に接種率上昇が見受けられる。子宮頸がん予防のためにも行政・教育・医療機関のはたらきかけを継続していくことが重要と考える。

P-24-6 子宮頸部細胞診における異型腺細胞症例の臨床的検討

友愛医療センター

正本真利子, 金子侑暉, 延壽桃子, 山田真司, 大城大介, 大久保奈緒, 野坂舞子, 比嘉 健, 大橋容子, 前濱俊之

【目的】子宮頸部異型腺細胞診 (AGC) は腺に異型を認めるが, 明らかな上皮内腺癌 (AIS) や浸潤性腺癌の特徴のないものと定義されている。頻度は0.1-0.8%と報告されており, その追跡調査では10-40%に異常病変がみられる。AGCの最終診断は子宮頸部だけでなく体部の病変も関連しており, 慎重な対応が必要である。今回, 当院にてAGCと判定された症例についてHPV検査も含めた臨床的解析を行った。【方法】2015年10月から2022年8月までにAGCと判定された61例について組織学的診断とHPV検査を施行した41例の解析も行った。【成績】AGC症例58例の年齢中央値は47歳(29-72歳)であった。最終的な臨床診断の結果は, 浸潤癌15例(頸部腺癌3例, 子宮体部類内膜腺癌13例), 子宮頸部上皮内病変22例(CIN1-3:18例, AIS:3例, CIN3+AIS:1例), 良性所見16例, その他4例(子宮内膜異型増殖症2例, 子宮内膜増殖症1例, LEGH1例)であった。子宮頸部病変(上皮内腫瘍+浸潤癌)のHPV陽性率は68%(17/25)であったが, AISと頸部腺癌に限定すると100%(7/7)であり, HPV型はすべて16型あるいは18型であった。【結論】子宮頸部細胞診にてAGCと判定された症例の26.2%(16/61)が浸潤癌の診断となり, その中では子宮体部類内膜癌の頻度が高かった。子宮頸部病変の頻度は40.1%(25/61)であり, HPV陽性率は68%であった。AISと頸部腺癌に限定するとHPV陽性率は100%であった。AGCの管理においてはHPV検査を導入することが子宮頸部病変の診断に有用と思われた。同様に, 体部病変の精査も重要である。

P-24-7 子宮頸がん検診へのHPV検査導入の課題—併用検診導入の経験から—

佐賀大

栗原麻希子, 秀島未紗子, 大石将平, 瓜生泰恵, 吉武薫子, 池田正純, 大隈良一, 徳永真梨子, 福田亜紗子, 梅崎 靖, 奥川 馨, 横山正俊

【目的】HPV検査併用検診プログラム導入の経験から, 子宮頸がん検診にHPV検査を導入した現況及び導入に伴う問題点について報告する。【方法】S市において2011年から2019年に子宮頸部細胞診とHPV検査の併用検診を受けた35,525人を対象とし, NILM/hrHPV+の検出率及びその後の経過について検討した。2016年までは細胞診は従来法で行い, 2017年以降は液状化細胞診(LBC)に変更した。2017年からS県では子宮頸がん検診の広域化を開始し, さらに2019年から全県下で30-44歳のHPV検査の無料化事業を導入した。NILM/hrHPV+例への1年後の個別通知による受診勧奨に加え, 未受診者への再勧奨も行い, 検診受診率の変化を検討した。また, 検診の広域化の効果についても検討した。【成績】NILM/hrHPV+は7.4%(2,612/35,525)で, 1年後の追跡精検で59.7%(630/1,055)が2年連続hrHPV+であり精密検査を行った。そのうち19.4%(205/1,055)にCINが, 3.5%(37/1,055)にCIN2以上の病変が検出された。受診勧奨のみでは1年後の受診率は42.6%(1,096/2,612)に過ぎなかったが, 受診勧奨及び未受診者への再勧奨を追加することにより1年後の受診率は60.8%へと上昇した。検診の広域化により受診者数の増加も認められた。【結論】HPV検査導入において, LBCの導入, 検診の広域化, 1年後の再受診勧奨を行うことは有用と考えられるが, さらなる受診率増加や未受診者管理のための適切なシステムの構築が必要と考えられる。

P-24-8 腹腔鏡下子宮全摘術後に発症した *Mycoplasma hominis* 腹膜炎の一例

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【症例】患者は46歳女性。両側内膜症性嚢胞, 子宮筋腫に対して腹腔鏡下子宮全摘術, 両側付属器切除術を施行した。術前抗生薬にCMZを投与した。経過良好で術後4日目に退院となったが, その夜発熱と下腹部痛を認め, 術後5日目に術後腹膜炎の診断で再入院となった。CTでは腹膜炎所見と, 陰断端に3cm大の血腫を認め, 同部位ドレナージ施行するも膿の排出はなく, ドレナージ液を細菌培養に提出した。抗生薬ABPC/SBT静注を開始したが, 発熱, 下腹部痛, CRP優位の炎症反応高値は継続し, 再入院後1週間後のCTでは腹水, 腹膜炎所見の増悪を認めた。血液, 尿, 陰分泌物の培養で起炎菌同定困難であったが, 陰断端ドレナージ液の長期培養でわずかにコロニー形成が認められた。グラム染色では菌体は同定できず, 質量分析(MALDI-TOF)を用いて *Mycoplasma hominis* (以下 *M. hominis*) が同定された。再入院後12日目からDOXY内服を開始し, 速やかに解熱と腹痛, 腹膜炎所見の改善が見られた。【考察】*M. hominis* は正常女性の10%程度が保菌する生殖器の常在菌の一種である。産婦人科系術後感染の起炎菌として症例報告が散見されるが, グラム染色や一般培養で菌の同定ができず, 診断に苦慮している報告が多い。当院では質量分析が導入されており, *M. hominis* 感染が診断可能であった。しかし, 一般的には同菌の感染を積極的に疑ってPCRを使用しなければ診断が困難である。治療は, β -lactum系, EM, AZM耐性を持つことが多く, TC系, CLDM, CPF, LVFX等を用いる必要がある。【結論】産婦人科系術後感染において, グラム染色で菌同定できず, β -lactum系抗生薬が無効である場合, *M. hominis* 感染を積極的に疑うことが重要である。

P-24-9 ロボット支援下子宮全摘出後に *Mycoplasma hominis* による多発皮下膿瘍を認めた一例

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ロボット支援下子宮全摘出術後に *Mycoplasma hominis* による陰断端膿瘍及び多発皮下膿瘍を経験したので報告する。症例は49歳, 1妊1産, 既往歴に虫垂炎手術と腎臓結石があった。子宮筋腫による過多月経を認め, ロボット支援下子宮全摘出術を施行した。術後3日目に38°C 台の発熱と白血球11,530/μL, CRP 15.24 mg/dl と上昇を認めた。造影CTで骨盤底に液貯留, 辺縁リング状の濃染を認め膿瘍形成が疑われ, タゾバクタム・ピペラシリン水和物 4.5g 6時間毎を開始した。術後12日目に改善傾向を認めていた白血球の再上昇を認め, 造影CTを施行し骨盤膿瘍は縮小したが腹壁下(ポート部)に多発膿瘍を認めた。膿瘍の穿刺吸引ではグラム染色で明らかな細菌を認めず, 白血球を多数認めた。術後15日目に陰断端離開が起こり陰断端縫合を行った。婦人科の原因不明の膿瘍として *Mycoplasma* 属, *Ureaplasma* 属菌の関与の可能性があり膿瘍の穿刺液を PPLO 培地で培養したところコロニー形成を認め, 質量分析検査で *Mycoplasma hominis* が同定された。その後, スルバクタムナトリウム・アンピシリンナトリウム 3g 6時間毎+ドキシサイクリン内服 200mg/日を開始し, 再手術後9日目に全身状態改善しアモキシシリン・クラブラン酸+アモキシシリンとドキシサイクリン内服で退院とした。現在, 再燃なく外来でフォロー中である。*Mycoplasma hominis* は *Mycoplasma* 属の一種で, 女性泌尿生殖器の常在菌である。マイコプラズマ専用培地を用いた培養検査や, ぬぐい液や穿刺液でPCR検査も可能である。婦人科術後骨盤内膿瘍は一定の頻度で認めるが, 通常の抗菌薬に抵抗性である場合は原因として *Mycoplasma hominis* も鑑別に挙げる必要があると考えられた。

P-25-1 不妊症例におけるナノポアシーケンサーを使った子宮内・腔内細菌叢解析

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【目的】全細菌が有する16SリボソームRNA遺伝子(16S)のDNA配列を解析することで細菌組成解析ができ, ヒト常在細菌叢解析で頻用されている。子宮内・腔内細菌叢は, 着床不全や慢性子宮内膜炎との関連が多く報告されているが, 不明な点が多い。他方, 圧倒的な迅速性を有するナノポアシーケンサー(ナノポア)は, 近年正確性も向上したため, 臨床応用が期待されている。すでに周産期領域では実臨床での応用が始まっており, 生殖補助医療への活用も期待されている。そこで, ナノポアを使って子宮内・腔内細菌組成解析を行い, 子宮内膜炎とdysbiosisとの関連を調べることを目的とした。【方法】2022年6月から2023年7月までの間1施設で, 不妊症を主訴に外来受診し, 子宮内細菌叢検査と子宮内膜炎検査を希望された26例から, 腔分泌物と子宮内組織を採取した。DNA抽出し, ナノポア(MinION Mk1C)を使って16Sのアンプリコンシーケンスを行い, 属・種レベルの細菌組成解析を実施した。子宮内膜のCD138陽性を子宮内膜炎と定義した。【成績】2時間のシーケンスで, 25例(96%)で解析に十分な5000リード以上のデータを取得でき, 判定不能な症例はなかった。属レベルの子宮内・腔内細菌叢解析では, 既存の子宮内細菌叢検査の結果と概ね一致した(感度78%, 特異度77-82%)。子宮・腔内細菌叢解析で陽性だった場合, 既存の子宮内細菌叢検査またはCD138検査で陽性となる確率はそれぞれ78・89%であった。【結論】ナノポアを使って子宮内や腔内の細菌叢解析を属・種レベルで実施し, 既存の検査と同等もしくはそれ以上の解析結果を得ることができた。今後, 症例数を増やしてさらなる詳細な検討を行う予定である。

P-25-2 ART困難症例において卵子成熟に関わるTUBB8に病的バリエントを認めた一例

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【目的】生殖補助医療(ART)困難症例の中でも卵子成熟障害症例の対応には苦慮する。今回, 12回の採卵で成熟卵子をほとんど得られず受精卵の全く得られなかった症例に対し遺伝学的な原因検索を行った。【方法】全エクソーム解析を行い卵成熟および受精に関わる遺伝子TUBB8に病的バリエントの有無を検索した。【成績】症例は27歳0妊0産。当院初診時25歳, AMH: 3.43ng/mL。前医の治療は採卵を2周期, 総採卵数23個, 受精卵0個であった。当院紹介後に採卵を12周期実施, 総採卵数126個, 成熟卵子24個(成熟率19%), 受精卵0個であった。卵巣刺激法はPPOS, Long法, 自然周期およびIVMを実施した。受精方法は一般体外受精, 顕微授精, Caイオンファ処理およびODO-ICSIを試みた。今後の治療方針決定のため不妊原因探索を目的とした遺伝学的検査を提案, 夫婦に遺伝カウンセリングの後, インフォームドコンセントを得て全エクソーム解析を実施した。解析の結果, 卵成熟に関わるTUBB8にミスセンスバリエント:c.1164G>A (p.Met388Ile)を認めた。なお, 本研究は遺伝学研究機関の臨床倫理委員会の承認を得ている。【結論】TUBB8は霊長類に特異的な遺伝子であり, 卵母細胞と初期胚で機能するが他の体細胞組織や精子形成には機能しない。そのためTUBB8の病的バリエントは男性の生殖機能に影響しないが, 女性では重症卵子成熟障害を発症し, 現時点では有効な治療法がなく生児獲得が望めない。患者の遺伝的な問題を明らかにすることは不妊治療の最後通告となる可能性があるため実施には慎重な対応が求められる。現在, 患者夫婦は第三者の配偶子を含めた治療も視野に入れ, 今後の治療を模索中である。

P-25-3 ヒト胚第一体細胞分裂では紡錘体形成が不安定であり、2細胞期での多核化の原因となる

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【目的】ヒト第一体細胞分裂は雌雄前核の融合に引き続き生ずる極めて動的なイベントである。その細胞生物学的な過程はヒト胚資料の調達困難も含め現在まで把握されていない。我々はヒト凍結融解2前核期胚23個を用いて雌雄ゲノムの融合および第一分裂紡錘体の形成および細胞分裂終了までのライブイメージングに成功した。ヒト生命の第一分裂に関するいくつかの知見を得たので報告する。【方法】受精卵の凍結保存中に治療を終結もしくは妊娠出産後に廃棄を希望し、研究利用に同意の得られた2前核期胚を融解して使用した。核および微小管に結合する蛍光標識プローブを用い、蛍光ライブイメージングを行った。23個のヒト凍結融解2前核期胚を第一あるいは第二分裂終了まで観察した。【成績】70%以上の胚(n=17/23)が2細胞期で多核を呈した。第一体細胞分裂紡錘体の形態には様々なバリエーションがあり、アスペクト比(縦横比)の低い紡錘体は、高い紡錘体と比較して2細胞段階で多核化する傾向を認めた。しかし、2細胞期で多核を有する胚の50%以上(n=4/8)が4細胞期では単核に修正された。また、マウスで報告されているゴノメリー(雌雄ゲノムが混合せずそれぞれの割球に分配される)がヒト第一分裂でも観察された(n=17/18)。【結論】ヒト第一分裂紡錘体は種々の形態を示し、縦横比が低い紡錘体が形成された胚では2細胞期で多核が生ずることが明らかになった。また、ゴノメリーがヒト第一分裂ではじめて観察された。ヒト生命の最初の体細胞分裂の過程が明らかになることで、タイムラプス胚発育動態観察やPGT-A等のART add ons技術のみならず、ヒト発生に関する今後の重要な基礎知見が得られると考える。

P-25-4 子宮移植への取り組み～ロボット支援ビッグドナー子宮採取術の試み～

昭和大

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【目的】子宮性不妊の女性にとって子宮移植は新たな生殖補助医療技術として期待される。ロボット手術は細かい血管の温存が可能であり、子宮移植の成功率が高く、海外ではドナーに対する子宮採取術にロボットを用いるケースが増加している。本学では開腹でビッグ子宮移植実験も試みているが、今回ヒトでの子宮採取術の前段階として、手術支援ロボットを用い、ビッグによるドナー子宮採取術を試みた。【方法】①月齢3か月、体重40kg、出産歴なし②月齢5歳5か月、体重39kg、出産歴ありの2頭のビッグを使用した。手術支援ロボットを用い、子宮動脈や卵巣動脈を確保し、子宮の血流に関連する子宮動脈は内腸骨動脈ごと、卵巣静脈は下大静脈の流入部で切断し、子宮グラフトを摘出する予定とした。安楽殺後にグラフトを開腹回収し、ヘパリン加生食で灌流し、グラフト内の血管が微小血栓などで閉塞していない事を確認した。【成績】いずれも子宮動脈は内腸骨動脈の分岐部、卵巣静脈は下大静脈の流入部で切断した。2頭目は左子宮静脈、左卵巣動脈の確保も行った。平均手術時間4時間24分、平均コンソール時間4時間2分。いずれも全身ヘパリン化の後、血管遮断10分後に安楽死を確認。12分後にグラフトを摘出、15分後にヘパリン加生食を用い子宮動脈から灌流を開始した。1頭目はグラフトが小さく、灌流が不可能であったが、2頭目は子宮動脈から注入したヘパリン加生食は卵巣静脈から流出し、灌流が良好であった。子宮全体が白色に変化したことを確認し実験終了とした。【結果】手術支援ロボットでのビッグドナー子宮採取術は可能であり、子宮グラフトは良好に灌流可能であった。今後再現性があるか確認が必要である。

P-25-5 Granulocyte colony-stimulating factor 皮下投与は前胞状卵胞の発育促進で卵巣予備力低下例のART胚発育と妊娠率を著しく増加する：前方視的無作為試験

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【目的】ART難治10例にGranulocyte colony-stimulating factor (G-CSF)を投与したところ、2か月後に3例が妊娠し、1例は45歳で排卵誘発剤なしに双胎だった。G-CSFは前胞状卵胞の発育を促進したと考え、倫理委員会承認、説明と同意のうえ、前方視的無作為試験(UMIN00013956)で、卵巣予備力低下症例に対し、G-CSF前投与により2周期後のART妊娠率改善とAMH増加を試みた。【方法】AMH<2ng/mL、42歳以下の卵巣予備力低下100症例を、G-CSF前投与群と対照群に振り分けた(各50例)。最初の2周期は外来治療し、その際、G-CSF群は各周期の高温初期に一回のみG-CSFを皮下注射した。次に両群ともlong法でART施行し、非妊娠例は凍結胚移植を継続した。血清AMHの変化も比較した。【成績】G-CSF前投与は、受精率、胚発育率、新鮮胚着床率を有意に増加した。新鮮胚移植による臨床と継続妊娠率(卵巣刺激あたり)は、G-CSF群で30%、26%、対照群で12%、10%と、ともにG-CSF群で有意に高かった。余剰胚の凍結保存可能例も、G-CSF群で有意に多かった。症例あたり累積出産率は、G-CSF群32%、対照群14%と、G-CSF群で有意に高かった(RR,2.8;95%CI,1.04-7.7)。産児は正常で、体重、出産週数、Apgar scoreも両群で差がなかった。年齢、day3FSH、AMH、G-CSF前投与のうち、年齢、G-CSF前投与のみが累積出産率と有意に相関した。またG-CSF前投与は有意に血清AMHを増加した。G-CSFによる有害事象はなかった。【結論】G-CSF前投与は卵巣予備力低下症例の胚発育およびART妊娠・出産率を著しく増加する。その機序は、前胞状卵胞の発育促進と示唆された。G-CSF前投与は、卵巣予備力低下に対する安全、容易で有効な新治療法である。

P-25-6 単一胚移植後の多胎妊娠のリスク因子と血中 estradiol との相関

加藤レディスクリニック

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【目的】単一胚移植が推奨されてから、日本における体外受精による多胎妊娠の頻度は3.2%まで低下し、単一胚移植では1.4%と報告されている。しかし単一胚移植であっても体外受精では一卵性双胎のリスクは増加し、周産期予後に重篤な影響を及ぼすことから、多胎のリスクを軽減する努力が必要である。このため我々は今回、単一胚移植後の多胎妊娠のリスク因子とその軽減の可能性について検討した。【方法】2014年から2018年の期間に当院で新鮮胚移植または凍結融解胚移植を施行した79,070周期を対象とした。移植周期では全て単一胚移植を行なった。【成績】79,070周期の移植周期に対して28,051例の子宮内妊娠(35.5%)を認め、多胎妊娠は279例(0.99%)で、Weinberg's differential ruleによる補正では単一胚移植後の多胎妊娠率は0.89%であった。多胎妊娠率は凍結胚盤胞移植の1.05%に比べ新鮮胚盤胞移植では2.65%と多かった(OR=2.81, 95% CI=1.56-5.10)。また多胎妊娠率は2日目分割胚移植の0.66%に比べ3日目分割胚移植では1.99%と多かった(OR=2.99, 95% CI=1.40-6.40)。凍結胚盤胞移植の移植当日のestradiol値 160.5 ± 95.8 pg/mlは新鮮胚盤胞移植の 170.8 ± 88.0 pg/mlに比べ低く、移植当日のestradiol値が60 pg/ml未満の周期の胚盤胞移植では、60 pg/ml以上の周期と比較して有意に多胎妊娠のリスクが低下した(OR=0.36, CI=0.15-0.88)。【結論】多胎妊娠は、分割胚移植では3日目移植より2日目移植、胚盤胞移植では新鮮胚移植より凍結胚移植で減少した。移植当日の血中estradiol値が低い周期では多胎リスクが低下する可能性が示唆された。

P-25-7 慢性子宮内膜炎の診断・治療法についての実態調査：IZANAMI project

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【目的】慢性子宮内膜炎(Chronic Endometritis; CE)は子宮内膜の持続的な炎症疾患であり、反復着床不全の女性に高率に認める。診断基準は生検した子宮内膜組織のCD138免疫染色が基本だが、明確には定まっておらず、本邦での診断法および治療法の実態は不明である。本研究ではCEの診断および治療法について本邦の実態を調査することを目的とした。【方法】本研究は生殖・内分泌委員会小委員会「生殖補助医療技術における技術導入の実態のための小委員会」が行った調査研究(IZANAMI project)の一環として実施した。ART実施施設を対象に2021年12月から2022年2月にかけてアンケート調査を実施し、CEの診断および治療法について情報収集した。【成績】調査に回答した437施設の内、339施設(77.6%)においてCEに関する診断および治療を取り入れていた。診断法として子宮内膜組織のCD138免疫染色を用いていた施設は214施設(63.1%)であった。一方、診断の補助に子宮鏡を用いている施設は241施設(71.1%)であり、子宮内マイクロバイオーム検査(218施設, 64.3%)および子宮内細菌培養検査(150施設, 44.3%)が続いた。CE診断のためのCD138陽性細胞のカットオフ値は、400倍顕微鏡下20視野あたり3-5個が最多(50.0%)であり、6-10個(26.2%)、11個以上(8.4%)が続いた。治療の第一選択は、ドキシサイクリンの投与(210施設, 61.9%)が最多であり、子宮内マイクロバイオーム検査で推奨される抗菌薬の投与(51施設, 15.0%)が続いた。【結論】CEの診断は子宮内膜組織のCD138免疫染色を用いていた施設が多かったが、その詳細はさまざまであり、保険収載に向け診断法および治療法の確立が重要であると考えられる。

P-25-8 MD-TESE 不成功夫婦に対する生殖心理カウンセリングがライフコース選択に与える影響

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【目的】非閉塞性無精子症と診断され顕微鏡下精巣内精子採取術で精子獲得できなかった患者夫婦を対象として、専用に開発された半構造化された生殖心理カウンセリングを受けた夫婦は、受けなかった夫婦に比べてライフコースの選択肢の1つである精子提供による生殖補助医療施設への受診を希望するか比較検討することを目的とした。【方法】アウトカム変数として、精巣内精子採取術日から10か月(300日)以内に精子提供による生殖補助医療の実施施設への紹介状作成日までの期間を観察した。【成績】カウンセリング群は非カウンセリング群に比べて累積紹介状未作成率が低かった。また、男性患者の染色体検査結果、パートナーの年齢、初診までの不妊期間が同じとき、この後に紹介状を作成する割合は2.931倍であった。【結論】非閉塞性無精子症と診断され顕微鏡下精巣内精子採取術で精子獲得できなかった場合、専用に開発された半構造化された生殖心理カウンセリングを患者夫婦に実施するとライフコースの選択を比較的早く検討、選択できる効果があることがわかった。非閉塞性無精子症と診断され顕微鏡下精巣内精子採取術で精子獲得できなかった場合に心理カウンセリングを提供することは、患者夫婦にとって夫婦の血のつながりのある子どもを持ってない悲しみのケアと今後のライフコース選択について夫婦で取り組む機会として有効である可能性が示唆された。

P-25-9 従来穿刺針 (20 ゲージ) と太さが異なる穿刺針 (20/17 ゲージ) による採卵成績の比較

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【目的】採卵には高い回収率, 速さ, 低侵襲性が求められ, 穿刺針の選択は重要である。吸引時間の短縮には 17 ゲージ (G) の太い穿刺針が, 出血や痛みの軽減には 21G の細い穿刺針が望ましい。当院では以前, 20 ゲージ (G) のシングルルーメン穿刺針を使用していたが, 近年開発された, 先端が細く (20G) 本体が太い (17G) シングルルーメン穿刺針を使用したため, 両穿刺針の臨床成績を比較した。【方法】2019 年から 2023 年までに当院で採卵をした患者で, 20G 穿刺針を使用した 189 例 (A 群), 20/17G 穿刺針を使用した 105 例 (B 群) を対象とした。年齢, 穿刺卵胞数, 獲得卵子数, 受精卵数, 採卵時間, 麻酔追加の有無を比較した。【成績】A 群, B 群において, 平均値と標準偏差はそれぞれ, 年齢で 40.4 ± 4.0 歳, 39.8 ± 4.38 歳, 穿刺卵胞数で 7.97 ± 7.07 個, 10.7 ± 8.44 個, 獲得卵子数で 4.51 ± 4.69 個, 6.66 ± 6.21 個, 受精数で 2.94 ± 3.68 個, 4.08 ± 4.46 個, 採卵時間で 9.86 ± 5.14 分, 7.79 ± 3.75 分, 麻酔追加の有無で 39.1%, 42.9% であった。穿刺卵胞数, 獲得卵子数, 受精卵数は B 群で有意に多く, 採卵時間は B 群で有意に短かった ($p < 0.05$)。年齢および麻酔追加の有無には有意差を認めなかった。なお, 穿刺卵胞数あたりの獲得卵子数 (回収率) は, A 群で 56.9%, B 群で 62.2% と B 群で有意に高かった ($p < 0.05$)。【結論】先端は細いが本体が太い穿刺針を使用した B 群では先端が同一の A 群と比較し, 穿刺卵胞数が多いにも関わらず, 採卵時間は平均で約 2 分短縮していた。また, B 群では A 群と比較し回収率も高かった。20G のような細い穿刺針を選択する場合, 本体が太くなった穿刺針 (20/17G) の使用は, 有用であると考えた。

P-25-10 生殖補助医療で出生した児の 12 歳時の体格は, 不妊症の親から出生した自然妊娠児と異なるのか〜日本で出生した生殖補助医療出生児の長期予後調査より〜

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【目的】生殖補助医療 (ART) で出生した児の出生体重は自然妊娠児と差があるが, 長期的な体格の違いについては結論が出ない。今回, 我々は日本で出生した ART 出生児の 12 歳時での体格を, 不妊症の親から出生した自然妊娠児と比較した。【方法】日本で 2008~2009 年に ART で出生した児の前向きコホート研究に参加した症例の中から, 12 歳まで追跡可能であった早産, 過期産も含む単胎児を対象とした。この内不妊症の親から出生した自然妊娠児 (非 ART 出生児群) を対照群とし, 新鮮胚移植児と凍結融解胚移植児を男女別に比較した。評価項目は身長, 体重で, 統計解析は重回帰分析を用いた (有意水準 5%)。【成績】解析対象者は, 非 ART 出生児 101 症例, 新鮮胚移植児 283 症例, 凍結融解胚移植児 350 症例であった。女児では, 身長, 体重ともに群間差を認めなかった。男児では, 身長に群間差は認めなかったが, 体重は交絡因子 (出産歴, 母親年齢, 親の体格) の調整の有無に関わらず, 新鮮胚移植児は非 ART 出生児より 3.5 キロ重かった ($p=0.023$)。また, 新鮮胚移植児と凍結融解胚移植児を初期胚移植群と胚盤胞移植群にわけ, 非 ART 出生児と比較した 5 群比較の解析では新鮮胚初期胚移植群で非 ART 出生児より体重が有意に 2.6 キロ重い結果であった ($p=0.017$)。【結論】12 歳時の体格は, 男児の新鮮胚移植群では非 ART 出生児群より有意に重かった。また新鮮胚初期胚移植群でも同様の傾向であった。第二次性徴の影響も考慮する必要がある。今後より大規模な検討が必要であると考えられた。

P-25-11 慢性子宮内膜炎疑い症例に対し先進医療技術: 子宮内細菌叢検査 (EMMA/ALICE) を施行した結果とその後の妊娠予後: 前方視的多施設コホート研究

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【目的】2022 年 4 月より先進医療技術に認定された子宮内細菌叢検査 (EMMA/ALICE) は慢性子宮内膜炎 (CE) を疑う症例に対し子宮内に存在する細菌の 16S rRNA 遺伝子配列決定に基づく次世代シーケンサー (NGS) 解析を行い, 感染の起炎菌となる細菌の有無を検査する目的で行われる。今回我々は, CE 疑い症例に対し子宮内細菌叢を施行し, 起炎菌との関連と検査後の妊娠予後について前方視的多施設研究を行った結果について報告する。【方法】2022 年 4 月から 2023 年 7 月までの期間, JISART 登録のある 12 施設において CE を疑う症例に対し子宮内細菌叢検査を施行した症例の結果と検査後の妊娠予後について追跡した前方視的コホート研究である。検討対象は検査施行同意時に研究への参加も同意が得られた 42 歳以下の患者とした。第一の検討項目を細菌叢正常群と抗菌薬が推奨される病原菌検出群の治療介入後の継続妊娠率とし, 統計学的検討を行い $p < 0.05$ を有意差ありとした。【成績】同期間に 527 名が本検査を受け, 抗菌薬が推奨される状態であった患者は全体の 26.2% ($n=138$) であり, 検出された細菌の上位 2 種は Gardnerella と Atopobium であった。一方, 子宮内細菌叢が良好であり治療介入の必要がない正常群は 25.6% ($n=135$) であった。同期間に妊娠予後が判明した 295 症例の中で, 検査後に施行した胚移植 4 回以内の累積妊娠率は着床率 87.8% ($n=259$), 臨床的妊娠率は 61.7% ($n=182$) であった。結果正常群と異常群の妊娠継続率は 53.5% ($n=54$), 56.8% ($n=25$) であり両群間での妊娠成績に有意差はなかった ($P=0.721$)。【結論】子宮内細菌叢検査により CE を疑う症例の起炎菌に基づく抗菌薬が検査後の良好な妊娠成績に寄与した可能性が示唆される。

P-25-12 多機関共同研究による卵巣予備能低下症例の不孕治療成績

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【目的】卵巣予備能低下症例の生殖補助医療成績について1採卵周期あたりの累積妊娠率を含め検討した。【方法】18施設の多機関共同研究により症例を集積した。2021年1月1日から12月31日までに採卵をおこなった症例（AMH<1.1ng/mL, 20歳以上40歳以下）を対象（同一症例については対象期間の初回採卵症例のみ）とし、胚移植結果については2022年10月31日までの治療周期を対象とした。【成績】609症例、採卵609周期が解析対象となった。うち新鮮胚移植を実施したものが45周期、全胚凍結されたものが449周期、卵もしくは良好胚が得られず胚移植にいたらなかった周期が115周期であった。対象患者の年齢（歳）、FSH（mIU/mL）、AMH（ng/mL）の平均±SDは、37.01±3.16, 11.51±7.16, 0.64±0.32であった。移植周期あたりの妊娠率は36.2%、採卵周期あたりの累積妊娠率は36.3%であった。年齢層別の解析では、20-29歳、30-34歳、35-39歳、40-41歳の移植あたりの妊娠率は、それぞれ47.4%、37.6%、37.9%、29.0%であった。【結論】AMH低値であっても移植あたりの妊娠率は年齢相応のものが見込めるが、1採卵周期の累積妊娠率も移植あたりの妊娠率と同等であり、採卵数が少なく胚移植にいたらなかった症例が影響していることが示唆された。このことは低卵巣予備能の生殖補助医療にあたって考慮すべき点であると考えられる。

P-25-13 凍結融解後の胚盤胞再拡張率における胚質評価の動態的指標としての有用性

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【目的】凍結融解後の胚盤胞再拡張率における胚質評価の動態的指標としての有用性を明らかにすることを目的とした。【方法】2017年1月より2022年12月のPGT, PRP, ERA後周期を除外した凍結融解胚盤胞移植周期を対象として後方視的観察研究を実施した。Gardner分類が3あるいは4の胚を対象として、ROC曲線を用いて臨床妊娠に対する再拡張率のカットオフ（CF）値を算出し、CF値以上を再拡張群、CF値未満を収縮群とした。再拡張率は融解後9-11分の間に最も胚が拡張した時点の胚実質面積/透明帯内側面積の比と定義した。収縮群、再拡張群、孵化群（凍結融解後のGardner分類が5.6）のART成績を比較した。次に再拡張率を含めた臨床妊娠に影響を与える可能性のある因子についてロジスティック回帰分析を行い、それぞれ調整オッズ比（aOR）を算出した。本研究は当院の倫理委員会の承認下で行った（承認番号M22266）。【成績】対象は再拡張群433周期、収縮群360周期（再拡張率CF値90.2% [ROC-AUC 0.63, p<0.05]）、孵化群210周期であった。3群の臨床妊娠率は41.5%/22.7%/41.3%であり、再拡張群、孵化群と収縮群に有意差を認めた（p<0.01）。流産率は30.0%/37.8%/30.9%（p=0.42）であった。ロジスティック回帰分析で統計学的有意な臨床妊娠に対する予測因子（aOR [95%信頼区間]）は胚盤胞の凍結融解後の再拡張率（2.0 [1.4-2.9]）母体年齢（0.90 [0.86-0.94]）、内細胞塊のグレード（1.55 [1.1-2.2]）、栄養外細胞のグレード（1.53 [1.1-2.1]）であった。【結論】胚盤胞の凍結融解後の再拡張不良はART成績へ有意に負の影響を与えた。再拡張率は胚の質を評価する客観的な動態的指標であることが明らかになった。

P-25-14 反復着床不全に対するERA検査の有用性

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【目的】本研究は子宮内膜の着床の窓（window of implantation）を特定する子宮内膜着床能検査（Endometrial Receptivity Analysis ; ERA[®]）の反復着床不全（Repeated implantation failure ; RIF）に対する有用性を明らかにすることを目的とした。【方法】2017年6月から2022年12月に2回の良好胚盤胞移植（Gardner分類で3BB以上）で妊娠不成立であったRIF患者において、ERA検査結果に基づき施行したホルモン補充下凍結融解良好胚盤胞移植（HR-FET）周期（ERA群）とERA検査を未実施である患者の3回目以降のHR-FET周期（non-ERA群）のART成績を後方視的に比較した。PRP, PGT-A, 2個胚移植、凍結胚が融解後の移植直前に収縮状態であった移植周期を除外した。本研究は当院の倫理委員会の承認下で行った。【成績】対象はERA群60例（112周期）、non-ERA群108症例（168周期）であった。年齢、BMI、血清ホルモン基礎値、血清AMH値は両群間に有意差を認めなかった。ERA群とnon-ERA群の着床率は41.0%/50.5%、臨床妊娠率は23.4%/36.3%、継続妊娠率は16.0%/22.6%、流産率は45.5%/37.7%であり、いずれも有意差を認めなかった。ERA群のreceptive群とnon-receptive群の着床率は37.5%/50.0%、臨床妊娠率は27.5%/34.3%、継続妊娠率は15.0%/18.7%、流産率は45.4%/45.4%であり、いずれも有意差を認めなかった。【結論】本研究では2回の良好胚盤胞移植で妊娠が成立しなかったRIF患者において、ERA検査結果に基づく胚移植はART成績を改善させなかった。形態学的良好胚盤胞の反復不成功をもってRIFと判断しERAを実施することの妥当性の検討が必要であると考えられ、今後正倍数性胚を対象とした検討が重要である。

P-26-1 帝王切開時所見からみた子宮内膜症と胎盤位置異常の関係について

日本医大

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【目的】子宮内膜症と前置胎盤の関連について多数の報告があるが、子宮内膜症の診断基準が明確でない。また子宮内膜症の術後症例で検討したものも多く、妊娠時子宮内膜症の合併の有無については言及されていない。そこで今回帝王切開時の腹腔内所見で子宮内膜症病変を確認した症例を対象とし、子宮内膜症と胎盤位置異常との関係について検討した。【方法】対象は2015年1月から2022年12月までに当院で帝王切開術した2357例のうち、帝王切開時に子宮内膜症病変を認めた症例とした。妊娠12週未満時の子宮全体像が記録にないもの、多胎妊娠を除外した。これらを生子宮内膜症合併妊娠とし、胎盤位置が正常であった群(normal (N) 群)と、胎盤位置異常を認めた群(malposition (M) 群)とに分け、妊娠初期時の子宮後屈の有無、帝王切開時の子宮後壁癒着の有無、胎盤の後壁付着の有無について後方視的にケースコントロール研究を行った。【成績】子宮内膜症合併妊娠は176例であり、N群は144例、M群は32例だった。子宮後屈かつ胎盤後壁付着症例はN群で4例(2.8%)、M群で5例(15.6%)とM群で有意に多く(OR 6.48; 95%CI: 1.63-25.71)、後壁癒着ありかつ胎盤後壁付着症例はN群で3例(2.1%)、M群で11例(34.4%)とM群で有意に多かった(OR 24.62; 95%CI: 6.34-95.58)。また子宮後屈かつ後壁癒着ありで胎盤後壁付着症例はN群で1例(0.7%)、M群で7例(21.9%)とより有意な差を認めた(OR 40.04; 95%CI: 4.72-339.62)。【結論】妊娠初期に子宮が後屈であり、子宮内膜症による子宮後壁癒着を認め、胎盤が後壁付着であるときに胎盤位置異常が発症する関連性が、子宮内膜症を帝王切開時の所見で診断した立場からも示唆された。

P-26-2 産科出血に対する治療的子宮全摘術の有用性；DPC データベースを用いた観察研究

埼玉医大総合医療センター

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【目的】産科出血は妊産婦死亡の主要な原因のひとつであり、播種性血管内凝固によりしばしば止血が困難となる。産科出血に対する治療は、輸液や輸血等の内科的治療と併行して、外科的治療による止血を要することも多い。外科的止血術にはバルーンタンポナーデ、子宮動脈塞栓(uterine artery embolization: UAE)、開腹止血術、そして開腹子宮全摘術があり、患者の容態や出血源を考慮して治療法が選択される。特に、子宮全摘術は最も手術侵襲が大きいが、救命目的に施行されることがある。産科出血に対する子宮全摘術についての研究は重要だが、治療目的に行われる子宮全摘術は、手術適応について一定のコンセンサスは存在せず、医療施設毎のマニュアルや、施設基準により手術適応を決めていると考えられる。各施設での実施件数も極めて少なく、臨床研究の報告は極めて少ない。【方法】2020年4月から2022年3月までの、Diagnosis Procedure Combination (DPC) データベースを用いた観察研究を行った。産科出血患者を抽出し、子宮全摘施行群と未施行群に分類した上で、主要評価項目である死亡率を比較した。【成績】計78,426例の産科出血患者が抽出され、そのうち615例(0.78%)で子宮全摘が行われた。死亡は子宮全摘施行群と未施行群で3/615 vs 9/77,811例 vs (487.8/10万 vs 11.6/10万, $p < 0.05$)であり、子宮全摘実施群で有意に死亡率が高かった。患者の重症度を出血量、年齢、原因疾患等で調整した後の感度分析解析でも、子宮全摘施行群で有意に死亡率が高かった。($p < 0.05$)【結論】産科出血に対する治療的な子宮全摘術を行った群は、子宮全摘を行わなかった群と比較して死亡率が高かった。

P-26-3 当院で経験した帝王切開癒着部妊娠に対してメソトレキセートの全身投与を行った9症例についての検討

順天堂大附属静岡病院

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【目的】帝王切開癒着部妊娠は大量出血や子宮破裂のリスクがあり、早期診断・治療が重要である。治療には手術療法、メソトレキセート(MTX)全身投与または局所投与、子宮動脈塞栓術などがあるが、MTXの全身投与は低侵襲で、妊孕性の温存も可能である。今回2016年から2023年に当院で経験したMTX全身投与を行った9症例について、MTXの全身投与の有効性及び安全性についての検討を行った。【方法】2016年から2023年の期間に帝王切開癒着部妊娠と診断され、子宮温存希望があり、MTX全身投与を施行した9例を後方視的に検討した。当院のプロトコルに基づきMTX 50 mg/bodyの単回もしくは複数回筋肉内投与を行った。【成績】9症例のうち6症例(67%)はMTX全身投与のみで病変の消失を認めた。うち3症例はMTX複数回投与(3~5コース)を要した。単回投与と複数回投与におけるhCGの中央値はそれぞれ9980mIU/ml (4397-30845)、23782 mIU/ml (9110-24334)であった。MTX全身投与後、追加治療が必要となった症例は3症例(単回2例、複数回1例)で、すべて子宮内容除去術を行った。多量出血により子宮動脈塞栓術及び子宮摘出を要した症例や輸血を必要とした症例、MTXによる骨髄抑制等の有害事象を認めた症例はなかった。病変消失までの日数の中央値は単回単独で165日、複数回単独で148.5日であった。2例(22%)で治療後に妊娠成立し、それぞれ37週、38週で帝王切開分娩となった。【結論】本検討では、MTX全身投与による帝王切開癒着部妊娠治療の高い有効性と安全性が示された。診断時hCGがより低値な程、単回投与で治療完遂できる可能性が高いが、単回投与と複数回投与のいずれも病変消失までおよそ5か月程度の期間を要した。

P-26-4 帝王切開後創部に胎盤付着あり，妊娠16週で子宮内胎児死亡に至った一例

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帝王切開創部にかかる前置胎盤症例は周産期リスクが高いが，妊娠12週以降に子宮内胎児死亡（Intrauterine Fetal Death：IUFD）となった場合の報告は少なく，管理方法は定まっていない．今回我々は前回切開創に胎盤が付き，前置癒着胎盤が疑われた症例において，IUFDに至った一例を経験したので報告する．症例は36歳G2P1，前回妊娠時は骨盤位のため帝王切開となっていた．既往歴なし．体外受精で妊娠成立し，近医で管理されていた．妊娠16週1日に胎児発育不全精査のため当科紹介され，その際IUFDを認めた．胎盤は前壁付着で下縁が内子宮口に接しており，前回の帝王切開創と思われる部分では血流が豊富であり癒着胎盤が疑われた．その時点で児娩出処置は困難と思われるため待機的療法の方針とした．2か月後には内子宮口付近の胎盤は自然退縮し剝離していたが，癒着が疑われる部位は豊富な血流を維持していた．少量の性器出血を認めるのみで感染徴候はなく経過していたが，フィブリノーゲンが緩徐に低下しており，子宮動脈塞栓術を行った上で胎児娩出の方針とした．IUFD確認後67日後に子宮動脈塞栓術を行い，胎盤血流の減少を確認した．2日後より頸管拡張開始し，翌日にゲメプロスト錠錠使用し，児娩出に至った．胎盤もスムーズに娩出された．児は24g女児であり，明らかなIUFDの原因は不明であった．出血は羊水込みで10gであり子宮内に明らかな遺残も認めず経過良好であった．前置胎盤症例での中期流産処置で子宮動脈塞栓術は必須ではないが，本症例のように癒着胎盤が疑われ胎盤娩出時の出血リスクが高い場合には子宮動脈塞栓術を考慮してもよいと思われる．

P-26-5 不妊治療前にプレコンセプションケアを考慮すべきであった痩せ過ぎ妊婦の2症例

神戸大

田中将之，谷村憲司，今福仁美，内田明子，喜多ともみ，益子尚久，高橋良輔，出口雅士，寺井義人

【緒言】痩せ過ぎ妊婦（妊娠前BMI<16.0）では早産や胎児発育不全などの周産期リスクが上昇する．不妊治療で妊娠した痩せ過ぎ妊婦2例を経験したので報告する．【症例1】40歳，3妊1産．体外受精，ホルモン補充周期による凍結胚移植で妊娠成立．妊娠前BMI15.8（体重39kg）．癒着胎盤既往のため当院紹介となった．画像検査で癒着胎盤が疑われたため計画分娩の方針となり，妊娠37週4日より分娩誘発を開始し，妊娠37週6日に2460g（-1.0SD），女児，Apgar Score（Aps）8点/9点を経膈分娩したが，癒着胎盤で多量出血したため膈上部切断術を行った．出血量は合計3133ml，RBC22単位，FFP16単位の輸血を要し，術後7日目で退院となった．【症例2】31歳，2妊1産．排卵誘発，人工授精で妊娠成立．妊娠前BMI14.1（体重36kg）．3絨毛膜3羊膜品胎，摂食障害合併のため当院紹介となり，妊娠21週2日から管理入院となった．摂食困難のため高カロリー輸液投与を行ったが，自身のボディイメージの歪みから輸液拒否，さらに早期の妊娠終結を希望した．断続的に高カロリー輸液を行い，分娩時には体重47kgまで増加したが，母体精神状態悪化のため妊娠29週6日に帝王切開で児娩出した．第1子1188g（-0.9SD），女児，Aps8点/9点，第2子1234g（-0.6SD），女児，Aps8点/9点，第3子932g（-2.3SD），女児，Aps8点/9点で，術中出血量は887ml（羊水込み）であった．母体は術後5日目，児は3児とも日齢106に退院となった．【考察】痩せ過ぎ女性では，栄養管理，メンタルヘルス，妊娠後のリスクに関する説明などのプレコンセプションケアを行い，癒着胎盤や多胎妊娠を回避できるように不妊治療法の選択について十分に検討する必要がある．

P-26-6 妊娠14週に診断された自然排卵周期の正所異所同時妊娠に対して期待的管理を行った1例

倉敷中央病院

寺井悠翔，福原 健，深江 郁，橋本阿実，黒田亮介，西村智樹，田中 優，伊藤拓馬，加藤 慧，清川 晶，長谷川雅明，本田徹郎

【緒言】正所異所同時妊娠（Heterotopic pregnancy，以下HP）はARTによって近年増加傾向であるが，自然排卵周期では約3万件に1件と非常に稀な疾患である．また，HPの約70%が妊娠5～8週，約20%が妊娠9～10週の間に診断され，妊娠11週以降の診断はわずか10%である．この度，妊娠14週に診断された自然排卵周期のHPに対して期待的管理により生児を得た1例を経験したので報告する．【症例】34歳．G2P1．妊娠8週に腹痛と不正性器出血を主訴に前医を受診し，腹水貯留を指摘された．妊娠9週に血性腹水の増大の診断で前医入院となった．入院中の妊娠11週に子宮右側に腫瘤を指摘されたが経過観察となった．退院後に腹痛が再度出現し，妊娠14週2日に当院紹介となった．エコー検査にて週数相当の子宮内児を認め，子宮外右側の腫大した卵管内に1.36cm長の胎児心拍のない胎芽を含んだ5cm大の嚢胞を認めた．嚢胞の周辺には豊富な血流を認めた．同日，緊急MRI検査でHPおよび右卵管の枯死卵と診断された．期待的管理の方針とし入院を継続したところ，症状は軽快し，病変が縮小したため妊娠17週3日に退院とした．その後，右卵管の壁肥厚は残存したが，嚢胞構造は妊娠26週に消失した．妊娠39週2日に経膈分娩に至った．母児ともに分娩後の経過は良好であった．【考察】HPでは子宮外児を手術で摘出する報告も多いが，子宮内児の流産となるリスクがある．HPに対して適応を見極めた上での期待的管理は選択肢となりうる．

P-26-7 大量出血後に子宮温存が可能であった帝王切開癒痕部妊娠の2症例

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【目的】帝王切開癒痕部妊娠 (CSP) は大量出血を来す可能性のある疾患であり, 子宮全摘を余儀なくされることもある。近年増加しているが治療方針は確立していない。今回大量出血後に子宮動脈塞栓術 (UAE) とバルーンカテーテルによる圧迫により子宮温存可能であった2症例を経験したため報告する。【症例1】24歳2妊1産。帝王切開後3か月で大量性器出血を認め救急搬送, 帝王切開癒痕部に胎嚢を認めた。胎児は7週相当で心拍あり, カラードプラーで胎嚢周囲に豊富な血流を認めた。持続出血を認め, ショックインデックス (SI) >1, 意識レベル低下あり緊急両側 UAE 施行。外出血は消失したが胎嚢周囲の血流と胎児心拍は残存した。3日後に胎嚢を吸引したところ噴出する出血あり, 癒痕部にバルーンカテーテル (ミニメトロ[®]) を留置し30mLで圧迫, 翌日抜去し止血を確認した。【症例2】25歳6妊5産 (帝王切開5回)。産後8か月で少量性器出血と腹痛のため近医受診し CSP と診断。その後大量出血と意識レベル低下を来し救急搬送となった。胎児は9週相当で心拍あり, 胎嚢周囲に豊富な血流を認めた。SI=1, 出血持続あり緊急両側 UAE を施行した。2日後に胎児心拍は消失したが周囲の血流は残存していた。胎嚢を吸引したところ出血が持続し, 症例1と同様ミニメトロ[®]を癒痕部に留置し止血, 翌日抜去した。【結語】CSP は正常内膜が欠損した癒痕部に着床することで異型血管が発達し大量出血を来す可能性がある。胎嚢周囲の血管は子宮動脈下行枝や腔からも栄養されるため両側 UAE のみでは完全に血流を消滅させることは不可能であったが, バルーンカテーテルによる圧迫を組み合わせることで止血を得られ, 子宮温存が可能であった。

P-26-8 自然発生した子宮内外同時妊娠

岡山赤十字病院

兼森雅敏, 角南華子, 山本梨沙, 柏原麻子, 佐々木佳子, 高取明正

【症例】23歳既婚, 0経妊0経産。【現病歴】無月経を主訴に当院を最終月経より6週4日で初診となった。既往歴に自閉症, 家族歴は特記事項なし。排卵誘発等の不妊治療歴はなし。初診時の腔鏡診, 内診では異常所見を認めず, 経膈超音波検査にて子宮内に胎嚢と思われるエコーフリースペースを認めた。7週5日, 外来受診時, トイレ行った後に意識消失あり転倒。腔鏡診にて外子宮口からの少量の性器出血を認め, 内診では右付属器領域に圧痛を認めた。経膈超音波検査にて子宮内にGS, 右付属器領域にGSとみられるエコー所見を認めた。子宮内外同時妊娠 (右卵管妊娠および正常妊娠) を疑い, 本人および家族に十分なインフォームドコンセントを行ったうえで, 同日腹腔鏡下手術を施行とした。【経過】腹腔内には約2000mLの血液が貯留し, 右卵管が腫大していた。同部位の妊娠が疑われ, 腹腔鏡下右卵管切除術を施行し, 病理組織検査にて右卵管妊娠であることが確認された。患者の術後経過は良好で, 術後3日目に退院した。以後の妊婦健診も異常なく経過し, 39週6日に経膈分娩にて生児を得た。【考察】子宮腔内と子宮腔外の同時妊娠が自然発生することは極めて稀であり, その頻度は約30,000件に1件と報告されている。本症例では初診時に超音波検査にて子宮内に胎嚢を確認したが, 右付属器の異常所見を確認するには至らなかった。再診時の超音波検査にて腹腔内の血液貯留を認め, 子宮内外同時妊娠の存在を疑い試験的腹腔鏡検査・手術を施行した。日常診療において子宮内に胎嚢が確認できたとしても, 子宮内外同時妊娠の存在を念頭に置き, 付属器領域等を注意深く超音波や内診により診察する習慣をつけることの重要性を再認識した。

P-26-9 双胎一児が帝王切開癒痕部妊娠, 流産後に妊娠継続した症例

自治医大

海平俊太郎, 堀江健司, 島田哲郎, 大草陽史, 小古山学, 鈴木寛正, 薄井里英, 大口昭英, 高橋宏典, 藤原寛行

【緒言】帝王切開癒痕部妊娠 (cesarean scar pregnancy: CSP) は帝王切開癒痕部に着床する異所性妊娠で, 妊娠継続させると子宮破裂や前置癒着胎盤を発症する危険性があるため, 通常, 妊娠中断が推奨される。一児が正常妊娠のため妊娠継続させた二絨毛膜二羊膜性双胎における一児 CSP 自然流産例の経過を示す。【症例】38歳, 2妊1経 (帝王切開), 凍結胚移植により二絨毛膜二羊膜性双胎を妊娠, 妊娠8週に多量出血し, 当科に搬送された。来院時に画像所見から, 一児の CSP 流産と診断した。輸血を要したものの保存的に経過観察し, 本人の強い希望もあり妊娠継続した。超音波検査上, CSP の血腫・妊娠成分は徐々に縮小したが, CSP 近傍の筋層血流は豊富で分娩時の大量出血を危惧して, 妊娠16週での退院後も外来で慎重に経過観察した。妊娠34週に管理入院を予定していたが, 妊娠33週5日に自宅で多量出血し, 近医へ救急搬送され, 出血性ショックのためそのまま緊急帝王切開で分娩 (1548g, 女児, Apgar 値1点/4点) した。輸血後も出血が持続しショックバイタルが改善しないため, 当院へ搬送された。造影CTでCSP部位に一致した造影剤血管外漏出を認め, 子宮動脈塞栓術を行い止血した。術後CSP筋層の血流は低下し, 再出血なく, 産褥11日目に退院した。【結語】双胎一児がCSP流産となったが, もう一児が妊娠継続した報告は非常にまれである。CSP流産は超音波検査で妊娠成分が同定できなくなったとしても, 着床部筋層の異常血管から大出血を来す危険性があるため, 慎重な妊娠管理を行うとともに, 帝王切開に際して十分な輸血, 術後の子宮動脈塞栓などの準備を整えることが望ましい。

P-26-10 右卵管妊娠に対する卵管切除術後に異所性妊娠を反復し腹膜妊娠の診断となった1例

防衛医大

菅沼奈弥, 高田美乃莉, 宮本守員, 海士洋平, 田中佑奈, 今氏晶梨, 岩間公隆, 三宅太郎, 吉本和矢, 加藤顕人, 笹 秀典, 高野政志

【緒言】異所性妊娠の手術後、10-15%に異所性妊娠が反復する。また異所性妊娠が反復した際に腹膜妊娠を発症するのはさらに稀である。我々は、右卵管妊娠に対する卵管切除後に、腹膜妊娠を反復した1例を経験したので報告する。【症例】34歳、5妊2産、右卵管妊娠に対して腹腔鏡下卵管切除の既往がある。下腹部痛で近医を受診。妊娠反応陽性、経陰超音波で子宮内に胎嚢はなく、ダグラス窩に貯留があり、異所性妊娠疑いで当院へ紹介受診。血清hCGは1944mIU/mlであり、経陰超音波は前院同様であった。翌日hCGは2614mIU/mlであり、MRIのT2で右子宮角及び右卵巣付近に辺縁低信号、内部高信号の腫瘍があり、残存した右卵管の異所性妊娠が疑われ、腹腔鏡下手術を施行した。オープンダイヤモンド法で腹腔内へ到達し、155mlの血液を吸引した。残存卵管はなく、右卵巣は正常で、左卵巣に黄体嚢胞があった。卵管切除痕から離れた子宮底部右側の漿膜に凝血塊があり摘出した。続いて子宮内容除去術を施行した。凝血塊及び子宮内容物には肉眼的に絨毛成分はなかった。再度腹腔内を観察し、胎嚢様構造物はなく、凝血塊に含まれていると考えて手術終了した。術後hCGは463mIU/mlと低下し、経過良好で退院となった。病理組織学的検査では、凝血塊に絨毛組織や栄養膜細胞があり、子宮内容物は正常内膜であり、子宮底部の漿膜に発症した腹膜妊娠と診断した。術後1か月でhCGは陰転化した。【結語】右卵管妊娠に対する卵管切除術後に腹膜妊娠となった症例を経験した。反復する異所性妊娠でも、腹膜妊娠は起こり得ることを考慮する必要があると考えられる。

P-26-11 右卵管間質部妊娠術後に左卵管間質部妊娠をきたし腹腔鏡下に治療した一例

兵庫県立西宮病院

萬家愛賀, 尹 純奈, 山野友加里, 森田康之, 大月萌詩, 古村恭子, 山部エリ, 浅野正太, 渡辺正洋, 増原完治, 信永敏克

【緒言】卵管間質部妊娠は異所性妊娠の2~4%を占める疾患であるが、片側の間質部妊娠術後に対側の間質部妊娠を発症する頻度は極めて稀であると考えられる。今回我々は右卵管間質部妊娠に対し腹腔鏡下右卵管切除および卵管角楔状切除術を施行後に、自然妊娠にて左卵管間質部妊娠をきたし、再び腹腔鏡下に治療した一例を経験したので報告する。【症例】33歳、4妊1産、月経周期不整、既往歴として当院にて11か月前に右卵管間質部妊娠に対し、腹腔鏡下右卵管切除および右卵管角楔状切除術が実施されている。術後hCGの陰性化を確認し、妊娠許可としたのち、今回自然妊娠が成立した。最終月経起算にて10週2日に近医受診にて、左子宮卵管間質部に胎嚢を認めたため、妊娠10週4日に当科紹介となった。当院受診時、自覚症状はなく、血中hCGは8400mIU/mLであった。経陰超音波検査にて子宮内腔に胎嚢を認めず、左卵管間質部付近に11mm大の胎嚢を認めた。卵管温存希望はなく、パソプレシンの使用に関して十分なインフォームドコンセントを得て、同日腹腔鏡下手術を施行した。左卵管間質部に約1cm大の未破裂の膨隆部分を認めたため、100倍希釈のパソプレシンを間質部膨隆部周囲に局注し、左卵管切除および卵管角楔状切除術を施行し、子宮筋層は吸収糸にて連続二層縫合を行った。術中出血量は5mlであった。病理検査にて絨毛成分を確認し、左卵管間質部妊娠の診断となった。術後経過良好で、現在外来にて慎重に管理している。【結語】異所性妊娠の既往のある患者はその再発リスクが高まるとされているが、稀ながら対側の間質部にも再発しうことに留意する必要がある。

P-26-12 凍結胚移植後に子宮-右卵管間質部の子宮内外同時妊娠をきたし腹腔鏡下異所性妊娠手術を施行した1例

東京女子医大

國司真央

卵管間質部との子宮内外同時妊娠は非常に稀であり、子宮内に近い治療方針に苦慮する。今回生殖補助医療で妊娠成立し、卵管間質部との子宮内外同時妊娠で腹腔鏡下異所性妊娠手術を施行した1例を経験したので報告する。34歳2妊0産、不妊治療反復不成功のため胚盤胞2個で凍結胚移植を受け、妊娠6週0日に内外同時妊娠を疑われ当院紹介となった。経陰超音波検査では子宮内と右卵管角~間質部に胎嚢を認め、どちらも胎児心拍を認めた。手術、薬物治療、自然待機の選択肢を説明のうえ、今後成長した場合の出血リスクが高いと考え、翌日腹腔鏡下間質部切開による内容除去術、右卵管切除術を施行した。子宮内の胎嚢と近い位置にあり、また今後の妊娠経過を考慮し卵管角を削りすぎないように注意を払った。術後の経陰超音波検査にて卵管間質部位に胎嚢、高輝度領域を認めないこと、子宮内胎児の心拍を確認した。術後経過良好で子宮内の胎児発育に問題はなく、術後5日目に退院となった。卵管間質部との子宮内外同時妊娠は稀であり治療方針、手術方法にさらなる検討をする必要がある。

P-26-13 中隔部分に胎盤が付着した不全中隔子宮症例に慎重な周産期管理を行い、生児を得た症例の経験を通して、診療所に適したハイリスク症例の分娩管理方法を考える

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双角子宮や中隔子宮などの子宮奇形は全女性の0.5%にみられ、不妊症の原因のひとつとして知られている。さらに、たとえ妊娠したとしても、子宮奇形の合併妊娠では、妊娠37週未満の早産率、常位胎盤早期剝離（早剝）発症率、帝王切開率が有意に高いことが報告されており、ハイリスク症例であることは言うまでもない。一方、出生数が減少し続けている現在、収益の大半を分娩数に依存する産科診療所ではいかにして分娩数を維持するかが最重要課題で、ハイリスク症例を分娩管理することの必要性を認識している。今回、われわれは不妊治療後、中隔に胎盤が付着していた不全中隔子宮症例に対して、待機入院し、早剝や胎児機能不全などの急変対応を回避することで、生児を得た症例を報告する。症例は35歳1経妊初産婦。1年間の不妊、骨盤MRI、HSGで、単頸双角子宮と診断されていた。タイミング法で、左子宮に着床。妊娠33週の経膈超音波断層法により、胎盤の主座は左前壁で、辺縁が子宮中隔に付着している不全中隔子宮と診断。妊娠35週に早剝を起こした症例報告を参考に、妊娠34週6日から、安静入院。妊娠36週0日に、骨盤位の診断で、選択的帝王切開を施行し、2190gの健康女児を得た。術中、子宮底部は双角子宮様で、膜様中隔は認めなかった。胎盤は後血腫を認めず、胎児面は全面が暗褐色を呈し、病理学的に新鮮な羊膜下血腫と診断された。近年、羊膜下血腫と胎児発育不全や胎児機能不全、早剝との関連性が報告されており、本症例では結果的に、人工早産が有効であったと考えられた。また、ハイリスクである子宮奇形合併妊娠症例に対しても慎重な周産期管理を行えば、診療所でも安全に分娩が行えることの可能性を示した。

P-26-14 子宮を温存し得た子宮内異所性妊娠の三症例

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【緒言】子宮内異所性妊娠である頸管妊娠（CP）や帝王切開痕癩部妊娠（CSP）は不用意な搔爬により止血困難な大出血を起こし、輸血や子宮全摘術を余儀なくされることがあるが標準治療は未だに定まっていない。我々は様々な経過を辿ったのちに、合併症なく子宮を温存し得た子宮内異所性妊娠の三症例経験した。【症例1】41歳1妊0産。体外受精妊娠。経膈超音波断層法にてCPの診断に至った。妊娠7週時に胎児心拍は認めず、約8週間経過観察をしたが自然排出なくMTX全身投与を3クール行った。その後も胎嚢が残留したため子宮鏡下手術療法の方針となった。【症例2】32歳2妊1産（前回帝王切開）自然妊娠。CSP疑いのため当院へ紹介。初診時妊娠6週相当で血中hCG値は13029.6mIU/mlで胎児心拍は不明瞭であった。約1週間後にhCG値が27597.1mIU/mlまで上昇がしたため、経膈的にMTX局注を行った。その後異常な出血は認めず約2か月で血中hCG値は3.7mIU/mlまで低下した。胎嚢の残存は認められたが、本人の希望あり他院へ紹介となった。【症例3】35歳5妊3産（前2回帝王切開）。他院にてCSPと診断された。MTX単回投与を3クール行ったが効果は得られず、当院へ紹介。当院初診時妊娠11週相当で心拍が確認され、血中hCG値は89906.9mIU/mlであった。経膈的に胎児心臓へKCL注入を行い、自然経過観察の方針とした。約2週間後出血にて来院。胎嚢排出が認められた。約1か月後に血中hCG値は21.7mIU/mlまで低下が認められ、その後異常な再出血なく子宮温存が可能であった。【考察】異所性妊娠では血中hCGの値に関わらず予想外の大出血を来すリスクがある。今回、状況に応じて適切な治療法を選択することで安全に子宮を温存し得たと考えられた。

P-27-1 妊娠22週未満の経膈分娩の際の胎盤位置に関する出血量の検討

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【目的】昨今、様々な要因により22週未満での娩出が増加傾向にあるが、胎盤位置により分娩方法に難渋する場合がある。本邦では一定の見解がない妊娠22週未満の娩出において、低位胎盤群（Group A）と常位胎盤群（Group B）とで大量出血リスク因子の同定と胎盤の位置による出血量を比較検討した。【方法】倫理委員会承認の下、診療録より抽出した2009年4月から2023年8月の22週未満での170例の分娩例のうち帝王切開例を除外した168例を対象とした。胎盤辺縁が内子宮口に重なるものを低位胎盤群（Group A）、それ以外をGroup Bと定義した。【成績】Group A群は43例（全前置胎盤11例、部分前置胎盤9例、辺縁前置胎盤12例、低置胎盤11例）。168例の内、出血量1000ml以上：7例（4.1%）であり、Group A群は3例が該当。低位胎盤自体が1000ml以上の大量出血のリスク因子とはならなかった。次にGroup A群の経膈分娩時の出血量の中央値は200mlで最大値は1675ml、Group B群の出血量の中央値は110mlで最大値は2197mlであった。Group A群の中央値はGroup B群の1.8倍を示し、出血量は有意に増加した（ $P=0.04$ ）。Group A群の中で全前置胎盤とその他の低位胎盤では有意に出血量で差異が認められた（ $P=0.003$ ）。【結論】本検討から妊娠22週未満ではGroup A群のGroup B群と比較し出血量は有意に増加させ、その中でも全前置胎盤が最も出血量を増加させることがわかった。一方で、低位胎盤が母体危機に直面させる大量出血の直接的なリスク因子とはならなかった。22週未満の経膈分娩の管理は胎盤の位置に限らず大量出血する症例が一定の割合で発生することが示唆され、出血への対応が可能な施設での経膈分娩が安全であることが示唆された。

P-27-2 生殖補助医療 (ART) 妊娠における潜在性甲状腺機能低下症と周産期予後についての検討

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【目的】潜在性甲状腺機能低下症 (SCH) とは、遊離サイロキシン (FT4) 値は正常であるが甲状腺刺激ホルモン (TSH) 値が高値であるものをいう。妊娠中の SCH の有病率は 2~5% と推定され、比較的高頻度で検出されるものであるが妊娠予後との関連性は明らかにされていない。今回我々は生殖補助医療 (ART) で妊娠成立し当院で出産に至った単胎妊婦を対象に SCH の合併が妊娠予後にどのような影響を及ぼすか検討した。【方法】2020年1月から2023年7月までに ART で妊娠成立した単胎妊婦のうち、当院にて分娩に至った 688 例を対象とした。このうち既往として甲状腺疾患を指摘されている 22 例、前置胎盤合併例 15 例を除外し、合計 651 例で検討を行った。SCH の診断基準は TSH 値 2.5uIU/L 以上と定義し、甲状腺機能が正常な A 群 (581 例)、SCH がありレボチロキシン内服していない B 群 (34 例)、SCH がありレボチロキシン内服している C 群 (35 例) に分け、周産期予後 (早産・妊娠高血圧腎症・FGR・分娩時出血量・胎盤用手剥離・輸血) について比較検討した。【成績】妊娠高血圧腎症・FGR・分娩時出血量・胎盤用手剥離・輸血は 3 群間で有意差を認めなかった。37 週未満での早産率に関しては有意差を認めなかったが、34 週未満早産に関しては A 群 6.2%、B 群 14.7%、C 群 0% であり、C 群で有意に低かった ($p=0.047$)。多変量ロジスティック解析において、34 週未満早産については妊娠高血圧腎症が有意なリスク因子 ($OR=3.65$) であったことに加えレボチロキシン内服が有意なリスク予防因子 ($OR=0.11$) であった。【結論】SCH 合併妊婦においてレボチロキシン内服は 34 週未満早産予防に寄与することが示唆された。不妊治療開始時に SCH を認めた場合レボチロキシン内服を推奨する。

P-27-3 前方前頭位分娩が母体・新生児転帰に及ぼす影響に関する検討

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【目的】前方前頭位は分娩中に発生する最も一般的な児頭回旋異常であり、分娩の遷延など対応に苦慮することが多いが、日本で前方前頭位の分娩転帰を検討した報告はない。今回我々は、前方前頭位分娩が母体及び新生児の転帰に及ぼす影響を検討した。【方法】2000年1月から2023年5月に当院で頭位経陰分娩で出産した妊娠 37 週以降の単胎妊婦を対象に、母体背景、分娩転帰及び新生児転帰について診療録を元に後方視的に検討した。【成績】当院で出産した 13958 例のうち、前方後頭位群は 13739 例 (98.4%)、前方前頭位群は 219 例 (1.6%) であった。母体の妊娠前体重、分娩時体重は前方前頭位群で有意に大きかったが、分娩時年齢や BMI、経産回数に有意差はなかった。母体転帰では、分娩時出血量の中央値 [四分位範囲] が前方後頭位群で 323 (211-498) g、前方前頭位群で 400 (267-590) g と前方前頭位群で有意に多かった ($p<0.001$)。前方後頭位群、前方前頭位群の器械分娩、会陰切開、3 度又は 4 度裂傷の頻度は、6.2% vs 25.1% ($p<0.001$)、40.8% vs 68.3% ($p<0.001$)、0.9% vs 2.7% ($p=0.047$) と前方前頭位群で有意に高かった。分娩時間、臨床的絨毛膜羊膜炎、分娩後入院日数に有意差はなかった。新生児転帰では、臍帯動脈血ガス pH < 7.1 の頻度が 0.7% vs 1.9% と有意差を認めた ($p=0.047$) が、児の体重や新生児仮死の頻度、NICU 入院率に有意差はなかった。【結論】前方前頭位分娩は、前方後頭位と比較して器械分娩が多く、分娩時出血量や会陰切開、重度の会陰裂傷が増加した一方で、新生児合併症は増加しなかった。分娩時に前方前頭位と診断した場合には、母体の有害転帰が増加することを念頭において管理することが重要である。

P-27-4 妊娠中に MRI で子宮体下部筋層に血管拡張を認めた症例の分娩管理についての後方視的検討

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【目的】妊娠中の経陰超音波検査にて、子宮筋層の拡張した血管が観察されることがある。この所見は胎盤の辺縁静脈洞との鑑別を要し、分娩時大量出血リスクの評価に苦慮する場合がある。今回、妊娠中に子宮筋層に拡張した血管を有する症例の管理について後方視的に検討した。【方法】当施設で 2020年1月から2023年8月までに分娩した症例のうち、妊娠中に MRI で子宮体下部筋層の血管拡張を指摘された 19 症例を対象とした。既往帝王切開後妊娠等の適応にて予定帝王切開で分娩した症例は除外した。対象について、妊娠中の警告出血の有無・分娩転帰・輸血療法実施の有無を後方視的に検討した。【成績】今回対象とした 19 症例中、分娩開始前に警告出血を認めた症例は 3 例、分娩経過中に出血量が増加し緊急帝王切開に移行した症例は 4 例だった。分娩時出血量の中央値は、経陰分娩症例で 993mL、帝王切開症例で 2397mL だった。経陰分娩で出血量が 500mL 以上の症例は 53.8%、さらに 1000mL 以上の出血をきたした症例は 30.7% だった。19 症例中 15 例で自己血 300~800 mL を貯血し分娩に臨んだが、3 例ではさらに同種血輸血を要した。分娩経過中に内診時に血管破綻をきたし、止血に難渋するケースもみられた。一方で、経過中に血管拡張が自然に縮小し、分娩時出血も少量であった症例も 5 例認めた。【結論】妊娠中に経陰超音波検査にて子宮筋層の血管拡張を認めた際には、MRI を用いた診断を行い、内診を行う際には血管破綻する可能性に十分留意して実施する必要がある。さらに、前置胎盤や低置胎盤の管理同様、事前に自己血を貯血しておくなど、大量出血に備えた準備が必要であると考えられ、高次周産期医療機関での妊娠管理が考慮される。

P-27-5 分娩時における2本の臍帯動脈血 pH 値の差異について

滋賀医大

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【目的】分娩時の臍帯動脈血 pH は2本の血管の一方を無作為に選択し測定する。しかし、以前我々は、片側の臍帯動脈血流途絶がある症例で、2本の臍帯動脈血 pH の差異 (Δ pH) が0.2となる症例を経験した。そこで、分娩時の2本の臍帯動脈血 Δ pH が増大する症例がどのような症例かを明らかにすることを目的に本研究を行った。【方法】本研究は倫理委員会の承認後に前向きに行った。2020年4月から2021年10月の間に当院で分娩となった166例を集積できた。評価項目は妊娠週数、出生体重とその胎児発育曲線に対する Z-score, Apgar score, 臍帯巻絡の有無, 臍帯附着部異常の有無, 臍帯断面積, 臍帯動脈拡張期血流の逆流・途絶の有無, 2本の臍帯動脈血の pH 等であった。【成績】 Δ pH の中央値は0.007(四分位点0.004, 0.016)で、 Δ pH>0.05が9例(5.4%)、 Δ pHの最大値は0.086であった。 Δ pHを目的変数、上述の評価項目を説明変数とした重回帰分析を実施した結果、出生体重の Z-score ($p=0.027$)、臍帯動脈拡張期血流の逆流・途絶 ($p=0.006$)、臍帯動脈血 pH ($p=0.012$)の各々が Δ pH と有意に関連した。【結論】測定機器の誤差では説明できない臍帯動脈血 pH の差異を認める例を少数ではあるが認めた。それらは、出生体重の Z-score が小さい場合、臍帯動脈拡張期血流に逆流・途絶がある場合、臍帯動脈血 pH が低い場合に特に顕著であった。これらの結果は、分娩時ストレスで臍帯動脈の血流波形が変動しやすい状況下では2本の臍帯動脈血 pH に各々変化を生じ、双方の pH 値で差異を生じる可能性を示唆するものと考えられた。

P-27-6 ターニケット法と子宮内バルーンを併用した前置胎盤に対する手術方法

三重大

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【目的】前置胎盤は妊娠の高齢化、不妊治療の普及、帝王切開分娩の増加に伴い、増加傾向にある。帝王切開時には大量出血を来すことがあり、子宮摘出を要する場合がある。術中出血量軽減かつ子宮摘出回避のために当院で行っている前置胎盤に対する手術方法について紹介する。【方法】当院における前置胎盤に対する手術方法のポイントは、①児娩出後、子宮を腹腔外へ出し、子宮峡部をネラトンカテーテルでターニケットした上で胎盤娩出を試みること、②子宮筋層縫合前に胎盤剥離面からの出血抑制および Ferguson 反射を介した子宮収縮促進目的に子宮内バルーンを経腹的に留置することである。2014年6月から2022年12月までに、前置胎盤63例(全前置胎盤35例、部分前置胎盤6例、辺縁前置胎盤22例)に対して、本手技を行った。【成績】63例のうち、40歳以上、生殖補助医療での妊娠、帝王切開既往、子宮手術・子宮内操作既往の症例数はそれぞれ、13例(20.6%)、20例(31.7%)、11例(17.5%)、14例(22.2%)であった。また、分娩週数、術中出血量の中央値は37.1(31.9-38.7)週、1,334(541-12,496)mlで、輸血は13例(20.6%)で要した。本手技を行っても止血困難で、子宮摘出となった症例が1例(1.6%)あり、術中に癒着胎盤と診断した症例であった。【結論】ターニケット法と子宮内バルーンを併用した前置胎盤に対する手術方法は、簡便であるため、施設を問わず汎用性が高く、出血のコントロールに有用であると考えられる。

P-27-7 当院における経陰分娩後の癒着/固着胎盤と ART 妊娠との関連性について

石川県立中央病院

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【目的】近年、ART 妊娠の増加により癒着・固着胎盤の増加が指摘されている。特に経陰分娩後の癒着胎盤では、分娩前予測が不可能であり緊急対応となることが多い。当院における特に経陰分娩後の癒着・固着胎盤について検討する。【方法】2010年1月から2023年6月までの期間に当院で経陰分娩後に癒着/固着胎盤と診断した62例。癒着/固着胎盤の定義は臨床的にを行い、当院分娩例については児娩出後30分以上娩出されず用手剥離を試みた症例とした。固着胎盤は用手剥離にて遺残なく娩出でき、出血少量例とし、癒着胎盤は、用手剥離が困難か剥離可能も一部残存を強く疑う症例、および出血1000ml以上の症例とした。病理学的癒着胎盤には子宮摘出例以外に胎盤に子宮平滑筋の付着が認められた症例も含めた。【成績】62例の内訳は、固着胎盤19例、癒着胎盤43例、病理学的癒着胎盤は16例となった。初産婦は47%(29)、分娩年齢35≤の妊婦73%(45)、産褥母体搬送37%(23)であった。多量出血(3000ml \leq)を29%(18)にみとめ、輸血は48%(30)に行った。また処置としてUAEを13%(8)、子宮全摘6%(4)に行った。癒着・固着胎盤の61%(38/62)、癒着胎盤の79%(34/43)、病理学的癒着胎盤の94%(15/16)がART由来であった。【結論】経陰分娩後の癒着・固着胎盤は増加しており、その多くはART妊娠であった。予測困難のため夜間や緊急搬送が多く、さらには子宮温存希望者も多いことから、多くの医療資源と医療現場への負担を生じている。ART妊娠の母体への危険性を再確認すべきである。

P-27-8 帝王切開時の子宮筋層縫合糸・方法の違いが子宮癒痕部および子宮筋層の非薄化に与える影響

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【目的】帝王切開率は年々増加傾向にあり、帝王切開癒痕症候群は重要な術後合併症として注目されている。子宮筋層縫合糸・方法の違いが、術後の子宮癒痕部および子宮筋層の非薄化に与える影響について明らかにすることを目的とした。【方法】2021年3月から2023年9月に、帝王切開で子宮下部横切開が施行された症例を対象とし、以下の3群について後方視的に解析した。A群は、1層目：1-0号吸収性縫合糸・単結節縫合、2層目：0号Spiral糸・減張連続縫合、B群は、1層目：0号Spiral糸・連続縫合、2層目：0号Spiral糸・減張連続縫合、C群は、1層目：1-0号吸収性縫合糸・単結節縫合、2層目：1-0号吸収性縫合糸・減張連続縫合とした。Spiral糸はすべてSTRATAFIX® Spiral PDS plus®を使用した。評価項目は術後1,3か月の経腔超音波検査での癒痕（陥凹部の深さ $\geq 2\text{mm}$ ）の割合および残存筋層の厚さとし、3群間で比較した。本研究は、倫理審査委員会の承認を得て行った。【成績】A群79例、B群162例、C群86例が登録された。母体背景に有意差を認めなかった。癒痕の割合は、術後1か月で、B群で有意に低く（A群83.5%、B群54.9%、C群83.7%、 $p < 0.001$ ）、術後3か月では、A、B群で有意に低かった（A群43.1%、B群34.3%、C群65.2%、 $p = 0.002$ ）。残存筋層は、術後1か月で、A、B群がC群と比較し、有意に厚かった（A群 $12.1 \pm 2.6\text{mm}$ 、B群 $11.5 \pm 2.5\text{mm}$ 、C群 $9.9 \pm 3.5\text{mm}$ 、 $p < 0.001$ ）。術後3か月でも同様の結果であった（A群 $9.4 \pm 2.3\text{mm}$ 、B群 $10.9 \pm 3.2\text{mm}$ 、C群 $7.4 \pm 2.6\text{mm}$ 、 $p < 0.001$ ）。【結論】Spiral糸を用いた無結節有棘縫合では、癒痕の割合は減少し、術後の残存筋層は厚くなることから、帝王切開癒痕症候群の減少につながる可能性がある。

P-27-9 ジノプロストン腔用剤における子宮頸管熟化不良因子の抽出

熊本大

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【目的】国内臨床試験におけるジノプロストン腔用剤の子宮頸管熟化成功率（投与後12時間以内にBishop score (BS) が7点以上、又は経腔分娩のいずれかに至る割合）は約50%であるが、本施設は本剤を使用しても子宮頸管熟化が不良な症例を多く経験する。今回われわれは、周産期ハイリスクを扱う本施設の背景も踏まえ、子宮頸管熟化の不良因子を抽出することを目的とした。【方法】2021年4月から2023年9月の間に総合周産期母子医療センターである当施設で子宮頸管熟化目的に本剤を使用した症例を対象として後方視的検討を行った。高齢、経腔分娩歴、肥満、糖代謝異常の有無、妊娠高血圧症候群（HDP）の有無、使用時の妊娠週数およびBishopスコアについて症例を2群に分け、子宮頸管熟化成功率をFisherの直接検定を用いて比較した。【成績】対象は44症例で、年齢の中央値は36（21-43）歳、35歳以上は6例（25%）、初産は36例（81.8%）であった。BMIの平均値は $22.9 \pm 6.7\text{kg/m}^2$ 、 $\text{BMI} \geq 25\text{ kg/m}^2$ の肥満例は18例（40.9%）、周産期合併症として糖代謝異常が18例（40.9%）、HDPが15例（34.1%）を占めた。使用時の妊娠週数は中央値39週4日（37週0日-41週4日）であり、使用前Bishopスコア2点以下が21例（47.7%）であった。本剤による子宮頸管熟化成功例は11例（25.0%）と臨床試験と比較し低い成績であった。子宮頸管熟化成功率は肥満例（有り11.1% vs 無し34.6%、 $p = 0.155$ ）、糖代謝異常例（有り11.1% vs 無し34.6%、 $p = 0.155$ ）、HDP例（有り13.3% vs 無し31.0%、 $p = 0.282$ ）で低い傾向がみられた。特に24時間以内の経腔分娩率は肥満症例で有意に低い結果となった（有り11.1% vs 無し42.3%、 $p = 0.043$ ）。【結論】母体の肥満や糖代謝異常、HDPの合併は本剤による子宮頸管熟化を阻害する可能性がある。

P-27-10 当院における50歳以上の高年妊娠の周産期予後

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【目的】近年、高年妊娠が増加している。当院での高年妊娠における母児の周産期予後について検討した。【方法】2013年1月から2022年12月に当院で周産期管理を行った26,855分娩のうち、分娩時年齢が40歳以上の4,036例を対象とし、合併症、分娩転帰について後方視的に検討した。【成績】総分娩数26,855例のうち、40~44歳をA群（3,728例）、45~49歳をB群（279例）、50歳以上をC群（29例）とした。多胎率はA群で2.0%（双胎76例）、B群では9.3%（双胎24例、胎児2例）、C群では10.3%（双胎2例、胎児1例）であった。C群で生殖補助医療を用いて妊娠した28例のうち、23例は卵子提供による妊娠であった。37週末満の早産となったのは各8.9%、12.5%、13.8%であった。C群で早産となった原因は多胎、子宮内感染であった。C群では4例に誘発・促進を行った。初産婦経腔分娩の平均所要時間は各845分、908分、912分であった。帝王切開分娩率は各35.3%、51.6%、81.5%であり、経腔分娩のうち器械分娩に至ったのは各25.0%、33.6%、40.0%であった。C群で輸血を行ったのは8例であり、分娩後平均オキシトシン投与量は8.8単位であった。平均出生時体重は各2,997g、2,902g、2,626gであった。SGA (Small for Gestational Age) 児はC群で7例（多胎は3例）であった。NICU入院率は各12.9%、18.6%、30.3%であった。Apgar scoreや臍帯血pHには差がなかった。【結論】C群ではほとんどが卵子提供による妊娠であり、A群B群と比べ多胎率・帝王切開率が高く、経腔分娩であっても器械分娩を行う割合が高かった。多胎による早産・SGA児が多く、年齢に伴ってNICU入院率も上昇した。年齢の上昇に伴い周産期のリスクは上昇し、より厳重な周産期管理が必要である。

P-27-11 当院における無痛分娩の検討～陣痛発来後の麻酔開始の有効性について～

琉球大

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【目的】硬膜外麻酔による無痛分娩により第二期分娩時間の延長・器械分娩が増加すると指摘されており、それに伴う弛緩出血、産道裂傷および大量出血の発生に備える必要がある。本邦では日中の計画無痛分娩を行う施設が多く、合併症の増加が危惧されている。当院では陣痛発来後に麻酔開始としており、自然陣痛発来後の麻酔開始が分娩転機や新生児予後に影響を与えるかについて明らかにすることを目的とした。【方法】2020年1月から2022年12月までの当院での36週以降の単胎、初産婦の経陰分娩例286人のうち硬膜外麻酔による無痛分娩を施行した群34人と麻酔なしの群252人について母体背景、妊娠経過、分娩転機、新生児予後について比較検討した。【成績】患者の年齢、妊娠前BMI、既往症など母体背景に有意差はなかった。経陰分娩に至った例において無痛群で分娩第2期が有意に長かった[86.5分(40-175) vs 50分(26-92)*, $p < 0.05$]。分娩第1期、分娩総時間に有意差はなかった。またオキシトシンによる陣痛促進施行率[17(50%) vs 97(38%)], 器械分娩率[2(6%) vs 32(13%)], 緊急帝王切開率[8(24%) vs 47(19%)]に有意差はなかった。分娩時出血量[312g(54-1485) vs 407g(76-2220)*], 産道裂傷[3(9%) vs 37(15%)], 児のApgar Score5 分值 < 7 点[1(3%) vs 4(2%)], 臍動脈血pH[7.30(7.12-7.63) vs 7.30(7.04-7.33)*], NICU入室率[13(38%) vs 79(31%)]に有意差はなかった。*中央値(範囲)【結論】自然陣痛発来後の無痛分娩開始はオキシトシン使用を増加させず、分娩転機や児の予後に大きな影響を与えなかった。

P-27-12 当院での身体的・精神的ケアが必要な妊婦の母乳導入率と、母乳育児を導入するためのサポート状況について

弘前総合医療センター

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【目的】当院では、ほぼ全例の褥婦に対し産褥2週間での母乳外来で産褥期のトラブルを確認し精神的ケアも行っている。身体的・精神的ケアが必要な褥婦の母乳外来・産褥1か月健診での母乳導入率を比較し、当院でのサポートが有効であるか検討する。また褥婦に対し母乳育児関連のアンケートを実施し更なる改善点を模索する。【方法】母乳導入率について2019年～2022年の4年間、当院で単胎を分娩し産褥1か月健診を施行した妊婦1862人を調査対象とした。母乳外来と産褥1か月健診での母乳導入率を比較し、①何らかの疾患により当院に搬送または紹介になった妊婦、②帝王切開施行妊婦、③妊娠高血圧症候群妊婦、④妊娠糖尿病妊婦、⑤低出生体重児を分娩した妊婦、⑥母乳外来でEPSPD9点以上であった妊婦について、母乳導入率を算出した。母乳育児関連のアンケートについて2021年3月～7月に分娩した褥婦に対し、①妊娠中に希望した栄養方法、②母乳育児実施状況、③サポートに対する満足度等を集計した。【成績】母乳率は母乳外来で52.8%、産褥1か月健診で58.4%と上昇した。①～⑥の全てで上昇し、特にEPSPD9点以上であった妊婦では33.5%から54.2%と、高い上昇率であった。しかし妊娠高血圧症候群妊婦の産褥1か月健診時の母乳導入率は37.1%と低値であった。一方、サポートに対する評価について、妊娠中に母乳育児を希望した妊婦は64.3%であったが、実際の完全母乳栄養導入率は45.2%と低値であった。【結論】身体的・精神的サポートの充実により母乳育児の導入は可能になると考えられ、それにより産褥期のメンタルヘルス向上にもつながると推測される。今後も母乳育児を希望する妊婦のサポートを継続する方針である。

P-27-13 当院における産褥搬送症例に関する検討

琉球大

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【目的】当院へ産褥搬送された症例を調査しその課題を明らかにする。【方法】2017年1月から2023年9月までに当院へ産褥期に搬送された70症例について母体背景、原因疾患、出血量、輸血量、治療内容について後方視的に検討した。【成績】分娩後異常出血(primary PPH)が25例(35.7%)、その内訳は弛緩出血(n=15)、産道損傷(n=4)、子宮頸羊水塞栓症(n=2)、胎盤遺残(n=2)、子宮切開部の動脈損傷(n=1)、仮性動脈瘤破裂(n=1)であった。後期分娩後異常出血(late PPH)が10例(14.3%)であり、その内訳はRPOC(n=5)、弛緩出血(n=3)、仮性動脈瘤破裂(n=2)であった。Primary PPHの分娩様式は経陰分娩21例(84%)、帝王切開4例(16%)であった。到着時SI 1.0以上が36%(9例)、出血量の中央値は2000g(1028-3280)であり、76%(19例)に輸血、24%に子宮動脈塞栓術が施行され、子宮摘出を要した例はいなかった。分娩後異常出血以外の原因による搬送が35例であり、その内訳は産道血腫(n=17)、呼吸不全(n=4)、膀胱損傷を伴う腹腔内出血、子宮筋腫の変性、後腹膜血腫、胎盤遺残、子宮内感染、産褥HELLP症候群がそれぞれ1例、その他8例であった。【結論】分娩後異常出血は産褥搬送の50%を占め、大量輸血やIVR、ICU管理など集学的治療を行うことで子宮摘出を回避できた。産褥搬送の原因は多岐にわたり、原因検索と平行した迅速な治療の開始が重要である。

P-27-14 当センターでの患者希望による計画無痛分娩の現状

大阪はびきの医療センター

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【目的】当センターでは2017年から患者希望による無痛分娩を開始し、無痛分娩件数は年々増加傾向である。麻酔管理は自家管理で、原則計画無痛分娩としている。誘発週数については、初産婦は39週、経産婦は38週を目安としている。計画無痛分娩の現状について初産婦と経産婦に分けて検討し、今後の課題について検討する。【方法】2022年1月から12月に当センターで無痛分娩を実施した215例のうち、陣痛発来などで予定外に無痛導入となった35例を除外し、計画無痛分娩を行なった180例について分娩様式を検討した。さらに、緊急帝王切開3例を除外した177例について、初産婦と経産婦でそれぞれ母体年齢、分娩時間、日勤帯での分娩率（日勤は平日9時から17時半とした）、分娩時出血量、Apgar score 1分値と5分値、臍帯動脈血液ガスpHについて検討した。【成績】180例のうち、初産婦は69例（42%）、経産婦は111例（57%）であった。分娩様式については、帝王切開率は有意差を認めず、初産婦で2.9%（2/69例）、経産婦で0.9%（1/111例）だった。吸引分娩率は初産婦と経産婦で46%（32/69例）vs 10%（12/111例）と初産婦で有意に多かった（ $p < 0.001$ ）。経産婦のうち有意差を認めたのは、Apgar score 1分値8.4 vs 8.7（ $p = 0.03$ ）、分娩時間584分 vs 316分（ $p < 0.001$ ）、日勤帯での分娩率61% vs 82%（ $p = 0.002$ ）、分娩時出血量425ml vs 332ml（ $p = 0.004$ ）であった。【結論】初産婦の計画無痛分娩では、吸引分娩率が高く、分娩時出血が多かった。また、分娩時間が長く、分娩が当直帯にかりやすいことがわかった。初産婦の計画無痛分娩を安全に行うために、誘発方法や誘発時期などの検討が必要と考えられる。

P-28-1 児童相談所問題に対する医学的、法的、人権的、行政的、教育的アプローチの必要性について小畑会浜田病院¹, 東京大医療倫理学教室², 石渡産婦人科病院³生月弓子¹, 高橋しづこ², 佐藤智子³, 合阪幸三¹

【目的】2023年4月こども家庭庁が発足、189ダイヤルや児童虐待の社会的認知上昇もあり、令和4年度の児童相談所による児童虐待相談対応件数は21万9,170件、前年度より11,510件（+5.5%）増え、過去最多を更新。見相の人手、専門的知識不足、連携や調整不備、精神的重圧、疲労等もあり、悲惨な児童虐待死事件の未然防止に至らぬ一方、見相の体制や権限強化による誤認、怨恨や軽微な虐待通報より、親子双方の事情聴取なく、生物的親子、家族の長期分離、長期間の面会禁止、信書の開封や検閲等通信制限、一時保護中の通学禁止、所在不明、学習遅滞、施設での虐待、ハラスメント、保護児童一人に月45万円に及ぶ金銭的インセンティブ、安易な精神薬投与や医療保護入院、ICやカルテ開示請求禁止など人権侵害や違法行為が否めず、国際人権条約が無視された現状に対し、国連子どもの権利委員会から重要勧告を受けている。未成年の帰宅困難児相保護症例経験から見相行政の現体制改善を目的に報告する。【方法】見相保護下の未成年のケースレポート、裁判判例精査。【成績】医師、ソーシャルワーカー、弁護士、子ども代理人、自治体、厚生労働省、こども家庭庁の職員や法務局の人権擁護委員等外部機関の介入により、1年に及ぶ面会禁止解除、保護下の環境改善整備、家族の再統合、帰宅への調整開始。【結論】児童相談所の問題点は、守秘義務など閉鎖性から深刻な現状を知る機会が少ないが、医学、法曹、人権、行政、教育など関係機関の多角的介入により、児童虐待の早期発見、早期解決が期待され、今後の各専門家の積極的連携、人権擁護や法遵守、新たな法改正や整備、児童福祉司国家資格化や認知が必要不可欠である。

P-28-2 地方産婦人科女性医師のキャリア形成と育児の両立における問題点

佐賀県医療センター好生館

光 貴子, 北川早織, 山崎温詞, 久本菜美, 神下 優, 八並直子, 金井督之, 室 雅巳, 安永牧生

【目的】妊娠・出産・育児と仕事の両立は、女性医師自身のキャリア形成及び人材の確保の点から重要であるが、その両立は未だに多くの困難を伴っている。本研究では、地方の産婦人科女性医師がキャリア形成と育児の両立において有する問題点を明らかにすることを目的とした。【方法】佐賀県内を中心に、産婦人科医師（男性医師も含む）及び女性医師の配偶者を対象にアンケート調査を行なった。統計学的処理はJMP Pro15を使用し、フィッシャーの正確確率検定、 χ^2 検定、マンホイットニーのU検定で検討した。【成績】回答数は産婦人科医師43（回答率86%）、配偶者16（84.2%）であった。子供を有する女性医師のフルタイム勤務者と短時間勤務者の比較では、サポート体制や子供の数で有意差を認めず、未就学児の存在（ $p = 0.0022$ ）、医師年数の少なさ（ $p = 0.0016$ ）で時短勤務者が有意に多かった。産後の復職時の不安な点は手術（78.9%）、分娩業務（57.9%）が多かったが、子供を有する女性医師は、男性医師や子供のいない医師と比較して現在の手術執刀（ $p = 0.025$ ）、手術助手（ $p = 0.01$ ）、分娩業務（ $p = 0.015$ ）を行う割合が有意に少なかった。女性医師とその配偶者の比較では、週平均労働時間に有意差を認めなかったが、家事時間は女性医師が有意に多く（平日中央値：医師4.75（1~10）、配偶者1（0~3）時間）、早退も女性医師が有意に多かった（ $p = 0.001$ ）。自由記載では複数主治医制や働き方の多様性についての記載が見られた。【結論】子供の成長と共に仕事にかかる時間を増やすことはできる。それまでの間にキャリア向上の機会を減らさないため、執刀や分娩等の機会確保、家庭内のワーキングシェアが課題として挙げられた。

P-28-3 高齢期女性のヘルスケアに関わる要因について (コロナ禍の生活への影響調査から)

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【目的】日常生活が自立している高齢者に対して、コロナ禍の生活と健康への影響についてアンケート調査を実施、高齢者自身の日常生活への影響の認識を、先行研究の他世代の結果と比較し、高齢期の女性のヘルスケアに関わる要因と性差を分析する。【方法】2023年8月に実施した生涯教育講座に参加した高齢者93名(男性30名:平均年齢75.5歳,女性63名:76.5歳)に対して、無記名のアンケートを配布し、本研究の趣旨に同意した方から得た回答を分析した。コロナ禍の生活と心身への影響、健康感、受診行動、性別役割の認識に関する質問に、対象者自身が回答を記入した。【成績】①現在の健康感、男女とも8割が健康と回答。②コロナ禍の生活と健康への影響は、家族の世話・家事負担感の増加の認識は、有配偶女性42%、離死別女性14%、男性1割(先行研究の20-60代女性全体では4割,男性4.5%)。③家計管理の主体が男性にあると認識する女性の方が、負担感の認識が高率。④医療機関への受診抑制は有配偶女性18%、離死別女性33%(先行研究の女性4割,男性2割)。⑤受診抑制のなかった高齢者の8割が現在も持病のため通院中と回答。【結論】社会活動に参加可能な高齢者では、コロナ禍での家族の世話や家事の負担感、医療機関の受診抑制は、他世代と同様に女性の方が高率であり、配偶者の有無や同居家族で差異を認めた。高齢者にも家庭内の役割分担に性差が認められ、内閣府が示したコロナ下の女性への負担増大は、高齢者にも存在した可能性がある。高齢化や女性の社会進出で、家庭内での女性の役割が複雑化する中、高齢期女性の生活とヘルスケアに影響するジェンダー要因について、今後さらに研究を進める必要がある。

P-28-4 本邦初、月経カップを用いた現代日本人女性の月経重量に関する前向き観察研究～現代女性の月経重量はどのくらいですか?～

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【目的】長年、経血量は37-43mlが正常とされ、140ml以上を過多月経と定義されている。本邦女性の月経量に関する調査は近年少ない。現代女性の月経重量を月経カップを用いて測定することを目的とした。【方法】月経のある18-49歳の女性を対象とし、月経カップユーザーにwebアンケート調査を施行し被検者を募集し、24時間で150名が希望された。適格基準(子宮筋腫、子宮内膜症、卵巣腫瘍、定期的内服薬剤なし等)に適合した70名を対象とした。月経/月経量/月経カップに関するアンケート調査ならびに、3サイクル月経周期を連続して月経重量を被検者が専用アプリに記録した。主要評価項目は1サイクルの月経重量平均値と中央値とした。副次評価項目は未/経産婦、年齢別に分けそれぞれで月経重量を検討した。さらに自己申告月経量について実際量との評価を行った。【成績】68名、202月経が解析対象となった。年齢別18-29/30-39/40-49歳でそれぞれ14/33/21名、未/経産婦別28/40名、自己申告月経量は少/普通/多でそれぞれ2/47/19名であった。1サイクル月経重量の平均値±SD:98.4±52.7g,中央値82.3g,95%CI:[91.4-105.7g]であった。未経産婦と経産婦の検討ではそれぞれ平均値±SD:110.0±54.2g,中央値95.5g,平均値±SD:90.5±50.1g,中央値75.2gであり未経産婦が有意に多かった(p<0.01)。年齢別の月経重量に有意差を認めなかった。申告月経量の普通と多い群の実際の月経重量平均値は同等であった。普通の正答率は77%であり23%は過小評価し、多いの正答率は21%であり79%は過大評価だった。【結論】現代女性の月経重量研究を行い、正常とされる月経重量が明らかになった。自己申告月経量の主観は実際量と比較すると過小評価が問題であると考えられた。

P-28-5 HPVワクチン接種に関する学生等の意識調査と集団接種の試み

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【目的】令和4年4月よりHPVワクチン(HPV)接種の積極的勧奨が再開されたが、接種率は依然として低い。特にキャッチアップ(CU)接種は令和6年までの期限付き措置であり、接種率の向上は直近の課題である。HPVへの意識を調査し、接種率向上に向けた対策を検討した。【方法】本学在籍の学生・職員を対象に、2023年6月に保健管理センターよりHPVへの認識や接種希望に関するアンケートを行った。【成績】男女～名に配布し、1333名が回答。キャッチアップ(CU)接種対象者は606名であった。606名中、自身がCU対象者であると認識があったのは437名(72%)、CU接種終了時期を知っていたのは232名(38%)。未接種者423名中266名(62%)が学内での接種を希望し、56名は今年度で卒業予定であった。「接種を希望しない・わからない」が、116名(19%)で、その理由として「副反応が怖い」が最も多かった。【考察】アンケート内容から協議を行い、CU接種希望者に対して機会を設けることが必要と判断したため、直ちにHPV接種を大学病院にて実施する体制を整えた。卒業予定者を優先して180名の集団接種を行い、学内多職種連携の元、キャンパス間のバスの運行、事前情報収集、行政手続き案内、接種会場での産婦人科医との個別相談、内科医による集団接種不適合例や接種後副反応症例へのサポートを提供した。【結論】対象者の多くはHPV接種に前向きであり、大学内の多職種連携により、医療系以外の学部生への接種機会の提供に繋がった。正しい知識の提供と副反応への対応強化を行い、身近に接種機会を設けることで、より接種を推進できる可能性がある。

P-28-6 日本の若年層におけるSRHRに関する大規模意識調査～LEP服用や頸がん検診を避ける最大の理由は「お金がかかる」という誤った認識

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稲葉可奈子

【目的】日本の若年層におけるSRHR（セクシャル・リプロダクティブヘルス&ライツ）に関する意識調査。国際NGO ジョイセフが隔年で実施している調査を監修し、経時変化を分析した。【方法】交際経験がある全国の15-29歳を対象に、調査機関によるwebアンケート調査（匿名）を2023年8月に実施。【成績】有効回答は5800人（男性：2350人、女性：3156人、どちらでもない：294人）。避妊せずに性交渉をしたことがある割合はコロナ禍に減少、避妊しなかった理由の1位は「大丈夫だと思った」。もし自分/相手が妊娠したらどうするつもりだったか→「産む/産んでもらうつもりだった」が2019年44.9%→2021年33.3%→2023年34.4%。男女とも傾向は同じ。「緊急避妊薬を飲めばいいと思った」が2019→2023年（男性8%、女性4%）で増加傾向。ピルの月経コントロール、避妊の効果については4-5割が理解しているが、33%は値段が高いと認識（10代女性では44.5%）。ピルを服用していない理由の1位は「お金がかかる」で2021年37.9%→2023年45%、2位は「副作用が心配」。子宮頸がん検診を定期的に受診しているのは20代前半は18.8%。20代後半の35.9%は未受診。20代後半の子宮頸がん検診受けない理由は、「面倒だから」33.5%、「お金がかかるから」31.3%。※抄録に掲載しきれない結果についても発表時に詳報する。【結論】LEP、避妊、子宮頸がん検診など女性がSRHRを享受する上で重要な要素を「お金がかかる」という理由で避けられていることが明らかとなった。実際には自己負担が少ないものもあり、必要な情報が対象者に届いていない可能性が示唆される。国民の健康に寄与するには、制度整備だけでなく正しい情報の普及啓発も不可欠である。

P-28-7 過去2年間における医学部学生のHPVワクチンアンケート調査とその差異についての検討

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【目的】2022年度からHPVワクチンの積極的推奨が言われている。しかしながら、接種率増加に反映されていない。我々は、2022年に医学部学生に対し接種の目的と接種率などについて調査した。積極的推奨から1年経過した2023年においてHPVワクチンについて意識変化があるかアンケート方式で調査した。【方法】(1)医学部学生130名に対して、Googleフォームで作成したアンケート調査票を用いて質問する。その後、結果を集計し、Googleフォーム内のデータをオフラインでエクセルへ入力した（倫理承認番号MH2022-059）。(2)過去2年間のHPVワクチン接種率についてt検定を用い検討した。【成績】アンケート回答率は71%であった。平均年齢22.8歳であり、回答者の内訳は女子が46人、男子が55人であった。子宮頸がんワクチン接種歴の有る男子学生は1人(0.02%)、女子学生は70.7%であった。「子宮頸がんは予防できる」の質問については、男女ともに100%認識していた。HPVワクチンの子宮頸がん予防効果について「パートナーへの感染を防ぐ」が86%。ワクチン接種率は、2022年と2023年とで比較し有意差はなかった。9価ワクチンを接種率は昨年に比べ16.6%増加していた。特記することは、男子学生の接種者が1人いたことである。HPVワクチンの予防効果について、2022年の男子学生は40%のみであったが、2023年は約100%となった。HPVワクチンの情報源については、授業が51%、SNSは13%で家族が12%であった。【結論】1年間と短い期間であるが、女子・男子学生ともHPVワクチン予防効果についての意識が高まっていると考えられる。医学部の講義は学生自身の知識のみならず、同世代に向けて啓発活動に貢献すると期待する。

P-28-8 当院における性虐待被害児に対する被害確認診察の現状

旭中央病院
古賀千悠、藪田薫理、布施史織、鈴木拓真、市川瑛美、小川美咲、森脇隆太、北村翔一、高橋健太、大藏慶憲、小林康祐

【目的】近年児童相談所による児童虐待対応件数は年間20万件を超え、この30年間で約20倍に増加している。そのうち性虐待として報告されているものは1%程度であるが、約20%の女性が子どもの頃に性虐待被害を受けているとのWHOによる報告もあり、日本では性虐待が見逃されている可能性も否定できない。当院では児童相談所からの依頼で性虐待被害児に対する被害確認診察を行っており、被害児が女児の場合には小児科医だけでなく産婦人科医も同席し対応している。当院における診察の現状について報告する。【方法】2022年1月から12月に当院で小児科および産婦人科合同で診察した女児は34人であった。このうち同胞が性虐待を受けていたため被害の開示はないものの診察に至った8人を除く26人について分析した。【成績】平均年齢は12(5-17)歳、被害内容は乳房や陰部への接触が多かったが挿入被害を開示した児も7人(27%)認められた。問診時に多くの児が被害について語ったが、被害はなかったと語った児も2人おり、1人は挿入被害を事前に開示していた児であった。性虐待以外の虐待も受けていた児が12人(46%)。母に対してDVが認めらる児は9人(35%)見られた。【結論】挿入被害などの重大な被害にあっても診察室で開示できない児もおり、診察時の問診の重要性が確認できた。また性虐待だけでなく身体的、精神的虐待も受けていた児が約半数に上っており、母に対するDVを認める家庭も多かった。性虐待の開示がなくても他の虐待および家庭環境から性虐待の可能性を考慮し対応する必要がある。

P-28-9 病院職員に対するヒトパピローマウイルス (HPV) ワクチン認知度アンケート調査

青森県立中央病院
石原佳奈

【目的】ヒトパピローマウイルス (HPV) ワクチンの積極的接種勧奨の再開とキャッチアップ接種が開始となり1年半が経過した。全国的に接種率は上昇しているものの十分とは言えない。医療従事者に対し HPV ワクチンの認知度についてのアンケートを行い、HPV ワクチン接種率向上のため今後すべきことを模索するため。【方法】2023年9月にA総合病院職員に対し、無記名アンケート調査を行った。HPV ワクチンや定期接種、キャッチアップ接種、男児への接種拡大について知っているか、女性へは自身のワクチン接種の有無や検診受診についてのアンケート調査を行った。【成績】A総合病院の職員1580名中788名から回答(回答率50%)を得た。HPV ワクチン自体を知っていると答えた人は84%だったが、定期接種やキャッチアップ接種導入については知っている人は71%、38%であった。男児への接種が可能であることを知っている人は22%だった。10代~29歳の女性では、HPV ワクチンを定期接種もしくはキャッチアップ接種で受けている人は61% (68/110人)で、自治体からの案内や親からの勧めが接種動機であるとの回答が多かった。定期的な子宮頸がん検診率は78% (495/636人)と高かった。自由記載には、副反応への不安、安全性に対する情報が少ないなどの記載が複数認められた。HPV ワクチンや子宮頸がんに対する勉強会参加希望率は77%であった。【結論】医療従事者でも HPV ワクチン自体を知っている人は多かったが、キャッチアップ接種の認知度は低く、ワクチンの正しい理解が不足していることもわかった。勉強会参加希望率は高く、勉強会を開催し、勉強会聴講後の意識変化についても調査したい。

P-28-10 HPV ワクチンの普及を目指した当院での取り組み

愛媛大
田口晴賀, 宇佐美知香, 大塚沙織, 河端大輔, 中橋一嘉, 加藤宏章, 宮上 暉, 横山真紀, 安岡稔晃, 森本明美,
松元 隆, 杉山 隆

【目的】HPV ワクチンの積極的勧奨が再開になったが、全国的に定期接種・キャッチアップ接種ともに実施率が低いのが現状である。当院では HPV ワクチンの普及を目指し、医学部生および病院職員を対象にキャッチアップの集団接種を行ったため報告する。【方法】愛媛大学医学部の医学科・看護学科、愛媛大学医学部附属病院職員の中でキャッチアップ対象者は約750程度と考えられた。今回は HPV ワクチンを1回も受けていない者、県内に住民票がある者を対象とし希望者を募った。募集にあたっては、子宮頸がん予防についての情報をリーフレットにして情報提供を行った。また、使用するワクチンは2023年4月よりキャッチアップ接種にも使用できるようになった9価ワクチンを採用した。実施の運用に関しては、コロナワクチンの集団接種のノウハウを持った感染制御部の医師・看護師・薬剤師・病院事務の協力を得た。【成績】【結論】対象者の内、希望のあった85名に対してキャッチアップの集団接種を行った。現在までで2回目の接種まで終了したが、問題となる接種後症状の出現はない。実際の接種人数は対象者の約15%程度と考えられたが、医療従事者及び医学部生であり一般対象と比較して既に接種済の者も一定数存在した。接種者からは、友人や親戚にも接種を奨めたという声もあり、また今回対象としなかった県外に住み票がある学生からは帰省時に接種しようと思うという声もあり、波及効果はあったと感じている。定期接種に加え、2024年度末までのキャッチアップのさらなる接種普及を目指し、今後も取り組んでいきたい。

P-28-11 当院における性被害児への診察と行政連携の検討

福岡大
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【目的】子どもへの虐待はいまや世界での社会問題となっている。当院を診察のため来院した性被害で児童保護された児童の傾向を評価し、考察する。【方法】2018年から5年間で当院を受診した性被害疑いの児童50名を対象に、年齢、被疑者、裂傷の程度、などを評価した。【成績】年齢は3歳から18歳と広範囲にみられた。児童50名中、明らかに外陰部裂傷を認めたものは1例であった。【結論】外陰部の裂傷がないからといって、性被害を受けたと断定は困難である。

P-28-12 子宮頸がん検診における細胞診・HPV 併用検診と HPV 単独検診の検証

友愛医療センター

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【目的】細胞診・HPV 併用検診 (HPV 併用) は子宮頸がん検診の診断精度を向上させているが、過剰診断率が上昇していることが問題である。当院データより、HPV 併用の検証と効率的運用について検討した。さらに HPV 単独検診の有用性について解析した。【方法】2008年4月より2021年12月までの検診症例 105,096 例を対象とした。HPV 検査は同意のもと希望者に行い、6,078 例に実施した。年代別に細胞診陽性例、細胞診陰性例での HPV 陽性率を分析し、HPV 陽性例では型分析を行った。細胞診陰性・HPV 陽性例では可能な限りコルポスコピー検査と生検を実施し、CIN の頻度とその年代別分布を解析した。さらに2010年から2021年における HPV 併用で HPV 陰性例における細胞診異常の頻度を分析した。【成績】細胞診陰性例での HPV 陽性率は 11.2% であった。年代別の細胞診陰性・HPV 陽性での HPV 頻度は 20代で 16.1%、30代で 14.1% で両年代間に有意差は認めなかった。40代は 9.2%、50代は 8.5%、60代は 7.8% で推移していた。細胞診陰性・HPV 陽性例において精査できた 330 例中 193 例 (58.5%) が CIN と診断された。さらに、年齢別に精査できた CIN : 131 例と non-CIN : 119 例を分析し、20-39 歳と 40 歳以降を比較検討した結果、20-39 歳で有意に CIN の頻度が高かった。2010年から2021年において HPV 陰性例 4282 例中 42 例 (0.98%) のみが細胞診陽性であり、HPV 単独検診においても細胞診異常を見逃す率は低かった。【結論】細胞診陰性・HPV 陽性例の CIN 検出率が 58.5% であり、HPV 併用検診の有用性が示された。また、HPV 単独検診の細胞診異常を見逃す率は低く、今後、子頸がん検診の選択肢となることが示唆された。

P-28-13 医学教育における VR 画像講義の試み

佐賀大

梅崎 靖, 山口加恵, 大石将平, 瓜生泰恵, 吉武薫子, 池田正純, 奥川 馨, 横山正俊

【目的】当院では臨床実習生に対する骨盤内の解剖講義に VR シミュレーション画像の利用を試みている。造影 CT 画像より作成した 3D モデルを VR 空間で自由に移動や回転をさせることができるため、複雑な立体構造で構成された骨盤内臓器の位置関係を理解しやすく、教育に適した教材として利用できると考えた。臨床実習生の解剖講義に VR シミュレーション画像を利用することで、骨盤内臓器や血管走向など人体の立体構造に関して、どの程度理解度が向上するかを検討した。【方法】造影 CT の DICOM 画像から臓器や血管、尿管等の 3D ポリゴンデータを作成して、WEB 上のデータサービスサイトで VR データに変換する。用意したヘッドマウントディスプレイにその VR データを展開することで、3次元空間上でのデータ閲覧を可能にしている。臨床実習生を VR シミュレーション群と書籍イラスト群の 2 群に分けて、骨盤内の解剖講義を実施した。講義終了後に理解度を確認する試験を実施し、その定着度を得点化して比較した。【成績】VR シミュレーション群は書籍イラスト群と比較して講義理解度の得点がより高く、正確に骨盤内の立体解剖を理解していることがわかった。また実習後のアンケート評価でも VR シミュレーションの印象が強く残り、高評価を得ていることがわかった。【結論】VR シミュレーション体験での少なからずの感動が知識の習得や学習意欲の向上に寄与していると考えられ、VR シミュレーション教育の可能性を感じた。

P-28-14 月経異常を TBL ; Team-Based Learning で能動的に学修する取り組み

近畿大

貫戸明子, 松村謙臣

【目的】医学教育モデル・コア・カリキュラムで「月経異常」は臨床推論の項目で取り上げられており、他の診療科では専門的には扱わない症候のため、産婦人科における学修方略を充実させる必要がある。今回 TBL を取り入れたところ得られた効果が学生にも教員にも非常に多岐にわたるので報告する。【方法】医学部学生に対しての系統講義の中で、婦人科学に充てられている 26 時間のうち最後の 3 時間を月経異常の TBL とすることをシラバスに記載し、講義の冒頭でも学生に伝えて周知。事前に学生を小グループに振り分け、事前学習はそれまでの講義の内容と重複するので割愛、まず iRAT (Individual Readiness Assurance Test) をオンラインで実施。時間内に回答してもらい、結果をもとに補足説明と質疑を重ね、月経異常についての理解を深めてからグループでの作業に移行。各グループで課題に取り組み、それぞれ発表。その後フィードバックまでを時間内に終えた。iRAT への回答、発表、別のグループからの質問への対応も評価に含めた。【成績】学生：能動的な参加、批判的思考と問題解決スキルの向上、自己学習の重要性の理解が認められた。教員：1 対多数形式でも LMS (Learning management system) 活用などで学生のニーズの把握と適切なフィードバックができることがわかり、インターネット環境があれば遠隔でも参加可能であったり、評価の際の集計作業なども効率化できた。【結論】臨床推論をする上で必要な知識と実践的なスキルの教育として TBL は学生と教員に様々な効果をもたらす。

P-29-1 術前化学療法が著効した高異型度漿液性進行卵巣癌症例に対するインターバル腫瘍減量手術の有無による予後の検討

名古屋大

國島温志, 池田芳紀, 吉田康将, 吉原雅人, 玉内学志, 清水裕介, 横井 暁, 芳川修久, 新美 薫, 梶山広明

【目的】進行卵巣癌に対してNAC (neoadjuvant chemotherapy) を行い画像上CR (complete response) と判定した時にIDS (interval debulking surgery) を行って予後に寄与するのか疑問に思うことがある。今回、化学療法のみあるいはNAC-IDS後にCRが得られた症例においてIDSの施行有無で予後が異なるのかについて検討した。【方法】2001年から2020年までに初回治療を行った高異型度漿液性卵巣癌症例183例のうち試験開腹または細胞診陽性でNACを開始した82例を抽出し、そのうち化学療法のみあるいはNAC-IDSでCRを達成した48例を対象として後方視的に検討した。OS (overall survival), PFS (progression-free survival) を用いて評価した。【成績】48例の内訳はIDSなし (画像上残存病変なし) 群12例とIDSあり (肉眼的残存病変なし) 群36例であった。各群の年齢の中央値はそれぞれ61 (37-84) 歳と60 (31-74) 歳で、臨床進行期の内訳はそれぞれIII期10例・IV期2例とIII期26例・IV期10例であった。化学療法サイクル数の中央値はそれぞれ8 (3-19) サイクル, 6 (4-14) サイクルであった。OSの中央値はそれぞれ107か月と69か月であり、両群に有意差は認められなかった ($P=0.15$)。PFSの中央値はそれぞれ未到達と15か月であり、同様に有意差は認められなかった ($P=0.18$)。【結論】今回の検討において、化学療法のみあるいはNAC-IDS後にCRとなった症例においてIDSの施行有無で予後に有意差を認めなかったが、化学療法のみでCRとなったIDSなし群の方がOSもPFSも長い傾向であった。本研究の限界は症例数が少ないことであり、真に差がない可能性と検出力が低いために差が出ていない可能性も考えられる。今後も更なる症例の蓄積と検討が必要である。

P-29-2 KELIM値を用いた卵巣癌に対するPARP阻害薬使用患者の現状把握と予後解析

京都大

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【目的】卵巣癌に対するオラパリブとニラパリブの使い分けは定まっていない。血清CA125値の動態を示すKELIM値はプラチナ感受性や予後に関わる。プラチナ感受性がバイオマーカーであるPARP阻害薬におけるKELIM値の意義はわかっていない。本研究の目的は、オラパリブとニラパリブの対象がリアルワールドで異なるかをKELIM値により検証し、KELIM値の臨床的意義を検討することである。【方法】当施設で2021年1月から2023年9月の間に卵巣癌に対してPARP阻害薬で治療した134例 (オラパリブ90例, ニラパリブ44例) におけるプラチナ感受性の根拠となったPARP阻害薬直前のKELIM値と治療成績を後方視的に検討した。KELIM値1以下を高値群, 1を超える症例を低値群とした。【成績】初発コホートにおいて、オラパリブを用いた20例中 (ベバシズマブ併用18例) 10例が高値群で, 19例中4例が高値群のニラパリブよりも多い傾向にあった ($p=0.0958$)。初回腫瘍減量術後にオラパリブを用いた9例全て再発を認めなかった。一方、ニラパリブを用いた11例中8例に再発を認め、高値群は低値群よりも無増悪期間が長かった ($p=0.0595$)。再発コホートでもオラパリブに高値群が多い傾向にあった ($p=0.1593$)。再発コホートのオラパリブを用いた症例では、無増悪期間、全生存期間ともに高値群は長い傾向にあった (無増悪期間649日と260日, $p=0.0654$; 全生存期間未達と1,043日, $p=0.1099$)。【結論】オラパリブと比較してニラパリブを投与する症例はKELIM値が悪い傾向にある。PARP阻害薬を投与する前のプラチナ治療中のKELIM値を用いてPARP阻害薬の効果を予測できる。

P-29-3 当院におけるプラチナ感受性再発卵巣癌に対するPARP阻害剤投与症例の検討

JCHO 徳山中央病院

平林 啓, 中川達史, 新井響子, 松尾美結, 樫部真央子, 高木遥香, 澁谷文恵, 山縣芳明, 沼 文隆

【目的】再発卵巣癌 (卵管・腹膜癌含む) に対するPARP阻害剤の臨床効果と有害事象について検討する【方法】2018年から2022年までにPARP阻害剤投与歴のないプラチナ感受性再発卵巣癌に対しPARP阻害剤を投与した25例について患者背景, 臨床効果, 有害事象について検討した【成績】投与薬剤はオラパリブ16例, ニラパリブ9例で組織型はHGS16, 明細胞4, 類内膜3, 未分化2例で初回治療からPARP阻害剤投与までの期間は6M-125Mで中央値33Mであった。前治療の化学療法は1-6レジメンで中央値2レジメン, 投与前にコンパニオン診断を含む遺伝子検査を施行したのは14例 (FD-1: 4, FD-1 liquid: 9, 他1)でBRCA変異3例, HRDを1例に認めた。PARP阻害剤の投与期間は1-45Mで中央値6Mであった。現在まで25例中2例が有害事象で中止, 16例がPDとなり中止, 7例は1年以上経過しCRであり現在も投与継続中である。PDにて中止した16例でPDまでの期間は3M未満3例, 6M未満8例, 6M以降が5例であり, PDまでの中央値は5Mであった。現在CRの7例の組織型はHGS4例, 類内膜2例, 明細胞1例で投与期間は12-45M, 中央値35Mであった。有害事象により7例中5例で減量・休薬を要した。有害事象は軽微なものを含めると全例に認め、重篤な事象としてはG3貧血6例 (24%), G3血小板減少6例 (24%), G2嘔気・嘔吐5例 (20%), G2疲労・倦怠感5例 (20%)に認めた。発現時期は投与初期の4週以内に発生するものが多かった。【結論】PARP阻害剤でCRが得られた7例中5例は投与後3年が経過しており長期予後も期待できる。個別化医療のためには組織型やプラチナ感受性以外のHRD statusを含めた遺伝子情報を知ることが今後重要になると思われる。

P-29-4 再発卵巣がんに対する PARP 阻害薬リチャレンジに関する有用性の評価

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【目的】近年, 学会レベルでは再発卵巣がんに対する PARP 阻害薬リチャレンジの有用性が報告されているが, 我々産婦人科医にとってはいまだ未知の領域である. 我々は PARP 阻害薬リチャレンジの安全性と有効性について当院での臨床経過を後方視的に検討した. 【方法】2020年4月1日から2023年8月31日までに PARP 阻害薬リチャレンジを施行した卵巣がん11例, 卵管がん2例, 原発性腹膜がん2例を対象とし, その安全性および有効性を評価した. 【成績】年齢中央値は65歳(49-82歳), PSは0が14例, 1は1例であった. 組織型は漿液性癌14例, 類内膜癌1例であった. 前治療レジメン数は2が6例, 3が7例, 4以上が2例であった. 前 PARP 阻害薬はオラパリブが11例, ニラパリブが3例, ルカパリブが1例に投与され, 投与期間中央値は8か月(1-28か月)であった. リチャレンジにはオラパリブが8例, ニラパリブは7例に投与され, 投与期間中央値は3か月(1-24か月)であった. 減量は6例, 休薬は5例におこなわれた. Grade3以上の血液毒性は白血球減少1例, 好中球減少4例, 貧血3例, 血小板減少2例に認めた. また Grade3以上の非血液毒性, 治療関連死は認めなかった. 観察期間中央値は16か月であり, PFS, OS中央値はそれぞれ5か月(2-NA), 28.5か月(16-NA)であった. 【結論】PARP 阻害薬リチャレンジは Grade3以上の血液毒性は認めるものの, 減量, 休薬をおこなうことで治療継続が可能であり安全に投与することができた. しかし有効性については今後の検討課題となると考えられた.

P-29-5 当院における HRD 検査の現況とオラパリブとペバシズマブ併用維持療法の意義に関する検討

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【目的】相同組換え修復欠損 (homologous recombination deficiency: HRD) は DNA 損傷修復機構の異常を示す分子機構であり, 卵巣癌をはじめとする多くのがんにおいて, 予後予測および治療効果予測のバイオマーカーとなることが知られている. とりわけオラパリブとペバシズマブ併用維持療法 (PAOLA レジメン) のコンパニオン診断として実地臨床で用いられている. 自験例における HRD 検査 (myChoice 診断システム) の現況とオラパリブとペバシズマブ併用維持療法の意義について検討した. 【方法】当院で myChoice 診断システムを実施した卵巣癌・原発性腹膜癌・卵管癌患者の臨床的特徴およびその結果に基づいて PAOLA レジメンを施行した症例の有効性と安全性を後方視的に検討した. 【成績】2021年2月以降, HRD 検査は62例に実施された. このうち28例で HRD 陽性であり (45.1%), そのうち8例で tBRCA バリエントが陽性であった (12.9%). HRD 陽性例の内訳は初発時実施が18例, 再発時実施が10例, 卵巣癌20例, 腹膜癌6例, 卵管癌2例, 組織型は高異型度漿液性癌24例, 類内膜癌1例, 明細胞癌1例, 腺癌 (不詳) 2例であった. HRD 陽性例のうち13例が PAOLA レジメンを施行し, 2例の増悪例を除く11例はすべて治療を継続しており, 無増悪生存期間中央値は9か月(2か月-28か月)であった. 特に tBRCA 陽性例は長期の無増悪生存を示す傾向であった. 13例のうち1例が肺塞栓症のためペバシズマブを中止したものの, 12例では治療中止となる有害事象を認めなかった. 【結論】当院における HRD 陽性例は45%であり, 既知の報告と同等であった. PAOLA レジメン施行例の多くが無増悪生存を維持しており, その有効性が示された.

P-29-6 当院における進行卵巣癌の治療成績

安城更生病院

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【目的】進行卵巣癌に対して求められる手術術式は, 肉眼的残存腫瘍を認めない complete surgery の遂行である. そのためには基本術式に追加して, 横隔膜, 腸管, 脾臓等を含む他臓器合併切除が必要となる場合がある. 当院では2010年以降, 横隔膜切除や脾臓摘出などの上腹部操作を含む手術にて complete surgery を目指している. 【方法】2010年1月から2022年12月の間に卵巣癌 III 期または IV 期と診断した症例218例に対して, その治療成績につき後方視的に検討した. 【成績】進行卵巣癌218例のうち, 手術療法を施行した症例は143例 (65.6%) であった. PDS 58例 (40.6%), NAC-IDS 73例 (51.0%), その他12例 (8.4%) であった. optimal surgery を達成した症例は PDS において49例 (84.5%), NAC-IDS において67例 (91.8%) であった. そのうち, surgical complexity score が8点以上の症例は34例 (29.3%) であった. 2002年1月から2009年12月の間に当院で進行卵巣癌に対して PDS または NAC-IDS を行った症例38例と比較して, optimal rate の改善を認めた (52.6% vs 88.6%, $p < 0.01$). また, optimal surgery を達成した症例の生存期間中央値は, 2009年以前は61.0か月であったのに対し, 2010年以降は96.0か月であった. 【結論】積極的な手術を行うことにより, optimal rate の上昇を認め, 生存期間中央値は既報よりも高い結果であった. 他科との連携を十分にとり, complete surgery の達成を目指すことが重要であると考えられる.

P-29-7 当科における進行卵巣癌初回治療後のPARP阻害薬維持療法

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【目的】進行卵巣癌治療はPARP阻害薬を保険診療として導入できるようになり、大きく変化しつつある。当科における進行卵巣癌初回治療後のPARP阻害薬維持療法について紹介する。【方法】当科で進行卵巣癌・腹膜癌に対する初回治療後の維持療法としてPARP阻害薬を投与した症例(経済的理由で2か月で中止した1例を除く)について、診療録を用いて後方視的に検討した。【成績】進行卵巣癌・腹膜癌初回治療後の維持療法として12例の患者にPARP阻害薬維持療法を行った。卵巣癌が9例、腹膜癌が3例であった。初回治療時の年齢中央値は56.5(43-83)歳、進行期はIII期が9例、IV期が3例、組織型は高異型度漿液性癌が11例、類内膜癌が1例であった。手術治療はPDSが8例(Complete surgeryが4例、5mm以下のOptimal surgeryが4例)、IDSが4例(Complete surgeryが4例)であった。gBRCA1変異陽性が4例、gBRCA2変異陽性が2例、HRDが5例(sBRCA2変異陽性を1例含む)、不明が1例であった。初回化学療法のサイクル数中央値は8(6-9)回、維持療法開始時の治療効果はNED/CRが11例、PRが1例であった。使用薬剤はオラパリブが6例、ニラパリブが5例、オラパリブ+ペバシズマブ併用が1例であった。Grade3以上の有害事象を4例に認め、Grade4の血小板減少2例、Grade3の貧血1例、Grade3の好中球減少2例であった。経過中7例に休薬・減量を要した。12例中1例に再発を認めて4か月で中止となったが、11例は再発なく継続中である。現在継続中症例の継続期間中央値は10(4-33)か月であった。【結論】進行卵巣癌初回治療後のPARP阻害薬維持療法は、有害事象により休薬・減量を要することが多いが、継続投与が可能でPFS/OSの延長が期待できる。

P-29-8 当科における進行卵巣癌に対する他臓器切除の安全性の検討

北里大
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【目的】進行卵巣癌のPDS-R0達成が、明らかな予後良好因子であると近年見直されている。当科ではR0達成のため積極的に他臓器切除を実施しており、その安全性を検討することを本研究の目的とした。【方法】当科で2020年4月から2023年6月までに治療開始した進行卵巣癌を対象に、診療録を用いて後方視的に検討した。統計解析に χ^2 乗検定を用いた。【成績】進行卵巣癌は63例であり、IIIA期9例、IIIB期4例、IIIC期35例、IVA期8例、IVB期7例であった。39例(62%)に審査腹腔鏡を実施し、うち6例(15%)にPDSを実施した。19例(30%)は審査腹腔鏡をせずPDSを実施した。PDS実施25例の手術完遂度はR0:60%, optimal:16%, suboptimal:24%であり、腫瘍残存は直腸が最多(20%)であった。他臓器切除を9例(36%)で実施し、横隔膜・直腸が各4例、横行結腸2例、小腸1例で、3例(12%)に一時的人工肛門を造設した。合併症は直腸穿孔1例(人工肛門)、神経損傷2例、膀胱損傷1例であった。一方、NAC-IDS実施34例の手術完遂度はR0:56%, optimal:18%, suboptimal:27%であり、腫瘍残存は小腸と横隔膜が各7例で最多(21%)であった。他臓器切除を13例(38%)で実施し、横隔膜・横行結腸が各5例、NAC-IDS3例、脾臓尾部・小腸・S状結腸が各1例で、3例(9%)に一時的人工肛門を造設し、合併症は認めなかった。NAC-IDSと比べPDSは合併症率が高いが($P < 0.05$)、重篤な後遺症は認めず、人工肛門造設率は同等であった($P = 0.69$)。【結論】他臓器切除の実施率、人工肛門造設率はPDSとNAC-IDSで同等であったが、合併症率はPDSで高かった。PDS-R0達成による予後改善効果と合併症の可能性を含む十分なICのもと、PDSを実施する必要があると考えられた。

P-29-9 当科における進行卵巣癌に対する審査腹腔鏡 Status of staging laparoscopy for advanced ovarian cancer

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【目的】近年、進行卵巣癌の治療において相同組み換え修復異常の遺伝子検査が導入されたため治療開始前の組織採取は重要度が増している。そのため、審査腹腔鏡は最小限の傷で組織採取を施行し早期に化学療法を開始することが出来るアプローチとして施行される機会が増えている。今回、我々は当科における進行卵巣癌に対する審査腹腔鏡について後方視的に検討した。【方法】2020年1月~2022年4月に当科で進行卵巣癌もしくは腹膜癌の疑いの術前診断で審査腹腔鏡を施行した8例について患者背景および治療成績について検討した。【成績】患者背景では、術後診断は卵巣癌7例、腹膜癌1例、進行期はIIIC期6例、IVA期1例、IVB期1例、組織型は高異型度漿液性癌7例、類内膜癌1例であった。治療成績では、6例で二期的根治術を施行し、complete surgery 3例、optimal surgery 2例、suboptimal surgery 1例であり、二期的根治術までの化学療法施行数は 6.2 ± 0.4 (5-7)回であった。術後補助化学療法はtri-weekly TC + bevacizumab療法3例、tri-weekly TC療法2例、PLD-C + bevacizumab療法1例であり、施行数は 4.3 ± 1.2 (3-6)回であった。維持療法はbevacizumab療法3例、olaparib療法2例、bevacizumab + olaparib療法1例であり、4例で再発を認め、suboptimal surgeryの1例を含む2例で治療継続中であった。再発した4例でPlatina free intervalは 17.3 ± 7.8 (5-26)か月であった。【結論】進行卵巣癌に対する審査腹腔鏡は初回腫瘍減量術で完全切除困難が予想される症例に対する治療のよい選択肢となる可能性があると思われた。

P-29-10 当院における卵巣癌・卵管癌・腹膜癌に対するHRD検査施行症例の検討

杏林大

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【目的】進行卵巣癌では、相同組替え修復欠損 (HRD) が約半数に認められ、HRD を呈するがん細胞には PARP 阻害薬による合成致死が期待できる。HRD status を調べる myChoice™ 診断システムの当院における検査状況について検討した。【方法】2021年7月から2023年1月に当院にて myChoice™ 診断システムを施行した卵巣癌・卵管癌・腹膜癌の24症例を対象とし、患者背景、HRD status、ゲノム不安定性 (GI) スコア、初回治療について検討した。【成績】症例は卵巣癌16例、卵管癌7例、腹膜癌1例であった。組織型は高異型度漿液性癌が19例と最多であった。全症例の50% (12/24例) がHRD陽性、GIスコアの中央値は35 (6-78) であり、漿液性癌では57.9% (11/19例) がHRD陽性、GIスコアの中央値は45 (7-78) であった。HRD陽性/陰性に分けた検討では、PDSのcomplete/optimal surgery完遂率はHRD陽性例で41.7%、陰性例で72.7%であった。PDS後のフォローアップ期間の平均は21.5か月で58.3% (14/24例) で再発を認めた。再発率はHRD陽性例、陰性例ともに58.3%であった。TFIは平均6.5か月であり、HRD陽性例で4.7か月、陰性例で8.3か月であった。HRD陽性でPAOLAレジメンを受けた7例のうち3例で再発を認め、TFIは平均6.0か月であった。再発を認めない4例では平均10.5か月、維持療法の継続ができていた。【結論】当院における対象症例のHRD陽性率は半数であり、既報と一致した。HRD陽性例の中でPAOLAレジメンを受けた症例は、長期に維持療法を継続している傾向が見られ、TFIが延長されている可能性が示唆された。

P-29-11 進行卵巣癌・高異型度漿液性癌に対する化学療法の反応性、HRDとKELIMスコアとの関連

慶應義塾大

地阪光代

【目的】進行卵巣癌の術前化学療法 (neojuvant chemotherapy : NAC) に対する反応の予測因子として、CA125の値を用いたKELIM scoreが提唱されている。進行卵巣癌におけるKELIM scoreとHRDおよび予後との関連について、自験例を用いて後方視的に検討した。【方法】対象は2021年4月から2023年8月までにIII期以上の卵巣癌、卵管癌または腹膜癌で高異型度漿液性癌と診断され、NAC後にInternal debulking surgery (IDS) を施行し myChoice 診断システムでHRD検査が行われた19例とした。KELIM score 1点未満の低スコア群と、1点以上の高スコア群の2群に分けて、初回治療終了後の無増悪期間 (PFS)、HRD陽性率などの関係性を比較・検討した。KELIM scoreは初回化学療法投与日から100日以内に少なくとも3回計測されたCA125の値で算出した。【成績】低スコア群は9例、高スコア群は10例だった。症例全体の観察期間の中央値は15か月 (1-97か月)、年齢中央値は58歳 (39-77歳)、PFSは10か月 (0-97か月)、HRD陽性例は11例、BRCA1/2変異陽性例は6例であった。低スコア群と高スコア群ではそれぞれ、観察期間は15か月 (8-97か月) と15か月 (1-65か月)、年齢は69歳 (52-77歳)、52歳 (39-76歳)、PFSは13か月 (2-97か月)、6か月 (0-27か月) (p=0.27)、HRD陽性例は3例、8例 (p=0.07)。BRCA1/2変異陽性例は1例、5例 (p=0.122) であった。両群間にPFSやBRCA1/2変異の有無では明らかな有意差は付かなかったものの、HRD陽性例は高スコア群に多い傾向であった。【結論】KELIM scoreで年齢、PFS、BRCA1/2変異に明らかな有意差は認めなかったが、KELIM scoreが高い群はHRD陽性が多い傾向を認めた。今後の更なる検討が望まれる。

P-29-12 当院におけるPARP阻害剤の治療経験

奈良県立医大

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【目的】PARP阻害剤の登場後、卵巣がんの治療戦略は大きく変化した。そこで、PARP阻害剤であるOlaparib、Niraparibの使用経験について検討した。【方法】初回治療日が2020年1月から2023年5月までの上皮性の進行卵巣癌51症例について後方視的に解析を行った。内容は患者背景、治療経過、有害事象である。【成績】51症例であり、そのうち漿液性癌は38例、明細胞癌が7例、類内膜癌は5例、未分化癌が1例であった。年齢の中央値は64歳 [31歳-81歳] であった。MyChoice診断システムで検査を実施した例は35例であり、HRDは13例、HRPは22例であった。sBRCAmtであったものは3例であり、3例中gBRCAmtであったものは1例であった。初回治療としてPDSを行った症例は20例であり、NAC+IDSが20例、生検+化学療法が11例であった。化学療法としてTC療法あるいはTC+Bevasizumab療法を行い、CRが17例、PRが25例、SDが5例、PDが4例であった。維持療法を行った33例のうち6例がOlaparib+Bevasizumab、17例がNiraparib、9例がBevasizumab、1例がOlaparibであった。再発例は26例であり、プラチナ感受性再発は12例であった。PARP阻害剤を使用している症例では、23例中9例で再発を認め、プラチナ感受性であったものはそのうち6例であった。有害事象によるPARP阻害剤の中止は2例であり、原因は赤芽球瘡とMDSであった。うちMDSは有害事象により死亡している。【結論】多くの症例でPARPを使用しており、現在も再発なく治療継続できている。他方で致死的な有害事象も発生しており使用には注意が必要と考えられる。その効果については今後長期的な観察が必要である。

P-29-13 維持療法にPARP阻害薬を用いた進行再発卵巣癌の予後～PARP阻害薬2剤の比較

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【目的】進行再発卵巣癌は一旦緩解状態に到達しても比較的短期間に再発することも多い。近年は主治療後にPARP阻害薬を用いた維持療法の効果が期待されている。本邦においては維持療法のためのPARP阻害薬としてオラパリブ(O)およびニラパリブ(N)が認可されているが、投与適格基準が多少異なっており、その有用性の比較についての議論も不十分である。2剤のPARP阻害薬の有用性・予後について後方視的に検討する。【方法】2018年4月から2023年3月までに当科で治療を行った進行再発卵巣癌で、主治療後にPARP阻害薬を用いて維持療法を施行した24例。うちO群12例(初発3例, 再発9例), N群12例(同3例, 9例)につき、1)BRCA遺伝子変異の有無, 2)維持療法中の増悪の有無, 3)PFSおよびOS, 4)有害事象などにつき後方視的に検討した。【成績】患者背景には差はなかった。1)BRCA遺伝子変異の有無は、O群ではBRCA陽性が4例, MyChoice陽性1例, BRCA陰性または不明が7例, N群では同0例, 1例, 11例であった。2)維持療法中の増悪は、O群で8例, N群で4例であったが、統計上有意差はなかった。増悪までの期間は、前者で14.5か月, 後者で4.8か月であり、O群で有意に長期間であった。3)2群間でPFSおよびOSに有意差は認めなかった。4)O群では消化器症状で投与中止した症例が2例あった。N群では有害事象で減量した症例はあったが、中止した症例はなかった。【結論】BRCA遺伝子変異の有無に関わらず投与されたNは、Oと同等の予後を示したが、増悪までの期間が短い問題点も指摘された。PARP阻害薬投与症例の適正な選択基準に検討の余地があると思われる。

P-29-14 プラチナ感受性再発卵巣癌に対して、オラパリブの長期服薬が可能であった症例の背景因子の後方視検討

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【目的】PARP阻害剤であるオラパリブは、プラチナ感受性の再発卵巣癌(PSR)および、初回化学療法後のBRCA遺伝子変異陽性卵巣癌の維持療法において無増悪生存期間を延長させる効果が認められている。PSRに対してオラパリブの長期維持療法が可能であった症例の背景因子を検討した。【方法】2018年4月～2021年5月まで当院でPSRに対して、オラパリブを投与した16例を診療録から後方視的に検討した。無増悪で2年以上服薬継続中の5例(CR群)と2年以内に再発した11例(PD群)に分類した。2群間における1)年齢2)プラチナ製剤コース数3)プラチナフリーインターバル(PFI), 4)オラパリブ服薬開始前のCA125値についてWelch's t testを用いて、 $p < 0.05$ を有意差ありとし検討した。【成績】CR群とPD群において、オラパリブ開始時の年齢: 52(46-64) vs 69(46-83)歳, 投薬直前のCA125 U/ml 14.2(6.2-36.7) vs 82.7(24.5-335)であり、年齢とCA125において有意差を認めた。プラチナ製剤コース数とPFIでは有意差を認めなかった。CA125を20 U/mlをカットオフ値とし、CR群は5例中4例でCA125が20 U/ml以下で感度が80%, PD群はいずれもCA125が20 U/ml以上であり、特異度100%でAUCは0.964であった。【結論】PSRにおいて、低年齢、服薬開始前のCA125カットオフ20 U/ml以下の症例では2年以上服薬継続できる可能性があり、長期服薬可能か否かの目安になり得る。

P-30-1 化学療法が著効した子宮頸部大細胞型神経内分泌癌の1症例

天津赤十字病院

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子宮原発の大細胞型神経内分泌癌は非常にまれな悪性腫瘍であり、確立された標準治療はなく、予後不良とされる。特に子宮頸部原発は若年発症の報告も多い。今回我々は、若年発症で急速に進行した子宮頸部大細胞型神経内分泌癌に対し、化学療法が著効した症例を経験した。症例は28歳、未経妊。下腹痛を主訴に救急受診し、内診、経膈超音波検査にて子宮全体の腫大や腹水貯留の所見を認めた。CT・MRI検査にて、子宮頸部左側から体部に広く浸潤するような腫瘍と、腹膜播種、骨盤内多発リンパ節腫大、多発肺転移を疑う結節を認めた。また初診の翌日に再度診察した際、膈前壁への浸潤を疑う潰瘍性変化が確認され、同部の生検による組織診にて大細胞型神経内分泌癌の診断であり、子宮頸癌IVB期と考えた。初診から数日のうちに咳嗽、呼吸苦、疼痛などの症状の増悪が進行したが、初診の12日後から化学療法VP-16/CDDPを開始したところ諸症状は著明に改善し、3サイクル終了時点で画像検査上も子宮、膈の腫瘍や播種、転移病変は消退した。現在6サイクルまで終了して、以降は厳重経過観察を予定している。子宮頸部大細胞型神経内分泌癌は初期ならば広汎子宮全摘術と術後化学療法または化学放射線療法が主に行われるが、手術不能の進行例に対しては化学療法や化学放射線療法が試みられるものの予後不良な報告が多い。化学療法のレジメンには様々な報告があるが、本症例では最も報告例の多いVP-16/CDDPを選択して著明な効果が得られた。今後の治療方針も含め、本症例に関し、若干の文献的考察を加え報告する。

P-30-2 妊娠中に子宮頸癌再発治療を要した一例

島根大

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【背景】子宮頸癌の若年化により、妊娠中に初めて子宮頸癌と診断・治療された症例は比較的多い。しかし、これまでに妊娠中に子宮頸癌再発と診断・治療された報告はない。我々は、妊娠22週で子宮頸癌再発と診断し妊娠中化学療法を行った症例を経験したため報告する。【症例】39歳時に前医でHSIL/CIN3の診断にて子宮頸部円錐切除術を施行された。子宮頸部円錐切除検体の病理診断はHSIL/CIN3・腺様基底細胞癌pT1a1, 切除断端陰性であった。円錐切除前のMRI検査にて左骨盤内リンパ節腫大を認めていたが、その後リンパ節の増大なく経過していた。41歳で自然妊娠成立(3妊0産)し、MRI検査にて左骨盤内リンパ節腫大増大、血液検査にてSCC上昇を認め妊娠22週で当院紹介となった。子宮頸部円錐切除検体再評価にて扁平上皮癌と診断された。PET-CT検査にて骨盤内腫大リンパ節のFDG集積を認めたため子宮頸癌再発と診断し、妊娠24週より化学療法(TC療法3コース)施行した。化学療法により腫大リンパ節の縮小、腫瘍マーカーの改善を認めた。妊娠34週で選択的帝王切開を行い、同時に子宮全摘術・両側付属期切除術・骨盤内リンパ節郭清術を施行した。摘出したリンパ節に腫瘍残存を認めたため、術後CCRT(同時化学放射線療法)を行った。【結論】我々は妊娠中に子宮頸癌再発と診断された症例を経験した。本症例をフォローしていき、妊娠中に子宮頸癌が再発した場合の治療について検討していきたい。

P-30-3 子宮頸癌の放射線治療後に発生した二次性子宮体部悪性腫瘍の3例

北里大

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【緒言】子宮頸癌に対する放射線治療の進歩により長期予後を期待できるようになった一方で、稀だが二次性癌を生じる事が報告されている。今回、子宮頸癌の放射線治療後の二次性癌として子宮体癌を発症したと考えられた3症例を報告する。【症例】59歳(G4P4), 87歳(G1P1), 48歳(G0P0)。症例1,2は子宮頸部扁平上皮癌でIIIB期(cT3bN0M0), 症例3はIIIC1r期(cT3bN1M0)の診断で同時化学放射線治療を行い寛解した。それぞれ治療後11年, 5年, 12年で偶発的に子宮腫大を指摘され当院に紹介となった。当院紹介から1~8か月の時点で子宮体部悪性腫瘍の疑いで子宮全摘を行い子宮体部明細胞癌IA期(pT1aN0M0), 子宮体部癌肉腫IB期(pT1bN0M0), 子宮体部癌肉腫II期(pT2N0M0)の診断となった。症例1は肥大型心筋症を合併しており術後抗癌剤治療を行わず経過観察の方針となったが、術後7か月で腹膜播種再発し抗癌剤治療を行い、術後31か月で原病死した。症例2は高齢の為に抗癌剤治療は行わなかったが、術後9か月で腔断端再発しBest supportive careの方針となり術後17か月で原病死した。症例3は術後抗癌剤治療を行い術後20か月で無病生存中である。【結語】放射線治療後の二次性癌3症例を経験した。放射線治療の影響により子宮内膜検査や手術が困難であり確定診断を付ける事に難渋したが、悪性疾患の存在が疑われる場合には、二次性癌の可能性を考慮しつつ適切な診断と治療を行う必要があると考えた。

P-30-4 子宮頸癌に対する放射線治療後に仮性動脈瘤を発症した3症例

筑波大

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仮性動脈瘤は、血管壁を形成する3層(内膜, 中膜, 外膜)の壁が欠け、漏れた血液が外膜と周囲の結合組織との間に瘤を形成したものである。仮性動脈瘤の原因は手術や外傷・感染などがあり、産婦人科領域では子宮内容除去術, 正常分娩後など子宮内操作後に生じることが報告されている。悪性疾患においては、放射線治療の後期合併症として、まれに仮性動脈瘤を形成することが報告されている。今回、子宮頸癌の放射線治療後に骨盤内に仮性動脈瘤を形成し、動脈塞栓術を要した3例を経験した。3症例とも放射線治療後1年以上経過しており、最長19年目で診断された。【症例1】放射線治療後7年、不正性器出血の増加を認め救急外来を受診し、右内腸骨動脈の仮性動脈瘤を診断され、緊急動脈塞栓術を施行した。2か月後に新たに仮性動脈瘤を指摘され、再び動脈塞栓術を施行した。【症例2】放射線治療後19年、大量の性器出血を認めた。仮性動脈瘤の破裂と診断され、動脈塞栓術, 左右総大腿動脈バイパス術を施行した。【症例3】放射線治療後2年、大量の性器出血にて救急搬送され、子宮動脈の仮性動脈瘤を診断され動脈塞栓術を施行した。さらに13年後に大量性器出血のため救急搬送となった。CTでは骨盤内血腫を形成し、最後は出血コントロールが困難となり、死亡となった。今回我々が経験した3症例は、腫瘍の再発はなく、放射線治療後に膀胱, 腔, 直腸に瘻孔を形成し、感染コントロールに難渋したエピソードがあった。仮性動脈瘤は破裂による大量出血のため、致命的な状態に陥る可能性が高い。まれな疾患であるが放射線治療後の管理において、仮性動脈瘤の存在を念頭において管理する必要がある。

P-30-5 子宮頸癌に対する手術・放射線治療を行い婦人科フォロー終了後に重篤な放射線晩期障害を来した4症例

箕面市立病院

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【目的】放射線治療後の晩期障害は治療が困難であり相当な期間を経過してから発症することもある。子宮頸癌の放射線治療後に発症した重篤な晩期障害の4症例を報告する。【成績】4症例で広汎子宮全摘術と術後の全骨盤照射が実施されていた。他院で手術が行われ、子宮頸癌のフォローは終了していた。【症例1】30歳で手術、照射。膀胱腫瘍、直腸腫瘍の状態。骨盤内は空洞形成され、感染を繰り返し、64歳で恥骨骨髓炎発症。両側尿管狭窄生じ、腎瘻造設。イレウス、誤嚥性肺炎を繰り返し71歳で死亡。【症例2】57歳で手術、照射。術後右腎瘻造設。イレウスの繰り返しあり、74歳で小腸炎、吸収不良状態。小腸穿孔を来した手術。76歳でS状結腸瘻孔、S状結腸小腸瘻となり、ストーマ手術もイレウス、骨盤内膿瘍となり死亡。【症例3】51歳で手術、照射。57歳でイレウス、小腸穿孔を来し小腸大量切除、短腸症候群となり吸収障害。左右尿管狭窄にて左右腎盂カテーテル留置。60歳で左腎瘻造設。尿路感染とCVポート感染を繰り返している。症例4:33歳で手術、照射。55歳で下肢リンパ管炎、大陰唇リンパ管腫発症。64歳で恥骨骨髓炎にて外科的治療を実施。65歳でイレウス、尿路感染を来し、左尿管狭窄に対して尿管バルン拡張。66歳で膀胱穿通にて保存的治療を行った。【結論】放射線晩期障害の根治的な治療は困難である。病状は進行性であり2症例では死亡に至った。尿路や腸管の合併症が特に問題となり、治療に婦人科が関与していない症例が多い。当院の症例でも3症例は治療のメインは外科や泌尿器科であった。婦人科で把握していない重篤な晩期合併症の症例が多く隠れていることが推測される。

P-30-6 ペムプロリズマブによるステロイド抵抗性 irAE 胆管炎に対してタクロリムスを導入した一例

静岡県立総合病院

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【緒言】免疫チェックポイント阻害薬 (ICI) には多彩な免疫関連有害事象 (irAE) が報告されるが、頻度 0.05% と報告される稀な irAE 胆管炎を経験した。【症例】40歳で子宮頸癌 (adenocarcinoma) IB1 期に対して広汎子宮全摘術、両側付属器切除術を行い経過観察していたが、4年で通院を自己中断した。左下肢痛が出現し54歳時にMRIで左臀部腫瘍、多発リンパ節腫大を認め、CTガイド下生検で子宮頸癌再発と診断し、パクリタキセル/カルボプラチン/ペバシズマブ/ペムプロリズマブ (Pem) 療法を開始した。3サイクルでPRの効果を得て、下肢痛に対するモルヒネ硫酸塩の使用量も著減した。CTで総胆管壁肥厚を認め、時折心窩部痛があったが、肝胆道系酵素上昇はGrade1であり、4サイクル目を実施した。Day9に心窩部痛の増悪、発熱を認め、肝胆道系酵素はさらに上昇し入院管理とした。PemによるirAE胆管炎と考えDay12にステロイドパルス療法を開始したが漸減途中で再燃したため、院内の臨床倫理委員会の適応外使用の承認を得てミコフェノール酸モフェチルやアザチオプリンを導入した。いずれも再燃し徐々にCTで肝内胆管拡張が増悪し、総ビリルビン (Bil) 12.0mg/dl まで上昇したためタクロリムス (Tac) を導入したところ、高 Bil 血症は改善傾向を認めている。irAE胆管炎発症後8か月経過したが再発腫瘍は縮小を維持し、化学療法は中断のまま Tac による治療を継続中である。【結語】腹痛や肝胆道系上昇を認めた場合、irAE胆管炎は重要な鑑別疾患である。ステロイド抵抗性 irAE胆管炎は死亡例の報告もあり、免疫抑制剤の有効性に関する報告は少ない中で、Tacによる高 Bil 血症の改善を認めた貴重な一例を経験した。

P-30-7 子宮頸部胃型 HPV 非依存性腺癌に対して術前化学療法後、手術療法を施行し完全奏功となった一例

三重大

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【背景】子宮頸部胃型 HPV 非依存性腺癌は治療抵抗性で、予後不良な疾患である。今回、子宮頸部胃型 HPV 非依存性腺癌に対して術前化学療法後、手術療法を施行し完全奏功となった一例を経験したので、その組織型特徴を含めて報告する。【症例】症例は70歳、5妊3産、下腹部痛を主訴に前医を受診され、CT検査で骨盤、傍大動脈多発リンパ節転移と子宮頸癌が疑われ、当院紹介となった。子宮頸部に5cm大の腫瘍あり、傍組織浸潤はなく、腔壁下2分の1まで浸潤していた。子宮頸部の生検で、核の濃染と腫大を示す腫瘍細胞が不整管状や索状、あるいは小胞巣状構造を形成して浸潤する腫瘍を認めた。背景に粘液を伴い、一部の腫瘍細胞は印環細胞の形態を示した。免疫染色でp16は陰性であり、子宮頸部胃型 HPV 非依存性腺癌と診断された。血液検査は、CA19-9:125.4U/ml, CA125:55U/mlと高値で、骨盤部MRIでは明らかな膀胱直腸浸潤や子宮傍組織浸潤はなく、臨床進行期分類IIIC2期、cT2a2N2M0と診断した。術前化学療法後、手術の方針とし、パクリタキセル+カルボプラチン+ペバシズマブ2コース施行後、CT検査で腫瘍縮小を確認し、1コース追加後、腹式広汎子宮全摘術+両側付属器切除+骨盤、傍大動脈リンパ節郭清術を施行した。病理組織は、淡明な細胞質を豊富に有する細胞と細胞質が乏しい細胞が混在し、未分化癌と胃型 HPV 非依存性腺癌が混在しており、ypT1bN2M0と診断された。術後化学療法3コース施行し、CT検査で完全奏功のため、現在外来経過観察中である。【結論】子宮頸部胃型 HPV 非依存性腺癌は化学療法抵抗性とされるが、短期間の化学療法から手術を施行することで、完全奏功を得ることができた。

P-30-8 広汎子宮全摘術の神経因性膀胱に与える影響

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【目的】広汎子宮全摘術では、子宮の傍組織を広範囲に切除するため、骨盤内の自律神経を損傷し、術後の膀胱機能の低下（神経因性膀胱）を高率に発症する。膀胱機能温存のためには骨盤神経叢膀胱枝の温存が重要で、現在多くの施設では自律神経温存術式が選択されている。当院でも全例、自律神経の温存に努めている。しかし、自律神経を温存した症例でも術後神経因性膀胱（排尿障害）の症状が遷延する症例が散見される。広汎子宮全摘術が術後の神経因性膀胱に与える影響を明らかにするため、関連する様々な要因を比較検討した。【対象および方法】2022年4月から2023年8月まで当院で広汎子宮全摘術を施行した23例の症例について、術後神経因性膀胱の症状が遷延している（自己導尿を継続している）群：CIC群とそうでない群：非CIC群について、術前に施行した排尿関連質問票（OABSS, IPSS, ICIQ-SF）による主観的評価と尿流測定による客観的評価、年齢、BMI、病期などの患者背景因子を比較した。【結果】CIC群と非CIC群では、両群間の患者背景因子のうち、術前の腫瘍径、術前のSCCの値に統計学的有意差を認めた。また術前の下部尿路症状では、CIC群と非CIC群で術前の残尿量に有意差を認めた。なお、CIC群において、術前の最大尿流量率が低い傾向があった。【結論】自律神経温存の広汎子宮全摘術後の排尿障害の有意なリスク因子として、腫瘍径、SCCは重要な患者背景因子と推測された。術前の残尿量もリスク因子となることが示唆された。

P-30-9 当院で治療した子宮頸部小細胞神経内分泌癌の3例

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子宮頸部小細胞神経内分泌癌は子宮頸部の神経内分泌腫瘍の中で最も多く、その65~80%を占めるとされる。しかし、子宮頸部における神経内分泌腫瘍の割合は1~1.5%程度と報告されており、稀な腫瘍の一つである。悪性度が高く早期症例でも転移再発が多く、予後はI期でも5年生存率65.5%と本邦の報告にあるように不良である。2001~2022年の期間に当院で初回治療した子宮頸癌は427例で、うち小細胞神経内分泌癌は3例（0.7%）であった。症例1、22歳IIA期治療は化学療法（P・CPT-11）先行し、広汎子宮全摘術施行。子宮頸部腫瘍は化学療法が完全奏功であったが、骨盤リンパ節転移は認めた。追加化学療法行い寛解したが、短期間で乳房転移等生じた。化学療法放射線治療行ったが、肝転移など多発転移生じ、初回治療より1年7月後に原病死となった。症例2、38歳Ib2期治療は化学療法（EP）先行し、広汎子宮全摘術施行。子宮頸部に腫瘍残存認めたが、骨盤リンパ節転移は認めなかった。追加化学療法行い寛解。初回治療より10年9月後無病生存。症例3、32歳IIB期治療は化学療法（EP）先行し、同時化学放射線治療施行。さらに追加化学療法を行い寛解。初回治療より3年9月後無病生存。子宮頸部小細胞神経内分泌癌は稀な腫瘍で標準治療が確立しているとは言えない。通常の子宮頸癌と異なり、化学療法がかなり重要で、使用薬剤も肺の小細胞癌に準じた薬剤が有効。予後も通常の子宮頸癌より不良で、集学的な治療戦略が重要である。

P-30-10 進行・再発子宮頸癌に対するペムプロリズマブ使用時の留意点：子宮頸癌に特有と考えられる有害事象を経験して

熊本大

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【目的】進行・再発子宮頸癌に対するペムプロリズマブ（Pem）の使用においては、さまざまな有害事象が報告されている。今回、我々は子宮頸癌に特有と考えられる有害事象を経験したため、その発生機序とPem使用時の留意点について考察を加えて報告する。【方法】2022年11月から2023年8月の間に当施設で子宮頸癌に対しPemが使用された16例（進行症例：IIIC2期1例、IVB期4例、再発例；IB1期2例、IB2期1例、IIIB期3例、IIIC2期1例、IVA期2例、IVB期2例）を対象に治療効果と有害事象を後方視的に検討した。【成績】年齢の中央値は52歳（26~70歳）で、治療期間は2~10か月であった。組織型は扁平上皮癌が11例、腺扁平上皮癌が1例、大細胞神経内分泌癌が2例、腺癌が2例で、初回治療として10例、術後補助療法として2例に同時化学放射線療法（CCRT）が行われていた。治療効果を判定しえた8例において、2例に部分奏効、3例に安定、3例に進行が認められ、Grade3の有害事象として、下痢、薬剤性中毒疹、発熱性好中球減少症、下垂体機能低下症、高血圧症が1例ずつに認められた。子宮傍組織進展を伴うbalkyな腫瘍と遠隔転移を有したIVB期の1例では、CCRT後の残存腫瘍に対しパクリタキセル+カルボプラチン+ペバシズマブ+Pemによる治療が行われ奏効がみられたが、Grade3の子宮出血と直腸腔瘻が認められ、2度の動脈塞栓術と人工肛門増設を要した。【結論】子宮頸癌のPem使用では、Bev併用による放射線照射部位での瘻孔形成のリスクが高まり、さらに、血管が豊富な子宮傍組織への進展例で、Pem著効による腫瘍組織の壊死・線維化による出血が惹起される危険性があることに留意する必要がある。

P-30-11 妊娠中細胞診にて ASCUS であったが産後の組織診にて頸癌 IIB 期の診断に至った 1 例

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【緒言】妊娠中の子宮頸部細胞診異常に対して、ハイリスク HPV 検査、コルポスコピー、生検組織診は非妊娠時と同様に行うことが推奨されている。妊娠中の細胞診で LSIL を認めたが組織診を施行せず、産後 2 週間の組織診で浸潤癌の診断に至った症例を経験したので報告する。【症例】34 歳、2 妊 1 産。妊娠初期に細胞診 LSIL、HPV18 陽性だったが、組織診は施行せず、中期の細胞診は ASC-US であった。29 週に切迫早産の管理目的に当院へ母体搬送された。切迫早産管理中から頸部は易出血性であり、疼痛のため腔鏡診による頸部の観察が困難であった。31 週に骨盤位で陣痛発来し緊急帝王切開を施行した。帝王切開後 2 週間の受診の際に多量出血の持続の訴えがあり、診察にて浸潤癌が疑われ、頸部組織診施行したところ扁平上皮癌の診断に至った。精査の結果 IIB 期と診断し、帝王切開から 57 日後に広汎子宮全摘、両側付属期切除を施行した。【考察】産科ガイドラインでは細胞診が ASC-US や LSIL の場合、組織診で浸潤癌と判明する可能性は極めて低く、コルポスコピーは分娩後に延期することも許容されると記載されている。本症例では細胞診では ASC-US、LSIL までしか検出しなかったにも関わらず、組織診にて浸潤癌の診断に至っており、細胞診と組織診に乖離があったと考えられた。【結語】切迫早産管理 2 週間のうちに帝王切開となり、産後 2 週間の組織診にて子宮頸癌 IIB 期と診断された症例を経験した。コルポスコピー、組織診を行うことで、治療を早期に開始できた可能性があった。

P-31-1 HBOC に対するリスク低減卵巣摘出術及び乳腺外科手術の合同実施に関する当院での取り組み

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【目的】2020 年より遺伝性乳がん卵巣がん症候群 (HBOC) 当事者に対する診療が一部保険収載され、当院でもリスク低減卵巣摘出術 (RRSO) の症例数は増えている。当院では乳腺外科と連携し、乳腺手術と同時に RRSO を施行しており、これまでの取り組みについて報告するとともに、その安全性について検討する。【方法】2020 年 4 月から 2023 年 4 月に当院にて RRSO を施行した症例を対象とし、診療録を用いて後方視的に検討した。【成績】RRSO 実施症例 47 例のうち 5 例 (10.6%) が乳腺外科と合同で、42 例 (89.4%) が婦人科単独で手術を施行していた。合同手術と婦人科単独手術で比較すると、手術時間の中央値は合同手術が 204 分、婦人科単独手術が 79 分と合同手術の方が長い。RRSO のみの時間で比較すると有意な差は認めなかった (中央値 82 分対 79 分; $p=0.666$)。RRSO における術中出血量は全ての症例で少量であり、術中・術後合併症も認めなかった。合同手術を行った 5 例に関して乳腺外科の手術内容を検討すると、4 例は乳腺のリスク低減手術であり、1 例が乳癌の初回治療として両側乳房全摘及び患側腋窩リンパ節郭清を施行していた。乳癌手術との同時手術でも大きな合併症なく施行可能であった。【結論】合同手術を実施するにあたり、臨床遺伝子診療科を中心に乳腺外科、婦人科で、その意義と対象症例について検討を重ね、導入が実現した。手術回数の減少、入院費用の負担減少から HBOC 当事者にとってメリットは大きく、今回の検討で安全性も確認できた。現在、合同クリニカルパスを作成中であり、さらに多診療科での連携を強化していく。今後も患者の病状・希望にあわせて安全な医療の提供に努めていきたい。

P-31-2 子宮頸部円錐切除術に対する Thulium : yttrium-aluminium-garnet laser (Tm-YAG レーザー) の有用性について

奈良県立医大

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【目的】円錐切除術の方法には、レーザー、メス、LEEP (electrosurgical excision procedure) 法、ハーモニックスカルペル (HS) があり、それぞれの方法や機器、器具の特長がある。しかし以前より熱凝固による診断精度の低下、正常組織の損傷が指摘されてきた。Thulium : yttrium-aluminium-garnet laser (Tm-YAG レーザー) による熱凝固の組織深達度は約 400 μm と少ないとされ、泌尿器科領域で利用されている。円錐切除術に Tm-YAG レーザーを用いることで正確な病理組織学的検索と正常組織の熱損傷を減らすことが可能かを検証した。【方法】当院で 2020 年 12 月から 2022 年 5 月に実施した円錐切除術のうち、Tm-YAG レーザーを用いた 10 例と、HS を用いた 10 例を対象とし、熱凝固の組織深達度について後方視的に比較検討を行った。熱凝固の組織深達度は、H-E 染色標本を鏡検し症例すべての切片で、筋層面の熱変性部の最大深度を計測した。また断端の陽性率・不明率、入院期間、出血量、手術時間、合併症の有無 (術後出血や頸管狭窄など) について検討した。【成績】組織深達度は、HS 群で 320-389 μm (中央値 300 μm)、Tm-YAG レーザー群で 201-243 μm (中央値 200 μm) で有意差を認めた ($p<0.01$)。断端の陽性率・不明率、入院期間、出血量、手術時間、合併症の有無に有意差は認めなかった。【結論】Tm-YAG レーザーは円錐切除術においても熱凝固の組織深達度が少ないことが改めて示された。正確な病理組織学的検索と正常組織の熱損傷を減らす利点がある。今後は長期的な追跡を行い、再発率や妊娠率などの検討を行っていく。

P-31-3 当科での審査腹腔鏡の現況

姫路赤十字病院

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【目的】進行卵巣/卵管/腹膜癌における PAOLA レジメン適応の判定検査である HRD 検査 (MyChoice™ 診断システム) は、2021 年 1 月に保険収載されて以来本邦でも急速に広まっている。HRD 検査は卵巣癌の治療方針を決定する際の一助となるがその測定には十分な組織量が必要なため当科では組織採取法として審査腹腔鏡を第一選択としている。今回、当科における進行卵巣癌に対する審査腹腔鏡の成績に検討を加え、その現況を分析することを目的とした。【方法】2021 年 1 月から 2023 年 3 月までに当科で施行した審査腹腔鏡 13 例について、進行期や組織型、HRD status、手術時間、出血量、治療開始までの期間などについて後方視的に検討した。【成績】13 例全例で組織型の確定診断が可能で、10 例が高異型度漿液性癌、2 例が癌肉腫、1 例が卵巣癌であった。HRD 検査は 13 例中 11 例に行われ、それぞれに対して最適と考えられる維持療法を選択した。HRD 例の 75% に PAOLA レジメンが適応されていた。HRP 例では、維持療法に移行できた症例はいずれも Niraparib が開始されていた。今回検討した症例はいずれも審査腹腔鏡による重篤な合併症は認めず、急性増悪した 1 例を除いて術後速やかに術前化学療法を開始することができた。導入当初は審査腹腔鏡から治療開始までに 2-3 週間と日数がかかっているが最近ではおおそ 8 日以内に治療開始できていた。また、IDS 施行例の 80% で complete surgery が達成されていた。【結論】HRD status によって個別に維持療法を選択することもでき、審査腹腔鏡は進行卵巣癌の治療方針を決定する上で有用と考えられた。

P-31-4 国産手術支援ロボット hinotori の導入と安全性について

神戸大

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【目的】婦人科領域において 2022 年から国産手術支援ロボットである hinotori サージカルロボットシステム (以下 hinotori) が保険診療で認可された。hinotori はアームがコンパクトであり、また衝突で停止するなど安全面に配慮された設計となっている。ハンドクラッチの搭載など、臨床導入後もアップデートが数回行われている。当院で実施している hinotori の治療成績や安全面について検討した。【方法】2022 年 9 月から 2023 年 9 月に行われた hinotori, da-Vinci X あるいは Xi を用いたロボット支援下手術において、hinotori 群と da-Vinci 群で手術時間や術後血液検査などについて後方視的に比較検討を行った。【成績】hinotori 群は 22 例 (悪性 11 例)、da-Vinci 群は 50 例 (悪性 23 例) であった。各群で患者背景、子宮摘出重量に差はなく、またロールインまでの所用時間やドッキング所要時間、術後入院期間や合併症有無などに差は認めなかった。コンソールから腔断端縫合終了までの時間は hinotori 群で低かった (hinotori 群 148 分 vs 176 分, $p < 0.01$)。また術後 1 日目、3 日目の CRP 値は hinotori 群で有意に低かった。両群間で術中合併症は認めず、Clavien-Dindo 分類の Grade II 以上の術後合併症についても差を認めなかった。【結論】hinotori ではアームの干渉による停止を避けるため、ポートや固定具の配置などに変更を加えている。hinotori 導入から約 1 年が経過しているが、現時点で hinotori を用いたロボット支援下手術は安全に施行することが出来ている。

P-31-5 高齢婦人科疾患患者における腹腔鏡手術とロボット支援下手術の安全性に関する検討

三重大

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【目的】高齢婦人科疾患における腹腔鏡手術とロボット支援下手術の安全性を比較検討する。【方法】当科で 2015 年 1 月から 2023 年 2 月までに施行した腹腔鏡手術と 2019 年 1 月から 2023 年 8 月までに施行したロボット支援下手術で手術施行時年齢が 65 歳以上の患者を全例抽出し、周術期合併症を後方視的に検討した。当科では腹腔鏡手術は頭低位 15 度程度の碎石位、ロボット支援下手術は頭低位 25 度の碎石位で行っている。【成績】腹腔鏡手術群は 67 例で悪性疾患 45 例 (うちリンパ郭清あり 28 例)、良性疾患 22 例であった。年齢中央値は 72 歳 (65-88)、BMI 中央値 23.6 (16.0-48.8)、依存症 (高血圧、糖尿病等) を 57 例に認めた。ロボット支援下手術群は 82 例で悪性疾患 65 例 (うちリンパ郭清あり 30 例)、良性疾患 17 例であった。年齢中央値 71.5 歳 (65-86)、BMI 中央値 23.7 (16.5-40.3)、依存症を 42 例に認めた。周術期合併症として腹腔鏡手術群では腸管損傷 2 例、膀胱損傷 1 例、腔壁裂傷 1 例、絞扼性イレウス 2 例、術後せん妄 2 例、腔断端血腫 2 例、認知症の増悪 1 例、低血糖 1 例、閉鎖神経障害 1 例、創部感染 1 例を認め、開腹移行例も 1 例認めた。周術期死亡例は認めなかった。ロボット手術群では皮下気腫 1 例、無気肺 1 例を認めたが、いずれも自然軽快した。開腹移行例は認めず、周術期死亡も認めなかった。【結論】今回の検討では術者や術式のバイアスがあり、純粋な比較検討はできないが、腹腔鏡手術の方が周術期合併症が多いように思われる。また、ロボット支援下手術が難しいような癒着症例で腹腔鏡手術が選択されている可能性もあるため、今後は症例を蓄積し、術者や術式、開腹手術既往等の条件を揃えた上での比較検討を行いたい。

P-31-6 後方アプローチによる腹腔鏡下子宮全摘術の検討—術者と尿管損傷の観点から—

小倉医療センター

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【目的】腹腔鏡下子宮全摘術 (TLH) において尿管損傷は重大な合併症の一つである。尿管損傷を予防するアプローチ法にはいくつかの方法があるが、腹腔鏡手術修練医には尿管の同定と授動の手術操作は難渋する手術手技のひとつである。当院では後方アプローチを用いて主に TLH を施行しており、今回、後方アプローチで TLH を行った症例を対象として、尿管損傷の予防となる尿管の同定・授動の手術操作が術者により影響を受けるのか、後方視的に検討を行った。【方法】2021年11月から2023年2月の間に当院で良性疾患に対して TLH を施行した症例を対象とした。技術認定医取得前の腹腔鏡手術修練医 (修練医) が執刀した A 群と日本産科婦人科内視鏡学会技術認定医 (技術認定医) が執刀した B 群に分けて患者背景や手術関連情報 (尿管同定、授動操作を含む) 及び手術関連合併症を検討した。【成績】対象は126例で、A群101例、B群25例であった。患者背景に差はなかった。尿管の同定から広間膜を開放するまでの時間は両群ともに差はなかった。尿管の授動・分離の時間は右側のみ B 群が有意に短かった ($p < 0.01$) が、尿管損傷や術後の尿管蠕動障害は両群ともに一例も認めなかった。【結論】後方アプローチを用い TLH を施行する場合、尿管損傷や術後の尿管蠕動障害がなかった観点から修練医は技術認定医と同様に尿管損傷を予防しながら TLH を完遂できる可能性がある。後方アプローチでは尿管の同定から尿管トンネル近傍までの分離操作を常に視認しながら施行でき、その後の操作も容易に尿管を視認できるため、修練医の不安やストレスが軽減しパフォーマンスが向上に繋がった結果安全に手術を完遂できるからだと考える。

P-31-7 ロボット手術のトロッカー位置を再考する～行う手技に合わせた配置変更～

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【目的】当院は da Vinci Xi サージカルシステム (以下 da Vinci) を用いた手術を行っているが、トロッカー配置は通常の横並び配置で開始した。da Vinci のトロッカー配置はガイドラインで決められてはいるが、原理を理解し安全に使用できれば配置変更も可能である。今回、行う手技・方法に合わせ、よりよいと思われる位置にトロッカー配置を変更できるかを検討した。【方法】当院のロボット子宮全摘は1番アームにフォースパイポラ、2番にカメラ30°斜視鏡、3番にスパチュラ、4番にベッセルシーラーを使用している。把持鉗子としても使用するベッセルシーラーの特徴は、「あご」が通常の把持鉗子と比較し長いこと、関節の可動域が60°までであることが特徴である。右側側方アプローチでは pelvic side wall の後腹膜を4番のベッセルシーラーで把持するため、トロッカー位置は通常的位置である必要があった。しかしアプローチを後方に変化させると Pelvic side wall の展開がなくなり、4番アームを頭側に配置させる必要性がなくなった。一方、4番のベッセルシーラーで陰管切開を陰の真横から行う手技は、可動域60°制限を考慮すると頭側から刺入するよりも、より尾側からの方が後陰壁に対して真横からアプローチできる。よって横並びに配置していたトロッカーを、4番のみ5cmほど尾側に配置した。【成績】手術全体に不具合はなく、4番のベッセルシーラーを用いた後陰壁の切開が容易になった。【結論】da Vinci Xi は横並びのトロッカー配置が導入には推奨されているが、ロボット子宮全摘の方法は統一されていないため、da Vinci の原理を理解すれば、自身が行う手技・方法に合わせたトロッカー配置へ変更することも可能である。

P-31-8 当科の腹腔鏡子宮全摘術における気腹法と吊り上げ法の比較

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【目的】腹腔鏡手術は低侵襲性や QOL に優れた手術であり、手術機器の改良や技量の向上により手術適応が拡大している。腹腔鏡手術における視野確保の方法として気腹法、吊り上げ法が用いられる。今回我々は当科の腹腔鏡子宮全摘術を気腹法と吊り上げ法で後方視的比較検討を行ったので報告する。【方法】2015年1月より2021年3月までに良性腫瘍に対し腹腔鏡子宮全摘術を行った173例 (気腹法: 84例, 吊り上げ法: 89例) を対象とした。手術は両群とも気管内挿管による全身麻酔下で行い、第1トロッカーは open 法で挿入した。周術期合併症、年齢、BMI、手術時間、出血量、Hb 低下値、術翌日 CRP、摘出子宮検体重量、平均在院日数を統計学的に比較した。周術期合併症は Clavien-Dindo 分類を用いて検討した。各群間の比較には t 検定を用い、統計学的解析には SPSS を使用した。 $p < 0.05$ を統計学的有意差ありとした。【成績】開腹手術への移行は両群ともになく、Clavien-Dindo 分類 Grade IIIa 以上の合併症は吊り上げ法で3例、気腹法で2例に認めた。年齢 (気腹: 47 ± 6.5 , 吊り上げ: 48 ± 7.26), BMI (気腹: 23 ± 4.9 , 吊り上げ: 22 ± 3.6), 摘出子宮検体重量 (気腹: 245 ± 118 , 吊り上げ: 232 ± 160 g) に有意差はなかった。Hb 低下値 (気腹: 1.2 ± 1.1 , 吊り上げ 1.5 ± 1.9 g/dl) に有意差はなかったが、気腹法が有意に出血量 (気腹: 64 ± 99.4 , 吊り上げ: 212 ± 303 g; $p = 0.0001$) は少なく手術時間 (気腹: 177 ± 47.0 , 吊り上げ: 203 ± 61.9 min; $p = 0.0017$) が短かった。入院期間 (気腹: 6.6 ± 0.9 , 吊り上げ: 7.6 ± 3.3 日; $p = 0.009$) は気腹法で有意に短く、術後 CRP (気腹: 2.7 ± 2.0 , 吊り上げ: 3.8 ± 6.5 mg/dl; $p = 0.0008$) も低かった。【結論】腹腔鏡子宮全摘術において、気腹法は吊り上げ法に比べ手術侵襲が少なく有用であると考えられた。

P-31-9 改良型ラッププロテクター[®]を用いた経腔的腹腔鏡下子宮全摘術 (vNOTES-LAVH)

大阪赤十字病院

岩見州一郎, 福田真優, 齊藤希実, 水野友香子, 定本怜子, 徳重 悠, 平山貴裕, 川田悦子, 小林弘尚, 前田万里紗, 中川江里子, 野々垣多加史

【目的】我々は2022年に経腔的腹腔鏡手術(以下vNOTES)を導入し, 良性子宮・付属器疾患に施行し, 現在100例強の経験がある。vNOTESに使用するリトラクターは腔壁に密着する症例もあれば, 密着せず滑脱・気腹ガス漏れが起こることもある。その原因はリトラクターのインナーリング径と形状, シースの材質にあると考える。密着するリトラクターを追求し, 現在当科では改良型ラッププロテクター[®](八光製)を使用している。今回, そのリトラクターを用いた経腔的腹腔鏡下子宮全摘術(以下vNOTES-LAVH)を紹介する。【方法】vNOTESは腔に内診指が2本入る症例を適応としている。vNOTES-LAVHは, 1. 腔門蓋を輪状切開, 2. タグラス窩腹膜・膀胱子宮窩腹膜を切開し腹腔内に到達, 3. リトラクターを装着, 4. 気腹し15度の頭低位, 5. 鏡視下に子宮摘出・腔式に子宮回収, 6. 腔切開部を閉鎖の順に行っている。【成績】5例に使用し, 全例vNOTESで手術を完遂し, 合併症を呈した症例はない。ポートは3~4本挿入し, 5mmフレキシブルカメラ(OLYMPUS製)とAESCULAP[®]Caiman Articulating type(B BRAUN製)・ENSEAL[®]G2 Articulating(Johnson & Johnson製)などの先端が屈曲するエナジーデバイスを使用することが多い。【結論】vNOTESは歴史の浅い手術であるがゆえに決まった形が確立されていない。試行錯誤している段階ではあるが, リトラクターは滑脱・気腹ガス漏れし難くコスト性に優れた, 改良型ラッププロテクター[®]を使用している。なお, 我々はvNOTESと同じ自然孔鏡視下手術である経肛門の内視鏡手術の手技・機器も参考にしている。今後, 更なる改良・工夫を加え, vNOTESがより施行しやすい手術になることを追求したい。

P-31-10 当院の腹腔鏡下子宮全摘術における手術時間延長に影響する因子についての後方視的研究横浜医療センター¹, 横浜市立大附属市民総合医療センター², 横浜市立大³田之井有華¹, 小林奈津子¹, 山崎 萌¹, 鈴木沙也香¹, 大野 菜¹, 平田 豪², 齊藤 真², 栃尾 梓¹, 向田一憲¹, 浅野涼子², 最上多恵¹, 宮城悦子³

【目的】当院における全腹腔鏡下子宮全摘術(total laparoscopic hysterectomy: TLH)の症例数は増加傾向で, 内視鏡技術認定医だけでなく専攻医による執刀も多く, 幅広い年代が経験する術式となりつつある。術前の予定より長い手術時間を要する症例も見受けられる。医師の働き方改革によって時間外労働の過度な延長は許容されないことから, 手術時間延長要因を把握することは重要であり, 術前に手術時間を要する症例をよりの確に評価することを目的とし, 手術時間延長に影響する因子を後方視的に検討した。【方法】院内倫理委員会の承認を得て, 当院で2022年4月から2023年8月までに子宮良性疾患に対して施行したTLH全111例について検討を行った。手術時間延長は手術時間の長い上位10%(延長群:P群)と定義し, その他の症例(N群)と比較検討した。数値データはt検定, カテゴリカルデータはカイ二乗検定を行った。【成績】全体の平均手術時間は, 197分だった。P群の手術時間は281分以上だった。子宮横径・検体重量・BMI30以上・術前からの癒着所見・術中癒着所見・卵巣嚢腫合併の6因子で有意差を認め, 既存報告と相違なかった。子宮横径の平均値は, P群で102mm, N群で79mmだった。検体重量の平均値は, P群で409g, N群で256gだった。また手術歴・内視鏡技術認定医の執刀または第一助手としての手術参加・経腔分娩歴については, 二群で有意差を認めなかった。【結論】手術時間延長に影響する因子について術前に評価することで, 専攻医でも予定手術時間内に安全に手術を行える可能性が示唆された。

P-31-11 当科におけるhinotoriの新規導入経験とDa Vinci手術との比較

浜松医大

伊藤敏谷, 東堂祐介, 成味 恵, 松家まどか, 柴田俊章, 村上浩雄, 安部正和, 伊東宏晃

【目的】当科ではこれまでDa Vinci Xiを用いてロボット支援手術を行ってきたが, hinotoriを2023年8月から導入し, 9月までに婦人科ロボット支援手術で保険適用となっている全ての術式を行った。【方法】手術は全例ロボット4アーム+補助ポートとし, 良性疾患に対する子宮全摘術2例, 骨盤臓器脱に対する仙骨腔固定術2例, 早期子宮体癌に対する子宮悪性腫瘍手術4例(そのうち骨盤リンパ節郭清術1例)を行った。【成績】これまでの手術成績の中央値[範囲]は, 年齢54[43-78]歳, BMI24[17-32], 手術時間169[142-400]分, ドッキング時間18[12-31]分, 出血量10[5-50]g, Clavien-Dindo分類3以上の周術期合併症は認めなかった。【結論】hinotoriではロボットアームをポートに固定しないため, アームを外せば即座に助手ポートとして使用できることや, 専用のジェネレーターのみでダブルパイポラが使用可能であることがメリットと考えられた。ベッセルシーラー非搭載であるため, 助手ポートから腹腔鏡用のベッセルシーラーを使用している。これに伴いポート配置を変更するなど, より良い術式を模索中である。Da Vinciとは異なるドッキング方法や操作感, ベッセルシーラー非搭載など留意点はあるものの, Da Vinciで行っていた全ての術式に対応可能であった。現在当科ではhinotoriを用いた手術を5件/月程度行っている。hinotoriによる手術の実際を提示し, これまでの症例データとDa Vinci手術の症例データとの比較を行う。

P-31-12 当院におけるロボット支援下手術の教育

杏嶺会一宮西病院

北川雅章, 竹下 奨, 早川卓治, 田中幸余, 小祝千夏, 坪内寛文, 福江千晴, 水川 淳

【目的】当院では2021年6月よりロボット支援下手術を開始した。導入当初から1年はプロクターによる執刀のみとして、ロボット手術導入から1年後に、その他術者の養成を開始した。当院での教育方針について報告する。【方法】対象術者は3名。2021年6月から2023年7月まで297件施行したうち、3名が執刀した80件を対象とした。【成績】良性子宮全摘は57件あり、子宮摘出重量中央値215g(43-1424)、総手術時間中央値151分(83-257)、コンソール時間中央値123分(61-223)、出血中央値少量(0-900)、BMI中央値23(18-35)、年齢中央値48(35-74)。摘出重量による手術時間のばらつきは多少認めたが手術時間は短縮傾向である。【結論】ロボット手術の習熟度は早いと考える。継続的に手術をすることでさらなる上達が期待できる。

P-31-13 当科における hinotori による婦人科手術の初期経験

鹿兒島大

大井帆波, 戸上真一, 永田真子, 小林裕介, 駒崎裕美, 窪凜太郎, 税所篤志, 水野美香, 築詰伸太郎, 小林裕明

【目的】当科では、2022年からda VinciXi[®]に加えて国産ロボット hinotori[™]を追加導入し、12月からの婦人科保険適用と同時に手術を開始したので初期経験を報告する。【方法】良性子宮疾患(骨盤臓器脱含む)と再発低リスク子宮体癌に対し、hinotoriで手術した症例を解析し、その特徴や今後に向けた改善点などを検討した。【成績】現在まで26症例(良性子宮腫瘍10例、仙骨腔固定術11例、子宮体癌5例)にhinotori手術を行った。中央値(範囲)で、年齢は59歳(38-77)、BMIは25.9(18-33.3)、手術時間は263.5分(150-612)、コックピット時間は201.5分(102-430)、ドッキング時間は15分(9-20)、術中出血量は30mL(5-105)、術後退院日数は6日(4-15)であった。開腹へのconversionはなく、術後に2症例で骨盤内感染を認めたが、保存的治療で改善した。体癌症例では全患者がセンチネルノードナビゲーション手術の臨床試験を希望し、全例でリンパ節郭清を省略できた。da Vinciと異なり、1)ドッキングフリーデザインのため術後のポート創部痛は軽いものの、テンディング操作によるワーキングスペースの拡大ができないこと、2)鉗子が干渉時アラームが鳴り、作業が中断しがちであること、3)鉗子のラインナップがまだ不十分なことなど、今後改善を要する点もあった。一方、画角が広いこと、可動式ビューワーにより術者の疲労が少ないこと、助手のワーキングスペースが広いことなどは利点であった。【結論】hinotoriでも婦人科手術に十分対応可能であるが、症例に応じた工夫や今後の機器や鉗子の改善を要する点もあった。

P-31-14 経膈回収における絹糸誘導法の有用性について

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【目的】当院では経膈回収をより安全でスムーズに行うため、回収袋の端にあるループに絹糸を1本結紮することで誘導糸を延長し、体外に残した絹糸を牽引することで回収袋を閉鎖し膈部へ誘導する方法(以下、絹糸誘導法)を2023年1月に導入した。従来は、回収袋の糸を鉗子でたぐりながら閉鎖し、左下腹部のポートの鉗子から膈部ポートに向かって鉗子を逆行性に通すことにより回収袋の糸を膈部に誘導していた(以下、従来法)。従来法では、鉗子の患者が干渉したり、鉗子がスコープに当たる危険性があった。絹糸誘導法の有用性を従来法と比較し検討した。【方法】2022年4月~2023年7月に当院において実施した腹腔鏡下卵巣嚢腫摘出術もしくは付属器摘出術156症例のうち、従来法で行なった症例63例と絹糸誘導法を行なった症例44例について回収袋に組織を搬入した直後から膈部まで誘導終了した時間を後方視的に検討した。回収袋を先に腹腔内に搬入した上で嚢腫摘出術を行なった症例や組織搬入後すぐに膈部へ誘導していない症例は除外した。統計学的手法はMann-WhitneyのU検定を用いた。【成績】従来法では、EZパース[®]使用例は33例で中央値34秒(13-110秒)、メモバック[®]使用例は30例で中央値58秒(27-430秒)であった。絹糸誘導法ではEZパース[®]使用例は26例で15.5秒(5-52秒)、メモバック[®]使用例は18例で21.5秒(6-67秒)であった。絹糸誘導法の方が組織回収袋の種類に関係なく搬出までの時間が有意に短縮した。安全性に問題が生じた症例は認めなかった。【結論】絹糸誘導法は簡便であり、術者の技量に関わらず安全に、より短時間で回収・搬出することが可能である。

P-31-15 子宮筋腫に対する子宮全摘術の術式選択（開腹，腹腔鏡下，ロボット支援下手術）に関する検討——当科における現状——JCHO 熊本総合病院
東矢俊光

【目的】子宮筋腫に対する手術療法の術式選択に関しては様々な要因が関与している。子宮全摘術に限定して、当科における開腹子宮全摘術（ATH）、腹腔鏡下子宮全摘術（TLH）、ロボット支援下子宮全摘術（RASH）の現状について検討し、今後の術式選択の改善と展望について考察する。【方法】2021年4月から2023年8月まで、当科にて手術した子宮筋腫手術例61例について、後方視的に検討した。【成績】TLHが最も多く29例（47.5%）、ATH：13例（21.3%）、RASH：7例（11.5%）、筋腫核出術8例（13.1%）、子宮鏡下粘膜下筋腫摘出術4例（6.6%）であった。70%近くが鏡視下手術であった。平均手術時間はATH：119分、TLH：151分、RASH：149分。平均出血量はATH：208g、TLH：112g、RASH：45g。平均摘出子宮重量はATH：1165g、TLH：318g、RASH：203g。手術合併症に関しては尿路損傷や腸管損傷などの重篤な例はなかった。【結論】TLHやRASHは出血量も少なく、十分な視野が得られると予想される症例は子宮全摘術の第一選択と考えられた。また術者の技量もあるが1000gを超える様な巨大筋腫症例は開腹手術が妥当と考えられた。やはり患者の安全を最優先した上で、より低侵襲の術式を選択すべきであろう。

P-31-16 TLH0件からのロボット手術立ち上げ2年間の変遷杏嶺会一宮西病院
竹下 葵，早川卓治，田中幸余，小祝千夏，坪内寛文，北川雅章，福江千晴，水川 淳

【目的】当院では2021年5月のロボット手術学会プロクター着任まで腹腔鏡下全摘術を施行していなかった。短期間ではあるが準備を経て同年6月よりロボット支援下手術を開始した。ロボット手術導入から約2年間の症例数の変遷について検討した。【方法】2021年6月から2023年7月までを対象とした。【成績】ダビンチXi一台を運用しており導入当初は術者一人、週一件で開始した。導入後は一日2件施行しつつ、他科が使用していない枠を活用し、また新規術者の育成を行った。その結果2023年7月までに症例数は297件（悪性：37件 仙骨腔固定術：53件 良性：207件）に到達した。悪性：郭清あり20件 中央値がそれぞれ年齢55歳（41-69）総手術時間180分（87-252）出血少量（0-30）、郭清なし17件 年齢57歳（41-82）総手術時間150分（65-236）出血少量（0-180）。仙骨腔固定術：シングル30件 年齢72歳（45-88）総手術時間146分（112-359）出血少量（0-200）、ダブル23件 年齢65歳（43-87）総手術時間202分（158-322）出血少量（0-50）、良性：800g未満182件 年齢47歳（28-74）総手術時間132分（57-355）出血少量（0-5180）、良性：800g以上25件 年齢48歳（41-68）総手術時間203分（128-277）出血少量（0-900）。【結論】他科との調整がスムーズであったこと、3名の術者を新たに育成し、現在は限られた手術枠ではあるが術者4人平均月14件ペースで施行している。TLH0件からのロボット支援下手術導入としては、症例数は順調に増加していると考えられる。

P-32-1 子宮内膜症におけるneuropilinを介したPI3 kinase-akt経路の発現異常について大分大
西田正和，須奈家栄，麻生咲季，青柳陽子，小林栄仁

【目的】neuropilin(NRP)は、細胞外領域とPDZドメインを含む細胞内領域を有する膜1回貫通型レセプターで、semaphorin(SEMA)やVEGFファミリーと結合することで軸索誘導や血管新生の制御を行う。SEMAは、もともと神経軸索の方向性を決定する神経軸索誘導調節因子として同定された分子群であるが、近年細胞増殖、血管新生、悪性腫瘍の転移など多くの機能を持つことが報告されている。今回、子宮内膜症の病因解明のため、子宮内膜症細胞と正常子宮内膜間質細胞におけるNRPの発現および、その下流にあるPI3kinase-aktのシグナル伝達や接着因子であるβカテニンについて検討を行った。【方法】今回の研究を行うにあたり、当大学のInstitutional review boardより許可を受けたのち、インフォーム・コンセントを得て卵巣子宮内膜症、子宮筋腫の採取した細胞を採取・培養し実験を行った。培養した子宮内膜間質細胞、子宮内膜症細胞を用いて、western法、免疫染色を行い、SEMA3BとNRP2の発現、PI3 kinase-akt, phosphorelated akt, βカテニンの発現について検討した。【成績】子宮内膜症細胞において、SEMA3B, NRP2, PI3kの発現増加しており、これに伴いphosphorylated aktの減少が認められた。また、接着因子であるβカテニンの発現の増強が認められた。【結論】子宮内膜症の病因には、種々の要因が複雑に組み合わさっている。今回の研究では、NRPを介する細胞伝達に着眼し、PI3k-Akt系に異常があることを発見した。更にその下流にあるβカテニンも発現が増強し、子宮内膜症の接着の機序に関与することが示唆された。今回の研究結果が子宮内膜症病態解明の一助を担う可能性がある。

P-32-2 子宮内膜症治療を目的としたSR-16234の分子基盤の検証

鳥取大

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【目的】SR-16234 (SR) は、主にエストロゲン受容体 α アンタゴニストとして作用するSERMである。子宮内膜症間質細胞 (ESCs) および子宮内膜間質細胞 (NESC) に対し、SRが細胞増殖や炎症・疼痛関連因子発現に与える影響を明らかにすることとした。【方法】卵巣子宮内膜症性嚢胞壁 (n=21), あるいは子宮内膜症を有さない女性の子宮内膜組織 (n=18, 分泌期) より間質細胞を分離培養した。骨盤内炎症を模倣してTNF- α を前投与した培養細胞にSR (10^{-6} - 10^{-8} M)を添加し、WST-8アッセイを用いて細胞増殖に与える影響を評価した。培養細胞におけるIL-6, IL-8, COX-2, ESRIおよびESR2 mRNA発現をRT-PCRで、培養上清中のIL-6, IL-8およびPGE2濃度をELISAで測定した。リン酸化I κ B α , ERK1/2およびAKTタンパク発現をウェスタンブロットで評価し、さらにNF- κ Bの核内p65タンパクを測定した。【成績】ESCsにおいて、TNF- α 単独添加と比較して、SR添加は細胞増殖を約20%抑制し、上記すべての炎症・疼痛関連因子の遺伝子発現とタンパク産生量を減少させた。SR添加は、リン酸化I κ B α 発現、核内p65タンパクを低下させたが、リン酸化ERK1/2およびAKT発現に影響を及ぼさなかった。一方、NESCにおいては、SR添加による細胞増殖および炎症・疼痛関連因子発現の変化はみられなかった。【結論】子宮内膜症細胞においてSRがもたらす細胞増殖抑制および抗炎症作用には、NF- κ B経路の阻害が関与していると推察された。

P-32-3 卵巣子宮内膜症性のう胞が卵胞顆粒膜細胞に及ぼす影響

名古屋大

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【目的】卵巣子宮内膜症性のう胞 (OE) は腹腔内に炎症を引き起こし不妊症の原因となるがその機序は明らかでない。また子宮内膜症女性の腹水ではTGF- β が亢進するとされており、TGF- β は顆粒膜細胞 (GC) においてVEGFを介して血管新生に関与するとされるが詳細はわかっていない。そこでOEのGCにおける血管新生の影響を解明することを本研究の目的とした。【方法】ヒト非黄体化顆粒膜細胞株 (HGrC1) にTGF- β を添加しqPCRでVEGF発現を評価した (n=3)。さらに9週齢のC57BL/6Nマウスを用い、OEモデルマウスを作製した。即ち、ドナーの子宮を細切し、PBS注入後に卵巣のうを切開したレシビエントの卵巣に付着させ、12週齢で病変採取した。PBS注入のみ行ったShamマウスも作製した。免疫染色にて顆粒膜細胞でのVEGFとCD31発現を比較し血管新生について調べた (各々n=3)。【成績】HGrC1にTGF- β を添加すると3時間でVEGFが約3.5倍上昇した (3.66 ± 1.20 , $p=0.004$)。さらに、OEモデルマウスにおいてsmall antral follicleでのGCでは、shamと比べVEGF (OE: 18.00 ± 18.80 , sham: 5.32 ± 8.83 (% area/follicle), $p<0.05$)とCD31発現 (OE: 53.49 ± 11.51 , sham: 43.59 ± 15.8 (% length/outer diameter), $p<0.05$)の亢進がみられた。なおsmall antral follicleより前の発育段階での卵胞のGCではVEGF/CD31ともに発現の亢進は認めなかった。【結論】正常卵胞は発育の後期で血管新生が亢進するが、OEにおける卵胞ではTGF- β によりVEGFが早期に発現し異常な血管新生をきたし、結果として卵胞の発育機能障害に寄与する可能性がある。

P-32-4 卵巣子宮内膜症性嚢胞の内容液漏出の影響を少なくした手術は再発を減らし、術後早期妊娠をもたらす?

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【目的】卵巣子宮内膜症性嚢胞 (EMoma) の手術の際の内容液漏出に生理食塩水 (NS) による腹腔洗浄を行うことが多いが、術後癒着予防の観点からNSでなく乳酸リンゲル液 (LR) による洗浄が望ましいとする報告がある。我々は2020年1月から腹腔洗浄液をLRとする内容液漏出の影響が少ない手術手順に変更し、本研究はその術後経過を評価することを目的とした。【方法】新手順は、嚢胞が1/3沈む程度にLR骨盤内貯留、吸引管で内容吸引除去しLRで洗浄、パンプレシ液性剥離法で嚢胞摘出・縫合する。2020年1月から2023年3月までの新手順群12例と2019年以前の従来法群49例の患者背景、術前不妊症率、嚢胞最大径、術後妊娠率、術後自然妊娠までの期間、再発率を比較検討した。術後妊娠希望例または妊娠例に限定した。統計はカイ二乗検定などを用いた。【成績】新手順/従来法ではそれぞれ平均年齢 $31.3 \pm 4.7/31.1 \pm 5.0$ 歳、術前不妊症率 75/92%, 嚢胞最大径 $5.8 \pm 2.7/6.0 \pm 1.6$ cm, ASRMスコア $51 \pm 33/58 \pm 33$ と背景に差はないが、術後経過では体外受精を含む妊娠率 75/51%, 術後自然妊娠率 50/39%, とくに術後自然妊娠までの期間 $4.3 \pm 4.8^*/15.6 \pm 13.6$ か月と再発率 $8.3^*/30.6\%$ と差をみた。とくに不妊症3例は新手順で術後一回の月経を経て自然妊娠した。文献的にウサギ実験モデルへのヒト嚢胞内容液を注入する癒着評価実験ではNS洗浄は逆効果で腹膜損傷を起こすとされる。【結論】EMoma手術の新手順により、術後再発が減り妊娠率が上がることで、早期自然妊娠も期待できることが示唆された。

P-32-5 包括的子宮内膜症術前診断法：NMS-EのEスコアの臨床的意義—子宮内膜症の手術時間を術前予測することは可能か?—

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【目的】子宮内膜症の重症度に基づいた手術時間予測はトリアージの観点から重要である。本研究の目的は、内診と経膈超音波検査のみで評価可能な包括的子宮内膜症術前診断法：NMS-EのEスコアとr-ASRMスコア、および手術時間との関連性を調べることである。【方法】MS-E (Numerical Multi-Scoring System of Endometriosis) は、子宮内膜症を四病変 (卵巣嚢胞：10点満点, 癒着：10点満点, 疼痛：10点満点, 子宮周辺病変 (主に深部病変)：3点×病変の数) に分類し、それぞれを内診と経膈超音波検査によってスコアリングする。これらのスコアを合算し、子宮内膜症の重症度を単一のEスコアとして示す。研究対象は、当院で子宮内膜症手術を受けた118例である。術前にNMS-Eを評価し、そのEスコアとr-ASRMスコア、手術時間、出血量、および臨床症状との関連性を調べた。【成績】術前の平均Eスコアは19.3 (6-36) で、r-ASRMスコアとの相関係数は0.770だった。Eスコアと手術時間・出血量との相関係数はそれぞれ0.664と0.199だった。一方、r-ASRMスコアと手術時間の相関係数は0.651であった。Eスコアと臨床症状との関連性については、月経痛との間にのみ弱い相関関係が見られた ($r=0.271$)。【結論】NMS-Eの重症度指標であるEスコアは、手術時間の術前予測を可能にした。手術時間 (分) = $6.0622 \times E$ スコア + 57.756。その精度は、術前評価が不可能なr-ASRMスコアのそれと同程度以上であった。

P-32-6 月経困難症に対するGnRH antagonistとジェノゲストを組み合わせた新しい治療法

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【目的】40歳以上の月経困難症に対しては、血栓症などの合併症が予測されるため、黄体ホルモン製剤を中心とした治療を行うのが望ましいとされている。ジェノゲスト (D) 0.5mgは優れた治療効果を有する反面、治療中に予期せぬ破綻出血を起こすことが欠点であるとされている。そこでこれを防止する新しい治療法の開発を試みた。【方法】研究開始に当たり、当院の倫理委員会にプロトコルをすべて公開し、審議に諮り許可を得た。対象症例には十分なインフォームドコンセントを行い、同意を得た。月経困難症のため薬物療法としてD 0.5mg錠 (朝, 夕2回投与) を選択した29例を対象とした。いずれも子宮に器質的な疾患を合併していない症例とした。これらをat randomにA:D投与前に2週間GnRH antagonist (40mg/day, G) を先行投与した群, 17例、およびB:先行投与なしにDを投与した群, 12例に分け、D投与前開始から不正子宮出血発現までの期間、D投与前の経膈超音波断層法による子宮内膜厚を計測し、比較検討した。【成績】D投与前開始時より不正子宮出血出現までの期間は、A, B群でそれぞれ、 76.7 ± 10.5 vs. 55.2 ± 15.2 daysとA群で有意に延長した ($p < 0.05$)。D投与前開始時の子宮内膜厚は、 0.3 ± 0.1 vs. 4.2 ± 1.7 mmとA群で有意に非薄化していた ($p < 0.01$)。【結論】Gを先行投与させるDの新しい治療法は、子宮内膜を非薄化させることにより予期せぬ破綻出血の発生を遅延させることが可能である。GとDを組み合わせることにより、患者のQOLに配慮した月経困難症に対する長期間の薬物療法が可能となる。

P-32-7 レルゴリクスの腺筋症病変に対する縮小効果の検討

神戸大

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【目的】本研究では、腺筋症の治療における子宮容積の縮小と臨床症状に対するRelugolix (REL) の有効性を明らかにすることを目的とした。【方法】REL (40mgを約20週間) を投与した後に、腺筋症または子宮筋腫に対する子宮全摘出術を受けた患者を対象として後ろ向きコホート研究を実施した。患者を術後病理診断によって腺筋症合併子宮筋腫 (グループA) と子宮筋腫のみ (グループB) の2群に分けた。主要評価項目は、治療前と治療開始後16週時点でのMRIを比較した子宮容積、腺筋症病変の容積および最大子宮筋腫容積の縮小率とした。副次評価項目は、治療開始後12週時点での無月経、骨盤痛、貧血の緩和率とした。【成績】合計56人の患者が本研究に参加した (グループAで20人, グループBで36人)。最大子宮筋腫容積の縮小率に関しては、両群間に有意差はなかった ($P = 0.297$)。REL治療後の子宮容積は、グループB (27%) と比較してグループA (43%) で有意に縮小し ($P = 0.00972$)、グループAでは腺筋症病変が61%も縮小した。群に関係なく比較すると、腺筋症病変 (61%) は最大子宮筋腫 (33%) より有意に縮小した ($P < 0.001$)。両群間で症状 (無月経, 骨盤痛, 貧血) の緩和率に統計学的有意差はなかった。【結論】RELは、子宮筋腫よりも腺筋症病変を軽減し、症状 (無月経, 骨盤痛, 貧血) を緩和するのに効果的であった。以上よりRELは子宮筋腫に対してだけではなく、腺筋症の術前治療としても活用されることが期待される。

P-32-8 GnRH antagonist を用いた子宮筋腫の逃げ込み療法—間隔を空けた投与方法による副作用防止について—

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【目的】閉経に近い症例に対する GnRH antagonist を用いた子宮筋腫の逃げ込み療法の有用性を検討した。【方法】研究開始に当たり、当院の倫理委員会にプロトコルをすべて公開し審議に諮り許可を得た。対象例には十分なインフォームドコンセントを行い同意を得た。手術を希望しない閉経直前の子宮筋腫症例 (49.4±1.5 歳) 20 例に対して GnRH antagonist 製剤を投与した。1 か月の連続投与後は、間隔を空けた投与方法 (1-2 日間隔) に変更して Hot flush (HF) の出現を予防した。HF の程度は VAS scale により検討した。【成績】HF の VAS 値は連続投与後は 8.8±1.3 であったが、間隔を空けた投与方法により 4.7±1.5 と有意に改善した (p<0.01)。HF が回復するまでの期間は 4.6±2.3days と短期間であった。治療開始 3 か月後より、すべての症例は無月経となった。6 か月の治療により 14 例 (70%) がその後 6 か月間閉経となった。本研究期間中の重篤な副作用は認められなかった。【結論】GnRH antagonist 製剤投与により HF などの副作用が出現した場合は、投与間隔を調整することにより速やかに回復することが可能である。このような投与方法により副作用を回避しつつ、閉経期直前の子宮筋腫の逃げ込み療法が安全に行われる可能性が示唆された。

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P-32-9 子宮腺筋症における妊娠 20 週前後の流早産の頻度

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【目的】子宮腺筋症では初期の流産と共に、本来妊娠が安定しているとされる 20 週前後の流早産も時に経験される。そこで、当院で子宮腺筋症と診断し、保存的手術の対象となった症例において、中期流早産の頻度を調査、術前後での変化も検討した。【方法】2002~2023 年に当院で子宮腺筋症核出術を施行した 2194 例中、妊娠経験があり (1131 例)、その詳細が明らかで (1042 例)、その転帰が人工妊娠中絶、化学流産のみであった 378 例を除いた 664 例、1129 妊娠を対象とした。今回は妊娠初期を妊娠 5 か月未満、中期を 5-6 か月、後期を 7 か月以降とした。【成績】術前の既往妊娠 1129 回のうち、妊娠の終了時期は初期 711 回 (63.0%)、中期 84 回 (7.4%)、後期 334 回 (29.6%) であった。このうち、中期流早産経験症例は 73 例で、10 例が中期流早産を繰り返し返していた。一方、術後には 446 例に 545 回の臨床的妊娠が成立し、中絶 10 回、妊娠継続中 14 回を除く 521 妊娠の転帰は、初期流産 159 回 (30.5%)、中期流早産 7 回 (1.3%)、後期での妊娠終了 355 回 (68.1%) であった。さらに術前に中期流早産を経験していた 73 例のうち、29 例に 32 回の術後妊娠が成立し、正期産 13 回、早産 4 回 (全例 intact survival)、流産 13 回、妊娠継続中 2 回で、中期流早産は 18 週での 1 例のみであった。【結論】子宮腺筋症核出術の適応症例では、20 週前後の流早産が 7.4% あることが判明した。保存的手術によって流早産率は有意に改善し、子宮腺筋症核出術が初期・中期流早産の改善に寄与する可能性が示された。

P-33-1 中期流産・超早産既往症例での子宮内及び腔内細菌叢の比較

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【目的】子宮内及び腔内細菌叢は不妊への関与のほか流早産など分娩転帰に関わる可能性が示唆されている。不妊症例について子宮内細菌叢は腔内と比較して多様性を有するとの報告があるが流早産症例での細菌叢分布に関しては明らかではない。今回、感染が想定される流早産既往症例での子宮内及び腔内細菌叢分布を比較した。【方法】12 週から 28 週の流早産既往があり流早産時の胎盤病理検査で絨毛膜羊膜炎を認めた症例 7 例を対象とした。非月経期に腔・子宮内膜を採取し 16S rRNA 遺伝子解析を用いて各細菌叢の関連性を検討した。【成績】Lactobacillus 属 (以下 Lac 属) は子宮内と腔内細菌叢とともに 7 例中 4 例に検出されたが、全体に占める割合では子宮内 21.4%、腔内 24.3% と低かった。種の解析では、L. Gasseri, L. iners が検出されたが L. crispatus, L. jensenii は検出されず子宮内と腔内で違いは見られなかった。Lac 属以外に検出された主な細菌は Bifidobacterium 属, Gardnerella 属, Atopobium 属で上位 4 属の割合に子宮内と腔内で違いは見られなかった。一方、検出された細菌叢数については、属では子宮内 3.7 (種で 4.4)、腔内 4.7 (種で 6.3) であり腔内で多かった。また子宮内ではなく腔内に検出されたものとして Aerococcus 属, Probotella 属があげられた。【結論】感染性流早産既往を有する子宮内細菌叢と腔内細菌叢は、Lac 属非優位群が多く分布に相違傾向を認めなかった。しかし占有率の低い細菌が腔内に多く検出され、多様性に相違がある可能性が示唆された。

P-33-2 妊娠28週未満の切迫早産症例における全身性炎症マーカー Gal-3 の有用性についての検討

県立広島病院¹、広島大²、広島大歯学科口腔外科学³

三浦聡美¹、中島祐美子¹、綱掛 恵¹、白山裕子¹、寺岡有子²、宮内陸美³、三好博史¹

【目的】早産と母体の全身性炎症の関連が考えられており、我々は一つの原因として菌周病について検討してきた。これまでの研究により、免疫調節因子である Galectin-3 (Gal-3) が早産症例の胎盤で高発現していることが明らかになった。また28週以降の出産直前の妊婦の血清 Gal-3 は、早産症例では正常産症例よりも有意に数値が上昇していた。ほかに19種類の因子を分析し、子宮頸管熟化や子宮収縮に関与する IL-6、IL-8、ストレス応答性サイトカインである Growth Differentiation Factor-15 (GDF-15) など、5種類が胎盤で高発現し、血清中에서도検出可能であることを同定した。中でも Gal-3 と GDF-15 はマーカーとして有用である可能性が示された。今回の検討では妊娠28週未満の症例で評価を行うこととした。【方法】2022年10月から2023年4月までに、切迫早産のため妊娠28週未満で入院し、妊娠34週未満で出産に至った12症例を対象とした。入院時に採取する血液検体を用いて、上記の5項目を測定した。対象群は正常産症例35例とした。【成績】早産症例の出産週数の中央値は25.5週(24~31週)だった。これまでの研究で、正常産症例から求めた妊娠14~27週の Gal-3 のカットオフ値は4500 pg/mL (2537~4112 pg/mL)、GDF-15 のカットオフ値は29500 pg/mL (16830~28308 pg/mL) だったのに対し、今回検討した12症例の Gal-3 は6528~16078 pg/mL、GDF-15 は15896~42676 pg/mL だった。【結論】先行研究同様、早産ハイリスク症例の抽出には Gal-3 と GDF-15 の測定が有用である可能性が示された。

P-33-3 胎盤病理所見に基づく胎児炎症反応症候群を予測する新規羊水バイオマーカーの検討

滋賀医大

桂 大輔、辻後一郎、所 伸介、笠原真木子、稲富絢子、菅田佳奈、星山貴子、全 梨花、岡田奈津実、喜多伸幸、村上 節

【目的】胎児炎症反応症候群 (FIRS) は新生児予後不良との関連が報告されているが、その発症を事前に予測することは困難である。既存の予測因子として IL-6 が報告されているが十分ではない。尿中好中球ゼラチナーゼ結合性リポカイン (NGAL) は敗血症の急性腎障害のマーカーとして注目され、炎症と相関することが報告されており、我々は胎児尿である羊水中に存在する NGAL が FIRS を予測する新規羊水バイオマーカーの候補となりえるかを検証した。【方法】当院で管理した単胎妊婦症例を対象に、分娩時に羊水を採取し、分娩後の胎盤臍帯病理から FIRS 群 (病理検査で絨毛膜羊膜炎と臍帯炎と診断) と non-FIRS 群に分類した。両群間で母体背景、羊水中 IL-6、NGAL を比較検討した。【成績】46症例を解析した。FIRS 群 (43.5%、20/46) と non-FIRS 群 (56.5%、26/46) に分けられた。IL-6 においては採取方法が数値に有意な影響を与えなかったが、NGAL においては、採取方法が数値に有意な影響を与えたため ($p < 0.001$)、経陰的と経腹的採取に分けて解析した。羊水中 IL-6 (45063 vs 2791 pg/mL; $p < 0.001$)、経陰 NGAL (2025 vs 420 $\mu\text{g}/\text{gCr}$; $p = 0.013$)、経腹 NGAL (1545 vs 131.5 $\mu\text{g}/\text{gCr}$; $p < 0.001$) において両群間で有意差を認めた。AUC (カットオフ値) は、羊水 IL-6 は 0.948 (11344 pg/mL)、経陰的 NGAL は 0.800 (1180 ng/mL)、経腹的 NGAL は 0.946 (708 ng/mL) であった。【結論】羊水 IL-6 と NGAL は FIRS に対して同等に高精度な予測因子である可能性が示唆された。

P-33-4 子宮内高度炎症例の周産期予後について

佐賀病院

神藤 愛、小野剛史、柏田浩伸、津田聡子、大島侑子、上妻友隆、野見山亮、津村圭介

【目的】子宮内高度炎症に対し SBT/ABPC および AZM 静脈内投与を中心とした抗菌薬治療を施行した場合の、周産期予後の現況を明らかにすること。【方法】2014年8月から2021年4月までの妊娠20週から33週で、頸管無力症や切迫早産で入院管理中に子宮内高度炎症を認めた26症例を対象とした。分娩時や陣痛発来後に羊水採取した例、診断時に分娩の方針とした例、羊水灌流を行った例は除外した。母体炎症所見を参考に羊水穿刺を行い、子宮内高度炎症 (羊水 IL-6 $\geq 11.3 \text{ ng/mL}$) を認めた場合には SBT/ABPC および AZM 静脈内投与を開始し、羊水グラム染色と培養結果で抗菌薬の選択と中止を決定する。培養陰性の場合でも再検査による羊水 IL-6 値の明らかな低下を認めなければ抗菌薬治療の継続する。感染合併の有無や起炎菌により3群に分類し、患者背景や周産期予後について検討した。【成績】最終解析対象は26例であり、感染合併12例 (ウレアプラズマあるいはマイコプラズマ・ホミニス8例、その他の細菌4例)、非感染14例であった。子宮内高度炎症の診断から分娩までの日数の中央値はそれぞれ8日、2日、2日であり、起炎菌の有無や種類に関わらず、有意差はなかった。【結論】切迫早産例において子宮内高度炎症を認めた場合、子宮内感染の有無に関わらず早期の分娩が報告されている。本研究でも同様に早期の分娩となることが確認できた。子宮内高度炎症の診断から分娩までの日数は起炎菌の有無や種類により有意差は認められなかったが、ウレアプラズマあるいはマイコプラズマ・ホミニス感染群の場合は分娩までの日数が延長している可能性が示唆された。

P-33-5 腹腔鏡下子宮頸管縫縮術による周産期予後に関する検討

長崎大

原田亜由美, 重富典子, 梶村 慈, 阿部修平, 永田 愛, 松本加奈子, 長谷川ゆり, 北島道夫, 三浦清徳

【緒言】経膈的な子宮頸管縫縮術が困難な症例に対して、経腹的子宮頸管縫縮術が報告され、国内外でもその有効性が報告されている。当院では難治性の流早産のハイリスク例に対して2014年より開腹による経腹的子宮頸管縫縮術を行っており、より低侵襲手術として2019年より腹腔鏡による経腹的子宮頸管縫縮術を行なっている。【目的】腹腔鏡下子宮頸管縫縮術による周産期予後を明らかにする。【方法】2019年4月から2023年4月までの期間に当院で施行した腹腔鏡下子宮頸管縫縮術9例について、周産期予後に関する情報を後方視的に調査した。【成績】腹腔鏡下子宮頸管縫縮術の手術施行週数は12週0日(11週5日から12週4日)、手術時間は163分(107~230)、出血量は1g(1~50)であった。全ての症例において妊娠中期から後期にかけて、胎児および胎盤の血流の評価を行なったが、妊娠経過に伴う臍帯静脈血流波形、静脈管血流波形および子宮動脈血流波形のPulsatility Indexは全て正常範囲であった。分娩方法は全て帝王切開分娩で分娩し、術中の合併症を認めなかった。妊娠継続中の1例を除く、8例のうち3例は妊娠35週に早産したが、その他の5例は妊娠37週-38週まで妊娠を継続できた。【結論】腹腔鏡下子宮頸管縫縮術は、子宮頸管無力症や子宮頸管短縮例で経膈的な手術操作が困難な症例に対して、周産期予後を改善する有効かつ安全な術式と示唆された。

P-33-6 子宮頸部円錐切除後の妊娠症例における周産期予後の解析

友愛医療センター

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【目的】子宮頸部円錐切除術(円切)は若年者の子宮頸部上皮内腫瘍(CIN)に対し、最も多く実施されている術式である。しかし、円切後の妊娠症例においては早産率の増加が多数報告されている。我々は円切後妊娠症例の周産期予後について早産例を中心に詳細に分析した。【方法】2006年4月から2022年5月までの、当院における円切後妊娠症例70例を対象とした。腺系病変と電気外科的ループ切除法は除外した。解析方法は周産期予後を早産例、切迫早産治療・正期産例(切迫早産治療のため入院治療を要した正期産例)、無治療正期産例の3群に分類し、その頻度を分析した。さらに3群間における円切での平均頸管切除長との関連性について解析した。【成績】円切後妊娠症例70例中、早産が16例(22.9%)、切迫早産治療・正期産例が19例(27.1%)、無治療正期産例が35例(50.0%)であった。早産例における平均頸管切除長は13.6mm、切迫早産治療・正期産例では13.3mm、正期産例では12.2mmであり、3群間に関連性は認めなかった。最終的に正期産となった全症例は54例あるが、そのなかで、切迫早産治療・正期産例が19例(35.2%)存在した。【結論】円切後妊娠症例の早産率は22.9%であった。また、正期産例のなかには切迫早産治療・正期産例が35.2%もあり、円切後妊娠症例は早産のみならず切迫早産治療・正期産例を増加させることが示された。円切の切除頸管長と周産期予後との関連性は認めなかった。

P-33-7 超早産児(在胎25週未満)のIntact survivalに関する予後予測因子に関する検討

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【目的】国内の周産期医療の進歩により早産児の新生児予後は向上したが、妊娠25週未満の超早産児については依然として精神発達遅滞等の後遺症が問題となっている。本研究では、総合周産期センター産科で妊娠25週未満で分娩に至った妊婦から出生した超早産児の新生児予後とその予後予測因子を検討することを目的とした。【方法】当院において2016~2022年の間に妊娠25週未満で分娩に至った30例(月齢中央値53.5か月)を対象とした。当院小児科医によって精神発達を評価されている。主要評価項目を「精神発達遅滞のない intact survival (IS)」, 副次評価項目を「生存」とした。母体年齢, 分娩週数, 入院から分娩までの日数, 入院時母体CRP, 出生体重, Apgar score5 分值(Aps 5'), 胎盤絨毛膜羊膜炎度数について、ロジスティック回帰分析, ROC解析を行った。【成績】「IS」例は14例(47%)であり、単変量解析では入院時母体CRP, Aps 5'が有意な相関因子であったが、多変量解析でAps 5'だけが独立予後因子となった(p=0.033)。ROC解析からAps 5'6点以上が「IS」の予後因子(感度65%, 特異度75%, p<0.001)となった。一方、「生存」例は23例(77%)であり、単変量解析では母体年齢, 分娩週数, 入院から分娩までの日数, 出生体重が有意な相関因子であったが、多変量解析では独立予後因子は抽出されなかった。【結論】在胎25週未満の超早産児の予後は、「生存」に対しては分娩週数, 出生体重等が関連因子となっていたが、「IS」に対しては予後因子ではなかった。Intact survivalを得る予後予測因子は分娩時Apgar score5 分值が重要であり、出生時の児の状態がintact survivalに直接的に寄与すると考えられた。

P-33-8 単胎妊婦における治療的子宮頸管縫縮術の予後とそのリスク因子の検討

長崎医療センター

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【目的】子宮頸管長短縮, 切迫流産の治療法として, 当院では子宮頸管縫縮術を施行している。今回, 当院における子宮頸管縫縮術の予後とそのリスク因子を後方視的に検討した。【方法】内診による子宮口開大・胎胞形成もしくは, 経陰超音波検査による頸管長短縮 (25mm 未満) 症例に対する縫縮術を治療的子宮頸管縫縮術と定義し, 当院で2017年から2022年に治療的子宮頸管縫縮術が実施された単胎妊婦を対象とした。術後1週間以内の分娩および22週未満の流産を予後不良群とし, そのリスク因子について後方視的に検討した。リスク因子として, 母体年齢, 手術週数, 既往歴 (流産, 早産, 頸部円錐切除術, 縫縮術), 術前血液検査結果 (CRP, 白血球数, 好中球%), および術前所見 (胎胞形成の有無, 頸管長) について評価した。【成績】対象症例は147例で, 母体平均年齢は32.7歳, 初産婦は23%であった。手術平均週数は妊娠21.8週, 分娩平均週数は妊娠35.8週で, 縫縮術から分娩までの平均妊娠延長週数は13.9週であった。予後不良群は, 術後1週間以内の分娩となった症例が5例, 22週未満の流産症例は7例であった。術後1週間以内の分娩のリスク因子は, 胎胞形成 (15% vs. 0.8%, オッズ比21.9 [95% 信頼区間2.15-222.5]), 好中球増加 ($p < 0.05$) であった。一方, 22週未満の流産関連リスク因子は, 胎胞形成 (21% vs. 5.2%, 5.0 [1.03-28.1]), CRP ($p < 0.005$) であった。【結論】従来の報告同様, 胎胞形成を認めた症例では予後不良となるリスクが高く, 在胎週数を延長できない可能性を含めた患者へ情報提供の必要がある。

P-33-9 妊娠23週0日から32週0日未満の破水症例における妊娠期間に関与する周産期因子の検討

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【目的】妊娠23週0日から32週0日未満の破水症例における臨床所見が妊娠期間に与える影響を検討した。【方法】2019年3月から2023年8月までに, 妊娠23週0日から32週0日未満に破水と診断した症例を対象とした。破水の定義は, 子宮口からの羊水の流出とし, バイオマーカー陽性のみの症例は除外した。当院では妊娠34週未満の破水症例では, 母体への出生前ステロイド投与の間のみ子宮収縮抑制剤を短期投与 (48-72時間) している。子宮収縮抑制剤投与期間中に分娩に至った症例を早期分娩群, 子宮収縮抑制剤投与終了後も妊娠延長できた症例を妊娠延長群として, 比較検討した。【成績】対象症例は49例認め, 破水診断時の妊娠週数の中央値は30週 (26-31週) であり, 早期分娩群は15例 (31%), 妊娠延長群は34例 (69%) であった。妊娠延長群での, 破水診断後から分娩までの期間の中央値は7日間 (3-58日間) であった。早期分娩群と妊娠延長群で比較した場合, 早期分娩群では破水診断時に体温37.5度以上の症例, 有痛性の子宮収縮がある症例が有意に多く ($P < 0.05$), 診断時の血液検査で白血球数も有意に高値であった (中央値14200 vs 9600 / μ L, $P < 0.05$)。胎盤病理検査における絨毛膜羊膜炎の頻度は両群に有意差を認めなかった。【結論】妊娠23週0日から32週0日未満の破水症例において, 入院時に体温37.5度以上, 有痛性の子宮収縮, 白血球数高値を認めた症例では, 妊娠延長群と比較して有意に早期分娩 (破水後72時間以内) に至った。

P-33-10 絨毛膜羊膜炎の早期発見における口腔内体温測定の見解の検討

宮崎大

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【目的】母体口腔内温と母体腋窩体温の絨毛膜羊膜炎 (CAM) 発症時の違いがあるかどうかについて検討する。【方法】2020年8月1日から2023年9月30日までに当院へ切迫早産の診断で入院となり, 当院で34週未満の早産となった症例を診療録から後方視的に検討した。検討項目は胎盤病理でのCAMの有無, 分娩週数, 入院時WBC・CRP, 分娩時WBC・CRP, 分娩時腋窩体温, 分娩時口腔内温とし, 体温測定は腋窩・口腔内ともに6時, 11時, 17時, 21時の1日4回測定し, 分娩時の直近の値を最終体温とした。検定はMann-Whitney U testを用いて $p < 0.05$ を有意とした。【成績】対象期間中に当院で切迫早産の診断で入院となり, 入院時に羊水穿刺を行って子宮内感染を否定し, 入院期間中に口腔内温測定を行い, かつ34週未満の早産となった症例は36症例であった。胎盤病理で25例にCAMを認め, 11例はCAMを認めなかった。CAMありの症例では分娩時のCRPが有意に高く, 分娩時の腋窩体温と口腔内温では有意差は認めなかったが, 口腔内温がやや高い傾向を認めた。また従来の絨毛膜羊膜炎を示唆する38°C以上の発熱を認めた症例は25例中3例しか認めなかった。【結論】従来の38°C以上の体温上昇を認める以前にCAMが発症しており, 口腔内温では有意差は認めなかったが, やや高い傾向を認めた。口腔内温を測定することでCAMの早期発見に寄与できる可能性がある。

P-33-11 新型コロナウイルス感染症 (COVID-19) 流行下における初産妊婦の *Ureaplasma* 及び *Mycoplasma* 陽性率についての考察

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【目的】新型コロナウイルス感染症 (COVID-19) 流行下における初産妊婦の *Ureaplasma* 及び *Mycoplasma* 感染の実態について、当院の症例をもとに検討した。【方法】2020年1月1日より2022年12月31日までに当院で分娩を行なった初産妊婦668例を対象とし、妊娠20週未満で陰分泌物 *Ureaplasma*, *Mycoplasma* 培養検査、および一般細菌培養検査を行い、かつ分娩予後が明らかとなっている症例に対して、診療録より後方視的に解析した。解析結果について、COVID-19が発見される前の2018年8月1日より2019年3月31日に当院で妊娠管理を行なった症例と比較した。【成績】対象668例のうち、*Ureaplasma* 陽性は230例 (34.5%)、*Mycoplasma* 陽性は19例 (2.8%)、*Ureaplasma* または *Mycoplasma* 陽性は235例 (35.2%) であった。*Ureaplasma* または *Mycoplasma* 陽性群の平均年齢は32.9歳、陰性群では平均34.4歳であった。また、同対照群の陰分泌物一般細菌培養検査において、*Lactobacillus* が有意ではない症例は272例 (40.7%) であった。【結論】COVID-19流行下において、妊婦の *Ureaplasma* 陽性率については、我々の施設における既報の値よりも若干上昇傾向を認め、かつ *Lactobacillus* が有意ではない症例の割合も上昇傾向を認めた。

P-33-12 妊娠中の性交渉と妊娠予後の関係についての研究

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【目的】妊娠中の性交渉が、妊娠経過にどの程度悪影響を与えるかについて、これまで諸外国で少数の臨床研究がなされたが、早産と関係がないという報告がある一方で、細菌性陰症の原因となり早産になる可能性が報告されている。日本人では未だ調査研究が行われていない。妊娠中の性交渉の有無と早産との関係を究明することを目的に、当院で前方視的研究を行った。妊娠中の性交渉の有無と早産との関係を調べ、副次評価項目として細菌性陰症 (以下 BV) との関係を探ることを目的とした。【方法】当院で妊婦健診を行い、2022年8月から2023年5月までに分娩した妊婦を対象に、アンケート調査を用いて、妊娠中の性交渉の有無と早産との関係を調べた。また、性交渉の有無と細菌性陰症との関係を調べた。倫理委員会の承認を得て、データの公表について全症例に文書による説明を行い、同意を取得した。【成績】対象は観察期間に当院で分娩した妊婦のうちアンケート回答のあった146人。初産婦54人、経産婦92人。平均年齢は30歳。14週以降で性交渉有り79人、性交渉無し67人。性交渉有り群で早産したのは1人 (1.3%) であり、性交渉無し群で早産したのは2人 (3.0%) で有意差はなかった。また、妊娠14週以降の性交渉有り群での BV 治療を行った (Nugent score 4点以上) のは12人 (15.2%) で、妊娠14週以降の性交渉無し群の12人 (17.9%) と有意差はなかった。【結論】妊娠中の性交渉の有無は、早産とも細菌性陰症とも相関を認めなかった。今後は症例数を増やして更なる検討が必要である。

P-33-13 当院における頸管長短縮症例へのプロゲステロン陰錠の使用経験について

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【目的】早産ハイリスク症例へのプロゲステロン陰錠の有用性を示す報告が複数あるが、本邦での使用報告はまだ少ない。早産予防のためのプロゲステロン投与は適応外使用であるため、当院では倫理委員会の承認を得て使用しており、その投与経験について報告する。【方法】当院では妊娠16週以降28週未満に子宮頸管長短縮を認めた症例のうち希望があった場合、早産予防のためにプロゲステロン陰錠を1日1錠、妊娠34週まで投与するプロトコルをとっている。今回の研究では、2019年10月から2023年9月30日までにプロゲステロン陰錠投与の対象となった症例のうち、単胎妊娠症例を対象として、母体背景、合併症の有無、妊娠転帰について記述的に評価することを目的とした。【成績】当該期間にプロゲステロン陰錠を使用した症例は85例であり、平均開始週数は23.0±3.1週、開始時の頸管長は19.3±5.8mmであった。初産婦は35例 (41.1%)、早産既往症例は15例 (17.6%)、子宮頸管縫縮術実施症例は20例 (23.5%) であった。80例 (94.1%) で34週までの予定投与を完遂し、妊娠37週、34週、28週未満の早産はそれぞれ17例 (20.0%)、13例 (15.2%)、4例 (4.7%)、GDM、HDPの合併は10例 (11.7%)、8例 (9.4%) であった。副作用での中断症例や、母児ともに薬剤の有害事象を疑う所見を呈した症例は認めなかった。【結論】症例数が限定する検討であるが投与症例での早産率は既報と同程度であり、母児ともに薬剤による有害事象を疑う症例は認めなかった。引き続き使用基準やその転帰について調査を継続する。

P-33-14 切迫早産妊婦への硫酸マグネシウム投与と早産児の症候性動脈管開存症の関連

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【目的】切迫早産妊婦への硫酸マグネシウム投与と早産児の症候性動脈管開存症 (patent ductus arteriosus: PDA) を検討する。【方法】2020～2022年の3年間に切迫早産治療のため硫酸マグネシウムを投与され早産となった単胎121例を対象に症候性PDAとの関連性を検討した。対象より染色体異常や多発奇形, 新生児死亡, 生後4日以内に手術を受けた例, 硫酸マグネシウム投与開始日に分娩した計31例を除外した。年齢, 初産産, ART妊娠, 前期破水, 絨毛膜羊膜炎, 分娩様式, 分娩週数, 出生体重, 使用薬剤, 母体血マグネシウム (Mg) 値, 臍帯血 Mg 値, 硫酸マグネシウム投与期間を検討した。【成績】硫酸マグネシウム投与期間 (週) は症候性 PDA で 1 (0-6), 非症候性 PDA で 3 (0-14) であった。症候性 PDA と関連する因子は妊娠 28 週未満の早産 (オッズ比 25.5 : 95% 信頼区間 5.2-251.7; $p < 0.01$), 1,500g 未満の低出生体重児 (31.5 : 4.4-1386.5; $p < 0.01$), 絨毛膜羊膜炎 (3.9 : 1.2-14.6; $p = 0.02$), 帝王切開分娩 (4.5 : 1.1-26.3; $p = 0.03$), 臍帯血 Mg 値 (3.0 : 1.2-7.7; $p = 0.02$), 硫酸マグネシウム投与期間 (0.8 : 0.6-1.0; $p < 0.01$) であった。分娩直前母体血 Mg 値と臍帯血 Mg 値の間に相関関係を認めた。また多変量解析において, 臍帯血清 Mg 値と硫酸マグネシウム投与期間は共に症候性 PDA と有意な関連はなかった (2.3 : 0.6-8.0; $p = 0.2$ と 1.2 : 0.8-1.7; $p = 0.4$)。【結論】切迫早産治療のための硫酸マグネシウム投与は, 投与量を病状に応じて調節すれば早産児の症候性 PDA 発症のリスクを上昇させることはない可能性がある。

P-34-1 計画無痛分娩の完遂例と未完遂例の比較から見た無痛分娩の有効性と安全性に関する検討

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【目的】無痛分娩を計画分娩で行う場合, 無痛分娩の完遂率や周産期合併症の問題が残る。本研究では, 脊髄くも膜下硬膜外併用麻酔 (以下 CSEA) を用いた計画無痛分娩の完遂率, 分娩経過, 分娩様式を検討した。【方法】2022年4月から2023年8月までに当院での麻酔科医師による無痛分娩を希望した低リスク妊婦 180 名 (初産 121 例, 経産 59 例) を対象とした。当院では全例が, 日中の計画無痛分娩とするが, 予定前に入院となった陣発・破水入院例でも状況によって無痛分娩を可能とした。【成績】無痛分娩を完遂した妊婦で重篤な周産期異常は認めなかった。計画通りの予定入院となったのが 88 例 (planned: P 群), 陣発・破水で予定前に入院となったのが 92 例 (before planned: B 群) であり, 無痛分娩の完遂率は P 群 65.9%, B 群 34.7% であった。経産婦 59 例は全例が経陰分娩であり, 無痛分娩完遂例 (41 例) は, 未完遂例 (18 例) に比して, 分娩時出血量が多かった ($p < 0.05$) が, 分娩の遷延や機械的分娩率の上昇はなかった。初産婦 121 例では, 帝王切開率は P 群 42%, B 群 15% で, その適応は P 群では分娩停止が最多であった。P 群の初産婦のうち, 帝王切開例では, 経陰分娩例に比して, 母体年齢と母体 BMI が高く ($p < 0.05$), CSEA が開始できなかった率が高かった ($p < 0.01$)。さらに初産婦の帝王切開例では分娩誘発に要した日数が長い傾向があった ($p = 0.053$)。【結論】経産婦では個々の希望に沿った分娩計画と無痛分娩の完遂率が高い。初産婦の計画分娩では分娩誘発に反応せず CSEA が開始できなかった場合に帝王切開率が高いことから, 初産婦の分娩誘発不良時には分娩計画の再設定か自然陣発を待つ等の細やかな対応が肝要であると考えられた。

P-34-2 分娩誘発におけるプロスタグランジン E2 の経口剤と腔用剤の効果比較

神戸大

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【目的】本邦では, 分娩誘発に用いるプロスタグランジン E2 (PGE2) として経口剤に加え, 2020 年より腔用剤が使用可能になった。PGE2 腔用剤, 経口剤のそれぞれで分娩誘発を開始した症例で分娩婦結に差があるかを後方視的に調べた。【方法】2020 年 1 月から 2023 年 8 月の間に当科において PGE2 で分娩誘発を開始した症例を, 腔用剤で開始した群 (V 群) と経口剤で開始した群 (PO 群) に分けた。2 群間で経陰分娩 (VD) 率, 誘発開始 24 時間以内の VD 率, 胎児機能不全 (NRFS) による帝王切開 (CS) 率, ならびに, VD 例では分娩誘発を実施した日数を分娩誘発日数と定義し, 比較した。なお, PGE2 腔用剤と経口剤の両方を用いた症例は除外した。【成績】V 群が 8 人, PO 群が 176 人で, PO 群では 160 人 (91%) でメトロイリンテルを併用していた。V 群と PO 群の患者背景の比較では, 母体年齢 (中央値 33 [範囲 27-43] 歳 vs 33 [20-45] 歳, $p = 0.6$), 経産婦 (3 人 [38%] vs 65 人 [37%], $p = 0.7$), 誘発開始週数 (38 [37-40] 週 vs 39 [34-41] 週, $p = 0.4$), 誘発開始前の Bishop スコア (2 [0-4] 点 vs 2 [0-10] 点, $p = 0.4$) に差を認めなかった。分娩婦結の比較では, VD 率 (V 群 71% vs PO 群 63%, $p = 0.7$), 誘発開始 24 時間以内の VD 率 (13% vs 16%, $p = 0.3$), 誘発開始 24 時間以内の NRFS による CS 率 (0% vs 3%, $p = 1.0$) にも差を認めなかった。一方, VD 例における分娩誘発日数は V 群で PO 群より短い傾向であった (1 [1-2] 日 vs 2 [1-7] 日, $p = 0.05$)。【結論】PGE2 腔用剤で分娩誘発を開始した方が, 経口剤で開始するよりも分娩誘発日数を短縮できる可能性がある。

P-34-3 当院の切迫早産母体搬送における早産リスクの検討

京都第一赤十字病院

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【目的】当院は総合周産期母子医療センターであり、近隣医院等から母体搬送の依頼を受けている。妊婦の希望も多様化してきており、母体および児の状態によっては搬送もとの分娩を希望するケースもある。36週を超えて搬送もとが受け入れ可能なら逆紹介をする場合もある。【方法】2022年度における当院の母体搬送応需システム記録より後方視的に、母体搬送の応需率、搬送理由、当院分娩率（逆紹介にならなかった割合）および切迫早産搬送例の早産リスク因子を解析した。【成績】母体搬送応需率は依頼198例中138例(69.7%)であった。当院分娩率は切迫早産で60%、前期破水で95%、HDPで87.5%であった。切迫早産に関して36週未満に分娩となった群（早群）と36週以降に分娩となった群（正群）に分け、リスク因子を抽出した。来院時週数および初産婦と経産婦での差はなかった。来院時頸管長は早群は 8.7 ± 11.5 mm、正群は 18.7 ± 9.4 mmで早群で有意に短く($p < 0.01$)、IVF-ET妊娠は早群で有意に多かった($p < 0.01$)。また経産婦のリスク因子は、切迫早産の既往は早群で有意に多く($p < 0.01$)、妊娠間隔は早群は 21.3 ± 9.5 か月、正群は 39.1 ± 30.2 か月で早群で有意に短かった($p < 0.05$)。【結論】当院へ切迫早産で母体搬送となった場合、来院時頸管長の短縮、IVF-ET妊娠、切迫早産の既往、前回からの妊娠間隔が短いことは早産のリスク因子であった。

P-34-4 当院の低置胎盤の管理、周産期予後

奈良県立医大附属病院

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【目的】低置胎盤は前置胎盤と異なり、分娩様式を含めた管理指針はガイドライン上、明確にされていない。当院での低置胎盤の管理と周産期予後について検討する。【方法】2020年4月1日から2023年3月31日までの3年間に当院の地域連携に前置胎盤、低置胎盤で紹介された症例のうち、分娩時に前置胎盤であった症例を除いた45例について検討した。【成績】45例のうち紹介時に前置胎盤であった症例は17例、低置胎盤であった症例は20例、常位胎盤であった症例は8例であった。分娩時に低置胎盤であった症例は12例、常位胎盤であった症例は25例であった。低置胎盤から常位胎盤にmigrationした症例は75% (15/20) であり、migrationした週数は平均33週であった。分娩方法の決定は出血のリスクを患者に伝えた上で希望があれば試験経陰分娩の方針としている。低置胎盤のうち5例は試験分娩を、5例は選択的帝王切開術とした。試験経陰分娩のうち4例は経陰分娩に成功し、1例は徐脈による胎児機能不全のため緊急帝王切開術を行なった。低置胎盤の経陰分娩の分娩時出血は平均376.5 (274-546) g、選択的帝王切開の分娩時出血は平均1275 (964-1679) gと帝王切開の方が出血が多い結果となった。自己血貯留した症例は経陰分娩で2例、帝王切開で3例であったが自己血を返血した例は0例であった。常位胎盤の経陰分娩の分娩時出血は平均577.5 (173-1568) gであった。【結論】低置胎盤の経陰分娩の症例は分娩時出血は比較的少なく、自己血返血もなかったため比較的 safely に経陰分娩を施行できる可能性がある。

P-34-5 当センターにおける3年間の巨大児分娩の現状

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【目的】巨大児のリスク因子として母体の耐糖能異常、肥満、妊娠中の過度の体重増加、巨大児分娩既往などが挙げられ、経陰分娩においては、産道損傷、分娩時の出血増加、肩甲難産による児の外傷など異常分娩の頻度が増加するとされる。当センターにおける出生体重4000g以上の巨大児の分娩経過と周産期合併症について検討した。【方法】2020年1月から2022年12月の当センターでの22週以降の単胎分娩を対象とし、経産回数および分娩様式別に診療録より後方視的検討を行った。経産回数については初産群（A群）、非子宮手術既往の経産群（B群）、子宮手術既往の経産群（C群）に分類した。尚、本検討においてC群の子宮手術は帝王切開術のみであった。【成績】対象期間中の単胎分娩5442例のうち、巨大児は75例(1.37%)、男女比は2.5:1であった。分娩週数は40週が36例(48%)で最も多く過期産は認めなかった。11例(14%)に耐糖能異常を認めた。A群、B群、C群はそれぞれ33例、31例、11例で、B群のうち巨大児分娩既往は6例(19%)であったが、28例(90%)で経陰分娩が可能であった。一方で、C群でVaginal birth after cesarean section; VBACに至ったのは27%に留まった。III・IV度会陰裂傷は認めなかった。児のNICU入院は経陰分娩で2例(4%)、帝王切開分娩で5例(18%)であり、新生児仮死は1例であった。3例(6.3%)で肩甲難産となったが、鎖骨骨折を認めたのは1例であった。【結論】巨大児の分娩では、母体背景や起こりうる周産期合併症について留意しながら分娩様式を検討する必要がある。

P-34-6 RPOC (retained products of conception) からの出血に対する IVR (Interventional Radiology) の選択に関する後方視的検討

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【目的】RPOC (retained products of conception) は流産または分娩後の子宮内妊娠組織遺残物を一括した概念で、近年増加傾向にある。治療の選択肢として IVR (Interventional Radiology) があるが、選択される状況の特徴は明らかではない。今回当院における RPOC からの出血に対する IVR の実施について検討した。【方法】当院研究倫理委員会の承認のもと、2013/10~2022/12 に流産または分娩後の出血で追加の処置や予定外の受診、他院からの搬送などを要した患者のうち、RPOC の診断となった35例の治療について後方視的検討を行った。流産又は分娩後10日以内の出血症例(早期群:17例)と11日以降の症例(後期群:18例)で、IVR 施行の有無や画像診断の有無、輸血を要する出血の有無を比較した。【成績】IVR を実施した症例は早期群で5.9% (1例/17例)、後期群66.7% (12例/18例)。造影CT等の画像検査を施行した症例は早期群で35.3% (6例)、後期群で83.3% (15例)と、上記2つの項目において後期群が有意に多かった ($p<0.01$)。早期群で画像検査をした6例はいずれも出血の原因血管が明確に同定できなかった。輸血を要する出血量の症例は早期群で29.4% (5例)、後期群で16.7% (3例)であり有意差はなかった ($p=0.37$)。hCG 値による治療の傾向は見られなかった。治療後に出血のコントロールがつかず子宮全摘など追加の治療を要した症例は両群ともに認めなかった。【結論】RPOC からの出血に対して、出血の原因となる血管が同定されたことが IVR の積極的な選択に寄与していると考えられた。本検討により、実臨床において出血を伴う RPOC に対する治療として、IVR は分娩から時間が経過し画像検査によって治療の有効性が期待される症例に対してより選択されることが示唆された。

P-34-7 高齢出産時代の安心安全なお産のための一戦略~Hybrid 帝王切開という選択肢~

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【目的】前置胎盤や癒着胎盤の胎盤付着異常症は、産科出血の中でも大量出血リスクが高くかつ事前予測が比較的可能な病態だ。出血量抑制手法の中で、動脈内バルーン遮断併用の有効性報告は近年増加しているが、手法や有効性にバラつきがあり安定的な手技とは言えない。一方で、不妊治療の保険診療適応による拡大等もあり、不妊治療妊娠、高齢出産は増加し、それに伴う胎盤付着異常症は今後更なる増加が予測され、より安全性・確実性の高い娩出法の確立は高いニーズが見込まれる。当施設での大動脈遮断バルーンカテーテル (IABO) での血流制御と自己血回収装置併用のハイブリッド帝王切開の有効性と安全性を検証した。【方法】直近7年間に胎盤付着異常症での帝王切開のうち、大量出血ハイリスクと術前判断した45例を対象とした単施設後方視的観察研究。Hybrid 帝王切開は、Hybrid 手術室で術中 IABO の血流調整を行い直視下止血困難時は即時血管塞栓術を行う帝王切開。従来法群 (C 群) と Hybrid 帝王切開群 (H 群) の二群に分け、患者背景、出血量、実失血量 (術中出血量-自己血回収装置での返血量)、同種血輸血量、手術手法 (皮切法等)、追加処置 (子宮摘出・血管塞栓術等) を検証した。【成績】C 群 (n=18) vs H 群 (n=27) で、前置付着率 (22% vs 52%) が H 群で高い以外は背景に有意差なし。術中出血量 (2641ml vs 1135ml)、術中実失血量 (1877ml vs 921ml)、同種血輸血量率 (33% vs 0%)、皮膚縦切開率 (100% vs 19%)、子宮内バルーン率 (67% vs 0%) は H 群で有意に低く、子宮摘出率 (6% vs 0%)、動脈塞栓術率 (6% vs 19%)、介入を要する術中術後合併症率 (6% vs 4%) に有意差なし。【結論】同戦略は高齢出産時代への有効かつ安全な一対策となる可能性がある。

P-34-8 初産と経産における児頭の骨盤内軌跡に関する検討

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【目的】経産婦における分娩所要時間は初産婦と比較してその半分程度であることは判明しているが、その機序は十分に解明されていない。経会陰超音波断層法は分娩進行を評価するのに大変有用であり、分娩進行の評価に用いられている。今回我々は、初産婦と経産婦の産道における児頭の軌跡に違いがあるのかを検討した。同一妊婦において、初産と経産分娩時における児頭の軌跡を比較し、経産婦分娩時の分娩所要時間が短い機序を解明することを目的とした。【方法】当院で2016年1月1日より2023年6月30日までに複数回経産分娩に至った36症例について検討した。初産経産分娩に至った症例を初産群とし、同一妊婦の第二子以降の経産分娩に至った症例を経産群とした。当院では分娩室に入室した時点の経会陰超音波所見を全例記録しており、これら2群間における分娩時間及び分娩室入室時の経会陰超音波パラメータ (Progression angle (以下 PA), Progression distance (以下 PD), Head direction (以下 HD)) を比較検討した。また、PA 及び PD より母体恥骨下縁より児頭先端までの距離を近似的に算出 (恥骨下縁児頭先端距離 = $PD / \sin (PA - 90^\circ)$) し、2群間におけるデータを比較検討した。【成績】初産婦と経産婦において、分娩室入室時より分娩までの所要時間に有意差は無かったが、分娩室入室時の経会陰超音波パラメータにおける PA, PD, HD は初産婦で有意に大きく、恥骨下縁児頭先端距離は初産婦で有意に短かった。【結論】経産婦の分娩における児頭の軌跡は初産婦に比較し母体恥骨下縁児頭先端距離が長いことが判明した。今後、分娩三要素に加えて、児頭の軌跡が分娩要素に追加される可能性がある。

P-34-9 前期破水に対する分娩誘発法による分娩転帰の検討

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【目的】前期破水に対する分娩誘発の際に頸管熟化処置を行うべきかどうかは子宮内感染の懸念などから議論が分かれる。分娩誘発方法の違いによる母体・新生児転帰の違いを明らかにすることを目的とした。【方法】当院で2017年8月から2023年8月に37週以降に分娩をした女性のうち前期破水を適応として分娩誘発を受けた者を対象とした。当院では前期破水に対する分娩誘発法として2020年6月にジノプロストン腔内留置用製剤を導入するまでは頸管熟化不良であっても子宮収縮剤のみを使用していた。導入後は頸管熟化不良な前期破水症例に対して収縮剤に加えてジノプロストン腔内留置用製剤を使用している。対象者をジノプロストン腔内留置用製剤導入前後の2群に分けて母体・新生児転帰を比較した。【成績】対象期間の対象者は1776例だった。導入前群1050例、導入後群726例に分類された。分娩時年齢、非妊時体重/BMI、分娩時体重/BMIに有意差はなかった。初産婦の割合は65.5%、70.7%と導入後群に多かった。経陰分娩率はそれぞれ85.7%、83.5%だった。母体背景(年齢、身長、体重、出産経験の有無)を共変量とした多変量解析の結果、有意差は無かった。新生児の転帰に差は無かった。【結論】前期破水症例に対してプロウベスを導入前後で経陰分娩率、新生児転帰の差は無かった。前期破水症例に対する適切な分娩誘発法についてはさらなる検討が必要である。

P-34-10 当院でのIVF-ET妊娠の分娩転帰に関する検討

JCHO 大阪病院

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【目的】IVF-ET妊娠での分娩に関しては、早産、前置胎盤、常位胎盤早期剝離、産後多量出血、誘発分娩、器械分娩、帝王切開分娩の増加などのリスクがあると報告されている。当院では全妊婦におけるIVF-ET妊娠の割合が高く、IVF-ET妊娠の分娩がリスクを伴うのであれば、当院ではハイリスクな分娩が増加している可能性がある。当院でのIVF-ET妊娠での分娩に関する分娩転帰を検証し、ハイリスクな分娩となっているかどうかを検討する。【方法】2018年4月から2023年8月までに当院で分娩となった症例を対象とし、診療録よりIVF-ET妊娠を抽出し、分娩転帰を後方視的に検討した。【成績】2018年1月から2023年8月まで当院で分娩となった症例は2691例で、うちIVF-ET妊娠は240例(8.9%)であった。IVF-ET妊娠の分娩転帰は、死産、双胎及び既往帝王切開を除いた209例中、経陰分娩は152例(72.7%)、帝王切開は57例(17.3%)で、HDPの診断に至った症例は27例(12.9%)であった。選択的帝王切開を除いた192例中、誘発分娩は123例(64%)、器械分娩は55例(28.6%)、胎盤用手剝離実施例は24例(12.5%)であった。経陰分娩となった152例で、出血量が500ml以上となったのは111例(73%)であり、輸血実施例は23例(15.1%)であった。選択的及び緊急帝王切開59例で、出血量が1500ml以上となったのは15例(25.4%)であった。【結論】当院におけるIVF-ET妊娠においても産後多量出血、器械分娩、誘発分娩、HDP、胎盤用手剝離の割合が高く、ハイリスクな分娩となっていた。

P-34-11 当院における超緊急帝王切開(Grade A)導入後の評価と今後について

岩手医大

佐藤貴紀、川村花恵、寺田 幸、羽場 巖、岩動ちず子、小山理恵、馬場 長

【目的】当院は県内唯一の総合周産期母子医療センターであり、ハイリスク妊娠や救急疾患に対応している。その中でも超緊急帝王切開は一刻も早い児の娩出を図る帝王切開術であり、当院では産婦人科医の経験年数に関わらず迅速に対応し母児の予後を改善すべく、2019年9月より超緊急帝王切開(Grade A)を導入した。Grade A導入後の現状を評価検討し、今後の課題を明らかにする。【方法】対象は、Grade A導入後の2019年9月から2023年9月までに当院で施行した超緊急帝王切開例である。評価項目は、決定(院内発生では宣言時、院外発生では当院到着時)から児娩出までの時間、産婦人科医の経験年数による影響、児の予後等とし後方視的に検討した。【成績】検討期間中のGrade A施行は21例であり、院外発生は52.4%(11例)、院内発生は47.6%(10例)であった。決定から児娩出までの時間は全症例とも30分以内であり、院外発生の中央値が10分に対し、院内発生では18分と有意に時間を費やしたが、児の予後に差はなかった。産婦人科医経験年数10年以上と10年未満との比較では、決定から児娩出までの時間や児の予後因子に有意差を認めなかった。【結論】当院では、Grade A導入前から今もなお各部署と連携し、年に1回以上のシミュレーションと振り返りを継続して行っている。その結果、全症例とも決定から30分以内の児娩出を可能とした。経験年数による児の予後への影響はなく、指導医のもと若手医師が迅速に対応できることを証明し得た。今後は、院内発生の時間短縮を課題とし、迅速かつ恒常的なGrade A運用と母児の予後改善を目標に取り組んでいく。

P-34-12 当院における胎盤用手剥離を要した症例の検討

桑名市総合医療センター

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【目的】胎盤用手剥離は、分娩後に自然娩出されない胎盤を手的に剥離し娩出する処置である。胎盤娩出に時間を要する場合は一部の胎盤剥離面から持続出血を認め、時にバイタルサインに異常をきたす可能性があり緊急処置が必要となる一方で、早急な人員の確保も重要となってくる。またその際は止血処置のみならず適切な全身管理を要する。胎盤用手剥離を要するリスクの算出と適切な管理方法の確立のため、当院における胎盤用手剥離症例を検討する。【方法】当院において2020年4月から2023年8月までに胎盤用手剥離を行った症例の診療録、助産録などを確認し、後方視的に検討する。【成績】当院では15例の胎盤用手剥離症例を認めた。出血量の中央値は1886gで、輸血を要した症例は6例(40%)だった。未経産婦が12例(80%)を占め、体外受精-胚移植を行った症例は13例(87%)であった。分娩室での処置が6例(40%)、手術室での処置が9例(60%)あり、手術室での処置はいずれも全身麻酔下で行われた。分娩室で処置を行った症例より手術室で行った症例の方が出血量は少ない傾向にあったが、統計学的有意差は認めなかった。手術室で全身麻酔にセボフルランを使用した症例は、使用しなかった症例に対して出血量が多い傾向であった。【結論】出血量や輸血を要する割合について有意差は認めないものの、胎盤用手剥離を行う場合は適切な全身管理と人員確保の点で手術室で実施する方が安全であると考えられる。セボフルランの使用は胎盤用手剥離困難症例の場合はやむを得ない場合もあるが、出血量が多くなる可能性があり注意が必要である。施設の状況にもよるが、胎盤用手剥離の際は積極的に手術室で対応することが望ましいだろう。

P-34-13 3回以上の反復帝王切開症例における皮膚横切開と縦切開の比較

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【目的】帝王切開の皮膚切開は美容的観点から横切開(Pfannenstiell法、またはJoel Cohen法)を選択することが多いが、次の帝王切開時に開腹や視野の確保に難渋する場合がある。3回以上の反復帝王切開症例での手術経過や児の予後を皮膚横切開と縦切開で比較した。【方法】対象は2020-2022年に当院で3回目以降の反復帝王切開を施行した症例。診療録を基に後方視的に検討した。【成績】前2回、3回、4回既往帝王切開症例はそれぞれ27例、13例、1例(計41例)で、正中切開が28例(M群)、横切開は13例(T群)であった。母体年齢、分娩時母体体重、分娩週数、児体重、アプガースコア5分値、臍帯動脈血pH、NICUの入室率に両群間の差はなかったが、術中出血量はM群が 675 ± 210 g、T群は 858 ± 290 gで有意差があった($p=0.02$)。卵管結紮術を施行したのはM群が7例、T群は3例でこれらを除いた31例の手術時間は、M群が 56 ± 12 分、T群は 75 ± 16 分でT群が有意に長かった($p=0.005$)。【結論】3回以上の帝王切開症例の皮膚切開方法は正中切開が多かった。多くの子供を希望する妊婦の初回帝王切開の皮膚切開方法は慎重に決定する必要があると思われた。

P-34-14 常位胎盤早期剥離のCouvelaire徴候の臨床的意義

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【目的】常位胎盤早期剥離の帝王切開時に観察されることのあるCouvelaire徴候は術後出血やDIC等と関連があるとされているが、報告は少なく詳細は不明である。本研究は常位胎盤早期剥離の胎児生存例の帝王切開を対象としてCouvelaire徴候の臨床的意義を明らかにする事を目的とした。【方法】2016年3月から2023年6月までに当院で帝王切開分娩により生産し、常位胎盤早期剥離と診断された妊婦90人を対象に診療録を後方視的に検討した。血液疾患合併妊婦は除外した。術中にCouvelaire徴候を認めたCouvelaire群24人と認めなかった正常子宮群66人の2群に分類し母体転帰(輸血、ICU・HCU入室)・新生児転帰(Apgar score5分値 <4 、臍帯動脈血pH <7.1 、新生児死亡)を比較検討した。【成績】母体背景では経産回数、妊娠高血圧症候群合併率に差はなかった。Couvelaire群で母体年齢は低く(中央値31歳 vs 34歳)、分娩週数は遅かった(中央値35.5週 vs 33週)。単変量解析では輸血(58% vs 32%, $p=0.023$)、ICU・HCU入室(29% vs 6%, $p=0.003$)はCouvelaire群で有意に多かった。両群に子宮摘出を要した症例はなかった。新生児転帰はいずれの項目も有意差はなかった。母体年齢・分娩週数を共変数とした多変量解析ではCouvelaire徴候は輸血・ICU・HCU入室の独立したリスク因子であった。【結論】胎児生存している常位胎盤早期剥離で術中にCouvelaire徴候を認めた場合は輸血や術後集中ケアを必要とする可能性が高い。急速遂娩の準備と並行し輸血手配や高次医療施設への搬送を考慮するべきである。

P-35-1 スマートフォンアプリを用いた妊産婦への栄養に関する知識調査と情報提供がもたらす効果に関する検討

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【目的】子宮内環境は低栄養でも過栄養でも周産期予後や次世代の疾病リスクに影響を及ぼすため、妊娠中の栄養管理が重要である。今回、現代女性が最も利用する情報収集ツールであるスマートフォンを用いて妊産婦の身体状況や栄養に関する知識を調査し、妊産婦にとって望ましい栄養に関する情報提供を行うことで知識の普及や行動変容がもたらされるか検討した。【方法】「妊娠・出産アプリ Baby プラス (HEARZEST+Co.,Ltd.)」利用中の妊産婦を対象に、妊娠中と産後1か月時にアンケート調査を実施した。令和3年度は基礎調査を行い、令和4年度は妊娠中アンケート終了後に漫画コラム閲覧や「食生活の10のポイント」のメール配信を行い、調査年度間で知識や行動変容に差がみられるか検討した。【成績】2021年10月～2023年3月の調査期間にのべ10,678名の妊産婦の参加を得た。産前産後のデータが連結可能であった解析対象者は令和3年度調査 (R3群) : 777名, 令和4年度調査 (R4群) : 273名であった。妊娠前の体格はR3群 : やせ (BMI<18.5) 16.3%, ふつう (18.5≤BMI<25) 74.1%, 肥満 (BMI≥25) 9.5%, R4群 : やせ 16.5%, ふつう 74.0%, 肥満 9.5% と、日本人若年女性層を反映した集団であった。「食生活の10のポイント」の認知度がR4群で有意に上昇 (オッズ比 1.98 (95% 信頼区間 : 1.48-2.64) したが、妊娠転帰や知識、実践行動に調査年度間で差はなかった。【結論】スマートフォンアプリを利用することで短期間に多くの妊産婦のデータを収集し得た。今回の情報提供は一方通行形式であり、実効性が高いとはいえない結果であった。

P-35-2 国際緊急援助隊医療チームにおける産婦人科医の役割. 2023年トルコ共和国地震被害に際し派遣を経験して

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 石川 源¹, 竹田津史野², 鈴木貴士³

【目的】国際緊急援助隊医療チーム (JDR Medical Team) は、海外の大規模災害に対して派遣される日本政府の援助チームである。2023年2月に発生したトルコ共和国南東部を中心とする地震被害に対して JDR Medical Team が派遣され、現地で野外診療所を展開。産婦人科診療を行ったのでその概要を報告する。【方法】JDR Medical Team がトルコ共和国の被災地で2023年2月16日～3月11日に野外診療所を展開。この間の診療記録に基づき総括した。【成績】24日間で1946名の患者を診療し、妊娠女性への診察は公式統計記録では53名。診療録からの抽出では58名以上におよんだ。分娩管理は1名で、経過中に他医療機関に母体搬送された。医療提供状況 : 一次隊 (2/10～3/1) 総員75名 (医師14名, 看護師29名) うち産婦人科医2名, 助産師1名。二次隊 (2/23～3/9) 総員65名 (医師12名, 看護師25名) うち産婦人科医1名。三次隊 (3/4～3/16) 総員41名 (医師6名, 看護師8名) うち助産師1名。【結論】今回 JDR Medical Team が野外診療所を展開したのは災害発生後のフェーズで重急症期にあたる。ほとんどの患者が避難所など自宅以外から来院しており、受診理由は、かかりつけ医が被災もしくは閉鎖して受診先が無くなったためだった。母子健康手帳は無く妊娠週数の特定に困難を要する患者も見受けられた。演者らは過去に JDR Medical Team における産科医不足を問題提起しているが (第72回日産婦 P-244「国際緊急援助隊医療チームは産科医師を必要としているが充足していない」) 今回派遣期間の全てにおいて産科医と助産師ともに充足することはできなかった。WHO の認証を受けた医療チームとして経産分娩や帝王切開への対応が求められ、対応力向上のため産科登録医の養成はなおも急務である。

P-35-3 当院で経験した完全未受診症例の問題点

沖縄県立中部病院

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【目的】当院は県内に2つある総合周産期母子医療センターの1つであり当該地域の完全未受診症例も取り扱っている。今回当院で1度も受診しないまま分娩となった症例についての傾向と問題点について検討を行った。【方法】2013年1月から2023年6月までの10年6か月のうちに当院で対応した完全未受診症例39例について診療録を後方視的に検討した。【成績】未受診症例は毎年1-6例みられ、平均年齢は27歳で初産婦16例, 経産婦は23例であった。院内出生は30例 (経産24例, 帝王切開6例) でこのうち子宮口全開大で受診した7症例の院内到着から分娩までの平均時間は14分であった。この他に自宅での分娩6例 (遺棄未遂1例含む), 他施設で分娩後に搬送された症例が3例であった。医学的問題として産道裂傷20例, 早産10例, HDP7例, VBAC3例, ICU管理2例, 輸血・子宮内胎児死亡・産褥の母体死亡も1例ずつ認めた。未受診となった理由は多岐にわたるが、初産婦の65%, 経産婦は87% で成人の同居人がいるにもかかわらず周囲に気付かれないケースや妊娠の指摘をうけるも受診しないまま妊娠が進行し分娩となるケースも存在した。分娩後に全症例に地域支援や保健師の介入を行っているが、産後健診の受診は初産婦では全例であったが、経産婦で40% と低い受診率であった。また経産婦症例の46% は不定期受診や未受診の既往があり3例は再度の飛び込み分娩となった。【結論】未受診症例における啓蒙活動や患者支援は重要であるが一定数は地域への介入が途絶えてしまい、未受診を繰り返す症例も見られた。このため救急室・新生児科・手術場との情報共有や救急隊員への病院前教育を行い安全に分娩対応が可能な体制作りも重要であると考えられた。

P-35-4 授乳婦に使用する薬剤検索ツールとしてのアプリ開発の検討

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【目的】授乳婦は治験の対象外であり使用する薬剤の情報は乏しく、添付文書も「授乳を避けさせること」と記載されていることが多い。薬剤師においても服用中の授乳の可否について指導内容は統一されおらず授乳可能であっても授乳の中止を指導している場合も見受けられる。そこで今回薬剤師が使用している情報源と指導内容を調査し、医療者向けの授乳中の使用薬剤情報検索ツールとしてアプリの開発を検討した。【方法】県内調剤薬局の薬剤師に対して、作成したGoogleフォームアンケートにて授乳婦への使用薬剤の情報源と授乳婦への指導について調査しアプリ開発について検討した。開発は企業と共同開発を行い、データベースとなる情報は周産期薬物療法に専門的に関わっている医師・妊婦授乳婦専門薬剤師がコンセンサスの得られている情報を用いて評価し作成した。【成績】回答は74名から得られた。91%が授乳中の薬について困った経験があった。授乳の中止については45%が添付文書で「授乳を避けさせること」と記載があれば中止を説明していた。授乳の再開について30%は説明しておらず、53%は薬剤の半減期を参考としていた。情報源は73%が添付文書を利用していた。アプリの検索ツールは92%が希望した。アプリの内容は授乳婦への処方薬の情報検索のほか、同効薬の一覧検索と専門家が評価した授乳継続の可否についての情報が検索できることとした。【結論】専門家が総合的に評価しており今までにないアプリでの検索ツールとなっている。定期的に情報の更新が可能なため比較的新しい薬剤にも対応可能と考えられる。これにより授乳中であっても治療と授乳が両立できることを期待する。

P-35-5 当院での過去13年間における10代の若年妊娠の実態

小倉医療センター
北川麻里江, 川上浩介, 宮原英之, 藤川梨恵, 小野結美佳, 石橋弘樹, 清水隆宏, 徳田論道, 川越秀洋, 大藏尚文

【目的】産婦人科診療ガイドライン2020では、未受診妊婦をハイリスク妊娠とし、関係機関での円滑な情報共有を行うことが推奨されていた。同ガイドライン2023の改訂に伴い、未受診妊婦だけではなく、若年妊娠や精神疾患合併、経済的問題を含む社会的支援を要する妊産婦を社会的ハイリスク妊産婦と定義され、子育て困難・児童虐待のリスクの高さを認識するとともに、ソーシャルワーカーなどが勤務する適切な医療機関への紹介が推奨された。今回、社会的ハイリスク妊産婦の中でも若年妊娠の子育て困難・児童虐待のリスクについて、当院の過去13年間の症例より検討した。【方法】2011年1月から2023年6月までに当院で分娩した10代の若年妊娠107例を対象とし、診療録から後方視的に検討した。本研究は当施設の倫理委員会の承認を得た。【成績】義務教育の対象年齢である13~15歳をI群、16~19歳をII群とした。I群が4例、II群が103例と、I群が少なかった。I群は2例(50%)が家族の強力な支援と多職種連携による社会的支援を導入して自宅へ退院となり、1例(25%)が特別養子縁組、1例(25%)が乳児院へ退院となっている。II群は99例(96.1%)が自宅退院、1例(1%)が特別養子縁組、3例(2.9%)が乳児院へ退院となっている。他のリスク因子としてI群の3例(75%)が不登校かつ未受診妊婦、II群の8例(7.8%)が未受診妊婦であった。【結論】10代の若年妊娠の中でも、分娩時年齢が13~15歳、不登校、未受診妊婦の症例は、多機関多職種の連携により強力に行う必要があった。また、子育て困難・児童虐待のリスクを予見し、子の退院先の検討を含めた社会的支援の提供が円滑に行える医療機関での管理の必要性を感じた。

P-35-6 外国籍妊婦受け入れ状況について

東京都立広尾病院
榊原咲弥子, 衣斐凜子, 五十嵐稔枝, 若林 晶

【目的】日本における在留外国人数は年々増加傾向にある。当院は周囲に大使館が多く存在していることから、以前より外国籍患者の受け入れを積極的に行っており、2017年にはJMIP (Japan Medegal Service Accreditation for International Patients)の認証を受けた。そこで今回当院で行っている外国籍妊婦への対応、受診数の変化について検証を行った。【方法】2015年4月~2023年3月の期間に当院で分娩を行った外国籍妊婦の人数、意思疎通言語、宗教食対応の状況などをカルテをもとに検証した。【成績】当院では主に言語対応と入院時食事対応を行っている。言語対応としては、コーディネーター、通訳者の配置、通訳アプリの利用、希望する職員に対し1年単位で英語研修などを行っている。入院時の対応としては、あらかじめ宗教的に制限される食種を確認したうえで食事を提供、病院で提供するミルクへの制限の聞き取り、必要時持ち込みミルクの対応を行っている。全分娩数に占める外国籍妊婦の割合は増加傾向にあり、コロナ禍後もその受診数は大きく減ることなく推移していた。それに伴い、入院時に宗教食対応が必要となる割合も増加傾向にある。入院助産を理由とした来院は少なく、大使館や知人の紹介、分娩費用などを理由に受診する患者が多い傾向にあった。【結論】当院における外国籍妊婦の受診割合は増加傾向にあり、それぞれの患者背景が異なることを考慮しながら今後ますます細やかな対応が必要とされると思われる。引き続き職員の語学研修を行うとともに、外国語での院内の案内板や掲示、書面の作成などを進めていく必要性、ご本人とのコミュニケーションの重要性を強く感じる場所である。

P-35-7 アニマルウェルフェアと SDGs 目標 15 の達成を目指した動物園飼育下大型類人猿の診療ネットワーク構築の検討—ヒトの妊婦健診をゴリラに実施した1例—

名古屋市立大附属西部医療センター¹、名古屋市立大²、上野動物園動物病院³、アトムメディカル株式会社営業推進部⁴、尾崎康彦¹、後藤志信²、井出祥子²、平野雄三³、佐藤由里⁴、杉浦真弓²

【緒言】多くの動物の貴重な命と引き替えに発展した医学や医療を還元するために、我々はヒトの産婦人科医療を大型類人猿に提供すると共に全国の動物園との診療ネットワークを形成してきた。動物園飼育下の妊娠中のゴリラに健診を実施し健康な仔を得たので報告する。【症例】本検討ではヒト医療の診断法及び検査基準を適応した。症例はA動物園飼育下の38歳の雌ニシローランドゴリラで6妊4産である。最終月経と尿中hCGの上昇から分娩予定日を推定した。妊娠32週頃より下痢を発症し体重は非妊娠時と比べ約15%減少した。尿検査では糖、タンパクや潜血は認められず、糞便検査でも潜血、寄生虫や病原性のある細菌は検出されなかった。止瀉薬を投与したが改善せず、妊娠37週3日に全身麻酔下で健診を実施した。超音波検査では胎仔は頭位で胎盤の位置や臍帯動脈血流に異常はなく、推定体重は約2,000gであった。NSTでは麻酔の影響と考えられる基線細変動減少が認められた。CT検査では胸腺腫大以外に異常はなく、子宮頸部細胞診はNILMでクラミジア及びGBSは検出されなかった。末梢血検査ではHb5.4g/dl、血小板数3万/μLで、骨髄検査で軽症の再生不良性貧血と診断された。妊娠39週2日に正常分娩に至った。仔は1,720g(生後2日目)の雌であった。分娩時に母体に病的な出血傾向は認められなかった。母乳栄養が確立できず生後約半年間は人工栄養とした。母体に対してはシクロスポリンを投与し血液所見の改善を認めた。【考察】ヒトの周産期医療が大型類人猿にも応用できることが示唆された。アニマルウェルフェアとSDGs目標15の達成のためにヒトの医療を還元することが重要だと考える。

P-35-8 未受診妊婦が民間あっせん機関を利用し特別養子縁組を行なった一例

産業医大

網本頌子, 近藤恵美, 齋藤佐真, 磯嶋裕佳, 飯尾一陽, 田尻亮祐, 金城泰幸, 吉野 潔

【目的】特別養子縁組は児童相談所と民間あっせん機関が担っているが、児童相談所の成立件数の方が2倍ほど多く、臨床現場では、民間あっせん機関の情報が乏しい。今回我々は、未受診妊婦が民間あっせん機関の特別養子縁組を希望し、民間あっせん機関と調整を行なった1例を経験したので報告する。【症例】20歳、2妊0産1回人工妊娠中絶術。「未受診妊婦がNPO法人を通じて特別養子縁組を希望している」と行政から連絡があり、未受診妊婦が民間あっせん機関の相談員と当院を受診した。児の父親は不明であり、姉以外の家族には今回の妊娠を知らせていない状況だった。BPDより同日を妊娠34週2日とし、分娩予定日を決定した。その後の妊娠経過は良好であった。妊娠36週5日に陣痛発来、破水の診断で同日緊急入院となった。分娩は問題なく経過した。児は2752g、Apgarスコア1分値8点、5分値9点であった。早産児であり新生児科に入院となった。母体は産褥2日目に退院となった。出生届は民間あっせん機関の相談員に渡し県外の養親がいる行政へ提出した。母体と児の面会は児の退院日に一度だけ、養親と共に行なった。児は日齢10に退院となり、県外の養親が自宅に引き取った。【考察】当院では民間あっせん機関を利用した特別養子縁組が行うことは初めてであり、民間あっせん機関による特別養子縁組が可能かの確認や調整手続きに時間を要した。【結論】法律的な側面が出てくる特別養子縁組だが、臨床現場が理解を深め、出産前から各所と連携し、医療側と民間あっせん機関、行政と環境調整を行うことにより、児が健やかに育ち、子どもの権利を護ることに繋がると考えた。

P-35-9 小児がんやAYA世代がんの治療後女性における妊娠・出産と循環器疾患、妊娠前カウンセリングについての意識調査

国立循環器病研究センター¹、国立成育医療研究センター周産期・母性診療センター母性内科²、大阪大³、三重大⁴、近畿大⁵、埼玉医大⁶、宮崎大⁷、京都大⁸、笹ヶ追奈々代¹、神谷千津子¹、金子佳代子²、三宅達也³、前沢忠志⁴、川崎 薫⁵、亀井良政⁶、桂木真司⁷、奥宮明日香⁸、柿ヶ野藍子¹、吉松 淳¹

【目的】近年、小児期やAdolescent and Young Adult (AYA) 世代のがん患者の生存率改善に伴い、治療後の晩期合併症や社会生活全般への影響が問題となっている。がん治療後女性の妊娠においては、産科合併症や循環器合併症の発症リスクまたは増悪などが報告されているが、そのような女性への情報提供は十分でない。そこで、がん治療後女性における妊娠前カウンセリングや心臓スクリーニング検査の普及状況を明らかにするため、アンケート調査を行った。【方法】全国12施設における18~39歳のがん治療後女性とがん治療を専門とする医師を対象に、2022年3月~2023年9月の期間にアンケート調査を行った。【成績】がん治療後女性16人、がん治療を専門とする医師34人から回答を得た。がん治療後女性16人のうち、14人(87.5%)にがんの治療前あるいは治療時に妊娠についての説明があった。そのうち、「治療により、妊娠中、心臓などの他の臓器の合併症が増える場合がある」と説明されたのは2人、妊娠前カウンセリングやスクリーニング検査を勧められたのは2人であった。その後、実際に妊娠前カウンセリングを受けたのは16人中3人(18.8%)であった34人の医師のうち、32人(94.1%)が、がん治療が妊娠に与える影響について説明していたが、そのうち、心臓などの他の臓器の合併症が増える場合があることを説明していたのは8人(25.0%)、妊娠前カウンセリングやスクリーニング検査を勧めていたのは14人(43.8%)であった。【結論】がん治療後の妊娠中の循環器疾患を含めた合併症のリスクについて、患者への周知は不十分であり、関係する診療科が連携した情報提供体制が必要である。

P-35-10 VR教材を用いた鉗子分娩の手法獲得への取り組み

杏林大

小島康嗣, 谷垣伸治, 山口恵吾, 三ツ矢紫音, 島田智子, 高屋敷瑞穂, 佐藤泰紀, 田嶋 敦, 小林陽一

【目的】VR (Virtual Reality) を用いた教育は、現実の状況に立ち会っている様な体験ができる新しい学習形態である。今回我々は、VRと実技訓練を併用した鉗子分娩の手法獲得を目的とする講習を行い、VRを用いた医学教育の有用性や問題点を検討した。【方法】産婦人科専門医取得前の医師22名、取得後9名が受講した。10分間の講義後に、鉗子分娩を、施行者目線を含め多方向から確認できる4分間のVR教材を視聴した。視聴後にネーグリ鉗子と骨盤・児頭の模型を用いた実技訓練を行った。講習前後に受講者の了承を得てアンケート調査を行った。【成績】講習前に鉗子分娩を単独で施行できる受講者はいなかった。急速遂娩に鉗子分娩を考慮したいと答えた受講者は講習前5/19名(26%)から、講習後29/31名(94%)に有意に増加し($p<0.01$)、専門医資格の有無に関係なく同様の傾向を認めた。鉗子分娩を難しいと感じていた受講者は13/19名(68%)であり、受講後も26/31名(84%)と減少しなかった($p=0.29$)。VRに対する肯定的な意見として、臨場感がある、指導者不在でも繰り返し学べるなどの意見があった一方で、VRである必要性を感じない、動画と変わらない、酔ってしまうなど否定的な意見もあった。【結論】臨床において鉗子分娩を単独で施行することは今回の受講のみでは困難であり、それに精通した医師による指導が必須である。指導できる医師は限られていることから、手技に慣れるための事前の訓練として、繰り返し視聴できるVRは非常に有用であると考えられた。しかし、VRである必要性に懐疑的な意見もあり、ハンズトラッキング機能(VR上に装着者の手を反映する機能)を取り入れるなど、改良の必要性が示唆された。

P-35-11 医学生に対する分娩・内診シミュレーターを用いた教育の効果千葉大¹, 君津中央病院²佐藤美香¹, 廣岡千草¹, 篠原佳子¹, 山本敬介¹, 廣澤聡子¹, 鈴木義也², 長澤亜希子¹, 岡山 潤¹, 中田恵美里¹, 尾本暁子¹, 甲賀かをり¹

【目的】産婦人科の講義の中で医学生に最も教えることが難しいのは分娩機転や内診である。骨盤を児頭が回旋しながら下降する、三次元でのイメージがつきにくいことが、分娩機転を理解しにくい最大の要因である。また内診は実際の患者で行うことが難しい。分娩と内診のシミュレーターを用いた実習のカリキュラム開発を行い、シミュレーター学習の効果を確認する。【方法】対象は、分娩シミュレーターアドバンスド[®]と、妊婦内診シミュレーター[®]を用いたシミュレーター実習を2022年10月から2023年7月までに受講した医学部4、5年生計87名。実習前後に、「分娩機転について説明できる」などの問いに対して、スケール4(できる)~1(できない)の4段階から選択させる自己評価アンケートと、分娩機転の知識を問う4問の多肢選択法テストを行い、前後比較をした。【成績】自己評価アンケートでは、「分娩機転について説明できる」という問いに対し実習前はスケール1, 2が60.8%, 3, 4が39.1%, 実習後はスケール1, 2が0.2%, 3, 4が97.4%と自己評価の有意な上昇がみられた。知識を問うテストの平均正解数(満点4)は、実習前は1.41から、実習後2.75と有意な上昇がみられた。実習後アンケートの自由記載では、分娩機転や内診についてシミュレーター実習を経験したことは印象に残り、有意義であるという回答が多くみられた。【結論】医学生に対する分娩・内診シミュレーターを用いた教育により、分娩機転や内診についての理解が深まることが確認できた。この取り組みは他の施設のカリキュラム開発にも役立つと考える。

P-35-12 出生数減少に伴う無痛分娩教育ニーズの変遷

株式会社 LA Solutions 代表取締役

入駒慎吾

【目的】日本の出生数は7年連続で減少し、2022年に過去最少の77万人台となった。そのため、分娩取扱施設は分娩数維持のために様々な施策を講じる必要に迫られた。最も効果的な施策の1つに、無痛分娩が上がるのはいままでのないだろう。ただし、日本特有の分娩取扱施設の分散や麻酔科医不足から、産科医による無痛分娩の麻酔部分の管理は避けることができない。しかし、産科医療現場は常に逼迫していて、十分な麻酔研修や麻酔に関する知識・技術のアップデートを受けることすら難しい状況にある。このような環境の中、無痛分娩を安全に管理するために教育を外部に委託する施設が増加した。今回、無痛分娩の安全性向上やその導入にあたり、教育を外部委託した施設の動向を調査し、出生数減少の側面に関して検討する。【方法】2017年から2023年の7年間に、無痛分娩教育を外部に委託した施設の推移とその施設の無痛分娩数を増加を後方視的に調査した。【成績】無痛分娩教育を外部委託した施設数は、2017年から順に、4施設、10施設、24施設、28施設、29施設、30施設、44施設であった。同期間の無痛分娩数は概算で、2017年から順に、713例、2324例、3238例、3475例、3685例、5230例、5530例であった。新型コロナウイルス感染症前後で、外部委託施設が急増していた。無痛分娩数の増加と合わせると、コロナ禍明けでは無痛分娩の新規立ち上げ(導入)施設が増加していると推測された。【結論】新型コロナウイルス感染症により出生数減少に拍車がかかったことにより、無痛分娩新規立ち上げのために教育の外部発注が増加していると考えられた。

P-35-13 当院における超緊急帝王切開シミュレーションの試み～いままでとこれから～

岡山大

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【目的】当院では、超緊急帝王切開術（GradeA C/S）を『手術決定後、一刻も早い児の娩出をはかる全身麻酔下での帝王切開術』と定めており、手術決定から15分以内の児娩出を目標としている。よりスムーズな娩出のためには各科・各部署との連携が不可欠であり、2015年より多職種を交えたシミュレーション(sim)を行ってきた。sim開始から8年が経過し、より臨場感のあるsimに向けての取り組みや、COVID-19流行前後の変化、その変遷について報告する。【方法】2015年から2023年におけるGradeA simについてシナリオ、参加部署やスタッフの経験年数、IOT使用の有無などについて過去資料や記録ビデオより後方視的に検討をおこなった。【成績】8年間で計6回のsimを行った。第3回simより産婦人科医による事前勉強会を開催した。院内発症5例、院外発症1例を想定したシナリオを作成、症例は常位胎盤早期剝離、臍帯脱出、胎児機能不全、子癇発作などとし、各回ともいずれもsimにおける到達目標を定めた。第5回(2020年)では、死戦期帝王切開のsimを初めて開催した。第5回を除き時間帯は人手の少ない当直時間帯に設定していた。第5回から、患者役は皮切も可能な妊婦シミュレーターを使用した。評価者はタブレット端末を用いて当日キャストの動きを評価、COVID-19流行後は、密を避ける為全体デブリーフィングは行わず、部署毎に意見を集約し、後日代表者間会議で最終的な改善点を共有した。【結論】定期的な院内simを繰り返すことで、多職種とも共通認識を持ち、速やかなGradeA C/Sに繋がっていると考えられる。引き続き安全性の確保の為にsim教育を継続していく予定である。

P-35-14 産婦人科医学教育における講義及び実習への反転教育の6年間の経験と課題

山梨大

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【目的】われわれは6年前から産婦人科の講義ならびに実習に反転教育を導入し、学修の効率化を図っている。この間、Covid-19の拡大により医学教育にさまざまな困難が生じたが、対面教育が可能となった現段階において、より効率的な教育方法を開発する目的で、これまで行ってきた反転授業に関して検討した。【方法】2017年度から2022年度までの産婦人科が担当する医学科3、4年生の講義のすべてについて、各教員が予習用の解説音声付きスライドを作成し、講義前に学生がWeb上で閲覧できるようにした。学生には、事前学習を指示し、その予習状況について各講義の冒頭で小テストを行って確認した。さらに、臨床実習についても、実習前に確認しておくべき内容を反転学習させた。反転教育の内容や効果については、講義・実習担当教員ならびに学生からの聞き取りによって経時的に評価した。【成績】この6年間の小テストの平均点は毎年ほぼ変わらず、80-90%の学生が反転学習をしている判断された。Covid-19の拡大に伴い反転授業に対応した講義を対面で行うことが少なかった2020年の小テストは他の年度に比較して有意に平均点が低かった。反転授業用の教材作成は毎年行っていたが、前年の教育ならびにその効果を踏まえて改訂した教員は少なかった。学生からの評価は、一貫して、学習効果が高まったものが多いが多数であった。【結論】以上より、日常的な反転学習は、講義ならびに実習の教育効果を高めることができるものと考えた。しかしながら、より教育効果の高い反転教育を実現するためには、反転授業において学習する内容を、その講義ごとに的確なものにする必要があると考えられた。

P-36-1 子宮筋腫の局所増殖巣における血管網の形成と阻害についての形態学的検討

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【目的】我々は子宮筋腫の病態について、栄養血管の破綻性出血による壊死部周辺の通常筋腫にマクロファージが関与して局所増殖巣が形成される機序を報告した。今回はこの通常局所増殖巣の血管網形成と阻害について検索した。【材料】閉経前直径5cmの出血巣を有する通常型組織の壁内筋腫6症例を用い、出血壊死部、局所増殖巣、通常筋腫部を検索部位とした。【方法】HE染色、免疫染色としてFib, FDP-D, TUNEL法, CD-68, Ki-67, CD-34, PDGFAさらに抗血管新生因子であるPEDF(色素上皮由来因子)およびHIF(低酸素誘導因子)の局在について検討し、SEM, TEMにても観察した。【成績】1.出血壊死部:FibおよびFDP-D陽性を示し、腫瘍血管は微小血栓により内腔が閉塞した壊死像を呈し、栄養血管に巨大な血栓がみられた。さら壊死部に一致してHIF陽性細胞が存在した。2.局所増殖巣:Ki-67陽性細胞は通常筋腫部の約3~5倍多く認め、CD-34陽性を血管新生部位に、さらにPDGF陽性と陰性の細胞が混在していた。一方、癥痕化を呈す部位ではIII型コラーゲンが増生していた。【結論】1.出血巣内はHIFの存在から種々の血管増因子とその受容体が誘導され周辺の通常筋腫に局所増殖巣が形成に関与すると推測する。2.局所増殖巣において筋腫細胞の産生する α -SMAやマクロファージ由来のPDGFAに刺激された細動脈血管周囲線維芽細胞が α -SMA陽性の筋線維芽細胞に形質転換しコラーゲン等の過形成が生じた結果、PEGF陽性、陰性の血管が出現し、血管網形成が阻害され、結果、さらなる虚血は子宮筋腫増大・壊死の一因となるものと考ええる。

P-36-2 子宮内膜症に対するHDAC10阻害剤の治療効果

大分大

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【目的】子宮内膜症の治療はホルモン療法が中心であるが、副作用や再発率が高いことから、新しい機序に基づく薬物療法の開発が求められている。Histone deacetylase (HDAC) 10は白血球細胞の増殖を促進することが報告され、阻害剤が治療薬として開発されている。一方、子宮内膜症におけるHDAC10の発現解析の報告はない。我々は遺伝子発現マイクロアレイで正常子宮内膜間質細胞と比較し、子宮内膜症間質細胞でHDAC10の発現が亢進していることを見出した。今回、2種類のHDAC10阻害剤について、細胞増殖能やアポトーシス抑制能、細胞周期制御能の観点から、子宮内膜症の治療薬としての有用性について検討した。【方法】HDAC10阻害剤 (Tucidinostat, TH34) を子宮内膜症間質細胞に添加し、細胞増殖能、アポトーシス耐性能、細胞周期に対する効果を評価した。また、Tucidinostatを子宮内膜症間質細胞に添加し、48時間刺激を行い、RNAシーケンス解析を行った。【成績】Tucidinostat, TH34のいずれも子宮内膜症間質細胞の細胞増殖を濃度依存性に抑制 (Cell Proliferation ELISA では96%抑制) し、アポトーシスを誘導 (Cell Death Detection ELISA で477%とアポトーシスが増加)、G0/G1期で細胞周期を停止させた ($p < 0.05$)。RNAシーケンス解析では、細胞増殖やアポトーシスに関わる複数の遺伝子の発現上昇を認めた。【結論】HDAC10阻害剤は子宮内膜症間質細胞の増殖抑制、アポトーシス誘導や細胞周期停止を引き起こした。RNAシーケンス解析の結果からは、子宮内膜症間質細胞に対してHDAC10はミトコンドリアを介するアポトーシス促進経路や、MAPK/Erk経路を介した細胞増殖に関わっていると考えられる。

P-36-3 TP受容体シグナルの子宮内膜症における役割解明

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【目的】子宮内膜症の進展には、血管・リンパ管新生が関与する。これまでの研究でシクロオキシゲナーゼ (COX) 由来のプロスタグランジンが病変内の血管新生を促進することが明らかになっているが、一方、同じCOX由来のトロンボキサン A₂ (TXA₂) の関与は不明である。そこでTXA₂受容体 (TP受容体) シグナルの子宮内膜症における役割解明を本研究の目的とした。【方法】雌性C57BL/6マウス (野生型, WT) とTP受容体ノックアウトマウス (KO) を用いた。ドナーの子宮内膜片を宿主の腹壁に移植するマウス異所性子宮内膜症モデルを作成した (WT→WT, KO→KO)。14日目の移植片について、面積、血管・リンパ管新生およびその関連因子について免疫染色やPCRで比較検討した。また、培養骨髄由来マクロファージをTXA₂受容体作動薬 (U46619) で刺激した反応について比較検討した。【成績】14日目の移植片面積、移植片内の血管密度、リンパ管密度、血管・リンパ管内皮マーカー、および脈管新生因子の発現は、KO→KOでより増加した。免疫染色で、移植片内のマクロファージはTPおよび血管新生因子 (VEGFA)・リンパ管新生因子 (VEGFC・VEGFD) を共発現した。KO→KOの移植片で、マクロファージの集積および抗炎症性マクロファージ関連遺伝子の発現が増加した。LPS処置下の培養骨髄由来マクロファージをU46619で刺激すると、脈管新生因子や抗炎症性マクロファージ関連遺伝子の発現はWT由来マクロファージで減少したが、KO由来マクロファージでは減少しなかった。【結論】TP受容体シグナルの阻害によって異所性子宮内膜の血管およびリンパ管新生が促進されることより、子宮内膜症の進展にTP受容体シグナルが関わっていることが示唆された。

P-36-4 当院での子宮筋腫に対する術前レルゴリクス投与症例の検討

和歌山県立医大

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【目的】子宮筋腫に対する低侵襲手術として腹腔鏡手術・ロボット支援下手術が広く施行されるようになってきた。手術においては術野やワーキングスペースの確保は大変重要であり、術前に子宮筋腫を縮小させることは手術の安全性向上、手術時間の短縮に繋がると考える。GnRHアンタゴニストであるレルゴリクスは子宮筋腫に基づく諸症状の改善とともに、子宮筋腫の縮小作用の効果も期待でき、それらに寄与すると考える。そこで、当院でレルゴリクスを使用した症例の有効性について検討した。【方法】2019年6月から2022年10月の間に、レルゴリクスを投与した症例について後方視的に検討した。【成績】レルゴリクス投与症例は84例、中央値として、年齢は46 (33-55) 歳、投与期間は112 (2-188) 日間であった。4例は有害事象 (月経量増量, 多汗, 不正出血, 膨疹) のため投薬を中止したが、その他の症例では重篤な合併症なく投与を継続できた。レルゴリクス投与前に貧血 (Hb: 12.0g/dL未満) を認めた症例は50例あり、36例 (72%) で貧血の改善を認めた。また、術前にMRI検査を実施した25例において、レルゴリクス投与における子宮体積 (MRIで子宮縦径, 横径, 前後径を計測し、楕円体として子宮縦径×横径×前後径×0.523として算出) の縮小率 (投与後/投与前体積) の中央値は40.7 (7.4-71.5) %であった。なお、25症例中、13症例 (52%) において40%以上の縮小を認めたが、40%以上縮小した群とそうでない群での筋腫の部位や個数の違いでの有意な差は認めなかった。【結論】子宮筋腫に対するレルゴリクスの投与により、術前に貧血の改善、および子宮体積の縮小が見込まれ、より安全な手術が実施できる可能性があり、有益であると考える。

P-36-5 腹腔鏡下手術とロボット支援手術のメリットとデメリットについての検討

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【目的】当院では、2022年11月からダビンチを導入、2023年9月で153症例のロボット支援手術(RASH+RSC)を行った。以前より当院の特徴として、既往帝王切開、内膜症などの癒着症例、巨大筋腫症例など多くの難症を腹腔鏡下にて行ってきた。しかし、その有用性から現在においては保険適応のある手術はほぼロボット支援手術に置き換わった。今回、ロボット手術のメリット、デメリットについて解析した。【方法】2022年1月から12月に行った、同一術者のTLH 78症例と2023年1月から9月までに行った同一術者のRASH 128症例を比較検討した。2022年11月からRASH症例はあるが、手技が安定した2023年1月からの症例を対象とした。BMI 25以上を肥満症例、500g以上を大きな筋腫とし、帝王切開、内膜症などを癒着難症例とした。【成績】TLHとRASHの比較では、肥満症例ではTLH群、手術時間188分、出血量は201g (n=20)、RASH群182分、70g (n=42)。癒着症例ではTLH群183分、147g (n=42)、RASH群181分、71g (n=65)。大きな筋腫症例はTLH群206分、238g (n=22)、RASH群220分、90g (n=25) でした。【結論】3種類の難症例いずれにおいても出血量はRASH群が明らかに少なく、手術時間はTLHとRASH群にほぼ差はなかった。むしろ、ロボットの設置時間を含めた時間なので、実質の手術時間はRASH群が短いと思う。実際に手術を行った感触では、ロボットに関節があることにより、血管の同定、選択的な止血が確実に行え、手術中のストレスも少なかったと考える。ロボット手術は難症例においてよりそのメリットを表すと考えられた。

P-36-6 過多月経を呈する粘膜下筋腫に対する経腹超音波ガイド下筋腫融解術(TCMM)併用MEA治療の成績

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【目的】過多月経を呈する粘膜下筋腫に対するマイクロ波子宮内膜アブレーション(MEA)と経頸管的マイクロ波筋腫融解術(TCMM: transcervical microwave myolysis)の併用治療の成績について検討した。【方法】マイクロ波治療を行った3-7cmの単一粘膜下筋腫径の125例を対象に検討した。全例にMEAにTCMMを併用した。TCMMは直線型のマイクロ波アプリケーションを使用し、超音波ガイド下に70Wの条件で焼灼した。麻酔は硬膜外麻酔と静脈麻酔で行い、全例日帰り手術で行った。【成績】年齢は平均45.2歳、平均筋腫径は5.3cm、平均手術時間は37.9分で、平均照射時間はMEA450秒、TCMM525秒であった。術後3か月で月経量がVAS score 3以下に減少した著効例は115例(92.0%)であり、無月経症例は42例(33.6%)であった。また、貧血は術後3か月で有意に改善した(Hb10.8 vs 12.8g/dl, p<0.001)。満足度(VAS満点10)は平均9.9であった。また、子宮筋腫の体積は、術後3か月で67.7%、6か月で79.0%収縮した。子宮内感染が4例(3.2%)あった。【結論】経腹超音波ガイドを用いたTCMMを併用したMEA治療は、3-7cmの粘膜下筋腫の治療に90%以上の有効性と満足度が得られた。office gynecologyにおける日帰り治療でも可能であり、子宮摘出術の代替療法となり得ると考えられた。

P-36-7 経腹超音波検査を用いた非侵襲的な癒着診断法:癒着スコアによる妊娠出産前後の骨盤内癒着状態の変化

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【目的】妊娠により妊娠前に存在する子宮内膜症性癒着を改善するかどうかを検討すること。【方法】子宮内膜症に対する経腹超音波検査を用いた癒着診断法:癒着スコアは、簡便かつ非侵襲的な検査であるため、子宮内膜症患者の術後の癒着状態を経時的に評価することが可能である。本研究では、当院で子宮内膜症手術を実施した131名のうち、術後に妊娠・出産し、かつ妊娠前後の癒着スコアを評価出来た患者14名において、妊娠前後の癒着スコアを10点満点で評価し、t検定を用い、有意差を検討した。【成績】当院で子宮内膜症手術を実施し、術後1か月と出産後の癒着スコアを評価出来た患者14件の術後1か月平均値は、4.07であったが、産後平均値は2.35と、有意に低下した(p=0.04)。その改善率は42.2%であった。また、妊娠方法の内訳は、7名が自然妊娠で、7名がART妊娠であった。自然妊娠7名の術後1か月平均値は、3.57であったが、産後平均値1.71であった(改善率52.1%)。ART妊娠7件の術後1か月平均値4.5であったが、産後平均値3であった(改善率33.3%)。【結論】妊娠出産を通して、子宮内膜症性癒着の改善が見られる可能性が示唆された。特に自然妊娠可能な状態の子宮内膜症性癒着は改善される可能性が高い。

P-36-8 頸部筋腫と筋腫分塊は TCR が best and must の選択薫風会佐野病院
井上滋夫

【目的】3500件超の子宮筋腫内視鏡手術を経験し「頸部筋腫は筋腫偽被膜との接合が疎で剝離が容易、筋腫分塊は頸管拡張せずにスコープを挿入でき筋腫基部の切離が容易」との事実に基づき、頸部筋腫と筋腫分塊の最適術式は TCR (transcervical resection) と考えたので、報告する。【方法】2011年以降に経験した頸部筋腫35例、筋腫分塊27例を後方視的に検討した。単シース持続灌流レゼクトスコープを用い筋腫核剝離を行った。剝離は低出力凝固モードのローラーボール電極で筋腫立ち上がり部から始め、剝離できなくなるところまで進めた。筋腫の挟針牽引が可能になれば直視下にメス・クーバー剪刀で筋腫を分割切離し、挟針できない場合は鏡視下にループ電極で切削し、剝離と切離・切削操作を反復し筋腫を摘出した。【成績】一次的完全摘出した頸部筋腫は28例、摘出筋腫重量は5gから532gで、100g以上の例が20例あり、これらの平均は251g、手術時間は13分から189分、平均118分であった。筋腫分塊は全例が一次的に完全摘出でき、摘出筋腫重量は5gから134g、平均39g、手術時間は5分から85分、平均22.9分であった。【結論】漿膜下筋腫でない頸部筋腫と筋腫分塊となった筋腫は大きなものも TCR 可能であった。頸部筋腫の筋腫核出術・子宮全摘術は子宮動脈と尿管の損傷の危険を伴い難易度が高く、有茎性筋腫の筋腫分塊の経腔捻除は出血・基部残存・子宮内反・子宮穿孔の危険性があり、茎が太い場合は開腹・腹腔鏡手術が行われている。TCRは腹腔鏡より低侵襲で入院・休業期間が短く、高額な消耗機材を要さず、医療費低減という社会的要求にも応えられるから、頸部筋腫と筋腫分塊の標準術式として普及することが望まれる。

P-36-9 巨大子宮筋腫はレルゴリクスで本当に小さくなるのか伯風会大阪中央病院
細川有美, 松本 貴, 天雲千晶, 相本法慧

【目的】GnRH アンタゴニスト製剤の経口薬として国内初となるレルゴリクス(レルミナ)が発売され、当院では腹腔鏡下子宮筋腫核出術を施行する際に術前投与を行なっている。レルゴリクス投与による子宮筋腫の縮小率や大きさを術前に評価できれば、実際の手術イメージが想定でき、より安全な手術が可能となる。今回、巨大子宮筋腫に対してレルゴリクスによる縮小率をMRIより算出し、摘出した検体重量と比較、検討した。【方法】2021年7月から2023年4月までに腹腔鏡下子宮筋腫核出術を施行した症例のうち、MRIにおける子宮筋腫の最長径が10cm以上の10症例を対象とした。レルゴリクス投与前後にMRIを施行し、画像から子宮筋腫の体積を算出し縮小率を推測した。また、摘出検体の重量とレルゴリクス投与後のMRIから算出した体積を比較検討した。【成績】投与前の子宮筋腫の最長径は10.8-15.6cm、体積は315cm³ - 1072cm³だった。9症例で子宮筋腫の縮小(縮小率12-70%)を認めたが、1症例は38%の増大率を認めた。レルゴリクス投与後に施行したMRIにおける体積と摘出検体の重量とに正の相関関係(相関係数0.801)を認めた。摘出重量と出血量とに相関関係を認めなかった。【結論】レルゴリクス投与後に施行するMRIによって、算出した子宮筋腫の体積と摘出検体の重量とに正の相関関係を認めた。手術時の子宮筋腫の大きさを予想できることから、術前に必要な準備ができ、より安全な手術を可能とすると考える。

P-36-10 子宮筋腫核出術症例における富細胞性筋腫の術前画像診断について琉球大
宮城真帆, 銘苅桂子, 知念柊子, 仲村理恵, 大石杉子, 平敷千晶, 関根正幸

【目的】富細胞性筋腫は良性腫瘍であるが再発しやすく、画像上、平滑筋肉腫との鑑別が必要である。富細胞性筋腫の頻度や診断率、画像所見と臨床経過を明らかにし、平滑筋肉腫との鑑別点を抽出することを目的とした。【方法】2017年1月から2023年3月の期間、当院で子宮筋腫核出術を施行した103例を対象とし、診療録より富細胞性筋腫の診断有無、画像所見、病理学的所見、臨床経過を後方視的に調査した。【成績】年齢中央値は38歳で、術式内訳は腹式子宮筋腫核出術35例、腹腔鏡下筋腫核出術67例、腹腔鏡補助下筋腫核出術1例であった。全症例の病理診断内訳は富細胞性筋腫1例(0.9%)、平滑筋腫54例(52.4%)、変性平滑筋腫45例(43.6%)、活動性核分裂型平滑筋腫1例(0.9%)、Adenomatoid tumor 1例(0.9%)、平滑筋肉腫1例(0.9%)であった。術前のMRI画像診断で富細胞性筋腫疑いと診断されたのは8例(7.8%)あり、全症例において拡散制限を有していた。そのうち病理診断で富細胞性筋腫と診断されたのは1例で、診断率は12.5%であった。その他は平滑筋肉腫1例、Adenomatoid tumor 1例、変性平滑筋腫2例、平滑筋腫3例であった。病理診断で富細胞性筋腫と診断された1例とその他7例との画像所見に有意な差は認めなかったが、平滑筋肉腫の画像所見上の鑑別点として「中心領域の造影欠損」や「出血」を認めた。【結論】MRI所見で富細胞性筋腫と診断された8例のうち1例に平滑筋肉腫を認めた。平滑筋肉腫の画像所見上の鑑別点として「中心領域の造影欠損」や「出血」が挙げられるものの、鑑別は容易ではなく、これらの所見を認める場合は平滑筋肉腫を念頭に、術式についてより慎重な対応が望ましい。

P-37-1 再発子宮頸癌に対してパクリタキセル、カルボプラチン、ペバシズマブ、ペムプロリズマブの4剤併用化学療法が著効した2例

東邦大医療センター大森病院

釘宮剛城, 小宮山慎一, 齋藤有沙, 土屋貴裕, 向井隆文, 長島 克, 中田雅彦

【緒言】進行あるいは再発子宮頸癌の新しい治療戦略として、KEYNOTE-826 試験で有用性が示されたパクリタキセル (T)、カルボプラチン (C) あるいはシスプラチン (P)、ペバシズマブ (BEV)、ペムプロリズマブ (PEM) の4剤併用化学療法 (もしくはBEVを除く3剤) がある。当院では、2022年11月より8例に4剤併用化学療法を施行した。転帰は、完全奏効 (CR) 3例、部分奏効 (PR) 1例であった。このうちの代表的2例につき報告する。【症例】著効した1例目は、52歳の子宮頸部腺癌 (IB2期) 術後、補助化学療法後の患者。腹腔内再発巣に対してTC+BEV+PEM 併用療法を施行、5サイクル施行後のCT検査で再発巣はすべてCRとなった。奏効期間は3か月であり、治療継続中である。有害事象としてgrade2の甲状腺炎による続発性甲状腺機能低下症を認めたため、現在レボチロキシン100 μg/日を補充中である。著効した2例目は、76歳の子宮頸部扁平上皮癌 (IIIC1期) 同時化学放射線療法後の患者。左鎖骨上窩及び後腹膜リンパ節再発に対してTC+BEV+PEM 併用療法を施行、5サイクル施行後のCT検査でCRと判定した。奏効期間は6か月であり、治療継続中である。有害事象としてgrade3の掻痒感をともなう中毒疹、40℃以上の高熱、一過性の意識消失発作 (尿失禁、便失禁) を認めたが、管理可能であった。【結語】進行あるいは再発子宮頸癌に対するTC+BEV+PEM4剤併用化学療法は有効であり、新しい標準治療になり得るであろう。

P-37-2 進行子宮頸癌合併妊娠に対して子宮内に胎児を残したまま同時化学放射線療法を行った一例

JA 旭川厚生病院

南川太一

【緒言】わが国では40歳前後をピークに浸潤子宮頸癌が増加しており、妊娠年齢の高年齢化に伴い子宮頸癌合併妊娠も増加している。浸潤子宮頸癌に対する治療遅延について明確な指標はなく、診断時の妊娠週数と進行期から個別に妊娠帰結時期および治療開始時期が検討される。しかし妊娠初期に、長期間の治療遅延を許容しがたいIII期以上の進行子宮頸癌が診断された場合の治療報告は少ない。今回我々はIIIC1期の進行子宮頸癌に対して、妊娠15週から子宮内に胎児を残したままCCRTを行った一例を経験したので報告する。【症例】30歳、3妊2産。妊娠10週に近医で子宮頸部細胞診H-SILを指摘され、妊娠12週に当院へ紹介された。陰部後唇に腫瘍の増生を認め、生検組織は扁平上皮癌であった。MRI検査で頸部腫瘍と右鎖骨節の腫大、内診では右基韧带浸潤を認めた。CT検査で明らかな遠隔転移病変を認めず、子宮頸癌IIIC1期と診断した。児の良好な予後が期待される週数までの治療遅延は許容しがたいと判断し、患者・家族と十分な相談の上、標準治療であるCCRTを早期に開始することとした。胎児の扱いについてはESMOのガイドラインを参考に、妊娠15週0日から子宮内に胎児を残したまま治療を開始し、21日目の診察で子宮内胎児死亡が確認され、38日目で児が娩出された。【考察】ESMOガイドラインでは第1三半期に照射を開始する場合は妊娠状態のまま、第2三半期には子宮切開で児を娩出後に開始することが推奨されている。本症例では第2三半期初めに治療開始するにあたり、第1三半期に準じて妊娠状態のままで行った。妊娠継続が不可能な進行子宮頸癌合併妊娠に対する治療においては、安全な治療遂行と十分な精神的配慮が求められる。

P-37-3 心電図異常から子宮頸癌の心臓転移の診断に至った一例

静岡県立総合病院

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【緒言】子宮頸癌の心臓転移は稀であり、生前に診断される症例はさらに少ない。全身倦怠感の訴えから心電図異常を発見し、心臓転移の診断に至った一例を経験した。【症例】52歳 (X年) で子宮頸癌 (扁平上皮癌) IIIC2p期 (ypT2bN2M0) に対し術前化学療法としてイリノテカン/ネダプラチン2サイクル施行後に広汎子宮全摘/両側付属器切除/骨盤・傍大動脈リンパ節郭清術を施行した。術後化学療法としてパクリタキセル/カルボプラチン/ペバシズマブ (Bev) 療法を6サイクル施行した。X+1年6月尿道周囲再発を認め、同時化学放射線療法を施行した。その4か月後に左鎖骨上窩リンパ節転移を認め、放射線治療を施行した。X+2年2月に傍大動脈リンパ節 (PAN)/頸部リンパ節転移を認め、PAN領域に放射線治療を施行した。照射終了直後に倦怠感、息切れの訴えがあり心電図を施行したところ、VI~V4, II, III, aVFに冠性T波を認めた。心エコーにて右心室内に血栓あるいは腫瘍を疑う占拠性病変を認め、突然死を回避する目的で手術適応とした。右室内を腫瘍が占拠しており、摘出腫瘍の術後病理診断は扁平上皮癌で、子宮頸癌の右心室転移と診断した。パクリタキセル/シスプラチン療法2サイクル施行後の心エコーで右心室内腫瘍の再発を認めノギテカン/パクリタキセル/Bevに変更した。2サイクル後、呼吸困難感、低酸素血症を認め、CTで肺塞栓、右心室内転移増大、肝転移を認め緩和ケアの方針とし、心臓転移診断後5か月で自宅にて永眠された。【結語】がん治療中にはよく遭遇する倦怠感や息切れ等の症状は、極めて稀ではあるが心臓転移の可能性がある。心臓転移の診断契機として心電図異常が重要である場合がある。

P-37-4 脈絡膜転移を来した子宮頸癌の一例

群馬大

尾池 妙, 中尾光資郎, 池田禎智, 平川隆史, 岩瀬 明

【緒言】脈絡膜転移は肺癌、乳癌等で報告されるが婦人科腫瘍では稀である。今回我々は脈絡膜転移を来した子宮頸癌の一例を経験したため文献の考察と併せて報告する。【症例】38歳、1妊1産。自治体検診にて筋腫分婉を疑われ、近医婦人科を受診した。組織診にて子宮頸癌の診断に至り、当院を紹介された。子宮頸部後唇に3cm大の腫瘤を認め、内診、組織診、画像検査より子宮頸部腺癌IB2期（日産婦2020）と診断し、広汎子宮全摘術、両側付属器摘出術を施行した。術後病理検査から粘液性癌IIIC1p期と診断し、追加治療としてCCRTを施行した。治療終了2週後に咯血があり、CTにて縦隔浸潤を伴う肺門部腫瘤を認め、生検から子宮頸癌肺転移と診断した。同時に胸部、季肋部の疼痛が出現し、FDG-PETを施行したところ骨、肝にも多発転移を認めた。化学療法を予定するとともに、咯血と疼痛に対する緩和照射を開始した。しかし炎症反応の上昇とPSの悪化により入院となり、同時期に急激な右眼の視力低下の自覚あり。頭部CTにて眼球後部にドーム状の濃度上昇域があり、眼科精査にて2ヶ所の脈絡膜腫瘍とこれに伴う漿液性網膜剝離を認め、脈絡膜転移と診断した。視機能保持目的での眼球照射も検討していたが、原疾患増悪による無気肺、胸水貯留から酸素化が悪化し、CCRT終了2か月後、脈絡膜転移の診断から15日後に死亡した。【結語】脈絡膜転移は他臓器転移を伴うことが多く、予後不良である。眼科的診察により診断され、原疾患治療としては化学療法、視機能保持には放射線治療、光凝固等が検討される。他科と連携して予後を見据えた治療計画が重要と考えられる。

P-37-5 子宮頸癌標準治療終了後に Best supportive care としていたが、その後にセミプリマブが著効した1例

静岡県立総合病院

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【緒言】セミプリマブは2022年12月よりがん化学療法後に増悪した進行または再発の子宮頸癌に対して投与可能となった抗PD-1抗体である。標準治療終了後に Best supportive care (BSC) としていた症例にセミプリマブを投与し、著効した1例を経験したため報告する。【症例】67歳時に不正性器出血を主訴に受診され、子宮頸癌（扁平上皮癌）FIGO StageIIIC1r (T2bN1M0)と診断した。術前化学療法としてイリノテカン/ネダプラチンを投与し、広汎子宮全摘、両側付属器切除、骨盤内・傍大動脈リンパ節郭清術を施行した。同レジメンで術後補助療法を行い初回治療終了とした。治療終了約1年後に傍大動脈リンパ節と陰断端に再発を認め、同時化学放射線療法で完全奏効を得た。再発治療終了約2年後に多発肺転移を認め、パクリタキセル/カルボプラチン/ペバシズマブ、ノギテカン/パクリタキセルを投与したが病勢進行し、MSI検査は陰性、癌遺伝子パネル検査 (F1 Liquid) でも治療に結びつく遺伝子異常は認めず BSC の方針とした。その9か月後にセミプリマブが使用可能となり投与を開始した。腫瘍熱、疲労感、肺転移による左背部痛、咯血を認めていたが3サイクル後にこれらの症状は消失し、SCCも正常化した(28.6→0.6ng/mL)。6サイクル後には治療前に認めていた最大径5cmの腫瘤の他、複数の肺病変は著明な縮小効果を認めた。副作用の出現なく現在も投与継続中で病勢は落ち着いている。【結語】再発子宮頸癌は有効な治療の選択肢が少ないことが課題である。複数のレジメンの投与歴がある症例でもセミプリマブで著明な効果を得られる可能性がある。

P-37-6 演題取り下げ

P-37-7 子宮頸管ポリープに発生した明細胞癌の1例

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【緒言】子宮頸管ポリープの悪性は稀で、ポリープ全体の約0.1%との報告があり、更に子宮頸部明細胞癌は、頸部腺癌の中でも4.9%と稀な組織型である。今回子宮頸管ポリープに発生した明細胞癌で、癌性腹膜炎が初発症状であった1例を経験したので報告する。【症例】59歳、未妊。腹部膨満感を主訴に前医を受診し、腹水貯留・腹膜播種を認め、卵巣癌疑いにて当院を受診した。審査腹腔鏡手術を施行した所、卵巣は肉眼的には所見を認めず、骨盤内から上腹部に及ぶ播種病変を多数認め、Optimal surgeryは困難と判断された。大網播種生検にて明細胞癌を疑う腺癌の診断であり、腹膜癌IIIC期としてPaclitaxel+Carboplatin (以下TC)療法施行後、腫瘍減量術を施行した。術後病理にて子宮頸管ポリープに局限する明細胞癌を認め、子宮頸部明細胞癌IVA期、ypT1b1NxM1の診断となった。がんゲノムプロファイリング検査FoundationOne®CDxも施行したところ、TP53の変異のみを認めたため子宮原発の悪性腫瘍の可能性が高いと判断し、術後はTC+Pembrolizumab療法を施行した。【考察】明細胞癌でのTP53変異の頻度は子宮体癌で約35%、子宮頸癌で約25%であるが、卵巣癌では10%程度との報告があり、本症例では術後病理診断や遺伝学的検査から子宮原発の悪性腫瘍の可能性を考え、治療選択を行った。但し、腫瘍減量術後の評価であることには留意すべきであると考え。【結語】今回我々は、子宮頸管ポリープに発生した明細胞癌の1例を経験した。本症例を通じて、特殊組織型は非典型的な臨床経過を辿ることも念頭におき、より適切な診断や治療選択へ繋げる一手として遺伝学的検査も有用であることを改めて認識することができた。

P-37-8 進行子宮頸癌に対してペムプロリズマブ・バクリタキセル・カルボプラチン・ペバシズマブ療法を行い免疫関連有害事象を起因とした敗血症性ショックを繰り返した一例

関西労災病院

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【緒言】ペムプロリズマブは多彩な免疫関連有害事象(irAE)を起こすが、irAE胆管炎や膵炎は稀である。今回我々はirAE胆管炎、膵炎を発症し、敗血症性ショックを繰り返した症例を経験したので報告する。【症例】57歳、1妊0産の女性。子宮頸癌cT4N1M0、stage IVA期と診断され、腫瘍の尿管閉塞による急性腎不全のため腎瘻増設後、ペムプロリズマブ・バクリタキセル・カルボプラチン・ペバシズマブ療法を6サイクル実施し、完全奏効となった。ペムプロリズマブ・ペバシズマブ維持療法を1サイクル実施後に、上腹部痛のため受診。肝胆系酵素の上昇・CTで閉塞機転を伴わない胆管の壁肥厚と拡張を認め、irAE胆管炎(Grade1)の診断で、絶食・抗生剤投与を開始した。入院13日目に発熱、急激な肝胆系酵素・炎症反応上昇を認め、敗血症性ショックとなった。irAE胆管炎の増悪(Grade3)に対してプレドニゾン(PSL)60mg(1mg/kg)を開始し、全身状態は改善したため、PSLを漸減したが、入院23日目に肝胆系・膵酵素再上昇を認め、再び敗血症性ショックを来した。CTでびまん性膵腫大と左腎腫大、周囲脂肪織濃度増強を認め、急性膵炎と尿路感染症の併発の診断で、補液、抗生剤、蛋白分解阻害薬を開始した。ステロイドに伴う膵炎も否定できないことから、PSLは早期漸減とした。集中治療により全身状態は改善し、人工呼吸器、持続的血液濾過透析(CHDF)は離脱できたが、現在も治療継続中である。【結語】irAE胆管炎、膵炎は稀だが急速に病態が進行する可能性があり、施設内チームによる連携と迅速な対応が重要である。

P-37-9 子宮頸癌に子宮留膿腫を合併し、抗生剤と経腔ドレナージで改善せず敗血症性ショックに至り、単純子宮全摘出術を施行した1例

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【緒言】子宮頸癌に伴う子宮留膿腫から子宮穿孔をきたした症例は少数報告されているが、穿孔をきたさず敗血症性ショックに至った症例の報告はない。今回、感染コントロールに難渋し治療途中でsalvage hysterectomyを施行した子宮頸癌の1例を報告する。【症例】60歳、既往歴に本態性血小板血症があり、 hidroキシカルバミドとアスピリンを内服中であった。子宮頸癌IIIC2期、扁平上皮癌(FIGO2018)に対し、同時化学放射線療法(CCRT)の方針とした。治療開始前から発熱と炎症反応高値を認め、子宮留膿腫が原因と考え抗生剤(SBT/ABPC)投与と経腔ドレナージを施行した。その後も解熱が得られず、汎血球減少を認めた。経腔ドレナージ後のMRI検査で子宮内腔の膿瘍は消失したものの子宮後壁筋層内に膿瘍形成が疑われた。抗生剤をTAZ/PIPCに変更するも汎血球減少は増悪し、抗生剤治療開始から5日目に敗血症性ショックをきたしたため、同日感染巣除去目的に単純子宮全摘出術を施行した。開腹所見では子宮頸部腫瘍が膀胱筋層に浸潤、壊死した腫瘍組織を認め、同部位の膿瘍は残存した。術後、循環動態は安定し血球も回復傾向にあり、術後9日目に抗生剤治療を終了した。術後2週間後より残存病変に対する放射線治療を再開し順調に経過している。【結語】子宮内膿瘍が制御困難となり敗血症性ショックをきたした子宮頸癌の1例を経験した。本態性血小板血症と本症例の経過の関連は明らかではないが、子宮穿孔をきたしていない場合においても保存的加療で改善がみられない場合、子宮摘出が重要感染のコントロールに有用であると考えられた。

P-37-10 子宮頸部腺癌再発に対する免疫チェック阻害剤 (ICI) 治療によるサイトカイン放出症候群 (Cytokine release syndrome; CRS) を発症した一例

産業医大

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CRSは過剰な免疫反応で、血中サイトカイン濃度が上昇することで起こる炎症性症候群である。子宮頸部腺癌再発へのICI投与後に発症したCRSに対してヒト化抗ヒトIL-6受容体モノクローナル抗体(トシリズムマブ)を投与した症例について報告する。子宮頸癌IIB期に対してCCRTを行い、治療後1年で腹腔内再発を認めためTC+Pem療法を開始した。2コースday23に発熱と腰部痛を主訴に受診、腎盂腎炎の診断で入院となり、抗生剤投与で退院となった。3コースday27に持続する高熱と倦怠感、皮疹を主訴に受診した。尿中白血球の検出から腎盂腎炎の疑いで入院したが、入院翌日よりインフルエンザ様の上気道症状や筋肉痛を認めた。さらに下痢を発症後まもなくショックバイタルに至ったため、腎盂腎炎による敗血症性ショックと判断してICU管理とした。CK上昇に伴う腎機能障害、LVEF20%の心機能低下から多臓器不全となり、人工呼吸器やCHDFを導入した。横紋筋融解、膵炎、多形紅斑、腸炎より、免疫関連副作用(irAE)と診断した。各種培養検査が陰性であること、血中フェリチンと可溶性IL-2Rの上昇を認めたことから血球貪食症候群を伴うCRSと診断し、3日間のステロイドパルス療法を実施した。その後も症状改善はなく、トシリズムマブを投与した。投与後4日目に心機能と酸素化の改善を認め抜管した。6日目にCHDF離脱、21日目に自宅退院となった。退院後はCRSの再燃は認めなかったが、腫瘍は再増大した。ICIによるCRSは敗血症との鑑別が困難であり、経過が急速かつ重篤であるため、その対応への理解は重要である。ICI療法後にCRSを発症し、ステロイドとトシリズムマブにより治療が奏効した症例について文献的考察を含め報告する。

P-38-1 前回妊娠時に子宮内胎児死亡となった症例における不育症スクリーニング結果と次回妊娠転帰の後方視的検討

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【目的】当科では、前回妊娠時に子宮内胎児死亡や早発型妊娠高血圧腎症、重度の子宮内胎児発育不全であった症例に対して、不育症スクリーニングを実施している。本研究では、前回妊娠時に子宮内胎児死亡となった症例に対する不育症スクリーニングの結果と、次回妊娠時に治療介入した際の妊娠転帰につき後方視的に検討したため報告する。【方法】前回妊娠時に子宮内胎児死亡となったため、次回の妊娠に向けて不育症スクリーニングを希望し、2013年から2023年までの間に当科を受診した31例を対象とした。不育症スクリーニングの検査項目は、抗カルジオリピン抗体、抗β2GPI抗体、ループスアンチコアグラント、甲状腺機能検査、Protein S活性、Protein C活性、第XII因子凝固活性、抗核抗体とした。不育症スクリーニングの結果と、次回妊娠時に治療介入した際の妊娠転帰につき後方視的に検討した。【成績】不育症スクリーニングの結果、抗リン脂質抗体症候群の診断基準を満たした症例が31例中8例(25.8%)あり、次回妊娠時に全例で低用量アスピリン・ヘパリン併用療法を施行し、8例中7例で生児を獲得した。妊娠経過中に妊娠高血圧腎症や子宮内胎児発育不全を発症した症例はいなかった。抗リン脂質抗体症候群の以外の症例では、23例中10例で低用量アスピリン内服、12例で低用量アスピリン・ヘパリン併用療法を施行し、23例中20例で生児を獲得した。妊娠経過中に妊娠高血圧腎症2例、子宮内胎児発育不全5例を発症した。【結論】前回妊娠時に子宮内胎児死亡となった症例では、次回妊娠に向けて原因検索を行い、適切な治療介入を行うことで妊娠転帰を改善することができる可能性がある。

P-38-2 ART妊娠成立後の初期流産に対する待機療法の後方視的検討

岩手医大

齋藤珠帆, 尾上洋樹, 村上一行, 佐藤千絵, 馬場 長

【目的】2022年4月より生殖補助医療(ART)が保険適用となったことでART妊娠は増加し、それに伴いART妊娠後の初期流産の方も増加している。初期流産に対しては薬物療法が未認可のため自然妊娠と同様に待機療法と手術療法が選択されるが、内膜愛護などの観点や手術療法の場合は入院が必要となる事から当院では待機療法を選択する事が増えている。今回ART妊娠初期流産症例の待機療法について検討した。【方法】2022年2月から2023年6月までに胚移植を行い、妊娠成立した妊娠10週までに稽留流産と診断された68例を後方視的に検討した。【成績】稽留流産68例のうち早期の手術療法を希望したのは5例(7.3%)であり、それらの理由としてはつわり、不育症による頻回の流産歴や胎嚢が大きいことが挙げられた。待機療法を選択した63例のうち自然排出されたのは58例(92.1%)、手術療法へ移行したのは5例(7.9%)だった。手術へ移行した症例は4週間以上待機期間をおいたものの自然排出が見られなかった症例だった。診断から自然排出までの期間を0-6日、7-13日、14-20日、21-27日、28日以降の割合で示すと43%、22%、26%、6.9%、1.7%であり、大部分が2週間以内に排出を認めた。待機療法中に13例が腹痛や性器出血で救急または予約外受診し、うち1例は出血が多く入院管理、輸血を施行した。また透明帯開口術施行の有無、高濃度ヒアルロン酸含有培養液使用の有無で自然排出までの期間に差はみられなかった。【結論】当院で期間中に待機療法を行った症例のうちのほとんどが2週間以内に自然排出がみられた。自然妊娠と同様にART妊娠後の初期流産に対しても待機療法は安全な管理法と言えるだろう。

P-38-3 不妊治療と就労の両立支援に関する当院の施策について

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【目的】不妊治療と就労の両立は極めて重要な課題であり、当院では専用アプリをはじめとしたDXによる患者支援に力を入れている。今回その有効性確認を目的に、当院で治療を受ける患者の就業状況と背景について調査・検討した。【方法】2022年5月～2023年5月の間に当院で不妊治療を受けた患者を対象に、文書による説明と同意を得た上で、不妊治療と就労についてオンラインにてアンケート調査を実施した。加えて、各診療内容ごとに患者の在院時間を検討した。【成績】対象患者は2379人で、369人から回答を得た(15.5%)。女性回答者のうち、仕事をしながら不妊治療を受けた経験があるのは、299人中248人(82.9%)、そのうち不妊治療を理由に就業状況を変更したのは60人(24.2%)、退職したのは15人(6.0%)であった。女性患者の在院時間は、初診日で平均1時間37分±38分(N=473)、再診日以降で一般不妊治療は50分±34分(N=960)、採卵周期(採卵術当日、術後を除く)は1時間27分±35分(N=1158)、胚移植周期(移植術当日、術後を除く)は1時間11分±36分(N=692)であった。【結論】国内の先行研究では就労と治療の両立困難を理由に23%の女性患者が離職するとされるが、当院における患者の離職率はそれより低い結果であった。当院では専用アプリによる診察予約や事前問診票記入、後日会計システムと院内処方等の施策により在院時間を削減しており、今回の調査においてこれらの取り組みとその効果も合わせて紹介したい。

P-38-4 提供精子による生殖医療を行うための精子バンク活動について

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【目的】提供精子による生殖医療を行うための精子バンク活動について報告する【方法】2021年4月から2023年3月までの活動について、後方視的に解析する【成績】と【結論】提供精子を用いた挙児方法は、AIDを中心として40年以上前から限られた施設を中心に行われてきた。しかし、子どもの権利としての出自を知る権利に関する情報が行き渡るにつれて、世界的にドナー登録を行う人が減少してきた。特に、新型コロナウイルス感染症の蔓延による、移動制限がさらにドナー登録の不足を加速させた。国内でAIDの登録施設に希望しても、新規希望者の受け入れの中止や、1年以上の待機期間の施設が増加した。さらにSNSを介した精子授受が盛んにおこなわれるようになり、多くの問題点が明らかにされた(Reprod Med Biol. 2021 Jun 14; 20(4): 554-556. doi: 10.1002/rmb2.12395)。この状況を改善するために、国内唯一の民間精子バンクを2021年4月に設立し、ドナー募集と提携医療機関への精子提供を開始した。しかし、この活動は2023年4月で一旦休止することになった。これまでの経験から(1)ドナー募集方法、(2)ドナー選択基準、(3)レシピエントの対象、(4)レシピエントの負担する費用、(5)現在の問題点について、海外の精子バンクとの比較を行うとともに、今後の展開に関して報告する。

P-38-5 「いざよく遊び、いざよく学び」—カードゲームによる新たな生殖医学教育—

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【目的】生殖医学は内分泌なども関わり、難解な部分もあることから、医学生や研修医にとって興味を持ちにくい分野である。今回、「遊ぶ」ことを通して、生殖医学を「学ぶ」、カードゲームによる新たな学習法を開発し、その有用性について検討した。【方法】対象は、2020年3月～2023年9月までの間に、本学医学部4年生、5年生で、産科臨床実習で「ゲームで学ぶ体外受精」を選択した学生である。実習1時間の中で、ゲームルールを解説後、ゲームを3回プレーして、ゲームを通して体外受精のプロセスや刺激法について学んだ。学習効果についてはゲームの前後でプレテスト・ポストテストを実施して評価をした。合わせて、実習後にアンケートを行い、ゲームについて学生が評価を行った。【成績】選択した学生は135人であった。プレテスト・ポストテストの正答率はそれぞれ72%、95%で、ゲーム後に正答率の有意な上昇を認めた(p=0.0001)。また、ポストテストの正答率は学生が一人(88%)よりも複数(95%)で参加した方が高い傾向を示した。アンケートでは、93%の学生がカードゲームを「楽しかった」と評価し、82%の学生が体外受精に関する知識が「増えた」と実感した。さらに93%の学生が「体外受精に興味を湧いた」、「採卵を見てみたい」と回答しており、生殖医学への興味も得られていた。【結論】カードゲームを通して、生殖医学に関する知識の習得ができることが示され、さらに複数名による学習の方が、より高い学習効果を得られる可能性が示唆された。また、産婦人科への興味を持つ機会作りにも有用である可能性も示され、新たな教育ツールとして有望であると考えられた。

P-38-6 トリオにおける大規模全ゲノムデータを利用した、夫婦間対立遺伝子における遺伝子変換の検出～インプリンティング異常症・常染色体潜性遺伝病における新規発生メカニズムの探求～

東北大

虎谷惇平, 立花真仁, 平賀裕章, 横山絵美, 渡邊 善, 齋藤昌利

【目的】DNAの二重鎖切断を起こした領域は修復が必要となる。修復に相同組み換え修復が用いられる際、ドナーDNAの一部がアクセプターアレルにコピーされることで、遺伝子変換が起こることが知られている。近年、いくつかのグループがCRISPR-Cas9を用いて受精卵のゲノム編集を目的とした研究に着手しており、DNA切断部位での遺伝子変換が報告されている。これらの研究結果は、父母いずれかのアレルに二重鎖切断が存在する条件下では、受精時や発生初期において夫婦ゲノム間でDNAのコピーが起こる可能性を示唆している。これらに着想を得て、日本人トリオの全ゲノムデータを用いて遺伝子変換が推測される領域を抽出し、一般集団における出現頻度や特性を評価することとした。【方法】東北メディカル・メガバンクが実施した三代コホート調査の参加者から、トリオで全ゲノム解析が終了している2304トリオを対象とした。なお、ヒト全ゲノムデータを用いた遺伝子変換の研究は前例がないため、独自のパイプラインを開発した。【成績】1トリオあたり平均で約1.2個、1件あたりのサイズが約30kbpの遺伝子変換が確認され、両親の由来に違いは認めなかった。また、ホットスポットが確認され、これは遺伝子変換が二重鎖切断に由来することを裏付けている。【結論】遺伝子変換は、減数分裂や体細胞分裂など特定の段階でのみ生じると認識されていたが、本研究により、発生初期の段階でも起こり得ることが示唆された。夫婦間の遺伝子変換により病的遺伝子がコピーされ得ることから、これまで原因不明とされていたインプリンティング異常症や常染色体潜性遺伝病の一部が、この現象が一因となっていた可能性が考えられる。

P-38-7 片側低形成腎および同側尿管の腔開口を伴うOHVIRA症候群の一例に対する臨床所見および治療戦略

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【緒言】OHVIRA症候群(Obstructed of hemi-vagina and ipsilateral renal anomaly)はさまざまな病型がある。今回、重複子宮の両側交通があるために診断が遅れ、慢性患側骨盤痛が持続増悪したために患側低形成腎および異所性開口した尿管および子宮全摘に至った一症例についてそれぞれのライフステージでの診断治療を見直し、文献の考察も含めて再考する。【症例】33歳3妊1産、骨盤腹膜炎、慢性骨盤痛にて当科入院となった。それまでに23歳7週にて自然流産、28歳39週で分娩停止にて帝王切開を受け、32歳妊娠16週での中期自然流産。入院後MRI、CT精査にて双頸双角子宮、左腔閉鎖、左低形成腎および左尿管異所性開口(左腔開口)の診断。その際左尿管は経血逆流による尿管留血腫及び周囲線維化を認めた。4か月後左腔閉塞術を施行。経血流出路確保され月経困難軽快。しかし妊娠を期待するも慢性骨盤痛の改善なく性交障害およびうつ病発症し38歳まで経過観察。疼痛が左尿管異所性開口部に一致するため外科的切除を希望。腹腔鏡下子宮全摘および左尿管・左腎摘出施行。術後慢性骨盤痛は軽快した。【考察】本症例は33歳まで左腔閉鎖に気づかず、月経困難および慢性骨盤痛にて生活に支障を及ぼしていた。慢性骨盤痛は慢性的な異所性尿管への経血逆流が原因であり、中期流産は経血流出路障害による子宮内膜炎の可能性を考えた。双頸双角子宮でありながら子宮腔部が1孔であることを疑問視されていたがOHVIRA症候群の診断に至らなかった。左尿管切除により症状軽快したが、早期に腔中隔切除できれば防止できたと考えた。

P-38-8 良性卵巣腫瘍の複数回再発後に医学的適応の妊孕性温存療法を施行した1症例

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【緒言】医学的適応の妊孕性温存療法は、悪性腫瘍以外にもその適応が広がりつつある。今回、複数回再発する良性卵巣腫瘍に対して、医学的適応の妊孕性温存療法を施行したので報告する。【症例】20歳、0妊0産、未婚。8歳時に成熟嚢胞性奇形腫茎捻転に対し腹腔鏡下左付属器切除術施行。術後7年後に右卵巣に18mm大の再発を認めた。経過観察するも術後11年後に増大傾向を認めたため腹腔鏡下右卵巣腫瘍摘出術を施行した。手術8か月後に再発を認め当科紹介となった。初診時、右卵巣に29mm大の腫瘍を認めた。再度の手術による卵巣機能低下の可能性があるので、妊孕性温存を希望された。当院倫理委員会承認の下、医学的適応の妊孕性温存療法を施行する方針となった。Anti-Mullerian Hormone (AMH)は8.32 ng/ml, Antral Follicle count (AFC)は6個であった。Progesterin Primed Ovarian Stimulation (PPOS法)にて調節卵巣刺激を15日間、合計3375IUゴナドトロピン投与を行い、経腔採卵を行った。結果、回収卵子数3個、うちMII卵子2個を凍結した。今後は再び妊孕性温存療法を施行し腹腔鏡下右卵巣腫瘍摘出術を施行する方針である。【考察】若年の良性卵巣腫瘍の複数回再発症例に対し医学的適応の妊孕性温存療法を施行した。調整卵巣刺激に対する反応が乏しく、回収卵数は年齢や卵巣予備能による予測よりも少なかった。【結語】良性卵巣腫瘍再発症例に対する妊孕性温存療法の有益性についてはまだ結論がでない。今回の症例から、卵巣の低反応性と少ない回収卵数により複数回の採卵が必要となる可能性が示唆された。そのため、今後は症例を蓄積し回収卵数を増やすための方法について検討していく必要がある。

P-38-9 若年女性に対する経腹超音波断層法が術前診断に有用であった Wunderlich 症候群の 1 例

トヨタ記念病院

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【緒言】今回我々は経腹超音波断層法が Wunderlich 症候群の診断に有用であった 1 例を経験したので報告する。【症例】症例は 14 歳, 0 妊 0 産, 初経は 12 歳。月経時の左下腹部痛を主訴に前医を受診した。腹部 CT で右片腎及び子宮奇形を疑う所見があり当科紹介となった。MRI で重複子宮と子宮左角と連続した左腔壁の留血腫と思われる嚢胞性腫瘤を認めた。右片腎, 重複子宮, 子宮頸部から左腔壁に留血腫を認め OHVIRA (Obstructed hemivagina and ipsilateral renal anomaly) 症候群または Wunderlich 症候群の術前診断で全身麻酔下に診察を行った。内診では左腔壁に柔らかい腫瘤を触知した。腔鏡診では子宮の右角の子宮腔部を認めた。経腹超音波断層法では左腔壁から子宮左角内腔に連続する留血腫を認めた。左角の子宮頸部の筋層は途中で断裂し, 子宮と左腔壁の連続性はなく, Wunderlich 症候群と診断した。左腔壁を切開し, 腔壁腫瘤の隔壁を十分に摘出し, 左角内の留血腫を十分に排出させ, 硬性鏡で左角を観察したが, 子宮腔部は確認できなかった。術後合併症はなく経過し, 術後 3 日目に退院となった。摘出した左腔壁の嚢胞壁は内膜腺を伴った子宮由来の組織であり, Wunderlich 症候群と最終診断した。術後 1 か月経過した現在, 再閉鎖なく経過している。【結語】Wunderlich 症候, OHVIRA 症候群は若年に発症することが多い。そのため経腹超音波断層法が難しい場合があり, MRI が有用とされているが, 鑑別診断に経腹超音波断層法が有用な場合もある。

P-39-1 不妊症女性の血中精子不動化抗体が認識する精子抗原の同定

兵庫医大

本田晴香, 陳 月焜, 脇本 裕, 柴原浩章

【目的】精子不動化抗体は不妊女性の約 3% に検出され, 免疫性不妊症の原因の一つと考えられる。本研究の目的は, 不妊女性の血中精子不動化抗体が認識する精子抗原を同定することであり, 得られた結果は免疫性不妊症による病態の解明や避妊ワクチンの開発にもつながると考えられる。【方法】運動性の良好なヒト精子を密度勾配遠心法で調製した後, 0.1% の sodium dodecyl sulfate (SDS) を用いて抗原タンパクを抽出した。一次元電気泳動法及び Western blot 法により, 精子不動化抗体陽性血清 (18 検体) が認識する精子抗原の検出を行った。次に, 二次元電気泳動を実施し, 陽性反応を示したすべてのタンパクに対し質量分析を行った。対照として, 精子不動化抗体陰性血清 (8 検体) を用いた。【成績】精子不動化抗体陽性血清 18 検体を用いて解析した結果, 32 種類の異なるスポットが二次元電気泳動により検出された。そのうち 15 検体はそれぞれ異なるスポットと反応したが, 3 検体は同一のスポットと反応した。これら共通のスポットは分子量 49K, 等電点 5.1 を示し, MS/MS 解析により Tubulin beta-4A (TBB4A) と同定された。同スポットは精子不動化抗体陰性女性 8 名においては反応しなかった。TBB4A は精子尾部の軸糸に存在し, また細胞内の微小管を形成するチューブリンの主要な構成タンパクである。【結論】以上の結果より, 精子不動化抗体陽性不妊症女性患者の血清は多様な精子抗原を認識することが明らかになった。また一部の精子不動化抗体は, TBB4A を認識し, チューブリンに結合して精子の運動を障害する可能性が示された。過去の研究においても, チューブリンの障害により精子の鞭毛運動が障害されることが報告されている。

P-39-2 精液所見のスコアリング化による配偶者間人工授精の妊娠予測の試み

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【目的】配偶者間人工授精 (artificial insemination with husband's semen: AIH) における精液所見を点数化することで AIH の妊娠予測スコアを作成することを目的とした。【方法】本研究は 2018 年 4 月より 2022 年 3 月までに施行した AIH 周期を対象とし, 後方視的に行った。生殖補助医療における採卵前の早発排卵に対してレスキュー目的で施行した AIH 症例は除外した。ROC 曲線を用いて, 臨床妊娠に対する精液各所見 (精液量, 精液濃度, 精子運動率, 精子前進運動率, 総運動精子数) の各項目のカットオフ値を独自に算出し, カットオフ値以上を 2 点, WHO 基準値 (2021) 以上からカットオフ値未満までを 1 点, WHO 基準値 (2021) 未満を 0 点とし, 10 点満点で点数化した。このスコアの臨床妊娠に対するカットオフ値を同様に算出した。倫理委員会の承認下に施行した (承認番号: M22238)。【成績】対象周期は 1270 周期 (362 症例), 年齢は 36.3 ± 4.3 歳であった。臨床妊娠予測のカットオフ値 (ROC-AUC [95% 信頼区間]) は精液量 6.5ml (0.48 [0.40-0.56]), 精液濃度 $52.0 \times 10^6/\text{ml}$ (0.57 [0.48-0.65]), 精子運動率 58.6% (0.56 [0.48-0.64]), 精子前進運動率 34.3% (0.54 [0.46-0.62]), 総運動精子数 107.48×10^6 (0.56 [0.47-0.64]) であった。精液所見のスコアの中央値は 6 点 (0-10) であった。精液所見のスコアによる臨床妊娠予測能 (ROC-AUC [95% 信頼区間]) は 0.60 (0.52-0.68), カットオフ値は 8 点であった。【結論】5 つの精液各所見を考慮したスコアの ROC-AUC は 0.60 であり, 個々の精液各所見よりも高い臨床妊娠予測能を示した。カットオフ値である 8 点未満である場合, 年齢なども考慮して生殖補助医療への早期ステップアップを検討することが考慮される。

P-39-3 人工授精 1380 周期の精液所見と妊娠例の検討

島根大

折出亜希, 金崎春彦, 岡田裕枝, 京 哲

【目的】人工授精は軽度の男性因子や原因不明のカップルなどを対象に体外受精移行前の一般不妊治療として広く用いられている。人工授精の妊娠率には年齢を含む様々な要因があり、精液所見との関連を示す報告も多いが一定の見解は得られていない。そのため人工授精（夫婦間）実施時の調整前及び調整後精液所見と妊娠率の関連について検討した。【方法】2018年1月から2021年12月までに当院で人工授精を施行した421名、1380周期の精液所見と妊娠率を後方視的に検討した。精液所見の正常下限基準値は2021年WHO基準を用いた。【成績】1380周期の人工授精中87周期で妊娠が成立した（6.3%）。妊娠群と非妊娠群では女性、男性共に年齢に有意差を認めず。調整前及び調整後精液所見は妊娠群、非妊娠群で量、濃度、総精子数、運動率、総運動精子数ともに差を認めなかった。調整前精液所見において運動率がWHO基準を満たしていない場合、基準値内にあった場合に比べて有意に妊娠率が低かったが、量、濃度が基準以下の場合と基準値内の場合で妊娠率に有意な差はなかった。調整後精子運動率が42%を超えない場合の妊娠率はなかった。調整前精液運動率と男性の年齢に負の相関を認めた。調整後運動率が基準を下回る場合の妊娠率はなかったが、調整前後共に基準値内である場合の妊娠率が他と比べて高かった。【結論】人工授精においては調整前後の精液所見のパラメーターは妊娠群、非妊娠群で差を認めなかったが、調整前精子の運動率がWHO基準を下回る場合の妊娠率は悪く、また調整後精子の運動率がWHO基準の42%下回る場合の妊娠率はなかった。人工授精においては精子運動率が重要であると考えられた。

P-39-4 慢性子宮内膜炎の診断方法と治療後成績の後方的検討

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【目的】慢性子宮内膜炎（chronic endometritis：以下CE）とは、子宮内膜局所の持続的な炎症を伴う疾患で、着床不全や反復流産、早産に関係することが知られている。CEの最適な診断方法、診断基準については統一見解がなく、子宮鏡検査、形質細胞の特異的マーカーであるCD138の免疫組織染色検査、原因菌の有無について次世代シーケンサーを用いて検索する子宮内微生物培養検査から総合的に診断されているのが現状である。今回CEの検査、治療後に胚移植を施行した症例の転帰について検討をした。【方法】2023年4月～2023年8月の間に当院リプロダクションセンターで3BB以上の良好胚凍結融解胚移植を施行し、反復着床不全、反復流産患者と診断し、CE検査を行った11症例を対象とした。CEの診断は月経終了後の子宮鏡、P+5のCD138陽性細胞（ ≥ 5 CD138（+）in20 HPFs）と子宮内フローラにより行った。CE+症例に対して抗菌剤+プロバイオティクスによる治療を行い、CE検査及び治療後の融解胚移植後の成績について後方視的に検討した。【成績】11例の症例背景の中央値は年齢37（29-42）歳、融解胚移植回数3.3（2-7）回、移植後の初期流産4/11例（36.3%）であった。子宮鏡でCE（+）と診断した3例は全例CD138陽性であり、そのうち2例がNLDMであった。CE検査、治療後の融解胚移植後の転帰はCE+3例のうち2例、CE-8のうち1例に成立し現在妊娠継続中である。【結論】CEの検査で子宮鏡とCD138免疫組織染色検査は高い相関関係を認めた。反復着床不全、反復流産のCE+症例に対して治療を行うことで妊娠率、妊娠継続率の改善を認めた。一方でCE-症例においては子宮内環境以外の要因が不妊に関与しているが示唆された。

P-39-5 子宮内膜症の妊孕能評価に非観血的所見は有用か？

高知大

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【目的】子宮内膜症（以下内膜症）の妊孕能の評価には、腹腔鏡下手術所見によるEndometriosis fertility index（EFI）が用いられている。しかし近年、卵巣機能低下の観点から、腹腔鏡下手術を施行しない症例も増加している。今回、観血的に診断した内膜症婦人につき、非観血的所見を用いた妊孕能評価が可能かについて評価検討した。【方法】2008年1月から2023年5月に、当院にて腹腔鏡下手術で内膜症と診断し、その後不妊治療と妊娠管理を行った62例を対象とした。62例を、IVFまでステップアップしたIVF群30例と、自然妊娠・タイミング療法・人工授精で妊娠に至った非-IVF群32例に群別した。評価方法は、観血的にはEFI、また非観血的には患者背景・自覚症状・内診所見・検査所見（画像と血液検査）とし、後方視的に比較検討した。評価・検討の時期は挙児希望の時点とした。【成績】IVF群は、EFIは有意に低値（ $p=0.001$ ）で、挙児希望の年齢は有意に高かった（ $p=0.042$ ）。また、自覚症状は月経時の疼痛スコアが有意に高く（ $p=0.039$ ）、内診所見は子宮可動性不良・タグラス窩硬結・挙上痛を有する割合が有意に多かった（ $p<0.001$ ）。一方、画像検査と血液検査は、内膜症性嚢胞の割合・嚢胞径・血清CA125値などに有意差を認めなかった。【結論】自覚症状・内診所見で両群間に有意差を認めたことから、より詳細な問診・細心な内診などの非観血所見が内膜症の妊孕能評価にも有用と示唆された。手術操作により卵巣機能低下となる可能性も指摘されており、内膜症における非観血所見の重要性が改めて認識された。

P-39-6 X-常染色体均衡型転座の一例

愛媛大

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【緒言】均衡型相互転座はおおよそ500人に1人にみられ、遺伝子の量的過不足がないため、表現型は基本的に正常である。今回、月経不順、挙児希望にて近医を受診し、染色体検査にてX-常染色体均衡型転座の症例を経験したので報告する。【症例】25歳、身長155cm、体重55kg、初経は14歳。その後順調に月経を認めていたが、23歳ごろより月経不順となり近医にてホルモン剤処方されていた。25歳で結婚し、挙児希望あるため不妊クリニックを受診した。FSH 46mIU/ml E2 10pg/ml未満であり、染色体検査施行した結果、46,X,t(X;19)(q22.1;p12)であったため、遺伝カウンセリング目的に当院へ紹介受診となった。夫婦でカウンセリングの希望があり、情報提供を行なった。その内容、X-常染色体均衡型転座であること、通常、正常X染色体が不活性化され、転座が起こっている異常X染色体側のみが発現することで遺伝子量の過不足が生じず表現型は正常となることが多い、Xq13.3-q26は卵巣機能不全の責任領域であること、X染色体の不活性化のパターンによっては、無月経、月経不順、不妊や精神運動発達遅滞、多発形態異常などを呈する場合もあることである。また、次世代への影響として、児が不均衡型の場合、均衡型の場合、またそれらを事前に予測することはできないこと、出生前検査等を説明した。夫婦で相談され、現在、外来にて卵胞発育を経過観察中である。【考察】X-常染色体均衡転座は、相互転座にX不活性化のパターン、不活性化の常染色体への影響などが加わり、症状を推測するのが非常に困難である。次世代への影響などを含めカウンセリングは慎重に行う必要がある。

P-39-7 Wunderlich 症候群に対し腹腔鏡補助下子宮頸部嚢胞開口術、体外受精・胚移植、不育症治療により挙児を得た一例

兵庫医大

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【緒言】Wunderlich 症候群は重複子宮、片側子宮腔閉鎖、患側の腎無形性や低形成を伴う稀な疾患で月経困難症を契機に診断されることが多い。今回挙児希望と月経困難症を契機に Wunderlich 症候群と診断され、子宮頸部嚢胞開口術後に体外受精・胚移植を施行し、その後不育症治療も並行し挙児を得た症例を経験したので報告する。【症例】30歳、0妊0産月経不順、下腹部痛を自覚し前医を受診した。高校生時、子宮形態異常と右腎臓欠損を指摘されていた。経陰超音波では子宮頸部後方に2cm大の嚢腫を認め、MRIでは重複子宮、右腎臓欠損、子宮頸部に血性嚢胞を指摘された。挙児希望および上記の精査加療目的に当院を紹介・受診した。腔鏡診では子宮腔部を1つ確認した。月経中時、子宮腔部右側に小孔を確認した。同部位より子宮鏡を挿入し経血の貯留と右子宮腔を確認した。月経困難症と挙児希望のため腹腔鏡補助下子宮頸部嚢胞開口術を施行した。術後、自然妊娠は成立せず、人工授精、体外受精とステップアップした。その後、左子宮に妊娠成立するも妊娠9週で染色体正常流産(46,XY)となった。そこで不育症に準じた精査を行い、抗リン脂質抗体陽性、プロテインS欠乏症、子宮内膜NK細胞分画異常を認め、それぞれに対する治療を並行しつつ凍結融解胚移植で左子宮に妊娠成立した。妊娠経過は問題なく経過し妊娠37週で骨盤位のため2,438g, Ap8/9の女児を帝王切開分娩した。母児ともに経過は良好であった。【結語】Wunderlich 症候群は術後自然妊娠、分娩の報告例がある。しかし本症例のように術後の妊娠成立・維持に苦慮する症例もあり術前から術後までの継続したフォローの重要性を再認識した。

P-40-1 症例報告：両上肢が胎児の背側に存在することによる重度の肩甲難産の解除法とその考察

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胎児は生まれ出る時に、両肩峰間を最小距離とするために、両上肢を胸の前で組む体勢をとる。しかしながら、上肢が胎児の背側に位置すると、肩をすばめることができず両肩峰間の距離が最大となり、肩甲の娩出は著しく困難となる。私達が経験した妊娠38週目の1回経産婦の分娩では、児頭が娩出された後に、恥骨上圧迫を併用したMcRoberts体位、Rubin法、Woods Screw法でも、肩甲を娩出できなかった。大きく会陰切開し、後在の腕の娩出を試みたが、腕は胎児の腹側には見当たらなかった。内診指を後在の肩から腕の方へ沿わせて確認すると、上肢は胎児の背部に存在した。示指から小指までの4本の指を、後在上肢全体を真っ直ぐな状態に保つようにひっかけて、胎児の背部から側面部を横切り、腹側へ移動させた。その後、胎児の胸の前を通して、後在肩甲とともに娩出させた。しかしながら、それでも、前在肩甲は恥骨から外れず、胎児は娩出されなかった。前在の肩から上肢を辿ると、これも胎児の背側にあった。これも上肢全体を真っ直ぐな状態に保ったまま胎児の腹側へ移動させると、その瞬間に前在肩甲は恥骨から外れ、胎児は娩出された。児は体重3586g, Apgar Score: 5/8, 臍帯動脈血ガスpH7.157, 骨折や神経損傷などの合併症はなかった。腕の娩出を試みる場合、腕の位置を肩から上肢を辿って確認することが重要である。背側にある上肢が、最も狭い胎児側面部を横切る時に腕の関節脱臼や骨折の危険性を伴う。上肢の各関節が曲がらず、上肢を真っ直ぐ保つ均等な力を上肢全体にかけるのがその防止策と思われた。また、前在上肢が児背側に位置することも、重度の肩甲難産となることを念頭に置くべきである。

P-40-2 当院での無痛分娩への取り組みと分娩管理について

桑名市総合医療センター

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無痛分娩は、麻酔などの手段を用いて、産痛を緩和しながら分娩を行うことの総称である。2020年度は日本全国で無痛分娩が505施設(全分娩取扱施設の26%)で実施され、その実施率は全分娩の8.6%であり、2007年の全国調査の2.6%に比べると増加傾向であることが伺える。しかし、約7~9割の普及率がある諸外国に比べると依然低い水準である。原因には麻酔科医・産婦人科医不足や周産期施設の非集約化、同分娩自体への理解の遅れなどが挙げられ、それを反映してか都市部での無痛分娩の普及率は地方に比べると高く、妊産婦の選択肢が地域・施設間によって制限されているのが現状である。当院では以前より医学的適応の無痛分娩は取り扱っていたが、昨今の状況を踏まえて、2022年12月から麻酔科と連携し、患者希望での無痛分娩を自費診療として開始した。当初は、麻酔科による硬膜外カテーテル留置術をされる計画無痛分娩のみとしていたが、2023年6月よりリスクに応じて産婦人科医によるオンデマンド無痛分娩の対応も始め、9月現在の取り扱い分娩数の18%を占める形となっている。それに伴い、従来の経陰分娩に比べての吸引分娩、出血時・癒着胎盤の対応などの対応は変遷してきた。地方の一施設での無痛分娩への取り組み、管理について文献考察も交えて発表する。

P-40-3 妊娠36週に発症した嵌頓を伴う子宮脱に対し、コルポイリントルの併用で経陰分娩に至った1例

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【緒言】子宮脱合併妊娠は10000~15000分娩に1例と稀な病態である。妊娠後期に発症する例はさらに少なく、その分娩方法については一定の見解が得られていない。今回、妊娠36週に子宮脱を発症し、コルポイリントル併用による分娩誘発で経陰分娩に至った1例を経験したので報告する。【症例】33歳女性、G3P2。前回妊娠時も子宮脱を認めたが、速やかに改善した背景がある。今回の妊娠経過は特記事項なく順調であったが、妊娠36週に子宮下垂感と不正性器出血のため前医を受診した。POP-Q stageIIIの子宮脱と子宮頸部の嵌頓による著明な浮腫を認め当科へ搬送、同日入院した。子宮脱は用手還納され、感染所見なく退院し、その後は自身で還納が可能な程度で経過した。分娩時の子宮脱の再発および嵌頓を懸念し、妊娠39週5日にコルポイリントルに蒸留水200mlを注入して分娩誘発したところ、子宮脱の発症なく子宮口の開大と展退が得られ、経陰分娩に至った。新生児は3250gであった。分娩後に弛緩出血を認めたが、子宮内バルーンポンプおよび腔内ガーゼ留置で止血した。産褥経過は良好であった。【考察】子宮脱合併妊娠は種々の合併症を有する。特に分娩時に子宮頸部が嵌頓すると帝王切開が施行される傾向にあることが文献的に指摘されており、経陰分娩のためには嵌頓の防止が重要と考えられる。コルポイリントル留置は簡便な手技であり、経陰分娩の遂行に有用な可能性がある。

P-40-4 当院で周産期管理をした OHVIRA 症候群の1例

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【緒言】OHVIRA症候群は重複子宮、片側腔閉鎖とその同側の腎欠損を症状とし、1/20000例に認められる稀な疾患である。今回我々はOHVIRA症候群の妊娠分娩管理を経験したため報告する。【症例】30歳、初産婦。既往歴として小児期よりOHVIRA症候群(重複子宮、重複腔(上部)、右側腔上部閉鎖、右腎欠損)と診断され、12歳時に右盲端腔壁切開を実施されている。非妊娠時の所見は子宮の大きさや、頸管長に左右差は認めなかったが、右側子宮の子宮腔部が未発達であった。今回、右側子宮に自然妊娠が成立し、管理目的で妊娠6週より当院で妊娠管理を施行。母児の状態として大きな異常は認めなかったが、腔切開側の子宮での妊娠であり経陰分娩が困難なことが想定された事、骨盤位が継続した事などから早期の帝王切開術が望ましいと判断され妊娠36週に選択的帝王切開術を施行し2258gの男児(Apgar score1分値6点、5分値8点)を娩出した。術後は問題なく母児ともに術後8日目に退院に至る。【考察】子宮形態異常は早産、骨盤位、前期破水、帝王切開のリスクの増加と関連しているとされており、中でもOHVIRA症候群の症状でもある重複子宮は他と比較して早産の割合が高いといわれている。分娩方法の決定に関しても腔壁の中隔を認める際は特に帝王切開を考慮する必要がある。その他患者の経陰分娩に対する懸念なども方針決定に重要な項目であり、本症例も患者の臨床的な背景を考慮して選択的帝王切開術の方針とした。【結語】OHVIRA症候群のような子宮形態異常を有する場合、分娩様式は正確な診断と患者への適切な情報提供のもと母児の状態の評価による多角的評価によって決定されるため、綿密なフォローが必要である。

P-40-5 当院における未受診妊婦症例の検討

静岡済生会総合病院

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当院では社会的ハイリスク妊婦を広く受け入れており、それには未受診妊婦も含まれる。部分的な未受診を含めると、当院では2021年4月から2023年9月の間に12名の症例を経験していた。うち3例は、分娩当日まで医療機関に一度もかかっていないものであった。その3例について報告する。【症例1】21歳、未婚、妊娠歴なし。職業は接客業。自宅トイレにて分娩し救急搬送となった。【症例2】36歳、既婚。2妊1産。職業はアルバイト。自宅トイレにて分娩し救急搬送となった。【症例3】27歳、未婚。2妊0産。職業は接客業でパートナー不明。足位で破水し救急搬送となり、緊急帝王切開となった。未受診となった理由や社会的背景は様々であるため、個々に応じた支援が必要であった。産後から退院までの短期間での支援とならざるを得ないため、他職種との連携がより肝要となる。我々がそれぞれに行った支援についても報告する。

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P-40-6 治療に難渋したB群溶連菌による帝王切開後膿瘍の1例

名古屋掖済会病院

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【緒言】Streptococcus agalactiae (Group B Streptococcus: GBS)は垂直感染による新生児感染症の原因菌として周知であるが母体感染の報告は少ない。今回、緊急帝王切開術後にGBSによる膿瘍のため開腹手術を要し、治療に難渋した症例を経験したので報告する。【症例】24歳、未産。破水および陣痛発来にて妊娠39週2日にて入院した。妊婦検診時スクリーニング検査にてGBS陽性、ペニシリン系抗菌薬にて発疹の既往あり、クリンダマイシン (CLDM)の予防的投与を行なった。母体発熱および胎児心音異常を認め、入院6時間後緊急帝王切開術を施行した。術後7日目に嘔吐、発熱および炎症反応上昇を認め、画像検索にて腹腔内膿瘍の所見もあり、術後腹膜炎の診断で開腹ドレナージ術を施行。抗生剤はCLDMに加えメロペネム (MEPM)を使用。膿瘍培養からはGBSが検出された。一旦はドレーン排液量は減少傾向となるも、帝王切開術後25日目、長期炎症波及による小腸穿孔をきたし再度開腹ドレナージ術を施行。ドレーン培養よりEnterococcus faeciumが検出されバンコマイシン (VCM)を追加。ドレーン交換、創部洗浄、中心静脈栄養継続し、症状は軽快傾向に転じ、帝王切開術後39日目より食事再開、術後47日目に抗生剤終了となった。【考察】本症例はペニシリン系抗菌薬にアレルギーがありCLDMを使用した。GBSがCLDM耐性株であったために感染が重篤化し治療に難渋した。ペニシリン系抗菌薬にて発疹や嘔気の原因がありアレルギーを疑う患者はしばしば遭遇するが、GBS陽性妊婦では、抗菌薬の選択や産褥、術後感染に注意する必要がある。

P-40-7 血液検査にて偶発的に発見した無症状急性妊娠脂肪肝の一例

日本赤十字社愛知医療センター名古屋第一病院

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【緒言】急性妊娠脂肪肝は稀な疾患で、嘔吐や上腹部痛を契機に発見され、急激な妊娠経過をたどることが多い。今回、無痛分娩前の定期採血にて肝酵素異常が判明し、重症化に至る前に急性妊娠脂肪肝を疑い、娩出に至った症例を経験したので報告する。【症例】症例は31歳、未産婦。前医にて妊娠経過は順調で、妊娠36週6日に無痛分娩前の定期検査のために血液検査を施行。AST 116/ALT 155と高値のため、2日後に再検。AST 277/ALT 385とさらに上昇傾向のため、妊娠37週3日に当院へ母体搬送となった。来院時腹痛などの自覚症状は認めず、軽度の腹部緊満感があるのみだった。当院の血液検査では、AST/ALTの上昇、低血糖、AT3の低下、腎機能軽度悪化を認めるも、PLTの低下は認めなかった。急性妊娠脂肪肝の診断基準は満たさなかったが、今後さらに肝酵素が上昇する危険性があると考え、terminationが望ましいと判断。初産で頸管熟化所見が乏しいことから、緊急帝王切開の方針とした。術中に出血傾向は認めなかったが、予防的にコンプレッション縫合を行い、手術終了とした。術後の血液検査にて肝酵素は著明に減少傾向となった。低血糖とAT3低値は遷延したが退院前に正常値まで回復し、術後8日目に自宅退院となった。【結語】無症状であるが肝酵素上昇を契機に偶発的に発見し、急性妊娠脂肪肝を疑った症例を経験した。血液検査にて肝酵素上昇を認めた場合は、無症状の場合でも急性妊娠脂肪肝を鑑別にあげた上で慎重な経過観察を行い、適切な娩出時期を決定することが重要である。

P-40-8 診断に難渋した正常卵巣萎縮転合併妊娠の1例

山口県立総合医療センター

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【緒言】卵巣萎縮転の多くは卵巣腫瘍に伴って発生するが、稀に正常卵巣が捻転することが報告されている。今回我々は、妊娠後期に急性腹症を発症し、診断に難渋した正常卵巣萎縮転の1例を経験したので報告する。【症例】症例は35歳、4妊2産。近医にて妊娠管理されていたが、妊娠36週4日に左下腹部痛が出現したため、当院へ救急搬送となった。超音波検査、血液検査、尿検査で明らかな異常は認めず、単純CT検査でも骨盤内や尿路系に明らかな異常は指摘されなかった。胎児のre-assuringも確認できたため、経過観察の方針とし、硬膜外麻酔による疼痛コントロールを行った。その後、左下腹部痛は消失したので、妊娠36週6日に一旦退院となった。しかし、妊娠37週0日に再び左下腹部痛が出現し、38℃台の発熱を認めたため、再入院となった。血液検査で著明な炎症反応の上昇を認めたため、再度単純CT検査を行ったところ、左卵巣の軽度腫大およびS状結腸の著明な拡張を認めた。正常卵巣萎縮転や腸疾患の可能性を考慮し、緊急帝王切開を行った後に腹腔内を精査する方針となった。脊椎くも膜下麻酔下に帝王切開を行った。児を娩出した後に腹腔内を観察したところ、正常大の左卵巣が捻転していたので、左付属器摘出術を行った。S状結腸は著明に拡張していたが、穿孔などは認めず、保存的加療の方針となった。病理組織検査で、浮腫と壊死を伴った正常卵巣組織と診断された。術後に麻痺性イレウスの治療を要したが、術後11日目に退院となった。【結語】診断に難渋した正常卵巣萎縮転合併妊娠の1例を経験した。妊娠中の急性腹症の鑑別疾患として、本疾患に留意することが必要である。

P-40-9 胎児機能不全に対する帝王切開の同意が得られず対応に苦慮した1例

国立成育医療研究センター

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【緒言】帝王切開が必要だが、妊婦が手術を拒絶する際の患者対応は困難である。今回分娩進行中に患者の判断能力が欠如し、対応に苦慮した症例を経験した。【症例】28歳、初産。精神疾患既往なし、膝靭帯損傷に対してボルト固定術の既往あり。ボルト固定術時の痛みの経験や創部に対する視覚的な忌避感から、妊娠中より帝王切開への恐怖を表出していたが、必要時の施行については承諾を得ていた。妊娠40週で分娩誘発を行い、その際に高度一過性遷延徐脈を認めたため、その時点で帝王切開の可能性を説明したが、激しい動揺を認め帝王切開を拒絶した。帝王切開となった場合には死にたい、殺してほしい、児も必要ない、などの発言があり、不穏状態やスタッフへの暴言などもあったため精神的異常を疑い精神科医に診察を依頼した。不穏状態で著しく判断能力の欠如を認めると判断し、産科・精神科・麻酔科医師と協議し帝王切開を行う場合は、鎮静と全身麻酔下で行う方針とした。この判断には夫の同意も得た。その後レベル4の胎児心拍数異常を認めたが、手術への拒絶を続け、最終的に興奮状態となったため、鎮静後、全身麻酔下で緊急帝王切開を行った。児は2804g、アプガースコア1/4、臍帯動脈血pH7.197であったが、蘇生後の経過は良好であった。分娩後も致死念慮やスタッフへの暴言などを繰り返したため、精神科管理目的で転院した。転院後は加療により精神状態は改善し、1か月健診時点では精神的には安定していた。【結語】帝王切開が必要であるにも関わらず、手術の拒絶をする妊婦に対する対応は極めて難しい。今回は妊婦の判断能力の欠如を判断し、帝王切開に踏み切った症例を経験した。

P-40-10 妊娠35週周産期心筋症に対して帝王切開を施行し、癒着胎盤であったため二期的に子宮全摘を行った症例

姫路赤十字病院

平田智子, 谷岡桃子, 谷村吏香, 楠元理恵, 西條昌之, 河合清日, 中山朋子, 関 典子, 小高晃嗣, 水谷靖司

癒着胎盤は産科危機的出血の原因となり、その管理方法は症例によって様々である。今回周産期心筋症に癒着胎盤を合併し、帝王切開後に感染症を生じ子宮全摘に至った症例を経験したので報告する。症例は26歳、G3P1既往に帝王切開と弛緩出血に対して子宮動脈塞栓術(UAE)がある。妊娠35週1日に呼吸困難感で当院を受診し、胸部Xpにて肺うっ血を認め、心臓超音波検査にて左室駆出率25%と低下を認めたため周産期心筋症と診断、同日緊急帝王切開を施行した。帝王切開時子宮前面に広く暗紫色の血管を認め、広範囲の嵌入胎盤を疑ったため胎盤剝離は行わず閉創し、止血目的でUAEを施行した。術中出血は2320ml、術中に赤血球製剤2単位と新鮮凍結血漿4単位を輸血したが、術後経過は良好で術後13日目に退院した。その後胎盤の自然脱落を期待したが術後46日目から発熱を認め、抗生剤加療を行うも効果なく、術後55日目に入院とし術後60日目に腹式単純子宮全摘+両側卵管切除術を施行し、術後経過は良好で子宮全摘後7日目に退院した。摘出子宮の病理結果は嵌入胎盤であった。今症例は術前に癒着胎盤の評価は十分にできておらず、術中に癒着胎盤の診断に至った。一期的に子宮全摘を行わなかったのはすでに出血量が多く、周産期心筋症を合併していたためこれ以上の侵襲は避けるべきと判断したためであるが、事前に診断が出来ていれば出血を減らし一期的に子宮全摘を行うことで感染を回避できた可能性がある。近年はUAEに限らず癒着胎盤のリスクとなる高齢妊娠やARTによる妊娠が増加しており、このような症例には癒着胎盤のリスクを念頭に置いて診療を行う必要がある。

P-41-1 妊娠36週以降の双胎妊婦における妊娠高血圧症候群の予測因子の検討

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【目的】妊娠36週に達した双胎妊婦において妊娠高血圧症候群 (HDP)、妊娠高血圧腎症 (PE) の予測モデルを構築し、母体予後の観点から分娩時期を探る。【方法】妊娠36週の双胎妊婦を対象とした後方視コホート研究である。妊娠36週未満のHDP、胎児治療、一羊膜双胎は除外した。評価項目は妊娠中のHDPとPEの頻度とし、母体背景、妊娠36週の院内高値血圧 ($\geq 130/80$ mmHg)・妊娠蛋白尿 (Up)・血液検査との関連をロジスティック回帰分析で調べた。関連因子を決定木分析に導入した。【成績】検討対象411例のHDPとPEの頻度はそれぞれ13.1%、5.3%であった。HDPの関連因子は高値血圧(調整オッズ比, aOR7.3 [95%CI3.3-16.3]), アンチトロンピン (AT) $< 85\%$ (aOR2.2 [95%CI1.0-4.7])で、PEの関連因子は高値血圧 (aOR6.1 [95%CI1.8-21.2]), Up (aOR5.7 [95%CI1.6-19.9])であった。高値血圧の61例のHDPの頻度は47.5%であり、それぞれ36週14.8%、37週27.5%、38週24.0%であった。Upの36例のPEの頻度は38.9%であり、それぞれ36週13.9%、37週21.9%、38週15.4%であった。血圧正常かつAT $\geq 85\%$ の妊婦のHDPは3.4%、血圧正常かつUpが無い妊婦のPEは0.6%であった。【結論】高値血圧や妊娠蛋白尿を合併した妊娠36週以降の双胎妊婦ではHDP・PEが増加する妊娠37週を超えない時期の分娩が考慮されるが、リスク因子が無い妊婦は妊娠38週までの待機的管理が期待される。

P-41-2 双胎妊娠における妊娠28週までの低用量アスピリン投与による妊娠高血圧腎症予防効果と安全性

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【目的】妊娠高血圧腎症 (PE) 予防において、海外の複数のガイドラインが双胎妊婦を含むPEハイリスク妊婦への分娩直前までの低用量アスピリン (LDA) 投与を推奨しているが、本邦では標準治療化しておらず、また妊娠28週以降は投薬禁忌である。双胎妊娠のみを対象としたLDA投与の有効性や短期間投与の意義についての検討は少ないため本研究で検討する。【方法】当院で分娩した双胎妊婦のうち、妊娠初期から妊娠28週までのLDA投与を受けたLDA投与群と、投与開始した2021年以前の1年間に分娩した非投与群について後方視的検討を行い、早産期PE発症率を比較した。また投与全例の有害事象を調べた。【成績】投与群は17例、対照群は25例であった。PE発症率は37週未満では各5.8%、8.0% ($P=1.0$)で有意差はなかった。34週未満では各5.8%、12.0% ($P=0.63$)で、有意差はないものの投与群で低下傾向を認めた。治療的頸管縫縮術のため投薬中断した症例を加えた20例に投薬中の有害事象はなかった。【結論】双胎妊娠のPE発症率は妊娠35週までのLDA投与群4.7%、非投与群9.8%と報告されており、本研究の自然発症率およびLDA投与群での減少率は同等であった。また妊娠28週でのLDA投与終了は妊娠後半の出血リスクを軽減すると推測されるが、短期間の投与でも特に早期のPE発症予防効果を期待できるかもしれない。双胎妊娠において、妊娠28週までのLDA投与はPE発症率を低下させる可能性がある。

P-41-3 血算から行う妊娠高血圧症候群の発症予測～平均赤血球容積の可能性

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【目的】妊婦健康診査で行う血算検査で、平均赤血球容積 (MCV) や赤血球分布幅 (RDW) に注目することは少ない。妊娠高血圧腎症の発症予測にsFlt-1/PlGFが用いられるようになったが、検査へのアクセシビリティの地域差があるため、実臨床で用いられる頻度は高くない。そこですべての妊婦に応用できるように血算検査でHDPの発症予測を行えないかを検討することとした。【方法】2013年から2023年に当院で分娩した妊婦のうち、中期・後期の血液検査結果のあった妊娠高血圧症候群 (HDP) の妊婦と、その分娩直前に分娩した健常妊婦1名を対象とした。対象者の妊娠初期、中期、後期の血算結果、胎盤重量、胎児体重について検討した。【成績】HDP47名と健常妊婦41名を対象とし、HDPの内訳は高血圧合併妊娠17名、妊娠高血圧13名、妊娠高血圧腎症12名、加重型妊娠高血圧5名であった。HDPを有した集団ではヘモグロビン、ヘマトクリット、MCV、RDWのうち有意にMCVが低値を示した (初期MCV86.7 vs 89.4 fL, $p=0.04$; 中期MCV88.4 vs 93.4 fL, $p<0.001$)。初期MCV89.3fLをカットオフとした場合、AUC: 0.70 感度0.71、特異度0.61で、中期MCV92.7fLをカットオフとした場合、AUC: 0.75、感度0.88、特異度0.59でHDPを予測した。【結論】本研究ではHDPで正常よりも有意にMCVが低値を示した。MCVを確認することで、妊婦健康診査で行う検査の範囲内でおおまかなHDPの発症予測を行える可能性がある。

P-41-4 妊娠高血圧症候群の臨床症状とsFlt-1の関連について

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【目的】妊娠高血圧症候群（HDP）は様々な要因によって引き起こされる疾患で原因となる病態生理については明らかにされていない。妊娠高血圧症候群の発症予測として母体血液中の血管新生因子阻害物質のsFlt-1及び血管新生因子PIGFの比であるsFlt-1/PIGFが有用であると報告されている。妊娠高血圧症候群の臨床症状や重症度は様々である。発症予測因子となるsFlt-1は血管内皮障害に関わっているとされており、それが臨床症状にどれだけ関与しているのか、その重症度も含め調査することで母体合併症の予測因子ともなり得るか検討する。【方法】当院で2022年11月から2023年8月までに当院で妊娠管理され、sFlt-1/PIGFを測定した40症例を対象に、sFlt-1/PIGFの数値と妊娠高血圧症候群の臨床症状（肝機能障害、進行性の腎機能障害、脳卒中、神経障害、血液凝固障害、子宮胎盤機能不全）の発現および重症度の関連を調査した。【成績】今回得られたsFlt-1の中央値は8567.5(27496-689)であり、sFlt-1/PIGF比は中央値220(658.3-1.9)であった。最終診断としてHDPに至った症例の病型はPE23例、GH4例、SPE6例、CH1例であった。全症例でのsFlt-1とそれぞれの臨床症状との間で有意な相関関係は認められなかった。PE症例23症例に限ると血圧上昇の有無とsFlt-1(9617 vs 1547.4 p<0.01)との間に相関関係が認められたが、他の臨床症状では有意差を認められなかった。【結論】HDPは様々な要因が交絡因子となり、複雑な臨床症状を呈する。血管内皮障害の指標の一つであるsFlt-1がPE症例の血圧上昇を反映していることは、PEと診断される症例が他の病型と病態が異なることを示唆していると考えられる。

P-41-5 当院の妊娠高血圧症候群フォローアップ外来の現状

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【目的】妊娠高血圧症候群（HDP）、妊娠糖尿病（GDM）に罹患した女性は、将来的に高血圧や脳血管障害、虚血性心疾患、糖尿病等の生活習慣病を発症しやすいことが明らかとなっている。当院では2014年よりHDP/GDMフォローアップ外来を立ち上げHDP/GDM既往女性の長期的フォローを行っている。この内、HDPフォロー外来のデータを分析し、今後の課題について検討した。【方法】2014年4月～2020年2月に当外来を受診したHDP既往女性172名の内、3年間以上継続してフォローしている116名について、産後1年、産後3年時点での血圧値、BMI、血液検査データの比較を行った。本研究は当院倫理委員会の承認を得て行った。【成績】分娩時平均年齢は34.7±4.5歳、平均BMI23.3±4.5、平均分娩週数38.1±2.1週、児の平均出生体重2711.8±567.7gであった。産後1年、産後3年での比較では、平均収縮期血圧が産後1年126.5±16.1/79.2±10.0mmHg、産後3年125.8±15.8/79.5±10.8mmHg、平均BMIが産後1年23.4±4.5、産後3年23.8±5.0mmHgであり、収縮期血圧やBMIに有意な変化は認められず、また各種血液検査データでも有意な悪化は認められなかった。【結論】HDP既往者の3年後のデータには有意な悪化を認めなかったが、個別に見れば既に高血圧症、糖尿病、さらに疑い例を含めた脂質異常症発症が認められた。このように介入を行っても各種疾患の発症率が存在するため、今後も引き続き当外来で生活指導や医療介入を行い生活習慣病発症予防に努めていくとともに、さらに適切なフォローアップ体制の構築を目指したい。

P-41-6 当院における妊娠高血圧症候群の分娩様式の検討

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【目的】妊娠高血圧症候群（hypertensive disorder of pregnancy；HDP）では、母体の合併症や児の予後を考慮して分娩様式が決定されるが、経陰分娩と帝王切開との周産期予後の比較検討を行った報告は少ない。今回我々は、当院におけるHDPの分娩様式の検討を行った。【方法】2010年から2022年までの期間にHDPと診断し、当院で分娩した603例の単胎妊婦を対象とし、患者背景、分娩様式、児の周産期予後を後方視的に検討した。【成績】HDP603例中、妊娠高血圧腎症（preeclampsia；PE）は368例（60.9%）、妊娠高血圧が152例（25.2%）、加重型妊娠高血圧腎症が5.3%、高血圧合併妊娠が8.6%であった。HDP全体では、449例（74.5%）が経陰分娩を試み、388例が最終的に経陰分娩となった（成功率86.4%）。PE群では、256例（69.6%）が経陰分娩を試み、215例が最終的に経陰分娩となった（成功率84.0%）。HDP全体で、経陰分娩を試みた症例と予定帝王切開で分娩に至った症例では、Apgar score5 値とNICU入院率に有意差はなかった。HDP全体で、経陰分娩を試み、最終的に経陰分娩に至った群（成功群）と最終的に緊急帝王切開で分娩に至った群（失敗群）において母体背景を比較したところ、失敗群で有意に母体年齢、初産婦の割合、肥満の割合が高かった。【結論】HDPの分娩では適切に症例を選択すれば、病型に関わらず、安全に経陰分娩を試みることができる。経陰分娩成功の予測因子として、母体年齢、初産婦、肥満が有用となりうる。

P-41-7 分娩後に臨床症状が顕在化した臨床的急性妊娠脂肪肝の一例

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【緒言】急性妊娠脂肪肝 (Acute Fatty Liver of Pregnancy, AFLP) は 7000~20000 妊娠に 1 例の稀な疾患で、母児ともに死亡率の高い疾患である。今回、臨床症状と血液検査から臨床的 AFLP と診断し、集学的治療を行った一例を経験したので報告する。【症例】27 歳初産婦、自然妊娠成立し前医での妊娠経過は順調であったが、妊娠 32 週に尿蛋白が出現していた。妊娠 33 週 6 日、血性帯下があり前医を受診した。胎児発育不全を指摘され、破水の診断で当院に緊急搬送となった。来院時に非重症域の高血圧、肝酵素上昇、腎機能低下、凝固能異常があり、胎児機能不全も認めため緊急帝王切開を行った。手術直後より非凝固性出血を認めた。また、一過性の意識障害と両上肢痙攣を認め、白血球増多・肝腎機能障害等の血液検査異常に加えて、多飲多尿や腹水貯留等の症状も出現し、臨床的 AFLP と診断した。術後 1 日目に呼吸苦と酸素需要が出現し、術後 3 日目には酸素需要の増大と著明な胸腹水貯留を認め、ICU で全身管理を行った。その後血液培養から緑膿菌が検出されたため抗菌薬治療を行い、術後 19 日目に退院となった。児は出生体重 1654g, Apgar score 4/9 (1 分/5 分)、臍帯動脈血 pH 7.26 であった。早産、低出生体重児のため NICU に入院となり日齢 28 で退院となった。【考察・結語】本症例では、AFLP に特徴的な悪心・嘔吐、上腹部痛、倦怠感などの臨床症状は分娩前には明らかでなかった。血液検査から母体の臓器障害、凝固能異常が著明であり、胎児発育不全、胎児機能不全も認めたことから急速遂娩し、母児を救命した。本症例のように分娩後に臨床症状が顕在化する AFLP も存在するという事を認識しておく必要がある。

P-41-8 分娩期に妊娠高血圧腎症・HELLP 症候群を発症し、緊急帝王切開術後に PRES・硬膜下血腫を認め集学的治療を要した一例

市立広島市民病院

坂井裕樹, 徳本佑奈, 田中奈緒子, 築澤良亮, 森川恵司, 植田麻衣子, 玉田祥子, 関野 和, 依光正枝, 上野尚子, 石田 理, 児玉順一

【緒言】HELLP 症候群は母体凝固異常・肝機能障害が急激に進行する重篤な周産期合併症である。今回、分娩期に妊娠高血圧腎症・HELLP 症候群を発症し集学的治療を要した一例を経験したので報告する。【症例】27 歳 1 妊 0 産。妊娠経過に特に問題なし。妊娠 39 週 6 日に陣痛発来し近医受診。頭痛・心窩部痛あり、血圧 180/110mmHg に上昇を認め周産期管理目的で当院搬送。ただちに降圧療法および硫酸マグネシウム製剤投与を開始。血液検査で肝酵素上昇 (AST 220U/L, ALT 148U/L, LD 516U/L)・血小板低下 (13 万/ μ L) を認め HELLP 症候群の診断で緊急帝王切開術を施行。ミシシッピプロトコルに従いデキサメタゾン投与も開始。術後一般病棟に入室したが、母体意識レベル低下など中枢神経症状を認めため集中治療室に入室。術後一過性に肝酵素上昇を認め、術後 16 時間後に T-bil 10.9 mg/dL, AST 1818 U/L, ALT 650 U/L, LD 4050 U/L まで上昇し術後 22 時間後にピークアウトを認めた。血小板は術後 2 時間後に 4.2 万/ μ L に急速に低下を認め血小板輸血 10U 行っても、術後 22 時間後に 1.9 万/ μ L まで低下を認め追加で 10U 血小板輸血を施行し、以降も血小板低下遷延し術後 4 日目にしてようやく自然回復を認めた。中枢神経症状については経時的に改善したが、術後 3 日目に視野障害の訴えあり、MRI・CT 撮像し後頭葉に T2 FLAIR で高信号領域および左頭頂葉円蓋部に血腫貯留を認め PRES・硬膜下血腫の診断。画像上 midline shift は認めず、保存的に降圧管理を継続し術後 12 日目に退院。現在外来でフォロー継続中である。【結語】分娩期に、急速に妊娠高血圧腎症を発症し HELLP 症候群や PRES を合併する例があることを念頭に置き、慎重な管理を行う必要がある。

P-41-9 PRES を契機に妊娠が判明した妊娠 20 週重症妊娠高血圧腎症の一例

市立広島市民病院

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【緒言】Posterior Reversible Encephalopathy Syndrome (PRES) とは可逆的な脳浮腫 (血管原性浮腫) を生じる高血圧性脳症である。今回、PRES を契機に妊娠が判明した妊娠 20 週重症妊娠高血圧腎症の一例を経験したため報告する。【症例】36 歳女性、片頭痛、うつ病の既往あり。X-2 日より頭痛を自覚。X-1 日近医内科救急病棟に搬送、収縮期血圧 200mmHg 以上、頭部 MRI にて両側後頭葉及び前頭葉皮質に T2 強調像及び FLAIR 像にて高信号を認め、PRES の診断で同院緊急入院となった。降圧治療開始され、X 日精査加療目的に当院脳神経内科へ紹介、救命救急センターに入院となった。来院時頭痛、視野障害を認め、血圧はニカルジピン投与下で血圧 169/100mmHg であった。尿蛋白 3+, 腎機能障害を認めため腎臓内科へ紹介、腎臓内科医が妊娠除外目的に尿中 hCG を調べたところ、陽性であり当科へ紹介となった。経腹超音波検査にて子宮内に妊娠 20 週 2 日相当の胎児を確認、未受診妊婦の重症妊娠高血圧腎症であることが判明した。神経症状、臓器障害を呈しており妊娠継続は困難と判断、母体適応で子宮切開による terminaion の方針となった。全身麻酔下に、子宮体部正中縦切開で児を娩出した。術後 ICU 管理施行。術後 1 日目に抜管、神経症状は改善傾向となり、X+6 日に一般病棟に転棟、降圧管理も内服で可能となり、X+12 日に退院した。現在循環器内科にて血圧管理を継続している。【結論】妊娠可能年齢の女性が PRES を認めた場合、妊娠高血圧腎症の可能性を念頭に置く必要がある。

P-42-1 エラストグラフィーを併用した腹腔鏡下子宮筋腫核出術 (LM) の3例

川崎医大

森本裕美子, 太田啓明, 岡本 華, 齋藤 渉, 河村省吾, 松本桂子, 松本 良, 杉原弥香, 塩田 充, 下屋浩一郎

【緒言】我々は Real-time Tissue Elastography® (RTE) という、組織の硬さをリアルタイムで画像化する技術を用い、腹腔鏡下腺筋腫摘出術における残存病変の切除方法について報告を行ってきた。多発子宮筋腫に対する LM では残存筋腫の確認に難渋することがある。術中に経腔超音波で残存筋腫を確認する方法は、術者自身がプローベを操作できない点や筋層切開部位を決定する点において困難である。今回、LM に対し RTE を導入した経験について報告する。【方法】腹腔鏡ポート配置は変形ダイヤモンドとし、全て 5mm トロッカーを使用した。RTE に用いる術中用プローベは後腔円蓋から経腔的に腹腔内に挿入した。エラストグラフィーで残存筋腫の有無を確認し追加核出を行った。【結果】LM に対する RTE を 2023 年 4 月に導入し、4 か月で 3 症例に対して使用した。多発子宮筋腫の 2 症例では、術前の MRI および超音波検査で同定し得た筋腫を全て核出し筋層縫合した後に、残存筋腫の確認で使用した。残存していた筋層内筋腫を同定し、切開部位を決定し追加核出を施行できた。粘膜下子宮筋腫の症例でも RTE を併用し、子宮内腔が周囲より赤く表示され筋腫は青く表示され、粘膜下筋腫と子宮内腔との位置関係を詳細に確認することができ、核出時の子宮内膜穿破の予防を容易に行えた。【結語】術中に経腔超音波を用いる方法とは違い、RTE の併用で残存筋腫核出の切開部位を容易に決定できた。また、粘膜下筋腫と内腔との位置関係を詳細に把握でき、内膜穿破を防ぐことができた。

P-42-2 トロッカーバルブ破損の経験から得たトロッカーの内部構造の熟知の必要性

藤井会石切生喜病院

中平理恵, 井上裕太, 橋口裕紀, 山本 彰, 古山将康, 山本久美夫, 田村一富

【緒言】腹腔鏡手術用機器の進歩に伴って器具破損の報告も増えている。トロッカーバルブの破損の報告例は少ないが、今回術中にトロッカーバルブの破損をきたし回収した症例を経験したので報告する。【症例】症例は 50 歳、子宮筋腫の診断のもと腹腔鏡下子宮全摘術を施行した。臍からカメラポートとしてアプライド社製の Kii パルレントロッカーを使用した。持針器による針の挿入や鉗子で癒着防止材の挿脱を行ったが抵抗感など全くなく、術中気腹漏れもなかった。手術終了直前に S 状結腸表面に約 1cm のゴム片を見つけ回収した。その場で術中使用した全ての器具を調べたが外見上欠損部はなく、カメラ用パルレントロッカーを分解して外側のダブルダックビルに割を入れて初めて内側のセプタムの一部に欠損部を認めた。回収したゴム片と一致することを確認し手術を終了した。【考察】録画ビデオを見直したが、いつ破損したゴム破片が腹腔内に落ちたかは不明であったので、その可能性を探るため針や癒着防止剤の出し入れを Kii パルレントロッカーのシールの内側から録画してバルブがどう変形しているのかを観察し、起こりうる破損の可能性を考察した。バルブが二重で立体的な複数弁のため使用感はいいが、破損した際は発見しにくい構造になっていた。また、当院で使用している他のトロッカーについても添付文書やカタログには記載されていないそれぞれのバルブの特徴、長所、短所を比較検討し、その多様性から術前の十分な理解が肝要であると考えた。【結語】トロッカーの改良が進み便利になる一方で、構造が複雑になり破損のリスクやその発見の困難さも伴うので、使用前の十分な理解が必須である。

P-42-3 VANH において尿管損傷を来した一例

仙台市立病院

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vNOTES (Transvaginal natural orifice transluminal endoscopic surgery) は腹腔鏡操作を経腔的に行うことで、腹腔鏡下手術と腔式手術の双方の利点を有する手術である。当院では 2022 年から vNOTES による子宮全摘出術 (vaginally assisted NOTES hysterectomy : VANH) を導入し、症例を重ねる中で、上記術式にて尿管損傷を来した一例を経験したので文献的考察を踏まえ報告する。患者は 41 歳女性。子宮頸部組織診にて CIN3 を指摘され X 年 Y 月 Z 日、円錐切除術を施行した。病理組織で子宮頸癌 (乳頭状扁平上皮癌, IA1 期) の診断となった。尿管侵襲は陰性、摘出標本断端陰性であった。単純子宮全摘出術の方針となり、VANH の方針となった。前回術後 42 日目に VANH を施行した。円錐切除後のためか子宮下垂が不良であったが、予定通り子宮全摘出は完遂し術終了となった。術翌日の採血で Cre0.89mg/dl と腎機能増悪を認め、超音波検査で左水腎症、同部位に圧痛を認めた。CT 検査で左水腎症、左腎造影遅延を認めたため、泌尿器科医師に依頼し逆行性尿路造影を施行したところ左尿管に閉塞起点を認め、左尿管損傷の可能性が示唆された。緊急手術となり、開腹し確認したところ、ちょうど尿管と子宮動脈が交差する高さで尿管断裂を認め、尿管膀胱新吻合術が施行された。術後腎機能および疼痛は速やかに改善し、良好に経過した。今回の症例に関しては子宮頸部円錐切除術から短期間での VANH となったことで、子宮頸部周囲の炎症のため尿管がより子宮頸部近くに位置していた可能性がある。今回の経験を生かし、今後も安全な手術を目指してゆきたい。

P-42-4 当院の緑内障合併患者における鏡視下手術の取り組み

安城更生病院

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【目的】鏡視下手術における頭低位や気腹の影響により、患者の眼圧は上昇することが知られている。緑内障合併患者においては、術後の視機能障害はそれらの手術の重大な合併症であるが、明確な対応についての指針は示されていない。今回、当院の緑内障合併患者における鏡視下手術の取り組みについて報告する。【方法】2022年4月から2023年7月までに、当院で行われた緑内障合併患者の鏡視下手術は5例であった。それらの症例において要した対応と術後の経過について検討した。【成績】5例のうち、全例が開放隅角緑内障であった。術式は腹腔鏡下左付属器切除術(TLSSO)が1例、ロボット支援下仙骨腔固定術(RSC)が3例、ロボット支援下子宮全摘術(RATLH)が2例であった。年齢は中央値64(46-71)歳、手術時間は中央値171(75-218)分であった。全例術前にかかりつけの眼科に病状照会し、23°の頭低位の可否を確認した。TLSSOの症例では、頭低位を回避し、仰臥位にて手術を行った。RSC症例のうちの1例では23°の頭低位の間に徐脈が出現し、眼圧上昇に伴う迷走神経反射の可能性を考慮し、頭低位から水平位に体位変換した。可能な限り、短時間の頭低位にて手術を進めた。その後の症例では、1時間に1度、5分間、頭低位から水平位に戻す時間を設けることで対応した。術中、術後の合併症は認めず、視野障害が出現した症例はなかった。【結論】当院では、術前に眼科にて頭低位の可否を確認し、頭低位を可能な限り避けつつ、必要時は1時間に1回頭低位から水平位に戻すという手順で手術を行っている。現在のところ視機能障害を含めた合併症はなく、緑内障合併患者においても安全に鏡視下手術を行うことができると考える。

P-42-5 術中超音波検査が Accessory and cavitated uterine mass (ACUM) の完全切除に有用であった一例

滋賀医大

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【緒言】Accessory cavitated uterine mass (ACUM) はミューラー管の発生異常が原因とされる、正常子宮筋層内にできる嚢胞性腫瘍である。この腫瘍は子宮筋層組織と、その内側に裏打ちした子宮内膜組織により構成される。月経困難症の原因となるため ACUM の摘出術も治療選択肢となるが、ACUM の外側は子宮筋層組織であるため、正常子宮筋層との境界は不明瞭である。術中超音波検査を併用することで、ACUM を破綻させずに摘出した症例を経験したので報告する。【症例】23歳、未妊未産。月経痛を主訴に近医を受診したところ、経腔超音波検査で子宮左側に4cm大の腫瘍を認めた。骨盤MRIでは子宮筋層内にT1およびT2強調画像で高信号を示す4cm大の腫瘍を認め、腫瘍と子宮内膜や卵管に交通はなかった。手術目的に当院に紹介受診となり、骨盤MRI画像からACUMを疑い腹腔鏡下嚢胞摘出術を施行した。腹腔内所見は、左円韧带付着部の子宮筋層が軽度腫大していたが、その他異常所見は認めなかった。右下腹部のポートから超音波プローブを挿入し腫瘍に当てると、腫大した筋層内に2cmの低エコー領域を認めた。腫瘍直上の子宮筋層に電気メスで切開を加えたが、腫瘍と子宮筋層との境界は不明瞭であった。超音波プローブを腫瘍や子宮筋層に当て低エコー領域を確認しつつ、嚢胞壁から1cmのマーシンをとり、腫瘍を牽引しながら破綻させずに摘出した。病理組織診断では、内腔面に子宮内膜組織を認め、その外側を子宮平滑筋組織が覆っており、ACUMの診断となった。【考察】術中超音波検査で嚢胞を確認しつつ、ACUMを腹腔鏡下に摘出した1例を経験した。術中超音波検査は、ACUMの子宮内膜組織を確実に切除するのに有用であると考えられた。

P-42-6 婦人科腹腔鏡手術後に生じた下肢コンパートメント症候群の3症例

大阪医科薬科大

橋田宗祐, 恒遠啓示, 村上 暉, 西江瑠璃, 土橋裕允, 田路明彦, 寺田信一, 古形祐平, 田中智人, 大道正英

コンパートメント症候群は、特に碎石位や頭低位の手術における合併症としても起こり得る疾患である。今回、当科において腹腔鏡手術後に下肢コンパートメント症候群を発症した3症例を経験したので報告する。1例目は、13歳、未妊、身長156cm、体重44kg、11cm大の子宮筋腫に対して腹腔鏡下筋腫核切除術を施行し、手術時間5時間17分、出血量1050mlであった。手術当日夜間よりコンパートメント症候群を発症した。内圧は30mmHg未満であり、緊急切開は行わず保存的に経過観察、理学療法を行った。術後3週間で独歩可能となり、術後2か月で日常生活に支障は無くなり、術後3か月で運動も制限無く行えるようになった。2例目は、52歳、1妊0産、身長166cm、体重58kg。子宮頸部腺癌1B2期に対して腹腔鏡下広汎子宮全摘術+両側付属器摘出術を施行し、手術時間10時間24分、出血量100mlであった。手術当日夜間よりコンパートメント症候群を発症した。内圧は30mmHg未満であり、緊急切開は行わず保存的に経過観察、理学療法を行い、独歩可能となったが術後1年経過後も右足首の背屈障害は持続している。3例目は、48歳、3産、身長156cm、体重72kg。多発子宮筋腫に対して腹腔鏡下単純子宮全摘術+両側卵管切除術を施行し、手術時間4時間37分、出血量少量であった。手術当日夜間よりコンパートメント症候群を発症した。内圧は30mmHg未満であり、緊急切開は行わず保存的に経過観察し、5日目には独歩可能、その後障害は消失した。碎石位、頭低位の手術を行う際には、コンパートメント症候群のリスクを認識し、周術期に様々な予防策や工夫を講じ、発症時には早期発見および適切な管理を行う必要がある。

P-42-7 全腹腔鏡下子宮全摘術後に発症し臨床的に診断した腔断端子宮内膜症の一例

名古屋市立大附属東部医療センター

倉本泰葉, 村上 勇, 近藤好美, 佐藤 玲, 石橋朋佳, 倉兼さとみ, 関宏一郎, 小島和寿, 中山健太郎

【緒言】肉眼的に腹腔内に子宮内膜症病変を認めない子宮筋腫の症例に対し、腹腔鏡下子宮全摘術 (TLH) を施行後、腔断端より周期的な出血を認め、臨床的に腔断端子宮内膜症と診断した症例を経験したため報告する。【症例】40歳、女性。5妊2産。既往歴は先天性耳瘻孔。子宮筋腫に伴う過多月経のため TLH の方針となった。つり上げ法、3ポート、気腹圧 8mmHg として型どおり手術施行。手術時間 132 分、出血量は 50g であった。腹腔内には明らかな内膜症病変を認めなかった。子宮は経腔的に細切し摘出した。術後より月に 1 回の周期的な性器出血を認めた。出血時、腔断端右側より茶褐色の出血をみとめ、軽度の膨隆を認めた。触診で軽度の硬結は認めたが経腔エコーでは所見を認めなかった。断端細胞診は NILM であった。骨盤部 MRI では腔断端左側に T1 強調像で点状高信号を示す部位を認めたのみで、腔断端子宮内膜症と臨床的に診断した。ジェノゲスト投与により性器出血は消失したが、倦怠感の症状により中止し、現在は無治療で経過観察中である。【結語】子宮内膜症の発症部位は多岐にわたり、好発部位である卵巣や子宮周囲以外に腹壁切開創や腔断端に生じるという報告もある。術後創部の子宮内膜症症例では腹腔内に内膜症病変を認める症例が多数であり、術中操作による子宮内膜症病変の移植や着生によるものであると考えられているが、本症例では腹腔内に内膜症病変を認めず、微小な内膜症があった可能性は否定できないが、子宮細切時に内膜が遺残し断端に生着したものと考えられた。子宮全摘術後に周期的な性器出血を認めた場合、腔断端子宮内膜症を考え精査する必要がある。

P-42-8 腹腔鏡下子宮全摘術での蛍光尿管カテーテル留置の有用性

松江市立病院

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【はじめに】子宮全摘術において、尿管損傷は最も懸念される合併症の一つであり、子宮の大きさや形、骨盤内癒着によってその危険性は高くなる。開腹術では尿管カテーテル留置によって、触診でその安全性を担保することができるが、触覚のない腹腔鏡下手術ではその同定が困難となる。近年、NIR (Near Infrared Ray) /ICG 蛍光画像を利用して、蛍光尿管カテーテルによる尿管の視認が可能になった。そこで術前に尿管損傷リスクが高いと予測された症例に術中に ICG 蛍光尿管カテーテルを使用したので報告する。【症例】2022 年 11 月から 2023 年 1 月の間に 3 例の腹腔鏡下手術、3 例のロボット支援下手術に使用した。6 例中 4 例が子宮筋腫、2 例が子宮体癌の症例であった。子宮筋腫の摘出標本は 315-820g で、多発筋腫もしくはタグラス窩に大きな筋腫核を認めていた。カテーテルは麻酔導入後に留置し、手術終了時に抜去した。ロボット支援下手術では Firefly モードを利用して尿管の明瞭な視認が可能であった。いずれも尿管損傷はなく、術後に軽度の血尿が見られたが、疼痛もなく、ADL に支障はなかった。【結語】腹腔鏡下手術において、蛍光尿管カテーテル留置は術中の視認に優れており、尿管損傷の回避に貢献することが期待できる。

P-42-9 右卵管癌と鑑別困難であった Meckel 憩室癌の 1 例

大阪はびきの医療センター

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Meckel 憩室は胎生期の卵黄腸管の遺残による先天性小腸憩室であり、一般集団の 0.3~2.9% にみられる稀な疾患である。特に Meckel 憩室癌の発生はまれであり、多くは進行してから発見され予後不良とされている。今回、右卵管癌が疑われたが試験腹腔鏡により早期に Meckel 憩室癌と診断し得た 1 例を経験したため報告を行う。症例は 73 歳女性。未経妊で閉経は 55 歳。既往歴に白内障・大腸憩室炎・逆流性食道炎がある。不正出血の既往があり 1 年毎に外来でフォローされていた。腔口狭小化により子宮体部細胞診採取が困難となったため精査目的に骨盤 MRI が撮影された。受診時に腹痛を含め特記すべき自覚症状はなし。骨盤 MRI で右下腹部に膀胱壁を圧排する管状の構造物を認め、同部位に拡散制限を呈しており悪性腫瘍の可能性も考慮された。造影 CT 検査で膀胱壁への壁外性の圧排の所見は確認できず可動性の高い病変と考えられ右卵管病変が疑われた。PET-CT 検査を実施したが同部位に異常集積を認めており右卵管癌が否定できなかったため、診断目的に試験腹腔鏡手術の方針とした。腹腔内所見は子宮は正常大で腹水はなく、両側卵管は正常であった。右虫垂も正常であったが 5cm 大に腫大した小腸病変を認めたため消化器外科にコンサルトとし、腹腔鏡補助下に小開腹で小腸を体外に牽引し小腸部分切除術を実施した。病理組織学的検査の結果、リンパ管侵襲を伴う Meckel 憩室癌 (pT2N0M0, pStageI) と診断した。今回、偶発的に早期発見された Meckel 憩室癌の症例を経験した。骨盤内の可動性良好な管状病変を認めた際は消化管疾患の可能性を考慮する必要がある、診断目的に試験腹腔鏡を実施することは有用であると考えられる。

P-42-10 子宮全摘出術後の腔断端出血に対する血管造影・動脈塞栓術の有用性についての検討

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【目的】子宮全摘出術後の腔断端出血の原因として仮性動脈瘤や動静脈奇形, 内腸骨系動脈分枝からの出血が知られているが, 対処法は確立されていない。腔断端出血に対して血管造影・動脈塞栓により止血を得た症例を経験したため, 文献的考察を加えて報告する。【症例】48歳, 5妊4産。過多月経を伴う多発子宮筋腫に対して6か月間レルゴリクスを内服した後に全腹腔鏡下子宮全摘出術を施行した。術後14日目に突然多量の性器出血を認め, 診察で腔断端左側より活動性の出血を認めた。血管造影にて右内陰部動脈より腔内への出血を認め, 両側内陰部動脈塞栓を行い止血を得た。以後再出血なく経過している。【考察】医中誌, Pubmedで20年間の子宮全摘出中後の腔断端出血について検索し, レビューを行った。腔断端出血の責任血管, 原因は様々であった。近年では血管造影・動脈塞栓により加療した報告がほとんどであった。経腔的または経腹的止血後に再出血し, 最終的に血管造影・動脈塞栓術で止血に至った報告も複数認められた。【結論】子宮全摘出術後の腔断端出血に対して, 血管造影・動脈塞栓は経腹的または経腔的アプローチよりも低侵襲で有用である可能性が考えられた。

P-42-11 腹腔鏡下子宮悪性腫瘍手術後に発症した well leg compartment syndrome の一例

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子宮体癌に対して碎石位で施行した腹腔鏡下子宮悪性腫瘍手術後に発症し, 保存的加療を行った well leg compartment syndrome (以下 WLCS) の1例を経験したため報告する。症例は36歳, BMI34, 子宮体癌1A期に対して腹腔鏡下子宮悪性腫瘍手術(腹腔鏡下単純子宮全摘出術, 両側付属器摘出術, 骨盤リンパ節郭清)を行った。術後1時間より下腿の疼痛を認めたが, 深部静脈血栓症を除外したのみで経過観察としていた。術後24時間で下腿の発赤・腫脹, 下腿径の左右差を認め, 血液検査でCKが31178U/L, ミオグロビンが6298ng/mLと高値であったためWLCSと診断した。発症から6時間以上が経過しており, 下肢の疼痛が改善傾向であったこと, 筋区画内圧が26-28mmHg程度であったことから減張切開を行わず, 保存的加療の方針とした。症状は徐々に改善し, 術後7日目から歩行可能となり, 術後23日目に自宅退院した。WLCSは碎石位, 頭低位, 長時間手術, 肥満等がリスク因子である。WLCSは治療が遅れた場合, 減張切開で期待できる治療効果が少なくなり, 不可逆的な神経障害や四肢切断, 腎不全等をきたす可能性がある。そのため本症例では, 保存的加療を行ったが, WLCSのリスクが高い症例では本疾患の可能性を考え, 早期の診断, 治療が重要である。

P-42-12 6~12か月放置された卵巣腫瘍茎捻転核出の一例と卵巣腫瘍茎捻転に対する手術治療の考察

誠光会淡海医療センター

十河進仁, 卜部 諭, 卜部優子, 鳥井裕子, 藤城直宣, 中川渥裕

【緒言】卵巣腫瘍茎捻転は卵巣への血友供給が阻害される緊急疾患である。妊孕性温存が必要な患者における, 卵巣腫瘍茎捻転ではしばしば腫瘍核出か卵巣摘出かで判断に迷う場面に遭遇する。今回6~12か月放置された卵巣腫瘍茎捻転を経験したため術中所見, 術後経過を文献的考察を含め報告する。【症例】28歳G0P0卵巣腫瘍, 月経困難症にて近医より紹介。左dermoid腫瘍, 右チョコレート腫の腫瘍の診断にて腹腔鏡下に両側卵巣腫瘍核出の方針とした。【術中所見】トロッカーは3mm2本, 5mm2本でダイヤモンド配置で行った。手術時間は2時間53分, 出血は20mlであった。腹腔内所見として左卵巣腫瘍は720度回転し大網がかぶり膀胱子宮窩に癒着している状態であった。左卵管は萎縮, 右卵巣腫瘍はグラス窩に位置するも内膜症性の癒着を認めた。左卵巣はコールドナイフの切開でも出血をしないほど血流が乏しい状態であったが, 出血を認めるような部位もあり, また今回, 右卵巣腫瘍も核出であり妊孕性の温存のため左卵巣腫瘍も核出とした。【病理結果】Mature teratoma of the left, Endometriotic cyst of the right【術後経過】経過良好で術後3日後に退院。外来にて低用量ピルを開始。術後3か月の外来でのエコーにて左卵巣にドップラー効果を認めた。【考察】本症例では, 術後感染症を認めず経過している。また, エコードップラーではあるが血流を確認できている。この症例をもとに腫瘍核出か卵巣摘出かの判断に関して文献的考察を含めて考察する。

P-42-13 全腹腔鏡下子宮全摘術時に偶発的に発見された完全重複腎盂尿管の2症例

飯田市立病院

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【緒言】近年、子宮全摘術の方法として、低侵襲な全腹腔鏡下子宮全摘出術 (total laparoscopic hysterectomy : TLH) が増加している。TLHは腹式単純子宮全摘術 (abdominal total hysterectomy : ATH) に比べ、尿管損傷の発生率が高いことが報告されている。今回良性疾患でのTLHにおいて、完全重複腎盂尿管を2例経験した。重複腎盂尿管は尿管奇形の中で最も頻度が高く、不完全重複腎盂尿管と完全重複腎盂尿管に分類される。術前に診断可能であれば、尿管損傷の予防策となりうる。そこで術前に超音波でスクリーニングが可能かどうかを検討した。【症例1】患者は43歳。3妊1産。既往歴に特記すべきものなし。前医にて貧血を指摘され、当科初診。子宮腺筋症と診断し、偽閉経療法後を行い、術前の超音波で水腎がなをいことを確認した。TLHを施行し、術中の膀胱鏡で左尿管口を2個認め、術後の超音波で左腎盂を2個確認し、左重複腎盂尿管と診断した。【症例2】患者は44歳。2妊2産。既往歴にパセドウ病。月経困難症で前医を受診、子宮腺筋症でフォローされていた。外科的治療を希望され当科初診。TLHを施行し、術中の膀胱鏡で左尿管口を2個認め、術後の超音波で左腎盂を2個確認し、左重複腎盂尿管と診断した。【考察】今回術中の膀胱鏡検査で偶発的に発見されたが、術前に診断できることにより、術中の合併症を回避できる可能性が期待できる。術前の超音波検査により重複腎盂の診断は簡便であり、重複尿管の予測に有用と考える。【結語】術前の超音波検査で、水腎の確認だけでなく、腎盂の数を確認することも重要である。

P-42-14 重症慢性閉塞性肺疾患・気管支喘息合併患者に腹腔鏡手術を行い、術後2日目に臍部創部離開を発症した一例

大阪赤十字病院

水野友香子, 岩見州一郎, 福田真優, 齊藤希実, 定本怜子, 徳重 悠, 平山貴裕, 小林弘尚, 川田悦子, 前田万里紗, 中川江里子, 野々垣多加史

【緒言】腹腔鏡下手術の視野確保には、一般的に全身麻酔下気腹法が用いられているが、慢性呼吸器疾患などで挿管・気腹による呼吸・循環への悪影響が懸念される場合、脊椎麻酔下手術や吊り上げ式腹腔鏡手術が有効である。ただ鏡視下手術といえども、ステロイド使用や咳嗽による腹圧上昇にて術後創部離開のリスクはある。今回、重症慢性閉塞性肺疾患 (以下 COPD) ・喘息の患者に対し、脊椎麻酔下に吊り上げ式腹腔鏡下手術を行うことで安全に手術を行うことができたが、術後2日目に臍創部離開を認めた症例を経験したので報告する。【症例】症例は81歳、合併症に COPD・喘息があり、卵巣腫瘍に対して脊椎麻酔下に単孔吊り上げ式腹腔鏡下両側付属器切除を行った。創部は定型的に吸収性縫合糸で筋膜・真皮を結節縫合した。術後経過は順調であったが、術後2日目に臍創部から大網の突出を認めた。同日、脊椎麻酔下に大網部分切除・腹腔内洗浄・非吸収糸で離開創部の再縫合を施行した。離開創部は、筋膜・真皮とも非吸収性縫合糸で結節縫合を行った。現在、術後110日目であるが腹壁癒着ヘルニアは呈していない。【考察】本症例では、長期に渡る吸入ステロイド使用と酷い咳嗽による腹圧上昇が、創部離開の要因となったと考えられた。全身麻酔に伴う呼吸障害等のリスクを考慮し術式を選択したが、結果早期の再手術となった。本症例での反省を通し、術後創部離開・腹壁癒着ヘルニアのリスクと、縫合の注意点を再度考察し、今後に生かしたい。

P-42-15 全腹腔鏡下子宮全摘出後に COVID-19 感染を契機に臍5mm 径ポートサイトの大網ヘルニアを発症した一例

石川県立中央病院

岩柿柚子, 津吉秀昭, 佐々木博正

【緒言】一般的に5mm径トローカー挿入部位の筋膜は、閉創時の縫合不要とされていることが多いが、稀にポートサイトヘルニアが見られることがあり、その発生率は0.003%程度と推定されている。今回5mm径からのポートサイトヘルニアを経験したので報告する。【症例】48歳、3経産。子宮筋腫に対して腹腔鏡下子宮全摘出術を施行した。手術時間1時間56分、ポート配置はダイヤモンド型で全て5mmポートを使用した。閉創は3-0吸収糸で皮下埋没縫合を行った。術後1日目から咳嗽が出現し、徐々に増悪。術後3日目強い咳嗽により腹圧がかかった際に臍創部より大網が脱出。ポートサイトヘルニアの診断で、局所麻酔下に大網を腹腔内に還納し再度3-0吸収糸で筋膜縫合と皮下埋没縫合を行った。術後4日目より39℃の発熱を認め、SARS-CoV2抗原検査陽性が判明しレムデシビル投与を開始。術後7日目まで39℃の発熱が持続したが、腹部CTでは再縫合を行った創部に異常を認めず、術後9日目ヘルニアの再燃なく退院となった。【結語】通常ポートサイトヘルニアは正中よりも鉗子操作による筋膜創が開大しやすい側方に発生することが多い。一方、咳嗽時の腹腔内圧は100~200mmH₂Oに達する場合があることが知られており、本例ではCOVID-19の反復する激しい咳嗽による内圧上昇のため、管腔臓器ではなく柔らかい大網の一部が最も圧の集中する臍部から脱出したと推定された。術後に咳嗽を認めることは稀ではなく、5mm径であってもポートサイトヘルニアを生じる可能性を念頭に早期発見に努めることが重要と思われた。

P-43-1 小細胞癌組織を含む極めて稀な卵巣明細胞癌の一例

大阪赤十字病院

平山貴裕, 福田真優, 齊藤希実, 水野友香子, 定本怜子, 徳重 悠, 小林弘尚, 川田悦子, 前田万里紗, 中川江里子, 岩見州一郎, 野々垣多加史

本邦では卵巣上皮性悪性腫瘍の中で明細胞癌は漿液性癌に次いで多い組織型である。しかし、明細胞癌に小細胞癌成分が含まれることは非常に稀であり、演者の知る限り同様の組織像を示す症例報告は見られない。今回我々は前述の組織像を呈した卵巣癌症例を経験したため病理所見を中心に報告する。症例は44歳、未経産、特記すべき家族歴や既往歴はなく不正性器出血を主訴に前医を受診した。偶発的に右付属器に38mm大の内膜症性嚢胞様腫瘍を指摘され精査加療目的で当院紹介となる。嚢胞病変に充実部はなく悪性を積極的に疑わず、未婚、未経産のため手術による卵巣機能低下を懸念され経過観察の方針となる。7か月後に同嚢胞は51mm大に増大したが充実部はなくジエノゲストを開始した。縮小傾向を得られ投与後8か月目には43mmまで縮小した。しかし、その3か月後には充実部を伴い106x80x94mmまで嚢胞は急増大した。遠隔転移なし、CA125高値(75.8U/ml)、卵巣明細胞癌I期疑いと診断し、腹式単純子宮全摘、両側付属器切除、大網部分切除を実施した。摘出した右付属器は70x65x50mmの多結節性充実腫瘍であり断面は白色から淡褐色調であった。腫瘍の大部分は淡明な細胞質を持つ高度異型細胞の充実性・腺管状・乳頭状胞巣が広がり明細胞癌の所見であり、肉腫様変化が散見し、リンパ管侵襲を伴う小細胞癌成分もわずかに認められた。他臓器に播種や転移はなく、術中被膜破綻のためIC期(腹水細胞診陽性)と診断した。術後化学療法を行い現在再発なく経過している。肉腫様変化や小細胞癌成分を伴った卵巣明細胞癌の報告はなく、ともに悪性度が高い組織型であるため慎重に経過観察をする必要があると考えている。

P-43-2 病理組織学的特徴より治療方針を決定した腹膜播種の1例

長崎大

小寺倫平, 原田亜由美, 西 真輝, 川下さやか, 阿部修平, 長谷川ゆり, 北島道夫, 三浦清徳

患者は47歳、0妊0産。既往歴、家族歴に特記事項なし。X年に卵巣腫瘍の診断で腹腔鏡補助下子宮筋腫核出術、右付属器摘出術、大網切除術、腹膜生検を施行し、右卵巣粘液性癌と診断された。その後、腹式単純子宮全摘出術、左付属器摘出術、骨盤及び傍大動脈リンパ節郭清術を施行し、右卵巣粘液性癌IIA期(pT2a, pN0, cM0)と診断された。術後パクリタキセル、カルボプラチン、ペバシズマブ療法(TC+Bev)6コースを行い、維持療法としてBev12コースを行った。2021年に小腸癌を疑われ、X+2年に腹腔鏡下小腸切除術+所属リンパ節郭清術を施行され、小腸癌、Tubular adenocarcinoma, pT4a (SE), cN0, cM0, cStageIIBと診断された。術後にオキサリプラチン、5-FU療法(mFOLFOX6)12コースが行われた。X+4年にフォローアップの造影CTで腹膜播種を認め、卵巣癌もしくは小腸癌の再発を疑われ、精査目的に当科を紹介された。腫瘍マーカーの上昇は認めなかった。造影CTおよびPET-CTでは腹膜播種の所見を認めた。卵巣癌もしくは小腸癌の再発を疑い、審査腹腔鏡および播種病変の生検を施行した。病理所見では腺癌が疑われ、免疫組織学的検査では消化管を示唆するマーカーであるCK20, CDX2が陽性、女性生殖器を示唆するマーカーであるCK7, PAX8, ER, PgRが陰性であった。この際、卵巣癌の初回手術時の病理組織を検討したところ、小腸癌の初回手術および2回目の手術と同様の免疫組織学的検査結果となり、また、小腸癌は正常小腸粘膜から癌への移行像を認めていたため小腸癌が初発であり、卵巣癌は転移性卵巣癌である可能性が示唆された。免疫組織学的検査は腫瘍の性質や転移性腫瘍の原発臓器の同定において有用と考えられた。

P-43-3 HRD陽性の卵巣扁平上皮癌にSTICを認めた一例

静岡済生会総合病院

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漿液性卵管上皮内癌(serous tubal intraepithelial carcinoma: STIC)は、卵管高異型度漿液性癌(HGSC)の前駆病変であり、一部の漿液性癌および腹膜癌の発生源地として考えられている。今回、HRD陽性の卵巣扁平上皮癌にSTICを認めた一例を報告する。患者は57歳、既往歴、家族歴に特記すべきことはない。両側卵巣腫瘍を認め手術目的に当院へ紹介となった。精査の結果、卵巣癌の疑いのため手術加療の方針となった。迅速診断で左卵巣扁平上皮癌、右卵巣低分化癌の診断のため根治術の方針とし、単純子宮全摘出術+両側付属器切除術+大網切除術+傍大動脈リンパ節郭清+骨盤リンパ節郭清を施行した。永久標本で、卵巣腫瘍は成熟嚢胞奇形腫やプレナー腫瘍を示唆する明瞭な所見は認めないが、左卵巣扁平上皮癌、右卵巣低分化癌であった。また、左卵管にSTICを認めた。手術進行期分類はIIIA1(ii)期、HRD陽性、BRCA1/2陰性であった。術後化学療法(パクリタキセル+カルボプラチン+ペバシズマブ)を行い、維持療法(オラパリブのみ)で経過を診ている。

P-43-4 17年前に診断された成熟嚢胞性奇形腫の悪性転化の一例

愛仁会千船病院¹, 近畿大²

永山明穂¹, 加嶋洋子², 和田知春², 太田真見子², 宮川知保², 松村謙臣²

卵巣の成熟奇形腫は全卵巣腫瘍の約20%を占める良性腫瘍である。悪性腫瘍の成分を伴うものは成熟奇形腫の悪性転化と呼ばれている。しかし、良性の成熟奇形腫を長期間フォローしたコホート研究で悪性転化した症例はなかった。成熟奇形腫が悪性化するのか、あるいは腫瘍発生時より急増悪するため悪性転化というのかは不明である。また、悪性転化には human papilloma virus (HPV) の関与が示唆されている。今回我々は、10年以上前に卵巣成熟奇形腫を診断され、そこから発生した悪性腫瘍の一例を経験した。症例は69歳女性2経産婦で52歳で閉経した。53歳55歳で左右の人工股関節置換術の既往がある。それぞれの術前検査のCT検査で骨盤内に10cm大の嚢胞性腫瘍が指摘されたが、産婦人科への紹介はされなかった。今回、嘔声を主訴に耳鼻咽喉科を受診し左反回神経麻痺を認めた。CTで骨盤内には脂肪成分、石灰化および充実部を伴う20cm大の嚢胞性腫瘍、総腸骨-傍大動脈、縦隔に多発リンパ節腫大を認めた。開腹術で被膜外への浸潤と腹膜播種を伴う右卵巣腫瘍を認め両側付属器切除を行った。術後病理検査では mature teratoma with squamous cell carcinoma と診断され、成熟奇形腫悪性転化 IVB 期と診断した。遺伝子パネル検査で、TMB high/HRD 陽性であった。HPV は検出されなかった。現在全ゲノムシークエンシングデータを解析中である。術後はパクリタキセル+カルボプラチン療法を6コース施行し partial response となり niraparib による維持療法を施行したが、progressive disease となった。現在、Pembrolizumab で治療し奏効している。本症例で遺伝子パネル検査は発癌メカニズムの解析と治療法の探索のために有用であった。

P-43-5 妊孕性温存療法を選択した IIIC 期巨大卵巣混合型胚細胞腫瘍の1例

横浜医療センター

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悪性卵巣胚細胞腫瘍は稀な疾患であり、比較的若年に発生し妊孕性温存などの治療方針に難渋することがある。今回我々は、腹腔内を占拠する巨大腫瘍として診断された、大網播種を伴う混合型胚細胞腫瘍、妊孕性温存療法の1例を経験したので報告する。症例は、20歳経妊0回の大学生。腹痛を主訴に近医を受診し、腹腔内腫瘍を指摘されて当科紹介初診。初診時、経腹超音波検査では臍上5cm程度に及ぶ充実性腫瘍が腹腔内全体を占拠しており、経直腸超音波検査では子宮は正常大で、ダグラス窩腹水を4cm程度認めた。血液検査では WBC 8,100 / μ l, Hb 10.0 g/dl, AFP > 20,000 ng/ml, LD 755 U/L と貧血や AFP の異常高値などを認めた。MRI 検査と造影 CT 検査では、未熟性奇形腫や卵黄嚢を含む長径 23cm の混合型胚細胞腫瘍が疑われ、腫瘍内部に出血を認め、被膜破綻、腹膜炎像、腹膜播種腫瘍を伴っていた。悪性卵巣腫瘍 III 期疑いで準緊急開腹術を施行した。血性腹水あり。左卵巣原発腫瘍は脆弱で、右付属器から膀胱子宮窩右側と S 状結腸間膜に浸潤を疑う強固な癒着を認めた。浸潤部分は残存させて左付属器摘出術を行った。大網結節を複数認め、これを全て含むように大網切除術を施行。他腹膜は肉眼的に正常だった。手術時間1時間41分、出血量は腫瘍内容液を含め 2220ml だった。病理診断は、混合型胚細胞腫瘍(卵黄嚢腫瘍+成熟奇形腫) IIIC 期, pT3cNXM0 分、大網腫瘍は卵黄嚢腫瘍だった。腹水細胞診は陰性。術後経過は良好で、術後19日目から後療法として BEP 療法を開始。4サイクル目施行時に AFP が陰転化した。エトボシド総投与量もふまえ、5サイクル終了後、残存腫瘍摘出術施行、経過観察中である。

P-43-6 患側付属器摘出困難であったが、その後プレオマイシン・エトボシド・シスプラチン併用療法で腫瘍縮小が得られた一例

旭川医大

土川 恵, 水崎 恵, 佐藤湊斗, 林なつき, 板橋 彩, 上田あかね, 市川英俊, 高橋知昭, 片山英人, 加藤育民

【緒言】卵黄嚢腫瘍の卵巣悪性腫瘍全体に占める割合は0.6%と稀な疾患である。治療として、腫瘍減量手術ののち、プレオマイシン・エトボシド・シスプラチン併用療法(BEP療法)を行うことが推奨されている。今回子宮と両側付属器が一塊となり、患側付属器摘出が困難であったものの、術後化学療法に反応した卵黄嚢腫瘍 IVB 期の一例を経験したので報告する。【症例】8歳, 126.8 cm, 21.6 kg, 生来健康【治療経過】X-6日に腹部圧迫感と発熱のため近医小児科受診、超音波検査で腹部腫瘍認め前医紹介となった。前医のCTとMRIで骨盤内に13cmの腫瘍と両肺に3mm程度の結節を認めた。血液検査では AFP 51357 mg/ml, LDH 2101U/L と著明な上昇も伴っており、卵黄嚢腫瘍 IVB 期の疑いで精査加療目的に当院紹介となった。X日、当院で患側付属器摘出術を試みたが、腫瘍の子宮背面や対側卵巣への直接浸潤を認め、妊孕性温存が困難と判断し生検のみに留めて閉経した。病理組織診断の結果卵黄嚢腫瘍の診断となり、画像所見と合わせて IVB 期(cT2aN0M1)の診断となった。X+13日に BEP 療法の1コース目開始。Day1, 8, 15にプレオマイシン 17mg, Day1-5にエトボシド 85mg とシスプラチン 17mg を投与した。X+28日にMRIを撮像したところ腫瘍の縮小が認められた。X+34日に BEP 療法2コース目を施行し X+49日に AFP は 900mg/ml, LDH 286U/L まで低下した。現在も治療継続中である。【結語】若年者の胚細胞性腫瘍は妊孕性温存のため腫瘍の一部生検に留めた場合でも、その後の適切な管理により病勢コントロールが可能と考える。

P-43-7 エストロゲン産生卵巣類内膜癌の3例

旭川医大

市川英俊, 土川 恵, 林なつき, 水崎 恵, 板橋 彩, 上田あかね, 高橋知昭, 片山英人, 加藤育民

【緒言】エストロゲン産生腫瘍は顆粒膜細胞腫や莢膜細胞腫などの性索間質系腫瘍が代表的であるが、上皮性卵巣腫瘍においてもエストロゲン産生を伴うことがあるとされる。今回我々は、閉経後女性で術前にE2高値を示し、術後にE2低下を認めた卵巣類内膜癌の3症例を経験したので報告する。【症例1】76歳3産。閉経後不正出血を主訴に前医を受診。子宮内膜14mmと肥厚、7cm大左卵巣腫瘍を認め当科紹介受診された。子宮内膜細胞診は異常なかったが、E2 108 pg/mLと高値を認めた。MRIで充実成分と囊胞成分が混在し顆粒膜細胞腫が疑われた。腹式単純子宮全摘術+両側付属器摘出術+大網部分切除術施行、最終診断は類内膜癌G3, pT1acN0M0であった。術後E2は低下した。現在術後1年6か月再発兆候なく経過している。【症例2】80歳2産。婦人科検診で左卵巣腫瘍指摘され前医を受診。MRIで顆粒膜細胞腫が疑われ当科紹介受診となった。E2 15.1 pg/mLと軽度上昇。腹腔鏡下両側付属器摘出術施行。最終診断は左卵管の類内膜癌G2, pT1c2cN0M0であった。術後E2は低下し、現在術後5か月追加治療せず再発兆候なく経過している。【症例3】84歳2産。肺癌follow up CTで骨盤内腫瘍指摘され前医を受診。E2 55 pg/mLと上昇。MRIで顆粒膜細胞腫が疑われ当科紹介受診となった。腹式単純子宮全摘術+両側付属器摘出術+大網部分切除術施行、最終診断は類内膜癌G1, pT1acN0M0であった。術後E2は低下した。現在術後2か月再発兆候なく経過している。【結論】ホルモン産生卵巣腫瘍は莢膜細胞腫と顆粒膜細胞腫で9割を占めるとされ、エストロゲン産生類内膜癌は稀ではあるが、鑑別診断の1つとして検討すべきと考えられる。

P-43-8 当院での子宮体癌に対するレンパチニブ・ペムプロリズマブ療法使用経験

大阪警察病院

塩見真由, 中村聡希, 苦居英梨彩, 原理紗子, 藤吉恵津子, 寺田美希子, 祝小百合, 徳川陸美, 邨田裕子, 細井文子, 西尾幸浩, 香山晋輔

【目的】進行・再発子宮体癌に対して2021年12月にマルチキナーゼ阻害剤のレンパチニブ(LEN)と免疫チェックポイント阻害剤のペムプロリズマブ(PEM)の併用療法が承認された。当院で経験したLEN+PEM療法の2症例について副作用マネージメントを中心に報告する。【方法】症例1は65歳、子宮癌肉腫ステージIA期、手術から5か月で腹膜播種再発、その後2回の再発に対して化学療法を行ったのち、術後4年7か月で肝転移を認め、LEN+PEM療法の方針となった。症例2は60歳、子宮体癌類内膜癌G2、ステージIVB期に対して術後化学療法を行ったが術後9か月で多発リンパ節転移を認め、LEN+PEM療法開始となった。【成績】症例1は治療開始10日目に急性胆嚢炎となり絶食・抗生剤加療にて改善した。また、PEM2コース目の投与3時間後に血圧低下・発熱・悪寒を訴えInfusion reactionが疑われた。以後、PEM投与前に前投薬を行い、症状緩和を得た。PEM7コース後には甲状腺機能低下症を認め、ホルモン補充療法を行った。PEM8コース後には胸部CTにてすりガラス陰影を認め、薬剤性肺炎が疑われたが、経過観察のみで症状改善した。症例2はPEM2コース後にGrade3の手足症候群を認めた。LENの休薬およびステロイド加療、減量を行った。【結論】子宮体癌に対するLEN+PEM療法の2症例を経験した。多様なirAEを認めたが、適切な時期で休薬や減量を行うことにより長期間の治療継続が可能であった。また、irAEを認めた際に、専門科への円滑にコンサルト可能な体制を構築することが重要である。

P-43-9 卵巣癌III期に対してneoadjuvant chemotherapy後に腹腔鏡下interval debulking surgeryを行った一例

三重大

加藤麻耶, 金田倫子, 小村勇二, 矢田貴大, 岡本幸太, 松本剛史, 吉田健太, 前沢忠志, 近藤英司, 池田智明

【緒言】卵巣癌の根治手術は、腹腔鏡の保険収載はされていない。今回卵巣癌IIIC期に対してneoadjuvant chemotherapy(NAC)を行い、自費診療で腹腔鏡下にinterval debulking surgery(IDS)を行った症例を経験したので報告する。なお、本研究は当院倫理委員会の承認を得ている。【症例】64歳、腹部膨満感を主訴に前医を受診され、腹部CT検査にて腹膜播種が疑われた。上部・下部内視鏡検査で異常は指摘されず、試験腹腔鏡手術(大網生検)にて漿液性癌と診断され、当科紹介となった。CA125は1615U/mL、MRI検査で両側付属器の腫大から卵巣癌または卵管癌が疑われ、IIIC期、cT3cN0M0の診断でNACとしてパクリタキセル・カルボプラチン療法を4サイクル施行した。NAC後のPET-CT検査では、両側付属器の腫瘍は縮小し、また両側付属器、腹膜播種、大網に優位なFDGの集積は認めなかった。MRI検査では、明らかな腸管浸潤はみられなかった。IDSとして、腹腔鏡下子宮全摘、両側付属器切除、大網切除を行い、腹腔内所見は一部大網に結節を認めるも、腹膜播種はなく、complete surgeryで終了した。手術時間は3時間11分、出血量は少量であった。術後の経過は良好で術後4日目に退院した。今後化学療法施行予定である。【結語】進行卵巣癌における腹腔鏡下のIDSは周術期合併症なく、安全に施行できた。今後症例を蓄積していく。

P-43-10 卵巣癌との鑑別に苦慮した後腹膜脂肪肉腫が急性腹症を来した一例

熊本赤十字病院

金城国俊, 村上望美, 中山真恵, 堀 新平, 山本文子, 井手上隆史, 荒金 太

【緒言】後腹膜腫瘍の頻度は全腫瘍の0.2%で、その約80%が悪性であり、その中で脂肪肉腫は14.7%と最多である。発生部位の特性により、多岐にわたる診療科で治療される。今回、卵巣癌との鑑別に苦慮し、急性腹症で緊急手術を施行した後腹膜脂肪肉腫と診断された一例を経験したので報告する。【症例】68歳3妊3産。卵巣腫瘍疑いで当科紹介受診となった。骨盤部のCT・MRI検査では子宮の背側に境界明瞭な148×70mm大の腫瘤を認めた。卵巣癌が疑われたが、子宮や両側付属器との連続性が明らかでなく、3D-CTの再構築により後腹膜腫瘍の可能性も考えられた。外科とも協議を行い合同での手術を計画した。手術待機中に腹痛の増悪あり、内診で腫瘍に一致して圧痛を認め、疼痛コントロール困難であり入院翌日に緊急開腹手術を施行した。肉眼的に後腹膜腫瘍である事が確認できた。腹式単純子宮全摘出+両側付属器切除+後腹膜腫瘍切除術を行い、摘出した腫瘍は580gで表面平滑、弾性軟であった。病理組織診断は脱分化型脂肪肉腫であった。術後経過良好で現在外来管理中である。【考察】後腹膜脂肪肉腫の多くは無症状で、診断時には卵巣腫瘍との鑑別を要する事も多い。治療は可能であれば腫瘍の完全切除が推奨されており、隣接する臓器に浸潤している場合は合併切除が必要になる事もあるため、術前の評価が重要である。本症例でも術前の3D-CTの再構築を含めた精査により、後腹膜悪性腫瘍の可能性も考慮し、術前に外科との協議が可能であった。【結論】術前卵巣癌との鑑別が困難であった後腹膜脂肪肉腫の一例を経験した。手術時に多岐にわたる診療科との連携が必要となることもあり、十分な画像評価と治療戦略を立てる事が重要と考える。

P-43-11 巨大卵巣癌に対して経皮ドレナージ後に挿管して腹式両側付属器切除術を施行し、術後に自発呼吸困難のため気管切開術を施行し人工呼吸器管理の下で化学療法を行った一例

大阪赤十字病院

定本怜子, 福田真優, 齊藤森実, 水野友香子, 徳重 悠, 平山貴裕, 小林弘尚, 川田悦子, 前田万里紗, 中川江里子, 岩見州一郎, 野々垣多加史

【緒言】巨大卵巣腫瘍摘出術は、機能的残気量の減少による低酸素血症、摘出時の肺静脈灌流の増加による循環動態の変動や術後の再膨張性肺水腫などのリスクがあり、周術期管理には注意を要する。巨大卵巣腫瘍術後に気管切開を施行し人工呼吸器管理下で化学療法を施行した症例を経験したので報告する。【症例】49歳、未妊。6年前から腹部膨隆感を自覚していたが受診せず、日常動作困難、呼吸困難が出現したため救急要請した。当院来院時の所見は呼吸数25回/分、心拍数72bpm、血圧126/86mmHg、血中酸素飽和度98%（酸素3L）、腹囲151cm、剣状突起に至る多房性の腫瘍を認め、仰臥位が困難だった。顔面・眼瞼・下腿に浮腫強く、造影CTでは52cmの粘性性境界悪性腫瘍疑いの診断だが、腰椎に広範な溶骨性変化を認めた。MRIは腹囲が大きすぎるため撮像できなかった。翌日、まず循環動態に留意しながら右側臥位にて経皮的に腫瘍内内容液18Lを1時間かけて吸引した後に、仰臥位と意識下挿管を施行し、腹式両側付属器切除術を施行した。右付属器は内容液と合わせて45.6kg、病理結果はhigh grade serous carcinomaとmucinous borderline tumorだった。再膨張性肺水腫は認めず術翌日抜管したが、低酸素血症とため同日再挿管した。巨大腫瘍で長期開引き延ばされていたため呼吸筋が弛緩しており自発呼吸困難で、術後9日目に気管切開を施行、BiPAPにて呼吸管理した。腰椎の病変は転移と判断、IVB期の診断に至り、パクリタキセル、カルボプラチンによる化学療法を3kur施行した。【結語】巨大卵巣腫瘍は周術期管理に注意を要し、周術期管理だけでなく、術後も長く呼吸器合併症が起こり得ることを念頭に置いておくべきである。

P-43-12 腹水細胞診で陰性を示し診断に難渋した卵巣神経内分泌癌の1例福井大¹, 福井県立病院²中村百合子^{1,2}, 山田しず佳¹, 井上理史¹, 北倉えり茅¹, 南部仁美¹, 大沼利通¹, 品川明子¹, 折坂 誠¹, 吉田好雄¹

【緒言】卵巣神経内分泌癌（NEC：Neuroendocrine carcinoma）は非常にまれな組織型で進行がはやく予後不良とされる。今回、進行卵巣癌が疑われたが、腎機能低下等の急激な全身状態の増悪があり、早期診断が必要であったが、腹水細胞診で悪性所見を認めず、腹水セロブロック作製により診断に至ったNECの症例を経験したので報告する。【症例】70歳G2P2下腹部痛を主訴に近医受診。CTで左卵巣充実性腫瘍、多発腹膜播種を認め、卵巣癌が疑われ当院紹介。審査腹腔鏡を予定したが、急激な腹水増加、腎機能低下のため、腹腔穿刺を行い腹水細胞診を提出した。しかし、初回腹水細胞診では悪性所見を認めず、2回目の腹腔穿刺で約3000mlの腹水を全量提出しセロブロックを作製できた。HE所見では、多数の炎症細胞に混ざって異型を有する上皮性細胞集塊を認め、免疫染色ではCD56、synaptophysinが陽性であり、NECの診断となった。WeeklyTC（パクリタキセル+カルボプラチン）療法を1コース施行し、一時的な全身状態の改善を認めたが、2コース目開始前に再び急激な腹水の増加、腫瘍の増大を認め、治療開始から35日目に永眠された。【考察】進行卵巣癌が疑われる例において、全身状態不良のために審査腹腔鏡による組織診断が困難な場合がある。腹腔穿刺による腹水細胞診は比較的侵襲が少なく早期に診断できるため多用されているが、採取量や血液混入量などの影響で診断に至らない場合がある。診断に難渋する際には、腹水セロブロック作製による組織診断が有用であり、早期診断・治療介入することができる。

P-43-13 ゲノムプロファイルによる腫瘍代謝特性からメトホルミン塩酸塩が寛解維持に関与していると考えられた卵巣癌症例の検討

総合病院土浦協同病院

遠藤誠一, 平野 拓, 大木崇広, 山中詩織, 小松紗友美, 秋田真友, 武内史緒, 竹谷陽子, 松岡竜也, 市川麻以子, 塚田貴史, 島袋剛二

【緒言】がん治療の個別医療における包括的ゲノムプロファイリング検査の重要性が認識されている。ゲノム情報に基づき考察される治療戦略は様々であるが、今回、臨床経過も包括し、腫瘍代謝の脆弱性をターゲットとしたメトホルミン塩酸塩投与が腫瘍増殖抑制に関与したと思われる症例を経験し報告する【症例】59歳 2012年不正性器出血を認め術前子宮筋腫の診断で開腹単純子宮全摘術施行。術後病理子宮体部類内膜癌 G1 stageIA。2018年卵巣がんの術前診断で開腹するも高度癒着のため不完全手術。卵巣類内膜癌の診断で化学療法施行。2022年経膈超音波検査にて35mm 充実成分を伴った嚢胞病変を認め、再発疑いにて当院紹介となった。当院MRIでは造影効果 拡散低下を伴う充実性、嚢胞性腫瘍、PETCTではSUVmax 12.4と集積を認めた。組織診断も兼ね腫瘍摘出を検討したが膀胱陰腫も認めたため、外科的介入は避け、個別的治療選択の目的で借用卵巣組織検体でのゲノムプロファイリング検査を行うこととした。バイオマーカー所見は特に異常なく、pathogenic な遺伝子所見はCTNBN1/PIK3CA/CDH1 ミスセンス変異、NOTCH3 ナンセンス変異およびSDHA エクソン 15 rearrangementを認めた。保険適応内での druggable な変異を認めず、PS0のため経過観察としたが、その後腫瘍縮小および腫瘍マーカーの低下を認めた。糖尿病既往に対してメトホルミン塩酸塩を内服しており、メトホルミン塩酸塩による細胞内糖代謝の変化がPIK3CA 経路に影響し腫瘍増殖を抑制している可能性が示唆された。【結論】ゲノムプロファイリング情報が個別化医療および drug repositioning による治療戦略を論理的に立案する上で有効である可能性がある。

P-43-14 予防的卵巣卵管摘出術を施行し、高異型度漿液性卵管上皮内癌を認めた遺伝性乳癌卵巣癌症候群の一例

虎の門病院

倉田奈央子, 馬場 聡, 宇津野彩, 福井大和, 神野雄一, 竹内 真, 吉田光代, 後藤美希, 東梅久子, 有本貴英

遺伝性乳癌卵巣癌症候群 (HBOC) に対し腹腔鏡下リスク低減卵管卵巣切除術 (RRSO) を実施し、術後に漿液性卵管上皮内癌 (STIC) と診断された症例を経験したので報告する。53歳, 2妊2産, 51歳時に右乳癌 stage IA, トリプルネガティブタイプと診断された。母が卵巣癌既往であるのに加え、4親等以内に他に乳癌4人, 前立腺癌2人の家族歴があり、生殖細胞系列遺伝子検査にてBRCA1 遺伝子に病的バリエーションを認めた。右乳癌に対する右乳房切除術と同時に予防的左乳房切除術を施行後、RRSOを希望し当科紹介となった。経膈超音波断層法にて付属器の腫大を認めず、血清CA125も7.9 U/mLと正常であり、予防的腹腔鏡下両側付属器摘出術を施行した。摘出検体は肉眼的には正常であったが、術後病理組織検査で左卵管管部に上皮内腺癌が認められ、STICの診断となった。切除断端陰性、腹腔内洗浄細胞診陰性であり、術後追加治療は実施せず、外来経過観察の方針とした。RRSO時にSTICを認めた症例ではその後の原発性腹膜癌の発症リスクが高いとの報告があり、今後も定期的な経過観察が必要と考えられる。

P-43-15 両側付属器切除後に下腸間膜動脈からの出血を呈した神経線維腫症I型の1例

安城更生病院

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神経線維腫症I型 (von Recklinghausen disease) は常染色体優性の遺伝病で、血管病変を合併することが知られている。本症例は53歳女性、全身のカフェオレ斑より神経線維腫I型と診断されていた。持続する腹痛で救急外来に受診。造影CTにて左卵巣腫瘍を指摘された。来院後は疼痛改善のため経過観察入院としていた。入院1日目の未明に腹痛が再燃し、左卵巣腫瘍捻転が疑われ、緊急開腹両側付属器切除術を施行した。術後13時間で急激な腹痛を訴え、Dynamic CTで下腸間膜動脈からの出血と周囲の血腫の所見が認められ、緊急開腹術施行し、下腸間膜動脈からの出血を止血して閉腹した。しかし再開腹術後3時間で疼痛再燃し、Dynamic CTで下腸間膜動脈からの再出血あり再開腹手術となった。下腸間膜動脈および腹部大動脈周辺からの出血は、血管や組織が非常に脆弱であり止血に難渋し、出血コントロール目的で腹部大動脈にステントグラフト留置を行った。また、S状結腸壊死と下行結腸の血流障害認め、横行結腸ストマ造設も行った。以後再出血は認めず、術後30日目に退院となった。機序は不明な点が多いが、神経線維腫症I型は動静脈の血管障害や出血合併症をしばしば発症するが、脆弱な血管壁組織の破綻に対して開腹手術で止血が困難な症例が存在することを念頭に置く必要がある。

P-44-1 白血病に対する造血幹細胞移植後20年で発症した子宮体癌の1例

岐阜県総合医療センター

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【緒言】子宮体癌はエストロゲンとの密接な関係があり、若年者における長期間の無月経はホルモン治療を検討すべきである。白血病に対する造血幹細胞移植後に閉経となり、20年後に子宮体癌と診断された1例を経験したため報告する。【症例】45歳、0妊。既往に慢性骨髄性白血病あり、25歳時に造血幹細胞移植を受けてから無月経となっている。ホルモン補充療法を受けたが嘔気が強いため治療継続を断念、以後婦人科への定期通院はされていない。X-11年より不正出血を自覚したが婦人科へ受診せず。X年8月不正出血の増加を自覚し当科へ受診。初診時E2 5.0 pg/mL, FSH 91.6 mIU/mL。内膜組織診よりEndometrioid carcinomaを抽出し、G3の可能性が示唆された。造影MRI・CTから一部骨盤内腹膜に造影効果を認めるが播種との診断に至らず、子宮体癌IA期の術前診断で開腹準込汎子宮全摘、骨盤内リンパ節郭清術を施行。右仙骨子宮靭帯から直腸右側の腹膜に明らかな肥厚あり生検に提出。手術時間3時間33分、出血量400g(輸血なし)。術後9日に退院。Endometrioid carcinoma, G3, pT3b, N0。筋層浸潤は1/2未満であるが生検した腹膜に転移を認め子宮体癌IIIB期と診断。再発高リスク群のためTC療法を検討中である。【考察】本症例では白血病患者に併発する閉経後20年で子宮体癌を発症した。造血幹細胞移植により卵巣機能が廃絶し閉経に至ったと考えられるが、微量なエストロゲンが分泌されていたことで子宮体癌の発症に至った可能性は否定できないと考える。癌治療後のヘルスケアに於いてホルモン補充療法は極めて重要であるが、治療開始時に治療の重要性を十分に説明する必要があると再認識した。

P-44-2 当院での再発子宮体癌に対するLenvatinib Pembrolizumab併用療法の治療経験について

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【緒言】再発子宮体癌に対するLenvatinib + Pembrolizumab併用療法(LEN+PEM療法)が保険適応となり、広く治療が行われているが、免疫チェックポイント阻害剤特有の有害事象など治療に難渋する報告も散見される。当院で3例経験したため報告する。【症例1】76歳。子宮体癌IIIC2期。初回手術後TC療法6コース施行し、8か月で傍大動脈リンパ節転移、多発肺転移を認め再度TC療法施行するも3コース施行後CTで転移巣の増大、肝転移の出現のためLEN+PEM療法へ。PEM2コース後に尿蛋白のためLENは中止。PEM3コース後のCTで病勢進行認めたためLEN+PEM療法は中止となった。【症例2】56歳。子宮体癌IIIC2期。初回治療後6か月で左鎖骨上窩など多発リンパ節転移を認めたためLEN+PEM療法へ。初回投与後19日目にirAE肝炎を発症。経過観察のみで改善を得られたが、治療継続は困難と考えAP療法を開始。3コース施行後のCTで完全奏効を得られ、現在経過観察中である。【症例3】68歳。子宮体癌IIIC2期。初回治療後CTで腹壁瘢痕部播種、傍大動脈リンパ節増大を認めLEN+PEM療法へ。高血圧、甲状腺機能異常を認めたため治療および経過観察が必要ではあるがPEM3コース後のCTで部分奏効を得られ、PEM5コース投与後も治療継続中。【考察】irAE肝炎では消化器内科と連携し、経過観察のみで改善を得られた。また、甲状腺機能異常、高血圧ではそれぞれ内分泌内科、循環器内科と連携し、経過観察ならびに内服治療を開始。LEN+PEM療法は他科との連携が必須であり、先の報告を参考とすることで迅速に対応し、良好な経過を得られたと考える。【結語】様々な有害事象を経験した。安全に治療を行うために他科と連携することが重要であると再認識した。

P-44-3 巨大嚢胞性病変を形成した低異型度子宮内膜間質肉腫の一例

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【緒言】子宮内膜間質肉腫は子宮筋層内に充実性に増殖し、腫瘍内部に出血・壊死をしばしば伴うが、巨大な嚢胞性病変を形成することは稀である。年単位の漸次的な増大がみられ、子宮筋層内に13cm大の多房性嚢胞性病変を形成した低異型度子宮内膜間質肉腫の症例を報告する。【症例】46歳、0妊0産。下腹部痛を主訴に近医を受診し、MRI検査で骨盤内に11cm大の嚢胞性腫瘍を指摘され、2か月後に当科紹介された。造影CT検査で13cm大の壁不整や充実部を伴う多房性嚢胞性腫瘍を認めた。MRI検査で子宮内膜との連続性はなく、卵巣腫瘍あるいは子宮後壁の筋層由来の腫瘍を疑った。血液検査でLDH 177 U/l・CEA 1.0ng/ml・CA19-9 13.9 U/ml・CA125 32.5U/mlと正常範囲内であった。診断目的に腹式単純子宮全摘出術・両側付属器摘出術を施行し、術中所見で子宮筋層由来の嚢胞性腫瘍があり、内部に黄色の粘稠度の低い液体を含んでいた。病理組織学的に、嚢胞壁は短紡錘形あるいは卵円形の異型細胞から成り、錯綜状に配列し不規則に浸潤増生していた。免疫組織学的に、腫瘍細胞はER・CD10・ α -SMA・desminに陽性であった。発生部位と病理所見から低異型度子宮内膜間質肉腫IB期(pT1BNxM0)と診断した。術後に再発なく1年経過している。【結語】画像検査で増大傾向のある子宮由来の嚢胞性病変を認めた場合、低異型度子宮内膜間質肉腫は鑑別の一つに考慮する必要がある。

P-44-4 当院の再発子宮内膜癌に対する Pembrolizumab+Lenvatinib 治療成績について

近畿大
佐藤華子

【目的】進行・再発子宮内膜癌に対して、2021年12月に Pembrolizumab+Lenvatinib 療法が保険承認され、期待が寄せられている。これまでの当院の治療成績や副作用マネージメントについて報告する。【方法】2021年12月から2023年7月までの20か月の間に、再発子宮内膜癌13例に Pembrolizumab+Lenvatinib 療法を行った。MSI status は dMMR が7% (1/13例)のみであった。組織型は類内膜癌が最多の38% (5/13例) だが、癌肉腫が27% (3/13例) と次いで多く、漿液性癌や脱分化癌も含まれている。【成績】AEは、高血圧、甲状腺機能異常、皮疹、関節痛や倦怠感、下痢は多くの症例で認められ、その他にも副腎不全、irAE 肝炎、肺炎などを認めている。Lenvatinib の用量は、2段階減量の10mgに減量する症例が多かった。当院の成績は観察期間がまだ短いながら、奏効率45%と非常に良好な成績を得られている。【結論】治療導入初期に、様々な副作用をコントロールしつつ、可能な限り減量せず継続することで、良好な治療成績が得られると考える。

21日(日)
日本語ポスター

P-44-5 肉腫様変化を認めた子宮体部原発の中腎様腺癌 Mesonephric-like adenocarcinoma (MLA) の一例

藤田医大ばんだね病院

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中腎様腺癌 Mesonephric-like adenocarcinoma (MLA) という用語は2016年に初めて用いられ、中腎腺癌と組織形態学的および免疫学的に顕著な類似性を持つが中腎腺癌と異なり中腎管の遺残や過形成が確認できないものとして報告された。その後子宮体部の中腎様腺癌は2020年のWHO分類第5版に新たな項目として追加となり近年卵巣や子宮内膜に発生する中腎様腺癌の報告が増えてきている。さらに子宮体部の中腎様腺癌に肉腫が混在する症例は報告が極めて少なく希少である。子宮体部原発の中腎様腺癌は約1-3%の頻度とまれであるが、他の組織型の子宮体癌と比較し進行期で発見され悪性度が高く予後も不良であることが報告されている。組織学的には細胞質内粘液を欠く低~中異型度の立方状ないし円柱状の細胞が好酸性の硝子様分泌物を含有する管腔を形成して増殖するが、裂隙状の空隙や乳頭状発育、充実性シート状、糸球体様、管腔状、索状、迷路状、小嚢胞状など多彩な増殖パターンがみられる。これらの組織の多様性に加え定義されてから歴史が浅く十分に周知されておらず診断が困難であると言われる。今回われわれは子宮頸癌と判断し術前化学療法を実施し手術を行ったところ、術後病理結果で肉腫成分が混在する子宮体部発生の中腎様腺癌であることが判明した症例を経験したため文献的考察を含め報告する。

P-44-6 子宮留膿症による子宮穿孔、汎発性腹膜炎を併発した子宮体部漿液性癌の一例

鹿児島市立病院

栢植竜太

【緒言】子宮留膿症は子宮頸管の狭窄や閉塞により子宮内腔に膿汁や壊死組織が貯留する疾患であり高齢者に多い。子宮留膿症による子宮穿孔は予後不良である。子宮留膿症の原因の22%は悪性腫瘍とされその多くが子宮頸癌である。今回われわれは子宮留膿症による子宮穿孔、汎発性腹膜炎を併発した子宮体部漿液性癌の一例を経験したため文献的考察を踏まえて報告する。【症例】48歳女性、4妊4産、未閉経で手術歴はなし。糖尿病、高血圧の既往があり近医内科で加療中であった。来院2日前に下腹部痛を自覚した。前医で腹部単純CTを施行されダグラス窩に腫瘍性病変を指摘され卵巣腫瘍茎捻転疑いで同日当院へ搬送となった。腹部造影CTで腹腔内および骨盤腔内に遊離ガスと膿瘍を認めた。子宮体部に充実性病変、子宮底部の筋層断裂を認めたことから子宮留膿症による子宮穿孔、汎発性腹膜炎と診断し同日緊急開腹手術を施行した。子宮底部背側に約5mmの穿孔部があり同部位から膿汁の流出を認めた。肉眼的に子宮内腔を占拠する充実性病変を認めた。感染コントロール目的に膈上部切開術および両側付属器切除術を施行した。術後経過良好であり、術後15日目に自宅退院した。永久病理検査の結果、子宮体部漿液性癌であったが穿孔部に病変はなかった。再発高リスク群であり術後33日目から補助化学療法を開始した。【結語】子宮留膿症による子宮穿孔を起こした子宮体部漿液性癌の一例を経験した。コントロール不良の糖尿病もその一因になったと考えられる。子宮体癌に対する根治術は必要ではあるが、救命には感染巣のコントロールが重要であり、患者の全身状態に応じて治療方法を選択する必要がある。

P-44-7 脂肪平滑筋腫として経過観察されていたが閉経期に増大が認められたため手術摘除が行われた子宮の脂肪肉腫の1例と文献的考察

明和病院

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【緒言】脂肪平滑筋腫と脂肪肉腫の鑑別は容易でない。【症例】閉経後、52歳時、卵巣嚢腫を指摘され受診した。長径4cmの子宮筋腫を認め、鑑別のためにMRI検査を行った。子宮体部前壁発生の39×32×41mmの腫瘤があり、T1強調画像、T2強調画像ともに低信号の部分と、淡く高信号の部分が混在していた。高信号の部分は脂肪抑制画像で信号抑制され脂肪成分で、脂肪平滑筋腫と考えられた。58歳時、腫瘤の増大を認めMRI検査を行った。49×40×49mm大であり、長径の増加は1.23倍、容積は1.85倍であった。悪性も念頭にいれ、子宮全摘と両付属器摘除を行った。完全摘除であり、腹腔内に播種や癒着、腹水を認めなかった。剖面は黄色で、出血や壊死を認めなかった。部分的に白色調の硬結部を認めた。組織学的に脂肪細胞の大小不同があり、短紡錘形腫瘍細胞が束状に増殖し、間質の細胞の大小不同、核の大小不同と核縁の不整と肥厚が認められた。免疫染色では、MDM2(一部に+)、CDK4(+), Desmin(+), Ki-67 index:1%であり、高分化脂肪肉腫と診断した。子宮限局であり、追加治療なしとした。術後3か月で再発を認めていない。【文献的検討】確認できた脂肪肉腫は19例であった。発症年齢は23歳を除くと、45~78歳、平均年齢は60.5歳である。症状は重複を含め、腫瘤感:12、出血:8、疼痛:4、圧迫症状:1である。病変部位は重複を含め、子宮体部:12、子宮頸部:6、韧带:2、子宮腔内:1である。初回治療は子宮全摘と両付属器摘除が多い。不完全切除は予後不良、子宮体部以外発生は予後不良である。高分化は予後良好、多形型は予後不良である。高分化の3例は再発なし。【結論】脂肪平滑筋腫が閉経後に増大を認めた場合は手術が必要である。

P-44-8 子宮体癌の多発皮下組織転移に対して化学療法が奏功した1例

総合病院土浦協同病院

東出 凌, 遠藤誠一, 平野 拓, 秋田真友, 武内史緒, 竹谷陽子, 松岡竜也, 北野理絵, 塚田貴史, 市川麻以子, 坂本雅恵, 島袋剛二

【緒言】子宮体癌の皮下組織転移は極めて稀であり、その予後は不良である。初期の子宮体癌の術後1か月で多発皮下組織転移が出現し、化学療法が奏功した1例を報告する。【症例】69歳、5妊4産。2型糖尿病の既往あり。4か月間持続する不正性器出血を主訴に前医を受診し、子宮内膜組織生検で腺癌の診断を得た。加療目的に当院を紹介受診し、診察で子宮内に充実性腫瘤を認めた。CTでは遠隔転移やリンパ節腫大は認めず、MRIでは病変は子宮内に限局していた。腹式単純子宮全摘術、両側付属器摘出術、大網部分切除、骨盤リンパ節郭清を施行した。病理組織診断は子宮体癌、明細胞癌成分を有する類内膜癌 Grade 3, Stage IBだった。術後経過は良好であったが、術後1か月のCTで多発皮下組織転移と腔壁腫瘤を認めた。腔鏡診で腔壁に3cm大の易出血性腫瘤を認めた。視診上表皮に明らかな病変はなかったが、触診で背部、腋窩、鼠径、臀部に弾性硬で可動性不良の最大径5cmの皮下腫瘤を触れた。PET-CTでそれぞれの腫瘤にFDG集積を認めた。腔壁腫瘤の病理組織診断は転移に矛盾しない所見であり、子宮体癌の再発と診断した。パクリタキセル・カルボプラチン療法を行い、1コース投与後から触診上速やかに病変は縮小し、3コース投与後のCTで臀部の皮下腫瘤以外の病変は消失した。現在も化学療法中である。【考察】皮下組織転移は血流とリンパ還流のどちらの流れからも生じると考えられており、診断時にはすでに全身に転移していることが多く、予後不良である。本症例では再発までの進行が非常に早く、予後不良であると推測されたが化学療法が著効した。切除不能な多発皮下組織転移に対して化学療法が有用な選択肢と推察された。

P-44-9 閉経後筋腫分娩の術前診断で子宮鏡切除後に子宮腺肉腫と診断された1例

大阪公立大

藤東温子, 安井智代, 栗津祐一郎, 内倉慧二郎, 野田拓也, 大上健太, 田坂玲子, 今井健至, 山内 真, 福田武史, 市村友季, 角 俊幸

子宮腺肉腫は良性の上皮細胞と悪性の間質細胞の増生を示す混合性腫瘍で、ポリープ状や隆起性病変として見られることが多い。子宮の悪性腫瘍の0.5%未満、子宮肉腫の約5%と稀な腫瘍であり、肉腫成分は低異型度子宮内膜間質肉腫であることが多く初期であれば比較的予後は良い。今回粘膜炎下筋腫の診断で子宮鏡下に切除したところ子宮腺肉腫と診断された症例を経験したので報告する。【症例】60歳、未妊、50歳時閉経、ホルモン治療歴なし。性器出血と下腹痛を主訴に前医を受診。1か月後当科受診時、超音波検査では子宮腔内に筋腫様腫瘤を認め、一部が子宮口から腔外に脱出していた。腫瘤の一部と子宮内膜の生検では悪性所見を認めなかった。またMRI画像上子宮腔内腫瘤のサイズは8×7×4.5cm辺縁整で子宮筋層は伸展非薄化していたが、積極的に悪性を示唆する所見を認めず粘膜炎下筋腫と考えられた。子宮温存希望が強かったため経腔的に腫瘤を切除する目的で入院となったが、外子宮口から脱出していた部分は入院待機中に自然脱落し入院時には症状も消失していた。残存腫瘤を子宮鏡下に切除したところ病理結果は子宮腺肉腫で、腹式単純子宮全摘出術と両側付属器摘出術を実施し、子宮腺肉腫IA期(pT1aNXMO)の診断となった。追加治療なく現在経過観察中である。【結語】子宮腺肉腫はポリープ様隆起病変を生じ、MRI画像上内膜ポリープや粘膜炎下筋腫と診断されることが多く生検程度の病理検査では診断がつきにくいとされている。性器出血が持続し子宮内に隆起性病変が認められる場合は、悪性所見に乏しい場合でも子宮腺肉腫の可能性も念頭に入れ、切除して病理診断を行うことが望ましい。

P-44-10 急速な進行を呈し子宮肉腫との鑑別に苦慮した子宮体部未分化癌の一例

気仙沼市立病院¹、東北大²、仙台市立病院³
橋本亮平¹、西本光男¹、谷口智紀^{1,3}、重田昌吾²

【症例】48歳、既往歴なし、2妊2産（経陰分娩1回、帝王切開1回）。過多月経あり、月経困難症あり。【現病歴】息切れを主訴に近医婦人科を受診し、Hb 4.8 g/dlの重症貧血を認め、当科紹介となった。骨盤造影MRIで子宮筋層内にDWI高信号域を伴う95 mm大の腫瘤を認め、子宮悪性腫瘍の疑いで手術の方針となった。術前CTでは病的腫大リンパ節、胸腹水、遠隔転移は認めなかった。子宮内膜細胞診は陰性、子宮内膜組織診では悪性を疑う異型細胞を認めた。【術中所見】子宮は新生児頭大に腫大し、漿膜面に腫瘍が露出していた。子宮内膜、子宮頸部、両側付属器、大網に肉眼的病変を認めなかった。膀胱子宮窩、ダグラス窩腹膜に小指頭大の結節を認めた。腹式単純子宮全摘術、両側付属器摘出術、腹膜病巣切除術を施行した。【術後経過】術後経過は良好であり、第8病日に退院した。病理組織にはrhabdoid cellを認め、vimentin, AE1/AE3, PgR, vimentin, CD10が陽性であった。右付属器転移、腹膜播種を認め、術中腹水細胞診は陰性であった。当初は子宮肉腫と診断されたが、高次施設にて子宮体部未分化癌 IIIA 期 (FIGO 2008), pT3aNXMO (UICC 第8版) の最終診断となった。術後第28病日のPET-CTで腹膜播種、多発リンパ節転移、骨転移、S状結腸浸潤を認めた。術後第41病日に術後補助化学療法としてTC療法を1コース施行したが、病勢進行に伴うPS低下のためBSCの方針となり、術後第76病日に永眠された。【考察】子宮体部未分化癌は子宮肉腫と類似した形態を示すことがあり、鑑別に際しては筋層浸潤の形態や免疫染色の結果を踏まえ総合的に判断する必要がある。いずれも進行が早く予後不良であるため、可及的速やかな診断、治療が望ましい。

P-44-11 ベンプロリズマブ・レンパチニブ併用療法中に首下がりで発症した重症筋無力症の一例

関西労災病院

堀内僚介、高田友美、浅井智奈美、澤本康平、山本実咲、大久保理恵子、下地香乃子、尾上昌世、吉岡恵美、後藤摩耶子、堀謙輔、伊藤公彦

【緒言】婦人科がんにに対してベンプロリズマブが使用されるようになったが、免疫関連副作用(irAE)を常に念頭に置く必要がある。子宮体がんに対し、レンパチニブ・ベンプロリズマブ併用療法(LP療法)中に、重症筋無力症を発症した一例を報告する。【症例】67歳、3妊3産の女性。10年前に尋常性天疱瘡、9年前に甲状腺乳頭がんの既往歴あり。現病歴として、6年前に子宮体部漿液性癌 IIIC2期に対して手術と術後補助化学療法を実施。術後2年で右肺尖部転移を認め切除術を実施。術後約3年半後に右肺から縦隔への再発、頸部～縦隔リンパ節転移、左大腿骨転移を認め、放射線治療を実施。術後4年で右肺門部・肺尖部・腸骨・大腿骨転移、鎖骨上リンパ節転移、腹膜播種を認めドキシソルビシン・シスプラチン療法を実施するも無効。右鎖骨上リンパ節転移は腕神経叢、C7椎間孔に浸潤しており、右腕に神経障害を認めた。この時点よりLP療法を開始した。2サイクル目のDay8に首がまわらないとの訴え、Day15に頭が上がりにくいとの訴えもあるも、右頸部の転移による症状と考え、3サイクル目を実施。3サイクル目のDay15に頭を挙上できず、視線が合わない状態となり、Day22に脳神経内科へコンサルトしたところ、irAEの重症筋無力症による「首下がり」と診断された。免疫グロブリン療法を開始し症状は軽快したが、約半年後に原癌死した。【結語】irAEは多岐にわたり、婦人科医が日常経験しない症状が含まれる。そのため、普段と違う症状を認めた際は、早期に他科にコンサルトすることが重要である。また、自己免疫疾患の既往を有する患者には特に注意が必要である。

P-44-12 傍大動脈リンパ節腫大を契機に診断に至った子宮体部原発悪性リンパ腫の1例

神戸医療センター

吉田 愛、白國あかり、浅見里紗、嘉納 萌、山崎友維、杉本 誠、武内享介

【緒言】子宮原発悪性リンパ腫は全子宮腫瘍中の0.05%と極めて稀である。今回傍大動脈リンパ節腫大の契機に診断に至った子宮体部原発悪性リンパ腫の1例を経験したので報告する。【症例】症例は72歳。検診で胸部異常影を認め、精査目的に施行した胸部CTで傍大動脈リンパ節腫大を指摘されて当院に紹介となった。消化器内科での検査で異常なく当科に紹介となった。経陰超音波にて子宮筋層のびまん性肥厚を認めた。子宮体部組織診は正常であった。画像検査にて子宮体部の腫大と骨盤内・傍大動脈リンパ節腫大を認めた。悪性リンパ腫の可能性を摘され血液内科と協議し、腹式子宮全摘術、付属器切除術、骨盤内リンパ節生検術を施行した。病理学的検索では子宮体部原発悪性リンパ腫であり、右骨盤内リンパ節転移も認めた。免疫染色でびまん性大細胞性B細胞リンパ腫の診断となった。血液内科にてR-CHOP療法を6コース施行。治療後の効果判定のPET-CTでリンパ節病変は認めず、現在術後1年で経過フォローとなっている。【考察】子宮原発悪性リンパ腫は極めて稀であり、組織型はびまん性大細胞性型が多いとされている。主訴としては不正性器出血が最も頻度が高く、他に腰痛や下腹部不快感などの症状も報告されているが、本症例ではこれらの症状は認めなかった。悪性リンパ腫においてリンパ節以外の臓器に発生する節外リンパ腫は約25%あることからリンパ節腫大を認める場合、子宮原発悪性リンパ腫の可能性を念頭に置き、積極的に精査加療を行う必要がある。

P-44-13 増大する子宮頸部筋腫より発生した悪性孤立性線維性腫瘍 (solitary fibrous tumor) の1例

津山慈風会津山中央病院

石川陽子, 片山菜月, 片山沙希, 岡真由子, 佐藤麻夕子, 河原義文

症例 45 歳 女性妊娠中, 子宮頸部に 3cm 大の筋腫を認め, 産後 1 か月健診でも同様のサイズであった。産褥 6 か月に, かかりつけ医にて既知の子宮頸部筋腫に対して定期受診をした際に 6cm と急な増大を認め, 精査加療目的に当院に紹介。MRI 検査では頸部筋腫の長径は 9cm に達し, T1 強調画像では低信号, T2 強調画像ではやや高信号も混在する像で, 拡散強調画像では高信号かつ一部 ADCmap 低信号を呈する箇所あり, Gd 造影画像では不均一に描出, 壊死変性を伴い, 肉腫を否定できない像であった。子宮全摘術を施行し, 術中周囲との癒着は認めず, 腫瘍断面は一部壊死と思われる軟組織が認められた。病理組織検査所見では HE 染色にて紡錘形細胞の増殖が密に増生する patternless pattern を認め, 免疫染色では CD34 陽性, STAT 6 陽性, a-SMA・c-kit・Desmin 陰性となり, solitary fibrous tumor : SFT の特徴的な所見を呈しており, 一部に悪性転化を示すものであった。子宮に発生する悪性転化を来した SFT は稀であり, 報告した。

P-44-14 当院で経験した再発子宮体癌に対する Lenvatinib/Pembrolizumab 併用療法の後方視的検討京都府立医大附属北部医療センター¹, 京都中部総合医療センター²沼田朋子¹, 山下 優¹, 北村圭広¹, 渡邊重矢², 菅原拓也¹, 黒星晴夫¹

【緒言】2021 年にがん化学療法後に増悪した切除不能な進行・再発子宮体癌に対して Lenvatinib/Pembrolizumab 併用療法 (LP 療法) の効能・効果が追加承認され, LP 療法の使用拡大とともに様々な免疫関連有害事象 (irAE) が報告されている。当院で LP 療法を行った 2 例を後方視的に検討し, 生じた irAE とその対策について検討した。【症例 1】子宮体癌, 類内膜癌, G1, stage IA。術後 11 か月目に陰断端・後腹膜に再発を認め化学療法を行なったが奏功せず LP 療法を開始した。初回投与後 21 日目に皮下・歯肉出血を認め, 血小板減少性紫斑病 (血小板数 2000 / μ L : Grade 4) を発症した。血小板輸血・ステロイド投与・大量免疫グロブリン静注療法により寛解し, LP 療法を再開したところ血小板減少は再燃しなかった。その後高血圧症や甲状腺機能異常, 上室性頻拍, 手足症候群が出現したが, 再発腫瘍は部分奏功を維持しており現在治療継続中である。【症例 2】子宮体癌, 類内膜癌, G1, stage IVB。術後化学療法後に再発を繰り返し, 4 回目の化学療法後 5 か月で肺病変が増大し, LP 療法を開始した。高血圧症や甲状腺機能異常, 皮膚症状を認めたが, Grade4 以上の有害事象は認めず, 2 サイクル投与終了後に完全奏功となり投与終了した。現在まで再燃なく無治療経過観察中である。【考察】殺細胞性抗がん剤と比較し, 一般に免疫チェックポイント阻害剤による血液毒性は少ないとされるが, 免疫チェックポイント阻害剤と分子標的薬の併用で血液関連 irAE が増加するとの報告もある。LP 療法の使用拡大に伴い今までと機序の異なる血液関連有害事象の出現が増加する可能性があり, 他科との連携を今まで以上に密にすることが重要である。

P-45-1 脊髄髄膜瘤胎児手術早期安全性評価試験の現状報告大阪大¹, 国立成育医療研究センター周産期・母性診療センター²遠藤誠之¹, 味村和哉¹, 木村 正¹, 和田誠司², 左合治彦², 小澤克典²

脊髄髄膜瘤患児に対して従来行われている脊髄髄膜瘤新生児手術と比較して, 神経後などの治療成績が良い脊髄髄膜瘤胎児手術を日本で施行できるようにすることを目的に, 2020 年度より AMED 難治性疾患実用化研究事業の支援を得て, 脊髄髄膜瘤胎児手術の早期安全性評価を臨床研究で行っている。2020 年のコロナ感染蔓延によって, 研究実施施設での新規手術実施が制限されたことなどの影響により, 臨床試験のリクルートを 2020 年 12 月頃まで一時中止をせざるを得なかった。全国の主な周産期センターの中で, 脊髄髄膜瘤を実際に出生前診断している施設から, 賛同を得た 30 施設で脊髄髄膜瘤ネットワークを立ち上げ, 脊髄髄膜瘤胎児手術の紹介体制を整備した。リクルート数は年々増加傾向にあり, リクルート開始から 24 症例の紹介があった。24 症例中, 胎児手術適応症例は 14 症例であった。そのうち 7 例が人工妊娠中絶, 4 症例が出生後治療, そして 4 症例が胎児手術を選択した。妊娠 22 週未満で紹介された 8 例中, 7 例 (87.5%) が人工妊娠中絶を選択した。胎児手術を選択した最初の症例は, 妊娠 25 週 0 日で胎児手術を実施した。しかし, 術後 5 日目に子宮内感染のため分娩となった。NICU にて治療を行ったが, 奏功せず, 生後 3 か月半で永眠した。第 2 症例目は, 妊娠 25 週 4 日で実施した。妊娠 34 週 3 日に腹緊増強により緊急帝王切開となった。児は妊娠中からキアリ奇形の改善を認め, 出生後にも両下肢の運動も保たれていた。脳室拡大は残存しているが, 増悪傾向はなく, シヤント留置もなく経過観察中である。第 3, 4 症例は, 胎児手術を行ったあと, 現在も順調に妊娠継続中である。

P-45-2 胎児のミトコンドリア三頭酵素欠損症に関連した急性妊娠脂肪肝の1例

岡崎市民病院

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【緒言】急性妊娠脂肪肝 (acute fatty liver of pregnancy: 以下 AFLP) は急激な肝不全の進行とともに母体死亡の原因となる重篤な疾患である。胎児の先天代謝異常に起因することが報告されている。今回 AFLP の疑いで帝王切開を行い、児がミトコンドリア三頭酵素 (trifunctional protein: 以下 TFP) 欠損症で死亡した1例を経験した。【症例】26歳。2妊1産。既往歴・家族歴は特記事項なし。【現病歴】X-2年7月自然妊娠で妊娠成立した。妊娠経過は良好であった。26週から推定体重-1.2SD程度で経過、33週4日に-2.0SDの胎児発育不全を認め、34週0日から管理入院となった。34週2日血圧123/94、腹部症状はみられなかったが、肝腎機能・凝固障害を認め AFLP を疑い、同日緊急帝王切開となった。1486g(-2.0SD)の女児を出生し、Apgar Score は1分値8点、5分値9点で、早産・極低出生体重児のため NICU に入院となった。児は日齢7に突然嘔吐、チアノーゼがみられた。心不全のためカテコラミン治療を開始したが、日齢8に死亡した。タンデムマスキリング検査で C16-OH、C18-OH の上昇で TFP 欠損症の疑いであった。遺伝学的検査では HADHB 遺伝子の複合ヘテロ接合を認め、TFP 欠損症と診断した。X年1月に次子を自然妊娠。遺伝カウンセリングを行い、出生前遺伝学的検査は希望されなかった。罹患児である可能性を想定し高次医療機関に転院となった。【考察】TFP 欠損症は常染色体遺伝性遺伝である。胎児が TFP 欠損症の場合には、母体はヘテロ保因者であり脂質関連の代謝機能が低下しており、妊娠後期に母体が AFLP や HELLP 症候群を発症することがある。AFLP や HELLP 症候群を発症した場合は児の先天代謝異常の可能性も考慮する必要がある。

P-45-3 出生後早期にボソリチド投与を開始した軟骨無形成症の一例

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【緒言】軟骨無形成症 (achondroplasia: ACH) は出生時から長幹骨の短縮など、多彩な症状を示す骨系統疾患である。線維芽細胞増殖因子3 (FGFR3) の病的バリエーションにより、FGFR3 が異常な活性化を起こし、軟骨内骨化を障害することが原因である。ACH 初の特異的な治療薬であるボソリチドは2022年6月に国内で承認され、国内外共に乳児への使用経験は少ない。今回、胎児期に ACH を強く疑い、乳児期に確定診断してボソリチド初回投与に至った症例を経験した。【症例】36歳。G1P0、自然妊娠し、前医で妊娠26週に四肢長幹骨短縮と胸郭低形成を指摘され、タナトフォリック骨異形成症疑いで精査管理目的で妊娠33週に当科紹介となった。当院初診時の超音波検査では BPD+3.6SD, FL-4.9SD, HL-4.8SD であったが、胸郭低形成は認めず、胎児ヘリカル CT にて大腿骨骨幹端軟骨骨化不全、腸骨方形化、椎体の扁平化、trident pelvis、骨幹端の軽度拡大・不整を認め、ACH の可能性が高いと判断した。出生前から両親にボソリチドの情報を提供し、出生後 ACH と確定診断した場合、早期に投与可能であることを説明した。その後、児頭骨盤不均衡疑いがあり妊娠37週で選択的帝王切開術を行った。出生後の児の外見所見 (前額部突出、鼻根部陥凹、両側三尖手)、単純 X 線検査、MRI、遺伝子検査で ACH と確定診断し、生後3か月にボソリチドの初回投与を開始した。【結語】妊娠中に胎児が ACH 罹患を強く疑われ、あらかじめカップルにボソリチドの情報提供や説明を十分に行っていたため、出生後早期にボソリチド投与を開始できた。

P-45-4 胎児期に右肺動静脈瘻と診断された稀な一例

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【緒言】肺動静脈瘻は肺動脈と肺静脈が異常吻合をきたす病態であり、多くは30-40歳代で労作時呼吸困難やチアノーゼを呈し発見される。肺動静脈瘻が新生児期に重篤なチアノーゼやアシドーシス、死亡の原因となることは極めて稀である。今回、胎児期に右肺動静脈瘻と診断された症例を報告する。【症例】26歳。2妊1産。自然妊娠。妊娠22週6日に胎児超音波検査で著明な心拡大と肺動脈の拡張を認め、先天性心疾患の疑いで前医より紹介となった。当院で行った胎児超音波検査では、心拡大 (心胸郭面積比55%) および右肺動脈と右肺静脈の拡張、右肺動脈と右肺静脈を交通するシャントを認めた。動脈管は狭窄し、逆行性血流が見られた。胎児水腫は認めなかった。胎児右肺動静脈瘻の診断で、循環器科とともに外来管理を行った。妊娠週数の経過とともに胎児の総心拍出量、動脈管逆行性血流の増加がみられたが、胎児水腫は認めなかった。妊娠34週0日に施行した MRI 検査では、右肺下葉肺底部 S10 近傍に右肺動静脈瘻を認めた。当科、新生児科、循環器内科、心臓外科でカンファレンスを行い、妊娠37週1日に帝王切開で分娩し、児は開胸手術を行う予定としていた。妊娠36週0日、胎動減少を主訴に救急受診し子宮内胎児死亡を確認した。病理解剖は希望されず、死亡時画像診断を行ったが、右肺動静脈瘻と死後の変化を疑う所見以外に新たな異常はなかった。【結語】胎児期に肺動静脈瘻と診断される症例は非常に稀である。胎児心循環機能を評価し、周産期管理を行ったが子宮内胎児死亡となった。

P-45-5 胎児診断した心臓横紋筋腫に対してシロリムスの経胎盤投与が奏功した1例

藤田医大

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【緒言】心臓横紋筋腫は結節性硬化症 (TSC) 患者の約半数にみられる良性腫瘍であるが、胎児期発症例で未治療の場合は約23%が新生児期までに死亡するとされている。左室流出路狭窄を伴う心臓横紋筋腫の胎児診断例に対し、シロリムスの経胎盤投与により腫瘍縮小と血行動態改善を得たので報告する。【症例】母は29歳、1妊0産。既往歴や家族歴なし。妊娠27週に胎児心臓腫瘍の精査目的に当院を紹介受診した。胎児心臓超音波検査で、最大径30mmの多発心臓腫瘍と心嚢水を認め、心臓横紋筋腫が疑われた。不整脈および腎腫瘍は認めなかった。胎児MRIで脳室上衣下結節を認め、Definitive TSCと診断した。心臓腫瘍は緩やかに増大し、左室流出路狭窄と心拡大が出現したため、当院臨床倫理審査委員会の承認の下、妊娠30週よりシロリムス2mg/日の経胎盤投与を開始した。シロリムスの目標母体血中濃度は10~15mg/dLとし、妊娠32週に3mg/日に増量した。妊娠34週には腫瘍は縮小傾向に転じ、心嚢水は減少し左室流出路狭窄も改善した。妊娠37週にシロリムスの投与を終了し、妊娠38週に選択的帝王切開術を施行した。出生児は女児で体重2,462g, Apgar score 8/9点 (1/5分)、臍帯動脈血pH 7.180であった。超音波検査で最大径22mmの心臓腫瘍を、頭部MRIで上衣下結節、皮質結節および右側脳室前角の腫瘍を認め、TSCと再診断した。日齢1よりエベロリムス0.1mg/日の投与を開始した。心機能は徐々に改善し、日齢39に退院した。【結語】胎児期発症TSCの心臓横紋筋腫には、シロリムスによる胎児治療が有効な選択肢となりうる。しかし本邦での治療実績は乏しいため、治療効果や安全性、症例選択基準等について検討が必要である。

P-45-6 胎児超音波にて食道拡張を認めた幽門閉鎖症合併表皮水疱症の1例

筑波大

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【緒言】表皮水疱症は表皮真皮間の蛋白遺伝子異常により、軽微な刺激で容易に水疱を生じるまれな遺伝性疾患である。幽門閉鎖症を合併する病型が知られており、その場合は重症で致死性が高いとされる。今回、胎児超音波検査で拡張した食道が描出されていたが、出生時より認めた皮膚異常により、幽門閉鎖症合併表皮水疱症の診断に至った症例を経験したので報告する。【症例】33歳、2妊1産。妊娠33週に羊水過多と胎児発育不全のため当院へ紹介となった。妊娠34週の胎児超音波検査で拡張し、蠕動する食道を認めたが、以降の診察では食道が描出されないこともあった。胃はやや拡張していたが、大きさも形状も一定ではなかった。十二指腸より上部の消化管通過障害が疑われ、妊娠37週の胎児MRI検査でも胎児食道の拡張を確認した。妊娠38週0日陣痛が発来し、自然分娩により1740gの女児を出産した。児は出生時より顔面と四肢にびらん、表皮欠損を認めた。胎児超音波所見と新生児皮膚所見より幽門閉鎖症合併表皮水疱症が疑われ、皮膚生検により単純型表皮水疱症と診断された。また日齢4に幽門閉鎖解除術が施行された。児は現在、皮膚感染加療と栄養管理を継続中である。【考察】幽門閉鎖症合併表皮水疱症は重篤であり、早期診断、出生前カウンセリングが望まれる。しかし、いくつかの特徴的な所見から胎児診断された報告はあるものの、典型像を示さない症例もあることや疾患自体がまれであることから、診断に苦慮することが予想される。胎児超音波検査で拡張した食道が確認される際には、幽門閉鎖症、さらにはその合併症として表皮水疱症を念頭においた診察を行う必要があると考えられた。

P-45-7 胎児診断で重症な呼吸障害が予測されたが救命可能であった総排泄腔遺残の一例鹿児島市立病院¹, 鹿児島市立病院新生児内科²谷口貴之¹, 橋本崇史¹, 齊藤大祐², 切原奈美¹, 谷口博子¹, 前田隆嗣¹, 上塘正人¹

【緒言】総排泄腔遺残は尿道、膈、直腸が一つの共通管(総排泄腔)に合流し、共通管のみが会陰部に開口する疾患で、発生頻度は約5万出生に1人と稀である。今回我々は胎児診断で重度の呼吸障害が予測されたが救命可能であった総排泄腔遺残の一例を経験したので報告する。【症例】33歳2妊1産自然妊娠、妊娠26週の妊婦検診で胎児腹水が疑われ妊娠28週で当院へ紹介された。初診時の経腹超音波検査で腸管拡張、両側水腎症、水腫症、鎖肛を疑う所見を認め、総排泄腔遺残と診断した。また、Amniotic fluid index 3.4cmと羊水過少を認め、29週以降は羊水腔は認めなかった。水腫症の悪化から腹部膨満が著明で横隔膜は挙上しており、出生直後から水腫症に対するドレーナージと高度の呼吸器管理を要すると判断した。在胎35週3日胎児機能不全 (recurrent late decelerations, variability minimum) のため緊急帝王切開で出生し、出生体重3179g Apgar score 1/6点で出生直後から人工呼吸管理を行い、遷延性肺高血圧に対する一酸化窒素療法と両側緊張性気胸に対する胸腔ドレーン留置を行った。日齢1で膈ドレーナージ術、経皮的膀胱瘻置設術、人工肛門増設術を施行し呼吸状態が安定したため日齢7で抜管となった。その後日齢34で膀胱瘻閉鎖となり、日齢53に自宅退院となった。【考察】総排泄腔遺残は、多彩な臨床像を示すが重症例では高度の尿路狭窄のため羊水過少や肺低形成を来し、出生直後から集学的なチーム医療を要するため、正確な出生前診断が重要である。【結語】本症例では胎児超音波検査により出生前から経時的に病態を評価し、関係各科で情報共有する事で円滑に出生後集学的な治療を行うことができた。

P-45-8 胎児期に進行性の脳破壊をみとめ孔脳症に至った COL41A 遺伝子変異の1例

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【緒言】孔脳症とは、大脳半球内に脳室との交通を有する嚢胞や空洞が見られる先天異常である。胎生期の感染症や脳梗塞、脳出血といった脳循環障害により発生すると考えられている。今回、妊娠27週より脳室拡大を認め、脳実質の破壊から孔脳症に至り、出生後にCOL41A遺伝子変異の診断となった1例を経験したので報告する。【症例】35歳、2妊1産、妊娠糖尿病と診断されていたが、近医で妊娠経過は良好であった。妊娠27週で側脳室の拡大が指摘され、妊娠30週から胎児発育不全(-2.5SD)も認めため、妊娠32週に当院に紹介となった。TORCH感染症スクリーニング陰性。胎児MRI検査で、小脳低形成、側脳室拡大、脳実質に腫瘍性病変や脳出血を示唆する所見を認めた。妊娠34週で再検したMRI検査では、脳室拡大、脳実質の破壊が進行しており、脳出血、孔脳症が疑われた。児の予後は短いと予想され、新生児科医師によるprenatal visitを行い、本人、家族と十分に相談した上で、計画分娩とした。誘発にて妊娠37週6日に分娩となった。胎盤病理で異常所見を認めなかった。児は1658g、Apgar score 1分値3点、5分値7点。自発呼吸は安定しており、低出生体重児のため、NICU入院した。眼球異常や甲状腺機能低下を認めたが、日齢30日で自宅退院した。児の遺伝子検査でCOL41A遺伝子異常症の診断となった。精神運動発達遅滞、症候性てんかんを認めるものの、生後1年以上の生存を得ている。【考察】COL41A遺伝子変異により、脳出血、孔脳症に至ると報告されている。本症例でもCOL41A遺伝子変異が孔脳症の原因と考えられた。胎児期の脳室拡大、脳出血を認める症例では、COL41A遺伝子変異を有する可能性を考慮する必要がある。

P-45-9 異なる転帰をたどった染色体構造異常2症例の出生前遺伝カウンセリングと周産期経過

宮崎大

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【背景】染色体異常は数的異常と構造異常に大別される。近年、出生前遺伝カウンセリングの重要性が広く認知され数的異常に関する情報提供は標準化されつつある。一方で、染色体構造異常は各疾患の発生頻度が少なく情報が限られているため、診断時の遺伝カウンセリングは慎重に進める必要がある。いずれも胎児形態異常を契機に診断された2症例を経験したが異なる周産期経過をたどった。【症例1】25歳G1P0妊娠17週に胎児水腫、小頭症を指摘され紹介受診した。遺伝カウンセリング後に羊水染色体検査を行い、G-分染法で13番環状染色体の一部が13モノソミーのモザイクを認めた。夫婦で相談を行い、妊娠継続を断念した。過去の報告は全て孤発例であったが、次子妊娠に際して、希望に応じて遺伝カウンセリングを行う予定である。【症例2】26歳G4P2近医で妊娠初期にNT肥厚を認めたが、更なる出生前検査は希望しなかった。妊娠20週に高度の胎児発育不全と心奇形を指摘され当院を紹介受診した。遺伝カウンセリング後に羊水染色体検査を行いFISH法で13,18,21番染色体の数的異常は認めなかった。妊娠22週にG-分染法結果が判明し、4番染色体短腕欠失症候群であった。当院での周産期管理を継続したが、妊娠33週で子宮内胎児死亡となった。第3子であり、現時点では両親の染色体検査は希望しなかった。【考察・結論】染色体構造異常は表現型や予後・遺伝形式が多様であり、診断時に丁寧な遺伝カウンセリングが重要である。また、次子再発率は突然変異もしくは均衡型相互転座由来により異なるが、両親の検査については遺伝の専門家による正確な情報提供を行い、受験意志の有無を尊重し慎重に進めることが必要である。

P-45-10 当院において出生前診断で先天性胆道拡張症が疑われた4症例

大分県立病院

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先天性胆道拡張症 (congenital biliary dilatation, 以下 CBD) の出生前診断は超音波検査で早いもので妊娠15-20週から同定される胎児の肝下面に存在する増大傾向を有する嚢胞像により行われる。本症は出生後早期に閉塞性黄疸や消化管通過障害のリスクを伴うため出生前診断が必要である。CBDを疑った4例を経験したので報告する。【症例1】31歳、1妊0産、妊娠24週に胎児肝下面に径17×12mmの嚢胞を認めた。嚢胞は次第に増大し、分娩前には径45×40mmとなった。妊娠40週0日に頭位経陰分娩となった。出生後も嚢胞が増大傾向で日齢19に根治術が施行された。【症例2】37歳、2妊0産、双胎妊娠の症例。妊娠28週に胎児肝下面に径17×14mmの嚢胞を認め、分娩前には径22×25mmと増大した。妊娠37週0日、選択的帝王切開分娩となった。出生後も嚢胞が増大傾向で日齢37に根治術が施行された。【症例3】30歳、1妊0産、側弯症のため妊娠34週に当科初診し、超音波検査で胎児肝下面に胆道系へと管腔構造を伴う約20×10mmの嚢胞を認めた。妊娠40週3日に頭位経陰分娩となった。児は合併症なく経過し、日齢115に根治術が施行された。【症例4】29歳、2妊1産、妊娠35週に胎児腹部腫瘤を指摘され、妊娠38週に当科紹介となった。胎児肝下面に約1cmの嚢胞を認めた。妊娠40週2日に頭位経陰分娩となった。児の経腹超音波断層法では嚢胞は右副腎由来で、腹部造影CTの所見から右副腎出血と診断した。腫瘤は生後4か月で消失した。CBDは鑑別診断として肝嚢胞、重複胆嚢、副腎腫瘍が挙げられる。出生前診断のためには胎児スクリーニング時期からの肝下面の嚢胞像の同定とサイズ変化の観察が重要である。

P-45-11 Cornelia de Lange 症候群の胎児超音波所見

北里大

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【緒言】Cornelia de Lange 症候群 (CdLS) は、胎児発育不全 (FGR) や特徴的顔貌、多毛症、上肢の異常などを呈する奇形症候群である。出生1万～8万人に1人の頻度で発生する稀な疾患で出生前診断は困難な場合が多い。今回、出生前診断に難渋し、出生後にCdLSと診断した一例を報告する。【症例】31歳、初産婦。前医の超音波検査で、妊娠27週にFGR、妊娠29週にはdouble bubble signと羊水過多を認めたため、当院を紹介受診した。当院の超音波検査では、上記の所見に加えて短頭、耳介低位、小顎、心室中隔欠損、左上大静脈遺残、右左手を認めたため21トリソミーなどの複合疾患を疑った。なお、患者は羊水染色体検査を希望しなかった。妊娠36週2日に臍帯潰瘍のリスクを考慮し選択的帝王切開を施行した。児は1760gの男児で、出生前診断の所見に加えて両側停留精巣、多毛(頭髪・眉毛・睫毛)、小さく上向きの鼻といった特徴的顔貌を認めたことからCdLSの診断に至った。出生後に胎児超音波所見を振り返ると、多毛・鼻といった特徴的な体表所見の一部が確認できた。児は十二指腸閉鎖根治術を施行され経過良好である。また、正常核型であったため遺伝子検査を予定している。【結語】本症例は胎児期に21トリソミーなどの複合疾患を疑ったがCdLSの診断には至らなかった。FGRに加えて上肢異常・顔面異常・先天性心疾患・消化管異常などの所見を認めた場合には、CdLSを念頭に置き、上肢や頭部・顔面の体表に焦点を絞って精査を行うことで、出生前診断につなげる可能性があると考えた。

P-45-12 乳癌発症後に妊娠が判明し、化学療法を施行しながら妊娠継続し出産へと至った一例

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中村一仁, 栗山千晶, 杉井裕和, 伊藤裕徳

【緒言】本邦において乳癌は女性の癌の罹患数として最も多く、その罹患率は30代後半から増え、40代後半から50代前半にピークを迎える。妊娠年齢は高齢化しており、乳癌合併した妊娠症例に遭遇する機会は高まっている。今回不妊治療中であった30歳女性に乳癌が判明し、精査中に妊娠が発覚したが、カウンセリングを経て化学療法を受けながら妊娠を継続し、出産まで至った一例を経験したため、妊娠の経過及び児の予後を含めて報告する。【症例】30歳女性、2妊0産、自然流産1回、結婚後2年経過するも妊娠しないため挙児希望のため、当科外来を受診。不妊治療中に右乳房腫瘍を自覚、乳腺外科診察にて右乳癌IIA期以上の診断となった。乳癌の精査目的にPET-CT、MRI検査等を施行。卵子凍結を検討していた所、妊娠4週であることが判明した。乳癌合併妊娠について当院での経験症例はなかったため、症例経験のある病院のセカンドオピニオンを受けた。カウンセリングを経て乳癌治療を受けながら妊娠を継続する方針となった。治療方針について産婦人科、乳腺外科と協議しながら推し進め、妊娠16週の際に右乳房全切除術及びリンパ節サンプリングを施行。後療法としてシクロホスファミド、アドリアマイシンを4コース施行し、産後にドセタキセルを施行する方針とした。児はFGR傾向ながらも発育を認め、妊娠36週6日に前期破水、同日経陰分娩にて出生。体重2176g、Apgar score 8/9(1分/5分)、児には房室中隔欠損を認めた。【考察】本邦では乳癌合併妊娠の妊娠継続率は少ないが、乳癌治療を受けながら生児を得ることができた。母児の将来のためにも適切かつ十分なカウンセリングが重要であると考えられる。

P-45-13 胎児18トリソミーの妊婦が破水時に常位胎盤早期剝離を発症し超緊急帝王切開となった2症例

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【緒言】18トリソミーは、胎児発育不全、羊水過多、心奇形、消化管閉鎖、手指重合など多彩である。今回我々は染色体検査で18トリソミーと診断、経陰分娩を試みたが破水時に常位胎盤早期剝離となり超緊急帝王切開を施行した2症例を経験したので報告する。【症例】症例1は36歳、1妊0産で不妊治療で妊娠成立し当院紹介となった。妊娠19週の超音波所見で胎児発育不全、小脳低形成や心室中隔欠損など認めた。羊水過多が著明で羊水除去し、染色体検査で18トリソミーが確定した。36週6日で破水し超音波所見で常位胎盤早期剝離を認め、超緊急帝王切開となった。児は男児、体重1454g、Apgar Score0/7点、pH6.864、BE-23.4mmol/Lであった。症例2は33歳、3妊1産で自然妊娠で胎児発育不全のため妊娠32週に近医より紹介受診となった。超音波所見で心室中隔欠損や食道閉鎖を疑った。羊水過多が著明で羊水除去し、染色体検査で18トリソミーが確定した。妊娠37週で分娩誘発中に破水し超音波所見で常位胎盤早期剝離を認め、超緊急帝王切開となった。児は女児、体重1674g、Apgar Score1/7点、pH7.230、BE-4.4mmol/Lであった。また食道閉鎖C型を認めた。【結論】今回2症例とも18トリソミーで羊水過多を認め、破水直後に常位胎盤剝離を発症した。羊水過多のある症例は破水時に常位胎盤早期剝離を引き起こす可能性がある。また18トリソミーの場合、小児科医や小児外科医による出生後の処置が必要である。そのため分娩時期の調整が必要で、かつ緊急帝王切開を避ける必要もあり、経陰分娩(分娩誘発)前の羊水除去または予定帝王切開を選択することで、羊水過多による常位胎盤早期剝離を防止できると考える。

P-46-1 常位癒着胎盤に対する新たな子宮温存手術～TURIP 法～

三重大

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【目的】近年、高齢妊娠、帝王切開率の上昇、体外受精の増加により、癒着胎盤は増加し、妊産婦死亡の原因としても散見される。常位癒着胎盤は、術前診断が困難であり、集学的治療の機会を逸しやすい。また、子宮動脈塞栓術や子宮全摘術は、妊孕性低下・喪失が問題となる。これらを解決する手術法として、TURIP(Tourniquet, UteRine Inversion and Placental dissection) 法を考案した。【方法】TURIP 法には3つのポイントがある。1つ目は、子宮峡部をネラトンカテーテルで結紮し、子宮への血流を遮断して出血量を抑えること、2つ目は、ニトログリセリンを静脈内投与し、子宮を弛緩させ、内反させ、癒着した胎盤を直視下で切除すること、3つ目は、胎盤剝離部位における子宮筋層の出血点を直視下で確実に縫合止血できることである。10例の未診断の常位癒着胎盤(帝王切開時に施行した7例、経陰分娩後に施行した2例、帝王切開後の再出血に施行した1例)に施行した。【成績】年齢、分娩週数、手術時間、術中出血量の中央値は、それぞれ40(38-41)歳、38(34-39)週、113(101-148)分、2,568(2,235-3,358)mlであった。全例で、周術期合併症はなく、一期的な子宮温存に成功した。また、術後3か月に、骨盤部MRIを施行し、子宮は瘢痕・死腔なく修復されており、月経再開後も問題を認めなかった。1例は、次の妊娠が成立し、癒着胎盤の再発なく、帝王切開で生児を得た。【結論】TURIP 法は、高度な技術や事前の準備を必要とせず、簡易であるため、未診断の常位癒着胎盤の妊孕性温存術として適している。帝王切開時に診断された症例だけでなく、経陰分娩時の緊急止血、帝王切開後の再出血による止血にも適用できる。

P-46-2 出血リスクの高い子宮鏡手術時における内腸骨動脈バルンカテーテル併用が、手術や妊孕性に与える影響について

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【目的】子宮鏡手術は低侵襲で妊孕性に配慮した術式であるが、大量出血リスクのある場合に妊孕性を低下させる可能性のある子宮動脈塞栓術(UAE)を必要となることがある。今回、我々は出血リスクが高いと判断した子宮鏡手術に際し、術中の動脈バルンカテーテル留置(balloon catheter; BC)が、手術やその後の妊娠予後に与える影響を後方視的に検討した。【方法】倫理委員会承認の下、2019年1月から2023年9月までに施行した内腸骨動脈バルンカテーテル併用子宮鏡手術9例(BC群; retained products of conception [RPOC] 7例、頸管妊娠1例、帝王切開癒着胎盤1例)を対象とした。患者背景、動脈阻血時間、手術時間、合併症、入院日数、術後月経再開までの日数、術後妊娠成績を、子宮動脈塞栓術(UAE; 2011年1月から2023年8月)を併用した子宮鏡手術12例(UAE群)と後方視的に比較検討した。【成績】両群間で患者背景に差はなく、BC群では内腸骨動脈阻血時間は30(19-49)分であり、カテーテル関連合併症は認めなかった。両群間で手術時間、術中出血量に差はなく、UAE群では1例の輸血施行症例を認めた。入院日数は、BC群2(2-3)日、UAE群6(3-10)日でBC群が有意に短かった($p < 0.05$)。手術施行から月経再開までの日数は、BC群30.5(28-42)日、UAE群30(19-240)日と差を認めなかった。BC群は術後7名に挙児希望があり、4名が妊娠、内2人が生児を獲得、1名は現在妊娠10週、1名は妊娠9週に稽留流産となった。UAE群は、フォローアップできた10名中4名が生児を得た。【結論】BCの併用はUAEと比べ、効果に遜色なく安全に施行できた。BC併用子宮鏡では、入院期間の短縮や妊孕性温存が期待できる可能性がある。

P-46-3 当院における骨盤位外回転術の成功率とその背景

ベルランド総合病院

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【目的】当院では骨盤位の経陰分娩を行ってならず帝王切開の適応としている。帝王切開率を減少させるため、単胎骨盤位に対して外回転術を施行している。今回その成功率、合併症、最終分娩転帰について検討した。【方法】2020年1月から2022年12月までの期間、当院で外回転術を行った36例を対象とした。当院では全例妊娠36週台で外回転術を行っており、術開始前にNSTでreactiveを確認し子宮収縮抑制剤の投与を行い、術中は超音波断層法で胎児心拍を確認しながら手術を行う。手術終了後と翌日のNST評価を行い退院としている。【成績】対象患者36例のうち、初産婦は18例、経産婦は18例であった。成功率は55.6%であり、うち初産婦では50%、経産婦では61.1% ($p=0.502$)と有意差を認めなかった。BMI、推定体重、羊水量、胎盤位置には有意差を認めなかった。合併症は全症例のうち15例(42%)で認め、出血が1例、破水により緊急帝王切開術を施行した例が1例、臍帯先進により緊急帝王切開術を施行した例が2例、術中に胎児心拍異常を認めたものが12例であった。最終分娩転帰については経陰分娩が17例(47%)、帝王切開術が19例(53%)であった。帝王切開の内訳は成功例の群で4例(20%)、不成功の群で15例(94%)であった。【結論】合併症のために緊急帝王切開に至った例は3例であった。しかし緊急帝王切開を行える体制と十分な周産期管理によりいずれの例でも母児ともに術後経過は良好で重篤な影響を最小限にできた。外回転術は合併症のリスクを伴うため患者への十分な説明と同意のもとで行うことが重要である。外回転術により全体の帝王切開率の低下につながり骨盤位の管理として妥当な選択肢となりうると考える。

P-46-4 子宮内容除去術後のRPOC発生率の検証(手動真空吸引法と掻爬法の比較解析)

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【目的】近年, 妊娠初期の流産手術および人工妊娠中絶の術式として母体低侵襲とされる手動真空吸引法(manual vacuum aspiration法:MVA法)が普及してきている。しかし, MVA法と従来から行われている掻爬法の術後の子宮内遺残(retained products of conception:RPOC)の発生率を評価した報告は少ない。自施設の症例で比較検証した。【方法】2020年1月から2023年6月に当院で妊娠12週未満に流産手術および人工妊娠中絶術を受けた症例を後方視的に調査した。対象を掻爬群とMVA群に群別し, その背景および術後のRPOC発生率, 追加治療率, 輸血率を算出し比較解析した。【成績】対象74例中, 掻爬群が46例, MVA群が28例だった。MVA群の平均吸引回数は 3.2 ± 1.2 回だった。流産手術は掻爬群で27例(58.7%), MVA群で24例(85.7%), 人工妊娠中絶は掻爬群で19例(41.3%), MVA群で4例(14.3%)だった($p=0.019$)。手術時の妊娠週数は掻爬群, MVA群ともに8[5-11]週だった($p=0.351$)。RPOC発生率は掻爬群で4例(8.7%), MVA群で3例(10.7%)だった($p=1$)。RPOC症例で経過中に追加治療(血管塞栓術)と輸血を要したのはMVA群の1例のみであった。【結論】今回の調査において, 妊娠初期の流産および人工妊娠中絶術後のRPOC発生率は, 処置の背景が異なるものの掻爬群とMVA群で有意な差を認めなかった。症例数を重ねた上でのさらなる検証が望まれる。

P-46-5 当院における選択的帝王切開の予定週数と予定手術日直前の緊急帝王切開移行率・時間外手術の検討

鴻仁会岡山中央病院

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【目的】産婦人科診療ガイドラインでは, 選択的帝王切開施行時期は各施設の診療体制に応じて決定するのが望ましいとされている。ACOGは妊娠39週以降での施行を推奨しているが, 緊急帝王切開・時間外手術が増加する可能性が指摘されている。手術予定日前に緊急帝王切開となった割合は38週で10-19%, 39週台で25%との報告がある。当院では単胎の選択的帝王切開を概ね妊娠38週後半~39週に設定しており, 緊急帝王切開移行率について検討を行った。【方法】2021年1月から2023年5月の間の当院での全分娩数2633件のうち, 帝王切開分娩の515件について後方視的検討を行った。妊娠38週台に予定した群(38週予定群)と妊娠39週台に予定した群(39週予定群)に分けて緊急帝王切開移行率を比較し, 時間外手術件数について調べた。双胎妊娠・前置胎盤を除外した。【成績】予定された選択的帝王切開は327件あり, そのうち38週予定群は155件, 39週予定群は166件であった。緊急帝王切開移行率は47件で, 38週予定群は13件(8.4%), 39週予定群は34件(20.5%)であった。時間外の緊急帝王切開は20件(42.6%)であった。仮に全例で妊娠38週台に帝王切開を行ったと仮定した場合に緊急帝王切開が回避できた症例は8例(時間外手術3例)のみであった。仮に全例で妊娠38週台に帝王切開を行ったと想定した場合に緊急帝王切開は18例増加すると推測された。【結論】選択的帝王切開が手術予定日より以前に緊急帝王切開となった割合は38週予定群・39週予定群ともに, 8.4%, 20.5%と既存の報告より若干少なかった。約半数近くが時間外に行われていた。各施設の診療体制に応じて選択的帝王切開の施行時期を設定することが望ましい。

P-46-6 妊娠29週で発症し付属器摘出術を要した黄体化過剰反応の一例

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黄体化過剰反応(Hyperreactio luteinalis:HL)は高hCG環境やhCGに対する過剰反応により卵巣腫大をきたす病態である。妊娠終結で退縮するため保存的加療が可能だが, 疼痛を伴う場合手術を要することがある。妊娠29週でHLによる卵巣茎捻転に対し捻転解除術により卵巣温存を試みたが, 再度子宮による圧迫で卵巣虚血となり付属器摘出術を余儀なくされた症例を報告する。症例は29歳, G1P0, 特に既往歴はない。自然妊娠成立し, 概ね順調に経過していた。妊娠29週1日, 右下腹部から側腹部の疼痛および嘔吐のため受診した。経腹超音波断層法で卵巣は右が11cm大, 左が6cm大と両側の多嚢胞性腫大を認め, 特徴的な画像所見と妊娠中の増大から黄体化過剰反応と診断した。右卵巣は側腹部に位置し疼痛部に一致していた。卵巣茎捻転を疑い手術の方針とした。腹腔鏡での観察にて180度の右卵巣茎捻転を認め, 腹腔鏡下捻転解除術, 卵巣多孔術による卵巣の縮小を図り卵巣を温存した。術後疼痛は消失したが, 4日目に右側腹部痛の再燃と右卵巣の再度の腫大を認め, 再捻転や圧迫による卵巣虚血を疑った。鎮痛薬で経過観察としたが症状が持続し, 妊娠30週0日で腹式右付属器摘出術を行った。右卵巣は初回手術時と同様に側腹部に位置し, 捻転は認めないが強い鬱血により暗赤色調を呈し温存不能と判断した。腫大卵巣の偏位により子宮に圧迫され血流障害が生じたと推測された。術後妊娠経過は順調である。本症例ではHLを術前に診断でき卵巣の温存を試みたが最終的には摘出を余儀なくされた。妊娠中期以降では卵巣の位置の修正は困難であり, 増大子宮による卵巣への圧迫が強い症例では卵巣の温存が困難な場合がある。

P-47-1 母乳哺育が妊娠糖尿病既往女性の産後早期の脂質プロファイルに与える影響

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【目的】妊娠糖尿病 (GDM) 既往女性は将来の2型糖尿病とメタボリック症候群のハイリスク集団である。母乳哺育はその発症予防に有効であることが知られているが、母乳哺育が産後の脂質代謝に及ぼす影響については一定の見解がない。今回、母乳哺育と産後早期の脂質プロファイルの関連を検討した。【方法】前方視的コホート研究として、単胎 GDM 妊婦を妊娠中に登録し、産後6~9週の耐糖能検査時(空腹時)の総コレステロール (T-cho)、中性脂肪 (TG)、HDL および LDL コレステロールを測定した。母乳強度は完全母乳 (=6) からミルクのみ (=1) まで6段階に設定し脂質と母乳強度の関連を検討した。また、80%以上母乳 (=4) 以上を高強度授乳 (HIB) と定義し、高TG血症 (≥ 150 mg/dL) および高LDL血症 (≥ 140 mg/dL) の調整オッズ比 (aOR) を算出した。【成績】対象は185例で分娩後7.3週に耐糖能検査を施行した。各脂質は T-cho 210 \pm 33, TG 73 \pm 49, HDL 72 \pm 1 および LDL 127 \pm 30 (mg/dL) であった。母乳強度は1から6まで各々2%, 6%, 7%, 8%, 16% および61% で、HIBは85%であった。HDL以外の脂質はいずれも母乳強度が強くなるほど有意に低下した。Non-HIBに対してHIBでは高脂血症の発症頻度 (aOR [95% 信頼区間]) が有意に低頻度であった (高TG血症 0.15 [0.04-0.56], 高LDL血症 0.24 [0.09-0.58])。【結論】母乳哺育は、GDM 既往女性の分娩後早期の脂質プロファイルを改善する効果が顕著であることを明らかにした。

P-47-2 我が国における妊娠糖尿病既往女性に対する産後血糖スクリーニングの実態—レセプトデータ解析によるリアルワールドエビデンス

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【目的】妊娠糖尿病 (GDM) は比較的多い妊娠合併症である。GDM 既往女性の一部で産後も持続する耐糖能異常を見逃さないために、産後のスクリーニングが有用である。産後の糖尿病管理を推進する観点から2020年度より在宅妊娠糖尿病患者指導管理料 (GDM 管理料) 2 が算定可能となったが、全国規模における実際の算定状況を含めた産後スクリーニング状況は不明である。本研究の目的は、レセプトデータを用いて我が国における産後スクリーニングの実施状況を明らかにするとともに、スクリーニング実施率に影響する因子を同定することである。【方法】JMDC 保険者データベースより、2012年4月から2021年1月までの間に、分娩日が特定でき、自己血糖測定のためにGDM 管理料1を算定されたハイリスク GDM 女性を抽出し、産後6-12週における75gOGTT 実施率を調査した。分娩日以前に糖尿病の確定病名が付与されている症例は除外した。【成績】データベースより2282人の対象女性を抽出した。コホート全体における産後6-12週における75gOGTT 実施率は29% (654/2282) であった。GDM 管理料2導入後の75gOGTT 実施率は33%であり、それまでと比較し上昇傾向であったが、GDM 管理料2の算定率は約13%と低値であった。産後6-12週における75gOGTTの施行率に関連する因子の検討では、分娩施設とGDM 管理施設が異なる場合に産後6-12週における75gOGTTの施行率が低いことが示唆された。【結論】本研究により、GDM 管理料2導入後もGDM 既往女性に対する産後スクリーニングの実施率が限定的であることが示唆された。産後スクリーニングの必要性についての認識を向上させ、2型糖尿病の早期発見・予防のための適切な医療体制を構築することが望まれる。

P-47-3 妊婦の栄養素摂取量と母児の血液サイトカイン濃度の関連

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【目的】妊婦の摂取栄養素と母児の免疫機能の関わりが注目されている。妊婦の多様な栄養素の摂取が、腸管免疫などを介して母児のサイトカイン濃度に影響を及ぼすとの仮説を想定し、その検証を試みた。【方法】倫理委員会の承諾の下、満期妊婦72例 (妊娠36週から38週) に選択的帝王切開を行った症例ならびに非妊婦37例 (25歳-43歳) から同意を得て、母体血並びに臍帯血を採取し、栄養調査票による調査を行った。食物繊維、飽和脂肪酸、不飽和脂肪酸、多価脂肪酸、エネルギー、酪酸、ビタミンC、ビタミンD、トコフェロール、 ω 3脂肪酸、 ω 6脂肪酸、食物繊維の摂取量と血液サイトカインアレイ解析 (IL-4, IL-8, IL-10, IL-12, IL-13, IL-17, G-CSF, IFN- γ , MCP-1, MIP-1 β , TNF- α) の関連を検討した。【成績】満期妊婦72例の中央値 (四分位) は、年齢34.0歳 (31歳-37歳)。臍帯血サイトカイン値は母体血より高値を示し、かつ正の相関あるいはその傾向を認めた。ビタミンC、トコフェロール、食物繊維総量、不溶性食物繊維、多価飽和脂肪酸の摂取量は母体血 TNF- α 値と正の相関がみられた。また、ビタミンCはIL-13値、MCP-1値と、 δ トコフェロールはIL-4値、IL-8値とも正の相関がみられた。非妊婦37例においてこのような相関はみられなかった。【結論】満期妊婦の摂取した栄養素は母児の血中サイトカイン値に関連する可能性が示唆された。

P-47-4 セルフリー DNA 濃度の運動負荷後の変化とクリアランス速度

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【目的】セルフリー DNA (cfDNA) とは、細胞外に存在する DNA であり、循環血液中にある cfDNA は非侵襲性出生前遺伝学的検査 (NIPT) や疾患の診断に有用なバイオマーカーとして注目を集めている。近年 cfDNA の生理学的意義について様々な研究が行われており、我々は血液中の cfDNA のメチル化部位が、短時間の経過で変化することを確認した。cfDNA に情報伝達物質としての役割があるならば、cfDNA の排出が速いほど、そのメチル化変化が生体の状態をリアルタイムに表す指標として意義をもつと考え、cfDNA のクリアランス時間に着目した。本研究では、健康男性に対する運動負荷後に血液検査を行い、cfDNA のクリアランス速度を明らかにすることを目的とした。【方法】運動負荷の1週間前に採血を行い肝腎機能に異常がないことを確認した男性被験者5名を対象とした。運動負荷直前に採血を行い、トレッドミルによる30分間の軽度の運動負荷を行った後に、運動終了直後とその10、20、30、60分後に採血を行い、cfDNA 濃度を TapeStation (Agilent) を用いて測定した。【成績】健康男性の運動負荷後の cfDNA の濃度は運動負荷終了後10分ほどで最高値に達した。その後徐々に減少し、cfDNA の半減期は約30分であり、約1時間後に運動前の濃度に戻ることが示された。【結論】血中の cfDNA の入れ替わりは速やかであることからリアルタイムに生体の状態を表す指標として用いることができると考えられ、その役割について今後も検討していく。

P-47-5 COVID19 流行前後における当院での社会的ハイリスク妊産婦に関する比較検討

市立岸和田市民病院
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【目的】COVID19 流行により出生数の減少や経済的・精神的不安の増加などが報告されてきたが、妊産婦について COVID19 流行前後での変化を検討した報告は少ない。当院は以前に社会的ハイリスク妊産婦に関する検討を行い本学会で発表を行った。今回当院における社会的ハイリスク妊産婦について COVID19 流行前後で比較検討し、その特徴の変化について調査することを目的とした。【方法】COVID19 流行第一波の開始である2020年1月29日から2023年6月30日までの期間に当院で妊娠22週以降に分娩となった妊産婦のうち社会的リスクを有する妊産婦を対象とし、その特徴や分娩の転帰につき後方視的に検討した。【成績】調査期間中の総分娩件数は459件で、2021年以降は軽度増加傾向であった。要支援対象妊婦は160人であり、要支援妊婦の占める割合は2020年39.7%、2021年33.8%、2022年36.7%、2023年23.4%であり、2021年以降はやや減少傾向であるが、概ね30%を超える高い割合で推移していた。要支援の理由はひとり親・ステップファミリー53.1%、経済不安33.8%、若年(若年妊娠の既往を含む)38.1%、精神疾患合併19.4%、未受診・受診遅れ19.4%で、COVID19 流行前と比較してひとり親・ステップファミリーの割合が有意に増加したが、経済不安や精神疾患合併の割合に有意な差は認めなかった。【結論】COVID19 流行前後で要支援妊婦の占める割合や、経済不安・精神疾患合併の割合に有意な変化は見られなかったが、依然として当院における要支援妊婦の占める割合が高く、公立病院としての社会的役割は大きいと考えられた。今後も地域の関連部署、医師助産師、MSW など多職種間で情報を共有し、継続した支援に努めていきたい。

P-47-6 指尖脈波から評価した妊産婦の自律神経機能評価について

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【目的】妊婦の自律神経活動を評価し、妊娠時期毎の特徴について検討することを目的とした。【方法】2021年1月~2022年10月の間に当院で妊娠分娩管理を行った妊婦を対象とした。指尖脈波から心拍変動を計測することで自律神経活動を解析する、簡易版自律神経活動測定器(以下:疲労・ストレス測定システム)を使用し自律神経機能を評価した。副交感神経・交感神経の活動状態を LF (Low-frequency power), 副交感神経の活動状態を HF (High-frequency power), 交感神経の活動状態を LF/HF 比で評価した。妊娠10週~20週までを群1, 妊娠21週~30週までを群2, 妊娠31週~40週までを群3, 産後1か月を群4とし、それぞれの測定値を比較した。Friedman 検定, 多重比較検定で統計解析を行った。【成績】合併症のない単胎妊婦の20人が対象となった。LF は群1が最も高値で、群2・群3で低下した後に群4で上昇し、妊娠時期毎に有意差を認めたが、多重比較検定では各群間で有意差はなかった。HF は妊娠週数が進むにつれて低値となり産後に上昇し、妊娠時期毎に、および多重比較検定にて群1・群3, 群3・群4間で有意差を認めた(P<0.05)。LF/HF 比は妊娠時期毎に有意差は認めなかったが、妊娠後期で最も高値となった。【結論】副交感神経の活動状態を表す HF は妊娠初期に最も高値で妊娠週数が進むにつれて低下傾向を示し、産後に回復した。交感神経の活動状態を表す LF/HF は妊娠時期による有意な変化は認めなかったが、妊娠後期で最も高値となった。妊娠期間を通じて副交感神経系の抑制と交感神経系の活性化が起こり、産後に回復することが示唆された。今後は産科合併症のある妊婦での比較検討をすることで、疾患と自律神経機能との関連性を明らかにしていきたい。

P-47-7 当院において産婦人科疾患に対して施行された経カテーテル動脈塞栓術 58 例の後方視的検討

日本医大

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【目的】経カテーテル動脈塞栓術 (TAE) は低侵襲でありながら止血効果の高い治療方法として、分娩後出血や子宮筋腫などの産婦人科疾患においてもしばしば用いられる。当院において産婦人科疾患に対して施行した TAE の治療成績を明らかにすることを目的とした。【方法】2013 年 1 月～2023 年 7 月までの期間に当院で TAE を施行した産婦人科症例を対象とし、診療録を基に后方視的検討を行った。【成績】TAE を施行した 58 例中、産科疾患は 47 例であり、内訳は RPOC が 16 例、子宮仮性動脈瘤が 14 例、子宮動脈静脈奇形が 7 例、弛緩出血が 3 例、癒着胎盤が 3 例、会陰腔壁血腫が 2 例、子宮型羊水塞栓症が 1 例、帝王切開癒着部妊娠が 1 例であった。一方、婦人科疾患は 11 例であり、内訳は悪性腫瘍による性器出血が 3 例、子宮全摘出術後の腔断端部出血が 2 例、骨盤内の仮性動脈瘤が 2 例、子宮筋腫による性器出血が 2 例、子宮筋腫手術時の出血予防目的が 2 例であった。TAE による止血効果または出血抑制効果が得られたのは産科疾患で 47 例中 43 例 (91.5%)、婦人科疾患では全例 (100%) であった。TAE での止血効果が得られなかった 4 例はいずれも産科 DIC を合併しており、TAE 施行時点までの出血量が 4000 mL 以上であった。TAE 施行後に子宮壊死を発症し子宮摘出を要した症例が 1 例確認されたが、その他に追加処置を要するような合併症は認めなかった。なお、TAE 施行後に妊孕性温存できた 45 歳以下の症例 46 例では、17 症例で合計 21 回の妊娠成立が確認された。【結論】当院において産婦人科疾患に対して施行された TAE でも奏効率が高いものであった。TAE の対象疾患は多岐に渡っており、産婦人科領域における TAE の有用性が示唆された。

P-47-8 当院における妊娠と薬外来

北海道大病院

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【目的】妊娠と薬情報センターは厚生労働省事業として、国立成育医療研究センター内に設置され、妊娠・授乳中の薬物治療に関して不安を持つ患者への情報提供を行なっている。当院は妊娠と薬情報センターが展開する「妊娠と薬外来」相談事業の協力施設の 1 つであり、妊婦及び妊娠を希望する女性に対して服薬に関する情報提供やカウンセリングを行っている。今回、過去 5 年の妊娠と薬外来における傾向に関して検討した。【方法】2017 年-2023 年 6 月までに当院の妊娠と薬外来を受診した 62 件を対象とした。症例の背景、相談の時期、使用薬剤の特徴について検討した。不安の改善に関する効果判定としてビジュアル・アナログスケールを用いて評価した。【成績】受診者の年齢の平均は 31.6 歳であり、妊娠前は 74.1% であった。疾患は精神疾患が 57%、アレルギー疾患が 11%、婦人科疾患が 11%、自己免疫性疾患が 5% であり、診断名はうつが 20% で最も多かった。相談薬剤数の平均は 6.7 種で多剤併用している症例が多かった。相談前平均不安度は 60.2 ± 4.23 で相談後は 16.4 ± 2.34 であり有意に改善していた。【結論】妊娠前の相談が多く、本外来で薬に関する情報を整理した後に妊娠に向かうことができるメリットは大きい。精神疾患が多く不安を抱える症例が多いことから、患者に寄り添ったカウンセリングが求められる。情報の整理が不安の解消につながる症例が多く、本外来の果たす役割は大きいと考えられる。

P-47-9 人口減少が進む島嶼での分娩数の変化から周産期医療の今後について考える

大島医療センター

瀬尾瑛美

【目的】当院は島で唯一の診療所として、開院から 20 年、急性期から慢性期まで島の医療を一手に担ってきた。島民である助産師 1 人と、医局派遣の産婦人科医 1 人が常駐し、ローリスクの分娩を取り扱っている。現在の島の人口は約 7000 人であり、20 年間での人口減少率は 2 割を超えている。出生数に至っては 20 年間で約 7 割減少している。過疎化と超高齢化が進む島での 20 年間の島内分娩と島外への周産期救急搬送症例を振り返り、島の周産期医療の現状を分析するとともに、今後の島内での周産期医療の在り方について検討したい。【方法】過去 20 年分の分娩記録と島外への周産期救急搬送要請記録を参照し、その件数と概要を参照した。【成績】20 年間で周産期死亡は 0 であった。島内での分娩数は 20 年で大幅に減少し、近年は 1 桁台が続き、2024 年の島内分娩数は 0 件であった。島内で健診を行い、分娩は島外を希望する妊婦が殆どである。【結論】島内での分娩件数の減少は顕著であり、分娩体制の存続を再検討する時期に来ていると言ってよいだろう。

P-47-10 当院における患者満足度向上のための取り組み

市立柏原病院

中島安紗海, 中野千晴, 末光千春, 井上 裕, 梶谷耕二

【目的】近年、核家族化・女性の社会進出が進んでおり、母親の育児に関する知識の早期取得・父親の育児参加が必要である。また様々な出産施設がサービス向上を行っており、各機関での診療サービスのアピールが今後より必要になるため、当院では患者の満足度向上に向けた取り組みを実施中である。【方法】Zoom による両親教室の開催、公式 LINE の運用、Instagram の開設を 2022 年 3 月に開始した。両親教室は月に 2 回の頻度で実施しており、アプリケーションをダウンロードした端末を所有していれば、自宅や会社の休憩時間などどこでも視聴できる点、以前は仕事等で現地参加不可の父親も視聴可能な点が長所である。Zoom は録画により見逃し配信として一定期間視聴可能な運用としている。次に公式 LINE は Zoom での両親教室の案内や重要な情報を配信しているが、最近では Zoom での両親教室の感想の投稿に応じてニューボーンフォトのクーポンを送信するサービスも提供している。最後に、Instagram は当院の新規患者獲得のための情報提供を目的に開始、施設紹介や当院の取り組みを月に 2 回程度のペースで更新している。出産費用の見える化に関する情報も Instagram 上で開示している。【成績】Zoom での両親教室の見逃し配信だが、配信開始時は視聴回数 約 10 回であったが、2023 年 9 月現在は 30 回/1 か月のペースと増加している。また、Instagram は投稿開始から約 1 年間でフォロワー 100 人を達成した。今回の発表は褥婦対象のアンケート結果も発表予定である。【結論】当院における患者満足度向上に向けた取り組みは患者層に浸透し活用されていると考える。アンケートの結果次第で新たなサービスの検討も積極的に取り組む予定である。

P-47-11 経膈分娩後の産褥 4 日目に静脈空気塞栓症から肺塞栓症を生じた一例

北里大病院

濱田奈実, 服部響子, 内坪 花, 高木さやか, 五十畑仁志, 五島裕之, 山崎 優, 吉村嘉広, 島岡享生, 関口和企, 大西庸子, 落合大吾

【緒言】静脈空気塞栓症は肺塞栓症の原因となることが知られている。経膈分娩後に静脈空気塞栓症を発症し、肺塞栓症に至った症例を経験したので報告する。【症例】患者は 38 歳、2 妊 0 産。30 歳時より 2 型糖尿病に対しインスリン治療を行っていた。今回自然妊娠にて妊娠成立し、妊娠 6 週 4 日当院を紹介受診した。妊娠中もインスリン治療を継続し、妊娠経過は良好であった。妊娠 39 週 2 日誘発麻酔分娩で出産した。産褥経過も良好で産褥 3 日目の退院診察で異常を認めず、翌日退院の予定であった。産褥 4 日目、朝食中に突然呼吸苦が出現し、経皮的動脈血酸素飽和度 (SpO₂) 85% と急激な低下を認めた。生体モニターの装着、酸素投与、輸液投与を開始し、全身管理を行いながら精査を進めた。心臓超音波検査で右室負荷所見を認め、造影 CT 検査では肺動脈末梢の造影が不良であった。しかし肺動脈内や深部静脈に血栓像はなく、子宮筋層内及び骨盤内の静脈に多量の空気混入を認めたため静脈空気塞栓による肺塞栓症と診断した。ICU に入室しネーザルハイフローで呼吸管理を行ったが、発症翌日 (産褥 5 日目) 酸素投与を終了した。なお発症後 2 日目 (産褥 6 日目) の単純 CT 検査では子宮筋層内や骨盤内の静脈の空気は消失していた。その後症状の再燃なく発症後 5 日目 (産褥 9 日目) に退院した。【結論】静脈空気塞栓症から肺塞栓症を生じた一例を経験した。静脈空気塞栓症が帝王切開を契機に発生した報告は散見されるが、経膈分娩後に発症した報告は稀である。産褥期に呼吸苦が生じた場合には、肺血栓塞栓症や周産期心筋症等を中心に鑑別診断を行うが、稀ではあるが静脈空気塞栓症から肺塞栓症を生じることも念頭に置かなければならない。

P-47-12 産前産後母子支援事業と連携し周産期管理を行った住居がない特定妊婦の検討

産業医大

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【目的】特定妊婦は 2020 年で約 8300 人と 10 年前の約 10 倍に増加していると報告されており、配偶者や家族の支援が得られず、住居を持たない妊婦は従来、行政機関に管理を委託された母子生活支援施設へ入居し、児は児童相談所を介して乳児院へ一時保護となる症例も多く見受けられた。2019 年の母子保健法の改正以降、各自治体では産前産後母子支援事業が推進されるようになったが、その運営体制については不明確な点も認められている。今回、当科で経験した産前産後母子支援施設と連携し周産期管理を行った特定妊婦 4 例について後方視的に検討した。【方法】当科で経験した特定妊婦のうち、産前産後母子支援事業を活用した症例 4 例について、電子カルテデータを用いて後方視的に検討を行った。【成績】症例の年齢の中央値は 31.5 歳 [25-35]、初産婦は 1 例、経産婦 3 例だった。分娩週数の中央値は 38 週 [37 週 3 日-38 週 6 日]、帝王切開症例は 2 例 (既往帝王切開後妊娠の適応) であった。住居がない理由として、パートナーからの DV が 2 例、精神疾患合併が 1 例、配偶者の支援不足が 1 例だった。精神疾患合併の 1 例は精神症状増悪に伴い、施設での対応が困難となり、産後は別の精神科へ入院、児は乳児院へ保護されることとなったが、他 3 例は産後も施設で 1 か月程度生活をし、母子での生活が可能と判断され現在は自立して生活をしている。【結論】産前産後母子支援施設と医療者、自治体とで連携を行い、住居がない妊婦も妊娠中から産褥期まで切れ目のない包括的な管理を行うことができた。特定妊婦の妊娠分娩の新たな生活の手段として、産前産後母子支援事業は有用と考える。

P-47-13 前期破水に伴う感染を契機に大動脈炎症候群および急性大動脈解離を発症した一症例

高知大

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【緒言】前期破水および感染を契機に大動脈炎症候群を発症し、動脈炎に伴う血管壁の脆弱性により大動脈解離を来した極めて稀な症例を経験したので報告する。【症例】34歳、初産婦、自然妊娠成立後、妊娠33週0日に前期破水の診断で当院へ救急搬送となった。抗生剤、母体ステロイド投与を行い感染症徴候と胎児機能評価に留意し妊娠期間延長を試みた。妊娠33週5日に感染症兆候出現のため緊急帝王切開を行った。術中経過には異常を認めなかったが、術後3日目に創部発赤、発熱および血液検査で高度炎症所見を認めたため創部感染と診断した。術後7日目に筋膜上を開放創とし、洗浄と抗生剤投与を連日継続した。しかし症状が増悪したため、最も疑わしい子宮創部感染を確認するため試験開腹、創部デブリードマンを施行した。子宮創部は術後変化と思われる軽度の炎症所見のみであり、臨床症状とは解離していた。一方、帝王切開術直後から胸部痛を訴えており、炎症の波及による呼吸器系・消化器系の症状として対応していたが、感染源検索の造影CT検査で大動脈弓部血管壁の肥厚、またPET/CT検査でFDGの大動脈血管壁への集積を認め、大動脈炎症候群と診断した。ステロイドの点滴・ミニパルス療法により炎症反応は低下したが、術後18日目に嘔声が出現し、造影CTにより大動脈起始部から弓部の大動脈解離を認めた。緊急開胸手術、人工血管置換術を施行し、術中に得られた組織の大動脈病理結果は大動脈炎に矛盾しない所見であった。【結語】帝王切開術後に正常に経過せず、炎症および感染兆候が収束しない場合には全身性炎症疾患を想起する必要がある。

P-47-14 妊娠37週に発症し、ウイルス感染症や他の皮膚疾患との鑑別に苦慮した妊娠性掻痒性蕁麻疹様丘疹(PUPPP)の一例

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【緒言】妊娠性掻痒性蕁麻疹様丘疹(PUPPP)は、通常腹部の妊娠線に沿った蕁麻疹様紅斑で始まり、腹部全体・臀部や四肢にも拡大し、激痒を伴う。今回我々は選択的帝王切開(CS)実施直前に、四肢の甲の水疱を伴う紅斑から発症し、ウイルス感染症や他の皮膚疾患との鑑別に苦慮した症例を経験したので報告する。【症例】35歳1妊0産、妊娠初期に一絨毛膜二羊膜双胎にて当院紹介。経過問題無く、妊娠37週2日に帝王切開予定であった。妊娠36週4日、水疱を伴う掻痒性皮疹が手足の甲から発症し、徐々に上下肢全体・下腹部・背部にまで拡大していった。発熱はなかったが鼻汁・関節炎を認め、ウイルス感染症の鑑別も必要と考えてCSは延期した。当初は近医皮膚科にて接触性皮膚炎の診断を受けていたが、当院感染症内科にもコンサルトし複数科で対応した。水痘・麻疹のIgG・IgM陰性、風疹HI抗体価8倍以下であったが、ペア血清で完全にウイルス感染を否定するためにはさらに時間が必要であった。また、発疹の発症様式からは妊娠性類天疱瘡も考えられた。そこで形成外科により皮膚生検も施行。真皮表層血管周囲のリンパ球を中心とした炎症細胞浸潤があり、蛍光抗体法では基底膜部にC3やIgGの沈着を認めず、PUPPPの診断であった。妊娠38週2日に選択的CS施行し、過剰な感染対策は回避することができた。術後経過は母児共に良好で母体皮膚病変も速やかに軽快、消失した。【結論】妊娠に伴う皮疹は、日常診療において比較的良好に遭遇する疾患であるが、時に重篤化し、その鑑別が困難なこともある。産婦人科医は妊婦の皮疹についても常に最新の知見を得ておくと共に、必要であれば複数科で、適切・迅速に対応する事が必要である。

P-48-1 当院におけるCTを用いた妊婦骨盤計測の検討

松江市立病院

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【目的】従来、妊婦の骨盤計測はX線検査による評価を行っていたが、現在、当院ではCT検査を用いた方法を採用している。採用当初の小数例の検討で、CT検査を用いた方法による被ばく低減や検査時間の短縮を報告した。その後の症例の増加を受けて、検査の安全性に対する追加検討を行うとともに、分娩様式および背景因子についても検討を加えた。【方法】2022年1月から2023年9月までに骨盤計測の際にCT検査が行われた50例を対象とした。被ばく線量および検査所要時間を記録し、X線検査を行った対照と比較検討を行った。分娩様式と背景因子については診療録から抽出し、後方視的に検討した。本研究は当院の倫理委員会の承認を得ている。【成績】平均被ばく線量は0.29mSy、平均検査時間は3.6分であり、X線検査(7.75mSy、10.1分)に比して有意に低線量かつ短時間であった。これらのうち明らかなCPDと診断した症例はなく、全例経陰トライとした。分娩様式は吸引分娩が2例、肩甲難産が1例あり、緊急帝王切開術は7例(分娩停止5例、胎児機能不全2例)であった。【結論】経陰分娩に至った症例と帝王切開術に至った症例では、背景因子に統計学的な有意差を認めなかったが、安全性は前回の報告同様に確認できた。今後、CT検査を用いた妊婦骨盤計測がX線検査に代わる新しい手法となることが期待される。

P-48-2 当院における無痛分娩と非無痛分娩の周産期予後の比較

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【目的】当院で開始した計画無痛分娩が分娩管理と周産期予後に及ぼす影響を明らかにすること。【方法】2022年11月から2023年8月までに正常産で経陰分娩となった経産婦のうち、麻酔科医による脊髄くも膜下硬膜外併用麻酔で計画無痛分娩を実施した症例を無痛群、実施しなかった症例を非無痛群とし、症例対照研究で2群間の比較検討を行った。評価項目は母体背景(分娩時年齢, BMI, 経妊回数, 経産回数, 不妊治療の有無, 流産回数, 人工流産回数, 前回分娩週数), 周産期成績(器械分娩率, 緊急帝王切開率, 胎児機能不全, 分娩週数, 分娩所要時間, 出血量), 新生児成績(出生体重, 低Apgarスコアの発生頻度, 臍帯動脈血pH, NICU入院率)とした。多胎や前期破水, 羊水量異常, 早産既往, 妊娠高血圧を除く妊娠高血圧症候群, インスリンを使用している糖代謝異常合併妊娠, 予定帝王切開の症例は除外し, ローリスク経産婦と定義した。無痛分娩は日勤帯(平日8時30分~17時00分)でのみ行われた。【成績】無痛群36例, 非無痛群337例のうち, 器械分娩率は13% vs 3%と無痛群で有意に高かったが, 緊急帝王切開率(0% vs 0.6%)や低Apgarスコアの発生頻度(2.7% vs 2.0%), 分娩所要時間(212分 [145-294] vs 223分 [153-392]) 胎児機能不全(8.3% vs 4.6%), NICU入院率(3.3% vs 5.5%)などは両群間で差はなく, その他の評価項目においても差はなかった。(P-value < 0.05)【結論】無痛群で器械分娩率が上昇したが, その他の周産期成績, 新生児成績においては差は認めなかった。ローリスク経産婦に限定したことにより安全に日勤帯で無痛分娩を導入することができた。

P-48-3 当院におけるジノプロストン腔内留置剤の使用経験

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【目的】ジノプロストン腔内留置剤(プロウベス[®])は症例によって陣痛発来する症例と, 使用後に機械的な頸管拡張を要する症例が存在する。【目的】当科で陣痛誘発のためにプロウベス[®]を使用した症例について分娩転帰と陣痛発来率を解析することでプロウベス[®]が有効な症例について検討する。【方法】2022年4月から2023年9月までに当院においてプロウベス[®]を使用した30症例を対象とした。分娩転帰, 使用後陣痛発来の有無, 年齢, BMI, 妊娠中増加体重, 誘発前Bishop score, 出生体重, 臍帯動脈血pH, Apgar scoreなどについて後方視的に検討した。【成績】30症例の中央値は, 年齢32歳(20-41), 非妊娠時BMI 22.1(17.9-37.9), 誘発時BMI 27.3(21.5-42.6), 妊娠中増加体重12.4kg(0-29.0), 誘発前Bishop score 2(0-2), 出生体重3152g(2832-3960), Apgar score 1分値8(5-9), 5分値9(7-10), 臍帯動脈血pH 7.306(7.084-7.374)であった。分娩転帰は経陰分娩24例(80%), その内プロウベス[®]留置中に陣痛発来したのは11例(37%)であった。使用後に機械的頸管拡張を要したのが7例(23%)であった。帝王切開となったのは6例(20%)であり内訳は, 分娩停止が5例(17%), 胎児機能不全が1例(3%)であった。使用中に陣痛発来した群と, 陣痛発来しなかった群とで比較した。誘発時と非妊娠時BMI, 年齢, Bishop score, 出生体重, Apgar scoreに有意差は無かった。【結論】プロウベス[®]は母体背景によって陣痛発来率に有意差が無く, また出生直後の児の状態についても差を認めないため, どのような症例についても安全に使用することが可能であると考えられる。

P-48-4 当院における超高齢妊娠の転機における検討

さいたま赤十字病院

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【目的】近年女性のライフスタイルの変化や不妊治療の進歩に伴い, 高齢妊娠が増加している。高齢での妊娠は母体や胎児に様々な影響があると言われている。今回45歳以上の超高齢妊娠が与える影響およびその転機について, 当院における症例を後方視的に検討した。【方法】当院における2020年から2022年までの40歳以上の分娩症例347例について, 初産婦の40~44歳154例 vs 45歳以上13例の緊急帝王切開率(フィッシャーの正確確率検定), 分娩回数に関わらず40~44歳327例 vs 45歳以上20例における1)分娩時出血量(経陰分娩群, 帝王切開群), 2)HDPの有無, 3)早産率, 4)児の入院率(1,2はt検定, 3,4はフィッシャーの正確確率検定)について検討を行った。【成績】初産婦の40~44歳 vs 45歳以上における緊急帝王切開率は45歳以上が有意に高かった(P<0.01)。分娩回数に関わらず, 45歳以上における経陰分娩群での分娩時出血量は有意に多かった(P<0.05)。帝王切開群での出血量は有意差を認めなかった。また, HDPの有無, 早産率, 児の入院率も群間で有意差は認めなかった。【結論】45歳以上の超高齢妊娠では40~44歳の妊娠に比べ緊急帝王切開率が高く, 経陰分娩時出血量も多かった。今後も症例を蓄積し, リスクに応じた対応を考慮することが必要である。

P-48-5 産褥期の突然死に対し病理解剖を施行し後腹膜出血が原因と考えられた2症例

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【症例1】30歳代, 初産, 鼠蹊ヘルニアと自然気胸4回の既往, 家族性高脂血症の合併あり。不妊治療でDD双胎妊娠成立し, 初期に予防的頸管縫縮術施行。27週頃左下肢に皮下出血を認め, 血液内科で血管性紫斑症の診断。33週4日蛋白尿陽性となり入院管理。34週0日子宮内胎児発育遅延, 第2子NRFSにて緊急帝王切開術施行し, 出血量710gで問題なく終了。術後7日目に38.1℃発熱, 抗生剤の内服等で発熱し術後9日目に退院。同日夜自宅で心肺停止状態で発見され当院へ搬送後死亡確認。病理解剖にて両側総腸骨動脈分岐部直上の腹部大動脈解離・破裂が死因と診断され, Ehlers-Danlos症候群が疑われた。【症例2】40歳代前半, 3経産, 既往歴合併症なし。前医にて妊婦健診を継続し, 時々収縮期血圧130mmHg台を認めた他異常なし。陣発入院しスムーズに分娩進行, 約5時間後38週6日にクリステレル法併用なく経陰分娩した。会陰裂傷I度, 出血2時間値まで214gと経過良好であり帰室。分娩約9時間後のスタッフ訪室時に心肺停止状態で発見された。蘇生措置に反応なく, 当院に搬送後に死亡確認。病理解剖にて左後腹膜に15×10×5cm大の後腹膜血腫を認め出血の主座と推定されたが, 明らかな破綻血管や動脈瘤は指摘されなかった。【考察】産後の後腹膜出血は重篤な産道裂傷や帝王切開での損傷にて起きうるが, 今回の2症例はこれらと異なる原因であった。産後の突然死に対し病理解剖を施行し, 2症例とも子宮や産道損傷の関与しない後腹膜出血が原因と判明した。その予知は非常に困難であるが, 病歴から結合織の脆弱性の有無を検討し, 産褥経過中のバイタル変化に注意することで, 早期発見や治療介入が可能かもしれない。

P-48-6 妊娠経過では指摘できなかった, 臨床的胎児間貧血多血症 (Twin Anemia-Polycythemia Sequence) の1例

武蔵野赤十字病院

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【背景】MD双胎やMM双胎などの一絨毛膜性の双胎は, 血管吻合の血流の不均衡により双胎間輸血症候群 (TTTS: Twin-twin transfusion syndrome) や胎児間貧血多血症 (TAPS: Twin Anemia-Polycythemia Sequence) をきたす場合がある。当院では推定体重や羊水量, 中大脳動脈血流速度 (MCA-PSV) 等で評価を行っている。今回, 妊娠経過では指摘できず, 分娩後に判明したTAPSを経験したため報告する。【症例】25歳, G3P1 (1SA, 1NVD)。X年2月自然妊娠でMD双胎を指摘され, 2~3週間毎に外来で推定体重, 羊水量, MCA-PSV等を評価し経過を診ていた。妊娠32週から妊娠管理目的で入院し, 約3~4日間隔で推定体重, 羊水量, MCA-PSVの測定を行い双胎間の血流不均衡の有無を確認した。MCA-PSV差はあるが定義を満たさず推定体重・羊水量に差を認めなかったため, 妊娠37週2日に予定帝王切開で分娩となった。娩出した胎盤に明らかな血管吻合は認めなかったが, 色調に差を認め, Hbも両児間に約8mg/dLの差を認め, 臨床的にTAPSと診断した。【考察】TAPSの胎児期診断の基準は①供血児のMCA-PSV>1.5Momかつ受血時のMCA-PSV<1.0Momもしくは②両児間のMCA-PSV差が0.5Mom以上とされている。本症例のようにTAPSの診断基準は満たさない程度のMCA-PSV差が持続して認められた場合でも, TAPSを発症している可能性を考慮し, 正確な測定が重要と思われる。一般的にMCA-PSVの測定は経腹エコーで行う場合が多いが, 胎位によっては経陰エコーを用いて血流測定を行うことで正確な診断につながる可能性があると考えられる。また, 予定通り妊娠37週2日に帝王切開で分娩としたが, 診断ができた場合の分娩週数についても議論の余地があると考えられる。

P-48-7 EP療法を行い完治に至った初期流産後RPOCの4症例

筑波大

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【緒言】RPOC (Retained products of conception) に対する治療法は待機療法, 子宮内容除去術, 子宮鏡下手術, 子宮動脈塞栓術など多岐にわたる。今回妊娠12週未満の初期流産後RPOCの4例に対してエストロゲン・プロゲステン製剤による治療 (EP療法) を行い, 全例で良好な経過が得られたので報告する。【症例】4例全例が生殖補助医療による妊娠であった。2例は自然に胎嚢が排出され, 2例は稽留流産に対して子宮内容除去術が行われた。流産後16-40日の経陰超音波検査で子宮内腔に腫瘍が認められ, RPOCと診断された。MRI検査は3例に施行された。腫瘍の長径は10-14mmであった。性器出血は1例では認められず, 3例では認められたものの少量であった。診断時の血中hCG+β II値は46.3-449.4mIU/mLであった。腫瘍内血流と子宮筋層の血流をカラーDプラ法により相対的に評価したところ, 4例全例で腫瘍内の血流は子宮筋層よりも少なかった。他の治療法も選択肢として提示した上で, インフォームドコンセントを得て全例にEP療法を行った。EP療法中に大量出血を来した症例はなく, 流産後81-114日で腫瘍および血流の消失を確認することができた。【考察】RPOCは遺残した組織が接着する子宮筋層に豊富な血管を増生させ, 大量出血の原因となる。そのため侵襲的治療を要することも少なくないが, 今回の4例ではEP療法で大量出血なく治療を完遂することができた。外出血が少量であり, 腫瘍径が小さく, さらに腫瘍内血流と子宮筋層血流の相対的評価により腫瘍内血管増生の程度が少ないと判断される症例では, EP療法は治療法の選択肢となり得る。

P-48-8 帝王切開癒痕症候群修復術後に正常産で分娩となった2例の周産期管理の検討

武蔵野赤十字病院

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【緒言】帝王切開癒痕症 (Cesarian Scar Disorder ; CSDi) は、帝王切開後の陥凹性癒痕の存在により過長月経・月経困難症・続発性不妊などをきたす病態で、近年子宮癒痕部修復術が多施設で行われている。当院で子宮癒痕部修復術を行い正常産で分娩となった2例の周産期管理に関して検討したため報告する。【症例1】37歳, 2妊1産。第1子を他院にて帝王切開で出産。2年間不妊治療を行うも妊娠に至らず、帝王切開癒痕部の非薄化(筋層厚1.5mm)および非薄化した筋層内部に嚢胞性病変を認め、当院に紹介。CSDiの診断にて、子宮鏡併用下開腹子宮癒痕部修復術を施行。術後3か月のMRI画像にて子宮体下部筋層厚は7.4mmに改善、嚢胞性病変は消失。術後10か月でタイミング法にて妊娠に至り、妊娠29週より癒痕修復部の筋層非薄化を認めたが頸管長短縮はなく、妊娠37週1日で選択的帝王切開を施行。【症例2】40歳, 2妊1産。第1子を他院にて帝王切開で出産。2年間不妊治療を行うも妊娠に至らず、帝王切開癒痕部の非薄化(筋層厚2mm)および非薄化した筋層内部に嚢胞性病変を認め、当院に紹介。CSDiの診断にて、子宮鏡併用下開腹癒痕部修復術および両側円靭帯縫縮術を施行。術後5か月のMRI画像にて子宮体下部筋層厚は4.4mm、嚢胞性病変は消失。術後10か月で顕微授精にて妊娠に至り、妊娠経過中は明らかな筋層非薄化を認めず、頸管長短縮もなく妊娠38週0日で選択的帝王切開を施行。【考察・結論】2症例共に、周産期合併症なく、正常産での健児を得た。近年、CSDi症例の増加とともにそれに対する子宮癒痕部修復術後妊婦の管理が増加することが予想される。CSDi術後における周産期リスクについて、報告する。

P-48-9 Mycoplasma hominis が起炎菌であった帝王切開術後膿瘍の3症例

富山大

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帝王切開術後の創部感染は2%前後、骨盤内膿瘍の頻度は0.2%未満と稀な合併症である。帝王切開術後膿瘍から *Mycoplasma hominis* が分離された先行報告は4件である(分娩後発熱の5%に *M.Hominis* が、20%に *Ureaplasma urealyticum* が関連すると報告される)。帝王切開術後に *M.Hominis* 起炎菌の膿瘍を形成した3例を経験した。1例は絨毛膜羊膜炎の早産での緊急帝王切開症例、1例は正常産での陣痛発来後に臨床的CAMと診断され緊急帝王切開となった症例、1例は胎児適応での予定帝王切開症例であった。3例とも術後3-4日目に発熱や炎症反応上昇を認め、抗菌剤開始や抗菌剤変更を行うも改善が得られず、膿瘍穿刺やドレナージ術などの外科的介入を行い、LVFXを追加し改善を得た。3症例とも膿瘍から *M. Hominis* が検出された。*M.Hominis* はβラクタム系やマクロライド系抗菌薬に抵抗性で特殊培地でしか検出できない。帝王切開術後に、保存的治療に抵抗性で、遷延する感染所見を認める場合には *M.Hominis* による感染を疑い、外科的介入やニューキノロン系抗菌薬投与を積極的にすることでより早期の改善を望むことができる可能性がある。

P-48-10 経膈分娩後後腹膜血腫に Isolated rectal buttonhole tears を合併し人工肛門造設に至った一例

三重大

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【目的】Isolated rectal buttonhole tears は腔および肛門括約筋の裂傷とは孤立した直腸裂傷である。非常に稀な産科合併症であり、管理方法に一定の見解はない。今回、後腹膜血腫に合併した Isolated rectal buttonhole tears の一例を経験したので報告する。【症例】33歳, 1妊0産。自然妊娠成立後、前医で妊娠管理されていた。39週に前期破水の診断で分娩誘発開始され、経膈分娩となった。産後に腰背部痛が出現し、ショック状態(心拍数110回/分、血圧88/40mmHg)と診断され当院に救急搬送となった。腔と肛門から鮮血の流出を認め、経腹超音波検査で子宮背側に血腫を認めた。造影CT検査で左内腸骨動脈末梢にextraを認め、後腹膜血腫と診断した。輸血の準備をしつつ、腔壁・会陰裂傷再縫合術で止血および血腫除去を試みるも腔側からの血腫除去は困難であり、IVRでの動脈塞栓術で出血点を同定し止血を得た。産褥1日に肛門出血の再発を認め、造影CT検査で骨盤血腫内にextraを認めた。再度動脈塞栓術を施行し止血を得た。総輸血量はフィブリノゲン製剤3g、新鮮凍結血漿-LR14単位、赤血球濃厚液-LR20単位であった。その後は出血なく経過し、産褥9日のCT検査で血腫は縮小傾向にあった。産褥10日に下部消化管内視鏡検査を施行され、10mm大の Isolated rectal buttonhole tears を認めた。産褥14日に腹腔鏡下回腸人工肛門造設術を施行され、術後経過良好のため産褥25日に退院となった。【結論】今回、後腹膜血腫に Isolated rectal buttonhole tears を合併し、人工肛門造設に至った一例を経験した。分娩後管理において、視認できる腔や会陰、肛門括約筋から孤立した直腸にも裂傷が生じうると認識することが大切である。

P-48-11 子宮底部横切開を施行したびまん性子宮平滑筋腫合併妊娠 (DUL: diffuse uterine leiomyomatosis) の1例

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【緒言】妊娠に子宮筋腫が合併する頻度は0.5~2%と高い。びまん性平滑筋腫 (DUL) は、3cm以下の無数の筋腫が子宮の筋層内から粘膜下に散在する非常にまれな筋腫であり、妊娠出産に至る例は41報告とさらに少ない。今回、子宮の増大により妊娠継続が困難となり、妊娠32週に子宮底部横切開で帝王切開術を施行したDUL合併妊娠について報告する。【症例】34歳、G1P0。31歳時、子宮鏡下に4.5cm大の粘膜下筋腫を摘出し、33歳時には、腹式に6cm大の筋層内筋腫核出術既往がある。自然妊娠が成立し前医で妊娠管理され、当院での管理目的で紹介となった。妊娠11週で既に子宮底は臍高であった。しかし、妊娠31週より、筋腫および妊娠経過に伴う子宮増大のため、嘔気、食欲低下などの腹部症状が増悪し、妊娠継続が困難となりて妊娠32週1日に帝王切開を施行した。術前に、超音波検査やMRI画像を確認したところ、出血量を可能な限り減らすのに最適な子宮切開部位は子宮底部右側のみであり、その他は胎盤または筋腫が散在していた。全身麻酔下で剣状突起から臍上に縦切開で開腹し、子宮は底部で筋腫を避けて切開した。児は1687g (-0.3SD)、Apgarスコア2/4であった。術中出血量は920gだった。産後、GnRH製剤投与した後、子宮全摘術施行予定である。【結語】子宮筋腫は頻度が高いが、中には子宮全周に筋腫が散在するDULであることがまれにある。通常、子宮底部横切開は、胎盤が前壁付着の全前置胎盤症例の出血を減らすために用いることがあるが、本例のように特殊な子宮筋腫合併症例では、子宮底部横切開も有用であると考察された。

P-48-12 当科での子宮頸管熟化剤使用症例の検討

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【緒言】ジノプロストン腔内留置用製剤は妊娠37週以降の子宮頸管熟化不全における熟化を促進する製剤である。当科でも2020年9月より使用開始し、症例数は現在までで66症例となった。そこで使用の意義の確認のため、後方視的に検討した。【結果・考察】内訳は初産婦61症例、経産婦5症例。経陰分娩に至った症例が35症例、帝王切開が31症例。帝王切開の理由は分娩停止が半数以上占め、胎児機能不全が9症例あった。9症例のうち、留置中に prolonged deceleration または severe variable deceleration を認め抜去した症例もあったが、抜去後にNSTは速やかに改善し、超緊急帝王切開となる症例はなかった。ジノプロストン腔内留置熟化剤のみで陣痛発来し、経陰分娩に至った症例が17例あった。翌日も誘発分娩を継続し経陰分娩に至った症例では、留置前、抜去後、翌朝の Bishop score 平均値はそれぞれ、2.4, 4.3, 6.3と上昇。また帝王切開となった症例でもそれぞれ1.5, 2.9, 4.1と上昇していた。初産で経陰分娩に至った症例では分娩第1期が平均で9.3時間と初産婦の平均と比較して短縮していた。これらの結果はジノプロストン腔内留置熟化剤が安全性を保ちつつ子宮頸部の熟化を促し、抜去後も長時間にわたって熟化促進していることを示唆していると考えられる。【結語】当科での66症例について検討した。ジノプロストン腔内留置用製剤のみで分娩に至った症例や、熟化を進行させて、分娩第1期の短縮や誘発分娩の総時間の短縮にもつながったと見られる症例もあった。今後も積極的に症例を重ねていき、より安全性の高い誘発分娩を目指したい。

P-48-13 合併症、既往手術症例に対して臍上皮膚切開アプローチを要した帝王切開術の二例

浜松医大

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【緒言】今回、子宮全体が子宮腺筋症で母体臍上に胎児が存在した早産 (症例1) と、先天性腸閉鎖症に対し0歳時に小腸切除術2回施行後、15歳時に骨盤内癒着性のう胞手術で膀胱損傷となった既往のある骨盤位 (症例2) に臍上皮膚切開、子宮底部切開で児を娩出し、帝王切開術を成し得た二例を報告する。【症例1】39歳、3妊2産。妊娠初診時には子宮全体に子宮腺筋症病変が占拠し、子宮底は臍上を越えていた。胎児は母体臍部より高い位置に存在し、横位であった。25週3日で破水、妊娠継続。経陰分娩は困難と判断した。MRIから子宮底前側の腺筋症が薄く、直下の胎盤が子宮腔内到達の指標となると判断した。25週5日、緊急帝王切開術を施行し、子宮底より808gの児を胎盤と一塊として娩出した。出血量は707gであった。【症例2】30歳、1妊0産IVFで妊娠。他院で管理中、既往かMRIを妊娠30週に施行した。胎盤前壁付着、膀胱子宮間の癒着と静脈洞形成を疑い、子宮前壁と腸管の癒着が考えられた。骨盤位のため帝王切開の方針であったが、15歳時手術では腹腔内に到達できなかったことから当院紹介となった。小腸切除創癒着の臍上部横切開でアプローチする戦略とした。小腸と腸間膜が膜状に子宮と癒着があり、剝離して子宮底部を露出させ子宮筋切開を行なった。子宮底部横切開で児頭から娩出させた。良好な子宮収縮で子宮底部が臍よりかなり下に移動したため、縫合に取り掛かるまでの出血により総出血が1715mLとなった。【結論】腹部に病変や手術歴がある場合、術前MRIを検査し、臨機応変に皮膚切開部位を決めること、子宮底部切開のような帝王切開手技を熟知することで慣れない上腹部アプローチでも安全に手術可能だと考えた。

P-48-14 経陰超音波検査による器械分娩後の肛門括約筋の評価の実際

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【緒言】近年日本では、高年妊娠や無痛分娩の割合が著しく上昇しており、それに伴い、器械分娩による分娩が増加している。器械分娩は産科的肛門括約筋損傷(OASIS)を引き起こし産後便失禁の原因となる。今回、当院で器械分娩施行後、便失禁症状を有した3症例に経陰的に3D経陰超音波を施行し、肛門括約筋評価と症例の経過を報告する。【症例1】43歳、3妊0産。妊娠40週2日、前期破水のため入院。妊娠40週4日、第2期短縮の適応で鉗子分娩を施行した。児の出生体重は3741gで、会陰裂傷は3bと診断し外肛門括約筋を修復した。産褥4日目に便失禁を認めたが、産褥31日目に症状は改善し、経陰超音波検査で外肛門括約筋の10時から12時に高輝度な部分を認め、外肛門括約筋の円形像も保たれていた。【症例2】36歳、1妊0産。妊娠39週0日、前期破水、陣痛発来のため入院。胎児機能不全の適応で吸引分娩および鉗子分娩を施行した。児の出生体重は3027g、会陰裂傷は2度と判断した。産褥2日目から便失禁の訴えあり、産褥36日目に症状は持続していたが経陰超音波検査で外肛門括約筋の欠損は認めなかった。経過観察により産褥78日目に症状が改善した。【症例3】41歳、4妊0産。妊娠39週3日、無痛分娩のため入院。妊娠39週4日、第2期遷延の適応で鉗子分娩を施行した。児の出生体重は3897g、会陰裂傷は2度であった。産褥4日目に便失禁の訴えあり産褥32日目に症状は持続しており、経陰超音波検査で外肛門括約筋の部分的欠損を認めた。【結論】OASISの管理において、症状の有無だけでなくの3D経陰超音波検査による客観的評価は管理方針決定に有用であると考えられた。

P-49-1 播磨・姫路地域における総合周産期母子医療センターとしての役割

姫路赤十字病院

谷岡桃子、中山朋子、谷村史香、楠元理恵、平田智子、西條昌之、河合清日、関 典子、小高晃嗣、水谷靖司

【目的】当院は2015年4月より総合周産期母子医療センターの指定をうけ、播磨・姫路地域の周産期医療の中核病院として24時間365日多くの母体搬送の受け入れをしている。今回、当院における母体搬送の現状を分析し総合周産期母子医療センターとしての役割を再認識すること目的とした。【方法】2015年4月1日～2023年3月31日までの8年間を調査対象期間として、母体搬送件数、搬送理由、搬送週数、搬送元地域、転帰など診療情報記録から後方視的に検討した。なお、今回の研究での母体搬送とは救急車による妊産婦・褥婦(妊娠12週以降～産褥期)の搬送を対象とし、当院での分娩症例については周産期予後についても検討した。【成績】母体搬送件数は年間117～183件であった。搬送理由としては切迫早産、妊娠高血圧症、産後出血などによる搬送がある。搬送元地域としては、播磨・姫路地域だけでなく、神戸市や大阪府からの搬送依頼もある。【結論】年々、搬送受け入れ件数は増えており、搬送理由も多岐にわたる。特に妊娠22週以降の母体搬送については基本的に全例応需しており、切迫早産については小児科と連携し超早産例の母体搬送も積極的な受け入れを行っている。また近年妊婦の高齢化による母体合併症の増加などにより、今後も母体搬送依頼が増えることが予想され、地域の周産期医療機関を機能的にバックアップできるようさらに体制を整えていく必要があると考えられた。

P-49-2 全前置胎盤に対する cesarean hysterectomy 症例8例の臨床的検討

日本赤十字社医療センター

磯野梨子、有馬香織、細川さつき、渡邊理子、山田 学、笠井靖代、木戸道子、宮内彰人

【目的】前置胎盤における帝王切開術では、種々の止血操作で止血が得られない場合や、胎盤剥離が困難である場合には帝王切開術から子宮全摘術に移行する cesarean hysterectomy (CH) が行われる。当院では事前に画像上で明らかな癒着胎盤が疑われる、術中に胎盤剥離が困難、帝王切開術中に出血コントロール不良であった症例以外では、極力子宮温存を試みている。当院で治療した全前置胎盤におけるCH症例について検討を行ったので報告する。【方法】2014年1月から2023年7月の間に当院で前置胎盤に対して手術を行なった症例について後方視的検討を行った。【成績】該当期間の全前置胎盤症例150例のうち、CHは8例であった。術前に超音波検査やMRI検査にて明らかな癒着胎盤と判断した6例は、帝王切開術時にCHの方針とした。術前は帝王切開術を予定しながら、緊急CHとなった症例は2例であった。CH症例の平均母体年齢は36.6歳(26～44歳)、平均分娩週数は32.9週(28～36週)、平均出血量は2820ml(1350～16985ml)であった。既往歴に帝王切開術7例、子宮手術1例、前置胎盤2例を有し(重複あり)、全例術中に自己血輸血返血を含む輸血を行なった。7例は切迫早産兆候を認め、術前より子宮収縮抑制薬を投与していた。事前の超音波、MRI検査で癒着胎盤の指摘は7例、3例は穿通、嵌入胎盤も疑われていた。全例病理学的に癒着胎盤であったが、穿通、嵌入胎盤はなかった。児は全例NICU入院となった。【結論】前置癒着胎盤が疑われる症例は大量出血のリスクもあり、十分な準備の上手術に臨むべきである。子宮温存の可否の判断は慎重に行い、事前にCHの必要性を判断することが重要である。

P-49-3 当院の分娩誘発における子宮頸管熟化法の後方視的検討

洛和会洛和会音羽病院
瀬尾晃司

【目的】無痛分娩を選択する妊婦の割合は全国で急激に増加しており、分娩誘発の重要性は高まっている。今回、当院において分娩誘発を行った症例について、子宮頸管熟化法を比較し後方視的検討を行った。【方法】2022年1月から2023年9月に当院で分娩誘発を行った46例について、分娩誘発開始から24時間以内に経膈分娩に至る、いわゆる誘発成功率と、子宮頸管熟化の代替パラメータとして Bishop score (BS) の変化を後方視的に検討した。【成績】予定日超過など未破水症例のうち、ジノプロストン腔内留置用製剤(プロウベス[®])で分娩誘発を開始した5例と、メトロイリントル挿入で開始した11例を比較した。プロウベス[®]で誘発成功したのが3/5例(60%)、緊急帝王切開が1/5例(20%)、メトロイリントルで誘発成功したのが2/11例(18%)、緊急帝王切開が3/11例(27%)であった。誘発処置開始から抜去までの Δ BSはプロウベス[®]が 2.2 ± 1.9 、メトロイリントルが 2.18 ± 2.0 ($p=0.49$)と有意差が無かったが、誘発処置開始から12時間後の Δ BSはプロウベス[®]が 4.6 ± 3.8 、メトロイリントルが 1.5 ± 2.1 ($p<0.05$)と有意にプロウベス[®]で増加していた。【結論】本研究ではプロウベス[®]抜去後に子宮頸管熟化が進んでいた。プロウベス[®]はメトロイリントルと比較して子宮頸管熟化をさせるため、誘発成功率が高いと考えられたが、時間調節性のないことが問題点の1つである。

P-49-4 体重増加目標変更後の当院妊婦における体重増加量の検討

横浜市立大附属市民総合医療センター¹、横浜市立大²
梅原琴乃¹、中西沙由理¹、鈴木琴音¹、終一哉¹、小嶋朋之¹、山本賢史¹、進藤亮輔¹、小畑聡一郎¹、笠井絢子¹、
田野島美城¹、宮城悦子²、青木茂¹

【目的】2021年3月に日本産婦人科学会は妊娠中の推奨体重増加量を変更した。この改訂により、妊娠中の体重増加量が変化したかについて検討した。【方法】2020年1月から2023年7月に当院で妊娠37週以降に分娩した、単胎妊婦で妊娠初期から病院の受診があった妊婦を対象とし、妊娠中の耐糖能異常合併妊娠は除外した。対象妊婦は妊娠初期に推奨体重増加量についてパンフレットを用いて保健指導された。旧基準の推奨体重増加量で指導された2020年1月-2021年7月に分娩した990症例、新基準の推奨体重増加量で指導された2022年1月-2023年7月に分娩した906症例を解析対象とした。2021年7月-12月は基準移行期間のため除外した。非妊時BMIにより、やせ・標準・肥満1度、肥満2度以上の4群に分類し、妊娠中体重増加量、出生体重、低出生体重児率について後方視的に検討した。【成績】基準変更前後で非妊時の体格分布を含む母体背景に有意差は認めなかった。妊娠中体重増加量は、やせ群では基準変更前後で10.8kgと11.1kg($p=0.94$)、標準群では10.7kgと10.4kg($p=0.14$)、肥満1度群で9.7kgと9.2kg($p=0.32$)、肥満2度以上群で7.4kgと6.7kg($p=0.44$)でありいずれの群においても有意差は認められなかった。出生体重、低出生体重児の割合についても変更前後で有意差は認めなかった。【結論】いずれの体格においても、変更前後の期間で妊娠中体重増加量に変化は認められなかった。パンフレットを用いて保健指導だけでは体重指導として不十分な可能性が示唆された。

P-49-5 切迫流・早産例に対する単繊維合成吸収糸二重縫縮による治療的子宮頸管縫縮術の検討

兵庫県立こども病院
金子めぐみ、辻麻亜子、長澤友紀、木原智子、内山美穂子、窪田詩乃、荒井貴子、松本培世、平久進也、船越徹

【目的】妊娠21~23週間に子宮頸管短縮を認めた切迫流・早産例に対する単繊維合成吸収糸二重縫縮による子宮頸管縫縮術(以下、縫縮術)の治療成績を検討する。【方法】2016年5月-2023年3月に当院に入院となった重篤奇形を有していない単胎妊娠例のうち妊娠21週0日-23週6日に頸管短縮(頸管長 ≤ 25 mm)を認めた138例を対象とし後方視的に検討した。入院時に絨毛膜羊膜炎、慢性早剥羊水過少症候群、前期破水、持続的な出血があるもの、陣痛発来しているもの、入院日に分娩となったもの、胎胞が腔内に充満しているもの、子宮口3cm以上開大しているもの、縫縮術が前医で施行されているもの、胎児死亡、死産、常位胎盤早期剥離となったもの、縫縮が1重縫縮となったもの等の53例を除外した85例を対象とし、縫縮術施行群をA群、非施行群をB群とし、入院日から分娩までの妊娠継続期間と出生体重を主要評価項目として、妊娠転機を検討した。【成績】A群は21例、B群は64例、両群の母体背景に差はなかった。A群の縫縮術施行週数は、22.7週(21週4日-24週0日)。妊娠継続期間のそれぞれの中央値は14.7週(9-18.0) / 13.1週(0.6-19.3)、出生体重のそれぞれの中央値は2,645g(1,660-3,790) / 2,352g(533-4,006)であった。妊娠継続期間は有意差を認めたが($P<0.05$)、出生体重に有意差はなかった($P=0.12$)。A群に縫縮術に伴う合併症はなかった。【結論】切迫流・早産で子宮頸管短縮のある症例を適応とした縫縮術は妊娠期間延長において有用である可能性が示唆された。

P-49-6 産褥の貧血に対する鉄剤投与および輸血による治療効果の比較検討

順天堂大附属順天堂医院

北村絵里, 竹田 純, 石田ゆり, 松澤奈々, 山本祐華, 板倉敦夫

【目的】産後の女性の4割以上が貧血と診断される。鉄欠乏性貧血の治療には鉄剤投与が一般的だが、ヘモグロビン(Hb)7.0 mg/dL以下では輸血を行うことも多い、しかし輸血は副作用や感染症のリスクがあり、可能な限り鉄剤での治療が望ましい。そこで、産褥にHb 7.0 mg/dL以下の貧血症例において鉄剤の有効性について検討する。【方法】2022年に当院で妊娠37週以降に分娩し、産褥3日目の採血においてHb 7.0 mg/dL以下であった25例のうち、産後2週間から1か月で採血を実施した症例を輸血群(13例)、鉄剤群(4例)に分類し、貧血の推移や合併症について検討を行った。【成績】年齢、妊娠週数、妊娠後期採血の貧血関連項目、出生体重、分娩時出血量などの背景に有意差は認めなかった。産褥3日目採血ではHb 6.4 ± 0.2 vs 6.4 ± 0.3 g/dL, $p = 0.86$ であり、その他の貧血関連項目でも有意差は認めなかった。輸血群では平均 4.6 ± 0.5 単位の赤血球製剤を投与した。産後2週間から1か月での採血では、Hb 12.1 ± 0.7 vs 11.8 ± 0.5 g/dL, $p = 0.31$ 、血清鉄 77.9 ± 9.7 vs 77.5 ± 11.6 μ g/dL, $p = 0.98$ 、総鉄結合能(TIBC) 327.3 ± 19.6 vs 307.8 ± 18.1 μ g/dL, $p = 0.48$ 、フェリチン 169.9 ± 46.4 vs 168.3 ± 37.2 ng/mL, $p = 0.98$ と有意差は認めなかった。【結論】産褥3日目に貧血を認めた症例において、輸血の有無で1か月健診時の貧血関連採血項目に差は認めず、鉄剤投与は有効である。

P-49-7 当院における分娩誘発と周産期予後についての検討

三重中央医療センター

村瀬結香, 山口恭平, 下村優莉奈, 稲井由佳, 榊原洗太, 柏原優花, 北村亜紗, 張 凌雲, 吉村公一

【目的】2020年4月にジノプロストン腔内留置用製剤が認可され、頸管熟化および分娩誘発の選択肢が増えた。これが分娩転帰や周産期予後に及ぼす影響について検討した。【方法】プロウベス腔剤導入前の2017年4月から2018年3月までの前期群39例と、プロウベス腔剤導入後の2022年4月から2023年3月までの後期群33例を対象とし、患者背景や分娩転帰を後方視的に比較検討した。【成績】前期群ではメトロイリント使用群が17例(43.6%)、後期群ではメトロイリント使用群が11例(33.3%)、プロウベス腔錠使用群が13例(36.4%)、両者併用群が6例(18.2%)であった。母体年齢の中央値は前期群で31.8歳、後期群で31.0歳であった。分娩週数の中央値は前期群で39.6週、後期群で38.1週であった。分娩誘発の適応は、母体適応(妊娠高血圧症候群、妊娠糖尿病)が前期群で14例(35.9%)、後期群で11例(23%)、胎児適応(FGR、巨大児)が前期群で2例(5.1%)、後期群で6例(6%)であった。経陰分娩数は、前期群で32例(82%)、後期群で22例(65%)であった。新生児出生体重の中央値は、前期群で3093g、後期群で2903gであった。Apgar score(1分値)の中央値は前期群で8(7-9)、後期群で8(2-9)、Apgar score(5分値)の中央値は前期群で9(8-10)、後期群で9(8-10)であった。【結論】分娩誘発の母体適応の変化や分娩誘発方法の多様化は、経陰分娩率に影響を及ぼす。今後症例をさらに蓄積し、より適切な分娩誘発方法を検討していきたい。

P-50-1 凍結胚移植前に子宮筋腫核出術施行し、術後病理で smooth muscle tumor of uncertain malignant potential (STUMP) と診断されるも不妊治療を希望され行った2例

岐阜市民病院

亀山千晶, 平工由香, 手塚慶吾, 東松明恵, 栗原万友香, 谷垣佳子, 柴田万祐子, 豊木 廣, 山本和重

【緒言】子宮平滑筋腫瘍のうち悪性度が不明な腫瘍を smooth muscle tumor of uncertain malignant potential (以下STUMP)という。術前診断には限界があり子宮筋腫として子宮筋腫核出術を行い術後病理でSTUMPと診断される例が少なくない。子宮体癌ガイドラインによると、筋腫核出術後の症例では年齢、挙児希望の有無、手術時の腫瘍残存の可能性などの因子を考慮し追加手術について個別化し検討する必要がある。今回不妊治療中に子宮筋腫核出術を行い術後病理でSTUMPと診断されたが、追加手術を行わず不妊治療を継続した2例を経験したため報告する。【症例1】35歳、0妊0産。凍結胚移植前に子宮筋腫核出を勧められ紹介受診。子宮筋層内に72mm大腫瘍あり、子宮筋腫を第一に考えるが筋腫内出血ありSTUMPの可能性も指摘。挙児希望強く十分な説明の上、開腹子宮筋腫核出術施行。術後病理で平滑筋肉腫を疑われたが、セカンドオピニオン受診し、最終的にSTUMPの診断となった。術後8か月目の造影CTは異常所見なく、不妊治療再開希望され許可とした。【症例2】38歳、0妊0産。凍結胚移植前に子宮筋腫核出術を希望され紹介受診。最大径36mmの多発子宮筋腫・左内膜症のう胞を認め、腹腔鏡下子宮筋腫核出術+左卵巣腫瘍摘出術施行。術後病理診断はSTUMPであった。術後1か月目の造影CTで異常所見なし。セカンドオピニオン受診後妊娠性温存を希望され不妊治療再開。術後11か月目の造影CT・MRIでも異常所見なく、術後18か月で妊娠成立した。【結語】STUMPはほとんど良性的経過を辿るが、術後9年目での再発や転移の例がある。筋腫核出術後に追加切除しない場合の再発率やフォローについて文献的考察を加え検討する。

P-50-2 鼠径ヘルニア手術に起因する子宮付属器滑脱ヘルニアを腹腔鏡下に修復した一例

甲南会甲南医療センター

前田美亜, 大和奈津子, 黒島瑞穂, 井関菜美子, 登村友里, 井上佳代, 村田友香, 山崎友維, 森田宏紀

【緒言】鼠径ヘルニアの脱出臓器は腸管が一般的であり、卵巣や卵管の滑脱は稀である。鼠径ヘルニア修復術の合併症として稀ではあるが手術操作に伴う卵巣・卵管の巻き込みや卵管閉塞の報告がある。今回、右鼠径ヘルニア手術に起因する子宮付属器滑脱ヘルニアを腹腔鏡下に修復した一症例を経験したので報告する。【症例】25歳0経妊0経産。生後4か月の際に右鼠径ヘルニア修復術を施行され、退院後も右鼠径部の膨隆を自覚していた。最近になり疼痛が出現したため近医でMRIで精査したところ、右鼠径部膨隆部位に一致して卵巣・卵管の脱出を認めたことから、子宮付属器滑脱ヘルニアの診断となった。消化器外科と検討の上、子宮付属器滑脱ヘルニアに対して腹腔鏡下鼠径ヘルニア修復術を行う方針とした。術中所見では卵巣動脈および円靭帯、卵巣・卵管は前回の鼠径ヘルニア修復術の影響で一塊となり鼠径管内に嵌入を認めた。腹腔鏡下にヘルニア嚢内部に到達し右付属器を腹腔内に修復し、ヘルニア門にメッシュを挿入した。卵巣動脈はヘルニア嚢に嵌入していた影響で伸長しており、卵巣捻転のリスクを考慮し腹膜に卵巣を固定した。術中卵管通水検査では左卵管は正常であったが右卵管の通過性は確認出来なかった。術後経過は良好で術後2日目に退院となった。【考察】鼠径ヘルニア手術の既往がある症例では、婦人科診察時に患側付属器への影響を考慮する必要がある。

P-50-3 卵巣癌との鑑別に苦慮した胃腸管外間質腫瘍の一例

佐賀大附属病院

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【緒言】多量の腹水を伴う骨盤内腫瘍を認めた場合、婦人科悪性疾患であれば卵巣癌を第一に疑う。今回、卵巣癌との鑑別に苦慮した胃腸管外間質腫瘍(EGIST: Extra-gastrointestinal stromal tumor)の一例を経験した。【症例】54歳2妊2産、腹部膨満感があり近医を受診し、腹部超音波で多量の腹水を伴う腹腔内充実性腫瘍を指摘され、当院へ紹介された。経膈超音波で骨盤内に15cmの充実性腫瘍を認めたが、腹部CT及び骨盤部MRIでは充実性腫瘍と大網との連続性があり、腫瘍と別に両側の付属器腫瘍が確認できたため、充実性腫瘍は卵巣癌の播種病変あるいは大網由来の腫瘍と考えた。初診時に血性腹水を除去、腹水細胞診でmalignant cellを認めた。以上の結果から卵巣癌疑いの診断で根治術の方針とし、子宮、両側付属器、大網を切除した。術中所見では子宮、両側付属器には病変を認めず、新生児頭大の充実性腫瘍を大網に認めた。病理組織診断でEGISTの診断となり、イマチニブ内服を開始した。経過中に腫瘍の再発、再発部からの出血を認め止血術を施行した。血液腫瘍内科、消化器外科で加療されている。【考察】GISTは消化管筋層に存在するカハール介在細胞(interstitial cell of Cajal: ICC)由来の腫瘍であると考えられているが、EGISTではそのICCが存在しない部位に発生する。EGISTは全GISTの1-5%程度と言われており、症状に乏しいため10cm以上の巨大な腫瘍を形成し発見されることが多い。本症例において、画像上は大網以外に病変を認めなかったが、多量の腹水を伴っており、卵巣癌や腹膜癌との鑑別が困難であった。播種病変を伴わない大網結節を認めた場合はEGISTの可能性も考慮する必要があると考えた。

P-50-4 SMARCA4欠損を認めた婦人科悪性腫瘍の2例

新潟大

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【緒言】SMARCA4はBRG1蛋白をコードするで、さまざまな遺伝子の発現・複製・分離・修復などに関わっている。SMARCA4欠損腫瘍は、急速に進行する悪性度の高い稀な予後不良の悪性腫瘍である。当時は胸部腫瘍領域で報告されていたが、近年では卵巣高カルシウム血症型小細胞癌や子宮体部未分化腫瘍での報告も散見される。しかしその数は少なく、治療方法は確立されていない。当科において、SMARCA4欠損婦人科悪性腫瘍の2例を経験したので、文献的考察を加え報告する。【症例1】33歳の未婚女性、傍大動脈リンパ節転移を伴う10cm大の左卵巣腫瘍を認め、本人の強い妊孕性温存希望により左付属器摘出術、大網部分切除術、傍大動脈リンパ節摘出術を行った。病理診断は高カルシウム血症型小細胞癌で、一部SMARCA4の発現消失を認め、リンパ節転移陽性でありIIIC期と診断した。術後早期にリンパ節の増大を認めたが、EP療法6サイクルにて寛解し、現在術後10か月経過時点で再発所見なく経過観察中である。【症例2】50歳、左鎖骨上リンパ節・縦郭リンパ節腫大を伴う子宮体部を占拠する巨大な子宮悪性腫瘍が疑われ、子宮内膜生検によりSMARCA4発現消失を伴う未分化癌と診断した。全身状態不良で手術は困難と判断、TC療法を5サイクル行ったところ著明な腫瘍の縮小を認め、単純子宮全摘術、両側付属器摘出術を行った。腫瘍はMSI-Highでもあり、術後のリンパ節病変の増大に対してpembrolizumabをベースとした治療を継続しており、現在術後6か月経過している。【結語】SMARCA4欠損腫瘍は、極めて進行が早く悪性度が高いとされる。婦人科領域においても、このような疾患概念を念頭におく必要がある。

P-50-5 虫垂粘液腫（腹膜偽粘液腫）が後陰門蓋部まで浸潤し長期に渡る帯下異常をきたしていた一例都城医療センター
古田祐美

腹膜偽粘液腫（pseudomyxoma peritonei；PMP）は虫垂や卵巣の粘液産生腫瘍が破綻することで腹腔内へ播種し大量のゼリー状粘液が貯留する病態である。その頻度は欧米での報告では100万人に1人と稀な疾患である。今回我々はPMPと診断し外科と合同手術により腫瘍の完全切除を施行した症例を経験したので報告する。【症例】73歳，2経産，閉経48歳。【既往歴】40歳～高血圧，54歳：急性心筋梗塞でステント置換術【主訴】長期の漿液性帯下【現病歴】約2年前より漿液性帯下のため前医で管理されており精査目的に当科紹介となった。【初診時診察】陰鏡診では子宮頸部に異常所見なし。後陰門蓋部に小嚢胞が多数見られ易破裂性でゼリー状の粘液の排出がみられた。子宮頸部，内膜細胞診はいずれも陰性。嚢胞の生検で腸型の組織が検出され外科と併診とした。【造影CT】子宮頸部背側に3cm大の腫瘤を認め虫垂との連続あり。【入院後経過】虫垂粘液腫の疑い（子宮腔壁浸潤）に対して開腹手術を施行。虫垂は長く骨盤内へ伸展し粘液腫を形成し可動性不良であった。横行結腸と大網，子宮後面と直腸，虫垂から連続する粘液腫瘍と右尿管とが強固に癒着しており手術は難航したが腸管や尿管の損傷なく癒着剥離でき子宮全摘+両側付属器切除+回盲部切除+D3郭清術を施行できた。病理結果で低異型度虫垂粘液腫瘍と診断。粘液腫瘍は腹膜，子宮頸部への浸潤を認め子宮内腔まで穿破していた。術後経過良好で退院した。【結語】PMPは稀な疾患であり虫垂や卵巣などが原発で，骨盤臓器への浸潤も多く報告されている。そのため骨盤臓器合併切除など大手術となる。治療に対しては本疾患に関した十分な知識と理解が必要である。

P-50-6 バルトリン腺嚢胞と間違えられた外陰富細胞性血管線維種（Cellular angiofibroma）の一例東邦大医療センター大森病院
向井隆文，齋藤有沙，小宮山慎一，長島 克，釘宮剛城，中田雅彦

【緒言】富細胞性血管線維種は外陰部に発生する非常に稀な間葉系腫瘍である。病理学的には良性腫瘍であり，外科的切除が治療の基本となる。鑑別疾患として侵襲性血管粘液種や血管線維芽細胞腫等が挙げられるが，これらは肉眼診断が難しくかつ管理指針が異なるため注意が必要である。一方でこれらの外陰腫瘍はバルトリン腺嚢胞と間違えられ，安易な穿刺で強出血を来すこともあるという。われわれはバルトリン腺嚢胞と診断された外陰富細胞性血管線維種の一例を経験した。【症例】51歳，0妊0産。10年以上前から外陰部の腫大を認め増大傾向であるため前医を受診した。バルトリン腺嚢胞を疑い，同医で穿刺を行うも内容液は吸引できず，腫瘍より多量出血を認めたため当院へ紹介受診となった。初診時に左外陰に手拳大の可動性良好な硬結を伴う腫瘍を認めた。MRIでは長径10cmの外陰皮下を中心とする腫瘍を認め，T2強調画像で高信号域内に葉状および結節状の低信号域を認めた。診断と治療を兼ねて，腫瘍の単純局所切除術の方針とした。術中所見では腫瘍と正常組織の境界は明瞭であり，残存なく腫瘍を摘出した。術後経過良好で第7病日に軽快退院した。病理学的には大小の拡張した血管とともに紡錘形および星芒状の異型の乏しい腫瘍細胞の増殖を認め，同部の免疫組織染色ではdesminが一部陽性，ERとPgRが陽性，S-100蛋白とSMAとCD34は陰性であった。以上より富細胞性血管線維種と診断した。術後18か月経過した現在，再発兆候を認めていない。【結語】外陰富細胞性血管線維種の一例を経験した。外陰腫瘍は肉眼診断が困難ゆえ，手術的摘出を行い病理学的に確定診断し，適切に管理することが肝要である。

P-50-7 “Floating fat ball sign”，別名“Boba sign（タピオカサイン）”という特徴的な画像所見を示した成熟奇形腫の一例公立豊岡病院組合立豊岡病院
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【目的】成熟奇形腫（mature teratoma）は通常，超音波検査やCT，MRIで脂肪成分を同定することで術前に診断することが可能である。また歯牙や骨成分もUS，CTで同定可能であり診断の一助となるが，多彩な画像所見を呈するため診断に苦慮することも多い。今回，術前の画像評価において“Floating fat ball sign”，別名“Boba sign（タピオカサイン）”，“Sack of marbles sign（ビー玉袋サイン）”，あるいは“Meat balls（ミートボール）”等とも呼ばれる特徴的な所見を示す成熟奇形腫の1例を経験したため報告する。【症例】53歳，女性，1経妊，1経産。15年前にMRIで80mm大の右卵巣奇形腫の診断を受けていた。フォロー自己中断しており，X年に近医受診し経腹超音波で20cmを超える骨盤内腫瘍を認めたため精査加療目的に当科紹介受診。MRIにて217×186×126mm大の巨大単房性嚢胞と，内部に10-30mm大の浮遊球を無数に認めた。嚢胞内容液はT2強調画像で高信号，T1強調画像で低信号と漿液性成分と考えられ，無数の浮遊球はT1強調画像T2強調画像ともに中等度の信号ではあったが脂肪抑制で信号低下し脂肪成分の含有が疑われた。また，浮遊球はすべてdiffusion画像で拡散制限を認めた。成熟奇形腫の術前診断で腹式右付属器切除を行った。手術時間は1時間20分，出血量は82mlであった。術後経過は良好であり術後8日目に退院となった。病理診断の結果，皮膚類似組織，軟骨を含む気管支類似組織，小腸粘膜と類似した組織がみられる成熟嚢胞性奇形腫であり悪性を疑う所見は認めなかった。【結論】“Floating fat ball sign”は成熟奇形腫に非常に特異的な所見でありその診断に有用である。

P-50-8 診断に時間を要した外陰部 Verrucous Carcinoma (疣状癌) の一例

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榊原秀也¹、浅野涼子¹

【緒言】疣状癌は高分化低悪性度の有棘細胞癌の稀な一型で、高齢女性が多い。外陰癌との鑑別を要するが、転移は稀である。今回、生検を繰り返すも診断に至らず、外陰部分切除により診断に至った外陰部疣状癌症例を経験した。【症例】45歳、2妊2産、44歳時に外陰部の搔痒感を主訴に近医皮膚科を受診した。その後生検を3回繰り返したが、良悪性の判別が困難であり、前医を紹介受診した。前医皮膚科で疣状癌を疑われ、部位から外陰癌も鑑別として挙がり、当院を受診した。陰核を主として右優位に両側大陰唇に及ぶ紅色で一部白色を伴う隆起性病変を64×49mm大で認めた。子宮、卵巣、腔内に異常所見はなく、両側鼠径リンパ節を触知しなかった。前医生検標本を再確認し、疣贅病変で悪性を否定できないものの確定する所見は認めなかった。腫瘍マーカーの上昇はなく、画像検査では異常所見を認めなかった。皮膚科にも併診し、外陰癌が否定できないものの、悪性未確定下での侵襲度を考慮し、診断的治療目的で外陰部分切除を行い、悪性であれば追加治療を行う方針とした。外陰部腫瘍から2mm離れた範囲で外陰部分切除術を行った。術後病理で圧排性浸潤と考えられる部分を一部に認め、病変の大きさと合わせて疣状癌の診断となった。一部断端に腫瘍が接しており、追加切除と所属リンパ節郭清を提案したが、追加治療の希望なく、経過観察中である。【結論】疣状癌は生検のみでは診断に至らないこともあり、その場合は病変を全切除し評価することが望ましい。病変が大きく複数回の生検でも診断がつかない場合には、二次的治療も視野にいれ外陰部分切除をすることで、診断および適切な治療選択が可能になると考えられた。

P-50-9 診断まで2年を要した外陰部バルトリン腺癌の一例

九州医療センター

古賀さくら、竹内 優、大塚裕一郎、永谷優華、荒木研士郎、中並弥生、田中大智、梶之浦佳奈、庄とも子、瓦林靖広、
藤原ありさ、小川伸二

【緒言】バルトリン腺癌は外陰癌の0.1~5%と稀な疾患であり、その15%がバルトリン腺腺様嚢胞癌と報告されている。比較的緩徐に進行し、臨床症状が非特異的であるため診断に時間を要する症例も少なくない。針生検が診断に有用であったバルトリン腺腺様嚢胞癌の一例を経験したため報告する。【症例】68歳、3経妊3経産。X-2年から右外陰部腫瘍を自覚した。X-1年に同部位に疼痛が出現し、近医を再診し2cm大の右外陰部腫瘍を認めたが自然経過観察で疼痛は軽快した。X年に再度同部位に疼痛が出現し、近医を再診し右外陰部腫瘍は3cm大に増大していた。バルトリン腺膿瘍を疑われ抗生剤加療をされたが症状は改善せず、前医を紹介受診した。右外陰部腫瘍は可動性良好で硬く触知された。骨盤MRI検査で悪性腫瘍が疑われた為、精査加療目的に当科を紹介受診した。右大陰唇皮下に3.5cm大の可動性不良な硬い卵形状腫瘍を触知した。吸引細胞診を施行し、偽陽性(N/C比の高い類円形~短紡錘形の小型異形細胞)であった。針生検を施行し組織生検結果はadenoid cystic carcinomaであったためバルトリン腺癌と診断した。造影CT検査では性状の異なる成分を含む外陰部腫瘍を認め、明らかな遠隔転移やリンパ節の腫大は認めなかった。形成外科合同で広汎外陰切除術を施行し、病理組織結果はバルトリン腺腺様嚢胞癌、IB期(pT1bNxM0)であった。術後は放射線治療を施行した。【結語】バルトリン腺癌の症状は非特異的であり良性疾患との鑑別が難しい為、早期に病理学的診断を行うことが望ましいと考える。

P-50-10 長期の免疫抑制剤投与による腔癌を発症したと思われる一例

東海大付属八王子病院

牧野田知奈美、原伸之介、牧野田佳、栗山裕貴、大岩一平、西島義博、前田大伸、村松俊成

【緒言】腔癌は非常に稀な疾患であり、女性生殖器がんの約1%程度といわれている。多くは高齢者に発症するが、32歳で腔癌の診断に至った一例を経験したので報告する。【症例】32歳、既婚、0妊0産。性器出血を主訴に前医を受診し、腔癌疑いで当院紹介受診となった。既往にクローン病があり、免疫抑制剤の投与が15年間行われていた。腔鏡診で、腔の著明な委縮と腔壁全体に腫瘍性変化を認め、易出血性であった。内診は、痛み刺激が強く施行不能であった。子宮頸部細胞診はNILM、内膜細胞診は疼痛により施行困難であったが、前医で偽陽性であった。また、腔壁生検にて扁平上皮癌の診断であった。腫瘍マーカーは、CEA 3.8、CA125 6.6、SCC 0.9であった。造影MRI検査では腔壁左側および後壁に造影効果を伴う肥厚病変を認めた。また、子宮筋層浸潤を伴う腫瘍性病変を認め、子宮体癌の可能性も考えられた。造影CT検査では多発肺転移を認め、PET-CT検査で多発胸膜転移、多発骨転移あり、腔癌IVB期の診断に至った。根治術や放射線療法の適応はなく、パクリタキセル+カルボプラチン+ペムプロリズマブの投与と、出血コントロールおよび疼痛緩和目的で放射線照射を行い、現在治療中である。【結語】今回我々は、若年で腔癌を発症した一例を経験した。長期の免疫抑制剤投与によりヒトパピローマウイルスの除去が妨げられる可能性は指摘されているが、今症例ではその影響による腔癌の発症が疑われた。今後さらなる症例の蓄積、因果関係の解明が望まれる。

P-50-11 外陰部に生じた明細胞癌の一例

大阪はびきの医療センター

梅原健耶, 長安実加, 坂元優太, 中谷沙也佳, 穂西実加, 安川久吉, 赤田 忍

【背景】外陰部に生じる上皮性腫瘍のほとんどが扁平上皮由来であり、外陰部原発の明細胞癌は非常に稀である。今回、外陰部原発の明細胞癌の一例を経験したので報告する。【症例】症例は63歳、2経妊2経産分娩、51歳閉経。既往に脳出血、症候性てんかんがある。家族歴に特記事項なし。2-3年前から緩徐に増大する外陰部のしこりを主訴に前医受診された。前医で腫瘍摘出術が行われ、明細胞癌が検出された。婦人科または泌尿器科由来の転移性腫瘍が考えられたため、紹介受診となった。腎臓MRIで異常認めず泌尿器科由来は否定的であった。内診で明らかな腫瘍を認めず、腫瘍マーカーはCA125が5.5U/mL、CA19-9が3.2U/mLと上昇を認めなかった。造影CT検査、造影MRIでは子宮筋腫のみで付属器に明らかな原発病変は認めず、PET-CT検査で異常集積は認めなかった。原発精査のため試験腹腔鏡を行い、腹腔鏡補助下腔式子宮全摘術および両側付属器切除術を行った。腹腔内に明らかな内膜症病変は認めず、肉眼的に付属器に異常所見を認めなかった。病理学的検索では腹水細胞診が陰性、子宮、両側付属器に悪性所見は認めず、外陰部原発の明細胞癌IB期(pT1bN0M0)の診断に至った。術後治療は行わず経過観察中であるが、現時点では再発や転移を認めていない。【結語】今回、外陰部原発の明細胞癌の一例を経験した。外陰部明細胞癌の症例は非常に稀であるが、そのほとんどは外陰部子宮内膜症と関連しているとされる。分娩時の会陰切開癒着部に異所性に内膜症病変が生じ、癌化した可能性が示唆されるが、明確な機序は定かではない。予後予測因子や治療方法については明確に確立されたものは無く、今後も症例の蓄積が必要である。

P-50-12 子宮炎症性筋線維芽細胞性腫瘍の一例

別府医療センター

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43歳、2妊2産。202X年8月に繰り返す過多月経と貧血を主訴に当院を紹介受診した。MRI検査で子宮前壁筋層内に長径8cmの境界明瞭な腫瘤を認め、拡散制限や壊死、出血性変化を認めず、富細胞性子宮筋腫の所見であった。子宮筋腫の術前診断で、子宮全摘出術の方針とした。GnRH療法を6か月間施行し、202X+1年1月のMRI検査で腫瘤は長径7.5cmであった。同年2月に腹腔鏡下単純子宮全摘出術、両側卵管摘出術を施行した。子宮は経腔的に細断しながら摘出した。術後病理診断は炎症性筋線維芽細胞性腫瘍(IMT)であった。IMTは軟部腫瘍の中で境界悪性腫瘍に分類される稀な腫瘍で、主に肺などの内蔵臓、軟部組織に発生するが、子宮に発生することは極めて稀である。免疫組織学的にIMTはDesminやSMAなどが陽性となるため、平滑筋腫瘍との鑑別に難渋しやすい。本症例はALK蛋白の発現を認めたことから、子宮IMTの診断に至った。

P-50-13 成熟嚢胞性奇形種に対する腹腔鏡下卵巣腫瘍核出術後に化学性腹膜炎をきたした1例

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【緒言】成熟嚢胞性奇形種は、術中の腫瘍破綻による内容液の漏出で化学性腹膜炎が発症すると報告がある。我々は、成熟嚢胞性奇形種に対する腹腔鏡下卵巣腫瘍核出術後に腫瘍内容液の漏出による化学性腹膜炎をきたした症例を経験したので報告する。【症例】16歳、0妊0産、月経困難症で近医を受診。右卵巣腫瘍の手術目的で当院へ紹介受診。骨盤MRIでT2高信号、脂肪抑制T1低信号である成熟嚢胞性奇形種に対して、腹腔鏡下手術を施行した。オープンダイヤモンド法で腹腔内に到達し、右卵巣9cm、左卵巣5cmと腫大していた。サンドバルーンで右卵巣腫瘍を穿刺し、吸引後に腫瘍を核出し、組織回収用バックに入れ回収した。穿刺時に腫瘍は完全破綻し、内容液が腹腔内へ漏出した。左卵巣腫瘍は漿液性内容液を吸引のみで終了し、腹腔内に漏出した脂肪や毛髪成分を含む腫瘍内容液を可能な限り回収し、生理食塩水で洗浄し手術終了した。術後1日目は発熱や腹痛なく、WBC20200/μl、CRP2.8mg/Lであった。夜間に39℃の発熱と腹痛があり、翌日WBC24300/μl、CRP20.7mg/Lと上昇していた。造影CTでダグラス窩に局限性腹膜炎があり、感染の可能性も考慮し抗生剤を開始した。術後6日目にWBC8100/μl、CRP2.0mg/Lと低下し、症状改善あり退院となった。腔培養はLactobacillus、血液及び尿培養は陰性であった。右卵巣腫瘍の病理組織学的検査では成熟嚢胞性奇形種の診断であり、悪性所見はなかった。【結語】成熟嚢胞性奇形種に対する腹腔鏡下卵巣腫瘍核出術後に発症する化学性腹膜炎は症状が強いので対策を検討していく必要がある。

P-50-14 原発巣および感染経路不明な膿瘍を伴う後腹膜腫瘍の一例

ベルランド総合病院

山下 央, 田村 聡, 姜 雅衣, 小川 萌, 益田真志, 松山佳奈子, 松木貴子, 濱田真一, 大西淳仁, 宮武 崇, 山崎正人, 村田雄二

症例は76歳, 1妊1産. 前医内科で撮像された腹部単純CTにて偶発的に右卵巢嚢腫を指摘され, 骨盤部単純MRIで約7cm大の充実成分を伴わない単房性の右卵巢嚢腫を認め, 当院紹介となった. 悪性所見は乏しく, 待機的に手術加療を行う予定であった. 当院初診から約4か月後に発熱を認めたため, 前医を受診し尿路感染症を疑われ, 入院の上で抗菌薬加療が行われていた. その後, 炎症反応は改善せず, 腹痛が出現したため, 当院搬送となり卵巢嚢腫茎捻転が疑われた. 腹腔鏡手術を行ったが, 術中診断で卵巢嚢腫茎捻転は認めず, 後腹膜腫瘍の診断となり, 原発巣の精査を行う方針とした. 術後, 骨盤部造影MRI, 腹部造影CTの結果, 膿瘍を伴う後腹膜腫瘍の診断となった. 上部, 下部消化管内視鏡にて腸管と腫瘍の交通は明らかではなく, 腫瘍の原発巣は不明であった. 抗菌薬加療を継続したが, 炎症所見の改善は乏しく, 外科にて腫瘍摘出術の方針となった. 入院11日目に腹腔鏡下腫瘍摘出術を行ったが, 術中の癒着所見が強く, 開腹手術に移行し腫瘍摘出を行った. 術後の病理診断では, 慢性の炎症細胞浸潤と線維化を認めるのみで, 原発巣は不明であり, また悪性所見は認めなかった. 本症例のように感染を伴い膿瘍化している後腹膜腫瘍の症例報告は少ない. 今回我々は, 原発巣および感染経路不明な膿瘍を伴う後腹膜腫瘍の一例を経験したため, 若干の文献的考察を踏まえて報告する.

P-51-1 当科における Mychoice™ 診断システムの結果と治療選択について

高崎総合医療センター

東 杏莉, 横山蓉子, 周藤 周, 黒住未央, 青木 宏, 伊藤郁朗

MyChoice™ 診断システムは2021年1月より保険適応となった, 進行性の卵巢癌・卵管癌に対する維持療法選択のための検査である. 当科において, 2021年4月から2023年3月までにHRD検査を提出した上皮性卵巢癌・卵管癌・腹膜癌を対象として, MyChoice™ 診断システムを用いた検査の結果とプラチナ製剤による化学療法, その後の維持療法の治療効果について検討した. 対象とした16例の検査結果は, tumor BRCA 病的バリエーション6例 (BRCA1:1例, BRCA2:5例) を含む陽性症例が9例 (56%), 陰性症例7例 (44%) であった. 当科症例では, 既存報告と比較しHRD陽性と判定される割合は同等であった. また, その検査結果を受け, プラチナ製剤後の維持療法の選択肢は①PARP阻害薬とベバシズマブを併用する, ②PARP阻害薬単剤を使用する, ③ベバシズマブ単剤を使用する, ④治療は行わず経過観察とする, に分けられていた. ①は2例, ②は8例であった. ①ではいまだ再発は認めず, ②も再発を認めた例は1例であり, ④と比較すると現状は予後良好であった. PARP阻害薬の使用が一般的となつてから, ③を選択する症例数は減少していた. PARP阻害薬では使用開始早期に貧血の進行や血小板減少が懸念される. 薬剤によって異なる副作用に注意しつつ, 今後も各治療群の経過を確認する必要がある.

P-51-2 卵管癌に合併した心タンポナーデの1例

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【緒言】心タンポナーデの内科的要因として癌性心膜炎が重要であるが, 卵巢・卵管癌における心タンポナーデの合併は稀である. 今回, 卵管癌に合併した心タンポナーデの症例を経験したので報告する. 【症例】82歳, 2経産. 61歳で右乳癌を発症, 79歳で右卵管癌 (IIIc期, 高異型度漿液性癌) を発症し, 遺伝学的検査で遺伝性乳癌卵巢癌症候群と診断されている. 初回治療として両側付属器切除術を行い, NAC療法 (パクリタキセル+カルボプラチン) 後に腫瘍減量術を施行し初回治療終了した. 以後, オラパリブを使用していたが, 初回治療後1年8か月に, 癌性胸水で再発した. 胸水除去後に胸膜癒着を施行し, ゲムシタビン+カルボプラチン療法を施行したが治療効果はSDであった. 化学療法を終了し緩和治療を主体とした外来管理の方針となった. 再発後1年6か月で労作時の呼吸苦, 全身倦怠感, 尿量減少が出現し, SpO₂:88%, 胸部X線で右胸水の増加を認め, 胸部単純CTで心とう液貯留を認めた. 少量であり経過観察としていたが, 数日後に呼吸増悪の進行と血圧低下があり, 心臓超音波検査で心とう液の増加を認め, 心タンポナーデと診断した. 心とう穿刺を行い, 850mLの血性排液を認め, 穿刺液の細胞診は陽性 (高異型度漿液性癌疑い) だった. 穿刺後は心とう液の再貯留なく心収縮能は改善し, 自宅退院となった. 【考察・結語】卵管癌に癌性心膜炎を合併し心タンポナーデを来した稀な一例を経験した. 本症例では, 心とう穿刺により状態改善を得て, 外来管理の継続が可能であった. 緩和治療に移行した症例において急激な呼吸状態の悪化を認めた場合, 心タンポナーデの合併を念頭に置いた管理と積極的な治療が必要である.

P-51-3 抗 NMDA 受容体抗体脳炎に対し複数回の腹腔鏡下手術を施行した1例

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【背景】抗 N-Methyl-D-Aspartate (以下 NMDA) 受容体脳炎の若年女性患者は6割に卵巣奇形腫を合併する。同腫瘍合併例では、腫瘍摘出が予後を改善するとされている。今回、我々は両側卵巣奇形腫を合併した抗 NMDA 受容体脳炎に対して3回の腹腔鏡下手術を行った症例を経験したので報告する。【症例】29歳0妊0産。前日からの幻覚・幻視及び躁病様の性格変化を主訴に当院の救急外来を受診した。腹部CTで両側に卵巣奇形腫の所見を認め、Probable 抗 NMDA 受容体脳炎の診断となった。腹腔鏡下に右側は付属器摘出を行ったが、左側は妊孕性温存のため卵巣腫瘍核出に留めた。術後に薬物療法も開始したが、痙攣発作が頻発し鎮静、人工呼吸器管理を要する状態が続いた。入院時に提出した髄液中のIgG型抗 GluN1抗体が陽性と判明し definite 抗 NMDA 受容体脳炎の診断になった。術後3か月のCTで左卵巣奇形腫の残存を認め、腹腔鏡下左卵巣腫瘍核出術を施行した。術後、痙攣発作は消失し人工呼吸器から離脱した。意識レベルは順調に改善したが、認知機能や高次機能などの改善が緩微であったため、薬物治療を追加した。2回目の術後4か月のCTで左卵巣奇形腫の再発を認めたが、症状が改善傾向であったため経過観察とした。しかし幻視の残存などがあり、腹腔鏡下左卵巣腫瘍核出術を施行した。術後、月経周期は正常で、神経症状は日常生活に支障がない程度に回復した。【考察】本症例では手術自体の治療効果を厳密に判定するのは難しいが、2・3回目の術後は一定の症状改善を認めた。本疾患で術後の経過が思わしくない場合、画像検査を繰り返し、腫瘍の残存・再発を認めた場合、積極的に手術を行うことが有用であると考えた。

P-51-4 腹水細胞診陰性で鑑別診断に苦慮し、TC+BEV療法が奏効した卵巣肺型小細胞癌の1例

総合病院土浦協同病院

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卵巣肺型小細胞癌は卵巣がんの組織型において非常に稀で治療法は確立されていない。腹水細胞診陰性で鑑別診断に苦慮し、審査腹腔鏡後にTC+BEV療法で治療を行った卵巣肺型小細胞癌の1例を経験したので報告する。47歳女性、0妊0産、外国籍。腹部膨満感と呼吸困難感を主訴に救急外来を受診し、CTで大量腹水、腹膜播種、多発リンパ節腫大、6cm大の骨盤内腫瘤を認め当科へ紹介となった。癌性腹膜炎が強く疑われ診断目的に腹水細胞診を施行したが腹水中に異型細胞は認めず陰性だった。その後さらに3回の腹水細胞診を行ったがすべて陰性で、確定診断には至らなかった。腫瘍マーカーは血清CEA 0.7 ng/ml, CA19-9 7IU/mlと正常値でCA125のみ38IU/mlと高値を示していた。診断目的に審査腹腔鏡を施行した。腹腔内に貯留していた腹水約7Lを吸引し、腹膜播種の一部を生検し術中迅速病理検査に提出した。腹水細胞診：陰性、組織診：低分化がんの診断を得た。免疫染色を追加しPAX8 (+), CD56 (+), ChromograninA (+), INSM1 (+), Synaptophysin (+)であり術後診断は卵巣肺型小細胞癌 StageIVB (肝転移あり)となった。患者の全身状態や希望を尊重しパクリタキセル・カルボプラチン・ペバシズマブ (TC+BEV) の投与を手術1か月後より開始した。化学療法1コース施行後より腹水は減少し、3コース投与後の治療評価CTでは原発巣、播種病変、肝転移、リンパ節転移の縮小と腹水の減少を認め部分奏功と診断し同治療を継続した。初回治療から6か月経過した現在も腫瘍縮小を維持している。【結語】進行卵巣がんで癌性腹膜炎をきたしているにもかかわらず腹水細胞診が複数回陰性となる例を経験した。また、卵巣肺型小細胞癌の治療としてTC+BEVが有用である可能性が示された。

P-51-5 帝王切開時の卵巣腫瘍摘出により診断された悪性卵巣甲状腺腫の1例

岩手県立二戸病院

千田英之, 小笠原敏浩, 阿部真璃奈, 齋藤達憲, 千葉淳美, 佐藤昌之

【緒言】悪性卵巣甲状腺腫の好発年齢は40～60代であり妊娠に伴っての悪性卵巣甲状腺腫の報告は稀である。今回我々は、帝王切開時の卵巣腫瘍摘出により診断された悪性卵巣甲状腺腫の1例を経験したため、若干の文献的考察を加えて報告する。【症例】31歳、1妊0産。既往歴に特記すべきことなし。前医で胎児頭殿長より分娩予定日を決定され、当院での妊婦健診を希望され妊娠10週で当科紹介となった。初診時の経陰超音波検査で、左卵巣に28mmの腫瘍性部分を認めていた。その後の妊娠経過は順調であり、低置胎盤のため妊娠38週で選択的帝王切開術を行った。手術時間1時間18分、出血量781g(羊水込み)。兄は2722gの男児であった。左卵巣が11cm×9cm大に腫大しており、正常卵巣部分を残して核出した。左卵巣腫瘍は187g。術後の病理組織検査の結果は悪性卵巣甲状腺腫であり、形態的に乳頭癌を考える所見であった。帝王切開術後37日目に、追加手術として左付属器摘出術および大網生検、腹膜生検を行った。手術時間1時間27分、出血量25g。抄録作成時点では病理組織検査の結果は未着であるが、乳頭癌に経過観察上有用な腫瘍マーカーがないため、1か月毎の診察および3か月毎のCT検査での慎重な経過観察を予定している。【考察】卵巣甲状腺腫の発生頻度は卵巣腫瘍の約0.5%で、その約0.1～0.3%が悪性転化すると報告されており、悪性卵巣甲状腺腫は稀な疾患である。妊娠に伴っての卵巣甲状腺腫の報告は稀であるが、妊娠の影響により急速に増大する可能性が指摘されている。【結語】帝王切開時の卵巣腫瘍摘出により診断された悪性卵巣甲状腺腫の1例を経験した。妊娠中の卵巣腫瘍の増大は甲状腺腫も念頭におく必要がある。

P-51-6 原発巣がSTICであった卵管癌 IV 期の 1 症例

京都第一赤十字病院

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【緒言】2022年12月の卵巣腫瘍・卵管癌・腹膜癌取り扱い規約病理編が改訂された。高異型度漿液性癌(HGSC)の決定基準と漿液性卵管上皮内癌(STIC)の改訂点が最大のポイントである。HGSCの多くが卵管を起源として卵巣や腹膜へ転移・進展したものであることから、粗大な病変がない場合においても骨盤内にHGSCをみとめ、卵管にSTICやHGSCをみとめた場合卵管癌として取り扱われる。今回、転移性大腸癌を契機として診断された卵管癌で、原発巣がSTICのみであった症例を経験したため報告する。【症例】76歳。1経妊1経産。既往歴はパーキンソン病、子宮筋腫のため40歳時に子宮全摘術を施行。便通障害を主訴に前医を受診。腹部CTで横行結腸の腫脹と傍大動脈リンパ節腫大をみとめた。精査のため下部消化管内視鏡を施行した。横行結腸中間部に狭窄をみとめ同部位の生検を行い、婦人科由来のHGSCが疑われたため当科紹介となった。超音波検査、MRIで明らかな付属器の腫大はみとめず、PET-CTでは横行結腸腫瘍、傍大動脈領域や鎖骨上窩のリンパ節に集積があり、両側付属器には集積がなかった。原発巣検索のため、消化器外科と同時に手術を行う方針となった。消化器外科で横行結腸切除および吻合を行い、婦人科で両側の付属器を摘出。両側付属器は腹壁に埋もれるような状態で、両側とも正常大で明らかな腫大はなかった。病理組織学的診断で左卵管にSTICをみとめ、卵管癌pT1aN1M1, IVb, 転移性卵管癌の診断となった。【考察】進行卵管癌であっても原発巣の卵管にはSTICのみを認め、画像検査では診断ができない場合がある。病理組織診断でHGSCが疑われた場合、画像所見がなくとも積極的な卵管の病理組織の検索が重要である。

P-51-7 適切な腫瘍内容吸引により良好な周術期経過を得た巨大卵巣腫瘍の3例

新潟大

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【緒言】巨大卵巣腫瘍に対する手術では、腫瘍内容の吸引・腫瘍縮小が必要になることが多い。その際、急激な腹腔内圧低下により一気に静脈環流が増加し再膨張性肺水腫をきたす場合があり、慎重な手術計画ならびに周術期管理が必要となる。今回、術中の適切な速度での腫瘍内容吸引により、良好な周術期経過が得られた3症例を報告する。【症例1】56歳、長径30cm大の多房性粘液性腫瘍に対し、1本の吸引管を使用し、500ml/分で、計22分かけて計11.3Lの腫瘍内容を吸引して腫瘍を縮小させ、付属器摘出術を実施した。【症例2】67歳、20kg程度の体重増加と急激な腹部膨満のため受診した。長径40cmを超える巨大卵巣腫瘍に対し、2本の吸引管を使用して450ml/分で計56分かけて計25Lの腫瘍内容を吸引し、付属器摘出術を実施した。本例では腹部～下肢の浮腫がひどく術後の静脈環流増加、体液コントロールが困難と判断し、術後1日目まではICU管理、2日目から一般病棟に転棟したが、その後20日間でさらに25kgの体重減少を認め、腫瘍内容と合わせ計49kgの減少となった。リハビリは術後13日目から介入し、長期臥床による筋力低下を認めていたが、体重減少とともに徐々にADLの上昇を認め、術後20日目に退院した。【症例3】57歳、長径34cm大の多房性粘液性卵巣腫瘍に対し1本の吸引管を使用して500ml/分で計20分かけて計10.1Lの腫瘍内容を吸引し、両側付属器切除を行った。これら全ての症例で、術中のバイタルサインの大きな変動や呼吸状態の悪化、術後の再膨張性肺水腫を認めず経過した。【結語】巨大卵巣腫瘍に対しては、450-500ml/分程度での腫瘍内容吸引により、安全な手術並びに周術期管理が行える可能性がある。

P-51-8 多発リンパ節転移、トルソー症候群を呈するも原発巣の特定が困難であった卵管癌の1例

弘前総合医療センター

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【緒言】卵管癌の転移経路として、骨盤内臓器への直接進展や、腹腔内臓器への播種性進展の他に骨盤・傍大動脈領域へのリンパ節転移が多いとされる。今回、我々は深部静脈血栓症(DVT)、腎梗塞および小脳梗塞を発症するも原発巣の特定に苦慮した卵管癌の1例を経験したので報告する。【症例】73歳、3妊2産。右下肢浮腫を主訴に近医内科を受診し、DVTの診断で内服による抗凝固療法が開始となった。1か月後に右背部痛で再受診し、CT検査で右腎梗塞に加え左腋窩リンパ節、腹部傍大動脈リンパ節、左腸骨リンパ節等、全身のリンパ節腫大を認め、悪性リンパ腫疑いで当院血液内科に紹介となった。PET-CT検査では腫大したリンパ節に陽性集積を認めた。CA125:1001U/mlと高値で婦人科悪性腫瘍も鑑別に挙がり左腋窩リンパ節生検の方針となった。しかし生検前に両側小脳梗塞を発症し、ヘパリン点滴による抗凝固療法が開始となった。左腋窩リンパ節生検の病理検査で、serous carcinoma, p53陽性、PAX8一部陽性、ER陰性、WT-1陰性で生殖器由来が考えられた。DVTの診断から45日経過後に当科紹介、64日目に腹式子宮全摘術+両側付属器切除術+大網切除術+左骨盤リンパ節生検術を施行した。左卵管遠位側が2cm弱に腫大し内腔に充満する腫瘍を認め、高異型度漿液性癌でリンパ管侵襲が著明であった。子宮筋層の一部に腫瘍のリンパ管浸潤が確認されたが卵巣は正常大であった。PET-CTを再評価し、左腸骨リンパ節の陽性集積が疑われた所見は卵管癌の集積であったと考えられた。【結語】卵管癌は原発巣が非常に小さくとも、全身転移の可能性があることを念頭に置き診断することが重要である。本症例に関して文献的考察を加え報告する。

P-51-9 再発を繰り返す成人型顆粒膜細胞腫の2例

横浜市立大

今井雄一, 松永梨沙, 飯島崇善, 長たまき, 紙谷菜津子, 小河原由貴, 永井康一, 石寺由美, 水島大一, 倉澤健太郎, 宮城悦子

成人型顆粒膜細胞腫は、境界悪性から悪性に分類される性索間質性腫瘍であるが、多くは早期に発見され比較的良好な疾患である。今回われわれは、再発を繰り返す成人型顆粒膜細胞腫の2例を経験したので報告する。症例1. 40歳, 2妊2産。8年前に成人型顆粒膜細胞腫 IA 期に対して、腹式単純子宮全摘術, 両側付属器摘出術, 大網切除術を施行した。初回手術からおよそ3年後に骨盤内再発し, 再発腫瘍切除術を施行した。以降腹腔内に広範囲の再発を繰り返し, これまでに計5回の再発腫瘍切除術を施行し, いずれも肉眼的に完全切除を達成している。本人希望で化学療法は施行しておらず, 外科的切除のみ施行しているが, 再発までの期間が徐々に短縮している。症例2. 70歳, 4妊3産。8年前に成人型顆粒膜細胞腫 IIB 期に対して, 腹式単純子宮全摘術, 両側付属器摘出術, 大網切除術, 骨盤および傍大動脈リンパ節郭清術を施行した。術後補助化学療法としてTC療法を追加し, 初回治療を終了した。初回治療終了よりおよそ3年後に骨盤内再発し, 再発腫瘍切除術を施行した。以降骨盤内に限局した再発を繰り返し, これまでに計3回の再発腫瘍切除術を施行している。4回目の再発と診断したが, 高度癒着のため外科的切除は困難で, カルボプラチンアレルギーのため使用できるレジメンが制限されており, 新たな治療レジメンを検討している。成人型顆粒膜細胞腫に対するエビデンスレベルの高い化学療法レジメンは存在せず, 再発時には可能な限り外科的切除をおこなうことで予後改善が期待されている。一方で, 外科的切除にも限界があり, 再発を繰り返すたびに手術の難易度は増加する。有効な化学療法レジメンの確立が望まれる。

P-51-10 急速な再発経過をたどった卵巣上皮性境界悪性腫瘍の2例

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【緒言】卵巣上皮性境界悪性腫瘍は予後が比較的良好な疾患である。再発症例については再発腫瘍が境界悪性腫瘍か浸潤癌かで予後が分かれるものの, 5年全生存率は50%との報告もある。当院で経験した急速な再発経過をたどった症例を, 文献的考察を加えて報告する。【症例1】61歳2経産。X年12月に左卵巣腫瘍に対し開腹手術施行, 迅速病理診断は境界悪性腫瘍の疑いであり, 腹式単純子宮全摘術, 両側子宮付属器摘出術, 大網切除術, 骨盤内リンパ節生検施行, 最終病理診断は漿液粘液性境界悪性腫瘍 Stage1A pT1aN0M0であり, 術後経過観察の方針とした。X+5年7月腹部膨満感あり受診, 腹水は認めないものの多発肺転移, 多発リンパ節転移あり。8月VATS生検で腺癌であり, 臨床経過としては卵巣境界悪性腫瘍の再発を疑う所見であった。同月化学療法の方針とするも, アレルギー出現し, ほかに化学療法を検討している間に癌性リンパ管症の急激な増悪に伴い酸素化不良となり, 10月に永眠した。【症例2】72歳2経産。Y年6月右卵巣腫瘍に対し, 腹腔鏡下右子宮付属器摘出術施行。病理診断は粘液性境界悪性腫瘍であり, 術中腫瘍破綻あり Stage1C1 pT1c1NxM0と診断した。Y年7月経過観察目的に当院紹介初診。Y+8年少量の腹水出現あり, CA19-9 1391と上昇あり。MRI, CTで腹膜播種疑いであり, Y+8年8月腹式単純子宮全摘術, 左子宮付属器摘出術, 大網切除術施行。癌性腹膜炎の状態であった。パクリタキセル+カルボプラチン併用療法2回施行するも効果に乏しく, 再発病変による閉塞から両側水腎症, 腸閉塞を併発し, Y+8年12月永眠された。

P-51-11 低分化型セルトリ・ライディッヒ細胞腫の一例

加古川中央市民病院

西田友美, 房 正規, 熊谷美咲, 清水香陽子, 中筋由紀子, 佐藤沙貴, 市橋さなえ, 宮本岳雄, 太田岳人

セルトリ・ライディッヒ細胞腫はあらゆる年齢層に発生するが, 平均年齢は25歳と若く, 卵巣腫瘍全体の0.5%に満たない稀な腫瘍であり, 様々な程度の分化を示すセルトリ細胞, ライディッヒ細胞, 未熟な性腺間質細胞で構成される腫瘍である。高分化, 中分化, 低分化となるにしたがって予後が悪くなり, 良性, 境界悪性, 悪性として取り扱われ, 低分化型セルトリ・ライディッヒ細胞腫は卵巣悪性腫瘍全体の0.1%とされる。手術療法は概ね卵巣癌に準じたものとなっており, 妊孕性温存に対する考え方も同様である。今回われわれは低分化型セルトリ・ライディッヒ細胞腫 IC1期と診断し, 患側付属器摘出術を施行し, 術後化学療法を行わずに5年間再発なく経過した症例を経験したので報告する。症例は25歳, 未経妊, 未経産。月経不順を主訴に受診した前医で骨盤内腫瘍を指摘され, 精査加療目的に当科紹介受診。造影MRIで25cm大の多房性嚢胞を認め, 左卵巣由来の境界悪性腫瘍以上が疑われた。CA125は45.0U/mLと軽度上昇を認めたが, CA19-9, CEA, E2の上昇は認めなかった。腹部症状が強くなり, 早期治療を希望されたため, 5日後に患側付属器切除術+腹腔細胞診, 腹腔内精査を行った。腫瘍内容物を吸引し, 縮小後に付属器切除を行った。腹腔内に左卵巣以外に肉眼的に病変は認めなかった。術中迅速は行わず, 永久病理組織診断で低分化型セルトリ・ライディッヒ細胞腫 IC1期の診断に至った。I期症例における再発リスク因子として, NCCNガイドラインでは腫瘍の破綻, 進行期 IC 期, 低分化の組織型, 腫瘍径10cm以上が挙げられており, 本症例は高リスク群であるが, 術後化学療法は行わずに, 治療後5年再発なく経過している。

P-51-12 当科で経験した卵管移行上皮癌の一例

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福田修司, 本田 裕, 伊勢田侑鼓, 梅木崇寛, 隅井ちひろ

【緒言】原発性卵管癌の90%以上が漿液性癌と類内膜癌が占めており、移行上皮癌は極めて少なく、標準治療も未確立である。今回、当院で卵管原発の移行上皮癌の一例を経験したので文献的考察を加え報告する。【症例】63歳、G1P0。約3か月持続する不正性器出血を主訴に前医を受診。骨盤内に13cm大の一部充実成分伴う腫瘍性病変を指摘され、精査目的に当院を紹介受診。諸検査の結果、左卵巢癌IA期相当と診断した。開腹すると左卵管と左卵巢は一塊となり、子宮、直腸、S状結腸と強く癒着していた。左付属器を術中迅速病理検査に提出したところ悪性所見を認め、子宮全摘術、右付属器摘出術、左骨盤リンパ節生検、大網部分切除術を追加した。さらに、S状結腸と直腸へ腫瘍の浸潤がみられたため、S状結腸・直腸切除、単孔式人工肛門造設術を施行した。術後病理組織検査で左卵管移行上皮癌IIB期と診断され、術後補助化学療法としてパクリタキセル・カルボプラチン療法(TC療法)を計6コース投与し、現在術後6か月経過し無再発生存中である。【考察】卵管癌は、卵巢癌に準じた治療、すなわち初回手術での可及的腫瘍減量術とプラチナ製剤を含む術後補助化学療法が一般的に施行される。卵管癌はリンパ行性の播種・転移が多く、再発部位として遠隔リンパ節が多いとされる。卵管移行上皮癌はここ10年間で約20例の報告があり、化学療法や放射線療法への感受性は良好で、他の組織型より予後が良好との報告がある。化学療法については、本症例のようにTC療法を術後補助化学療法として行った症例の他、尿路移行上皮癌に準じたレジメンを再発例に行い効果があった症例もあり、まだ一定の治療戦略は定まっていない。

P-51-13 術前に骨盤内腫瘍のみを認め術中診断が困難であった卵管癌IIB期の1症例

秋田大

金子恵菜実, 平川威夫, 菅原多恵, 牧野健一, 清水 大, 寺田幸弘

【症例】42歳女性、未経産。非定型抗酸菌症の既往があり1年ごとに定期検診を受診している。母に乳癌と大腸癌、母方叔母に子宮癌の既往歴がある。現病歴：X-2年より粘膜炎下筋腫による過多月経を認め近医産婦人科で低用量エストロゲン・プロゲステン配合薬を処方されていた。X年2月経陰超音波にて6cm大の卵巢腫瘍を指摘され、X年3月精査加療目的に当科紹介受診した。MRIにて子宮背側に充実性部分を伴う6cm大の嚢胞性腫瘍を認めた。CA125は247.0U/mL。卵巢悪性腫瘍や子宮頸部腫瘍の術前診断で、X年4月開腹手術を施行した。画像で指摘された腫瘍は子宮頸部背側と直腸の間に発育し、両側付属器は肉眼的に正常大で腫瘍とは離れて確認された。腹水細胞診は陰性。子宮頸部腫瘍と考え、子宮全摘術、両側卵管切除術を施行した。腫瘍摘出時に直腸の漿膜・筋層欠損を認めたため低位前方切除術を追加施行した。術後病理検査にて摘出腫瘍は高異型度漿液性癌であり、右卵管采にも同成分を認めた。骨盤内進展を伴う卵管原発高異型度漿液性癌と考えられた。初回手術より1か月後に両側卵巢摘出術、骨盤・傍大動脈リンパ節郭清術、大網切除術を施行した。摘出組織に転移所見は認めず、右卵管癌IIB期の診断に至った。術後治療としてTC療法6コースを施行している。【考察・結語】卵管癌は稀な腫瘍であり、術前診断される割合は0-10%と低く、術中診断においても約50%の症例で見逃されたという報告がある。本症例でも術前・術中診断には至らず、術後病理結果で卵管癌の診断に至った。骨盤内腫瘍を認めた場合、卵管原発腫瘍も想定し検索を行うことが必要である。

P-51-14 巨大卵巢嚢胞性顆粒膜細胞腫の1例

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卵巢顆粒膜細胞腫は卵巢悪性腫瘍全体の2.7%と稀な疾患で腫瘍は充実部が主体であることが多い。今回我々は巨大卵巢嚢胞の診断で術後に顆粒膜細胞腫と診断した症例を経験したので報告する。症例は56歳。性交経験なし。腹部膨満感を自覚して近医を受診。超音波検査で骨盤内腫瘍を指摘され当科紹介。性器出血は4か月前に自覚もその後なし。巨大卵巢嚢腫疑いにて精査。末梢生化学検査出血傾向異常なし。腫瘍マーカーではCA125のみ軽度上昇(65.9U/ml)。MR画像では右側付属器領域に114x208x238mmの境界明瞭な巨大多嚢胞性嚢胞性腫瘍を認め内部に明らかな充実成分なく隔壁以外に有意な造影効果を認めなかった。拡散制限や周囲への浸潤傾向もなく粘液性腫瘍が疑われた。開腹手術により右卵巢を摘出。迅速病理検査の結果で性索間質腫瘍が疑われ最終的に子宮、両付属器、大網切除術を施行した。術直後の血中E2値は36.2pg/mlであった。嚢胞壁は黄色調の厚い被膜からなり、嚢胞内充実部は明らかでなかった。組織学的に嚢胞壁はびまん性にシート状増殖を示す異型細胞から成り、異型細胞は比較的均一で細胞質に乏しく核分裂像が散在性に観察され一部には壊死や出血、変性を伴っていた。免疫染色ではcarletinin, EMA, CK7, p53, CD10等が陰性、 α -inhibin, WT-1, SF-1, melan-A, CD56, ER, PgR, Ki-67等が陽性所見を確認。さらにFOXO2遺伝子変異も確認され、最終的に成人型卵巢顆粒膜細胞腫と診断された。子宮内腔には内膜ポリープを認めた。卵巢顆粒膜細胞腫は悪性性索間質腫瘍の70%を占め、高エストロゲンによる出血などの症状から推測することは可能であるが本症例のように嚢胞優位の腫瘍では術前診断が困難となる場合があるため注意が必要である。

P-51-15 2週間のNiraparib投与で血小板数1,000/mm³まで減少した1例

鹿兒島大

福西優花, 水野美香, 大井帆波, 川原裕史, 小林裕介, 永田真子, 築詰伸太郎, 戸上真一, 小林裕明

【緒言】Niraparib (NIRA) の血小板減少の副作用は約40-60%と国内外より報告されている。今回、NIRAを2週間投与し、休業後に血小板数が1000/mm³まで減少した症例を報告する。【症例】72歳女性。併存症：右下腿深部静脈血栓症(抗凝固薬内服)既往歴；ステロイド糖尿病。現病歴；前医で診査腹腔鏡を行い、高異型度漿液性癌と診断され紹介となった。腹膜癌IIIC期として、術前化学療法Paclitaxel+Carboplatin(TC)±bevacizumabを3コース施行後、子宮全摘術、両側付属器摘出術、大網切除、播種切除を施行。術後TC3コース施行後、画像で完全奏効を確認。HRD score 35。術前bevacizumab使用中に新たな静脈血栓を発症したことより、維持療法はNIRA200mg内服を開始。投与開始9日目前後にインフルエンザ罹患しノイラミナーゼ阻害薬、症状は軽微であった。14日目採血で血小板7万/mm³と減少したため、NIRAは休業とした。休業後2週間後の受診時、前日からの鼻出血と下肢の皮下出血の訴えがあった。血小板は1000/mm³へ減少しており、鼻出血止血処置、抗凝固剤の中止、血小板輸血を施行。WBC440 μ l、Hb8.0g/dlと汎血球減少もみられ、骨髄穿刺を施行。血小板輸血は投与2日後には2万/mm³へ減少し8日間で計60単位投与された。全ての血液毒性がG1に回復するのに約8週間を要した。【考察】本症例の汎血球減少はNIRAによる血液毒性と診断された。化学療法中の血液毒性は好中球減少G4を2回認めた程度で、血小板減少は見られなかった。NIRA投与直前の血小板19.2万/mm³であり、今回のイベントは予測困難であった。NIRA投与にあたり、休業後も減少がみられること、時に急激に減少する症例があることに留意したい。

P-52-1 BMIによって子宮体がん開腹手術の安全性はどの程度異なるか

四国がんセンター

日比野佑美, 横山貴紀, 藤本悦子, 坂井美佳, 大亀真一, 竹原和宏

【目的】子宮体がんは肥満患者の多い疾患である。肥満症例は手術自体の難しさに加え、糖尿病などの合併症を有することが多く周術期管理に難渋することがある。BMIによって開腹手術の安全性がどの程度異なるかを明らかにする。【方法】2020年～2022年までの3年間に当院で子宮体がんと診断し開腹で子宮摘出を行った109例を対象とし、手術時のBMI、術式別の出血量と手術時間、周術期合併症、高度肥満症例への減量介入と結果を後方視的に検討した。【成績】標準体重(BMI<25)68例(62.4%)、肥満(25 \leq BMI<30)31例(28.4%)、高度肥満(BMI \geq 30)10例(9.2%)。糖尿病罹患率は全体で6.4%、高度肥満群では20%だった。郭清なし群は56例で、BMIと出血量、手術時間との間に相関関係は認めなかった。PLA群は17例で、BMI \geq 30で有意に手術時間が延長していた($p=0.002$)。PALA群は36例で、BMI \geq 25で有意に出血量が多かった($p=0.021$)。周術期合併症は全体で7例あり、術式別では郭清なし群5例、PLA群1例、PALA群1例、BMI別では標準体重4例(7.1%)、肥満1例(3.2%)、高度肥満2例(20%)だった。高度肥満の10例中7例で主治医から減量指導が行われ、4例は口頭指導のみで2.5kg～9kg(3～9%)の減量を達成し、3例は入院等の積極的な介入を行い2kg～24kg(2～22%)の減量を達成したが周術期合併症が2例で生じた。【結論】積極的な減量介入の有効性については症例数が少なく検討の余地があるが、BMIによって手術の安全性に違いがあり、手術待機中に可能な限りの減量を行うことが望ましいと考える。

P-52-2 プラチナ投与歴を有する子宮体癌再発症例に対するプラチナ製剤再投与の治療効果の検討

信州大

山田 靖, 竹内穂高, 安藤大史, 井田耕一, 小原久典, 宮本 強, 塩沢丹里

【目的】子宮体がん治療ガイドライン2023年度版では、切除不能な病巣を有する子宮体癌再発症例に対して、プラチナ製剤の投与歴のない場合にはプラチナ製剤を、投与歴のある場合にはペムプロリズマブを含む治療が推奨されている。そこで当科における切除不能な病巣を有する子宮体癌再発症例に対するプラチナ製剤の治療効果について検討した。【方法】2012年1月から2022年12月までに当科で初回治療を行い、その後切除不能な病巣で再発した子宮体癌38例について、プラチナ投与歴なし9例(A群)とプラチナ投与歴あり(29例)に分け、診療録から後方視的に検討し、RECISTガイドラインに従い再発後のプラチナ含有化学療法の治療効果判定を行った。【成績】前回治療終了から再発までの期間中央値はA群12か月、B群10か月と有意差はなく、奏効率はA群8/9例(89%)、B群11/29例(38%)と有意にB群で低かった($p=0.021$)。一方、B群の9例(31%)は、評価可能病変がないためにPR判定ができずnon-CR/non-PDと効果判定され、2例(7%)はSDと判定された。これらを加えた病勢制御率はA群9/9(100%)、B群22/29(76%)であり、B群で低いものの有意差はなかった($p=0.566$)。A群とB群の無増悪生存期間(PFS)と全生存期間(OS)の中央値はそれぞれ15か月対10か月($p=0.121$)、中央値到達せず対27か月($p=0.182$)で、共にB群で短い傾向にはあったが有意差はなかった。【結論】切除不能な病巣を有する子宮体癌再発症例に対して、プラチナ投与歴のある症例においても、プラチナ製剤の再投与は高い病勢制御率を有しており、治療選択肢となり得ると考えられた。

P-52-3 当院における子宮癌肉腫の予後調査

三重大

渥美麻子, 松本剛史, 綿重直樹, 牧野麻理恵, 岡本幸太, 金田倫子, 吉田健太, 前沢忠志, 田中博明, 近藤英司, 池田智明

【目的】子宮癌肉腫は婦人科腫瘍の中でも予後不良の腫瘍である。当院における子宮癌肉腫の治療成績を明らかにする。【方法】2012年1月から2022年12月の期間に、当院で子宮癌肉腫と診断された42例において、臨床情報を後方視的に検討した。初回治療開始時点からの全生存期間、無増悪生存期間、5年生存率を解析する。【成績】年齢は中央値66歳(35歳~85歳)、進行期はIA期:13例, IB期:10例, IIA期:3例, IIIA期:3例, IIIB期:2例, IIIC期:6例, IVB期:5例であった。初回手術例41例, 初回化学療法例1例であり、全体の再発例は18例(42.8%)であった。進行期別の全生存期間はIA期:58か月(9か月~115か月), IB期:66.5か月(9か月~134か月), IIA期:30か月(11か月~34か月), IIIA期:19か月(0か月~77か月), IIIB期:21.5か月(5か月~38か月), IIIC期:13か月(5か月~26か月), IVB期:13か月(1か月~57か月)であった。無増悪生存期間はIA期:11か月(5か月~52か月), IB期:9か月(4か月~10か月), IIIA期:14か月, IIIB期:13か月(4か月~22か月)であった。5年生存率はI期:47.8%, II期:0%, III期:9.0%, IV期:0%であった。【結論】子宮体癌I期症例の5年生存率は90%以上とされているが、今回の検討では子宮癌肉腫I期症例の5年生存率は47.8%であり、予後不良であった。

P-52-4 当院における早期子宮体癌に対する低侵襲手術についての後方視的検討

杏林大

澁谷裕美, 渡邊百恵, 百村麻衣, 松本浩範, 森定 徹, 小林陽一

【目的】早期子宮体癌に対する低侵襲手術は複数のRCTにより開腹手術と比較し、再発率、予後に差はないとされ、現在では多くの施設で行われている。今回、当院において施行した早期子宮体癌に対する低侵襲手術の症例選択の妥当性や治療成績について後方視的に検討した。【方法】2013年7月から2023年7月の10年間に、術前検査にて類内膜癌G1/2、子宮内膜異型増殖症(AEH)、腺癌疑い、臨床進行期IA期に対して低侵襲手術を施行した141例(腹腔鏡119例, ロボット22例)について後方視的に検討した。術後診断が術前診断と同様であったものをControl群、類内膜癌G1/2以外の組織型とされた症例をup grade群、進行期IB期以上をup stage群とした。【成績】術前病理診断は類内膜癌G1/2:113例, 腺癌4例, AEH:18例で、子宮口閉鎖により病理診断がつかずMRIにて子宮内膜ポリープやIA期とされたのが5例であった。術後診断は類内膜癌G1/2:131例, G3:4例, 特殊型:6例で、up grade群は10例(7.1%)であった。手術進行期はIA期120例, IB期12例, II期4例, III期4例, IV期1例, up stage群は21例(14.9%)で、IA期ではup grade群は6例(4.3%)であった。腫瘍最大径、CA125値はControl群とup grade・up stage群とで有意差を認め、無病生存率にも有意差を認めた。後療法施行は23例, 再発は5例(3.5%)で認め、部位は腔断端2例, 肺転移1例, 腹膜播種・骨盤内リンパ節転移2例, 4例はup stage群で1例はup grade群でもあった。【結論】早期子宮体癌では低侵襲手術の適応とされた症例においても術後up gradeやup stageとなることもある。今後症例をさらに蓄積し、早期子宮体癌における低侵襲手術の安全性、有効性を検討したい。

P-52-5 テストステロン投与下トランスジェンダー男性における女性生殖器臨床病理学的検討

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【目的】トランスジェンダー男性(TGM)は、長期に渡るテストステロン(T)投与を必要とすることが多いが、女性生殖器に対するT投与の影響は不明な点も多い。T投与下TGMにおける子宮、付属器の病理学的特徴を明らかにする。【方法】2020年7月~2022年12月までにT投与中のTGMに対して内性器摘除術を行った症例(A群)について、摘出検体の病理診断レビューを行った。また、T投与中のTGMにおける婦人科悪性腫瘍症例(B群)についても併せて後方視的検討を行った。【成績】A群は43例、年齢中央値は30歳(19~44歳)、術前T投与期間中央値は5.3年(0.7~18.4年)であった。病理学的所見では、子宮頸部重層扁平上皮には、萎縮・移行上皮化生が34例(79%)、前立腺化生が7例(16%)でみられた。子宮内膜には萎縮調の所見が41例(95%)でみられ、このうち22例(54%)では、一部に増殖期の所見がみられた。卵管周囲や卵巣門では、中腎管遺残の輪精管上皮様変化が13例(30%)でみられた。B群は2例で、いずれも子宮体癌の診断であった。症例1は30歳、術前T投与期間は2年、病理学的所見では類内膜癌grade3, StageIVBの診断で、免疫組織化学染色でわずかにNKX3.1陽性像を呈した。症例2は37歳、術前T投与期間は7年、病理学的所見では類内膜癌grade1, StageIIの診断で、腫瘍の一部は中腎様腺癌様の所見を呈した。【結論】T投与中の子宮、付属器は、非腫瘍例・腫瘍例ともに特徴的な所見を示した。特に、非腫瘍例の子宮内膜は、萎縮調を呈するだけでなく約半数で部分的に増殖期内膜を伴っており、子宮体癌との関連については今後の研究が期待される。

P-52-6 進行・再発子宮体がんに対する Lenvatinib-Pembrolizumab 併用療法—当科における経験から見たもの—

滋賀医大

谷口健太郎, 天野 創, 高橋顕雅, 西村宙起, 出口真理, 山中弘之, 信田侑里, 米岡 完, 中村暁子, 小川智恵美, 辻俊一郎, 村上 節

【目的】がん化学療法後に増悪した切除不能な進行・再発の子宮体がんに対して、2021年12月にLenvatinib-Pembrolizumab併用療法(Len-Pem療法)が新たな治療選択肢として加わった。当科における治療成績から得た知見を報告する。【方法】2022年2月から2023年9月までに当科でLen-Pem療法を施行した症例について後方視的に検討した。【成績】Len-Pem療法が施行されたのは12例で年齢の中央値は59歳(57-71)であった。全例にミスマッチ修復(MMR)蛋白の免疫染色あるいはMSI検査のいずれかを施行しており、MMR deficient (dMMR)が2例、MMR proficient (pMMR)が10例であった。観察期間の中央値が12.5か月(2-19)の時点における最良効果はCR5例、PR2例、SD2例、PD3例であった。dMMRの2例はCRとPDであり、全体としての奏効率率は58.3%、pMMRの症例で60%を占めた。CRが得られた5例中4例は現在継続中であり1例は副作用により中断しているが、全例が無再発生存している。一方PDとなった3例のうち1例は原病死に至ったが、放射線療法を選択したdMMRの1例は治療中にimmune-related adverse eventsと思われる副腎機能不全を発症したが著効し、pMMRの1例もTC療法が著効し現在無病生存となっている。【結論】進行・再発子宮体がんに対するLen-Pem療法は効果が得られた症例で長期間の維持が期待でき、一方でPDであった症例の後治療の効果が好影響をもたらす可能性も示唆される。以上からLen-Pem療法は進行・再発子宮体癌治療の早期に導入するメリットがあると考えられた。

日本語ポスター
21日(日)

P-52-7 子宮体癌に対する腹腔鏡下手術における腹腔細胞診陽性症例の検討

虎の門病院

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【目的】2018年4月より当科では術前診断IA期の子宮体癌に対して、腹腔鏡下子宮全摘術および両側付属器摘出術を行っている。その際に当科では、腹腔細胞診陽性の症例に対しては、大網部分切除術および骨盤リンパ節郭清術を追加する方針としている。腹腔細胞診陽性症例における追加術式についてはガイドラインで明確に定められた方針はなく、施設により方針が異なっているのが現状である。これまでの症例を検討し、当科における方針を再検討することとした。【方法】2018年4月から2023年8月の期間における、当科の腹腔細胞診陽性症例を後方視的に検討した。【成績】71症例の術前診断IA期の子宮体癌に対して、腹腔鏡下子宮全摘術および両側付属器摘出術を施行した。その全症例で術中に腹腔細胞診を迅速病理診断に提出した。そのうち11症例で腹腔細胞診陽性を認め、大網部分切除術を追加した。また、腹腔細胞診陽性症例のうち同意が得られなかった3症例と、重症の合併症があった1症例を除いた7症例に対しては骨盤リンパ節郭清術を追加した。術後病理診断による病期は2例がIB期であり、組織型は類内膜癌G1が7例、G2が4例であった。骨盤リンパ節に転移を認めた症例はなく、現在のところ腹腔細胞診陽性であった全ての症例で再発を認めていない。【結論】子宮体癌に対する腹腔鏡下手術では、腹腔細胞診陽性であっても骨盤リンパ節郭清術の省略を積極的に考慮した方が良い可能性がある。

P-52-8 術前の吸引内膜組織診で子宮内膜増殖症と診断された場合の子宮内膜全面搔爬術による病理診断の有用性

大阪急性期・総合医療センター

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【目的】子宮内膜生検の組織採取には吸引組織採取や全面搔爬術が行われている。当センターではこれまで、吸引組織診で類内膜上皮内腫瘍(EIN)と診断された症例は、全面搔爬術による病理検査を行わずに手術することも多かった。しかし、EINのうち30%程度は術後に子宮内膜癌へとupgradeされることが知られており、癌の組織型などによっては追加手術が必要となる可能性がある。生検方法による正診率を明確にすることを目的とする。【方法】2013年8月から2023年9月までに当センターで吸引組織診を行い子宮内膜増殖症の診断となった症例のうち手術治療を行った69例について、吸引および全面搔爬による病理診断と術後病理診断を比較して、その診断精度を後方視的に検討した。【成績】年齢の中央値は52歳(28-82歳)、BMIの中央値は23.6(13.4-42.5)であった。吸引による診断は44例(63.8%)がEINであり、残り25例(36.2%)が異型を伴わない子宮内膜増殖症であった。術前組織診を吸引のみで行ったのが49例(71.0%)、吸引・全面搔爬を併用したものが20例(29.0%)であり、術後に診断がupgradeする割合は両者を併用した方が有意に低かった(51.0% vs 25.0%; p=0.03, Fisher正確率検定)。さらに術中迅速病理検査を提出した33例についても、両者を併用した方が吸引のみを行った方よりもupgradeする割合は低い傾向にあった(36.0% vs 25.0%; p=0.68)。また、術後にupgradeされた症例の中には、追加手術を行ったものが3例あった。【結論】術前の吸引組織診で内膜増殖症と診断した場合、吸引単独よりも全面搔爬を併用した方が術後病理診断を正確に反映しており、適切な術式を選択し患者の負担軽減につながる可能性が示唆された。

P-52-9 後期高齢者における臨床進行期 I 期の子宮体癌に対する治療法と予後の検討

奈良県総合医療センター

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【目的】75歳以上の後期高齢者の子宮体癌の治療では、認知症などの基礎疾患により治療を縮小する場合がある。今回、後期高齢者における臨床進行期 I 期の子宮体癌患者の治療法と予後について検討した。【方法】2013年1月から2023年6月の間に当院での初診時年齢が75歳以上の子宮体癌 I 期の患者を対象とした。リンパ節郭清、術後化学療法などを施行した標準治療群 (S 群)、子宮摘出のみを施行した姑息的手術群 (P 群)、放射線治療のみを行った放射線治療群 (RT 群) に分け、予後は log-rank 検定、合併症は χ^2 検定を用いて検討した。【成績】対象患者は46例で、S 群は18例 (IA/IB 期 12/6)、P 群は22例 (同 14/8)、RT 群は6例 (同 3/3) であった。それぞれの年齢中央値 (範囲) は、76.0 (75-81) 歳、81.0 (75-88) 歳、84.0 (79-88) 歳であり、S 群は他の群と比較して有意に若年であった (P 群 $p=0.0329$, RT 群 $p=0.017$)。全患者の41例 (89.1%) が基礎疾患を有しており、RT 群はその他の群と比較して認知症の患者が有意に多かった (S 群 $p=0.00141$, P 群 $p=0.00342$)。全生存期間は3群間で有意差はみられなかった ($p=0.302$)。手術療法において Clavien-Dindo 分類 Grade3 以上の有害事象は S 群が P 群より有意に多くみられ ($p=0.033$)、RT 群において有害事象は CTCAE Grade2 の放射線腸炎を1例認めた。【結論】後期高齢者における子宮体癌の I 期ではどの治療群であっても全生存期間に差はみられなかった。術後合併症を考慮すると子宮摘出のみ、あるいは放射線治療も推奨できると考えられる。今後さらなる症例の蓄積を行う必要がある。

P-52-10 子宮体癌に対するレンパチニブ・ペムプロリズマブ (LP) 療法の治療効果に関わる因子についての検討

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【目的】LP 療法の治療効果に関わる因子について検討する。【方法】2014年1月から2023年6月までに子宮体癌の診断で当院にて治療した全症例を対象とする。そのうち進行・再発のため LP 療法を施行した症例について、治療効果や有害事象に加えて患者背景・疾患特性に関する情報を電子カルテより抽出する。また従来の化学療法を施行した症例との比較検討も行う。【成績】LP 療法を施行したのは22例で、年齢中央値は67.5歳 (52-78歳) であった。組織型は低異型度類内膜癌6例、高異型度類内膜癌3例、漿液性癌7例、明細胞癌2例、その他4例で、マイクロサテライト不安定性検査は2例で陽性であった。また前回治療からの無治療期間中央値は1.5か月 (1-53か月) であった。未評価・評価不能の7症例を除いた奏効率は40% (6/15) で、治療3か月後の病勢制御率は73% (11/15) であった。有害事象の発現率は100% で、Grade3 以上も59% (13/22) と高率に認め、有害事象による治療中止は4例であった。治療効果について、年齢・組織型・無治療期間に特定の傾向は認めなかった。【結論】LP 療法の治療効果に関わる患者背景・疾患特性に特定の傾向は認めなかった。

P-52-11 再発子宮体癌に対するレンパチニブ・ペムプロリズマブ併用化学療法 自験例の検討

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【目的】進行・再発子宮体癌に対するペムプロリズマブ・レンパチニブ併用療法が保険適応となり、約2年を迎える。自験例について、奏効率や副作用を後方視的に検討した。【方法】保険適応以降に併用化学療法を開始し、CT 検査で RECIST 判定を行った症例を対象とし、後方視的に検討した。【成績】対象患者は11例であった。年齢中央値は66歳 (34-82歳)、BMI21.9 (17.7-32.2)、7例が初回診断時に III 期以上の進行期であった。組織型は類内膜癌3例、漿液性癌3例、明細胞癌・混合癌・中腎様癌が各1例、KEYNOTE775 試験で除外されていた癌肉腫2例が含まれていた。3例でマイクロサテライト不安定性検査を施行しており、いずれも MSS であった。術後補助化学療法を除き、8例で前治療の化学療法が行われていた。併用療法の投与コースは中央値で6コース (1-15)、レンパチニブの内服治療強度の指標を示す RDI は66.8% (25-100%) であった。DCR (disease control rate) は63.6% (7/11) であった。再発時の 1st ラインとして本治療を行うまたは引き続いて追加治療 (放射線治療) を行った場合、奏効が得られていた。副作用は、高血圧 (45.4%) や甲状腺機能異常 (45.4%) のほか、血小板減少 (27.2%) や筋肉痛 (27.2%) が続き Grade3 以上の重篤な有害事象は血小板減少、好中球減少、蛋白尿、胆管炎がみられた。副作用の出現時期は治療開始1か月以内に特に集中しており、高血圧や甲状腺機能異常といった頻度の高い副作用は治療開始から約2か月程度までの間に観察された。【結論】進行期の症例、漿液性癌や癌肉腫など予後不良な組織型の症例が多くみられたが、DCR は比較的保たれていた。治療開始 1-2 か月に副作用の出現に注意を要する。

P-52-12 当院で経験した EIC (endometrial intraepithelial carcinoma) の後方視的検討

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【目的】子宮体部 endometrial intraepithelial carcinoma (EIC) は、稀な腫瘍ではあるが予後はかなり不良とされている。一方、その管理方針に関しては報告がまだ少ないのが現状である。今回、我々は当院で経験した EIC の症例からその治療方針に関する考察を行う。【方法】当院で 2011 年から 2023 年の間に EIC という診断に至り治療を行った 9 症例について後方視的に検討を行った。【成績】診断時の年齢の中央値は 67 歳 (52-74) であった。全例で内膜ポリープを合併していた。診断時の進行期分類 (FIGO2008) は、IA 期が 3 例、IB 期が 1 例、IIIA 期が 1 例、IVB 期が 4 例であった。組織型は、漿液性癌が 7 例、明細胞癌が 1 例、類内膜癌が 1 例であった。予後は、初回手術から 3 か月以内の死亡が 2 例、2 年生存率が 2 例 (うち 1 例は、再発後に診断が確定しその 3 か月後に死亡)、生存 (経過観察中) 4 例、lost follow が 1 例 (2nd line 化学療法の後 BSC となり転医) であった。【結論】EIC における急速な転移様式は、卵管を通じての腹腔内への腫瘍細胞の播種が示唆され、血行性転移やリンパ行性転移とは異なることが推定される。このことより、ステージングとしてのリンパ節郭清を含む根治術は必要であるが、治療効果という面においては化学療法の方が優位に立つものと考えられる。また、術後に EIC の診断が確定せずとも、内膜ポリープに併存する子宮体癌においては、EIC の可能性も念頭に置き病理検索を行い術後の化学療法の必要性を考慮する必要がある。

P-52-13 術前に良性の子宮体部腫瘍と診断し腹腔鏡下腔式子宮全摘 (TLH) を施行し、術後に子宮体癌と診断された症例についての検討

徳島大

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【目的】子宮内膜ポリープや子宮粘膜炎下筋腫は良性の子宮疾患であり、悪性疾患の鑑別のために子宮内膜細胞診や子宮内膜組織診、子宮鏡検査などが診断の根拠となりえるが、時に子宮体癌との鑑別に難渋することがある。今回我々は良性の子宮体部腫瘍の診断で TLH を施行し、術後の病理組織診断にて子宮体癌と診断された症例について後方視的に検討した。【方法】当院で 2018 年 4 月～2023 年 3 月までの間に、良性の子宮体部腫瘍の術前診断で最終的に TLH を施行し、術後に子宮体癌と診断された症例の臨床症状、検査所見について後方視的に調べた。【成績】該当症例は 5 例で、術前診断は 4 例が子宮内膜ポリープ、1 例が子宮粘膜炎下筋腫であった。受診の契機は 3 例が不正性器出血、2 例は検診 USG であった。子宮内膜細胞診は 4 例が陰性、1 例が疑陽性であった。子宮内膜組織診は 3 例で悪性所見なし、2 例は未実施であった。その他の検査として、4 例は骨盤部造影 MRI を施行し子宮内腫瘍を認め、3 例で腫瘍内にわずかに造影効果不良域を指摘された。2 例は子宮鏡検査を施行し、1 例は子宮内膜の一部に粗造な隆起、もう 1 例は子宮腫瘍にわずかな異型血管を認めた。TLH は子宮良性疾患に準じて施行された。摘出した子宮の病理診断は全例が類内膜癌 grade1, stage1A であった。全例とも現在まで再発なく経過している。【結論】既報では良性の子宮疾患に対して子宮全摘後に子宮体癌と診断される確率は 1% 未満との報告が多く、予期しない子宮体癌の合併はまれながら回避が困難と思われる。一方で子宮内膜細胞診や組織診で陰性の子宮内腫瘍に対して、悪性腫瘍の鑑別に骨盤 MRI や積極的な子宮鏡下の観察が診断の一助となる可能性が示唆された。

P-53-1 Dienogest による子宮内膜症治療と並行し生殖補助医療 (ART) の調節卵巣刺激により得られた胚の妊娠・出産後に

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【目的】子宮内膜症合併不妊症例に対し、本疾患治療薬である Dienogest を継続内服し調節卵巣刺激を行い、良好胚獲得後に内服を終了し妊娠を目指す治療の有効性について我々はこれまで報告してきた。本治療の分娩予後についてはまだ報告数も少なく、先進的な治療であるため継続した妊娠・出産予後の報告が重要である。今回我々は Dienogest 連続投与により得られた胚の 2022 年 12 月末までに分娩した症例を後方的に検証した結果を報告する。【方法】当院にて同意が得られ ART 治療を行なった子宮内膜症合併患者 378 症例を対象とした。Study 群 (Dienogest 連続投与群, N=153) は Dienogest 継続内服中に、調節卵巣刺激を施行し良好胚を全胚凍結とした。Control 群は同期間に当院にて他の調節卵巣刺激にて採卵、凍結胚移植を行い妊娠・分娩に至った群 (N=225) とした。統計的検討として unpaired t-test, Mann-Whitney U test 及び Chi-square test を用い、 $P < 0.05$ を有意差ありとし検討を行った。【成績】患者背景として AMH、基礎 FSH 値、BMI に有意差は認めなかった。また子宮内膜症手術歴・子宮腺筋症については Study 群が有意に多いという背景差は認められた。分娩予後については分娩週数 (中央値 [四分位範囲]) (S 群 39.0 [37.0-40.0], C 群 39.0 [38.0-40.0], $P=0.84$)、出生体重 (平均 \pm SD) (S 群 $3002.4g \pm 484$ vs. C 群 $3034.2g \pm 443$, $P=0.513$) と有意差はなく、分娩方法、児の先天奇形発生率においても両群間での有意差は認めなかった。【結論】Dienogest 継続内服により獲得した胚の出生予後についても、他の誘発法と比較し周産期合併症、児の先天異常などの上昇はなく良好であった。今後は長期的な児の予後についても検証を行う必要がある。

P-53-2 複数胚移植の治療成績に関する研究

島根大

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【目的】当院では単一胚移植を複数回行っても妊娠に至らなかった場合本人の希望で複数胚移植を実施している。当院で行った過去6年間の複数胚移植の治療成績について検討した。【方法】2017年1月1日から2022年12月31日までの6年間に当院にて実施した単一胚移植, 2個胚移植及び2段階胚移植の治療成績について検討した。年代別, 移植胚のグレード別に評価を行った。【成績】同期間に当院で実施した単一胚移植は2214周期, 2個胚移植は781周期, 2段階胚移植は169周期であった。妊娠率はそれぞれ25.0%, 23.4%, 28.4%と2段階胚移植で高い傾向にあったが統計学的な有意差は得られなかった。年代別にみると35-39歳以外の年代において単一胚移植, 2個胚移植, 2段階胚移植の順で妊娠率が高かった。複数胚移植について胚のグレード別に検討したところ, 2個胚移植の場合は胚盤胞2個移植で妊娠率が最も高く, 次いで良好初期胚(G1, G2)2個移植の成績が良かった。2段階胚移植において2回目に移植する胚盤胞を良好胚盤胞(3BB以上), 不良胚盤胞(3BB以下)で比較したところ, 初期胚の質に関わらず良好胚盤胞移植で妊娠率は有意に高かった。2回目移植の胚盤胞のグレードが同じである場合, 1回目で移植する胚を良好初期胚, 不良初期胚(G3以下)で比較しても妊娠率に差は認められなかった。多胎率は単一胚移植で1.3%, 2個胚移植で17.5%, 2段階胚移植で10.4%であった。流産率は単一胚移植で22.8%, 2個胚移植で30.1%, 2段階胚移植で20.8%であった。【結論】2段階胚移植の場合1回目移植の初期胚の質にかかわらず胚盤胞の質が治療成績に関係すると考えられた。複数胚移植に関してはその適応を含め詳細な検討が必要と思われた。

P-53-3 低刺激周期を基本とするART施設の臨床成績～2021年全国統計との比較～

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【目的】当院は採卵周期は低刺激を基本とし, 胚移植は全例単一胚移植を徹底している。この治療方針の意義検証のため全国統計との比較により客観的評価を行い, 毎年本会に報告している。2021年の臨床成績を報告する。【方法】【対象】2021年1月～12月に当院でARTを施行された症例。【方法】当院成績とARTデータブックの全国統計を比較し検討を行った。【成績】当院の採卵周期(n=20,282)の刺激方法の内訳は, 自然9.8%, クロミフェン単独66.5%, クロミフェン+ゴナドトロピン20.4%, その他3.2%, 平均採卵個数2.1個であった。全国統計との比較(当院 vs. 全国統計)では, 総治療周期の平均年齢(歳)は39.4 vs. 37.8, 総治療周期あたりの生産率(%)は11.6 vs. 13.6, 移植あたりの生産率(%)は29.4 vs. 25.2であった。多胎率(%)は0.9 vs. 3.1であった。年齢別に検討すると, 生産率で当院が全国統計に比べ劣った年齢層はなく, 総治療周期あたりの生産率は43歳で当院成績が良好であった。また移植周期あたりの生産率は, 30歳～45歳において当院が良好であった。【結論】施設として総治療周期あたりの生産率は全国統計より劣るが, これは例年通り当院の症例が全国平均より高齢であることに起因しており, 年齢別の検討では非劣性が示された。ただ, 例年は年齢別検討において全国統計よりも優位な成績であったが, 2021年はほぼ同等であった。理由は定かではないが, 全国統計において2021年は2020年より1万人近く多い出生児数であり, 新型コロナ流行による胚移植控え後, より良好な胚が選択され移植された可能性や, PGT-Aの普及が要因かもしれない。この傾向が継続するのか, 今後も継続して検討を行っていきたい。

P-53-4 少子高齢化社会における高年女性の生殖補助医療成績の検討

順和会山王病院

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【目的】生殖補助医療の成績は年齢に依存し, 保険適用にも年齢制限がある。当院では成績を提示した上で, 患者が希望すれば年齢制限を設けず治療を行っており, 採卵周期数の60%以上を40歳以上が占める。年代別の生殖補助医療の成績を分析しその意義を検討した。【方法】2018年から2022年の5年間に実施した胚盤胞および初期胚による凍結胚移植の妊娠成績(胎嚢確認)を採卵時年齢別に分析した。39歳以下をA群(採卵周期数, 以下同1288), 40-42歳をB群(同921), 43-44歳をC群(同565), 45歳以上をD群(同523)とした。【成績】凍結胚移植は2650周期行い, 妊娠率はA群1473周期452(30.7%), B群729周期127(17.4%), C群288周期中16(5.5%), D群160周期中3(1.9%)と年齢とともに低下した。胚盤胞と初期胚で比較するとそれぞれA群33.9対22.6%, B群22.9対8.6%, C群8.1対3.7%, D群5.8対0%であり, 全年代で胚盤胞移植が優れていた。移植に要した採卵周期数はA群0.87, B群1.26, C群1.96, D群3.27と年齢により増加した。【結論】B群, C群, D群の妊娠成績からわかるように, 40代では生殖補助医療の成績が年齢により急激に低下するが, 一定数の妊娠は得られている。人口統計によれば2022年40-44歳の出産は46336人(6.0%), 45歳以上1658人(0.22%)と近年増加している。生殖補助医療の適用の成果と考えられるが, 低い妊娠率が示すように莫大な費用を必要とし費用対効果は十分とはいえない。成績改善の努力とともにプレコンセプションケアにより妊娠出産の早期化にも努めるべきと考える。

P-53-5 初回採卵周期の新鮮胚移植における妊娠成立を予測する因子の検討

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【目的】本邦の ART 出生児は凍結融解胚移植による妊娠がほとんどを占め、新鮮胚移植による妊娠は1割に満たない。しかし新鮮胚移植は time to pregnancy を短くする事ができる可能性から再注目されており、他にも凍結操作による胚へのダメージの回避、凍結融解コストの削減、凍結融解胚移植よりも周産期リスクが比較的低いなどといった利点が挙げられる。今回、当院で新鮮胚移植を行った症例を調査し、初回採卵周期に新鮮胚移植を実施することが有用である症例を予測する因子を検討することとした。【方法】2012年1月～2022年12月の間に当院で初回採卵周期において単一新鮮胚移植を行った392例を対象に、臨床的妊娠が成立した群と不成立であった群、生児を獲得した群としなかった群に分類し、それぞれにおいて妊娠成立に関連しうる患者背景、血中ホルモン値、超音波検査所見について比較した。【成績】臨床的妊娠率は40.8% (232/392)、生児獲得率は全体が32.1% (126/392)であった。新鮮胚移植を実施した胚 stage は分割期胚が84例、胚盤胞が308例であり、臨床的妊娠率はそれぞれ28.6% (24/84)と44.2% (136/308)で、生児獲得率はそれぞれ22.6% (19/84)と34.7% (107/308)であった。生児を獲得した症例は年齢が低く (35歳 vs 36.5歳, $p < 0.001$)、胚移植時の内膜が厚かった (10.5mm vs 10.1mm, $p = 0.025$) が、不妊要因や ICSI 実施の有無に差はなかった。【結論】初回採卵時の新鮮胚移植は若年層で OHSS に留意しつつ実施することで time to pregnancy 短縮に寄与しうる可能性が示唆された。

P-53-6 挙児希望数と将来の妊孕性を意識した有効胚数獲得と OHSS の重症化予防を両立するプロトコール

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【目的】第16回出生動向基本調査によると、平均挙児希望数は2.01人と複数挙児を希望する患者は多い。そのためには、患者の将来の妊孕性低下を意識した至適有効胚数を獲得する調節卵巣刺激(COS)が重要である。COSを行う際には卵巣過剰刺激症候群(OHSS)の重症化予防は必須であり、当院のプロトコールの有用性を紹介する。【方法】2022年7月から2023年8月まで当院で行なった採卵833周期のうち、OHSSの診断となり重症化予防プロトコールを行った93例を対象に後方視的検討を行なった。全例 GnRH Antagonist 法によるCOSを行い、排卵誘発中に16mm以上の卵胞が15個以上発育した場合 Le-trozole 5mg/day x 5days②maturation trigger に GnRH Agonist のみ使用③trigger 同日より Cabergoline 1.0mg/day x 7 days④採卵当日より GnRH Antagonist 0.25mg/day x 3days の4項目いずれか、もしくは全てを行い全胚凍結とした。採卵術後5日目にOHSSの経過観察を行なった。【成績】年齢は27-44歳(平均35.7歳)、左右総 AFC6-82個(平均25.3個)、AMH 1.05ng/ml-22.24ng/ml(平均5.11ng/ml)、採卵数7-54個(平均25.1個)、獲得有効胚盤胞数(Gardner分類CCを除く)は1-13個(平均4.2個)であった。術後診察では卵巣最大長径は30.5-88.3mm(平均48.9mm)、44例が軽度腹部膨満感を自覚するのみであったが、小骨盤以上に及ぶ腹水貯留を1例認めた。採卵翌周期の月経開始までの日数は3-7日(平均4.2日)であった。【結論】ART開始時の年齢と挙児希望数、将来の妊孕性を考慮した目標有効胚数獲得は患者ごとに異なり、患者ごとに適したCOSの選択は重要である。特にAMH高値やPCOS症例に本プロトコールを用いることで、OHSS重症化リスクの軽減が期待される。

P-53-7 クロミフェン周期分割胚移植の内膜厚別妊娠率の検討—新鮮胚移植と凍結胚移植の比較—

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【目的】クロミフェン周期採卵後の分割胚移植で内膜厚が臨床妊娠率に与える影響を新鮮分割胚移植、凍結融解分割胚移植各々で検討し特徴を把握する。【方法】2019年1月1日から2023年4月30日までにクロミフェン採卵の新鮮分割胚移植あるいは凍結融解分割胚移植でプセリリンによるトリガー時と移植時の内膜厚を測定し得た周期を検討し、内膜厚が臨床的妊娠に与える影響を検討した。ホルモン補充周期は除外した。【成績】新鮮分割胚移植は235周期、平均年齢は35.7歳であった。臨床妊娠率は23.4%であった。移植時内膜厚別の臨床妊娠率は内膜8.0-10.0mm:15.8%(n=38), 10.1-12.0(n=117):21.4%, 12.1-14.0(n=74):25.7%, 14.1以上(n=6):83%であった。トリガー時の内膜厚別の臨床妊娠率は内膜厚7.0mm未満:17.6%(n=51), 7.1-8.0:24.2%(n=91), 8.1-9.0:16.7%(n=36), 9.1-10.0:34.3%(n=35), 10.1mm以上:27.3%(n=22)であった。他方、凍結融解分割胚移植は512周期で平均年齢は34.8歳であった。臨床妊娠率は38.5%であった。移植時内膜厚別の臨床妊娠率は内膜厚8.0-10.0mm:32.0%(n=97), 10.1-12.0(n=289):37.0%, 12.1-14.0(n=125):44.8%, 14.1mm以上(n=1):100%であった。トリガー時の子宮内膜厚別の臨床妊娠率は、内膜厚8.0mm未満:41.9%(n=31), 8.0-8.9:35.2%(n=128), 9.0-9.9:37.0%(n=108), 10.0-10.9:39.5%(n=114), 11.0-11.9:35.6%(n=45), 12.0-12.9:45.8%(n=48), 13.0-13.9:35.3%(n=17), 14.0mm以上:38.1%(n=21)であった。【結論】クロミフェン周期における妊娠率の差異は、凍結融解分割胚移植ではより薄い内膜厚でも臨床的妊娠が認められることにあると考えられた。

P-53-8 プロゲステロン陰錠併用ホルモン補充周期下での移植日の血中エストラジオール値とプロゲステロン値が臨床成績に及ぼす影響の検討

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【目的】ホルモン補充周期 (HRT) 下における凍結融解胚移植 (FET) 当日の血中エストラジオール (E_2) 及びプロゲステロン (P_4) 値と臨床成績との関連には様々な報告がある。当院ではプロゲステロン陰錠を用いた HRT での FET を行っており、移植当日の E_2 と P_4 値を計測しているものの、追加の黄体補充は原則として施行せずに移植を行っている。本研究ではプロゲステロン陰錠を用いた HRT における移植当日の E_2 , P_4 値と臨床成績の関連を検討した。【方法】2019 年 1 月から 2022 年 12 月の期間にプロゲステロン陰錠投与下での HRT-FET を行った症例 1120 周期を対象に、移植当日の血中 E_2 及び P_4 値と臨床的妊娠率を検討した。エストラジオール経皮吸収型製剤は月経 4 日目以内に 4 枚隔日貼付の固定法で開始し、子宮内膜厚 ($\geq 7\text{mm}$) を確認するとともに血中の E_2 及び P_4 値を測定し、移植日を決定した。プロゲステロン陰錠は 300mg/day 固定用量とし、妊娠判定日まで継続した。FET 日の P_4 値と生化学妊娠、臨床的妊娠、流産との関連を検討した。【成績】対象症例の平均年齢は 37.7 歳 (± 4.3) であり、933 例 (83.3%) が胚盤胞移植であった。生化学妊娠率、臨床的妊娠率および流産率は 43.5%、28.6%、20.3% であった。FET 日の E_2 値は 434.9 (± 289) pg/mL, P_4 値は 13.4 (± 3.9) ng/mL であった。 E_2 及び P_4 値と生化学妊娠、臨床的妊娠および流産に有意な関連は認めず、胚盤胞移植に限った解析においても有意差は認めなかった。【結論】プロゲステロン陰錠併用ホルモン補充周期下凍結融解胚移植における移植当日の血中 E_2 及び P_4 値と臨床成績に有意な関連は認めなかった。移植当日の血中 E_2 及び P_4 値の測定意義は乏しい可能性が示唆された。

P-53-9 両パートナーともに均衡型染色体相互転座を有する不育症カップルに対し、PGT-SR により得られた交互分離胚を移植し生児が得られた胎盤限局性モザイクの 1 例

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カップルのどちらかあるいは双方が均衡型染色体相互転座 (RTL) 保因者の場合流産の原因となりえ、着床前胚染色体構造異常検査 (PGT-SR) が対処法の選択肢の 1 つとなる。また、胎盤にのみ染色体異常を認める胎盤限局性モザイク (CPM) が存在し、周産期異常に関連することが指摘されている。今回、両パートナーともに RTL を有する不育症カップルにおいて、PGT-SR により生児が得られ、胎盤絨毛の解析で CPM が疑われた症例を経験したので報告する。症例は 3 回の流産歴のあるカップルで、精査により両パートナーの RTL が判明し PGT-SR 施行の方針となった。5 周期の採卵で得られた胚盤胞 20 個に対し PGT-SR を施行した。13 検体で転座領域及び染色体コピー数の解析が可能で、1 個が転座部分正常あるいは均衡型で異数性モザイク、2 個が正常あるいは均衡型で異数性、1 個が不均衡型で正数性、9 個が不均衡型で異数性の結果であった。正常あるいは均衡型で異数性モザイクの胚盤胞を移植し、妊娠が成立した。羊水染色体検査の結果は 46,XX であり、妊娠経過は順調で、妊娠 37 週骨盤位のため選択的帝王切開術を施行した。児に顕著な形態異常はみられなかった。カップルの同意の元、胎盤絨毛の染色体コピー数解析を行った。STR 解析で母体 DNA の混入がないことを確認の上、胎盤絨毛 4 検体を解析した。結果はそれぞれ、① 46,XX, ② モノソミー 17 (低頻度モザイク (LM)), モノソミー 19 (高頻度モザイク), モノソミー X (LM), ③ モノソミー 19 (LM), ④ モノソミー 19 (LM) であり、CPM が疑われた。両パートナーとも RTL 保因者のカップルにおける PGT-SR での移植胚選択は意義があると考えられた。また、PGT-SR, PGT-A や羊水細胞の解析では検出されないまま絨毛内に異数性細胞が存続しうることが確認された。

P-53-10 「重篤な遺伝性疾患を対象とした着床前遺伝学的検査」(PGT-M) 新見解のもとでの申請症例の検討

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PGT-M は、出生する可能性のある重篤な遺伝性疾患に対する妊娠中絶を回避し、身体的、精神的負担を軽減することを目的とする。日本では 1998 年に日本産科婦人科学会が発表した見解に則って運用されてきた。この旧見解における重篤性の定義として、成人に達する以前に日常生活を著しく損なう状態が出現したり、生存が危ぶまれる状態になる疾患と定められた。その後 2022 年 1 月に重篤性の定義が改定され、成人発症疾患を一律に除外しない方向性が示されたうえ、治療方法がないかあるいは高度かつ侵襲度の高い治療を行う必要のある状態であれば申請可能となった。今回我々は新見解以降の当院からの PGT-M 申請の現状をまとめた。当院に PGT-M を目的として遺伝カウンセリングに来院された症例数は 2023 年 9 月現在 19 症例であり、そのうち申請を行った症例が 8 症例、初回カウンセリング後に申請を希望しなかった症例が 5 症例、今後申請予定症例が 6 症例である。申請症例のうち認可されたものは 5 症例 (AchoondrogenesisIb・Leigh 脳症・Sengers 症候群・EDHS 1 異常症・ α サラセミアメジャー)、申請中 1 症例、再審議のため追加の意見書を求められたものは 2 症例 (ADPKD・Holt-Oram 症候群) である。認可症例は旧見解の重篤性の定義を満たす症例であるのに対し、再審議の 2 症例は新見解のもとではじめて承認の可能性が出てきた疾患である。新見解以降に症例申請が可能となった症例は増加したといえるものの、当院からの症例申請で現時点で承認が得られているのは旧見解の重篤性の定義に合致する症例のみである。クライアントが抱える背景は様々であり、旧見解の重篤性定義に合致しなくとも PGT-M を希望される例は今後も続くと思われる。

P-53-11 薬物療法・嚢胞穿刺・ARTのコンビネーションにより子宮内膜症性卵巣嚢胞の病勢抑制と不妊治療とを一元的に行い妊娠・分娩にいたった症例

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【緒言】子宮内膜症性卵巣嚢胞（以下 EmCyst）合併不妊症では、生殖補助医療（ART）を前提とする場合は EmCyst に手をつけずとする指針が多い。一方、EmCyst の位置によっては卵巣穿刺が困難であったり、採卵により PID を誘発したりすることがある。今回、薬物療法による EmCyst の病勢抑制を継続しつつ、EmCyst 内容吸引～調節卵巣刺激～採卵～全胚凍結～融解胚移植を行い、妊娠・分娩が成立した症例を経験したので報告する。【症例】29 歳 GOP0、近医より紹介受診となった両側 EmCyst を合併する原発性不妊症例。ART の方針としたが、EmCyst の位置的に卵巣穿刺が困難と考えられたため、まず EmCyst の病勢抑制目的でジエノゲスト（DNG：1 mg/日）の投与を開始・継続した。次いで経腔的 EmCyst 内容吸引を施行し、さらに DNG を継続使用しつつ嚢胞穿刺 13 日後より progestin-primed ovarian stimulation (PPOS) で調節卵巣刺激を行い採卵を施行（13 個）、顕微授精を行い計 5 個の胚を全胚凍結した。その後 DNG を Relugolix（40mg/日）に変更し継続投与を行いつつ、開始 9 日後より並行してエストラジオール/プロゲステロンによるホルモン補充下に融解単一胚盤胞移植を施行したところ妊娠が成立した。妊娠経過は順調で、妊娠 39 週 4 日で正常経陰分娩となった。【考察】採卵困難な EmCyst 症例に対して、薬物療法・経腔的嚢胞内容吸引・ART を組み合わせることにより、EmCyst の管理と ART とを一元的に行って妊娠並びに分娩に結びつけることができた。本法は、全経過を通じて常に薬物療法を行うことにより EmCyst の病勢抑制をしつつ手術を回避することが可能で、全て外来診療レベルで完結できるものであり、同様の症例に対して有用であると考えられた。

P-53-12 公的助成により実施した社会的卵子凍結による卵子を用いた ART 実施後の転帰

順天堂大附属浦安病院

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【緒言】がん患者の妊孕性温存を目的とした卵子凍結は本邦でも広く普及し始めている一方で、社会的卵子凍結については広く普及しているとは言い難く、転帰についての報告も少ない。今回、社会的卵子凍結を行い、その凍結卵子を用いて ART を実施した症例を経験したのでその転帰について報告する。【方法】2016 年 4 月から 2018 年 3 月の間に、千葉県浦安市から提供された研究資金で治療費を助成し、市内在住の 35 歳未満の未婚女性を対象に社会的卵子凍結を実施した。その 34 例に対し、研究期間終了後に凍結卵子を用いた ART を実施した。症例の治療経過と転帰について後方視的検討を行った。【結果】採卵時の平均年齢は 32.8 歳、平均卵子獲得数は 8.3 個であった。卵子凍結後に自然妊娠、一般不妊治療、体外受精・胚移植などにより妊娠した症例を認めた。3 例に凍結卵子を用いた顕微授精を行い、1 例は受精するも胚発育不良のため胚移植を実施しなかった。2 例は良好胚盤胞が得られたため胚移植を実施した。【症例 1】37 歳、1 妊 0 産、34 歳時に 7 個卵子凍結し、採卵から 3 年 7 か月後に凍結卵子を使用した顕微授精を行い、得られた良好胚盤胞を 1 個移植し、妊娠成立した。妊娠経過は問題なく、正期産に至った。【症例 2】40 歳、0 妊 0 産、34 歳時に 10 個卵子凍結し、採卵から 6 年後に凍結卵子を用いた顕微授精を行い、得られた良好胚盤胞を 1 個移植し、妊娠成立するも妊娠 8 週で流産となった。【結語】35 歳未満の未婚女性に対し社会的卵子凍結を行うことにより、将来的な妊娠方法の選択肢となる。一方で、卵子凍結実施から卵子使用まで長期間にわたるフォローアップが必要となる可能性が示唆された。

P-53-13 ホルモン補充周期から自然周期胚移植に変更し、妊娠成立した反復着床不全の一例

信州大

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凍結融解胚移植では自然な排卵後に移植する自然周期と薬剤を用いて子宮内膜を調整するホルモン補充周期があり、両者の生児獲得率に有意差はないが、ホルモン補充周期では生理的な排卵時よりもエストロゲンが高値となることがあり、子宮内膜の胚受容能低下に関連するとの報告がある。今回、ホルモン補充周期にて形態良好な胚盤胞を 4 回（計 5 個）胚移植するも妊娠に至らない反復着床不全であったが、自然周期に変更後に速やかに妊娠が成立した 1 例を経験したため報告する。症例は 33 歳、1 妊 0 産の女性で 27 歳時に児希望のために当科を受診した。28 歳時に両側卵巣子宮内膜症性嚢胞に対して、腹腔鏡下子宮内膜症病巣除去術を行い、術後 2 か月で自然妊娠が成立したが流産となった。以降、自然妊娠が成立せず、31 歳時に体外受精・胚移植にステップアップした。計 4 回採卵を行い、ホルモン補充周期にて Gardner 分類 BB 以上の胚盤胞 5 個（AA, BB, AB×3 個）を胚移植するも妊娠成立しなかった。子宮鏡検査、子宮内膜着床能検査などを施行したが、反復着床不全の原因は特定できなかった。胚移植周期の黄体ホルモン開始前日の E2 は平均 478 pg/mL（394～606）とやや高値（ ≥ 400 pg/ml）であったため、自然周期胚移植に変更した。月経 14 日目に主席卵胞は 16mm、E2 164pg/mL であり、翌日に HCG1 万単位を用いて、排卵を促し、HCG 投与 7 日目に Gardner 分類 5AB の良好胚を 2 個移植し、単胎妊娠が成立した。現在妊娠 16 週であり、妊娠経過は良好である。自然周期のホルモン補充周期に対する優位性は証明されていないが、反復着床不全症例においては移植周期の E2 を測定し、高値である場合は自然周期胚移植の検討が有効である可能性が示唆された。

P-54-1 当院で受け入れた分娩後異常出血による搬送症例の検討

北里大

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産科危機的出血は妊産婦死亡の主要な原因の一つである。当院の近隣地域の分娩数は年間約 9000 件だが、当院は地域で発生した産科危機的出血を 24 時間体制で 100% 受け入れ、造影 CT 検査の段階から Interventional Radiology (IVR) 専門医と連携し治療を行っている。しかし、適切な労務環境の構築と現行の医療体制継続を両立することが困難になりつつある。そこで、これまでの実態調査を目的に分娩後異常出血のため当院で受け入れた搬送症例を検討した。【方法】2019 年 4 月から 2023 年 3 月に当院で受け入れた分娩後異常出血による搬送症例を診療録から抽出し、後方視的検討を行った。【結果】該当症例は 4 年間で 71 例だった。搬送元は開業医 50 例 (70.4%)、総合病院 20 例 (28.1%)、救急隊からの直接依頼 1 例であった。夜間・休日帯の搬送は 44 例 (61.9%) で、来院時にショック症状を呈していた症例は 24 例 (33.8%)、播種性血管内凝固症候群を発生していた症例は 20 例 (28.1%) であった。IVR 適応症例は 27 例 (38.0%) で、そのうち夜間・休日帯の事例は 15 例だった。これは、分娩後異常出血による搬送全体の 21.1%、休日・夜間帯搬送の 34.0% に相当した。なお、IVR 適応症例の原因は腔壁血腫・裂傷 6 例、弛緩出血 4 例、臨床的羊水塞栓症 2 例、仮性動脈瘤破裂 1 例、癒着胎盤 1 例、産褥出血 1 例であり、15 例の平均出血量は 5059.7g であった。なお子宮摘出例はなく、全例、後遺症なく救命できた。【考察】分娩後異常出血の治療法として IVR は低侵襲かつ有用だが、治療には IVR 専門医と産科医の協働が必須だった。周産期医療における真の働き方改革の実現には、産科医のみならず IVR 専門医など関連領域も含めた検討が大切である。

P-54-2 分娩後腔壁血腫に対する IVR の有効性および合併症の検討

山梨大

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【目的】分娩後の腔壁血腫は一般的に外科的処置を行うが、状況により interventional radiology (IVR) を選択することがあり、その有効性および合併症について後方視的に検討した。【方法】2013 年 1 月から 2023 年 9 月までに発症した分娩後の腔壁血腫に対して IVR を施行した 15 例を対象とし、患者背景、妊娠合併症、DIC スコア、輸血量、IVR に要した時間、IVR 奏功および合併症の有無、残存血腫の経過、次の妊娠経過等について検討を行った。【成績】2 例が 1 産、他の 13 例は初産婦であり、母体年齢の中央値は 30 歳 (21-37)、分娩週数の中央値は 40 週 (35-41) であった。全例が腔壁血腫であったが 2 例は後腹膜血腫へ進展していた。妊娠高血圧症候群 4 例、HELLP 症候群および常位胎盤早期剥離を 1 例ずつ認め、DIC を発症した症例は 5 例であった。分娩誘発あるいは促進が 10 例、補助経陰分娩が 5 例で施行されていた。IVR に要した時間の中央値は 59 分 (36-136) であり、塞栓物質はゼラチンスポンジのみが 11 例、n-butyl-2-cyanoacrylate (NBCA) を要した症例が 4 例であった。DIC 症例を含め全例で止血が得られ、追加治療を要さず救命可能であり、感染や壊死などの IVR の関連する合併症は認めなかった。IVR 後の残存血腫径の中央値は 8cm (2-11) であり、基本的には残存血腫の除去術を行わず経過観察としたが疼痛管理も可能であり、産褥 1-2 か月後には血腫消失を確認した。5 例が再度妊娠し、4 例が正常経陰分娩し、1 例が現在妊娠中である。【結論】分娩後の腔壁血腫は IVR により合併症を認めず止血可能であり、残存血腫の除去も不要である可能性が示唆された。

P-54-3 当科における最近 10 年間の Cesarean hysterectomy 症例の検討

札幌医大

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【目的】帝王切開時、様々な止血操作に抵抗性で止血されない時、例えば癒着胎盤等で胎盤剝離不可能な時、同時に子宮摘出が行われる。こうした症例では術前診断は難しく、リスクのある症例では常にその可能性を念頭に手術に臨む必要がある。2014 年 1 月からの 10 年間に当科で施行した帝王切開時子宮摘出 (Cesarean Hysterectomy) 症例につき、その臨床背景、特徴、対処法等につき検討した。【方法】2014 年 1 月より 2023 年 10 月までの約 10 年間に当科で経験した Cesarean Hysterectomy 症例 23 例につき、診療録より後方視的に臨床データを収集した。【成績】当該期間の Cesarean Hysterectomy 症例は 23 例、同期間当科全帝王切開症例の 1.5%、全分娩の 0.7% であった。15 例が最初から子宮摘出を決定し、うち 12 例は侵入胎盤以上の癒着胎盤疑いであった。23 例中 8 例が術中の止血困難等による子宮摘出であった。子宮摘出症例のうち子宮全摘出術は 13 例、子宮陸上部切断術は 10 例に施行された。術中総出血量は中央値 3405ml (760-20710ml)、全子宮摘出症例 23 例中 19 例で自己血含む輸血を行った。癒着胎盤疑い等出血増加の可能性が高いと判断した 7 例で総腸骨動脈バルーン閉塞術 (CI-ABO) 併用を行った。【結論】帝王切開率の増加、妊娠高齢化に伴ういわゆる ART 妊娠の増加などに伴って、近年は癒着胎盤に伴う Cesarean Hysterectomy が増加してきている。こうしたハイリスク症例に対する術前の十分な準備、診断精度の向上が望まれる。

P-54-4 胎児徐脈に対する超緊急帝王切開術時に Spontaneous Hemoperitoneum in Pregnancy (SHiP) と診断した1例

近畿大

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【緒言】 Spontaneous hemoperitoneum in pregnancy (SHiP) は、妊産婦における外傷、子宮破裂、卵巣出血、異所性妊娠を除く急性腹腔内出血であり、発症機序は不明であることもあるが、近年子宮内膜症との関連も指摘されている。妊娠26週に母体急性腹痛と胎児徐脈を認め、超緊急帝王切開術時にSHiPの診断に至った症例を報告する。【症例】33歳初産婦、子宮内膜症の既往あり。妊娠26週6日右側腹部から上腹部にかけての激痛を突然認め、当院に救急搬送となった。前医での胎児心拍陣痛図モニターでは異常を認めなかった。受診時のバイタルサインは脈拍92回/分、血圧99/66mmHg、SpO₂(室内気)100%、体温36.5度であった。胎児心拍陣痛図モニターにて胎児徐脈(70-90bpm)を認めた。超音波断層法にて常位胎盤早期剝離を疑う所見を認めなかったが、胎児徐脈は回復せず全身麻酔下に緊急帝王切開術を施行した。術中所見では、上腹部に多量の血液貯留と横行結腸右側近傍の大網に鷲卵大の凝血塊を認め、大網からの出血によるSHiPと考えられた。術中出血量は約2Lであり、輸血(RBC16単位、FFP20単位、クリオプレシビテート12単位、血小板10単位)とフィブリノゲン製剤3gを投与した。新生児は、出生体重971g、Apgar score1点/4点、臍動脈血pH6.90、BE-17であり、新生児仮死のため新生児集中治療室に入院となった。【結語】妊産婦のショックを伴う急性腹痛症ではSHiPを念頭におき、経腹超音波検査での腹腔内出血の検索を行うことが、輸血や人員確保など手術準備に有用と考える。

P-54-5 産褥出血に対する子宮動脈塞栓術(UAE: Uterine artery embolization)により止血が得られたがその後子宮壊死により子宮摘出を施行した一例

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【緒言】子宮動脈塞栓術(UAE: uterine artery embolization)は分娩後異常出血に対して高い止血成功率を認める一方、約1-2%に子宮壊死が起こりうる。今回、分娩後異常出血に対するUAE後に子宮壊死を起こし子宮全摘出に至った症例を経験した。【症例】39歳、3妊1産。妊娠初期より前医で妊婦健診を受診し、妊娠38週4日に骨盤位のため予定帝王切開術を実施された。術後1時間から性器出血の増加を認め、輸血投与や子宮内バルーンタンポナーデを行ったが、術後4時間での総出血量3970mLとなり当院へ搬送となった。当院で造影CT検査により子宮底部の動脈性出血を認め、両側子宮動脈に対して吸収性ゼラチンスポンジを用いたUAEにより止血を得て、15日目に退院した。UAE後59日目に腹痛で再入院した。発熱や悪臭ある帯下を認め、骨盤内炎症性疾患に対して抗菌薬治療を実施したが、症状改善に乏しかった。UAE後69日目の骨盤部造影MRI検査により子宮底部を中心に子宮壊死を疑われ、単純子宮全摘術を施行した。術中所見は、子宮底部から体部が白色化し、内腔は黄色調であった。病理組織学に子宮間質部の広範囲に壊死、出血、変性像を認めた。術後7日目に退院した。【結語】分娩後異常出血に対するUAEは有効な治療法であるが、子宮壊死という重篤な合併症を惹起する可能性がある。UAE後に遷延する発熱や腹痛、悪臭を伴う帯下を認め、抗菌薬治療の効果が乏しいときは子宮壊死を疑い、造影MRI検査を行うべきである。

P-54-6 大量出血をきたした子宮頸部静脈瘤合併妊娠の一例

岐阜大

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【緒言】妊娠中の子宮頸部静脈瘤は稀ではあるが、破裂すると大量出血をきたしうる病態である。圧迫や縫合による止血が可能な場合もあるが、明確な管理方法は定まっていない。今回我々は妊娠34週で子宮頸部静脈瘤から大量出血をきたし、帝王切開術後に動脈塞栓術にて止血可能であった症例を経験したので報告する。【症例】31歳、G1P0。凍結胚移植で妊娠成立、辺縁前置胎盤のため31週時に当院紹介となった。34週2日に性器出血を主訴に受診され、陰鏡で展開すると子宮腔部より大量の出血あり、圧迫するも止血困難なため同日緊急帝王切開術を施行した。手術終了後、術前に腔内に充填したガーゼを抜去すると子宮腔部から大量の出血を認めた。造影CT動脈相で明らかなextravasationはないものの、圧迫では止血されず子宮への血流減弱目的に動脈塞栓術を施行した。両側子宮動脈、右腔動脈、両側内陰部動脈をゼラチンスポンジで塞栓し、止血を得た。翌日の診察で子宮腔部に破綻した静脈瘤の痕跡を確認したが再出血なく、術後8日目に退院となった。産後1か月健診時には子宮腔部の静脈瘤が消失している事を確認し終診となった。【考察】妊娠中の子宮頸部静脈瘤は胎盤位置異常症例に合併しやすく、子宮内部からの出血と鑑別するためにも事前の診断が重要である。また妊娠後期は子宮への血流が増加しており止血が困難となる場合がある。動脈塞栓術は妊娠性温存可能で手術と比較し患者負担の少ない手技であり、今回のような止血困難例には良い適応であると考えられた。

P-54-7 経膈分娩後の子宮出血に対して OB バルーンを経膈的に使用し止血を得た 2 例

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【背景】OB バルーンは前置胎盤の帝王切開に特化して開発されたバルーンである。今回、経膈分娩後の子宮出血に対して OB バルーンを経膈的に使用し止血を得た 2 例を経験したので報告する。【症例 1】32 歳 1 妊 0 産自然妊娠成立。妊娠経過異常なし。妊娠 40 週 6 日に微弱陣痛のため分娩促進を行い経膈分娩となった。児娩出後より子宮出血あり、経腹超音波で子宮頸管内～体下部に 9cm の血腫を確認。子宮内バルーンタンポナーデ目的に OB バルーンを使用した。子宮側バルーンを 300ml、腔側バルーンを 100ml で拡張し子宮内に挿入し止血を得た。出血はバルーン挿入までで 1960g、挿入後 2 時間で 100g であった。【症例 2】34 歳 1 妊 0 産 IVF-ET で妊娠成立。妊娠経過異常なし。妊娠 41 週 0 日に微弱陣痛のため陣痛促進を行い経膈分娩となった。児娩出後より弛緩出血あり、子宮収縮剤を使用するも出血持続。バクリバルーン挿入を試みたが滑脱し、OB バルーンを挿入し止血を得た。出血は OB バルーン挿入までで 2466g、挿入後 2 時間で 10g であった。RBC4 単位、FFP4 単位の輸血を要した。【考察】OB バルーンの特徴は、①本体が太く適度な硬さでコシがあること②ダブルバルーンであることである。本体の太さとコシにより、収縮した子宮体部に押し出されることなく子宮内への挿入が可能である。また、ダブルバルーンの特徴を生かし、腔側バルーンを頸管内に留置後に子宮側バルーンを拡張させることで、より確実に子宮内にバルーンを留置できる。更に、ダブルバルーンによってシングルバルーンよりも広い面積を圧迫止血できる。OB バルーンは、経膈分娩後の子宮出血に有用である。

P-54-8 救命し得た臨床的羊水塞栓症の 1 症例

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救命し得た臨床的羊水塞栓症の 1 症例を経験した。症例は 38 歳初産婦。妊娠 39 週 6 日に高血圧を認め (144/97mmHg)、入院管理し安静で血圧は改善。妊娠 40 週 5 日にオキシトシン投与による分娩誘発を施行した。子宮口全開後に高度遷延一過性徐脈が出現したため、吸引娩出術 (子宮底圧迫法併用) を試み、3 回目の施行後に母体の意識消失・筋硬直が出現。顔面にチアノーゼが出現し呼吸停止を認めたため直ちにバックバルブマスク換気を行い、全身麻酔による緊急帝王切開術を開始した。術前の収縮期血圧 153mmHg が、胎児胎盤娩出直後に突然収縮期血圧 66mmHg に低下し低血圧が持続したが、腹腔内出血量は多くなく子宮収縮も良好であった。以前経験した羊水塞栓症例も児娩出後に突然血圧低下を認めたことから羊水塞栓症を疑い、血中フィブリノゲン (fib) 採血と新鮮凍結血漿 (FFP) の確保・投与準備をおこなった。手術終了直後に経膈的に多量出血 (3668g) を認め、子宮収縮も不良となり、血中 fib 値は 50mg/dl 未満であった。臨床的羊水塞栓症と診断し、可及的速やかに FFP (合計 5040ml) やフィブリノゲン濃縮製剤 (3g) の投与を行い、出血は軽減するも持続するため子宮動脈塞栓術も施行し止血に成功した。分娩時に突然の血圧低下があれば羊水塞栓症を疑い、血中 fib 値の測定や FFP の確保投与、フィブリノゲン濃縮製剤投与を躊躇せず行うことが重要と考える。

P-54-9 母児共に救命しえた非癥痕子宮破裂の一例

神戸市立医療センター中央市民病院
山田野々花、前田振一郎、金澤怜佳、川本佳与子、元山貴仁、荻野敦子、山添紗恵子、松林 彩、三木通保、青木卓哉

【緒言】子宮破裂は母体死亡に至った産科危機的出血の原因として 2 番目に多い重篤な疾患である。なかでも非癥痕子宮破裂は 8000-15000 分娩に 1 例と非常に稀であり癥痕子宮破裂より重症となりやすい。今回、産科危機的出血をきたしたが母児共に救命しえた非癥痕子宮破裂の一例を経験したため報告する。【症例】38 歳 G2P1 (VD1) 胚移植で妊娠成立。予定日超過に対し前産科クリニックで妊娠 40 週 5 日に分娩誘発を開始し、同日胎児機能不全のためクリステル圧出法+吸引分娩 1 回施行し児娩出に至った。児は Apgar2/3 pH6.7 のため他院に搬送され、母体は SI : 1.5 程度の産科危機的出血のため当院搬送となった。到着直後の産科 DIC スコア 8 点、Hb6.3g/dL、持続的な外出血は少量であったにも関わらず不安定な循環動態が続き輸血や昇圧剤を要した。造影 CT で左子宮動脈からの出血と左広間膜内の血腫貯留を疑う所見を認め、まずは TAE で出血部位の評価と止血を試みる方針とした。左子宮動脈を NBCA で塞栓し止血及び全身状態の安定を得た。翌々日の MRI により左広間膜内の血腫に加えて子宮左壁の広範な筋層断裂の所見を認め同日緊急開腹手術を施行した。手術所見では子宮左壁広間膜内に男子手拳大の血腫が貯留し左卵管付着部直下から左頸部上まで筋層が全層に渡って断裂し子宮内腔と交通していた。漿膜はからうじて保たれ不全子宮破裂の状態であった。子宮温存希望はなく子宮全摘術を施行した。術後経過は問題なく術後 6 日目に退院した。【結論】急速墜娩を行った際に外出血量に見合わない不安定な循環動態を認める場合は子宮破裂の可能性を念頭に置く必要がある。

P-54-10 Retained products of conception (RPOC) に対する管理・治療についての検討

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Retained products of conception (RPOC) は妊娠終了後に生じる子宮内組織遺残物の総称であり、近年増加傾向にある。待機的管理で、3~5 か月までに8割が消失するが、RPOC 径が大きいものや血管増生の強いものは、大量出血により、子宮動脈塞栓術や外科的治療(子宮全摘術、子宮鏡下切除術)を必要とすることもあり、管理方法に関しては一定の見解が得られていない。【症例1】35歳、2妊1産、自然妊娠。妊娠16週1日に中期中絶を行った。産褥27日目、子宮内に4cm大の腫瘍と子宮後壁の血管増生像を認めた。産褥73日目に性器出血量が増加し、peak systolic velocity (PSV) 40cm/secの血流を認め、GnRH製剤を開始した。産褥84日目に大量出血をきたし、緊急子宮動脈塞栓術を施行した。【症例2】33歳、1妊0産、凍結融解胚移植妊娠。妊娠40週6日、分娩第2期遷延のため、吸引分娩により児娩出となった。産褥34日目、子宮内に4cm大の腫瘍とPSV 62cm/secの血流を認めた。子宮鏡、造影MRIで精査した後、外科的治療を提示した。今後の妊孕性温存を希望したため、子宮鏡下切除を計画していたところ、産褥60日目に自然消失した。過去の文献から、RPOC 径 \geq 4cm、PSV \geq 80cm/secといった出血リスクの高い症例に対して、予防的な外科的治療も選択肢とされるが、上記2例のように臨床経過は一様ではなく、妊孕性温存の有無、施設の緊急時の体制など、他の要因も考慮する必要がある。また、症例1のように、活動性に大量出血をきたした際の対応についても、施設毎に、患者状況に応じた適切な選択肢を考えておく必要がある。今回、自験例10例とこれまでのエビデンスから、RPOC に対する管理プロトコルについて考案したため、提案する。

P-54-11 子宮破裂・前置癒着胎盤による産科危機的出血を生じたが集学的医療により救命し得た一例

富山大

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【緒言】癒着胎盤・子宮破裂による大量出血では子宮摘出を行っても止血困難となることがある。今回、子宮破裂・前置癒着胎盤に対し子宮摘出を施行したが危機的出血が持続し、集学的治療により救命し得た一例を経験したので報告する。【症例】37歳 G3P1 (妊娠35週で破水・臍帯下垂のため緊急帝王切開、常位癒着胎盤あり) 若年性特発性関節炎 (JIA) に対し PSL 5mg, セルトリズマブペゴルで加療され疾患活動性は安定していた。IVF-ET 妊娠し、妊娠19週5日に後壁付着の全前置胎盤、るいそう (BMI4) のため入院した。妊娠22週6日に警告出血があり、塩酸リトドリン、硫酸マグネシウム点滴を行った。妊娠24週2日にショック、腹腔内液体貯留を認め、Hb: 6.7g/dLの貧血を認めた。造影CTで穿通胎盤からの出血が疑われ、緊急帝王切開を施行した。子宮体部後壁左側の子宮破裂・胎盤露出を認め、児娩出後に子宮全摘術を施行した。子宮摘出後も止血困難であり、術中に放射線科医により両側内腸骨動脈塞栓術(ゼラチンスポンジ)を施行した。産科DICに対しフィブリノゲン製剤9g, 多量輸血(輸血量11,790mL: RBC42単位, FFP38単位, PC20単位), エプタコグアルファ3.3mgを投与し、完全止血は得られなかったが出血量減少を認めたため閉腹した。術中出血量は14,190mLであった。しかし、術後も腹腔内出血が持続し、再度放射線科医により両側内腸骨動脈塞栓術(NBCA使用による永久塞栓)を施行し止血を得た。【考察・結論】本症例では塞栓が2回必要であり、永久塞栓により止血が得られた。止血困難症例であっても動脈塞栓術で止血可能となり得るため、術中を含めた放射線科との連携の重要性が再度認識できた。

P-54-12 帝王切開中に子宮限局型羊水塞栓症を発症したが、子宮温存に成功し、術後のMRIにて子宮筋層の浮腫を認めた1例

岩国医療センター

栗山千晶, 中村一仁, 杉井裕和, 伊藤裕徳

【緒言】羊水塞栓症とは約2万~3万分娩に1例と頻度は極めて低いものの妊産婦死亡の原因としては産科危機的出血、頭蓋内出血・梗塞に次いで多くなっている。今回帝王切開術中に子宮限局型羊水塞栓症を発症したが子宮温存に成功し、術後のMRIにて子宮筋層の浮腫を認めた症例を経験したので報告する。【症例】32歳2妊1産。前医にて妊婦健診施行され、血圧上昇傾向を認め妊娠34週6日よりニフェジピン内服を開始。しかし妊娠35週3日に受診時も収縮期血圧150mmHg, AST47U/I, ALT51U/Iと軽度高値であり妊娠高血圧腎症の発症が疑われ当院へ紹介搬送。来院時血圧120/100mmHgで当院での採血でもAST45U/I, ALT57U/Iと軽度高値を認めたが、明らかなHELLP症候群を疑う所見は認めず入院し安静にて経過観察の方針とした。入院4日目に収縮期血圧が160mmHgを超えニフェジピンの定期内服を開始。しかし入院5日目に再度血圧が160/100mmHgとなった為硫酸マグネシウムの点滴を開始。入院8日目の採血にてAST76U/I, ALT98U/Iと更なる上昇を認め妊娠36週3日で緊急帝王切開術を施行した。児娩出後急速に子宮弛緩が増悪し大量出血が持続、輸血製剤や子宮用手圧迫を継続し子宮弛緩と非凝固性の出血は改善した為子宮摘出はせずに閉腹。総出血量は3370ml。経過より子宮限局型羊水塞栓症が疑われた。術後1日目に現状確認のためMRIを撮影したところ子宮切開部付近に浮腫性肥厚を認めた。【結語】近年子宮限局型羊水塞栓症の病態について子宮を中心に発症したアナフィラクトイド反応と考えられている。今回羊水塞栓症後に撮影したMRIでみられた切開部にて一致した子宮筋層の浮腫はこの仮説を裏付ける一助になると考えられた。

P-54-13 帝王切開後に産科危機的出血を来した一例

大阪南医療センター

寺山奈央, 矢野恵子, 太田 裕, 岩井恵美, 金村昌徳

【緒言】産科危機的出血は、分娩時異常出血の中でも生命を脅かすものであり、その原因としては弛緩出血が最も多く、続いて羊水塞栓、胎盤早期剥離、子宮破裂等があげられる。今回我々は帝王切開後に危機的出血をきたした一例を経験したため報告する。【症例】42歳、1妊0産、他院でART後妊娠成立し、妊娠管理目的に紹介受診となった。過去に2度の筋腫核出術の既往があった。妊娠経過は順調で、38週3日に選択的帝王切開術を施行した。術時間は1時間39分、出血量は羊水込みで1430mlであった。術後の内診で悪露の流出を認めなかったため、頸管拡張をおこない、子宮収縮が良好であることを確認したのち手術室を退出した。帰室直後に悪露の急激な増加を認めショックバイタルとなったため、腔内に連結ガーゼを挿入し圧迫止血および輪状マッサージを行った。腹部造影CTで子宮動脈より活動性の出血を認めたため、子宮動脈塞栓術を施行した。右子宮動脈からの活動性の出血を認めた。子宮動脈塞栓術後は子宮出血も消退し、経過良好で術後8日目に退院となった。最終出血量は4477mlであり、輸血はRBC 24単位、FFP 24単位、PC 60単位を行った。【結語】帝王切開後に産科危機的出血を来した一例を経験した。本症例はIVF-ETによる妊娠、高齢妊娠であり、弛緩出血のリスクが高いことを認識し、帝王切開でも危機的出血に備え、術前からパルンタンポンナードや輸血の準備を行うべきであった。本症例では子宮動脈塞栓術で速やかに止血を得られ、再出血なく経過したことからも産科危機的出血に対する子宮動脈塞栓術は有用な対処法と考えられる。

P-54-14 当院で経験した産褥子宮内反症の2症例

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【緒言】産褥子宮内反症は報告により8,000分娩~10,000分娩に1例と稀な疾患だが、発症とともに同時に激しい疼痛と多量出血を伴い、短時間でショック状態に移行する可能性のある疾患である。全身状態悪化の前に超音波検査などで早期診断を行い、適切な子宮用手整復を施行できれば保存的治療の成功率は高いとされる。当院で経験した子宮内反症2例を文献的考察を含めて報告する。【症例1】40歳、初産。妊娠40週1日、陣痛発来し入院。分娩に至った。児娩出後10分で胎盤娩出し内診・経腹超音波を施行し子宮内反症の診断に至った。徒手整復を試みたが子宮収縮と疼痛で困難であった。分娩第3期までの出血量は1950g、ショックバイタルとなった。手術室で脊髄くも膜下麻酔を行い子宮弛緩が得られたため徒手整復を施行。手術室での出血は1500gであり、RBC10単位、FFP4単位を輸血した。その後子宮内にバルーンを挿入、10連ガーゼで圧迫しICUへ入室。産科DICスコア8点であり治療を行った。その後の全身状態は安定しており、翌朝に子宮内バルーン抜去とした。その後一般病棟での管理となり産後8日目に自宅へ退院。【症例2】24歳、初産。妊娠39週4日に陣痛発来し来院。翌日に経陰分娩に至った。児娩出後10分で胎盤娩出したが直後に子宮内反症と診断。緊急弛緩のため塩酸リトドリンおよびニトログリセリン投与を行い、超音波ガイド下に徒手整復を施行し、腔内ガーゼ圧迫とした。出血量は分娩第3期までで750g、処置中の出血750gの計1500gであった。翌日にHb7.3mg/dLと低値であったが外出血は少量であり、ガーゼを抜去、鉄剤の投与のみで加療し、産後6日目に退院とした。2症例とも産後経過も良好であり再発を認めていない。

P-55-1 妊娠を契機に診断され遺伝カウンセリングを施行した筋強直性ジストロフィー合併妊娠の2例

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【緒言】切迫早産に対する治療を契機に筋強直性ジストロフィーが疑われ、遺伝カウンセリングを施行した2症例を報告する。【症例1】30歳女性、1妊0産。32週6日で他院より切迫早産と羊水過多で当院に母体搬送。リトドリンによる副作用で、CK1043U/mlまで上昇し、硫酸マグネシウムに切り替えた。36週5日に完全破水があり経陰分娩で出生。児はアプガースコア1分値1点、5分値3点で重症新生児仮死のため他院へ搬送後、看取りとなった。問診で把握ミオトニアのエピソードと父方の弟が筋強直性ジストロフィーであったことが判明し、斧様顔貌、胸鎖乳突筋の萎縮から筋強直性ジストロフィーが疑われた。遺伝子検査でCTGレポートがあり、筋強直性ジストロフィーの診断となり当院で遺伝カウンセリングを施行。【症例2】33歳女性、1妊0産。31週0日に切迫早産の診断で管理入院。リトドリンと硫酸マグネシウムの点滴を開始。CK1000U/mlまで上昇し両大腿に筋肉痛が発生。把握ミオトニアがあり神経内科併診の上、筋強直性ジストロフィーの疑いでリトドリンを中止。37週0日で部分前置胎盤に対して選択的帝王切開術施行。児はアプガースコア1分値8点、5分値9点。遺伝子検査ではCTGレポートあり筋強直性ジストロフィーに対して遺伝カウンセリングを施行。児についても当院小児科でフォロー継続中。【結語】リトドリンによる副作用を契機に筋強直性ジストロフィーの診断となり、産後遺伝カウンセリングへと連携できた。産婦人科、神経内科、小児科、遺伝診療部で連携することで産後も患者本人に加えて血縁者を含めた対応が可能となる。

P-55-2 心疾患を有する成人女性の妊娠前（プレコンセプション）ケア戦略を考える

富山大

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医療分野の発展に伴い、生殖可能年齢まで生存する先天性心疾患患者や、若年で診断される遺伝性不整脈等の患者数、高齢妊娠の増加などにより心血管疾患合併妊娠数が増加している。心血管疾患合併妊娠は、ハイリスク分娩となることは言うまでもなく、本来であれば本人が妊娠・出産のリスクを十分に理解し、産科医および原疾患主治医との密な連携のもと妊娠を希望するかも含めてライフプランの選択を行う必要がある。一方で妊娠後に初めて産婦人科を受診するケースもあり、管理に難渋することも多い。実際当院で管理した心疾患合併妊娠患者32名のうち、内科主治医より妊娠許可されていた症例は13例(40.6%)であった。妊娠中に心不全となった症例は4例(13%)であった。早産は6例(19%)で、内3例は母体心不全発症による人工早産であった。心不全発症者のうち1例は、切迫早産治療のため、硫酸マグネシウムおよびベタメタゾン投与を行い右心不全を発症した。別の症例では大動脈基部置換術の既往および濃厚な家族歴からマルファン症候群疑いの患者が、病識の乏しいまま妊娠し、帝王切開後5日目に大動脈離解を発症した症例も経験した。こういった症例から、妊娠前(プレコンセプション)ケアの重要性を痛感し、各診療科との連携により漏れなく情報収集・共有を行えるよう拳児希望や既往歴、内服薬、家族構成等が確認できるリスク評価のためのチェックリストの作成および、生殖可能年齢に達した心疾患患者に対して、より早期からの産婦人科受診を促すシステムの構築が必要であると判断した。今回、プレコンセプションケアに関して当院で実施している外来や作成したリストの例を提示する。

P-55-3 妊娠初期の腹部内臓静脈血栓症を契機に診断に至った先天性アンチトロンビン欠乏症の1例

東海大

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【緒言】先天性アンチトロンビン(AT)欠乏症は、ATの量的もしくは質的低下により若年性血栓傾向を呈する遺伝性血栓性素因であり、妊娠期の静脈血栓塞栓症(VTE)のリスクが高い。またAT欠乏症におけるVTEで最も頻度が高いのは深部静脈血栓症であるが、門脈や上腸間膜静脈などの腹部内臓静脈血栓症を来すことも稀であるがあるとされている。今回腹部内臓静脈血栓症の発症を契機に先天性AT欠乏症と診断された症例を経験したため報告する。【症例】32歳2妊1産。妊娠9週で上腹部痛があり近医内科を受診したが症状の増悪傾向あり総合病院に搬送となった。超音波検査で門脈本幹、右枝、左枝、上腸間膜静脈、脾静脈に広範な血栓を認めたため加療目的で当院搬送となった。直ちにヘパリン静注が開始されたが、検査にてAT活性低下を認め、また同胞に肺血栓塞栓症の既往があることからAT欠乏症を疑った。経過中腸管壊死の所見を認めず、その後血栓の拡大傾向もなかったためヘパリン皮下注射に変更して第26病日に退院となった。遺伝カウンセリング施行後に遺伝子検査が施行され、SERPINC1遺伝子に病的変異を認めた。現在外来にて経過観察中である。【結語】妊娠初期のVTEにおいては血栓性素因を有している可能性が考えられるが、家族歴なども聴取しAT欠乏症などの遺伝性疾患についても考慮する必要がある。また腹部内臓静脈血栓症におけるAT欠乏症の割合は少ないものの、若年発症例では原因疾患として想起することが多いが、その明確な基準は定まっておらず今後の検討課題と考える。

P-55-4 妊娠中期に急性腹症を契機に疑われ、妊娠中に進行が見られた虫垂痛合併妊娠の一例

北里大

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【緒言】虫垂痛の発生率は1/1000万と低く、虫垂痛合併妊娠に関する報告は少ない。今回、我々は妊娠中期の急性腹症を契機に疑われた虫垂痛合併妊娠の一例を経験したので報告する。【症例】38歳、2妊1産。妊娠23週に急性腹症を発症した。前医では、超音波検査にて右付属器領域に約7cmの腫瘤を認め、付属器膿瘍の診断で抗生剤加療が行われていた。しかし、症状改善せず、妊娠25週に当院母体搬送となった。MRI検査では直腸腫瘤も認め、腫瘍マーカー高値(CA19-9:62U/ml, CEA:257ng/ml)も踏まえて大腸癌を疑い、内視鏡生検を2回施行したが悪性所見は得られず経過観察を行なった。しかし、腹部症状は改善しないため、妊娠28週に胸・骨盤部造影CT検査を施行した。その結果、妊娠子宮の頭側に6×3cmの腫脹した虫垂を認め、虫垂痛のダグラス窩転移、直腸浸潤を強く疑った。その後、妊娠29週に頻回の便潜血と陰性壁への直腸腫瘍が浸潤を認めたため、関連診療科で協議の上、虫垂痛合併妊娠として妊娠30週2日に帝王切開および虫垂切除術を施行した。術後病理診断は原発性虫垂痛であり、術後35日目から抗瘤剤治療を開始した。現在、術後1年で経過観察中である。【結語】妊娠中期に悪性腫瘍を疑った場合には、腫瘍生検により悪性像を病理学的に確定診断することで分娩時期を決定することも多い。しかし、本例のように、複数回の生検でも悪性像が確定診断できない場合もある。そのような場合でも、臨床的に悪性を強く疑う場合には、臨床症状に注意を払いながら画像診断で再評価し分娩時期を決定することも必要な場合があると考えた。

P-55-5 血管型エーラス・ダンロス症候群合併妊娠の2症例

信州大

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【緒言】血管型エーラス・ダンロス症候群 (vascular Ehlers-Danlos Syndrome: vEDS) は、コラーゲンの異常に伴う結合組織の脆弱性が特徴の遺伝性疾患である。動脈や腸管の破裂により突然死の原因となり、妊娠中には誘因なく子宮破裂をきたし母体死亡となりうる。【症例】【症例1】26歳、3妊1産の女性で、今回は妊娠32週の胸部大動脈瘤破裂で母体はショック状態となりパッチ修復術にて救命されたが、児は脳性麻痺となった。分娩後の遺伝子検査でvEDSと診断されている。妊娠5週に当科を初診し、妊娠18週から切迫流産の診断で入院した。管理入院を継続し、vEDS合併及び既往帝王切開後妊娠の適応で妊娠34週に選択的帝王切開術を施行した。術中出血量は550gで合併症はみられなかった。【症例2】27歳、2妊0産の女性で、vEDSの家族歴があり、妊娠前に遺伝子検査でvEDSと診断された。妊娠10週に当科を初診し、妊娠22週からβ1遮断薬セリプロロールの内服を開始した。経過は順調であったが、合併症の発症を監視する目的で妊娠28週より管理入院とした。vEDS合併の適応で妊娠34週に選択的帝王切開術を施行し、術中出血量は800gで合併症はみられなかった。【考察】vEDSは6~25%で母体死亡すると報告され妊娠のリスクは極めて高いが、妊娠管理や分娩時期に関しては定まっていない。我々は、妊娠継続の危険性を十分に説明して、妊娠28週以降は管理入院とし、妊娠34週で帝王切開を施行することで、いずれの症例においても母児の不良な予後を回避しえた。【結語】今回、vEDS合併妊娠の2症例を経験した。妊娠中の定まった管理方針はないが、嚴重に周産期管理を行うことで重篤な合併症なく管理して生児を得ることが可能であった。

P-55-6 Stiff person 症候群合併妊娠の一例

香川大

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【緒言】Stiff person 症候群 (SPS) は予期せぬ騒音や刺激などの環境要因により、体幹や四肢の痙攣などの症状が現れる神経免疫疾患である。非常に稀な疾患であり、有病率は100万人に1人と推定されている。今回 SPS 患者の周産期管理を経験したため報告する。【症例】25歳、1妊0産。既往歴に汎下垂体機能低下症、両側股関節亜脱臼などがある。19歳時 SPS と診断された。ステロイドパルス療法や免疫グロブリン療法、バクロフェン髄腔内注射、ジアゼパムにより症状軽減後は、タクロリムス水和物内服と A 型ボツリヌス毒素注射で加療されていた。自然妊娠したため神経内科より紹介となった。妊娠中は内服薬を継続し、注射薬は中止したが症状が増悪なく経過した。妊娠33週3日で妊娠高血圧腎症 (PE)、子宮内胎児発育不全のため管理入院を開始した。その後、PE 増悪と胎児機能不全のため妊娠35週5日に全身麻酔下で緊急帝王切開術を行った。新生児所見は1788g (small for date), 41.6cm, Apgar score 1分後4点, 5分後9点, 臍帯動脈血 pH: 7.27 の男児であった。術後疼痛による SPS の症状出現はなく、産褥13日目に軽快退院。産後1か月までの間、SPS 増悪はみられなかった。児は早産児のため NICU 加療後、日齢33日に自宅退院した。【考察】SPS 合併妊娠の報告例は Pubmed を用いて検索したところ9例あり、多くの症例で妊娠中に症状が軽減している。本症例も妊娠中に一部の治療を中止したが、症状は増悪なく経過した。SPS 患者においては適切な薬剤調整と疼痛管理により増悪なく周産期管理が行える可能性がある。【結語】SPS 患者の周産期管理を経験した。SPS 患者の周産期管理において適切な薬剤調整と疼痛管理が重要であると考える。

P-55-7 意識障害を来した細菌性髄膜炎合併妊娠の1例

大津赤十字病院

大西佑実, 多賀悠希子, 堀川陽平, 左古寛知, 石田憲太郎, 中村彩加, 星本泰文, 多賀敦子, 金 共子, 藤田浩平

【緒言】細菌性髄膜炎は生命を脅かす重篤な疾患であるが、妊娠中の細菌性髄膜炎の報告はほとんどなく、その予後は不明である。【症例】39歳、4妊2産、第二子妊娠時に妊娠17週で絨毛膜羊膜炎、敗血症性ショックでの子宮内胎児死亡の既往がある。今回、自然妊娠にて妊娠成立し、近医にて管理されていた。妊娠33週2日より発熱を認め、翌日より JCSII の意識障害も出現し、救急搬送となった。頭部 CT では頭蓋内病変は認めなかったが、副鼻腔炎の所見を認めた。発熱と項部硬直を認めたことから髄膜炎が疑われ、髄液検査にて好中球優位の細胞数増多や糖低下の所見を認めた。髄液培養検査及び血液培養検査より肺炎球菌を認め、菌血症を伴う細菌性髄膜炎の診断となった。抗菌薬やステロイド開始後も、発熱が遷延し、意識障害は JCSIII まで悪化した。DIC へ移行する懸念や胎児への影響も考慮し、妊娠33週3日で全身麻酔下での緊急帝王切開を行った。新生児は2046g, Apl/2/4点, 臍帯動脈血ガス pH7.284 であり、新生児仮死にて NICU 入院となった。母体は術後 ICU 管理としたが、術翌日に抜管し、発熱や意識障害は徐々に改善した。髄膜炎後に一過性に高次脳機能障害や認知機能障害等を認めたが、リハビリにて改善し、術後3週間で退院となった。新生児は出生後に急性呼吸窮迫症候群を認めたものの順調に経過し、修正40週3日で退院した。【考察】今回、妊娠中の細菌性髄膜炎にて帝王切開分娩となった1例を経験したので、文献的考察を加えて報告する。

P-55-8 妊娠29週に気腫性腎膿瘍を発症した一例

北里大

木島 華, 吉村嘉広, 五十畑仁志, 山崎 優, 五島裕之, 服部響子, 島岡享生, 関口和企, 大西庸子, 落合大吾

【緒言】気腫性腎膿瘍は、腎盂・腎実質・腎周囲にガス貯留を認める尿路感染症である。死亡率は約25%と予後不良な感染症であり、軽症例では経皮的ドレナージ、重症例だと腎摘出といった侵襲的治療を要する。糖尿病を背景とした報告例が散見されるが、妊娠中発症の報告は稀である。今回我々は、妊娠29週に気腫性腎膿瘍を発症した一例を経験したため報告する。【症例】32歳1妊0産。2型糖尿病と腎盂腎炎の既往歴を有するも、排卵誘発剤にて妊娠成立した。糖尿病合併妊娠で妊娠初期に当院を紹介受診し、妊娠経過は順調であったが、妊娠29週4日に発熱と右側腹部痛が出現した。炎症反応上昇と右腎叩打痛から尿路感染症を考へ抗生剤にて加療した。しかし、臨床症状は改善せず抗生剤の変更とMRI検査を行った。その結果、右腎臓内と被膜下に限局した含気のある膿瘍を認め、重症度分類(Huang分類)class2の気腫性腎膿瘍と診断した。非妊娠時には本重症度では経皮的ドレナージが推奨される。しかし、妊娠継続下で安全に効果的な経皮的ドレナージを行うことは困難と考へ、抗生剤加療にて妊娠継続の方針とした。そして、発熱や腎臓叩打痛などの臨床症状、超音波検査による膿瘍径の経時変化、血液検査、によって抗生剤治療の効果を判定し、治療効果が乏しい場合には児を娩出し経皮的ドレナージを行う計画とした。幸い、抗生剤加療にて病状改善し、妊娠37週に分娩に至った。【結語】本症例は、妊娠29週に気腫性腎膿瘍を発症し治療方針の決定に難渋した。治療方針の決定には、児の未熟性、抗生剤の長期投与に伴う薬剤耐性出現の可能性、侵襲的治療の介入時期、といった諸問題を関連診療科間で検討することが重要だった。

P-55-9 薬疹と鑑別を要した妊娠性類天疱瘡(pemphigoid gestationis:PG)の一例

産業医大

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【緒言】妊娠性類天疱瘡(pemphigoid gestationis:PG)は妊娠もしくは産褥期に発症する自己免疫性水疱症であり、発症頻度は50,000分娩に1例と稀である。今回、切迫早産治療中の妊婦に発症し、薬疹と鑑別を要したPGの症例を経験した。【症例】38歳、2妊1産。前医で切迫早産の診断で妊娠26週3日よりリトドリン塩酸塩の点滴静注が開始された。妊娠30週頃より四肢を中心に水疱を伴う紅斑を認め、薬疹の診断で薬剤を変更されたが、皮疹は増悪し、妊娠34週0日に子宮収縮抑制剤を中止された。その後も改善を認めず、口唇まで水疱が出現したため、妊娠34週5日に当院へ紹介搬送となった。当院初診時、手掌・膝・足に掻痒を伴う1-4cm大の緊満性水疱が散在し、体幹・四肢に浮腫性紅斑を多数認めた。血液検査で抗BP180抗体は676U/mlと高値であり、蛍光抗体直接法で表皮真皮境界部にC3が線状に沈着していた。以上よりPGと診断し、プレドニゾロン(PSL)25mg/日を開始し、皮疹は改善を認めた。妊娠39週6日に陣痛発来し、頭位経産分娩で女児を娩出した。児には皮疹の出現は認めなかった。PSL内服開始後98日目(産褥2か月)に中止し、皮疹の再燃なく経過している。【考察】本邦におけるリトドリン塩酸塩使用中に紅斑型薬疹を発症した切迫早産の報告例と比較し、本症例は点滴刺入部に皮疹を認めず、薬剤中止後に皮疹が改善しなかった。これらがPGの特徴と考へ、薬疹を除外することができるのではないかと考へた。【結語】薬物治療中の妊婦に皮疹が生じた場合には、薬疹以外にもPGなどの皮膚疾患を鑑別にあげることが大切であると考えた。

P-55-10 肝外門脈閉塞症および門脈閉塞症合併妊娠の一例

岩手医大

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【緒言】肝外門脈閉塞症は、肝門部を含めた肝外門脈の閉塞により門脈圧亢進症をきたし肝機能障害や食道静脈瘤、門脈大循環シャント等の合併症が生じる症候群である。今回、我々は肝外門脈閉塞症および門脈血栓症を発症するも小児科、消化器内科と循環器内科との連携によって生児を得た一症例を報告する。【症例】38歳の初産婦。既往歴:6歳時に高アンモニア血症を発症。肝外門脈閉塞症による門脈大循環シャントを合併。その後、蛋白制限、高アンモニア血症治療剤により日常生活を送っている。現病歴:自然妊娠により妊娠成立。妊娠8週6日で、下腿浮腫著明のため当科紹介となった。妊娠17週4日に造影CT施行し、肝外門脈閉塞、門脈内血栓、左肺動静脈瘻の診断となった。また、入院時検査にてATIIIの活性が59%でありATIII欠乏症と判明した。妊娠18週2日より予防的抗凝固療法としてヘパリン皮下注1万単位/日を開始。妊娠30週3日、頸管長短縮のためリトドリン内服開始となった。妊娠36週1日、胎児機能不全徴候を認め緊急帝王切開術となった。その際にATIIIを補充した。出血量は1610g(羊水込み)。出生児は女児で体重2580g、アプガースコア1分値8点、5分値9点であった。術後、母体はヘパリン持続点滴施行となり、術後11日目、経過良好のため、ヘパリンからワーファリン内服へ切り替え同日退院となる。【考察】妊娠中は循環血液量の増加により静脈瘤破裂、高アンモニア血症、肺高血圧症発症等のリスクが増加する。本症例は、門脈血栓症を併発していたため、妊娠中から術前後の肺血栓塞栓症を懸念し慎重な周産期管理を必要とした症例であった。

P-55-11 遺伝性血管性浮腫3型合併妊娠の一例

秋田大

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【緒言】遺伝性血管性浮腫 (HAE) は主に C1 インヒビター (C1-INH) の異常により全身に血管性浮腫発作が生じる常染色体優性遺伝疾患である。HAE は3つの型があり、最も稀な3型は C1-INH に異常がないにも関わらず、同様の血管性浮腫発作をきたす。その病態は解明されていないが、妊娠やエストロゲン製剤の関連が報告されている。喉頭浮腫による気道閉塞をきたす可能性があり迅速な対応が求められる。当院で管理を行った HAE3 型合併妊娠の一例を報告する。【症例】26 歳, 1 妊 0 産。幼少期より血管性浮腫発作を認め、23 歳時に HAE3 型と診断された。自然妊娠成立後、近医で妊婦健診されていたが、血管性浮腫発作が複数回出現したため、妊娠 31 週に当科に紹介された。発作時には選択的ブラスキニン B2 受容体拮抗薬の皮下注射により症状は寛解した。当院紹介後より発作の長期予防としてトラネキサム酸の内服を開始し、以後発作は認めなかった。発作時の気道閉塞に備え救急科・麻酔科と連携した上で、妊娠 38 週 6 日に計画分娩とした。分娩時の発作予防として C1-INH 製剤を投与した。胎児機能不全のため、吸引分娩にて児娩出に至った。分娩経過中に血管性浮腫発作は認めず、分娩後もトラネキサム酸の内服を継続し、発作なく経過した。児は Apgar score 1 分値 8 点, 5 分値 9 点であり、出生後問題なく経過した。【結語】他科との密な連携のもとトラネキサム酸内服と分娩時の C1-INH 製剤の静脈投与を行うことで発作の出現なく安全な周産期管理を行うことができた。本症は症例数が限られ、周産期管理における一定の合意には至っていない。HAE は適切な予防により母児共に安全な管理が期待されるため、今後更なる症例の蓄積が望まれる。

P-55-12 汎血球減少を契機に発見された急性骨髄性白血病合併妊娠の1例

岐阜県立多治見病院

松川 哲

【緒言】急性白血病が妊娠中に発症する頻度は約 10 万妊娠に一人と極めて稀である。今回我々は、自覚症状なく妊婦健診における定期的な血液検査で偶発的に白血病が発見された 1 例を経験したので報告する。【症例】28 歳, 2 妊 1 産, 帝王切開既往あり。妊娠 26 週の検診で WBC1500/ μ l, Hb7.4g/dl, Plt8.9 万/ μ l と汎血球減少認めため、27 週に当院に紹介受診された。血液塗抹標本で芽球の出現を認め、骨髄検査にて急性骨髄性白血病と診断され、入院管理となった。術前ステロイドと血小板、濃厚赤血球輸血を行い、妊娠 28 週 0 日, 帝王切開施行した。術後 7 日より寛解導入療法開始し、術後 30 日骨髄穿刺で血液学的寛解確認後退院。現在 2 コース目の地固め療法中である。児は出生体重 1128g で NICU 入院となり、生後 70 日に明らかな合併症なく退院した。【結論】白血病では早期診断、早期治療開始が重要であるが、妊娠中に発症した場合、その発症時期により妊娠を継続しながらの化学療法、または速やかな分娩後の化学療法との選択に希な疾患であり難渋する。妊婦健診の血液検査では白血球数や血小板数にも注意し、必要に応じ検査値の経過観察や塗抹検査など字を实地することが白血病などの血液疾患の早期発見につながる可能性がある。

P-55-13 修正型電気けいれん療法を施行した重症うつ病合併妊婦の周産期管理経験

北里大

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【緒言】修正型電気けいれん療法 (mECT) は薬物療法の効果が乏しい精神疾患に対し有効な治療法だが妊婦への治療報告は少ない。妊娠中後期に mECT を施行した重症うつ病合併妊娠の一例を報告する。【症例】30 歳, 1 妊 0 産。自然妊娠にて妊娠成立し、妊娠初期に情緒不安定、不眠、希死念慮が出現し不安障害と診断された。オランザピンとロラゼパムの内服では症状改善せず、妊娠 30 週には自殺企図が出現し重症うつ病の診断で精神科に入院した。薬剤をデュロキセチンとベリデンに変更したが改善なく、他害行為を認めた。関連診療科と協議し、プロポフォールによる麻酔下で mECT を施行し、処置後の血圧上昇に備えて降圧薬を準備した。また、処置前後には胎児心拍数陣痛図 (CTG) を装着し集中的な胎児監視を行った。妊娠 32 週以降、合計 7 回 mECT を施行した。処置後の CTG では、子宮収縮増強や胎児頻脈、基線再変動の減少を認めたが、数時間で自然回復した。mECT にて精神症状は著明に改善し、妊娠 37 週 0 日に誘発麻酔分娩で 2290g の女児を出産した。Apgar score は 1 分値 3 点, 5 分値 6 点, 臍動脈血 pH 7.24 だったが、一過性多呼吸にて NICU 管理を要し日齢 20 に軽快退院した。母は産後 7 日目より mECT を 5 回施行し、産後 31 日目に退院した。【結語】mECT は母の精神症状改善に有効だった。既報では、妊娠中後期の mECT は、子宮収縮増強や早産などの有害事象や、一過性徐脈の出現や基線細変動消失といった CTG 変化も散見される。我々は、mECT 前後の胎児監視で常に急速速娩に備えたが、幸い児への有害事象は認めず良好な周産期予後を与えることが出来た。

P-55-14 遺伝性QT延長症候群を合併する若年女性に対して遺伝カウンセリングを行った2例

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QT延長症候群 (long QT Syndrome : LQTS) は, torsade de pointes (TdP) と呼ばれる重症心室性不整脈により失神や突然死を来しうる遺伝性疾患である。LQTSは一部の疾患を除き常染色体優性遺伝疾患であり, 遺伝子型により増悪因子が異なり, 治療方針も異なる。妊娠や分娩といったストレスが致死性不整脈の誘因とされ, 児が発症した場合は子宮内胎児死亡や乳幼児死亡の原因となる。今回, 妊娠可能年齢のLQTS患者2例に対し遺伝カウンセリングを実施した。【症例1】21歳時に意識消失し, 循環器内科を受診した。家族歴からLQTSが疑われ遺伝カウンセリング, 遺伝学的検査を行い KCNH2 遺伝子変異を認めLQT1と診断した。内服治療を開始し経過観察としていたが26歳時に結婚を機に挙児希望あり, 妊娠に備え皮下植え込み型除細動器を留置した。【症例2】7歳時にプールで失神し心電図からQT延長を指摘, 以後無治療経過観察となっていた。38歳時に自然妊娠し, 当院受診となった。妊娠25週0日に遺伝カウンセリング, 遺伝学的検査を実施し KCNQ1 遺伝子変異を認めたためLQT1と診断した。 β 遮断薬内服を行いながら37週1日に帝王切開術で児を娩出した。児の先天性LQTスコアは家族歴のみの1点であったため, 児は臨床症状があれば遺伝学的検査を行う方針となった。妊娠可能年齢のLQTS患者においては, 母体死亡もしくは重度の有害事象が起こりえるため, 循環器内科・産婦人科により妊娠前に情報提供を行うことが望ましい。

P-56-1 産婦人科領域における不定愁訴の自律神経測定機器を用いた客観的評価と, 精油を用いたアロマセラピーによる不定愁訴改善効果についての検証

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【目的】不定愁訴を有する患者及びボランティアにおいて, アンケートを含む主観的及び自律神経活動評価を行いアロマセラピーが有効か検証する。【方法】同意をえて, 12種類のアロマオイル(以下精油)から1種類選んでいただき, 専用のディフューザーを用い朝, 晩30分間のアロマセラピーを行った。そして介入前, 4, 8, 12週間後に以下の計測を行った。SML, SDS及びQIDS-R, VASによるアンケート, 自律神経活動評価を行った。自律神経活動評価はハートリズムスキャナー(米国Bio-com社)を用い, 静かな個室で安静後に, 指先にモニターをつけ測定した。この機器により, 心拍変動(heart rate variability)の自律神経バランスダイアグラムの測定を行った。【成績】有症状ボランティア9例, 悪性腫瘍8例, 更年期障害, 産褥, 良性腫瘍が各2例の23例で検討した。平均年齢46.3歳。選択した精油は, オレンジスイート12例, レモンマートル4例, ベルガモット2例, ひばり2例, その他3例。精油吸入12週間後の結果は吸入前と比べ, (1)疲労・肩こり・不安・イライラのVASを改善した。(2)SMIは, 平均36から26.4点に有意に減少した。(3)SDS値は, 平均41から36.1点と有意に低下した。(4)QIDS-R値は, 平均5.6から3.2点と有意に低下した。(5)自律神経バランスダイアグラムによる評価で, 「最適バランス」ないし「リラクゼーション反応」を示したのは, 16例中10例(62.5%)であった。(7例は開始前から最適のため除外)中止や有害事象は認めなかった。【結論】アロマセラピー介入による研究を安全に行うことができた。いずれの評価においても改善が見られた。今後症例を増やし対象を絞って検討する予定である。

P-56-2 酸化バランススコアと更年期症状に関する検討

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【目的】体内の酸化ストレス状態を評価する指標として, 酸化促進因子と抗酸化因子のスコア化による酸化バランススコア(oxidative balance score, OBS)が用いられている。OBSと様々な疾患との関連が調査されているが, 更年期症状との関連は明らかではない。本邦の中老年女性におけるOBSを新たに作成し, 関連する更年期症状を調査した。【方法】中老年女性592名を対象とし, 更年期症状はMenopausal Health-Related Quality of Life Questionnaire, Hospital Anxiety and Depression Scaleを用いて評価した。簡易型自記式食事履歴質問票を用いて食習慣を, また生活習慣についても調査した。摂取栄養素と生活習慣における酸化促進因子(摂取エネルギー量, 脂質, 飽和脂肪酸, n-6系脂肪酸, 鉄, アルコール, 喫煙, BMI, 腹囲), 抗酸化因子(ビタミンC, E, A, n-3系脂肪酸, ゲニステイン, 運動)をスコア化し, 総OBSと更年期症状との関係について重回帰分析を用いて調査した。【成績】年齢中央値は51.0歳で, OBSを4分位群に分類するとOBSと血管運動神経症状(VMS), うつ症状, むかつき・吐き気症状, 生活満足度, 社会的健康度に有意な関係を認めた。単回帰分析で有意差を認めたVMS, うつ症状, 生活満足度, 社会的健康度に加え, 年齢, 閉経状況で調整し重回帰分析を行うと, OBSとVMS(回帰係数 $[\beta]$ 0.09, 標準誤差[SE] 0.10, p値0.031), 社会的健康度(β 0.13, SE 0.08, p値0.005)に有意な関係を認めた(寄与率0.08)。【結論】体内の酸化ストレス状態が高いとVMSの症状が強く, 社会的健康度が低いことが示された。中老年女性において体内酸化ストレス状態の緩和はVMSや社会的健康度を改善する可能性が示唆された。

P-56-3 更年期障害評価尺度 (Menopause Rating Scale : MRS) 日本語版の作成

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【目的】更年期障害女性の診療では、多彩な更年期症状を把握する上で、自記式評価票の使用が不可欠である。しかし、現在、日本国内で用いられている評価表は信頼性および妥当性の検証がされているものが無く、またほとんどが日本独自のものであるため、海外との比較が不可能である。一方、海外で使われている更年期障害尺度の一つとして Menopause Rating Scale (MRS)がある。11項目と簡便な上、点数化による比較が可能である。原版はドイツ語だが英語への翻訳後、アジア圏を含む25カ国語以上に翻訳され、更年期障害やその治療効果の評価に使用されている。そこで我々は、MRS日本語版の作成を行った。【方法】自施設の倫理審査委員会の許可を得たのち、尺度翻訳のガイドラインに従い、系統的に翻訳作業を行った。【成績】原著者からの日本語版作成許諾を得たのち、2名の日英バイリンガル翻訳者によって順翻訳を行った。順翻訳について議論し作成した暫定日本語版について、別の日英バイリンガル翻訳者による逆翻訳を行い、原著者に、翻訳結果に乖離が無いことを確認いただいた。その後、暫定日本語版について更年期障害当事者による認知デブリーフィングを行い、さらに、内容妥当性の検証として、多職種からなるエキスパートパネルによる各項目の必要性および適切性の評価を行った。I-CVI/Ave=0.85であり、パネルからのコメントを踏まえ表現を再検討し、日本語版MRSの完成となった。【結論】MRS日本語版を作成した。今後、信頼性および妥当性の検証をすすめ、日本の更年期医療における適用を目指す。

21日
日本語ポスター

P-56-4 遺伝性乳癌卵巣癌と診断された女性においてリスク低減卵管卵巣摘出術後の更年期症状と治療と課題

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【目的】遺伝性乳癌卵巣癌においてリスク低減卵管卵巣摘出術 (RRSO) は卵巣癌リスクを軽減する有効な予防法である。しかし閉経前のRRSOは医原性閉経から更年期障害を惹起する。RRSO例は発端が乳癌の発症であることが多く、ホルモン補充療法 (HRT) は禁忌となる。RRSO後の更年期症状とHRTに関する報告は稀であり、RRSO後の更年期症状とその治療を明らかにすることを目的とした。【方法】2008年4月~2023年3月に当院でRRSOを施行し閉経前であった28例につき診療録より臨床情報を後方視的に抽出した。【成績】RRSO時の年齢中央値は47歳 (35.50歳) であり、乳癌既往 (A群) が20例、未発症 (B群) は8例であった。術式はRRSOが10例、腹腔鏡下又は開腹下单純子宮摘出術+RRSOが18例であった。観察期間中央値は28か月 (6117か月)。更年期症状 (ほてり, のぼせ) は12例 (A群9例/B群3例) で認め、発症時期中央値はRRSO後5か月 (1~10か月) であった。1例経過観察, 9例漢方療法, B群3例でHRTを施行した。1例は漢方無効でありHRTへ移行した。HRT施行期間中央値33か月 (18~55か月)。使用薬剤はE2経皮2例, 1例E2経皮+天然型プロゲステロンであった。HRTは3例全例で症状改善した。観察期間中の有害事象は体重増加1例 (Gradel) であり、乳癌の新規発症は認めなかった。漢方療法では症状改善は5例 (44%) に留まり、脂質異常症をA群で6例認めた。【結論】RRSO後の更年期治療は乳癌既往では選択肢が非ホルモン製剤であり、治療効果の観点から課題が存在することが示された。

P-56-5 ホルモン補充療法は更年期手指関節症における手の痛みと上肢機能障害を改善する一後ろ向き症例対象研究一

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【目的】更年期に起こる手指の痛みは、ADL (activities of daily living) の低下と直結するため重大な問題である。ホルモン補充療法 (Hormone Replacement Therapy : HRT) は、筋肉痛や関節痛に有効と報告されているが、更年期手指関節症による手指の疼痛や疼痛による上肢の機能障害に対する治療効果は不明である。【方法】2019年4月から2022年3月までに手指関節痛を主訴とする更年期手指関節症に対して、治療導入した81例 (年齢中央値52歳) を後ろ向きに検討した。対象はHRT群68例、対症療法群 (漢方薬やサプリメント) 13例であり、いずれも鎮痛薬の併用はなかった。検討項目は年齢、閉経後患者割合、簡略更年期指数 (Simplified Menopausal Index : SMI)、うつ病簡易指標 (Self-Rating Questionnaire for Depression : SRQ-D)、罹病期間、疼痛の程度 (Visual analog scale : VAS)、上肢機能評価 (Disability of the arm, shoulder and hand : DASH) とした。VASとDASHは、治療前と治療後3か月で測定し、変化量をそれぞれ Δ VAS, Δ DASHとして算出した。治療法 (HRT/対症療法) と時期 (治療前/後) の二要因における反復測定分散分析を行い、交互作用を認めた項目については、その変化量について二群間比較 (t検定) を行った。【成績】治療前の患者背景に有意差はなく、反復測定分散分析でVAS, DASHにおいて交互作用を認めた (VAS (F=4.79, p=0.032), DASH (F=4.06, p=0.048))。 Δ VAS (HRT群 27.8±25.9, 対症療法群 10.3±25.8 (p=0.034)), Δ DASH (HRT群 35.0±39.5, 対症療法群 7.6±23.5 (p=0.048)) と、治療前後の差はいずれもHRT群で有意に大きかった。【結論】HRTは更年期手指関節症による手指疼痛と上肢機能障害を改善することが示唆された。

P-56-6 骨盤臓器脱における腹腔鏡下円靭帯腔固定術 (Kakinuma 法) と腹腔鏡下仙骨腔固定術 (Shull 法) の中期成績の後方視的比較検討

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【目的】骨盤臓器脱 (POP) における腹腔鏡下仙骨腔固定術 (LSC) が保険収載され、新たなアプローチとして普及し、当院でも施行してきた。しかし、腹腔内の高度な癒着が予想される症例や、メッシュ特有の合併症であるびらんや感染を起こしうるリスクの高い易感染性患者など、LSC を選択しにくい症例では、患者自身の組織を用いた修復 (NTR) を選択する機会も少なくない。NTR の一つとして腹腔鏡下仙骨腔固定術 (Shull 法) を導入したが、重度の骨盤臓器脱では有効な修復が行えないことがある。Shull 法の問題を解決する方法の一つとして、仙骨子宮靭帯よりもさらに解剖学的に高位にあり、組織学的に強靭な円靭帯に陰断端を固定する術式、Kakinuma 法を考案した。本研究の目的は、従来の NTR 法である Shull 法と、新たな NTR 法である Kakinuma method を後方視的に臨床的比較検討することである。【方法】2017年1月から2022年3月までに、POP に対して術後1年以上の経過を観察し得た症例のうち、Shull 法 40 例 (Shull 群)、Kakinuma 法は 38 例 (Kakinuma 群) について、後方視的に検討を行った。【成績】Shull 群の平均手術時間は 140.5 ± 31.3 分、平均出血量は 91.3 ± 95.0 ml、Kakinuma 群はそれぞれ 114.3 ± 21.9 分、 26.5 ± 39.7 ml で、Kakinuma 群では、Shull 群に比べて有意に手術時間は短く ($P < 0.001$)、また、出血量も少なかった ($P = 0.003$)。再発は Shull 群で 6 例 (15.0%) に、Kakinuma 群では 2 例 (5.3%) 認め、Kakinuma 群では、Shull 群に比べて有意に再発は少なかった ($P = 0.015$)。【結論】POP における Kakinuma methods は、POP における新たな NTR の術式になりうる事が示唆された。

P-56-7 当院で手術を施行した骨盤臓器脱 228 例の臨床的検討

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【目的】骨盤臓器脱に対する腔式子宮全摘出術+前後陰壁・会陰形成術 (Native Tissue Repair, NTR) の術後再発割合は約 20% であると報告されている。当院で NTR を施行した骨盤臓器脱症例の術後成績を検討した。【方法】2014年3月から2023年3月までに当院で NTR を施行した骨盤臓器脱 228 例の患者背景と術中・術後経過を後方視的に検討した。【成績】患者の年齢中央値は 75 歳、分娩回数中央値は 2 回、平均 BMI は 24.1、閉経割合は 98%、POP-Q stage は III-IV が 81.1%、116 例 (50.9%) に術前治療歴を認めた。入院日数中央値は 6 日であった。術中・術後合併症として、膀胱直腸損傷 4 例、陰外陰部血腫 4 例、排尿障害 21 例、せん妄 7 例、肺血栓塞栓症 2 例を認めた。術後フォローアップ期間 0.3-96.5 か月 (中央値 8.0 か月) における再発は 43 例 (18.9%)、このうち POP-Q stage I 以下の無症状再発は 28 例 (12.3%)、有症状再発は 15 例 (6.6%) であり、Kaplan-Meier 法による 1 年無症状・有症状再発割合は 14.4%/7.6%、2 年無症状・有症状再発割合は 18.9%/10.5% であった。3 例 (1.3%) に再手術を行い、Kaplan-Meier 法による再手術割合は 1 年 0%、2 年 3.9% であった。【結論】骨盤臓器脱に対する NTR の当院での治療成績を報告した。膈上部の吊り上げや固定を伴わない術式であっても、再発や再手術の割合に関しては過去の報告とほぼ同様であった。しかし、一定の割合で有症状再発を認め、少数ながら再手術に至った症例を経験した。再発例、再手術例の検討では一定の傾向を認めなかったが、今後は膈上部の吊り上げを伴う術式の選択的導入が必要であると考えられた。

P-56-8 当院におけるロボット支援下腹腔鏡下仙骨腔固定術の導入経験

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【目的】骨盤臓器脱に対し当院では比較的若年者を対象として腹腔鏡下仙骨腔固定術 (LSC) を施行してきたがその治療効果の高さと安全性から高齢者にも適応を拡大しつつあった。最近当院でロボット支援下腹腔鏡下仙骨腔固定術 (RSC) を導入したので報告する。【方法】当院で 2021年12月から2023年2月までに POP-Q stage II-IV の骨盤臓器脱患者 12 名に対し RSC を施行した。コントロールは RSC 導入以前の同一術者の LSC 12 例とした。全例ダブルメッシュ法を行った。【成績】RSC 症例の患者年齢・BMI・手術時間・コンソール時間・出血量の平均値±標準誤差はそれぞれ 71.7 ± 1.6 歳、 21.6 ± 1.1 、 328.3 ± 11.8 分、 267.4 ± 11.8 分および 11.7 ± 5.3 g であった。LSC 症例ではそれぞれ 64.3 ± 1.5 歳、 25.6 ± 1.4 、 272.3 ± 9.2 分および $10. \pm 5.5$ g であった。年齢は RSC 症例で有意に高く、BMI は有意に低く手術時間は有意に長かった。出血量と分娩回数は両群間に有意差を認めず、重篤な術後合併症は発生せず、術後尿失禁は LSC の 1 例のみであった。RSC は LSC と比較して手術時間が長かったが、ラーニングカーブの早さにより短縮傾向にある。また LSC では難易度が高いと感じていた後壁メッシュの縫合固定は da Vinci 鉗子の多関節機能と骨盤深部での安定した 3D 拡大視野により妥協のないメッシュの縫合固定が可能になった。【結論】当院の RSC は高齢者にも施行しているが、重篤な術中合併症や再手術が必要な術後後遺症を認めず安全に施行できる術式であると考えられた。今後は手術時間短縮を目指すとともに当該術式の長期予後も含め検討を続けていく。

P-56-9 ロボット仙骨腔固定術 (RSC) への ALLY ポジショニングシステム導入後の成績

川崎医大

岡本 華, 太田啓明, 森本裕美子, 河村省吾, 齋藤 渉, 松本 良, 松本桂子, 杉原弥香, 塩田 充, 下屋浩一郎

【目的】ロボット手術では手振れが補正され、拡大視野で正確な手術操作可能なことが利点の一つであるが、RSCでは陸前後の剝離操作やメッシュ固定の際に第二助手が仙骨腔固定用チップ(Hoyte サクロチップ®)を保持するためブレが生じていた。当院ではブレ解消のため ALLY ポジショニングシステムを導入し、導入前後での成績を後方視的に検討した。【方法】2023年1月から9月までの期間に当院で行ったRSCを対象とし、ALLY ポジショニングシステム使用有群および使用無群を診療録から抽出した。使用無群では従来通り第二助手が仙骨腔固定用チップを保持し、使用有群では手術台に固定された ALLY ポジショニングシステムに仙骨腔固定用チップを取り付け、位置が決まったところで保持固定させた。【成績】対象期間内のRSC症例は26例であり、ALLY ポジショニングシステム使用有群7例、使用無群19例であった。両群間で手術時間や出血量、POP-Qスコアの変化率に有意な差を認めなかった。【結論】両群間において手術合併症、治療効果に有意な差は認めなかった。しかし ALLY ポジショニングシステムの使用はブレのない術野継続が可能であり、これは術者のストレスの軽減につながった。また、第二助手にとっても手術モニターを正面に見ることができない体勢で長時間仙骨腔固定用チップを保持することは身体的に厳しかったが、ALLY ポジショニングシステムが保持することで改善された。2024年4月からはいよいよ医師の働き方についても新制度が施行される。人員削減にも有用である可能性がある。

日本語ポスター
21日(日)

P-56-10 膀胱陰瘻は腹腔鏡下手術で安全かつ確実に治せる

亀田総合病院ウロギネ・女性排尿機能センター

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【緒言】膀胱陰瘻は、常時、尿失禁をきたし著しくQOLを阻害する疾患であり、婦人科手術に起因することが多い。膀胱陰瘻に対して従来、腔式手術が行われてきたが近年腹腔鏡下手術の有用性が報告されており、当院も腹腔鏡下に膀胱陰瘻閉鎖術を行なっている。今回、術式のテクニックを症例とともに報告する。【術式】まず瘻孔を同定する。瘻孔へのアプローチには2つの方法がある。1つめは膀胱を切開して直接到達する方法、2つめは陰壁と膀胱の間に剝離し到達する方法である。2つめでは放射線治療後や瘻孔のサイズが大きい難治性と思われる症例において、再発を防ぐために膀胱と陰壁の間に組織(ex. 腹膜フラップ)を介在させることが可能である。瘻孔周囲の瘢痕を切除し膀胱と陰壁間の剝離を行う。陰壁と膀胱を3-0吸収糸でそれぞれ縫合する。膀胱壁をテンションフリーで層を合わせて縫合することが再発予防のため最も重要である。【結果】当院で施行した腹腔鏡下膀胱陰瘻閉鎖術の5症例は、術後再発なく経過している。【考察】腹腔鏡下膀胱陰瘻閉鎖術では、腔式と比較して瘻孔の状態を詳細に観察可能であり瘻孔周囲の瘢痕組織の適切な切除、膀胱と陰壁の間の剝離、それらの確実な縫合が可能であった。当院では、瘻孔のサイズが小さい症例では瘻孔に直接アプローチする方法、放射線治療後や瘻孔のサイズが大きい難治性と思われる症例では、膀胱と陰壁の剝離により瘻孔にアプローチする方法で行なっている。難治性膀胱陰瘻は膀胱と陰壁の間に組織を介在させることで再発を減らす可能性がある。【結論】膀胱陰瘻に対して、婦人科医も腹腔鏡手術の技術が十分にあれば安全かつ確実に治療することができる。

P-56-11 当院における VANH (vaginally assisted NOTES hysterectomy) の初期経験

愛友会上尾中央総合病院

片倉雅文, 森つばさ, 井上亜結実, 波平制士, 中熊正仁, 江澤正浩

【緒言】Vaginal Natural Orifice Transluminal Endoscopic Surgery (vNOTES) は近年本邦でも普及が進んでいる。当施設での骨盤臓器脱 (Pelvic organ prolapse: POP) に対する Native tissue repair (NTR) 術式としての vNOTES を考察する。【症例】【症例1】70歳, 3産。前医で左卵巣腫瘍を指摘され、CA19-9が高値であり、精査加療目的で受診した。9cm大の卵巣腫瘍と子宮脱 StageIII を認め、VANH, BSO, 全腔閉鎖、後陰会陰形成術を施行した。術後病理は子宮・付属器ともに悪性所見を認めなかった。【症例2】47歳, 2産。過多月経、臓器下垂感を主訴に受診した。3cm径の子宮粘膜下筋腫と子宮頸管延長症の診断で、手術加療の方針とした。術中所見で子宮頸部延長のみでなく膀胱瘤も認め、生殖裂孔の開大も認めたため、VANHに加え、前後陰壁会陰形成術を追加した。【考察】POP症例と非POP症例で困難となる場面が異なり、利点も異なると考えている。POPに対する手術として本邦では仙骨腔固定術が広く行われているが、年齢、既往などによりメッシュ留置を躊躇する症例や卵巣腫瘍を合併している症例などに対し、vNOTESは治療選択肢として有用と思われる。vNOTESに適した腔の広い症例は、麻酔導入後にPOPがより重度であると診断されることも多く、腹腔鏡の手技に加え、NTR術式にも習熟しておくことが肝要と思われる。【結論】vNOTES施行にあたっては腹腔鏡とともに腔式手術の手技の獲得が重要であると考えられた。

P-56-12 腹腔鏡下仙骨腔固定術後に増殖性膀胱炎を呈した1例

公立宍粟総合病院

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【目的】当院では2018年から骨盤臓器脱 (pelvic organ prolapse; POP) に対して腹腔鏡下仙骨腔固定術 (laparoscopic sacrocolpopexy; LSC) を施行している。今回、LSC術後9日目に増殖性膀胱炎を呈した1例を経験したので症例について報告する。【症例】症例は73歳、3妊3産。POP stage2に対してLSCを施行した。術後9日目から残尿感、排尿時痛、頻尿の症状が出現しエブランチル内服で経過観察していたが改善せず、術後20日目に経腹超音波検査で右水腎症および膀胱内に腫瘤様病変を認め泌尿器科に紹介受診。膀胱鏡検査で尿道から膀胱三角までが著明に浮腫状変化を認め増殖性膀胱炎と診断された。抗プラスミン剤の内服を開始し術後34日後には症状が軽快。膀胱粘膜は正常化し水腎症も軽快した。【考察】LSCの術後合併症としてメッシュ関連合併症、新規尿失禁 (de novo stress urinary incontinence; de novo SUI) などの排尿障害、腸閉塞などの報告はあるが、増殖性膀胱炎の報告はこれまでに無い。増殖性膀胱炎は肉眼的血尿、排尿障害を契機に発見されることが多く、発症原因として慢性炎症や刺激、遺伝や免疫の関連が示唆され、抗菌薬や抗炎症剤による保存的治療が第一選択となることが多いが、悪性腫瘍の併存も報告されており、慎重な経過観察が必要とされている。本症例は、関節リウマチの既往があり、自己免疫性疾患に加え術中の物理的刺激により増殖性膀胱炎を発症したことが考えられる。【結語】術後合併症として増殖性膀胱炎にも留意するとともに、自己免疫性疾患などの慢性炎症を基礎疾患にもつ症例では壁瘻と膀胱の剝離操作の工夫が必要と考えられる。

P-57-1 根治的放射線治療を選択した高齢子宮頸癌患者75例の検討

東京都立駒込病院

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【目的】高齢者は標準治療を確立する臨床試験の対象外であることが多く、診療方針に関する明確な基準が無い。高齢子宮頸癌患者に対する根治的放射線治療は今後も増加することが予想され、高齢者特有の有害事象に関する情報蓄積および高齢者機能評価を含む診療指針の確立が望まれる。【方法】2011年1月1日から2017年12月31日に、当院で全骨盤照射50Gy+腔内照射24Gyを標準とし根治的放射線治療を開始した65歳以上の高齢子宮頸癌患者75例の診療録から急性期および晩期有害事象を後方視的に検討した。高齢者機能評価をGeriatric8 (G8)で行った。【成績】年齢の中央値は73歳 (87-66歳) (85歳以上: 3例, 75-84歳: 24例, 65-74歳: 48例)。G8スコアの中央値は12.5 (8.5-13.5)。扁平上皮病変67例、腺上皮系病変7例、未分化癌1例。進行期 (日産婦2018) はI期11例、II期27例、III期32例、IV期5例。38例に同時化学放射線療法が選択された。CTCAE v5.0でGrade3以上の、急性期有害事象は23例 (30.7%) (骨髄抑制23例、胃腸障害2例)、晩期有害事象は6例 (8%) (胃腸障害2例、尿路障害1例、リンパ浮腫1例、骨盤骨折2例)。他Grade2以上の骨盤骨折が9例 (12%)。52例 (69.3%) が根治的放射線治療を完遂。同時化学放射線療法群では18例 (47.3%) で化学療法の減量・中止を要した。G8スコアで治療の完遂率や有害事象の発生率に有意な傾向は認めなかった。【結論】過去の若年者を含む報告と比較し、今回の検討では高齢者において急性期、晩期の有害事象共に発生頻度の増加を認めなかった。一方で健康成人にとっては軽症の有害事象であっても、高齢者においてはQOLの著しい低下につながる可能性があることに留意が必要である。

P-57-2 子宮頸癌 IVB 期の治療方針

四国がんセンター

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【目的】子宮頸癌 IVB 期症例は転移部位や症状が多様で、治療方針に難渋することが多い。初回治療として化学療法が推奨されるが、根治が難しい疾患である。より良い治療方針を提示するために、当院症例における治療方針別の治療成績を検討した。【方法】2011年1月から2020年12月の期間に、当院で治療を開始した子宮頸癌 IVB 期 (日産婦2020, FIGO 2018) 28例を後方視的に検討した。局所に対する手術 (OP) や放射線療法 (RT) を施行した症例を主治療群として、全身化学療法のみ施行した症例 (化療群) と予後を比較した。予後の解析は、Kaplan-Meier 曲線および log-rank 検定を用いた。【成績】初回治療は、局所症状を含む全身状態を考慮して、主治医選択による治療方針がとられていた。化療群9例、主治療群19 (RT: 15, OP: 4) 例であった。主治療群のうち14例で全身化学療法を施行した。全体の無増悪生存期間および全生存期間の中央値は8.6か月、22.5か月、2年無増悪生存率 (PFS)、3年全生存率 (OS)、5年 OS は 25.0%、35.7%、30.6% であった。化療群の2年 PFS、3年 OS は 0%、11.1% に対して、主治療群の2年 PFS、3年 OS は 36.8%、47.4% であり、有意に予後良好であった ($p=0.0078, 0.0006$)。【結論】全身状態などから忍容性があると判断できる子宮頸癌 IVB 期での初回治療では、放射線療法や手術療法を検討しても良い可能性がある。

P-57-3 当科における進行・再発子宮頸癌に対するペムプロリズマブの使用経験

小牧市民病院

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【目的】KEYNOTE-826 試験の結果を踏まえ 2022 年 9 月に抗 PD-1 抗体であるペムプロリズマブ (Pem) と化学療法±ベバシズマブ (Bev) の併用療法が「進行または再発子宮頸癌」に対し保険承認された。予後不良な進行・再発子宮頸癌に対する治療効果が期待されており、当科での使用経験を報告する。【方法】当科において 2022 年 10 月から 2023 年 2 月まで進行・再発子宮頸癌に対して Pem 併用化学療法を施行した症例について有効性ならびに安全性を後方視的に検討した。【成績】上記期間中に 6 症例に対し Pem 併用化学療法を施行した。年齢の中央値は 58.5 歳 (33-72) で組織型は扁平上皮癌が 5 例、胃型腺癌が 1 例であった。進行期 (日産婦 2020) は IIB2 期 2 例, IIIc1 期 2 例, IVB 期 2 例であった。進行例 1 例, 再発例 5 例であった。コンプライメンタリー診断としての PD-L1 検査は 5 例に施行し, 3 例で CPS>1, 2 例は評価不能であった。G3 以上の有害事象は好中球減少が 4 例, 発熱性好中球減少症が 1 例, 血小板減少が 2 例, 腸炎が 2 例, 重度の皮膚障害が 1 例であった。1 例は腸炎のため 1 サイクルのみ Pem 休薬を要し 1 例が Pem により irAE のため治療中止となった。残り 5 例における最良効果判定は CR3 例, PR2 例で, 5 例すべて Pem+Bev による維持療法を施行中である。【結論】当院において進行・再発子宮頸癌に対する Pem 併用化学療法は有効であった。免疫チェックポイント阻害剤である Pem の投与により従来の化学療法とは異なる副作用マネジメントが必要であり, irAE を早期に発見し他領域と連携し適切に管理する必要があった。

P-57-4 子宮頸癌に対してセミプリマブを投与した 7 例の経験

千葉大附属病院

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【目的】2022 年 12 月にがん化学療法後に増悪した進行又は再発の子宮頸癌に対し PD-1 阻害薬のセミプリマブが国内製造販売承認された。当科におけるセミプリマブの初期使用経験を報告する。【方法】2023 年 4 月から 2023 年 8 月に当院でセミプリマブを 1 サイクル以上投与した 7 例につき, 効果と副作用を後方視的に検討した。【成績】年齢は 31-68 歳 (中央値 62 歳), 進行期は, 1B3 期 1 例, 3C 期 3 例, 4B 期 3 例, 組織型は扁平上皮癌 4 例, 腺癌 1 例, 腺扁平上皮癌 1 例, 小細胞癌 1 例であった。子宮摘出後は 4 例, 放射線治療後は 4 例 (重複あり) で, マイクロサテライト不安定性 (MSI) 検査は全例陰性であった。全例が TC/TP+Bevacizumab 療法の既往があり, 4 例が TC/TP+Bevacizumab 療法中に増悪し中止され, 3 例が TC/TP+Bevacizumab 療法終了後 6 か月以内に再発していた。既往レジメン数は 1 レジメン 2 例, 2 レジメン 4 例, 3 レジメン 1 例であった (同時化学放射線治療を除く)。セミプリマブ投与サイクル数は, 1 サイクルで終了が 3 例, 3 サイクルで終了が 4 例であった。1 サイクルで終了した 3 例のうち 2 例は病状進行, 1 例は発熱の副作用による中止であった。3 サイクルで終了した 4 例はいずれも病状進行のための中止であった。投与延期または不可となる Grade3 以上の副作用は, 上記の発熱の 1 件だけであった。セミプリマブによると判断される Grade1-2 の副作用の出現はなかった。【結論】本検討ではセミプリマブの奏功例はなく, 既報の 16.4% より低い成績であった。本研究の対象集団は本剤の承認直後であったため, より進行例が多かった可能性がある。副作用は 1 例のみで許容範囲と考えられた。さらなる症例の蓄積が望まれる。

P-57-5 当科における進行・再発子宮頸癌に対するペムプロリズマブ・パクリタキセル・カルボプラチン・ベバシズマブ併用療法とセミプリマブ療法の使用経験

関西労災病院

澤本康平, 堀内僚介, 浅井智奈美, 大久保理恵子, 下地香乃子, 尾上昌世, 吉岡恵美, 後藤摩耶子, 高田友美, 堀 謙輔, 伊藤公彦

【目的】進行・再発子宮頸癌に対するペムプロリズマブ・パクリタキセル・カルボプラチン・ベバシズマブ併用療法 (PemTCBev 療法) が 2022 年 9 月に, セミプリマブ療法 (Cemi 療法) が 2023 年 3 月に本邦で承認された。当科での両療法の使用経験を報告する。【方法】2022 年 12 月から 2023 年 7 月までに当科で治療を開始した症例について有効性と安全性を後方視的に検討した。【成績】PemTCBev 療法は 13 例に実施され, 組織型は, 扁平上皮癌 11 例, 粘液性癌 1 例, 明細胞癌 1 例であった。治療歴のない進行例が 4 例, 再発例は 9 例で前治療レジメン数の中央値は 1 (範囲: 0-3) であった。実施サイクル数の中央値は 6 サイクル (範囲: 3-15) で, PFS の中央値は 6.0+か月 (範囲: 2.9+) であった。効果判定を実施した 12 例のうち, CR は 5 例, PR は 7 例で奏効率は 100% であった。Grade3 以上の有害事象は白血球減少 5 例, 好中球減少 10 例, 貧血 4 例, 手足症候群 1 例, ALT 上昇 1 例, 下血 1 例, 胆管炎・膵炎 1 例であった。Cemi 療法は 2 例に実施され, どちらも腺癌であった。治療サイクル数の中央値は 3.5 (範囲: 3-4) で, PFS の中央値は 2.6+か月 (範囲: 1.7-3.5+) であった。治療効果は SD1 例, PD1 例であった。有害事象は Grade3 以上は認めず, Grade1 の甲状腺機能亢進症のみであった。【結論】PemTCBev 療法は高い奏効率を得られたが有害事象も多彩であり有害事象の出現に注意しながら治療を行う必要がある。Cemi 療法については更なる症例の蓄積が必要である。

P-57-6 進行または再発子宮頸癌に対する PTX+CBDCA+Pembro±Bev 療法の使用経験

九州労災病院

鏡 誠治, 西村和朗, 梶尾 悠, 和田 環, 土岐尚之

【目的】2022年9月に保険適応となった化学療法治療歴のない進行または再発子宮頸癌に対するペンブロリズマブ (Pembro) +パクリタキセル (PTX)+カルボプラチン (CBDCA) ±ペバシズマブ (Bev) 療法について、当院での使用経験を報告する。
 【方法】2022年10月から2023年9月までに当院で使用した計3例について検討した。【成績】【症例1】42歳, IIB期, 腺癌, 広汎子宮全摘出術後, 化学放射線療法 (CCRT) 後の照射野内再発。grade3の肝機能障害, grade2の甲状腺機能低下症が出現。2コース後に腫瘍マーカー正常化, 6コース後PET-CT 検査でPRと判断, 維持療法に移行したが, 3コース後のPET-CTで残存病変のFDG集積と腫瘍マーカーの軽度上昇あり, 当初のレジメンに戻して3コース施行中である。【症例2】56歳, IIIB期, 扁平上皮癌で, CCRT後の照射野内再発。grade1の皮疹が出現。PRで6コース後, 維持療法2コース施行中である。【症例3】53歳, IVB期 (多発肺転移), 腺癌の初回治療。grade2の肝機能障害が出現。PRで現在4コースまで実施している。腸管浸潤が疑われた1例以外はBevを併用した。治療効果は全てPRであった。【結論】再発症例は放射線照射野内再発で, 1例は腺癌であったが, 奏効した。6コース終了時点でPRの時, どのような場合にPTX, CBDCAを6コースを超えて続けるべきなのか, 維持療法になった後に再燃した時の方針はどうか, 高齢者の第1選択にすべきかなど, 実臨床では意見が分かれるところである。今後の症例の蓄積を待つ必要がある。

P-57-7 子宮頸癌に対し免疫チェックポイント阻害薬を使用した症例の後方視的検討

佐賀大

瓜生泰恵, 吉武薫子, 池田正純, 大隈良一, 栗原麻希子, 徳永真梨子, 福田亜紗子, 梅崎 靖, 奥川 馨, 横山正俊

【目的】2022年9月にペンブロリズマブが進行・再発子宮頸癌に対し適応となり, 2023年3月にセミプリマブが進行・再発子宮頸癌に対し保険収載された。今後, 子宮頸癌に対する免疫チェックポイント阻害剤の治療効果が期待されるが, 本邦での使用経験はいまだ少ないのが現状である。今回, 当院でペンブロリズマブもしくはセミプリマブを使用した子宮頸癌の治療成績について後方視的に検討した。【方法】2022年9月26日から2023年7月31日までにペンブロリズマブもしくはセミプリマブを使用した症例を抽出し, 有効性ならびに安全性を後方視的に検討した。【成績】進行子宮頸癌4例, 再発子宮頸癌9例の合計13例が該当した。ペンブロリズマブのみ使用は9例, セミプリマブのみ使用は1例, ペンブロリズマブとセミプリマブどちらも使用したのは3例であった。進行期はII期が4例, III期が5例, IV期が4例であった。組織型は扁平上皮癌6例, 腺扁平上皮癌2例, 腺癌5例であった。最良効果判定はCRが3例, PRが2例, PDが6例, 不明が2例であった。3例がペンブロリズマブ維持療法を行い, 1例は2コース後にPDとなったが, 2例は再発なく経過している。最長投与期間はペンブロリズマブ14コースであった。有害事象として, 自己免疫性貧血が1例に認められた。【結論】子宮頸癌における免疫チェックポイント阻害剤は奏功が得られる一方, 最終レジメンとして使用される場合の治療転帰は良好ではなかった。当院における使用経験について文献的考察も含めて報告する。

P-57-8 当院におけるIVB期子宮頸癌治療の後方視的検討

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【目的】IVB期子宮頸癌の予後は不良であり, 根治を目指せる状況は限定的である。子宮頸癌治療ガイドラインではペバシズマブを併用した全身化学療法を推奨しており, oligometastasisで照射可能な症例では放射線治療を選択肢としてあげているが, その選択に明瞭な基準はない。今回の検討では当科で管理したIVB期症例を後方視的に解析し, 治療の個別化に関する知見をうることを目指した。【方法】2016年から2021年に当院で管理したIVB期頸癌を対象に, 患者背景 (年齢, 組織型, 遠隔転移部位), 治療成績 (無増悪生存期間, 全生存期間), 有害事象を後方視的に解析した。緩和管理を主目的とした症例は除外した。【成績】治療方針は婦人科医と放射線医によって合議的に決定した。肺, 肝臓, 上腹部腹膜播種を含む症例は化学療法, その他は放射線治療を選択した。治療導入が化学療法であった群 (CT群) が12例, 放射線治療の群 (RT群) が12例であった。CT群, RT群の年齢の中央値は49歳 (44-76) /58歳 (40-82), 組織型 (SCC/non-SCC) は5/7 vs 9/3であった。CT群のレジメンはTP+Bev 7例, TP+Pem 1例, その他4例, RT群の照射方法はCCRTが7例, 単独照射が5例であった。RT群の2例は鎖骨上転移, 10例がその他の遠隔転移であった。2年無再発率はCT群で0%, RT群で50%, PFS中央値は12.1m/21.4m, OS中央値は26.9m/未達であった。有害事象はCT群, RT群でプロファイルが異なったが, 治療継続に影響する事象は生じなかった。【結論】CT群に比べRT群の予後が良好であったが, 治療選択によるものか, 腫瘍の局在によるものかは不明である。症例ごとに腫瘍の局在, PS, 臓器症状などを総合的に評価し, 治療の個別化を図ることが望まれる。

P-57-9 進行・再発子宮頸癌に対するペムプロリズマブ併用療法の導入初期症例の検討

名古屋大

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【目的】進行・再発子宮頸癌に対するペムプロリズマブ併用療法の使用実態, 導入後の初期成績を後方視的に調査した。【方法】2022年10月から2023年7月までに当院でペムプロリズマブ併用療法を行った進行・再発子宮頸癌16症例を検討した。【成績】年齢の中央値は44(34-70)歳, 初発1例(6%), 初回治療後の残存1例(6%), 再発14例(88%)であった。組織型は扁平上皮癌9例(56%), 腺癌3例(19%), 小細胞癌2例(13%), 低分化癌(生検では組織型確定困難)2例(13%)であった。Combined positive score (CPS) <1が1例(6%), 1≤CPS<10が6例(38%), CPS≥10が3例(19%), 未検査が6例(38%)であった。ペバシズマブ併用ありが13例(81%), なしが3例(19%)であった。化学療法歴なしが5例(31%), ありが11例(69%)で, 化学療法歴がない症例では5例全てでPR以上であり全例投与継続中であった。ほぼCRといえる症例(画像上痕跡のみ)が2例あった。化学療法歴がある症例11例のうち, PR2例(18%), SD1例(9%), PD8例(73%)で, 投与継続中は4例(36%)であった。免疫関連有害事象は2例に認め, それぞれ腸炎G2と好酸球増加症G1であった。前者では消化器内科の指示でペムプロリズマブの投与を中止した。【結論】症例数が少なく観察期間も短い, 化学療法歴がない症例では全例PR以上と良好な治療効果が得られていた。KEYNOTE-826試験で組み入れ不可であった化学療法歴がある症例では, 奏効率18%と低値に留まった。ペムプロリズマブ併用療法の効果を得るには症例選択が重要である。

P-57-10 子宮頸癌 pT2b 症例の病理学的検討～より根治性の高い広汎子宮全摘術を目指して～

国立がん研究センター中央病院

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【目的】浸潤子宮頸癌に対する広汎子宮全摘術は, 婦人科手術で最も高難度な術式であり, 子宮支持靭帯と子宮傍組織の処理が重要であることは言うまでもない。婦人科医にとって, 子宮傍組織浸潤を来した子宮頸癌症例の実態を知ることは極めて有意義と考えられ, 手術手技の向上にも繋がる。今回, 手術療法を行い pT2b と診断された子宮頸癌症例の病理学的特徴について検討したので報告する。【方法】2015-2023年に当科で手術療法を施行し, pT2b と診断された子宮頸癌39症例を対象とし, その病理学的所見を後ろ向きに検討した。【成績】年齢中央値は49歳(27-71歳), 組織型は扁平上皮癌22例, 腺癌10例(通常型5例, 胃型粘液性癌4例, 腸型粘液性癌1例), 神経内分泌癌又は神経内分泌癌が混在する癌6例, 子宮内膜症関連類内腺癌1例であった。進行期分類(FIGO2018)は, IIB期15例, IIIC1期22例, IIIC2期2例で61.5%に領域リンパ節転移を認めた。28例(71.8%)が治療前T分類からupstagingした。腫瘍径中央値は55mm(17-108mm), 脈管侵襲は全例に認められ, 腔断端陽性例は4例であった。子宮傍組織浸潤に関しては, 深部間質浸潤から連続浸潤した症例が32例, 脈管侵襲を介して非連続的に浸潤した症例を7例認めた。大部分広汎子宮全摘術が施行されたが, 定型的な靭帯処理が困難であった症例を3例に認めた。【結論】子宮頸癌 pT2b 症例は, 高頻度で領域リンパ節転移を来し, 非連続性に子宮傍組織浸潤を来す症例も認められたことから, 改めて広汎子宮全摘術における領域リンパ節郭清の徹底と子宮支持靭帯処理の重要性が示唆された。浸潤子宮頸癌に対する広汎子宮全摘術は, 定型的処理が困難な場合を想定することも重要であり, upstagingする可能性を常に念頭に置くべきである。

P-57-11 当科における Bevacizumab 併用療法が施行された進行再発子宮頸癌 45 症例の検討

王子総合病院

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【目的】BEV 併用化学療法後の維持療法の有無で無増悪生存期間(PFS)を比較・検討すること。【方法】・臨床予後の検討・二変量:カイ二乗検定・連続変数の解析: Mann-Whitney U 検定および Spearman の相関検定・生存期間の定義観察期間: 初回治療開始日から死亡または最終生存確認日まで無増悪生存期間(PFS): 治療開始日から再発・再燃確認日まで・PFS: カプランマイヤー法で推定し, ログランク検定を行った。・統計解析には, JMP Pro, version 17.0.0 を用い, $p < 0.05$ を有意差ありとした。【成績】初回治療における PFS は BEV 維持療法あり群で未達, 維持療法なし群で 9.0 か月で有意差を認めなかった ($p=0.2428$)。再発後一次治療における PFS は BEV 維持療法あり群で 14.9 か月, 維持療法なし群で 4.8 か月で有意差を認めた ($p=0.0026$)。【結論】・初回治療において BEV 使用例に限定した BEV 維持療法の有無で PFS に有意差は認めなかったが, 維持療法なし群は 4 症例のみであり, 症例の蓄積を要する。・BEV の保険収載が 2016 年であり, 現時点では BEV 使用の有無で観察期間に有意差を認めており, 引き続きの観察を要する。

P-57-12 子宮頸部高度異型性・上皮内がんに対する円錐切除術と腹腔鏡下子宮全摘術の比較検討

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【目的】子宮頸部高度異型性・上皮内がん(以下 CIN3)は子宮頸がんの前癌病変であり、円錐切除術で進行期を診断した上で、根治術として子宮摘出が勧められている。近年では腹腔鏡下手術が主流となっており、CIN3 に対して腹腔鏡下子宮全摘術(以下 TLH)を行う症例が増加している。当院でも 2020 年から TLH の症例が増加傾向であるが、2 期的な手術ではなく、1 期的な治療を希望される場合もある。円錐切除術などの従来の手術方法と比較し、TLH の術式選択について妥当性の検討が必要と考えた。当院における 2020 年からの CIN3 に対して TLH を行った症例に対して、治療成績などを後方視的に検討したので報告する。【方法】2020 年 4 月から 2022 年 12 月までに CIN3 に対して TLH を行った 26 名を、同時期に手術加療を行った名と比較検討した。TLH 症例の内 7 名は事前に子宮頸部円錐切除術を行い断端陽性となった症例だった。3 例は断端が熱変性などで評価不能であったが、術後再発を認めなかった。2 例は術後細胞診異常(LSIL)が再発し、現在もフォローを行っている。【成績】同時期に他の手術療法を行った症例と比較し、術後再発率に差は生じなかった。術後細胞診異常再発以外に合併症は認めなかった。【結論】CIN3 に対して TLH は有用な選択肢として提示が可能と考える。しかし通常の TLH と比較してより子宮頸部断端との距離を考慮した手術手技が求められることから、手術内容の工夫が求められる。

P-58-1 転移性卵巣腫瘍に対する切除手術後の予後に関する検討

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【目的】転移性卵巣腫瘍は他領域の悪性腫瘍でありながら婦人科医が手術治療を行う珍しい病態である。今回、当院の現状を確認する目的で切除手術後の予後を検討した。【方法】2015 年 10 月～2022 年 9 月に当科で切除手術を行った転移性卵巣腫瘍を対象に診療録を後方視的に検討した。子宮や卵巣原発の症例、初回治療時に切除を行った症例は除外した。術後全生存期間の検討には Kaplan-Meier 法を用い、多変量での検討には Cox の比例ハザードモデルを使用した。【成績】対象は 61 例で、年齢の中央値は 51 (22-82) 歳であった。原発臓器は、結腸・直腸 30 例、胃 19 例、その他 12 例であった。術式は付属器摘出が 49 例、子宮摘出及び付属器摘出が 12 例であり、片側付属器の温存が 5 例あった。全集団の生存期間の中央値は 26 か月であった。手術時 50 歳未満の症例は 34 か月であり、50 歳以上は 23 か月であった。結腸・直腸原発の症例は 28 か月、胃原発は 16 か月、その他は 35 か月であった。化学療法中に切除に至った症例は 18 か月で、経過観察中に切除に至った症例は 35 か月であった。残存腫瘍のない症例は 48 か月であり、残存腫瘍があった症例は 18 か月であった。以上 4 つの因子を多変量解析で検討したところ、残存腫瘍なし (HR=0.23) と手術前化学療法なし (HR=0.41) と胃原発 (HR=2.55) が独立して予後に関連していた。【結論】本研究では切除手術後の予後は 2 年以上あり比較的長期であり、その中でも良好な予後を期待できる症例があることが示唆された。検討した因子を勘案し主治医と手術適応について相談する必要があると考えられた。

P-58-2 CA125 はプラチナ感受性再発卵巣癌における維持療法の選択に有用か?

杏林大

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【目的】プラチナ感受性再発卵巣癌の維持療法としてオラパリブまたはベバシズマブの投与が提案されるが、それぞれの適切な選択基準は得られていない。本検討ではプラチナ感受性再発卵巣癌に対するオラパリブとベバシズマブの維持療法の効果について後方視的に検討した。【方法】当院において 2015 年 1 月～2023 年 7 月の間にプラチナ感受性再発卵巣癌の維持療法として、オラパリブ (Ola) を投与した 28 例とベバシズマブ (Bev) を投与した 21 例について、年齢、Platinum-free interval (PFI)、維持療法前レジメン数、維持療法中の無増悪生存期間 (PFS) の各項目について比較検討した。【成績】年齢は両群間で差を認めなかった。PFI はオラパリブ投与群が長く ($p=0.013$)、維持療法前レジメン数はベバシズマブが多かった ($p=0.002$)。両群の PFS は中央値が両群とも 12 か月と有意差を認めなかった。維持療法の効果を予測する因子として維持療法開始直前の CA125 のカットオフ値を 18 として両群の検討を行うと、オラパリブ群では CA125 が 18 未満症例で良好な PFS が得られたが (Log Rank : $p=0.025$)、ベバシズマブ群では CA125 による PFS の差を認めなかった (Log Rank : $p=0.866$)。また、オラパリブ群とベバシズマブ群のうち、CA125 が 18 以上の症例について PFS を比較すると、有意差を認めないものの、ベバシズマブ群の PFS が長い傾向にあった [Ola vs Bev : 6 か月 vs 11 か月 (中央値)], Log Rank : $p=0.260$]。【結論】オラパリブは維持療法開始直前の CA125 が 18 未満の症例で良好な PFS を得られる一方で、ベバシズマブ維持療法は CA125 に左右されず、CA125 が 18 以上の症例ではベバシズマブによる維持療法が良い選択となる可能性が示唆された。

P-58-3 進行卵巣癌に対する Debulking surgery 時の他臓器合併切除に関する後方視的検討

愛知県がんセンター

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【目的】進行卵巣癌(卵管/腹膜癌含む)に対する初回治療では、手術療法と薬物療法を中心とした集学的治療が行われるが、手術完遂度は特に重要な予後因子である。肉眼的腫瘍の完全切除を目指した Debulking surgery (DS) を積極的に行うためには、他臓器合併切除に際しての他科連携等といった体制を整えておく必要がある。また、高手術侵襲症例においても適切な時期と治療強度を保った化学療法を行っていくことは重要である。今回、当センターで DS を施行した際に、他臓器合併切除を要した進行卵巣癌症例について後方視的検討を行った。【方法】2019年1月から2023年5月において、III期以上の卵巣癌に対して DS を施行した 88 例を対象とした。他臓器合併切除の割合、入院期間、術後合併症の有無や術後化学療法開始までの期間、人工肛門に関する転帰等について検討した。【成績】年齢中央値は 61 歳 (34~77 歳)、進行期は III 期 55 例、IV 期 33 例、PDS : 35 例、IDS : 53 例であった。他臓器合併切除なし群 : 45 例、合併切除群 : 43 例であった。合併切除の数が多くなるにつれ、術中出血、手術時間、入院期間は延長する傾向にあったが、術後の化学療法再開までの日数に差は認めなかった。また腸管切除を要した 40 例のうち人工肛門造設術を施行した例は 17 例 (42.5%) 認めた。維持療法開始後 6 か月経過した時点での人工肛門閉鎖率は 75%、手術後から人工肛門閉鎖までの期間は中央値 161 日であった。【結論】他臓器合併切除を要した症例でも、術後化学療法開始までの期間に差は認めておらず、術後治療に与える影響は高くないと考えられた。施設毎に DS 後経過を随時検証することで、周術期体制や患者予後の改善に努めていくことが重要である。

P-58-4 卵巣明細胞癌におけるリンパ節郭清の治療成績に関する検討

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【目的】推定 I-IIA 期までの卵巣癌に対し、staging laparotomy として後腹膜リンパ節郭清が推奨されているが、早期卵巣癌の正確なステージングが目的である。リンパ節郭清に治療的意義はないとされているが、本邦で多い化学療法感受性の低い組織型である明細胞癌においては明らかではない。当院手術により明細胞癌と診断した症例の治療成績について検討したため報告する。【方法】2017年1月から2023年12月で卵巣癌に対して手術を行い明細胞癌の診断となった 41 例を対象とした。当院では推定 I-IIA 期の症例に対して系統的リンパ節郭清を行っている。推定 I-IIA 期 31 例中、PS 不良例や本人の希望、症状緩和が必要で待機的手術が困難の理由で 9 例がリンパ節郭清を省略していた。患者背景、ステージ、リンパ節郭清、再発率などを後方視的に検討した。【成績】年齢中央値は 54 (30-78 歳)、BMI 中央値は 21.8 (16.8-33.3) であった。術後病理診断では FIGO 分類で I 期 27 例、II 期 6 例、III 期 7 例、IV 期 1 例であった。系統的リンパ節郭清でリンパ節転移ありと診断されたのは 22 例中 1 例 (4.5%) であり、本症例は微小大網転移を認めたため IIIB 期と診断された。IIA 期まででリンパ節郭清あり 21 例とリンパ節郭清なし 9 例を比較した。再発は郭清ありで 3 例 (14.2%)、郭清なしで 2 例 (22.2%) 認め、統計学的有意差はなかった ($p=0.622$)。【結論】当院における明細胞癌のリンパ節郭清意義について検討した。自験例ではリンパ節郭清による術後治療の抽出はなく検査的意義は確認できなかった。郭清ありで再発割合が少なく治療的意義がある可能性も考えられた。いずれも少数であり、検査的意義、治療的意義ともに今後も症例を集積して検討する必要がある。

P-58-5 PARP 阻害薬治療歴のあるプラチナ抵抗性再発卵巣癌・腹膜癌に対する Gemcitabine+Bevacizumab 併用療法の効果

長野赤十字病院

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【目的】プラチナ抵抗性再発卵巣癌の治療においては、Gemcitabine+Bevacizumab (GEM+BEV) 併用療法の有効性が報告されているが、PARP 阻害薬投与後にプラチナ抵抗性となった患者における GEM+BEV 併用療法の効果は不明である。当院で PARP 阻害薬投与後にプラチナ抵抗性となり、GEM+BEV 併用療法を行った 9 症例についてその有効性を検討する。【方法】2021年2月から2023年9月の期間に、当院にて GEM+BEV 併用療法を行った PARP 阻害薬による治療歴のあるプラチナ抵抗性再発卵巣癌・腹膜癌を対象とし、効果および有害事象を後方視的に検討した。【成績】症例は卵巣癌 5 例、腹膜癌 4 例であり、組織型は全て漿液性癌だった。進行期は III 期 5 例、IV 期 4 例であり、PARP 阻害薬での治療歴は、Olaparib 3 例、Niraparib 4 例、両剤とも使用歴あり 2 例だった。GEM+BEV 投与開始時の平均年齢は 70.8 (53~82) 歳、前レジメン数の中央値は 3 (2~8) レジメン、投与サイクル数の中央値は 9 (2~17) サイクルだった。抗腫瘍効果は PR5 例、SD2 例、PD2 例であり奏効率は 55.6% であった。PFS は、中央値 6 (2~12) か月であった。Grade3/4 の有害事象は、好中球減少が 6 例、血小板減少が 1 例、高血圧が 1 例であり、消化器症状や脱毛など QOL を損なう有害事象はなかった。また、副作用による治療の中止はなかった。【結論】GEM+BEV 併用療法は、PARP 阻害薬投与歴のあるプラチナ抵抗性再発卵巣癌・腹膜癌においても有効であった。少数例ながら奏効率は高く、脱毛や消化器症状が少ないため長期間投与を継続できる例もあり、プラチナ抵抗性再発卵巣癌・腹膜癌の治療における有望な選択肢になると考えられた。

P-58-6 プラチナ抵抗性再発卵巣明細胞癌に対するペバシズマブ併用化学療法について

防衛医大

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【目的】卵巣明細胞癌は化学療法が奏功しづらく、プラチナ抵抗性再発となると有効な治療法がなく予後不良である。今回プラチナ抵抗性再発卵巣明細胞癌に対するペバシズマブ併用化学療法の効果を確認すること。【方法】1993年2月から2023年9月までの間に当院でプラチナ抵抗性再発卵巣明細胞癌と診断された症例を対象として後方視的に検討した。当院では2015年以降はプラチナ抵抗性再発卵巣明細胞癌に対して、全例に化学療法にペバシズマブを併用しており、2014年以前は化学療法にペバシズマブを併用した症例は無かった。治療にペバシズマブを併用した群をA群、治療にペバシズマブを併用していない群をB群とした。【成績】プラチナ抵抗性卵巣明細胞癌は35例あり、A群が15例、B群が20例だった。両群間に年齢やFIGO stage、手術後残存腫瘍、再発前化学療法数に有意差はなかった。プラチナ抵抗性再発の診断以降のPFS、OSはどちらにおいてもA群の方がB群よりも有意に延長した($p < 0.01$)。両群間のプラチナ抵抗性再発後のOSに関する多変量解析ではペバシズマブ併用の有無、FIGO stage (I/II期 vs III/IV期)が独立した予後規定因子であると考えられた。【結論】プラチナ抵抗性再発卵巣明細胞癌に対して、ペバシズマブ併用化学療法は予後を改善しうる。今後さらなる症例の蓄積が求められる。

P-58-7 当院において腹腔鏡下生検を実施した進行卵巣癌症例に関する後方視的検討

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【目的】腹腔内播種を伴う進行卵巣癌において、腹腔鏡下生検は病理学的診断や手術による完全切除の可否の判断において有用である。また腫瘍の遺伝子変異に応じた治療薬選択が広く行われるようになった近年では、治療前の腫瘍検体を採取する手法としても腹腔鏡下生検の重要性は増している。今回我々は当院の進行卵巣癌症例における治療経過や転機から、腹腔鏡下生検の有用性に関して検討を実施した。【方法】2021年1月から2023年7月までの期間に当院にて腹腔鏡下生検を実施したIII/IV期の進行卵巣癌患者9例を対象とし、患者背景や治療転機、予後に関して後方視的に検討した。【成績】9例のうち8例が高異型度漿液性癌、1例が明細胞癌であった。進行期はIIIB期1例、IIIC期6例、IVB期2例であった。腹腔鏡下生検の術時間は中央値59分(40-103分)、出血量はいずれの症例も少量のみであり周術期合併症は認めなかった。トロッカー数は臍部カメラポートを含めて4個(ダイヤモンド配置)であった症例が4例、3個(ダイヤモンド配置のうち右下腹部トロッカーを挿入しない)であった症例が5例であった。腹腔鏡下生検から化学療法開始までの期間は中央値10日(6-22日)であった。9例のうち化学療法後に腫瘍減量術が実施された症例は5例であり、いずれも残存腫瘍のない完全切除を達成した。HRD検査を提出した6例のうち5例でHRD陽性、1例は陰性であったが、いずれの症例も検体における腫瘍組織量はHRD検査に十分な量であった。【結論】腹腔鏡下生検は病理診断や遺伝子検査に十分な腫瘍採取が安全に実施でき、早期の化学療法開始も可能であることから、腹腔内播種を伴う進行卵巣癌症例において有用であることが再確認された。

P-58-8 PARP 阻害剤使用者における KELIM score を用いた検討

北海道大

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【目的】近年、CA125値から計算される、KELIM score が話題となっており、種々のバリテーションスタディが報告されている。KELIM score は化学療法感受性の良い指標になるとされているが、PARP 阻害剤 (PARPi) に関する指標としては不明である。PARPi を用いた初回維持療法を施行した患者の KELIM score を測定し、PARPi 内服期間、予後について後方視的に検討を行った。【方法】2018年1月から2023年7月までに卵巣がん・卵管がん・腹膜がんと診断され、初回維持療法としてOlaparib単剤(O群)、Niraparib単剤(N群)、もしくはOlaparib+Bevacizumab(P群)のいずれかを施行した者を対象とした。対象の患者79名のうち、2名を除外した77名についての検討を行った。本研究にあたり、倫理審査委員会より承認を得た(実施許可番号:指022-0390)。【成績】年齢中央値63歳、使用PARPiは、Niraparibが39名(50%)と最も多く、次いでPAOLA 23名(29%)、Olaparib15名(19%)だった。全体における維持療法の平均継続週数は54週、中央値は45週だった。KELIM scoreの中央値はN群1.1、P群1.1、O群1.2だった。KELIM scoreがfavorableと分類される割合は、N群では51%、P群では69%、O群では全例がfavorableだった。維持療法継続期間にはstage(3or4)とIDS(R0orOther)に有意差を認め、KELIM scoreには有意差を認めなかった。【結論】PARPi使用患者は比較的KELIM値が高い傾向にあり、KELIM scoreのみでは初回維持療法の継続期間に有意な差はなかった。初回維持療法の長期継続のためには、KELIM scoreだけで判断せず、IDSの際にR0を達成するということが重要である。

P-58-9 当科で Bevacizumab 併用療法が施行された進行卵巣、卵管、腹膜がん 110 症例の検討

王子総合病院
佐多綜一郎

【目的】日本での保険収載より 10 年が経過した血管新生阻害薬である Bevacizumab (以下 BEV) の当科での使用データに基づき、卵巣・腹膜・卵管癌に対するその有効性を明らかにする。【方法】当科で BEV 併用化学療法、あるいは BEV を使用した維持療法のいずれかを施行された進行卵巣・卵管・腹膜癌 110 症例を後方視的に統計学的手法を用いて解析し、奏効率、病勢制御率、無増悪生存期間、全生存期間などを算出する。また、それらの結果を臨床試験の結果や他のリアルワールドデータと比較検討する。【成績】当科の初回治療での BEV 併用化学療法の奏効率は 80.4% であり、再発一次治療では 66.7% であった。PFS 中央値は初回治療で 29.5 か月、再発一次治療で 11.5 か月であった。初回治療で BEV 併用化学療法を施行した症例の OS 中央値は 52.8 か月となった。いずれも、臨床試験や他のリアルワールドデータと同程度の結果を示した。【結論】当科での使用においても、BEV は化学療法との併用で奏効率の上昇に寄与し、PFS を延長した。

P-58-10 卵巣・卵管・腹膜癌 2B 期症例の検討

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【目的】ガイドライン上、2B 期以上と考えられる症例に対する手術では、臨床的にリンパ節転移を認めない場合は、骨盤・傍大動脈リンパ節の郭清は実施しないことが推奨されている。3 期、4 期の進行卵巣癌に対しては PARP 阻害剤を用いた維持療法が適応となっているが、T2b の場合、骨盤内臓器への広範囲の癒着・浸潤が存在した場合においてもリンパ節転移が陰性であれば 2 期のままであり PARP 阻害剤を用いた維持療法の適応とならないのが現状である。上記から、2B 期の症例についての治療法や予後について検討した。【方法】当院で 2011 年 1 月から 2021 年 12 月までの間に治療を開始した、卵巣癌・卵管癌・腹膜癌の症例のうち、予後の追跡が可能な 156 例を調査の対象とした。【成績】上記対象症例のうち術後の病理診断で 2B 期 (FIGO2014) となった症例は 16 例であった。うちリンパ節郭清を行った症例は 9 例であった。組織型は漿液癌が 8 例、類内膜癌が 4 例、明細胞癌が 2 例、粘液性癌が 1 例、未分化癌が 1 例であり、内膜癌が発生母地と考えられる組織型が約 1/3 を占めていた。6 例で再発を認め、うち 2 例は BRCA 変異陽性であり再発治療後に PARP 阻害剤での治療を行なっている。T2b であったが、リンパ節転移があり 3 期となった症例は 3 例であり、うち 2 例が再発している。PARP 阻害剤は初回維持と再発治療後の維持療法で 1 例ずつ使用されている。【結論】報告によりばらつきはあるが、pT2 期のリンパ節転移の頻度は 20~50% とされている。術前の画像や術中所見でリンパ節転移が疑われる場合は積極的にリンパ節郭清を行うことも考慮すべきであるとともに、腹膜生検を含めた正確なステージングが重要であると思われる。

P-58-11 当院における進行卵巣癌初回治療における HRD 検査の検討

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【目的】当院では進行卵巣癌症例に対して初回治療時に HRD 検査を実施し、HRD 陽性例に対してはベバシズマブとオラパリブの併用維持療法を原則的に第一選択としている。今回我々は、当院における初回卵巣癌に対する HRD 検査の現状について検討を行った。【方法】2021 年 4 月~2023 年 9 月までの間に当院において施行した進行卵巣癌の初回治療例の HRD 検査の結果と、HRD 検査を施行して維持療法に移行した症例について後方視的に検討した。【成績】対象症例は 17 例であった。HRD 陽性/tBRCA1 病的バリエーション有りが 1 例 (6%)、HRD 陽性/tBRCA2 病的バリエーション有りが 2 例 (12%)、HRD 陽性/tBRCA 病的バリエーション無しが 6 例 (35%)、HRD 陰性が 6 例 (35%)、inconclusive が 2 例 (12%) であった。tBRCA 病的バリエーション有りの 3 症例のうち、1 例が gBRCA 病的バリエーション有りであった。癌種は卵巣癌 12 例、腹膜癌 3 例、卵管癌 1 例、後腹膜腫瘍 1 例、であり、組織型は高異型度漿液性癌が 14 例、類内膜癌、明細胞癌、卵巣成熟嚢胞性奇形種の悪性転化がそれぞれ 1 例であった。HRD 検査検体採取時期は 6 例が PDS、5 例が IDS、4 例が試験開腹または審査腹腔鏡、2 例が経皮的針生検であった。HRD 検査陽性の 9 症例のうち、2023 年 9 月時点で維持療法に移行したのは 7 例であった。治療の内訳は、5 例がベバシズマブ+オラパリブ併用療法、2 例がニラパリブ単剤療法であった。併用療法を選択しなかった 2 例は、血栓症既往、高血圧によってベバシズマブ投与が不適と判断された。【結論】当院における進行卵巣癌症例の HRD 陽性率は 53% であり、既報と同程度であったが、2 例の inconclusive 症例を認めた。今後症例数を増やして検討が必要である。

P-58-12 当院におけるHRD検査症例の臨床アウトカム

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【目的】進行卵巣・卵管・腹膜癌における初回治療において、当科ではHRD検査(myChoiceTM診断システム)を全例で提出しており化学療法前の組織検体を原則としNAC症例は診査腹腔鏡を可能な限り施行している。導入後2年半が経過したHRD検査における当科での臨床アウトカムについて報告する。【方法】当院において2021年1月から2023年6月の期間に卵巣・卵管・腹膜癌にてHRD検査を施行した65例中、初回治療中にHRD検査を施行した42例(46例中4例を研究非同意などで除外)について治療及び有害事象を含む臨床経過を電子カルテより抽出・解析した。【成績】初回治療時に提出された検体は35/41例(85%)が化学療法前検体であり10例が診断的腹腔鏡、21例にPDSが施行されていた。結果は21例(51%)がHRDであった。そのうち11例のtBRCA陽性症例であり現在までに3例がHBOCの診断に至っている。初診から初回化学療法開始までの期間中央値は診断的腹腔鏡及びPDSで統計学的な差を認めず(24 vs 29 days)、診断的腹腔鏡においてもPDSと同等の治療開始時間を要した。観察期間の中央値22か月(範囲:7-55M)。PAOLAレジメンが施行された10例中3例で減量(1段階:2例,2段階:1例)されいづれも貧血によるものであった。再発1例を除く9例が現在継続中である。【結論】診断的腹腔鏡は検査手技にも関わらず化学療法開始までの期間を短縮するメリットは認めず、HRD陽性時の維持療法PAOLAレジメンにおいては貧血がRDIの規程因子である可能性がある。

P-58-13 当科におけるBevacizumab併用療法が施行され消化管穿孔を起こした卵巣癌9症例の検討

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【目的】GOG218試験の結果から、Bevacizumab(以下、BEV)併用療法により卵巣癌の無増悪生存期間は非併用療法群と比較して有意に延長されることが示されたが、全生存期間の延長に優位差を認めなかった。一方で、BEVには消化管穿孔という重篤な合併症を呈することも知られている。今回我々の施設で経験した消化管穿孔症例に対して、その背景などを検討しリスク因子の抽出を試みた。【方法】2013年10月~2023年3月までの期間にBEV併用療法または維持療法を行なった。卵巣癌110症例の診療記録を基に、年齢、癌種、Stage、BEV併用治療回数、再発治療回数、骨盤内放射線照射歴、消化管浸潤病変を後方視的に調査し、消化管穿孔のリスク因子を同定するために多変量解析を行った。【成績】BEV併用療法または維持療法を使用した卵巣癌症例で消化管穿孔が発生したのは9例、消化管穿孔率は8.18%(9/101例)であった。放射線治療歴または消化管浸潤病変を持つ症例では消化管穿孔発生に優位差を認めた(それぞれP=0.0309, P=0.0022)。【結論】卵巣癌において骨盤内照射歴や消化管浸潤病変は、BEVを使用する際の消化器穿孔リスクになるため注意を要する。

P-59-1 帝王切開癒痕部に生じた子宮腺肉腫の一例

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【緒言】子宮腺肉腫は良性腺上皮と肉腫成分から構成される混合腫瘍で、葉状のポリープ様隆起性病変を形成し、その大半は子宮内膜に発生するとされている。今回、帝王切開癒痕部の筋層内に外方に突出する多房性囊胞性腫瘍を認め、術中迅速診断で子宮腺肉腫と診断し、腹式単純子宮全摘+両側付属器切除を行った1例を経験したため報告する。【症例】34歳、1妊1産(常位胎盤早期剝離、帝王切開)。検診のため前医を受診し、子宮体部腫瘍の診断で精査加療目的に当院へ紹介となった。MRIで子宮体下部前壁筋層内に多房性囊胞性腫瘍を認めた。子宮内膜細胞診は陰性、子宮鏡検査は帝王切開癒痕部に一致してやや血管走行が目立つ程度であった。悪性を否定できないため手術の方針とした。術中所見として、子宮体下部前壁に5cm大の弾性軟の腫瘍を認めた。術中迅速組織診断で提出した子宮より子宮腺肉腫の疑いと診断されたため、両側付属器切除を追加した。最終診断として、子宮筋層の1/2以上に浸潤しており子宮腺肉腫pT1cの診断となった。追加治療はせず外来で経過観察している。【考察】子宮腺肉腫は子宮内膜発生が大半であり、内膜細胞診やポリープ切除組織より術前診断が可能な場合もあるが、本症例では内膜に異常所見を認めなかった。調べた限りでは帝王切開癒痕部に生じた子宮腺肉腫の報告はなかった。原因として帝王切開に伴い筋層内に入り込んだ内膜組織が影響している可能性や、偶発的に帝王切開癒痕部に発生したことなどが考えられた。

P-59-2 再発子宮体癌に対するレンパチニブ・ペムプロリズマブ療法中に難治性口腔粘膜炎のため治療継続困難となった1例

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【目的】レンパチニブ (Len)・ペムプロリズマブ (Pem) 療法は、高血圧や手足症候群の他、免疫関連副作用 (irAE) など多種多様な副作用を認める。今回我々は Pem が原因と思われる難治性口腔粘膜炎のため治療継続困難となった再発子宮体癌の1例を経験したので報告する。【症例】62歳、X-6年に子宮体癌に対し腹式子宮全摘術、両側付属器摘除術、骨盤内および傍大動脈リンパ節郭清を行い、術後診断は pT1aN0M0、類内膜癌 G3 であった。X-1年に骨盤内再々発 に対しパクリタキセル/カルボプラチン療法を6コース施行したが、progressive disease となったため、Len・Pem 療法を開始した。高血圧・手足症候群および血小板減少のため Len の一時休業および減量を必要とした。Pem6コース後口腔粘膜炎 (Grade2) のため Len を休業したが、症状増悪し食事摂取困難 (Grade3) となった。歯科口腔外科にて、半夏瀉心湯・アズノール®軟膏およびうがい液・デキサメタゾン軟膏・エビシル®口腔溶液の使用およびセルフケアを開始した。直後に irAE 腸炎を発症したため、Pem を休業し絶食およびステロイド療法を行ったところ、irAE 腸炎とともに口腔粘膜炎の改善を認めた。Len・Pem 療法を再開したが、手足症候群のため Len は休業となり、Pem10コース投与後再度口腔粘膜炎 Grade3 を認めた。Pem の休業および上記対処療法を行うも改善に17週間を要したため、Len・Pem 療法を中断した。【結語】重症の口腔粘膜炎は患者の QOL を大きく損ない、難治性の場合治療継続が困難となりえる副作用と認識すべきである。

P-59-3 術後に卵巣癌との重複癌が判明した若年子宮体癌の1例～卵巣切除の必要性について～

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子宮体癌の標準術式は子宮と両側付属器の切除であるが、若年子宮体癌患者に対して両側卵巣切除を行うと、更年期症状だけでなく脂質異常症・骨粗鬆症・心血管系疾患の発症など、将来の健康状態に悪影響を及ぼし、45歳以下で両側卵巣切除した場合には死亡率の上昇も報告されている。しかし、若年子宮体癌患者は、有意に卵巣癌との重複癌や卵巣への転移が多いことも知られている。今回、若年子宮体癌に対して手術施行し、術後に子宮体癌と卵巣癌の重複癌と判明した1例を経験したため、卵巣切除の必要性も含め文献的考察を加えて報告する。症例は37歳未妊妊、高血圧・BMI:42.1と高度肥満あり、不正出血を主訴に前医受診し子宮内膜組織診で類内膜癌 G1 のため当科紹介。術前診断子宮体癌 IA 期に対してロボット支援下単純子宮全摘、両側付属器切除を施行した。術中迅速病理組織診で筋層浸潤認めため骨盤リンパ節郭清を追加した。術後病理診断で、子宮体癌 (類内膜癌 G1)、pT1aN0M0, StageIA 期と卵巣癌 (類内膜癌 G2)、pT1aNxM0, StageIA 期の重複癌と判明した。追加手術や術後補助化学療法は希望されず、現在約2年経過し無再発である。子宮体癌と卵巣癌の重複癌患者は、それぞれの単独癌患者よりも若く、さらに低悪性度かつ早期である傾向がある。卵巣癌の原因に内膜症性嚢胞の悪性転化説が知られているが、近年がんの遺伝子変異を有する子宮内膜細胞が月経血の逆流を受けて卵巣に生着することによって引き起こされる可能性も指摘されている。若年子宮体癌症例では、卵巣癌との重複癌や卵巣転移も懸念されるため、卵巣温存の適応について慎重な検討が必要である。

P-59-4 子宮体部に同時発生した明細胞癌および類内膜癌の1例

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子宮体部に組織型が異なる腫瘍が発生する症例は、症例報告としては散見されるものの、その具体的な頻度は不明である。今回、子宮体部に明細胞癌および類内膜癌が不連続に同時発生した症例を経験したため、報告する。症例は46歳、2経妊1経産1中絶、併存症として糖尿病と高血圧、緑内障あり。検診で子宮頸部細胞診 ASC-US に対し近医を受診し、ハイリスク HPV 検査陰性であった。経膈エコーで子宮内膜に10mm大のポリープ様病変を認め、経過観察となった。3か月後に血性帯下の訴えあり施行した子宮体部細胞診検査で陽性 (adenocarcinoma) であったため当院紹介受診した。腫瘍マーカーはCEA125, CA19-9ともに上昇を認めず。MRI では子宮底部に浅い筋層浸潤を伴う腫瘍と、子宮体下部から頸部付近まで筋層の2分の1を超える浸潤を伴う腫瘍が指摘された。また造影 CT ではダグラス窩腹膜播種と右付属器転移を疑う病変が指摘された。臨床的に子宮体癌 III 期と診断し、腹式準広汎子宮全摘・両側付属器切除・腹膜播種切除・大網部分切除を施行した。病理検査で、底部の病変は類内膜癌で ER (+), PgR (+), p16 (-)。体下部の病変は明細胞癌で ER (-), PgR (-), p16 (-) の診断となった。明細胞癌病変は筋層の2分の1以上浸潤しており、また頸部間質浸潤を認めた。右卵巣病変・腹膜病変は明細胞癌の転移の診断となった。2つの子宮内膜病変は連続しておらず、組織学的診断・免疫染色結果が異なることから、別起源の子宮内膜癌の重複と考えた。子宮体癌 IVB 期 (pT3bN0M1) と診断し、術後に TC 療法を6コース施行した。現在残存病変なく、経過観察を継続している。

P-59-5 骨盤臓器脱に対して前後壁経腔メッシュ手術を施行後、子宮体癌が疑われ治療した1例

大阪警察病院

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【目的】骨盤臓器脱 (POP) に対して前後壁経腔メッシュ手術 (AP-TVM) 施行後、子宮体癌が疑われ、当院で子宮体癌に対する手術、メッシュの再留置を経験したので報告する。【方法】患者は83歳、3妊3産、閉経52歳、10年前にPOPに対してAP-TVMを施行している。その後経過は特に問題なく当院を一旦終診となっていた。既往歴に虫垂炎手術、左足首開放骨折手術、白内障手術があり、現在非結核性抗菌症にて定期的フォロー中である。今回、排尿困難で近医産婦人科を受診し、経腔エコーで留水腫、子宮体癌が疑われたため、前医へ紹介となった。前医の経腔エコーでも同様の所見であったが、子宮口が完全閉鎖しており、子宮内腔のサウンディングが困難で、組織採取はできなかった。骨盤造影MRIでも子宮体癌が疑われたが、AP-TVM術後のため、手術時メッシュの剝離困難が予想されたため、当院での治療目的に紹介となった。術前検査では子宮体癌 stage Ia の診断となり、診断、治療目的に手術の方針となった。【成績】年齢、既往歴を考慮し、術中迅速病理組織診断には提出せず、開腹子宮全摘術、両側付属器摘出術、メッシュ断端固定術を施行した。術中子宮全摘の際に触診でメッシュのアームを残せるか確認をしながら子宮全摘術を施行し、最終的に断端に再度メッシュを固定し、手術を終了した。術後最終病理組織診断は子宮がん肉腫 pT1aNxM0 であった。年齢、合併症から追加治療はなしの方針となった。【結論】今回、POP後の悪性腫瘍手術で再度メッシュ留置術を施行し、現在悪性腫瘍、POPともに再発なく経過フォローをできている症例を経験した。

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P-59-6 診断に苦慮した高異型度子宮内膜間質肉腫の一例

大阪はびきの医療センター

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高異型度子宮内膜間質肉腫 (High-grade endometrial stromal sarcoma: HGESS) は子宮内膜間質に由来する異型の強い腫瘍で、希少疾患かつ新しい疾患概念であるため治療法に関するエビデンスが乏しい疾患である。今回、術前に子宮内膜間質肉腫が疑われ、病理検査でHGESSと診断した1例を経験したため報告する。症例は57歳女性、2妊2産。閉経後の不正性器出血を主訴に近医を受診した。経腔超音波検査で子宮内膜肥厚を指摘され、子宮体部組織診で子宮内膜間質肉腫疑いのため当院を紹介受診した。骨盤MRIで長径54mm大の境界不明瞭な拡散制限を伴う充実性腫瘍を認めた。胸腹部造影CTではリンパ節腫大および遠隔転移は認めなかった。腹式単純子宮全摘術および両側付属器切除術を実施した。術中所見では腫瘍の子宮漿膜面への露出を認めた。病理検査では子宮体部筋層内に好酸性細胞質を持つ類上皮あるいは紡錘形細胞が充実性胞巣を形成し浸潤性に増殖する腫瘍を認めた。Cyclin D1, BCORに有意な陽性所見は見られなかったが、脈管侵襲が多く、pan-TRK, CD10が陽性であることからHGESS (pT1N0M0) と診断された。術後化学療法としてパクリタキセル+カルボプラチン併用療法を行い、再発や転移を示唆する所見なく経過している。HGESSでは進行度に依存するが5年生存率が約40%と予後不良な疾患であるが、子宮外病変の切除を含めた完全摘出後の術後補助化学療法が有用であるとの報告もある。若干の文献的考察を加えて報告する。

P-59-7 レンバチニブ/ペンプロリズマブ併用療法の導入により長期の病勢制御が得られた再発子宮体癌の一例

東邦大医療センター大森病院

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【緒言】再発子宮体癌は難治性かつ極めて予後不良であり、有効な化学療法に乏しかったが、KEYNOTE-775試験の有効性に基づき、2022年よりレンバチニブ/ペンプロリズマブ併用療法 (LEM+PEM: LP療法) が実地臨床に導入された。その一方で、本療法に特有な有害事象の管理の難しさが指摘されており、長期投与の“足かせ”となっている。当院においてLP療法を比較的長期間投与し、病勢制御が得られた再発子宮体癌の一例を経験したので報告する。【症例】60歳代女性、子宮体癌 Stage IIIA、類内膜癌 G1、X年10月に前医で初回手術施行 (単純子宮全摘出術+両側付属器摘出術+骨盤リンパ節生検)、術後にTC療法 (PTX+CBDDCA) を6サイクル施行し、経過観察となった。X+5年4月に多発肺転移、肝転移、腹膜播種、ダグラス窩腫瘍直腸瘻のため、子宮体癌再発疑いで当院紹介初診となった。同年5月に試験開腹術および人工肛門増設術を施行、子宮体癌の再発およびMSI陰性 (pMMR) を確認した。その後TC療法3サイクル (アレルギーで中止) およびAP療法 (ADM+CDDP) 8サイクルで部分奏効 (PR) に至るも、ADMの総投与量上限となった。そこでX+6年8月よりLP療法を導入した。有害事象のためLEMの休業、減量 (最終的には中止) およびPEMの休業を要したものの、最良効果判定は不変 (SD) であり、8か月間の病勢制御が得られた。その後に肺転移巣の増悪を示したため、本人希望で best supportive care となり、X+7年6月に転院となった。【考察】LP療法の導入により比較的長期の病勢制御と担癌生存が得られた一例であった。本療法は支持療法に加え休業や減量のタイミングを工夫することが治療を長く継続するコツとなると考えられた。

P-59-8 子宮内感染と疼痛のため緊急手術を行ったところ術後に平滑筋肉腫と判明した一例

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平滑筋肉腫は子宮体部悪性腫瘍の1~2%とまれな疾患であり, 特異的な症状が乏しく, 子宮筋腫との鑑別は困難である。MRIで境界不明瞭で, 内部の出血像などの所見を呈す場合もあるが, 超音波のみで子宮筋腫と診断され経過観察されることも多い。今回我々は子宮内感染と疼痛のため緊急入院し手術を行ったところ平滑筋肉腫と判明した一例を経験したので報告する。症例は51歳, 2妊2産, 半年前まで月経周期正順であったが, 5か月前から不正出血が持続し, 下腹部に腫瘤感を自覚していた。2か月前より下腹部痛が出現し前医を受診したところ巨大子宮筋腫を疑われた。炎症反応上昇あり, 抗生剤とホルモン剤を処方された。その際の頸部および内膜細胞診は異常なかった。その後も疼痛持続したため, 当院紹介となった。経膈超音波で子宮内に10cm大の腫瘤を認め, 子宮内からは黄白色の組織片が排出していた。体温は38.3度, 血液検査でWBC19,400/ μ L, CRP8.9mg/dlと上昇を認め同日入院とした。CT, MRI所見では子宮体癌や子宮肉腫を疑う腫瘤とその内部にはガスを認め, 壊死に感染を伴っていると考えられた。また, 肺内に多発小結節影を認めた。夜間から疼痛増強し, 鎮痛薬でも疼痛コントロール出来ないため, 翌日に単純子宮全摘出術と両側付属器摘出術を行った。子宮は新生児頭大に腫大しており, 右側結腸と子宮は炎症性に癒着していた。摘出子宮の後壁腫瘤に割を入れるとかび臭があり, 断面は辺縁整の筋腫様で腫瘤内腔は脆弱な緑灰色の組織に置換されていた。病理組織診断は平滑筋肉腫であった。PET-CTで多発肺転移と骨盤内リンパ節転移を疑う所見も認め, FIGO分類IVB期であった。現在, 化学療法中である。

P-59-9 子宮鏡検査が診断に有用であった子宮体癌の2例

虎の門病院

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【緒言】子宮内膜細胞診は偽陰性となることがある。今回, 子宮内膜細胞診陰性だが子宮鏡検査により子宮体癌を疑い, 診断, 治療に至った2症例を経験したので報告する。【症例1】72歳0妊0産。不正出血主訴に受診, 超音波検査にて子宮内腔に3mm大のポリープ様病変を認め, 子宮内膜細胞診はclass IIであった。子宮鏡検査にて右卵管角近くに異型血管を伴う乳頭状隆起病変を認め子宮体癌を疑い, 引き続き子宮内膜組織診を施行, Endometrioid adenocarcinoma, G1の診断であった。子宮体癌IA期の術前診断に対して腹腔鏡下子宮全摘術, 両側付属器摘出術, 大網部分切除術を施行, 術後病理診断はEndometrioid adenocarcinoma, G1, pT1aであった。【症例2】33歳0妊0産。不正性器出血主訴に受診, 超音波検査にて子宮内腔に粘膜炎下筋腫を疑う1.5cm大の腫瘤像を認め, 子宮内膜細胞診はclass Iであった。子宮鏡検査にて子宮底部から突出する異型血管を伴う乳頭状隆起病変を認め, 子宮悪性腫瘍または変性を伴う粘膜炎下筋腫の疑いに対して子宮鏡下腫瘍摘出術を施行した。病理結果はEndometrioid adenocarcinoma, G2の診断であり, 画像精査の結果子宮体癌IA期の診断, 腹腔鏡下子宮全摘術, 両側付属器摘出術を施行した。術後病理診断はEndometrioid adenocarcinoma, G2, pT1aであった。【結語】超音波上子宮内腔病変を疑う場合は子宮内膜細胞診が陰性であっても子宮鏡検査を併用することでより正確に子宮体癌の診断につながると思われた。

P-59-10 切除不能な子宮体部原発大細胞神経内分泌癌に対し化学療法を行った一例

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【緒言】大細胞型神経内分泌癌(Large cell neuroendocrine carcinoma, 以下LCNEC)は子宮体部悪性腫瘍の1%未満と稀な腫瘍であり, 予後不良である。今回我々は, 切除不能な子宮体部原発のLCNECに対し, Pembrolizumab+Lenvatinibを含む3レジメンにわたり化学療法を施行した一例を経験したため, 報告する。【症例】34歳女性, 0妊。不正性器出血・腰痛・股関節痛を主訴に近医を受診するも経過観察とされていたが, 紹介元救急外来を受診し, CTにて骨盤内腫瘤及び両側肺野の多発結節影を指摘され, 当院紹介となった。内診では少量の性器出血と陰壁・右大陰唇に疼痛を伴う硬結を触知した。経膈エコーでは子宮はびまん性に腫大していた。子宮内膜吸引組織診にて組織型はLCNECであり, 多発転移を伴うIVB期と診断した。神経内分泌腫瘍として, 小細胞肺癌の治療に準じ, CDDP+VP16を3コース施行しSDであったが, 4コース目施行後にPDとなった。続いて切除不能な子宮体部の適応にてPembrolizumab+Lenvatinibをコース行うもPDであった。MSI検査も陰性であった。再度小細胞肺癌の治療に準じAmrubicin(以下AMR)単独療法を2コース実施したが, 病勢進行に伴う全身状態の悪化を認め, 積極的治療は終了とした。AMR終了後のCT評価ではPDであったが, 腫瘍マーカーは低下を認めた。治療終了後約9か月後に自宅でお看取りとなった。【結語】LCNECに対する治療は確立されていないが, 本症例では組織型に応じた化学療法にて一定の効果を得た。今後は組織型・ゲノム検査結果に応じた化学療法を施行することで, より有効な治療効果を得られる可能性がある。

P-59-11 術後早期より腔再発を認め急速に進行した子宮癌肉腫の1例

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【緒言】子宮肉腫は婦人科腫瘍の中でも特に予後不良の腫瘍であり標準的な治療は確立されていない。手術施行後早期より肉腫成分の腔壁再発を認め、急速に進行した子宮癌肉腫の症例を経験したため報告する。【症例】62歳0妊、尿閉を主訴に受診し、腔より脱出する腫瘤を認めMRI検査で腔内に充満する巨大な腫瘤を認めた。病理組織診で間葉系悪性腫瘍が疑われ、子宮肉腫疑いの臨床診断のもと手術を施行した。子宮底部から発生した有茎性腫瘍が子宮腔内から腔内へ連続性に存在し、腫瘍重量により子宮底部は内反していた。腹式子宮全摘出術、両側付属器摘出術を施行し、腔壁に一部腫瘍の癒着を認め摘出または焼灼した。術後病理組織診で子宮底部から発生した類内膜癌 Grade2 と腔内を占める高異型度間質肉腫の連続性をもつ子宮癌肉腫で、腔壁浸潤を認めることからpT3bNXM0の診断となった。局所制御目的に放射線治療を行う方針とした。術後低アルブミン血症が遷延し術後19日目に退院となり、術後31日目の外来受診時に数センチの腔壁腫瘍と出血を認め、腔壁再発と診断し早急な治療開始を提案したが受け入れられず、術後38日目に5cm大に腫瘍は増大し肺転移を認めた。腫瘍出血が増加したため術後45日目より止血目的に放射線治療を行い一過性の腫瘍縮小を認めたものの再度尿閉ならびに出血増強を認め、前者は尿道バルン管理、後者に対しては経動脈的塞栓術を施行し、現在緩和治療中である。【結語】子宮癌肉腫に対して手術治療を施行したが術後早期より腔壁再発を認め、急速に進行を認めた1例を経験した。腔壁浸潤を認める場合、腔壁の合併切除を考慮し、また術後可及的速やかな術後補助療法を行うことが重要と思われた。

P-60-1 本邦の多嚢胞性卵巣症候群の診断基準における抗ミュラー管ホルモンの位置付けとカットオフ値に関する検討

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【目的】2023年に欧米の多嚢胞性卵巣症候群(PCOS)の診断基準(Rotterdam基準)に抗ミュラー管ホルモン(AMH)が組み込まれたがカットオフ値は示されていない。国内でもこれまでAMH、胞状卵胞数(AFC)の全国的な調査研究はなく、本研究では本邦の診断基準におけるAMHの位置付けとカットオフ値を検討した。【方法】全国の国公立大学病院、生殖補助医療登録施設(643施設)を対象に症例調査を行った(日産婦 本邦におけるPCOSの診断基準の検証に関する小委員会)。解析対象は日産婦2007で診断したPCOS群538例、排卵障害のないコントロール群863例とした。AMHとAFC、年齢、BMI、LH、テストステロン等との相関を検討し、それらを説明変数としてAMHの重回帰分析を行った。年齢階層別にAMH、AFCカットオフ値(感度95%以上)を設定した。アクセス、エクルーシスの測定値は回帰式からルミパルスに換算して検討した。【成績】AMHは各年齢階層でPCOS群が有意に高かった。AMHは両群で年齢と有意な負の相関を、AFCと有意な正の相関を示したが、BMIとは相関しなかった。重回帰分析ではAFCのみが有意で、偏相関係数は0.381であった。AMHカットオフ値は、アクセス、ルミパルスでは20-29歳が4.4ng/mL、30-39歳が3.1ng/mL、エクルーシスではそれぞれ4.0ng/mL、2.8ng/mLであった。Rotterdam基準版のカットオフ値も別途設定した。AFCカットオフ値は全年齢階層で10個以上であったが、施設間のばらつきが大きかった。【結論】血中AMH濃度を規定する因子はAFCであり、卵巣所見を補完し得る。本邦の診断基準に適したAMHカットオフ値を、年齢階層、測定系別に設定した。AMHは卵巣所見を客観的に評価でき、PCOSの診断精度の向上に資する。

P-60-2 性ステロイドホルモンとプロラクチン発現に関する検討

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【目的】性ステロイドは視床下部-下垂体-性腺軸におけるフィードバック機構に重要な役割を果たす。今回我々は性ステロイドホルモンの存在が下垂体プロラクチン発現にどの様に影響するのかを検討した。【方法】ラットプロラクチン産生GH3細胞における性ステロイドホルモンによるプロラクチン遺伝子発現をプロモーターアッセイ及び定量PCRで測定した。卵巣摘出ラット及び有卵巣ラットにおける下垂体プロラクチン発現及びステロイド補充効果、卵巣摘出ラットにおける視床下部ドーパミンおよびTRH遺伝子発現についても併せて検討した。【成績】GH3細胞においてエストラジオール(E2)刺激はプロラクチンプロモーター活性を上昇させなかったが、プロラクチン遺伝子発現は有意に増加した。プロゲステロン(P4)、男性ホルモンであるジヒドロテストステロン(DHT)にプロラクチン増加効果は無かった。卵巣摘出により下垂体プロラクチン発現は減少し、E2の補充はプロラクチンの減少を抑制した。P4、DHT補充に効果は無かった。正常雌ラット(卵巣あり)にE2刺激を行うと、下垂体プロラクチン発現は増加した。P4、DHT投与で変化は認めなかった。卵巣摘出ラットの視床下部ドーパミンおよびTRH遺伝子発現に変化はなかった。【結論】下垂体プロラクチン発現はE2により直接的な影響を受けていると考えられた。

P-60-3 エストロゲンの視床下部への影響—ラット視床下部オキシトシンの動態について—

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【目的】エストロゲンは性腺に作用するだけでなく、中枢神経を含む全身に作用する。オキシトシン (OXT) は視床下部の視索上核 (SON) と室傍核 (PVN) で産生され、下垂体後葉 (PP) から血中に分泌される。OXT の作用には、分娩・射乳の末梢作用と、直接脳内に作用する中枢作用があるが、エストロゲンの OXT への影響は不明である。OXT 産生を定量評価できる OXT-monomeric red fluorescent protein 1 (mRFPI) トランスジェニック (TG) ラットを用いて、エストロゲンと視床下部 OXT との関連を検討した。【方法】成熟雄性・雌性の OXT-mRFPI TG ラットを用い、動物実験倫理委員会の承認を得た。雄群と雌群 (発情前期, 発情期, 発情後期, 休止期, 両側卵巣摘出術 (OVX)) 群, エストロゲン補充群 (低用量エストラジオール (E2) 35.8pg/日, 高用量 E2 514.1pg/日) 群に分けた。蛍光顕微鏡で視床下部 (SON・PVN) と PP の OXT-mRFPI 赤色蛍光輝度を測定した。次に OXT ニューロンを選択的に活性化できるコレシストキニン 8 (CCK-8) を OVX 群と OVX に高用量 E2 投与群にそれぞれ投与し、摂食量と免疫組織化学法を用いて検討した。【成績】OXT-mRFPI TG ラットの SON, PVN および PP の mRFPI 赤色蛍光輝度は、発情期に有意に高く、OVX 群では低かった。エストロゲン補充では、低用量 E2, 次に高用量 E2 投与の順で蛍光輝度が高くなった。E2 と CCK-8 を投与した場合に、摂食量が最も少なく、免疫組織化学法では視床下部 OXT ニューロンの Fos が最も強く発現した。【結論】エストロゲンにより、視床下部 SON・PVN の OXT 蛍光輝度は変化した。エストロゲン投与は OXT 産生を増加させることを証明した。臨床上、エストロゲン補充療法の更なる効果が期待できる。

P-60-4 本邦の多嚢胞性卵巣症候群患者の表現型に関する全国症例調査の集計結果

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【目的】本学会の多嚢胞性卵巣症候群 (PCOS) の診断基準 (2007) を検証し、診断基準の改定案を作成するために、全国症例調査により本邦の PCOS 患者の表現型, LH 測定時期, 臨床的アンドロゲン過剰症 (AE) 採用の影響等を検討した。【方法】全国の国公立大学病院および生殖補助医療登録施設 (643 施設) を対象に症例調査を行った (日産婦 本邦における PCOS の診断基準の検証に関する小委員会)。PCOS 895 例を解析対象とし、体型, 月経異常, 内分泌所見, 生化学的・臨床的 AE の発現と集積状況等を検討した。【成績】肥満 1 度以上 (BMI \geq 25) が 26.0%, 肥満 2 度以上 (BMI \geq 30) が 10.3% に見られた。月経異常の内訳は、希発月経 59.9%, 無排卵周期症 22.0%, 第一度無月経 18.1% であった。LH, LH/FSH 比およびそれらが高値を示す割合は 2007 年の調査と概ね同等であり、測定時期による検討では、月経 2-3 日目, 4-6 日目の検査に比べ、月経不順の初診時等に 1cm 以上の卵胞が存在しない状態で行った検査が有意に高かった。アンドロゲンは全体の 67.5% で評価され、その 9 割で総テストステロン (T) が測定されていた。T 測定例の 33.2% が高値を示し、LH, LH/FSH 比の高値に T 高値を加えることで内分泌異常の検出率は 6.2% 上昇した。臨床的 AE を 1 項目でも有する症例は全体の 14.6% であり、各有病率は多毛 13.5%, 尋常性痤瘡 10.4%, 低声音 3.5%, 陰核肥大 0.9% であった。T 高値に加え多毛を AE に追加することで、AE と判定できる患者は 30.4% 増加した。【結論】本邦の PCOS 患者の表現型を示した。高 LH 検出率は月経 2-6 日目では低い。診断基準への多毛採用は、診断精度を向上させ、多毛治療の端緒となり、国際基準との整合性向上など診療上の意義が大きい。

P-60-5 本邦の多嚢胞性卵巣症候群患者における肥満の有無による内分泌異常に関する検討

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【目的】多嚢胞性卵巣症候群 (PCOS) 患者における内分泌異常所見の肥満による影響について検討した。【方法】全国の国公立大学病院, 生殖補助医療登録施設 (643 施設) を対象に症例調査を行った (日産婦 本邦における PCOS の診断基準の検証に関する小委員会)。解析対象は日産婦 2007 で診断した PCOS 症例 895 例で、アンドロゲン過剰症 (AE) の発現率と集積状況等の内分泌異常について、肥満群 (BMI \geq 25, 233 例), 非肥満群 (BMI $<$ 25, 662 例) に分けて検討し、更に肥満度分類別 (日本肥満学会) に細分化して評価した。【成績】テストステロン (T) は BMI と有意な正の相関を示し、T 高値率は肥満群 43.0%, 非肥満群 29.4% で肥満群が有意に高く、肥満度分類別でも有意差を認めた。臨床的 AE の発現率は、1. 多毛 (13.5%), 2. 尋常性痤瘡, 3. 低声音, 4. 陰核肥大の順で高く、1~3 は肥満群が有意に高く、1, 3 は肥満度分類別にも有意差を認めた。臨床的 AE を 1 項目でも有する症例は肥満群 31.2%, 非肥満群 9.7% で肥満群が有意に高く、肥満度分類別にも有意差を認めた。生化学的 AE (T 高値), 臨床的 AE (多毛) いずれかによる AE の判定では、生化学的 AE 単独に比べ、AE 検出率が肥満群で 40%, 非肥満群で 25% 上昇した。LH と BMI は有意な負の相関を示したが、LH/FSH 比と BMI は相関を示さなかった。LH 高値率は肥満群で有意に低かったが、肥満度分類別では有意差を認めなかった。LH/FSH 比の高値率は肥満群, 非肥満群の間で有意差を認めず、肥満度分類別にも有意差を認めなかった。【結論】肥満 PCOS は、非肥満 PCOS に比べ臨床的および生化学的 AE の頻度が高く、LH 基礎値が低い。診断基準に多毛を採用することによる AE 検出率の向上は、肥満群で大きい傾向があった。

P-60-6 慢性炎症が卵巣機能に与える影響について

まつみレディースクリニック三田
松見泰宇

【目的】我々は凝固亢進状態をネオセルフ抗体検査が検出できることを報告してきた。本研究では慢性炎症状態をこの検査を用いて検出し、これが卵巣機能に与える影響を解析することを目的とした。【方法】ネオセルフ抗体価と慢性炎症状態を示す補体消費量との相関を解析するため、倫理委員会の承認のもと不妊症女性 58 例に対して、血清中のネオセルフ抗体価と補体濃度 (C3, C4, CH50) を測定し、相関を解析した。慢性炎症状態と卵巣機能との関係を解析するため、AMH を測定した 66 例を、PCOS 症例と non-PCOS 症例の 2 群に分け、PCOS 症例を AMH 値が 4.3 ng/ml 以下と以上の群に分け、AMH 値が 4.3 ng/ml 以上の群 (高 AMH 群) からネオセルフ抗体価が陰性 (カットオフ値 73.3 U/ml) で凝固亢進状態にない症例 23 例を抽出し、AMH 値とネオセルフ抗体価との相関を解析した。この集団における血清補体濃度とネオセルフ抗体価との相関についても解析した。【成績】58 例の検討では、ネオセルフ抗体価が高いほど C4 濃度は有意に低下していた (相関係数: -0.33, $P=0.0116$)。C3 および CH50 濃度との間には相関はなかった。PCOS (高 AMH 群) でネオセルフ抗体価陰性の 23 例の検討では、ネオセルフ抗体価が高いほど、AMH 値も有意に上昇し (相関係数 0.44: $p=0.034$)、AMH 値が高いほど C4 濃度も有意に低下した (相関係数 -0.43: $p=0.04$)。AMH 値と C3 および CH50 濃度との間には相関はなかった。【結論】ネオセルフ抗体価の上昇は慢性炎症を示す補体消費量と正の相関があり、この検査を用いて慢性炎症状態を検出できることが明らかとなった。AMH 値が高い PCOS 症例では、凝固亢進を伴わない慢性炎症が卵巣機能に影響を与えている可能性が示唆された。

P-60-7 多嚢胞性卵巣症候群 (Polycystic ovary syndrome ; PCOS) 患者における世代別変化の検討

徳島大
湊 沙希

【目的】多嚢胞性卵巣症候群 (Polycystic ovary syndrome ; PCOS) を有する女性の身体所見や理学所見に世代別に傾向があるのかを後方視的に解析することを目的とした。【方法】2003 年 11 月から 2023 年 3 月までに当院で治療中もしくは経過観察中の PCOS 患者 339 例を対象とした。身長、体重、BMI、体脂肪率、ウエスト、ヒップ、多毛・ニキビの有無、血圧、総コレステロール (TC)、トリグリセリド (TG)、LDL コレステロール (LDL-C)、HDL コレステロール (HDL-C)、HbA1c、空腹時血糖 (FBS)、空腹時インスリン (IRI)、HOMA-IR、LH、FSH、E2、テストステロン (T)、遊離テストステロン (freeT)、デヒドロエピアンドロステロンサルフェード (DHEAS)、卵巣体積を診療録より抽出し、30 歳未満、30 歳代、40 歳以上の世代別に検討した。【成績】30 歳未満は 30 歳代と比べて BMI、血圧が有意に低く、ウエスト、体脂肪率は他の 2 群と比べて有意に低かった。40 歳以上は他の 2 群と比べて左右卵巣平均体積、多毛またはニキビの出現率が有意に低かった。40 歳以上は他の 2 群と比べて FSH、TC は有意に高く、LH/FSH、T は有意に低かった。30 歳未満は他の 2 群と比べて TG が有意に低く、LDL-C は 40 歳以上と比べて有意に低かった。30 歳代は他の 2 群と比べて FBS が有意に高く、HbA1c は 30 歳未満と比べて有意に高く、IRI、HOMA-IR は 40 歳以上と比べて有意に高かった。【結論】PCOS 女性においてメタボリック症候群に関わる血圧、ウエスト、TG、FBS は、30 歳代から増悪する傾向にあることが判明した。

P-60-8 若年で AMH 低値を示す症例の背景因子について

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【目的】AMH (抗ミュラー管ホルモン) は卵巣予備能の指標であり高齢では低値となるが、若年でも低値を示すことがある。この場合妊娠可能年齢の短縮が予測され可及的早期の妊活が勧められるが、現在妊活前の女性が AMH を測定することは一般的ではない。そこで低値となるリスク因子が明らかとなればリスクを有する集団にプレコンセプションケアとして AMH 測定を勧めることができるかもしれない。今回、35 歳未満で AMH 低値を示した症例の背景因子について検討を行った。【方法】対象は 2020 年 1 月から 2022 年 12 月に T 不妊治療施設を初診し AMH 測定が行われ、測定日の年齢が 25-34 歳であった女性。年齢の影響を考慮し 25-29 歳と 30-34 歳に分け、AMH 低値群 (1.2ng/mL 未満) と非低値群について、背景因子を比較した。【成績】25-29 歳 78 人、30-34 歳 241 人で、AMH 低値群はそれぞれ 21.8%、36.1% であった。BMI、不妊期間、妊娠歴および子宮筋腫・子宮内膜症の頻度について、両群間で有意差を認めなかった。月経周期について、頻発月経 (頻発と正常を繰り返すものを含む) の頻度が 25-29 歳 (低値群: 非低値群、31.3% : 4.9%)、30-34 歳 (31.8% : 10.5%) ともに AMH 低値群で有意に高かった。また、30-34 歳については正常周期の割合が AMH 低値群で有意に低くなっていた (52.9% : 69.9%)。【結論】若年齢においても月経周期短縮が認められた場合には卵巣機能低下を示唆すると考えられた。AMH 低下が報告されている子宮内膜症は関連が認められなかったが、今回の対象が若年で、進行した子宮内膜症症例が少なかったことが影響した可能性があると考えられる。

P-60-9 経膈超音波検査による子宮角度の算出とその臨床的意義について

山梨大

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【目的】これまで予備的検討で、骨盤内における子宮の傾きが月経周期で変化し、経膈超音波検査を用いて子宮角度評価が可能であることを認めている。我々の考案した子宮角度評価法を用いて、凍結融解胚移植 (FET) 患者の月経・排卵・着床期における子宮角度変化および、不妊治療の転機への関連について検討した。【方法】倫理委員会承認の下、2022年5月~2023年4月に当院でFETを行った子宮前屈例を対象とし、月経2or3日(月経期)・E2最高値日(排卵期)・胚移植日(着床期)に子宮角度を算出した。子宮角度は、①子宮体部角度: 経膈超音波プローベに角度計測機を装着し地面に対しプローベが水平となるように挿入しその垂線と子宮体部のなす角度、②子宮体部-頸部角度: 子宮体部と頸部のなす角度、と定義した。子宮角度が移植周期内どのように変化しているか及び角度が妊娠成立に関連するかについて検討した。【成績】検討期間で168周期のFETをおこなっており、そのうち前屈例は110周期だった。①子宮体部角度の平均値と標準偏差は月経期 $15.2 \pm 22.4^\circ$ 、排卵期 $21.9 \pm 24.4^\circ$ 、着床期 $15.0 \pm 26.9^\circ$ であり、月経期から排卵期、排卵期から着床期の角度の違いはそれぞれ有意差を認めた ($p < 0.01$)。②子宮体部-頸管角度は、月経期 $136.2 \pm 29.8^\circ$ 、排卵期 $138.3 \pm 28.7^\circ$ 、着床期 $137.0 \pm 30.9^\circ$ であり有意差はなかった。子宮角度と妊娠成立については、本検討内では傾向がなかった。【結論】子宮体部は月経期に前屈方向に、排卵期にはやや直立気味に、着床期に再度前屈方向に変化することがわかった。この角度の変化が妊娠成立や周産期転機にどのように関連しているかについては、今後さらに症例を蓄積していく必要がある。

P-60-10 子宮内膜異型増殖症に対する妊孕性温存治療後の不妊治療中に慢性子宮内膜炎と流産を繰り返した症例

筑波大

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【目的】子宮内膜搔爬術は慢性子宮内膜炎 (CE) のリスク因子となる。今回我々は子宮内膜異型増殖症 (AEH) に対して、妊孕性温存療法 (FPT) 後に IVF で生児を獲得したが、治療中に CE と流産を繰り返した症例を報告する。【症例】38歳, 3妊1産。4年の不妊期間を経て、前医で不妊治療を開始した。多発子宮内膜ポリープを認め、子宮内膜搔爬術を施行した。病理検査にて AEH と診断されたため、当科紹介となった。2回の子宮内膜搔爬術を含む FPT 後、寛解を得たため不妊治療を開始した。AIH 反復不成功後、IVF の適応となった。初回の凍結融解胚移植 (FET) 後に妊娠が成立したが、妊娠10週で流産となった。その後3回の FET で妊娠成立せず、反復着床障害の精査目的で子宮鏡検査を施行し CE と診断した。ドキシサイクリンの投与後、再度 FET を施行して妊娠成立、妊娠27週で生児を獲得した。半年後第2子希望にて再診されたが、AEH が再発したため、再度、2回の子宮内膜搔爬術を含む FPT を施行した。寛解後、FET 施行前に子宮鏡検査を行い CE と診断した。前回と同様に加療後 FET を行い妊娠成立したが、部分胎奇胎となり子宮内容除去術を施行した。半年後、AEH が再発したため、再度、2回の子宮内膜搔爬術を含む FPT を実施、寛解後に採卵して1個の良好胚を凍結した。今後は、子宮内膜生検と並行する CE の迅速な診断と治療後に FET を行う予定である。【結論】本症例において、AEH 治療等の目的で頻回の搔爬後も妊娠・生児を獲得できたが、CE と流産を反復する結果となった。妊娠を希望する患者には、子宮内膜侵襲を最小限にする工夫と、胚移植移前の CE の対策が有用と考える。

P-60-11 様々な先天性子宮腔形態異常により子宮腔留血症をきたした3例についての検討

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【緒言】思春期における子宮腔留血症は子宮及び腔の様々な形態異常により発生するが、その頻度は稀であり、診断、対応に苦慮することが多い。今回、特徴的な先天性子宮腔形態異常により子宮腔留血症を呈した3例を経験したため、文献的検討を含め報告する。【症例1】13歳, 月経歴なし。4.5か月前から周期的な下腹部痛があり近医を受診したところ骨盤内に巨大な腫瘤を認め当科紹介となった。腔口は陥凹しており MRI で腔下部が同定できず、MRI, 経膈超音波で上部腔盲端との距離は13mmと推定され、腔下部欠損症の診断でドレナージ及び上部腔と腔前庭部を吻合する単純再建術を行なった。【症例2】15歳, 月経歴なし。腹痛を自覚し近医受診。骨盤内腫瘤を認め、腔口は膨隆、貯留した血液が透見され処女膜閉鎖と診断。処女膜切開術を実施された。【症例3】12歳, 初経11歳で月経は順調であった。月経痛や臀部痛が増強するため婦人科受診。MRI で重複子宮, 重複腔, 左腔閉鎖による腔・子宮・卵管留血症を認め、左腎形成不全, 右水腎症もあり OHVIRA 症候群と診断し左腔中隔の開窓術を行なった。【結論】子宮腔留血症は先天性形態異常の種類によって月経発来前にも月経発来後にも生じうる。急性腹症で搬送されるものも多く、思春期女性であり会陰部の診察は躊躇われるが、十分な術前評価が重要であるため慎重な対応が必要であると考えられた。

P-61-1 重症妊娠悪阻罹患中の Refeeding syndrome が原因と考えられる子宮内胎児死亡の2症例

香川大

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【緒言】Refeeding syndrome は、低栄養状態にある患者に急激な栄養補充を行った際、血糖や電解質異常により重篤な合併症をきたす病態である。今回我々は、重症妊娠悪阻患者に発症した Refeeding syndrome と、子宮内胎児死亡の症例を経験したため報告する。【症例】【症例1】29歳、3妊2産。妊娠9週頃より悪阻が出現し、妊娠17週まで外来通院にて補液加療を受けていたが症状改善せず、約2か月間で8.1kgの体重減少を認め、妊娠17週で前医に入院し補液開始となる。入院2日目に低カリウム血症の増悪、低リン血症の出現、歩行困難が出現したため、加療目的に当院に搬送となった。搬送時、腹部超音波検査にて子宮内胎児死亡を認めた。電解質補正と補液を行った後、分娩誘発を行い流産となった。【症例2】34歳、1妊0産。妊娠5週頃より悪阻が出現し、外来と短期間の入院にて補液加療されていたが、症状改善せず、非妊時より20kgの体重減少を認めたため、妊娠20週に再入院となった。補液開始後、低カリウム血症、高CK血症、下肢筋力低下を認め、当院に搬送となった。搬送時の血液検査にて低K血症の増悪、低P血症の出現を認めており、搬送直前の前医での経腹超音波検査で子宮内胎児死亡を認めた。当院で電解質補正と補液を行った後、分娩誘発を行い流産となった。【考察】妊娠悪阻は適切な補液を行い症状が改善する時期を待つことで、児の予後は良好な例が多い。しかし今回、症状が長期化することで重度の電解質異常を引き起こし、胎児死亡に至った2症例を経験した。2症例とも輸液の開始直後に胎児死亡が起きており、Refeeding syndrome が関連した可能性を考えた。

P-61-2 膀胱拡大術後の二分脊椎術後女性の妊娠・分娩管理

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【緒言】近年、膀胱拡大術後の二分脊椎患者における妊娠・分娩例が報告されるようになってきたが、まだその数は少ない。今回我々は、幼少期に膀胱拡大術を施行された二分脊椎術後患者の妊娠・分娩管理を経験したので報告する。【症例】36歳、未産婦。二分脊椎修復術、胃を用いた膀胱拡大術、腸閉塞や尿路感染による複数回の入院加療歴。脊椎係留症候群などの既往がある。凍結融解胚移植にて妊娠し、妊娠初期より当院で管理した。妊娠15週に腎盂腎炎および両側水腎症にて入院、妊娠17週で右、妊娠23週で左に腎瘻を造設した。その後も度々尿路感染症を発症、抗菌薬内服にて加療した。また、ピロリ菌や胃酸による膀胱炎や外陰皮膚炎も認めた。妊娠36週6日に腎盂腎炎にて入院、その後癒着性イレウスを発症したため、妊娠中断の方針とした。分娩様式としては、周辺臓器損傷のリスクが高いことから経膈分娩を目指すこととした。また、緊急手術時の対応について関連各科と事前に綿密な情報共有を行った。妊娠37週4日より分娩誘発を開始したものの、翌日分娩停止し緊急帝王切開を行った。全身麻酔導入後、両側尿管ステントを腎側より留置し手術開始、子宮前面には拡大した膀胱および大きく偏位した尿管を認めた。手術時間は2時間15分、出血量1780ml、児は3092gの男児であった。腸管癒着剝離を行い、膀胱・尿管損傷がないことを確認の上手術を終了した。術後は腹腔内感染および薬剤性の汎血球減少により約1か月の入院加療を要した。【考察】膀胱拡大術後の二分脊椎女性の妊娠・分娩のリスクは高い。関連各科と連携した症例ごとのきめ細やかな管理が必要と考えられた。

P-61-3 当科における様々な場面での遠隔分娩監視装置の活用経験

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【緒言】遠隔分娩監視装置（以下iCTG）は従来型の胎児心拍陣痛計を、超小型化かつ通信機能を持たせたもので、例えば地理的条件などで通院困難な妊婦の為に開発された。当科ではiCTGを6年間にわたり日常的に使用してきた。使用の中で当初の想定を超えた活用場面も出てきた。今回我々はこのような当院での6年間のiCTG活用事例を報告する。【場面1. : 対面診療が困難な状況下で】最近ではもっぱらCOVID-19罹患妊婦に使用してきた。隔離病棟やホテル、自宅で療養する妊婦に貸し出し、自己装着することで、医療者は非対面でモニタリングできる。実際これで異常を発見し、緊急帝王切開を行った事例もある。さらに、罹患産婦の経膈分娩管理にも利用することで、スタッフの長時間の病室内滞在を回避出来た。【場面2. : 院内-外の医療者間での情報共有】例えば時間外のCTG装着時などで、現場担当者が経験の浅い医療者の場合、判読に不安なケースがある。iCTGではデータは全て登録した端末にリアルタイムで送信される為、病院外にいるオンコール医師データを共有し、ディスカッションしたり判断を仰いだりできる。実際このような場面でも、遅滞なく母体搬送の判断が出来た事例がある。【場面3. : 母体搬送中に】母体搬送では原則救急車内でiCTGを使用するようにしている。車内で一過性徐脈を確認した為、到着と同時に情報を提示できた例がある。但し病院間の情報共有システムはまだ十分とは言えない。【結語】当科でのiCTGの活用事例を3つ報告した。他にも活用場面は広がっているが、病院間の連携にはまだ課題も多い。今後iCTGの有効な活用のためシステムを構築し有効に活用されることを望む。

P-61-4 当院におけるジノプロストン腔用剤の使用成績

愛媛大

内倉友香, 中橋一嘉, 井上翔太, 今井 統, 矢野晶子, 宮上 眸, 横山真紀, 松原裕子, 藤岡 徹, 松元 隆, 松原圭一, 杉山 隆

【目的】ジノプロストン腔内留置用製剤は、2020年1月、妊娠37週以降の子宮頸管熟化不全における熟化の促進を効能または効果として承認を取得したプロスタグランジンE2製剤である。当院では、2020年10月よりジノプロストン腔用剤を導入した。今回、当院における子宮頸管熟化不全症例に対するジノプロストン腔用剤と器械的熟化法の臨床成績を後方視的に比較検討した。【方法】対象は、2020年10月から2023年3月までの間に妊娠37週以降の単胎妊娠で、子宮頸管熟化不全に対し当院でジノプロストン腔用剤を使用した46例（腔用剤群）と2019年1月から2023年3月までに器械的熟化法を施行した43例（器械群）を対象とし、後方視的に比較検討を行った。【成績】両群間において患者背景に差を認めなかった。全体の経陰分娩率は両群に差を認めなかったが（腔用剤群 vs. 器械群；50% vs. 58%, $p=0.441$ ）、腔用剤群では陣痛促進剤使用率が低かった（50% vs. 81%, $p=0.004$ ）。特に初産婦では、腔用剤群で促進剤使用率が低く（47% vs. 88%, $p=0.002$ ）、24時間以内に経陰分娩となる割合が高かった（32% vs. 11%, $p=0.031$ ）。また、両群間で新生児予後の差を認めなかった。【結論】ジノプロストン腔用剤の使用は、従来の器械的熟化法に比べ促進剤使用率が低く、特に初産婦において24時間以内に分娩となる頻度が高いことが判明した。ただし、胎児機能不全や頻回の子宮収縮が生じる可能性があるため、使用方法については慎重な管理が必要となる。

P-61-5 遠隔分娩監視装置 iCTG を活用して在宅管理を行った子宮破裂ハイリスクの2症例

亀田総合病院

石川瑞季, 門岡みずほ, 小沼圭祐, 宮崎聖子, 三谷尚弘, 古澤嘉明, 末光徳匡

【緒言】遠隔分娩監視装置 iCTG は在宅で妊婦自身での胎児/子宮収縮（UC）評価を可能とする。我々はハイリスク妊娠、胎児発育不全での在宅管理の有用性を報告したが、今回は子宮破裂ハイリスク例での有用性や課題を報告する。【症例】①34歳4産、帝切既往4回。32週から子宮筋層非薄化と軽度の腹痛を認めるも入院拒否され iCTG で在宅管理とした。測定回数遵守率68%、胎児健康性評価に足る有効データ率80%だった。UC 検出率は全計測中67%だが各々少数で、在宅管理を完遂し35週より管理入院、36週4日に有痛性子宮収縮を認め切迫子宮破裂を否定しえず緊急帝切施行。②26歳1産、帝切既往1回。前回分娩後半年で妊娠し31週で子宮筋層非薄化を認めるも入院は困難で iCTG での在宅管理とした。測定遵守率46%、有効データ率90%、UC 検出率32%であった。36週3日健診時に UC と異なる腹痛を訴え、切迫子宮破裂疑いで緊急帝切施行。ともに筋層の高度な非薄化を認め切迫子宮破裂と最終診断し、児は一過性多呼吸にて NICU 入室するも経過良好で退院した。【考察】子宮破裂は突発的に発生し迅速な診断と治療を要す重篤な産科救急疾患である。切迫状態の兆候には UC 増強、胎児心拍異常、腹痛等があり、iCTG で UC と胎児心拍を客観的に評価し在宅管理を行った。1例目は UC 検出率良好で UC が頻でない旨確認し在宅管理を完遂できた。2例目では育児都合で測定遵守率が低く、在宅管理の恩恵の最大化は困難であった。【結語】子宮破裂ハイリスク例の iCTG 在宅管理には切迫破裂兆候の客観的評価・長期入院回避と医学的/社会的利点がある。患者の遵守に加え、在宅管理特有の早期介入困難など課題があり、症例の選定基準を含めて検討を継続したい。

P-61-6 妊娠高血圧腎症との鑑別を要して娩出時期に苦慮した Mirror 症候群の一例

金沢大

広多見和子, 齊藤実穂, 細野 隆, 鏡 京介, 松岡 歩, 折坂俊介, 山崎玲奈, 藤原 浩

【緒言】胎児水腫に続発し、母体の全身浮腫や肺水腫・胎盤浮腫が発症する場合があります。Mirror 症候群と呼ばれる。今回我々は拡張型心筋症によって胎児浮腫となり、Mirror 症候群を発症した一例を経験し、妊娠高血圧腎症（HDP）様の症状出現から娩出時期の検討に苦慮したため報告する。【症例】30歳1妊0産。自然妊娠し近医で妊婦健診を行っていた。24週3日の健診時、胎児水腫を認めたため当院へ紹介となった。超音波で拡張型心筋症による胎児水腫と診断した。出生しても生命予後は大変厳しいと判断し、ご夫婦と相談の結果、児の発育を見守る方針とした。経過で児の心拍出は徐々に低下し、児の腹水増加・浮腫増強、母体の羊水過多を認めた。妊娠29週頃より母体の異常な体重増加と浮腫が出現し、30週に入ると血圧の上昇と蛋白尿、母体胸水貯留が出現し、HDP の発症様式としては急激な増悪であった。この時のヘマトクリット値は血液の希釈を示しており、Mirror 症候群が鑑別に上がった。母体の状態から妊娠終了が必要と判断し、30週1日に緊急帝王切開術を行った。児は出生後啼泣・体動を認めず、蘇生を試みるも、循環動態確立の見込みがなく、看取りとなった。母体は術後利尿薬等にて治療を行い、症状の改善を認めた。【考察】Mirror 症候群の臨床症状は HDP と類似しているが、HDP と異なり胎児生存率は胎児原疾患を問わず7%と非常に低く救命できない場合が多い。重症例では母体の肺水腫・心不全に至る場合があり、分娩後大出血のリスクも半数弱と高くなっており、胎児の生存が困難な症例では早々に妊娠中断の判断が必要になると思われる。稀な疾患であるが、発症様式や血液検査所見から鑑別することが重要である。

P-61-7 リトドリン塩酸塩の使用を契機に薬剤性横紋筋融解症を発症し筋強直性ジストロフィーが疑われた一例

佐賀大

山口加恵, 山本徒子, 大石将平, 瓜生泰恵, 池田正純, 吉武薫子, 栗原麻希子, 徳永真梨子, 福田亜紗子, 梅崎 靖, 奥川 馨, 横山正俊

【背景】子宮収縮を伴う切迫早産に対して子宮収縮抑制剤を使用する頻度は高いが、副作用の危険が上回る場合もあり適正な使用が求められている。【症例】39歳3妊0産。A病院で顕微授精-胚移植で妊娠成立した。妊娠中期より同じ姿勢を保つと足の動かしづらさが出現した。B病院で妊娠管理し、31週0日に頻回の子宮収縮および頸管長短縮を認め切迫早産の診断でリトドリン塩酸塩の持続静注を開始しC病院に救急搬送となった。救急車内で両上下肢の筋痙攣を認めた。C病院に到着し、血液検査でCK、肝酵素、LDH上昇を認め横紋筋融解症を疑い、当院搬送となった。胎児に明らかな異常はなく、頸管長は14mm、胎児心拍陣痛図では子宮収縮は7回/30分、reassuring fetal statusであった。血液検査ではCK、肝酵素、LDH上昇を認め、尿は褐色尿、ミオグロビン高値を認めた。リトドリン塩酸塩による薬剤性横紋筋融解症と判断した。横紋筋融解症に対しては大量輸液を行った。リトドリン塩酸塩投与前より下肢の筋力低下を疑う病歴があったため筋疾患の精査を行ったが異常所見はなかった。31週5日にCK、肝酵素、LDHは正常化した。切迫早産に対しては安静で経過観察し、33週3日に陣痛発来、骨盤位のため緊急帝王切開を施行した。児は男児、出生体重2134g、Apgar score1分6点、5分8点であった。管理目的にNICU入院となった。産褥経過は良好で産褥6日目に自宅退院となった。児は早産児としての合併症なく経過し、日齢25日(修正37週0日)で自宅退院となった。【結論】リトドリン塩酸塩投与を契機に発症した横紋筋融解症では、筋強直性ジストロフィー等の筋疾患を鑑別にあげることがある。

P-61-8 卵管間質部妊娠に対する子宮温存卵管切除術後に生児を得た一症例

誠光会淡海医療センター

中川渥裕, 十河進仁, 鳥井裕子, 藤城直直, 卜部優子, 卜部 諭

【緒言】卵管間質部妊娠は全卵管妊娠の2.4%程度を占め、母体死亡率は2.25%である。卵管間質部妊娠に対する子宮温存術は線状切開や楔状切除などがあり、胎嚢が4cm未満なら線状切開、4cm以上なら楔状切除が定説である。今回、妊娠週卵管間質部妊娠に対して楔状切除にて子宮温存後に生児を得た症例を経験したので報告する。【症例】30歳、4妊1産で20XX年に左卵管間質部妊娠に対して当院にて左卵管切除術と子宮楔状切除術を施行した。近医にて不妊治療を継続し体外受精(IVF-ET)で妊娠成立し、子宮切開術後であるため当院での妊娠分娩管理を希望し紹介受診となった。妊娠経過は34週より周期的な腹痛を訴え、切迫早産の診断で入院安静管理となるが、その後症状は出現せず、妊娠37週での予定帝王切開術の方針となった。帝王切開術中所見は子宮菲薄化した箇所は認めず、定型通りの帝王切開術を行った。手術時間：時間分、出血量820mL、胎児は男児で体重3454g、Ap8/8、臍帯血pH7.402であった。術後経過は良好で術後7日目に退院となった。【結語】卵管間質部妊娠後に生児を得た症例を経験した。文献的考察を交えて発表する。

P-61-9 胎児母体間輸血症候群による子宮内胎児死亡の1例

洛和会音羽病院

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【緒言】胎児母体間輸血症候群(FMT)は、分娩前または分娩中に胎児血液が母体血液中に流入して発症し、胎児水腫、子宮内胎児死亡や重篤な後遺症の原因となる。厚生労働省の人口動態調査において2021年の満22週以降の死産2231例のうち胎児失血によるものは60例(2.7%)と報告されているが、既報では死産のうちFMTの頻度は1.13%と報告されており、原因不明の死産の中にもFMTが含まれる可能性がある。今回、特に誘因なく発症したFMTによるとみられる子宮内胎児死亡の症例を経験したので文献的考察を加えて報告する。【症例】31歳、G1P0。自然妊娠し妊娠経過は良好であった。妊娠32週の前医での妊婦健診では特に異常を指摘されなかった。妊娠33週頃に胎動減少を自覚し、妊娠34週2日に妊婦健診のため当院を紹介受診した際、胎児心拍が停止しており子宮内胎児死亡と診断した。児推定体重は1867g(31週5日相当)であった。破水や性器出血、腹痛、発熱はなく、超音波検査および血液検査において胎盤早期剝離、凝固異常、感染を示唆する所見はなかった。胎児水腫以外の胎児形態異常は指摘し得ず、不規則抗体は陰性であった。同日より分娩誘発を開始し、7日目に経陰分娩に至った。胎盤に肉眼的血腫はなく、病理組織診で絨毛内血腫を認め絨毛内胎児血管の破綻が示唆された。入院時に採取した母体血でヘモグロビンF5.2%、AFP9220ng/mlと高値であり、FMTによる子宮内胎児死亡と考えられた。【結語】血液検査結果から胎児死亡の原因を鑑別したことによって、今回の病態や今後の再発等について患者へ情報提供することができた。子宮内胎児死亡の原因検索において、ヘモグロビンFおよびAFP測定は有用である。

P-61-10 周産期心筋症の2例

長野赤十字病院

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周産期心筋症は心疾患の既往のない妊産婦が心不全を呈する疾患である。妊娠高血圧症候群に合併した周産期心筋症の2例を報告する。【症例1】34歳, 14妊8産, 喫煙者, 36週3日の健診時に妊娠高血圧腎症と診断されたが, 本人の希望で帰宅した。翌日呼吸苦で救急搬送され, SpO₂低下と胸部レントゲンで心拡大と肺水腫を認め, 全身麻酔下で緊急帝王切開を行った。術後, 心臓超音波でEF32%の左室壁運動低下を認め, 周産期心筋症による急性心不全と診断した。循環器内科による治療で心機能は改善し産褥12日で退院した。【症例2】41歳, 1妊0産, 29週から37週の間で13.8kgの体重増加と浮腫を認めた。37週2日尿蛋白陰性だが高血圧を認め妊娠高血圧と診断した。翌日から分娩誘発したが分娩に至らなかった。39週0日自然陣痛発来したが, 胎児機能不全のため緊急帝王切開を行った。術後1日目に重症域高血圧を認め硫酸マグネシウムを投与した後, 呼吸苦が出現し, 酸素需要は最大9Lまで上昇した。胸部レントゲンで心拡大と胸水貯留, 心臓超音波でEF45%の左室壁運動低下を認め, 周産期心筋症による急性心不全と診断した。循環器内科による治療で心機能は改善し産褥14日で退院した。妊娠中の体重増加, 浮腫, 息切れなどは健常妊婦も自覚する症状であり, 病的と捉えず診断が遅れがちである。今回の2症例では早期に周産期心筋症の可能性を考慮し心機能の評価を行なっていればより早期から適切な管理が出来ていた可能性がある。周産期心筋症は比較的稀な疾患だが急激に増悪し母体死亡に至る可能性があり, 疑わしい症状を認める場合は周産期心筋症を鑑別に挙げ早期に心機能を評価することが重要である。

P-61-11 生児を獲得したが出生後臨床的侵入奇胎となった胎児共存奇胎の一例

岡山大

谷 和祐, 末森彩乃, 中藤光里, 大羽 輝, 三苦智裕, 三島桜子, 大平安希子, 桐野智江, 牧 尉太, 衛藤英理子, 増山 寿

【緒言】胎児共存奇胎とは, 子宮内に正常胎児と全胎状奇胎とが双胎として発生し, 発症頻度はおよそ10万妊娠に1例と非常に稀である。妊娠高血圧症候群や出血, 早産といった周産期合併症だけでなく存続絨毛症のリスクも高くなる。今回我々は妊娠32週で生児を獲得したが出生後臨床的侵入奇胎となった胎児共存奇胎の一例を経験したので報告する。【症例】34歳, G3P2, 自然妊娠成立後近医受診, 胎児共存奇胎疑いで妊娠12週に当院紹介となった。初診時の血中hCGは456323mIU/mLと高値であり, 超音波検査で正常胎児と胎盤と嚢胞性胎盤を認め胎児共存奇胎と診断した。妊娠継続によるリスクについて十分なインフォームドコンセントを施行したが妊娠継続を希望された。妊娠15週に羊水検査施行, 46, XXで正常核型であった。妊娠31週5日に頸管長短縮, 性器出血を認め切迫早産で入院管理となった。tocolysisを施行するも前期破水となり, 陣痛発来し妊娠32週2日に経陰分娩となった。児は1405gの女児, Apgar Score8点/9点であった。胎盤病理結果より胎児共存全胎状奇胎の診断となった。分娩後5週で血中hCG3619mIU/mL, CTにて多発肺転移を指摘。絨毛癌診断スコア0点, FIGO Scoring2点で臨床的侵入奇胎の診断でアクチノマイシンDによる化学療法を施行中である。【考察】胎児共存奇胎は合併症のリスクが高く重症な周産期管理を要するが, 生児を得られる可能性もある。また統発症としては臨床的侵入奇胎が多く, 化学療法により寛解率・生存率も高い。妊娠・分娩後についての十分なインフォームドコンセントが必要ではあるが, 妊娠継続も選択肢の一つとなると考えられる。

P-61-12 虫垂子宮内膜症の癒着が子宮復古により牽引され急性腹症, 多量の腹腔内出血を来した産褥早期の一例

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【緒言】子宮内膜症の開腹手術時, 子宮後面の癒着剥離はその視野確保の困難さから, しばしば用手的に行われる。また, 産褥子宮は大きく柔らかいため腹腔鏡下の子宮後面の視野の確保は困難な場合が多い。産褥早期の急性腹症に対して審査腹腔鏡を行い, 虫垂と子宮の癒着が子宮復古により牽引され自然剥離し, 術中大量出血した症例を報告する。【症例】3回経産婦, 産科クリニックで自然経陰分娩し, 産褥5日に退院。退院当日, 急性腹症のため夜間急病センターを受診。造影CTでは肝周囲まで広がる多量の腹腔内出血を認め, 絞扼性イレウスまたは卵巣出血として当科へ救急搬送された。子宮は超乎拳大で多量の腹腔内出血と右付属器周囲に圧痛を認めた。産褥早期の卵巣出血は考えにくく, 外科と相談し絞扼性イレウスとして審査腹腔鏡を行った。腹腔内にはすでに約1000mLの出血を認め, 絞扼性イレウスの所見はなかった。子宮背面右側に凝血塊が多量に付着しており卵巣出血が疑われたが, 右卵巣からの出血はなく卵管の癒着もごく軽度であった。しかしながら, 右仙骨子宮靭帯付近に虫垂が索状に癒着しており, 子宮復古により牽引されて一部自然剥離し出血していた。ここが今回の出血点および腹痛の原因と考えられた。出血と大きな産褥子宮のため視野確保が困難な中, 虫垂の癒着剥離を試みた。途中突然湧き上がるような出血を認め, 止血困難と判断し緊急開腹手術へ移行した。圧迫止血しながら子宮広間膜内を展開し, なんとか止血した。その後虫垂を摘出して閉腹した。術後の病理結果は虫垂子宮内膜症の診断であった。【結語】産褥早期の急性腹症, 腹腔内出血として牽引による癒着剥離と虫垂子宮内膜症を経験した。

P-61-13 妊娠12週に子宮筋腫表在血管破綻により発症した Spontaneous hemoperitoneum in pregnancy (SHiP) の一例

鹿児島市立病院

齋藤もとみ, 中村俊昭, 三浦美沙, 前田隆嗣, 谷口博子, 切原奈美, 上塘正人

【緒言】Spontaneous hemoperitoneum in pregnancy (SHiP) は妊娠中から産褥期における非外傷性の急性腹腔内出血であり、早産、周産期死亡、母体死亡のリスクとなる重要な疾患である。既存の報告では子宮内膜症からの出血が多い。今回我々は子宮筋腫表在血管が破綻し、SHiPを発症した症例を経験したため報告する。【症例】33歳、未妊、検診目的で前医を受診し子宮前壁に最大径10cm大の筋層内筋腫を認めた。手術目的で当院を紹介受診され、偽閉経療法のち手術予定としたが自然妊娠した。妊娠12週2日に下腹部痛を主訴に前医を受診し子宮筋腫変性痛の診断で入院管理を開始したが、妊娠12週4日に症状持続と炎症反応上昇のため当院に搬送された。来院時、下腹部全体の反跳痛と圧痛、血圧低値(78/48mmHg)、貧血の進行(Hb9.1mg/dL)、炎症反応高値(WBC16900/μL、CRP3.84mg/dL)を認めた。経腹超音波断層像およびコンピューター断層造影像にて最大径16cm大に腫大した子宮筋腫と大量の血性腹水を確認した。出血点が不明であったため腹腔内大量出血による出血性ショックの診断で試験開腹術を施行した。腹腔内に大量の血腫を認め、子宮筋腫表面表在血管が破綻し静脈性に出血していたためこれを縫合止血することで止血を得た。血腫を含む術中出血は2660mlであった。術後は再出血なく経過し術後15日で自宅退院とした。【考察】子宮筋腫表在血管の破綻によるSHiPはまれである。症状のみでは子宮筋腫変性痛と判別が困難であるが初期対応の遅延が生命予後に影響する可能性もあり、経腹超音波断層像で腹水の有無や貧血を確認することはスクリーニングとして重要である。

P-62-1 脛体部痛に対して脛体尾部切除術後に妊娠糖尿病を発症した一例

伊勢赤十字病院

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【緒言】脛切除術後はインスリン分泌能の低下により耐糖能異常が生じ得る。今回、脛体部痛に対して脛体尾部切除術後に妊娠糖尿病を発症した一例を経験したので報告する。【症例】39歳、1妊0産。37歳時に脛体部粘液嚢胞腺癌 StageIIA に対して脛体尾部切除術+幽門側胃切除術を施行された。術後補助化学療法としてS-1療法(テガフル、ギメラシル、オテラシルカリウム)を1年間行い、再発なく経過した。術後2年で自然妊娠成立した。推定胎児体重が+2.3SDと在胎不当過大のため、妊娠29週に75g経口ブドウ糖負荷試験を行い、空腹時血糖78mg/dl、1時間後血糖187mg/dl、2時間後血糖75mg/dlの結果であり、妊娠糖尿病と診断した。食事指導を行い、血糖、HbA1cは正常値で経過した。妊娠40週1日に妊娠糖尿病、分娩予定日超過のため、分娩誘発目的に頸管拡張を開始した。妊娠40週2日に非重症妊娠高血圧症、頸管熟化不全のため、帝王切開術にて分娩となった。新生児所見は男児、出生時体重3565g(1.26SD)、Apgar score 1分値8点(皮膚色-2点)/5分値9点(皮膚色-1点)、臍帯動脈pH7.306であった。全身状態良好であり、特別な処置は必要としなかった。産褥母体は血圧正常となり、高血糖なく推移した。産褥79日目の75g経口ブドウ糖負荷試験は正常型であったが、血圧は正常高値が持続している。次児妊娠希望があるため、耐糖能や血圧管理を継続している。【結語】脛切除術後は耐糖能が低下し、妊娠糖尿病の発症リスクは上昇すると考えられる。今後は次回妊娠に向けて、脛癌再発、血圧、耐糖能に関してインターコンセプションケアが重要である。

P-62-2 骨髓異形成症候群合併妊娠

伊勢赤十字病院

村上菜々子, 日下直子, 若林慧美里, 萩元美季, 紀平知久, 奥川利治, 田中浩彦, 前川有香

【緒言】特発性血小板減少性紫斑病(以下ITP)は、妊娠中に比較的良好に経過するが、除外診断であることから、最初の診断が修正される場合がある。今回、第一子妊娠時にITP合併妊娠と診断されたが、第二子妊娠中に骨髓異形成症候群(MDS)が疑われ、産後に行った骨髓検査の結果MDSと診断された症例を経験したので報告する。【症例】37歳、3妊1産、第一子妊娠時にITP、2型糖尿病と診断された。第二子を自然妊娠し、ITPおよび2型糖尿病合併妊娠のため妊娠初期より当院で血液内科・糖尿病内科と併診した。妊娠16週よりインスリン自己注射を開始し、血糖コントロールは良好であった。血小板数は妊娠20週で2.8万と減少し、プレドニン(PSL)内服を開始した。しかしPSLを増量しても血小板数は増加せず、大球性貧血も併発、白血球数も減少し、造血障害が疑われた。MDSを疑い、分娩時には免疫グロブリン大量療法は行わず、分娩直前の血小板輸血に対応し、産後に骨髓検査を施行する方針とした。妊娠37週1日に自然破水したため、濃厚血小板30単位を輸血し、血小板数が7万と改善した状態で経陰分娩に至った。新生児の血小板数は正常であった。産後6日目に骨髓検査を行い、MDS(WHO分類MLD、IPSS-R:3 low risk)の診断に至った。【結語】第一子妊娠時にITPと診断されていたため、第二子妊娠中も当初はITPとして治療していたが、治療効果がなく、汎血球減少がみられたことからMMDSを疑った。MDSは妊娠中に増悪するが、産後は自然に改善している。しかし、IPSS-Rによる予後評価はlow riskでも無治療での生存期間中央値は5年程度であり、今後も血液内科で慎重な管理が必要である。

P-62-3 妊娠中の深部静脈内血栓症を契機に先天性 AT 欠乏症の遺伝子診断に至った家系

近畿大

黄 彩実, 川崎 薫, 城玲央奈, 森内 芳, 葉 宜慧, 松村謙臣

【緒言】先天性アンチトロンビン (Antithrombin: AT) 欠乏症は常染色体優性の遺伝疾患である。妊娠中は血栓塞栓症、流死産、胎児発育不全を発症することもある。悪阻による脱水と安静に起因する深部静脈血栓症を契機に先天性 AT 欠乏症の遺伝子診断に至った症例を報告する。【症例】24 歳初産、既往歴なし。妊娠 8 週右鼠径部痛と右下肢腫脹を認め、紹介となった。血液検査では D タイマー上昇 (46.0ug/mL) と AT 活性低値 (58%) を認めた。下肢超音波検査にて右外腸骨から総腸骨静脈に血栓を認め、深部静脈血栓症と診断した。実母に妊娠中の AT 低下を伴う深部静脈血栓症の既往があることより先天性アンチトロンビン欠乏症と考え、未分画ヘパリン静脈内持続点滴 (目標 APTT1.5-2.5 倍) と ATIII 製剤 (目標活性 \geq 70%) による抗凝固療法を行った。妊娠 15 週下肢超音波検査にて血栓の縮小を認め、未分画ヘパリンは皮下注射 (10000 単位/日) とした。妊娠 26 週血栓は消失した。妊娠 40 週陣痛発来し、AT 活性 80% 以上を目標に AT 補充を行った。同日経陰分娩に至り、出血量は 340g であった。新生児に AT 活性低下を認めなかった。分娩後に未分画ヘパリンはワーファリンに置換し、PTINR 目標達成後 AT 補充は終了した。周産期管理と同時に先天性 AT 欠乏症に関する遺伝カウンセリングを行い、実母は遺伝子検査にて AT 分子の構造異常に影響する SERPIN1 遺伝子変異が検出された。本人は分娩後に遺伝子検査を行い、同様の異常を認めた。【結論】家族歴に関する詳細な問診により親子の先天性 AT 欠乏症の遺伝子診断に至った。

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P-62-4 短腸症候群合併妊娠の 2 例

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後藤清美, 豊福一輝, 林下千宙, 小山尚子, 穴井麻友美, 内田今日香, 川野道子, 中村恭子, 佐藤祐輔, 広瀬奈津子, 杉山佳歩, 高尾圭純

【はじめに】短腸症候群は、様々な理由で小腸の大量切除が必要となり残存小腸が短くなってしまったために栄養の吸収が障害された状態である。腸管からの吸収で栄養素を十分に摂取できないため、早期から中心静脈栄養が必要となる。妊娠中は必要な栄養素量が増加するため、本症を有する妊産婦は母体の全身状態や胎児推定体重を確認しながら適宜カロリー調節が必要となる。さらに、病態により周産期合併症の併発にも注意していく必要もあり慎重な管理が要される。今回、妊娠・出産に至った短腸症候群の 2 例を経験したので報告する。【症例①】28 歳, G1P0。慢性特発性偽性腸閉塞症 (CIIP) の診断で中学生時に大量小腸切除を施行されている。自然妊娠成立し、かかりつけ当院小児外科より紹介受診。カテーテル感染を 4 回発症し入院加療が必要であったが、妊娠経過は良好であった。妊娠 37 週時に選択的帝王切開術施行。2941g の女児を出産した。術中出血量 2550g。compression suture とバクリバルーン併用止血を行った。術後 1 か月に子宮切開創部の壊死を疑う所見を認めたが抗生剤投与のみで症状軽快し、以後の経過は良好である。【症例②】22 歳, G1P0。腸管神経節細胞僅少症の診断で 1 歳より在宅中心静脈栄養法管理を受けている。自然妊娠成立し、当科紹介受診。妊娠経過、胎児発育は順調であった。妊娠 38 週に分娩誘導を行い、経陰分娩に至った。児は 2830g の女児であった。出産後経過良好で産褥 5 日に母児共に退院した。【結論】短腸症候群合併妊娠は栄養状態の影響で不妊症となりやすく、さらに妊娠中も胎児発育不全等の合併症を起こしやすいが、妊娠前からの慎重な栄養管理により良好な周産期予後を期待できる。

P-62-5 新規乳癌治療に応じて管理した妊娠期乳癌の一例

聖マリアンナ医大

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【目的】近年、新規抗がん剤が次々に開発され臨床応用が進み、化学療法の選択肢が変化している。今回我々は、乳癌における化学療法が変化している中で妊娠期乳癌症例を経験したため報告する。【症例】34 歳 4 妊 2 産。既往歴特記事項なし。自然妊娠成立後、近医で妊婦健診を施行していた。右乳房腫瘍感を自覚したため、妊娠 28 週 5 日、精査目的に当院乳癌外科受診となった。精査の結果、右乳癌 (Triple Negative type) cT2N0Mx, StageIIA 相当の診断となった。妊娠 32 週 1 日、周産期管理目的に当科紹介となった。当院受診時には腫瘍径は 3cm 大であったが、2 週間後には 6cm 大に増大し、早急な治療が必要であったため、妊娠 32 週 5 日に AC 療法が開始された。その後、産婦人科および乳腺外科で協議を行い、病状が急激に増悪しており術前化学療法として TC 療法+ペムプロリズマブが最良の治療であるため、ターミネーションが必要という結論に至った。さらに新生児科と協議を行い、分娩後の新生児対応についての体制を整え、妊娠 36 週 0 日に分娩誘発の方針となった。妊娠 36 週 0 日、経陰分娩となり、児は男児、出生体重 2632g, Apgar score8/9 であった。分娩後すぐに妊娠中施行困難であった乳癌の追加精査を行った。産褥 4 日目退院となり、退院後 9 日目に TC 療法+ペムプロリズマブが開始され、現在乳癌治療が継続中である。【結論】既存の文献では妊娠中に比較的安全に使用できる AC 療法を行い、妊娠 37 週を待つことが望ましいと考えられてきたが、ペムプロリズマブの出現により再検討の時期に至ったと考えられる。今後、最新の知見をもとに、母児にとって最良の分娩時期ならびに方法の検討が必要と考えられる。

P-62-6 脈管病変が広範囲にわたり帝王切開術の開腹操作に工夫を要したクリッペル・トレノネー・ウェーバー症候群合併妊娠の1例

熊本大病院

前田菜々, 岩越 裕, 山元康寛, 岸本かおり, 小寺千聡, 田山親吾, 大場 隆, 近藤英治

【緒言】 Klippel-Trenaunay-Weber 症候群 (KTWS) は広範囲にわたる混合型脈管奇形や軟部組織、骨の肥大を特徴とし、妊娠例では病勢の増悪や血栓塞栓症、分娩時の大量出血が問題となる。今回我々は、腹壁に広範囲の脈管病変がみられ、帝王切開術の開腹操作に工夫を要した KTWS 合併妊娠の一例を経験したため報告する。【症例】 39 歳 1 妊 0 産、小児期より同疾患と診断され、4 歳で右大腿切断術が施行された。今回タイミング法により妊娠成立し、妊娠 6 週に当科紹介となった。診察では右半身の下半部腹壁から腰部、臀部、外陰部まで広範囲に脈管病変が認められ、経膈分娩時に外陰部の病変を損傷し大量出血をきたす恐れがあることから、分娩は帝王切開術の方針とした。妊娠中の抗凝固療法は希望されず、定期的な凝固検査のフォローが行われた。妊娠 33 週の骨盤部 MRI 検査では、妊娠前と比較し下腹部腹壁の病変が右側から正中を超えて一部左側まで進展していた。通常の正中切開では病変の損傷による大量出血が予想され、病変を避けて正中より 1 横指左側で下半部縦切開を行う方針とし、妊娠 37 週に全身麻酔下での帝王切開術を施行した。切開創右側の皮下、脂肪層、筋膜付近に脈管病変が集簇しており、バイポーラーで焼灼止血しながら開腹操作を進め、単回使用開創器を用いて腹壁を圧排止血しつつ術野を確保した。その後の操作は問題なく終了し、出血量は 265g で児は 2285g であった。分娩後は抗凝固療法を 4 週間継続し、血栓形成はみられなかった。【結論】 腹部の脈管病変が正中を跨ぐ KTWS 合併妊娠の帝王切開術では、脈管病変の正確な評価と詳細な手術方法の検討が術中出血量の軽減に寄与することが示唆された。

P-62-7 呼吸器症状が妊娠の影響で見過ごされ、出産後にリンパ脈管筋腫症を疑った1例

亀田総合病院

小沼圭祐, 門岡みずほ, 小林美弥香, 石川瑞季, 竹沢亜美, 安田幸矢, 網師本健佑, 宮崎聖子, 三谷尚弘, 末光徳匡, 古澤嘉明

【緒言】 リンパ脈管筋腫症 (lymphangiomyomatosis : LAM) は、平滑筋様の腫瘍細胞 (LAM 細胞) が増殖し、肺などに多発性嚢胞を形成する緩徐進行性かつ全身性の腫瘍性疾患であり、結節性硬化症を伴う遺伝性の場合もある。妊娠可能年齢の女性に好発し、肺病変による呼吸困難感や自然気胸を契機に診断されるが、その病勢にはエストロゲンの関与が推測され、妊娠が病態を増悪させるとされる。また、30% 以上で合併するとされる腎血管筋脂肪腫 (AML) は妊娠中に増大、破裂のリスクがある。今回、労作時呼吸困難が妊娠の影響で見過ごされ、出産後に LAM を疑った1例を経験したので報告する。【症例】 33 歳 3 妊 2 産、既往歴なし。妊娠 34 週で当院紹介。妊娠経過順調で妊娠 39 週 3 日に無痛計画分娩で入院した。入院時に SpO₂ 93% と酸素化低下を認め、妊娠中期から労作時呼吸困難があるも妊娠の影響と考え申告していなかったと判明した。胸部単純写真で両側下肺野に粒状影を認めたが、慢性経過で症状も軽微であり分娩方法の変更を要す急性疾患ではないと判断し、結核等を考慮し感染対策を行い同日経膈分娩に至った。翌日の胸部 CT にて、両側肺野びまん性に境界明瞭な薄壁を有す嚢胞を認め、LAM が強く疑われ気管支鏡生検にて今後確定診断予定である。【考察】 呼吸困難感健康常妊婦でも認める症状で併存疾患が見逃される可能性がある。LAM は妊娠による増悪、気胸合併リスクがあり、AML 合併例では破裂リスクも有するため、妊娠/出産前の診断が望ましい。本症例のように呼吸器症状が妊娠により見過ごされる危険があり、患者、医療者ともよくある症状と安易に考えず、疾患を有す可能性も考慮し、慎重な問診や評価を行うことが重要である。

P-62-8 妊娠中の尿路結石性疼痛に対してフェンタニルの使用を要した一例

市立三次中央病院

藤田真理子, 西本祐美, 張本 姿, 熊谷正俊

【緒言】 妊娠による腹部増大や尿路結石により水腎症を呈する妊婦はまれではない。多くは軽症であり、補液や鎮痛薬によりコントロール可能である。しかしコントロール不良の疼痛や尿路感染、切迫流早産を合併すると臨床的に問題となる。今回我々は妊娠中に発症した尿路結石により激しい疼痛が遷延し、最終的にフェンタニルを使用して疼痛コントロールを行った症例を経験したので報告する。【症例】 26 歳、3 妊 2 産。第 1 子を 35 週で早産、第 2 子妊娠中に右尿管結石の既往あり。妊娠 28 週に背部痛を主訴に受診し、左尿管結石と左水腎症を認めたため入院加療した。アセトアミノフェン、ペンタゾシン、ブチルスコポラミンを使用するも耐え難い背部痛が持続し、嘔吐、子宮収縮も認め管理不良であった。D-J 尿管ステントを留置し、一時改善したがステントによる膀胱刺激症状が強引に抜去した。症状は再燃し、疼痛管理目的に緩和ケア内科に相談し十分なインフォームド Consent の上、妊娠 31 週からフェンタニル持続皮下注を開始し、3mg/日まで漸増して痛みは緩和した。フェンタニル貼付剤 10mg に切り替え、以降はアセトアミノフェンの併用により外来での疼痛管理が可能となった。切迫早産に対してリトリン塩酸塩の内服を行っていたが、妊娠 35 週 2 日に陣痛発来し 2175g の男児を出産した。新生児薬物離脱症候群は認めなかった。産後はロキソプロフェンとアセトアミノフェンで疼痛管理出来たため、フェンタニル貼付剤は漸減し、産後 6 日目に中止した。結石は産後 14 日目に自然排石された。【結語】 疼痛コントロール不良の妊娠中の尿路結石に対してフェンタニルの使用が有効であった。

P-62-9 エクリズマブ投与し分娩に至った発作性夜間ヘモグロビン尿症 (PNH) 合併妊娠の1例

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【緒言】発作性夜間ヘモグロビン尿症 (paroxysmal nocturnal hemoglobinuria: PNH) は血管内溶血を主徴とする造血幹細胞疾患であり, PNH 合併妊娠では血栓症や出血や貧血, 流産, 死産などのリスクが大きく慎重な管理を要する。今回 PNH 合併妊娠に対し, エクリズマブ (Ecu) 投与と赤血球・血小板輸血を行い, 有害事象の発生なく管理した症例を経験したので報告する。【症例】25歳, ベトナム人, 1妊0産。自然妊娠。既往歴・家族歴なし。妊娠初期の検査で汎血球減少を認め, 妊娠20週, 当院血液内科・産科を受診した。Hb8.1g/dL, 血小板5.3万/ μ Lと血球減少を認めた。腎機能低下や葉酸欠乏は認めなかった。妊娠24週, CD55・CD59欠損血球を認めPNHと診断した。赤血球・血小板とも輸血依存であり, 輸血を行いながら妊娠31週よりEcu投与を開始した。溶血所見はやや改善したが輸血依存状態が持続した。下肢超音波検査とDダイマーで血栓症を否定した。妊娠39週1日, 陣痛発来。分娩前に血小板20単位を輸血し分娩に至った。児は3194g男児, UApH7.30で全身状態は良好。分娩時の出血量は378gだった。産褥1日よりヘパリン投与を開始し, その後ワルファリン内服に変更した。産褥5日に母児共に経過良好で退院した。その後もEcuの投与と輸血, 抗凝固薬の調整を行い, 有害事象なく経過した。【考察】産科・血液内科の連携によりPNH合併妊娠に対し分娩前よりEcuを投与し, 重篤な合併症なく分娩することができた。Ecu投与による溶血の抑制と輸血・抗凝固療法が効果的であったと考えられる。

P-62-10 Evans 症候群, 抗リン脂質抗体症候群合併妊娠の一例

岡崎市民病院

青山 章, 森田剛文, 榎原尚敬, 吉川麻里奈, 木村真梨子, 根井 駿, 河井啓一郎, 井土琴美, 白崎茉莉, 野坂和外, 後藤真紀, 榎原克巳

【緒言】Evans 症候群は, 突発性血小板減少性紫斑病 (ITP) に自己免疫性溶血性貧血 (AIHA) を合併する病態である。今回我々は Evans 症候群および抗リン脂質抗体症候群合併妊娠の周産期管理を経験したので報告する。【症例】39歳, 1妊0産。既往にIgA 血管炎, Evans 症候群, 多発性脳梗塞, 脾梗塞, 腎梗塞, 心筋梗塞を発症した際に発覚した APS, また子宮頸部高度異形成に対し円錐切除術がある。ワルファリン内服を行っていたが, 凍結融解胚移植にて妊娠成立し, ヘパリン注射に切り替えた。また, PSL3mg/日内服を行っていた。妊娠30週 EFW1229g (-1.5SD) と asymmetrical FGR を認めた。その後も FGR はあるが発育は認め, その他特記事項認めなかった。妊娠36週低用量アスピリンの内服は中止した。妊娠39週 EFW 2274g (-2.2SD) UAPI 1.07, MCAPI 0.997 と発育は認めたが brain sparing を認め, 妊娠40週2日に誘発分娩の方針とした。しかし誘発中に胎児徐脈を繰り返したため, 帝王切開術の方針とした。出生児は Ap8/9, 体重2446gであった。術後経過は問題なく, 術後1日よりヘパリン再開とし, 術後6日目で退院とした。【考察】周産期管理において Evans 症候群は血小板減少や貧血の進行, 治療としてのプレドニゾン投与による感染症のリスクなど注意を要する。また APS は抗凝固療法を行うため出血のリスクがあり同様に注意を要する。今回の症例はあらかじめ合併していることが分かっており, 当初から血液内科と連携して妊娠管理を行い, FGR は認めたものの, 重篤な合併症のない経過で管理を行えた。また, 今回の症例では Evans 症候群や APS と FGR の関連は明らかではなかった。【結語】Evans 症候群および抗リン脂質抗体症候群合併妊娠の一例を経験した。

P-62-11 大理石骨病合併妊娠の一例

奈良県立医大附属病院

脇 啓太, 赤坂珠理晃, 上林潤也, 樋口 渚, 日野友紀子, 前花知果, 山中彰一郎, 牧野佑子, 市川麻祐子, 川口龍二, 木村文則

大理石骨病は, 破骨細胞の機能不全による骨吸収障害により, びまん性の骨硬化を呈する症候群である。破骨細胞の形成や機能に関連する複数の遺伝子異常が原因とされている。破骨細胞機能不全をもたらす原因は多相であるため, 遺伝的異質性の高い疾患であり, 症状も早期に発症する重症の新生児型/乳児型, 中等度の中間型, 軽症の遅発型まで多様である。未熟骨の成熟への置換が障害される結果, 骨は硬化しているにもかかわらず脆い。また, 過剰な未熟骨は骨髓腔の狭小化をもたらし, 骨髄機能不全(貧血, 易感染性, 出血傾向, 肝脾腫など)を引き起こす。頭蓋底の骨肥厚による脳神経症状(難聴, 視力障害, 顔面神経麻痺)を呈することもある。現在国内での患者数は約100人と稀な疾患である。今回我々は, 大理石骨病合併妊娠の一例を経験したため報告する。症例は39歳1妊0産。25歳時に健康診断の胸部レントゲンで骨硬化像を指摘されたことを契機に大理石骨病と診断された。兄も大理石骨病を指摘されている。36歳時に変形性股関節症で手術治療の既往がある。顕微鏡精で妊娠成立し, 周産期管理目的に当院を紹介受診された。股関節手術に伴う股関節の開排制限と大理石骨病による病的骨折リスクを勘案し, 分娩は帝王切開の方針とした。妊娠経過に特記異常はなく経過した。妊娠37週1日に前期破水および骨盤位の診断で緊急帝王切開となった。出生児に明らかな異常は認められていない。術後経過も良好であり, 通常退院された。大理石骨病は症例数も限られており, 分娩様式や妊娠管理について一定の見解はない。前もって妊娠中や分娩のリスクについて話し合い, 方針決定していくことが重要である。

P-62-12 妊娠後期に心不全症状をきたし、変性性僧帽弁閉鎖不全症による慢性心不全の急性増悪と診断した一例

総合病院土浦協同病院

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【緒言】変性性僧帽弁閉鎖不全症は重症の僧帽弁閉鎖不全症に最も多い原因であるが、若年女性において発症することは珍しい。妊娠後期に未指摘の慢性心不全の急性増悪をきたした症例を経験したので報告する。【症例】29歳, 1妊0産。既往歴は特になく、凍結融解胚移植で妊娠成立し、一絨毛膜二羊膜双胎の診断で妊娠9週4日に当科を紹介受診した。妊娠経過中に血圧の上昇は認めなかったが、妊娠34週から下腿浮腫と臥位で増悪する呼吸苦と咳嗽が出現した。妊娠35週2日に1週間で3kgの体重増加と全身の浮腫、蛋白尿、胸部レントゲンで胸水貯留を認めたため、管理目的に入院した。妊娠35週3日に努力様呼吸を認め、SpO₂が90%まで低下し、乏尿をきたしたため緊急帝王切開術を施行した。術中もSpO₂の低下が持続し、酸素投与を要した。術後の経胸壁心臓超音波断層法で僧帽弁の形成不全による重度僧帽弁逆流と左室駆出率の低下を認めた。変性性僧帽弁閉鎖不全症の所見であり、慢性心不全の急性増悪と判断し、強心薬や利尿薬を投与し治療に当たった。術後4日目には強心薬と利尿薬の投与を終了し、経過良好で術後7日目に退院した。以降症状の再燃なく経過しており、今後は僧帽弁閉鎖不全症に対する手術を検討している。【考察】産褥期の心不全症状をきたす原因には妊娠高血圧症候群に伴う肺水腫や周産期心筋症があるが、本症例のように背景に心臓弁膜症が認められる場合がある。妊娠中・産褥期の心不全症状の出現は母子共に生命に関わるため、適切な診断と迅速な治療介入が必要である。

P-63-1 感想レポートの計量テキスト分析から大学生プレコンセプションケア講義のあり方を考える

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【目的】プレコンセプションケア（以下プレコン）の導入が望ましい年齢層へのリテラシー向上を目的に、当該地域の非医学系大学生（以下大学生）を対象にプレコンの講義を実施した。講義終了後に提出された感想レポートの計量テキスト分析のデータから、今後の講義のあり方を検討した。【方法】上述の大学生カリキュラム「予防の医学」において、日本思春期学会性教育認定講師資格を有する産婦人科医より、プレコン概論、月経困難症、デートDV、子宮頸がんワクチンなどのテーマに基づいた90分間の講義を実施した。学生は3形式（A：本会場、B：サテライト、C：動画視聴）のいずれかで聴講し、感想レポートを自由記載形式でGoogle Formsにて提出した。レポートをもとにKHCoderで計量テキスト分析を行い、大学生における講義の理解や当事者意識について、性別や講義形式による差の有無を解析し、講義のあり方を考察した。【成績】A151名、B151名、C219名の計521名が聴講し、全体の性差は男性51.8%、女性47.6%、回答せざるが0.6%であった。レポート文字数はA>B>Cの順で有意に多く、女性が男性より有意に多かった。会場別にはA、BともにCより「感情」「知識」「当事者意識」に関連する語句の出現頻度が有意に高かった。性差別の出現頻度の特徴として、女性において「月経」「ワクチン」「子宮頸がん」といったより具体的な語句が多く出現していた。【結論】大学生の感想レポートにおける計量テキスト分析データから、プレコンの講義形式としてリアルタイム（本会場またはサテライト）が望ましいと考えられた。また講義内容として、女性のみならず男性にもより当事者意識を持つ契機となるような内容が望ましいと考えられた。

P-63-2 性別違和（Gender dysphoria）を抱える中高生に関する、アンケート調査票を用いた大規模実態調査

日本医大

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【目的】性別違和とは、出生時に割り当てられた性別と自分の性自認との間の不一致から生じる心理的苦痛を指し、多くは思春期に感じられる。性別違和の若者は自殺未遂や自傷行為で入院する傾向が強いため、集団の中では適切な対応が必要だが、中高生における一般人口レベルでの正確な実態は不明瞭である。そこで我々は、学校側と協力して性別違和に関する実態調査を行った。【方法】本研究は所属施設の倫理委員会の承認を得て行った。中学校3校、高等学校1校（すべて男女共学）が参加し、webベースでのアンケート調査票を用いて性別違和の有無とユトレヒト性別違和スケール値の回答を解析した。「性別に関する違和感がない」をA群、「違和感あり」をB群、「どちらともいえない」をC群とした。【成績】全体で966名がアンケートに参加し、回答数はA/B/Cが886/12/68であった。ユトレヒト性別違和スケールの平均値・中央値はそれぞれ、A/B/Cが35.9・34.5/57・56.5/46.1・47で、A群と比較してB群とC群はそれぞれ有意に高値であった。広義の性別違和と診断されるスケール41点以上の生徒の割合は全体で30.4%であり、A/B/Cでは27%/83.3%/66.2%であった。B群とC群に絞った解析では、「生まれつきの身体の性別は女性だが違和感あり」が17人でスケール平均値・中央値がそれぞれ59.7・54、「生まれつきの身体の性別は男性だが違和感あり」が7人で48・48、「当てはまるものなし」が36人で44.1・44.5であった。【結論】日本において中高生を対象とした同様の研究報告はなく、今回の実態調査は貴重な基礎的データである。ユトレヒト性別違和スケールが高値の生徒には、専門医の紹介など適切な対応が必要となる可能性がある。

P-63-3 先天性心疾患合併女性における月経異常

榑原記念病院

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【目的】医療の進歩により、心疾患合併患者の予後は著明に改善されてきており、とりわけ先天性心疾患（CHD）合併患者の多くが成人期を迎えることが可能となっている。そういった中で、CHD 合併女性の生涯にわたるヘルスケアが大切になってきている。生涯をより良く過ごせるように、また現在だけでなく未来の QOL 改善のために、心疾患合併女性特有の健康問題に着目する必要がある、その一つとして月経異常がある。これまでに CHD 合併女性ではチアノーゼ性心疾患や手術回数が月経異常を来すリスク因子といわれているが、CHD 合併女性と月経異常に関する報告は少ない。そこで、本研究では CHD 合併女性の月経異常の現状とリスク因子について調査することを目的とした。【方法】2019 年 1 月から 2022 年 12 月の 4 年間に、月経異常を主訴として当科を受診した CHD 合併女性 113 例について、患者背景や月経異常の内容について後方視的に調査した。性染色体疾患が診断されている例は除外した。【成績】初診時の年齢の中央値は 19 (11-47) 歳であり、複雑型心疾患が 62 例 (55%)、フォンタン術後は 48 例 (42%)、機械弁置換術後は 11 例 (11%) であった。内服薬として抗凝固療法は 66 例 (58%) であり、抗血小板薬は 65 例 (58%) だった。原発性無月経は 4 例 (3.5%) に認め、初経年齢に与える背景因子としてフォンタン術後と患者の身長であった。また抗凝固療法もしくは抗血小板薬内服例の多くが過多月経や月経困難症を抱えていた。【結論】CHD 合併女性の月経異常は、個々の背景にある CHD の病態と密接に関連している可能性があることが示唆された。

P-63-4 当院における初経遅延の原因とその後の月経・妊娠の可能性

日本赤十字社愛知医療センター名古屋第一病院

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【緒言】日本産科婦人科学会では、2017 年に満 15 歳以降満 18 歳未満で初経を認めない状態を初経遅延と定義し、診断・治療の介入基準とした。初経遅延の原因とその後の月経、妊娠について検討する。【方法】2009 年 4 月から 2022 年 12 月に当院産婦人科に受診歴があり、15 歳時点で自発的な月経のない症例を対象とした。初経遅延の原因と治療、月経・妊娠の有無につき後方視的に検討した。【結果】初経遅延例は 106 例であった。原因として、卵巣性無月経が 71 例 (67.0%) を占め、ターナー症候群 41 例、骨髄移植後 20 例が含まれていた。中枢性 (視床下部・下垂体) 無月経は 16 例 (15.1%) で、腫瘍などの治療に起因するものが 6 例、染色体異常、Prader-Willi 症候群、多発内臓奇形、キアリ奇形、腔中隔合併例を各 1 例ずつ認めた。子宮・腔奇形は 14 例 (13.2%) で、うち 12 例は子宮欠損であった。その他アンドロゲン不応症 4 例、PCO が 1 例であった。腔奇形術後の 2 例を含む 9 例 (8.5%) で 15 歳以降の自発的な月経を認めたが、うち 5 例は 18 歳以降であった。中枢性無月経の 5 例が不妊治療により、また卵巣性無月経の 1 例にホルモン療法中の自然妊娠を認めた。無月経、稀発月経によりホルモン療法を 86 例に開始した。【考察】当院の初経遅延例では 9 割以上が原発性無月経に移行し、8 割でホルモン療法の介入を要した。合併症などにより妊娠を許容できない例も含めると、将来的に自己の卵子・子宮による妊娠が可能と思われる例は 2 割弱であった。初経遅延例に対する早期の診断と介入はヘルスケアの観点からも重要であるが、同時に妊孕性の評価につながる可能性があり、慎重な診断と、本人の成長に合わせたケアやカウンセリングの継続が重要と思われた。

P-63-5 月経困難症や PMDs が関係していると思われた不登校女児へのホルモン療法について

三原赤十字病院

保谷茉莉

不登校とは「学校に行っていない状態」を表す一般用語で、不登校児には様々な病態の背景を持つ子供が含まれる。身体症状を伴うために不登校となる例では、度々小児科や内科を受診し、身体疾患、精神疾患、発達障害などの検索を受ける。今回、当院では、不登校に月経随伴症状 (月経困難症や PMDs) が影響していると思われた女児・若年女性が、ホルモン療法や漢方治療によって症状が軽快し、不登校状態が改善したと思われるケースを複数経験したため報告する。14 歳～18 歳の女児、若年女性 4 名、めまいや倦怠感、腹痛などの症状を呈し不登校になった。受験や進級ができない例もあった。すでに小児科や内科で、不登校児に認められやすい疾患 (過敏性腸症候群や起立性低血圧、脳脊髄液減少症、うつ、摂食障害など) の検索はされており、診断されたもの、疑いの域を出ないものなど、さまざまであった。全例で何らかの投薬・加療を受けたが症状が軽快しないとして、当科を受診した。月経歴を中心とした詳細な問診により、元来の症状が月経前から増悪すること (PME)、PMS 特有の下腹部膨満感や嘔気なども併発すること、月経痛もあり、鎮痛剤を使用するが効果が不十分であること、などが明らかになった。これらの月経随伴症状に対し、ホルモン療法や漢方治療を開始した。全ての女児において、月経痛と月経前増悪の症状が改善し、めまいや倦怠感など、登校を妨げる症状が軽快した。その結果、通学日数が増加し進級や進学が可能になった。以上より身体症状を呈する不登校女児に月経随伴症状があれば、婦人科も介入することで不登校状態の改善が期待される可能性がある。

P-63-6 血液凝固異常の関係した過多月経

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【初めに】過多月経はよく経験する症状であるが、血液凝固異常の症状として過多月経を呈する症例がある。今回過多月経の原因が血液凝固異常であると推定される症例4例を報告する【症例】症例1は月経異常の主訴で受診した症例で、ほとんど毎日性器出血が起こっていた。当初は29歳であるが、子宮摘出を希望していた。過多月経を起こす器質的疾患が否定できたので、凝固検査を行ったところ、フォンウィルブラント因子活性が34%で血液型がO型であったため、低フォンウィルブラント因子血症と診断し、トラネキサム酸の投与を開始した。出血量が劇的に減少し、月経周期が安定してきたが、Pictorial Blood Loss Assessment Chart (PBAC) スコアで150~200点程度になっており、月経血量は多い状態であると思われる。症例2は以前より鉄欠乏性貧血を指摘され、過多月経が原因であると想定されていた。しかし、過多月経の原因と思われる婦人科疾患は見いだせなかった。父親が血友病Aであるので、血友病Aの絶対保因者であることから、第8因子の低下による子宮出血と考え、トラネキサム酸の投与を開始した。今回経験した4例中3例は、フォンウィルブラント因子低下症例で3例とも血液型O型であった。【結論】器質的疾患が認められない過多月経症例で、特に血液型O型の症例では、血液凝固異常がある可能性を考慮すべきである。

P-63-7 当院で経験した処女膜閉鎖症の二例

成田赤十字病院
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【目的】通常処女膜閉鎖症 (imperforate hymen: 以下IHと省略) では腔内に留血腫を認めるが、一旦血腫が除去されてしまうと腔部位の同定が困難となる。そのような状況下で腔の部位を再度同定し根治術を行った当院の一例を報告する。【方法】通常通り腔内に留血腫を認めるIHに根治術を実施した症例と腔内の留血腫が除去された後に根治術を施した一例とを比較し、腔の同定が難しい場合の工夫について検討する。【成績】(症例1)尿閉にて当院救急外来受診し、小児科医より卵巣腫瘍疑いにて紹介された月経未発来の12歳6か月の女兒。超音波検査、CTにて拡張した腔内に著明な留血腫を認めIHと診断し、緊急で腰椎麻酔下に閉鎖している腔の菲薄化部分を十字切開し、腔壁を外反させるように単結節縫合。術後は規則的な月経発来を認め、術後6か月経過するが、再閉鎖は認めていない。(症例2)激しい下腹部痛のため当院救急科外来受診し、小児科医より、卵巣腫瘍・卵巣出血疑いにて紹介された月経未発来の13歳女兒。超音波検査、CTにて腔内に留血腫を認め、下腹部痛の鎮痛制御不能であるためIHと診断し緊急腔穿刺により血腫除去後に、全身麻酔下に根治術を行った。腔内の留血腫が除去された状態では腔部位の同定が難しく、膀胱・直腸損傷のリスクがあり、膀胱に生食、腔内にインジゴ生食を注入して腔部位を十分に再拡張させた後に症例1と同様に根治術を実施した。術後3年間外来で経過観察したが腔再閉鎖は認めていない。【結論】腔内に血液が貯留した状態での処女膜閉鎖症は容易であるが、一旦血腫除去してしまうと腔部位の確認が困難となるため、解剖学的部位を同定する工夫が必要となる。

P-63-8 自己肯定感、孤独感、心理的苦痛、月経前症候群の関連性検討～女子高校生を対象とした横断的研究

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【目的】我が国における若年女性の自己肯定感の低さはジェンダーギャップにおける重要課題である。自己肯定感の低さはうつ病や摂食障害、危険行動等の様々な不適応の指標と関連する。孤独感は心理的な苦痛をもたらし、うつ病等の精神疾患リスクを高める。思春期女性は、ストレスに脆弱であり、孤独のハイリスクとされている。一方、月経前症候群(PMS)は月経前の不快な精神、身体症状を特徴とし、ストレスが誘因の一つとされる。本研究では、自己肯定感、孤独感、心理的苦痛、PMSとの関連性を検討した。【方法】対象は、女子高校生1518名で、2022年12月に自記式アンケート調査を行った。PMS症状評価にはPSQ、心理状態評価として、Rosenberg自己肯定感尺度(RSES)、Kessler心理的苦痛尺度(K6)、改訂UCLA孤独感尺度(R-UCLA)、COVID-19恐怖尺度を使用した。月経周期整で、調査票に回答した1003例を解析した。【成績】自己肯定感、孤独感、心理的苦痛、PMS症状と有意な負の相関関係を認めた($r=-0.484, -0.396, -0.382$)。多重解析の結果、孤独感、心理的苦痛、PMS症状が自己肯定感と独立して関連する因子となった。構造方程式モデリングを用いた解析から、孤独感が自己肯定感、心理的苦痛、PMS症状を説明するモデルと、自己肯定感が孤独感、心理的苦痛、PMS症状を説明する良好なモデルが作られ、それぞれの26%・16%・19%と25%・16%・16%を説明することが明らかとなった。【結論】孤独感と自己肯定感の低さは、女子高校生のwell beingに悪影響を及ぼす重要な健康課題であり、相互に関連しあうものと思われた。医療従事者や学校保健関係者が留意すべき点が明らかとなった。

P-63-9 月経前症候群と月経前不快気分障害の診断・治療に医師の性差が影響する～日本産科婦人科学会女性ヘルスケア委員会調査報告二次解析結果

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【目的】月経前症候群 (PMS) / 月経前不快気分障害 (PMDD) は、月経前の不快な精神・身体症状を特長とし、女性の QOL を著しく障害する。医師・患者関係において、性差は治療薬選択などの様々な側面で影響を及ぼすことが知られている。産婦人科医における PMS および PMDD の診断と治療の性差を検討することを目的とした。【方法】2021 年 9 月～11 月に実施した、日本産科婦人科学会全会員を対象とした PMS/PMDD に対する診断・治療に関する実態調査結果を二次解析した。PMS/PMDD 診療に従事し、性別を報告した 1257 人 (男性 619 人, 女性 638 人) のデータを使用した。【成績】傾向スコアで調整した多重ロジスティクス回帰分析の結果、女性産婦人科医は男性よりも PMS/PMDD 患者の治療に従事する頻度が高かった (オッズ比 [OR] 1.74; 95% 信頼区間 [CI] 1.36-2.21)。診断法に関しては、PMS/PMDD の診断基準に記載のある「症状日誌による前向き評価」を使用して診断する頻度は、男性より女性の方が多かった (OR, 2.88; 95% CI, 1.80-4.60)。一方、治療法については、OC/LEP や漢方治療を第一選択薬として選択する者は男女差を認めなかったが、治療効果に関する十分なエビデンスを有する SSRI を選択する女性医師は男性より少なかった (OR, 0.39; 95% CI, 0.17-0.89)。【結論】日本の産婦人科医における PMS/PMDD の診断と治療法の選択には男女差がみられた。医師の性差といった医療と直接関係のない要因を調査することにより、日本における PMS・PMDD 診療の改善において、これまでとは違った側面からの貢献が期待できる。

P-63-10 月経前症候群月経前気分不快障害の診断・治療の現状と問題点～産婦人科医と精神科医を対象とした女性ヘルスケア委員会全国調査結果～

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【目的】月経前症候群 (PMS), 月経前不快気分障害 (PMDD) は、日本の社会での認知が乏しく、治療に関しても普及していない。月経前に身体・精神の双方に様々な症状が現れる為、産婦人科と精神科のどちらを受診すべきかが問われ、各科で診断・治療方針が異なる。産婦人科医と精神科医を対象に、PMS・PMDD に対する診断・治療の実態を調査した。【方法】日本産科婦人科学会女性ヘルスケア委員会調査として、2021 年 9 月末～11 月末に日本産科婦人科学会 (産婦人科医 16732 名)、2021 年 12 月上旬～2 月中旬に日本精神神経科診療所協会 (精神科医 1670 名) を対象に Web 調査を実施した。【成績】アンケートに回答した産婦人科医中の開業医 409 名と、精神科医 262 名を比較した。PMS・PMDD の診断・治療の実践者は、産婦人科 97.3%, 精神科 79.8% であった。PMS は産婦人科が診るべきという回答が両科ともに多く、PMDD は精神科が診るべきという精神科回答者が多かった。診断方法は「漠然とした問診のみ」が両科ともに最も多く (産婦人科 83.5%, 精神科 86.6%)、症状日誌による前向き評価は少数であった (産婦人科 6.6%, 精神科 9.7%)。薬物治療は複数回答可の場合、産婦人科が OC/LEP 98.0%, 漢方薬 (加味逍遙散 78.6%), SSRI 40.3% に対し、精神科は SSRI 91.1%, 漢方薬 (加味逍遙散 73.3%) で OC/LEP は 2.8% とごく少数であった。第一選択薬に絞ると、産婦人科は OC/LEP 77.4%, 漢方薬 18.9% に対して、精神科は漢方薬 42.1%, SSRI (持続投与) 32.8%, SSRI (黄体期投与) 20.6% という割合になった。【結論】回答した多くの産婦人科、精神科の医師が PMS・PMDD の診療に従事していたが、診断方法については診断基準と実臨床との乖離が認められた。治療についても日本独自の方法を実施していることが明らかとなった。

P-63-11 月経前障害 (PMDs) に対する経口ホルモン製剤の有効性

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【目的】PMS (月経前症候群) を含む月経前障害 (premenstrual disorders: PMDs) は精神面と身体面に多彩な症状を呈する疾患で、有経女性に影響を与えている。治療としてはセルフケアなどの非薬物療法と、ホルモン製剤などの薬物療法に大別されるが、低用量エストロゲン・プロゲステロン配合薬 (LEP) やプロゲステロン製剤による治療効果に関する報告は少ない。経口ホルモン製剤別に治療前後の症状比較を行い、有効性について検討した。【方法】2022 年 5 月から 2023 年 7 月までに単科産婦人科施設を受診し、PMDs または PMDs と月経困難症を併発した症例に対して、経口ホルモン製剤による治療を選択した 207 例 (年齢 27.6±7.5 歳) を対象とした。ドロスピレノン・エチニルエストラジオール錠 (DRSP/EE) (周期投与, 連続投与), レボノルゲストレル・エチニルエストラジオール錠 (LNG/EE) (周期投与, 連続投与), ノルエチステロン・エチニルエストラジオール錠 (NET/EE), ジエノゲスト錠 (DNG) の各ホルモン製剤別に、治療前後の月経随伴症状測定尺度 (MDQ) の得点について、後方視的に診療録調査を行った。【成績】DRSP/EE (周期投与, 連続投与), LNG/EE (周期投与, 連続投与), DNG の各製剤において、治療後は治療前と比較して、MDQ の総合得点と下位尺度 (痛み, 水分貯留, 自律神経反応, 負の感情, 集中力, 行動変化, 抑制因子) が有意に低下し、下位尺度の気分高揚は有意に上昇していた。【結論】経口ホルモン製剤のうち、DRSP/EE, LNG/EE, DNG は PMDs の症状改善に有効な可能性がある。

P-63-12 女性の心身症状に対する酸棗仁湯の応用

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酸棗仁湯は不眠症に頻用されるが、『金匱要略』の条文「虚勞・虚煩」に注目すると、本来「体力が弱って元気がなく、胸中が何となく煩わしく気持ちが落ち着かない」者に用いる漢方薬である。五臓論でストレスの調節や全身に血を蓄える働きは肝が、睡眠など自律神経を整える働きは心が担う。肝は母・心は子の関係にあり、肝が血虚になると心も血虚になり、心身が乱れる。酸棗仁湯はこれを治す。女性は月経、妊娠・出産、仕事・家庭環境など多くのストレスに曝され、それらに適応し恒常性を保っているが、抗えないと心身が疲弊する。この Hans Selye の学説を漢方医学的に考えると、肝血虚から心血虚が生じる過程と似ている。今回、女性の心身症状(産科、婦人科各3症例)に酸棗仁湯が奏効した。産科の1例は、25歳で自然妊娠が成立し、悪阻、続いて完全流産かつ半年前の胎児水腫に連続して生児を得られなかったことがストレスになり、ひとり煩悶し朝まで眠れず、日中は急激な眠気や倦怠感が生じた。酸棗仁湯を処方し3~4週で入眠でき、7週で倦怠感は消失した。婦人科の1例は、42歳で腹痛を主訴に受診し左卵巣内膜症性嚢胞と診断したが、腹痛は体の冷えや人前での緊張から生じ、決まって軟便した。白衣高血圧を認めた。過多月経や持出血が続き、倦怠感を覚えた。気持ちが焦り汗を掻きやすく、日常生活に支障を来した。酸棗仁湯を処方し5週で腹痛・肛門痛は消失し、焦燥感や緊張は半減した。ストレスにに対し患者がどのように立ち向かうか次第で心身症状は様々な形態をとり得るが、虚勞・虚煩する者は、酸棗仁湯が不眠症だけでなく、背景因子が複雑に絡んだ諸症状を解してくれる。

P-63-13 婦人科外来診療における全人的視点の重要性について

ポートサイド女性総合クリニックビバリータ
清水なほみ

【目的】婦人科外来診療において見逃しがちな患者背景をいかにして読み取るかを考察する【方法】「更年期症状」「月経前の不調」という一般的な訴えが主訴であったが実際は症状の背景にDVや虐待による複雑性トラウマが潜んでいた3症例について検証する【成績】いずれの症例も複雑性トラウマが確認できたのは本人からの自己申告であった。長い症例は初診時から10年以上たって判明している。投薬時の問診の中で、複雑性トラウマの可能性を認識して誘導した症例もあるが、自己申告がなければ気づけずに見逃した可能性も考えられた。複雑性トラウマに配慮した診察に切り替えてからは、カウンセリングとの相乗効果が見受けられた。【結論】婦人科外来診療においては、その患者背景に様々な生活背景や成育歴がありうることを念頭において全人的視点を持つことが重要と考えられた。

P-64-1 当院における進行子宮頸癌に対する weekly バクリタキセル・カルボプラチン併用同時化学放射線治療+tri-weekly TC 強化療法の成績と CCRT 従来法との比較

奈良県総合医療センター
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【目的】OUTBACK 試験で進行子宮頸癌に対する CCRT 後の強化療法の有効性は否定された。今回、当院における weekly バクリタキセル (T)・カルボプラチン (C) 併用同時化学放射線治療 (CCRT)+tri-weekly TC 強化療法の治療成績を検討した。【方法】2011年から2017年3月にシスプラチン (P) を毎週 40mg/m² で5-6回投与した16例 (P群) と、2017年4月から2023年9月に毎週 T : 35mg/m², C : AUC2 を5-6回投与し、RT 後強化療法として tri-weekly TC 療法 (T : 135mg/m², C : AUC5) を3回施行した37例 (TC群) の治療成績を検討した。両群間の比較には log-rank 検定を用いた。【成績】P群とTC群の患者背景は、年齢中央値は63 (35-75) 歳と63 (45-78) 歳、臨床進行期 (FIGO2018) はIIA期2例, IIB期9例, IIIB期4例, IVA期1例とIB期2例, IIA期3例, IIB期14例, IIIA期2例, IIIB期8例, IIIC期3例, IVA期4例, IVB期1例, 組織型 (扁平上皮癌/非扁平上皮癌) は14例/2例と29例/8例, weekly TC 療法のサイクル数の中央値は5 (2-6) と5 (1-6), 観察期間中央値は76.0 (17.2-118.6) か月と35.1 (5.7-83.9) か月であった。TC群における強化療法施行率は72.9%, 施行サイクル数中央値は3 (1-3) であった。治療成績は、3年PFSは62.5%と61.1% (p=0.40), 3年OSは81.3%と78.0% (p=0.99), 3年局所制御率は85.7%と82.8% (p=0.40), 3年累積遠隔転移率は32.7%と26.3% (p=0.90), 有害事象 (G3≤, 非血液毒性) 発生率は31%と24%であった。TC群での強化療法有無別の3年OSは有80.6%と無70.0% (p=0.09) であった。【結論】併用レジメンは異なるが、OUTBACK 試験同様、強化療法の有効性は認めなかった。weekly TC 併用 CCRT においては、強化療法を行わなかった場合は、従来の CCRT より治療効果が減弱する可能性がある。

P-64-2 進行、再発子宮頸癌9例に対するベムプロリズマブ療法の有効性、安全性の検討

筑波大

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【目的】KEYNOTE-826 試験の結果を受け、本邦では2022年9月に進行、再発子宮頸癌に対するパクリタキセル、カルボプラチン、ペバシズマブ、ベムプロリズマブ療法(TC-Bev-Pem療法)が承認され治療選択肢が広がった。化学療法、血管新生阻害薬の有害事象に加え、新たに免疫関連有害事象(irAE)などを経験した。当院の進行、再発子宮頸癌に対するTC-Bev-Pem療法の経験を報告する。【方法】対象は2022年12月から2023年8月にTC-Bev-Pem療法を導入した進行、再発子宮頸癌9例で、治療導入から2023年9月までを観察期間とし、治療の有効性と有害事象について後方視的に検討した。【成績】年齢中央は60(41-68)歳。進行期I期1例、III期5例、IV期3例。前治療は手術+化学療法2例、CCRT4例、NAC+手術2例、CCRT+手術1例、組織型は扁平上皮癌5例、腺癌2例、小細胞神経内分泌癌2例。前レジメン数中央値は1(0-6)であった。最大治療効果はCR2例(22%)、PR1例(11%)、SD6例(67%)であった。無増悪生存期間の中央値は5(1-8)か月であった。有害事象はGrade4の骨髄抑制、放射線照射後の症例のうちGrade3の出血性膀胱炎2例、膀胱陰瘻・直腸陰瘻1例を認め外科的処置を要した。irAEは甲状腺機能障害1例を認めレボチロキシシン投与で治療を継続している。【結論】進行例でも完全奏効した症例を認め、治療に難渋する進行、再発子宮頸癌に対する治療の選択肢が広がった。一方で治療中止に至る有害事象も経験し、慎重に選択し、管理することが必要である。

P-64-3 当院における再発子宮頸癌に対するセミプリマブの使用経験

大阪医科薬科大

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【目的】EMPOWER-Cervical1試験により、プラチナ製剤投与後に増悪を認めた再発子宮頸癌に対するセミプリマブの有効性が示された。実臨床での有効性と安全性を検討することを目的とし、当院における使用経験について後方視的に検討を行った。【方法】2023年4月から7月までの間、当院でプラチナ製剤投与後に病変増悪を認めた子宮頸癌に対しセミプリマブの投与を行った6症例を対象に、後方視的に電子カルテより抽出、解析を行った。【成績】6症例(組織型:扁平上皮癌2例、腺癌2例、腺扁平上皮癌1例)の年齢の中央値は61.0歳(56-73)、PSは全例で0であった。治療期間の中央値は13週(8-17週)、投与回数の中央値は3.8回(2-5)であった。既治療レジメン数の平均値は2(1-3)であり、6例中3例にペバシズマブの投与歴があった。最良評価効果はPartial response1例、Stable disease4例、Progression disease1例であった。有害事象は、1例にGrade2の甲状腺機能低下症を認めたが、ホルモン補充により治療継続可能であった。また、その他にGrade1の下痢、倦怠感、関節痛、貧血、ぶどう膜炎の発症がみられたが、全て治療継続に問題はなかった。重篤な免疫関連有害事象は現時点で発症はみられなかった。【結論】セミプリマブは予後が厳しいことが予想される再発子宮頸癌症例に対し、比較的安全に治療継続が可能な有効な選択肢と思われる。一方で今後、有効性と安全性についてさらなる経過観察とデータ集積が必要であると考える。

P-64-4 上部消化管内視鏡スコープを用いた子宮頸部病変の観察の当院での取り組み

石川県立中央病院

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【目的】消化器領域にて使用されている拡大観察・画像強調観察が可能な軟性内視鏡を用いた子宮頸部観察(以下子宮内視鏡)が、子宮頸癌の診断能向上に寄与するといわれている。当院では臨床研究として子宮内視鏡を用いた子宮頸部観察を行う患者を対象に子宮内視鏡を行っている。診療科の垣根を超えた当院での子宮内視鏡の取り組みについて報告する。【方法】令和4年9月よりCIN3に対して子宮内視鏡を用いた観察を行う患者を対象に、手術前に子宮内視鏡を行った。内視鏡操作は消化器内科医が行い、別室で産婦人科医がモニタリングや所見の確認を行なった。コルポスコピー、子宮内視鏡、術後病理検査の対比を行い、子宮内視鏡所見についてカンファレンスを行った。【成績】令和4年9月から令和5年8月までの12か月間で、症例は34例であった。酢酸加工後の所見は事前のコルポスコピー所見と比較しても遜色なかった。拡大観察や狭帯域光観察ではコルポスコピーでは観察できない血管走行の異常が指摘できたが、局所生検は行なっておらず、病理検査との対比は困難であった。【結論】明瞭な子宮頸部の観察が可能で、コルポスコピー以上の精度をもった検査となる可能性がある。診断体系の確立のために、病理診断との対比やCIN3以外の組織の所見など今後も症例の蓄積が必要である。

P-64-5 子宮頸癌に対するペムプロリズマブ併用療法の使用経験

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【目的】進行・再発子宮頸癌に対する初回化学療法にペムプロリズマブを追加することで、無増悪生存期間（PFS）ならびに全生存期間（OS）の改善が第三相試験（KY-826）で示された。しかしながら、実臨床においてはKY-826の対象外となる患者も少なからず存在するため、その有効性と安全性を検討することを目的とした。【方法】2022年10月から2023年9月に当院で進行・再発子宮頸癌に対してペムプロリズマブ併用療法を施行した症例について、診療録より後方視的に検討した。有効性については奏効割合、PFS、OSをRECIST ver. 1.1に従い、安全性については有害事象をCTCAE ver. 5.0に従って評価した。【成績】対象は12例で、年齢の中央値は50（35-73）歳、組織型は扁平上皮癌8例、胃型腺癌2例、腺癌1例、癌肉腫1例であった。治療歴については化学療法2レジメンが1例、放射線が7例であった。PD-L1検査はCPS \geq 10が5例、CPS \geq 1が9例、不適・未実施が3例であった。投与サイクル数の中央値は5（1-11）、総合最良効果はPRが6例（67%）、SDが2例（22%）、PDが1例（11%）、未評価が3例で、奏効割合は67%であった。KY-826の対象外である特殊組織型の3例においても1例のPRを認めた。観察期間の中央値は2.5か月で、PFS、OSの中央値は5.2か月（0.8未達）と8.5か月（0.8未達）であった。Grade3以上の有害事象は4例（33%）に認められ、有害事象による治療中断は多形紅斑の1例のみ（8.3%）であった。【結論】ペムプロリズマブ併用療法は実臨床においても高い有効性を示すことが示唆された。また、KY-826対象外の症例においても有効性を認めており、その効果を予測するバイオマーカー等の更なる確立が必要と考えられた。

P-64-6 当院における進行再発子宮頸がんに対する bevacizumab を用いた薬物療法

愛媛大

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【目的】当院における進行再発子宮頸がんに対する bevacizumab を用いた薬物療法について、その有効性と安全性を検討する。【方法】2016年5月より2021年12月に初回の全身化学療法を開始した59例を対象とし、診療録を用いて後方視的に検討を行った。【成績】対象症例は、bevacizumab 併用ありが46例（78%）、併用なしが13例（22%）であった。bevacizumab を併用しなかった理由は血栓症や腫瘍の腸管への浸潤の疑いなどで放射線治療を理由とした症例は無かった。bevacizumab を併用した症例の83%に骨盤への放射線治療歴があった。bevacizumab を併用したレジメンはTP療法15例（33%）、TC療法31例（67%）で、抗がん剤のサイクル数の中央値は6であった。抗がん剤終了後も bevacizumab 単剤で維持療法を行っていたものは21例（46%）で、投与期間の中央値は9.5サイクルであった。維持療法によりPFSが延長する可能性が示唆された。有害事象として注目される瘻孔形成は1例（2%）であった。【結論】進行再発子宮頸がんに対する bevacizumab 併用療法は既報と同様に安全に使用可能であると考えられた。今後も症例ごとの背景と治療薬の特性を考慮して適切な治療方法を検討し経験を蓄積していくことが必要である。

P-64-7 高齢子宮頸癌患者における放射線治療についての検討

杏林大

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【目的】75歳以上の高齢子宮頸癌患者では手術と比して放射線治療を選択するケースが多い。今回放射線治療を行った高齢子宮頸癌患者の治療成績や安全性について検討を行った。【方法】2014年1月から2022年12月までに放射線治療を施行した75歳以上の子宮頸癌患者28例を対象とし年齢、進行期、治療法、治療完遂率、有害事象、予後について、手術ではなく放射線治療を施行した非高齢者（75歳未満）と比較検討した。【成績】高齢者群は年齢中央値81歳（75~91歳）、組織型は全例が扁平上皮癌（SCC）であった。進行期（FIGO2018）はI期5例（17.9%）、II期11例（39.3%）、III期12例（42.8%）。治療法は放射線単独（RT）17例（60.7%）、同時化学放射線治療（CCRT）11例（39.3%）。非高齢者群は33例で年齢中央値56歳（31~74歳）、組織型はSCCが32例（97.0%）、非SCCが1例（3%）。進行期はI~II期5例（15.2%）、III~IV期28例（84.8%）。治療法はRT5例（15.2%）、CCRT28例（84.8%）。高齢者群ではCCRTの割合が低かった。両群とも全例で予定した放射線線量を施行できた一方、CCRTにおける化学療法では予定した5サイクルを完遂できたのは高齢者群4例（36.4%）、非高齢者群13例（46.4%）と高齢者群で低い傾向にあった。高齢者群ではGrade3の悪心や下痢等の非血液毒性症例が多く、非高齢者群ではGrade4の血液毒性やアレルギー症例が多かった。高齢者群の予後は3年以上観察し得た17例において再発6例（35.3%）、死亡3例（17.6%）であった。【結論】高齢者であっても標準治療は可能であり一定の治療効果と予後が見込められると思われたが、CCRTに際しては非血液毒性に対する十分な対処が必要と考えられた。

P-64-8 当院における子宮頸癌 CCRT の治療成績の検討

徳島大

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【目的】子宮頸癌の主治療の一つとして同時化学放射線療法 (concurrent chemoradiotherapy: CCRT) が広く施行されているが、子宮頸癌 CCRT 後残存・再発症例は治療に難渋することが多い。そこで我々は当院で初回治療として CCRT を施行した子宮頸癌患者の治療成績について調べた。【方法】当院における子宮頸癌患者で、2020年1月から2023年4月までに初回治療として CCRT を施行した 48 症例について、年齢、stage、組織型、腫瘍径、残存・再発の有無に関して後方視的に検討した。【成績】年齢は 29-81 歳 (中央値 62.5) であった。stage は IB1 1 例、IB2 2 例、IIA 1 例、IIB 10 例、IIIA 1 例、IIIB 12 例、IIIC 1r 10 例、IIIC2r 7 例、IVA 4 例であった。組織型は SCC 36 例、AC 8 例、ASC 2 例、NEC 1 例、carcinosarcoma 1 例であった。腫瘍径は 10-150mm (中央値 52) であった。CCRT 後残存なし 39 例、あり 9 例であった。CCRT 寛解後再発なし 37 例、あり 4 例であった。残存あり症例 9 例の腫瘍径は 48-150mm (中央値 72) であり、残存なし症例 39 例の腫瘍径 (中央値 48) よりも有意に大きかった ($p < 0.05$)。9 例中 6 例で DOD あるいは PD となり BSC となった。再発症例 4 例の腫瘍径は 60-90mm (中央値 75) であり、再発なし症例 37 例の腫瘍径 (中央値 53) よりも有意に大きかった ($p < 0.05$)。うち 2 例は RT で寛解、1 例はセミプリマブで SD、1 例は TC+Pem+Bev で PR となった。【結論】CCRT 後残存を認めた症例は予後が非常に悪いと考えられた。CCRT 後残存・再発症例は治療に難渋することが多いが、分子標的治療薬の開発・応用が進むことで子宮頸癌再発患者のさらなる予後の改善につながる事が期待される。

P-64-9 当院における子宮頸部広汎子宮全摘術の検討

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【目的】広汎子宮頸部摘出術は早期子宮頸癌における妊娠性温存手術の一つである。近年、本邦では生殖年齢女性の子宮頸癌発生率が増加傾向であり、本手術の必要性が高まっている。今回、当院で実施した広汎子宮頸部摘出術に関して、臨床背景および腫瘍学的/周産期予後について検討した。【方法】2008 年から 2023 年 3 月までに当院で広汎子宮頸部摘出術を実施した 6 例を対象に、年齢、病期、その後の妊娠の有無と妊娠方法、周産期合併症に関して後方視的に調査した。なお、当院で本手術を実施し、妊娠時の周産期管理は関連施設で実施した。【成績】手術時年齢は中央値 28 歳 (24-38 歳)、病期は IA1 期 2 例、IA2 期 2 例、IB 1 期 2 例、組織型は扁平上皮癌 5 例、腺癌 1 例であった。観察期間中央値は 71.3 か月 (6-149 か月) であり、全例で無再発生存であった。分娩転帰は、5 例で計 7 回の妊娠を認め、1 例で中期流産、6 例では生児を獲得した。妊娠方法は自然妊娠 5 例 (71.4%)、IVF-ET 2 例 (28.6%) であり、分娩週数中央値は 35 週 4 日 (26 週 3 日-38 週 0 日) であった。【結論】当院で広汎子宮頸部摘出術を実施した症例における腫瘍学的/周産期予後は良好であった。本術式の実施には腫瘍及び周産期専門施設の連携が重要であると考えられた。

P-64-10 当院における再発子宮頸癌に対するセミプリマブ投与の現状

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【目的】本邦では 2022 年 12 月に R2810-ONC-1676 試験の結果に基づき、「がん化学療法後に増悪した進行又は再発の子宮頸癌」の適応でセミプリマブ療法が承認された。セミプリマブは免疫チェックポイント阻害剤であり、従来の抗癌剤とは異なる有害事象が生じる可能性がある。これまで当院でセミプリマブ療法を施行した再発子宮頸癌症例について、有害事象を含む治療の現状を報告する。【方法】当院において 2023 年 7 月以降にセミプリマブ療法を施行した再発子宮頸癌症例を対象に、患者臨床背景、有害事象および治療効果について後方視的に検討した。【成績】対象は 6 例で、年齢 40-76 歳 (中央値 48.5 歳)、初回治療時の進行期は IB1 期 2 例、IB2 期 1 例、IIIA 期 2 例、IIIC2 期 1 例で、組織型は扁平上皮癌 2 例、腺癌 3 例、腺癌と神経内分泌腫瘍の混合型が 1 例であった。初回治療の内訳は、広汎子宮全摘術 3 例、CCRT 3 例、初回治療から最初のセミプリマブ投与までの期間は 8-81 か月 (中央値 36 か月)、再発部位は小骨盤腔、外陰部、眼窩等であった。PD-L1 発現状況 6 例中 3 例で評価いづれも陰性であった。有害事象は、1 例で Grade I の悪心、頭痛を認めたのみで、セミプリマブ中止に至るような重篤な免疫関連有害事象は現時点では認めなかった。治療効果については、1 例で 2 サイクル投与後に腫瘍マーカーの低下を認め、4 例治療継続中、1 例は原疾患増悪により死亡に至った。【結論】セミプリマブ療法の治療効果や有害事象に関する報告は、特に腺癌において少なく、今後も症例を蓄積し治療効果や安全性について検討すべきである。

P-64-11 当科における進行・再発子宮頸癌に対する化学療法+ペムプロリズマブ併用療法の検討

岡山大

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【目的】2022年に進行・再発子宮頸癌に対する治療として化学療法+ペムプロリズマブ併用療法が保険収載された。今回当科における投与の現状、および有効性について報告する。【方法】根治治療困難な進行・再発子宮頸癌に対して当科で化学療法+ペムプロリズマブ併用療法を開始した18症例を対象とした。全身治療としての化学療法の治療歴のある症例は除外し、少なくとも1度は画像による治療効果判定を行った。【成績】患者背景は、年齢中央値59歳(35-74歳)、初発症例は7症例、再発11症例であった。腫瘍検体のPD-L1発現陽性(combined positive score; CPS)の検査提出は6例で、全て陽性(CPS \geq 1)であった。ペムプロリズマブの総投与サイクルの中央値は4.5サイクル(1-13)、現在11例が投与継続しており、6例は病勢進行、1例は有害事象のため投与を終了している。最良治療効果は部分奏効が12例(66.7%)、病勢維持が4例(22.2%)、病勢進行2例(11.1%)で、そのうち化学療法を終了し維持療法を開始した8例については維持療法中の最良治療効果は維持4例(50%)、病勢進行4例(50%)であった。初発症例で併用治療6サイクルを終了した3症例では、いずれも化学療法終了後の治療効果は縮小維持から部分奏効であったが、維持療法開始後3-4サイクルで増悪し、2次治療に移行した。【考察】KEYNOTE-826試験では併用化学療法は6サイクル以上の投与も許容されていたが、今回初発治療において維持療法に移行した3例はいずれも3-4サイクルで病勢進行していた。【結論】維持療法移行へのタイミングは今後検討が必要である。

P-65-1 卵巣癌におけるプラチナ製剤に対する感受性とFdx1の発現の関連性についての検討

神戸大

高橋良輔, 山中啓太郎, 寺井義人

【目的】我々は先行研究でプラチナ抵抗性卵巣癌細胞株において、鉄-硫黄タンパク質であるFdx1が強発現していることを見出した。Fdx1はすい臓がんや肺がんにおいて予後予測因子となる可能性が報告されていたが、シスプラチン耐性と関連性については報告がなく、我々はFdx1の発現抑制により*in vivo*においてシスプラチンへの感受性が改善することを報告した。今回、臨床検体においてFdx1の発現と臨床的意義についての検討を行った。【方法】2013年1月から2020年3月までに当院で手術を行った卵巣癌・卵管癌・腹膜癌症例において摘出した45検体からTissue Microarrayを作成。対象をプラチナ感受性群と抵抗性群の2群に分け、それぞれの群で免疫染色によるFdx1の発現を確認した。【成績】45症例のうち、プラチナ感受性群は28症例、プラチナ抵抗性群は17症例であった。組織型は両群共に漿液性癌が最多であり、非漿液性癌の割合に有意差を認めなかった。診断時の進行期および初回手術におけるcomplete surgeryの割合にも有意差は認めなかった。免疫染色では2+以上と判定した割合はプラチナ感受性群では64%であったのに対し、プラチナ抵抗性群は88%であり、プラチナ抵抗性群で発現が高い傾向が見られた($p=0.07$)。また、3+と判定した症例は両群併せて6症例であり、4症例が類内膜癌であり、2症例は漿液性癌であった。予後に関してはプラチナ感受性群がPFS(progression free survival)が18.2か月に対してプラチナ抵抗性群で5.8か月と有意にプラチナ感受性群が長い結果であった。【結論】プラチナ抵抗性腫瘍ではFdx1が強発現しており、Fdx1の発現がプラチナ製剤に対する感受性の予測および予後予測因子になりうる。

P-65-2 Arid1a/Pik3ca 共変異卵巣癌マウスモデルにおけるIL-6とIL-17の腫瘍免疫に与える影響

近畿大

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【目的】卵巣明細胞癌(ovarian clear cell carcinoma; OCCC)はIL-6高産生腫瘍で、腫瘍免疫に影響を与えている可能性がある。臨床試験の結果から、免疫チェックポイント阻害薬が奏功する可能性が示唆されているが、未だ新規の適応はない。【方法】高IL-6産生腫瘍を形成するArid1a/Pik3CA共変異卵巣癌マウスモデルを樹立し、抗体薬を投与して治療効果と免疫に及ぼす影響を検討した。【成績】抗IL-6抗体(a-IL-6)投与群で有意に生存期間が延長したが、免疫チェックポイント阻害薬と併用しても相加効果を認めなかった。腫瘍細胞をフローサイトメトリーで解析したところ、a-IL-6を投与したマウスでは、腫瘍内に浸潤するTリンパ球数は増加したが、CD4+T細胞の機能低下とCD8+T細胞数の低下を認め、抗体薬併用による相加効果が得られない原因の一つであると考えられた。この腫瘍から樹立した細胞株をC57BL/6野生型マウスに皮下投与し同様にa-IL-6を投与したが、治療効果は得られなかった。【結論】Arid1a/Pik3ca共変異卵巣癌マウスモデルに対して、a-IL-6は一定の抗腫瘍効果を認めたがICIとの併用効果を認めなかった。腫瘍から樹立した細胞株に対して同様の治療効果を認めなかったことから、IL-6の影響は腫瘍微小環境を介している可能性が示唆された。

P-65-3 広範囲な子宮浸潤があり、子宮肉腫の診断で手術した成熟嚢胞性奇形腫の悪性転化の一例

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【緒言】成熟嚢胞性奇形腫のうち悪性転化は約1-2%と稀であるが、化学療法や放射線療法に抵抗性があり、一般的な上皮性卵巣癌と比して予後が悪い。そのため、術前診断と完全切除が予後に大きく影響するが、画像検査による術前診断は困難とされている。【症例】67歳、未経産、腹痛、便秘症を主訴に前医を受診し、CTで右卵巣腫瘍、右水腎症を認め、精査加療目的に同日当院紹介となった。MRI画像にて、右付属器領は8cm大に腫大していたが、脂肪成分を含み、成熟嚢胞性奇形腫と考えられた。またそれに接し、双角子宮の右側に内部に嚢胞性変性を伴う8cm大の腫瘤と、腫瘤の尿管浸潤を認めた。拡散制限を伴い、子宮体癌あるいは子宮癌肉腫が疑われ、手術加療の方針となった。術中所見では、卵巣腫瘍と子宮は一塊となっており、尿管、虫垂や腸管も腫瘍に固着していたため、単純子宮全摘術、両側付属器切除に加え、泌尿器科、外科より膀胱尿管新吻合術、S状結腸切除術、虫垂切除術を施行され、肉眼的病変は全て摘出した。腫瘍を剥離最中に、一塊になった腫瘍が破綻した。腫瘍の迅速組織診を提出し、扁平上皮癌の診断であった。術前保存血の検査からSCCが110ng/mlと判明した。術後病理診断は成熟嚢胞性奇形腫の悪性転化、卵巣癌 Squamous cell carcinoma IIIB期 (pT3bNXMX) であり、現在化学療法中である。【結語】本症例は術前に診断が困難であった成熟嚢胞性奇形腫悪性転化の一例である。画像診断と成熟嚢胞性奇形腫の悪性転化について、文献的考察を踏まえて報告する。

P-65-4 プロゲステロンは卵巣がん細胞の膜型受容体を介したトポイソメラーゼI発現抑制とフェロトーシス誘導によりイリノテカン感受性を増強させる

自治医大

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【目的】プロゲステロン (P4) は P4 受容体 (PR) 陰性の卵巣がんに対して、膜型受容体 (mPR) を介した非ゲノム作用によって迅速な細胞死を誘導する。卵巣がんの抗がん剤感受性に対する P4 の影響とその機序を検討した。【方法】PR 陰性かつ mPR 陽性の2種の卵巣漿液性がん細胞株を対象とした。1) 卵巣がん細胞に 100 μ M の P4 を 30 分間接触させた後、シスプラチンあるいはイリノテカンの活性型である SN38 を各々 0~32 μ M, 0~3.2 μ M 濃度で 48 時間接触させ、生細胞数を WST-1 アッセイで計測、濃度依存曲線を作成し IC50 値を求めてコントロールと比較した。2) 100 μ M の P4 を 30 分間接触させた卵巣がん細胞の、イリノテカンの標的であるトポイソメラーゼ I 発現を qPCR で測定した。3) アポトーシス、ピロトーシス、フェロトーシス、ネクロトーシスの各阻害剤をそれぞれ 100 μ M 濃度で 1 時間接触させた卵巣がん細胞に、100 μ M の P4 を 30 分、引き続き SN38 を 48 時間接触させ、生細胞数を WST-1 アッセイで計測した。【成績】1) P4 を接触させた卵巣がん細胞の SN38 感受性は、P4 非接触卵巣がん細胞に比べて著明に増強した。シスプラチン感受性に差はみられなかった。2) P4 を接触させた卵巣がん細胞のトポイソメラーゼ I 発現は P4 非接触卵巣がん細胞に比べて低下した。3) P4 と SN38 を接触させた卵巣がん細胞の中で、事前にフェロトーシス阻害剤で処理した卵巣がん細胞のみ、生細胞数が多かった。【結論】P4 は卵巣がん細胞に対して mPR を介した非ゲノム作用により、トポイソメラーゼ I 発現を低下させ、フェロトーシスを誘導することによってイリノテカンの感受性を増強させることが示された。P4 と抗がん剤を併用した卵巣がん新規治療戦略の可能性が示唆された。

P-65-5 FDX2 欠損は卵巣がん細胞株に、細胞老化様の増殖停止または細胞死をもたらす

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【目的】卵巣がんの新規代謝ターゲットを探索する。【方法】ゲノム編集技術 CRISPR/Cas9 を用い、卵巣がん細胞の増殖に不可欠な代謝関連遺伝子をスクリーニングした。その結果、鉄硫黄クラスター生合成遺伝子が複数同定された。鉄硫黄クラスターはミトコンドリアで合成され、種々のタンパクに配位する。このような鉄硫黄タンパクは、生体内で様々な役割を担っている。我々は、今回同定された鉄硫黄クラスター生合成遺伝子のうち、FDX2 に注目した。卵巣がん細胞株を親株として、FDX2 発現/欠損を誘導できる細胞株を樹立し、FDX2 の機能についてさらなる検証を行った。【成績】FDX2 欠損細胞は不可逆的な増殖停止を呈し、その形態は平たく膨張していた。さらに、FDX2 欠損は、SASP (Senescence-associated secretory phenotype) 因子の上昇と、p53/p21 経路の活性化をもたらした。細胞老化の存在が示唆された。また、FDX2 欠損は、多くの鉄硫黄タンパクの発現低下を引き起こし、その中には鉄制御や好気呼吸に関わるタンパクが多く含まれていた。種々の生化学的な検証から、FDX2 欠損は、鉄制御や好気呼吸の機能を低下させることで活性酸素種と DNA 損傷応答を誘導し、細胞老化様の増殖停止をもたらしている可能性が示唆された。また、TP53 欠損下では、FDX2 欠損は、増殖停止ではなく、カスパーゼ依存性の細胞死を誘導した。【結論】鉄硫黄クラスター生合成は卵巣癌の増殖に重要であると分かった。FDX2 欠損は卵巣がん株の増殖を抑制するが、その転機は TP53 ステータスによって異なり、細胞老化または細胞死が誘導されると考えられた。

P-66-1 新型コロナウイルスワクチン接種後に発症していた免疫性血小板減少症により子宮粘膜下筋腫捻除術後の止血に難渋した1例

市立奈良病院

藤井 肇, 原田直哉, 延原一郎, 春田典子, 東浦友美, 赤坂往倫範

【緒言】特発性血小板減少性紫斑病は、オプソニン化された血小板が脾臓等の網内系細胞に補足され、貪食されることが主因であることから、近年、免疫性血小板減少症 (immune thrombocytopenia : ITP) と呼ばれるようになってきている。今回、新型コロナウイルス (COVID-19) ワクチン接種後に ITP を発症していたために、子宮粘膜下筋腫の捻除術後の止血に難渋した患者について報告する。【症例】57歳、既往歴は SLE (寛解) と甲状腺機能低下症。手術5週間前に plt は $22.8 \times 10^9/\mu\text{L}$ であった。筋腫分娩となった子宮粘膜下筋腫に対して経腔的に子宮鏡併用下で捻除術を行った。術直後より出血を来し、plt が $0.3 \times 10^9/\mu\text{L}$ 、幼若血小板比率 20.7%、PAIgG $170\text{ng}/10^9\text{cells}$ となっていた。造影 CT で著明な子宮内腔への造影剤の漏出を認め、新鮮凍結血漿 6 単位、濃厚血小板 20 単位を輸血し、ヒストアクリルを用いた子宮動脈塞栓術で止血した。改めて問診を行うと2週間前に COVID-19 ワクチン (BNT162b2) を接種していたことが判明した。血小板減少を来すその他の疾患が否定的なことから、ワクチン接種後に発症した ITP と診断した。術後1日目より prednisolone 1mg/kg 内服、7日目には γ グロブリンを5日間投与したが、plt は上昇せず止血が得られなかったため、継続的に輸血 (濃厚血小板 110 単位、濃厚赤血球 4 単位) を行った。21日目からトロンボポエチン受容体作動薬を開始し、prednisolone 1mg/kg 内服と併用とし、38日目に plt $17.8 \times 10^9/\mu\text{L}$ と改善したため退院となった。【結語/考察】ワクチン接種後の ITP 発症には注意が必要である。本症例では手術後に COVID-19 ワクチン接種が判明したが、術前のワクチン接種歴の聴取が重要であることを改めて痛感した。

P-66-2 病理診断が平滑筋腫であったが悪性の転帰をたどった症例

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大久保大孝

【目的】子宮の平滑筋腫瘍には、良性の平滑筋腫、悪性度不明な平滑筋腫瘍 (STUMP)、平滑筋肉腫が挙げられる。子宮平滑筋腫瘍の良性・悪性の病理組織学的鑑別は、①細胞異型、②核分裂像、③凝固壊死などの所見によって総合的になされる。STUMP は、臨床的には悪性としての経過をとることが少なくない。今回、初回手術では平滑筋腫の診断であったが、数年後腹腔内再発し STUMP と診断された2症例を経験したので報告する。【方法】症例1, 70歳。排尿困難主訴にて4年前当科初診。腫瘍は T1 強調像で低信号、T2 強調像で高信号であった。明らかな悪性所見無く、変性子宮筋腫の診断にて腹腔鏡下子宮全摘術施行。腫瘍は水腫様変性しており、回収袋に入れ腔より回収した。術後病理診断はやや細胞密度が高いものの、壊死もなく平滑筋腫との判断であった。術後3年6か月、腹腔内に播種性病変を多数認め、開腹手術施行したところ主病変の腫瘍断面は黄白色でやや変性を疑う肉眼所見であった。組織診断は STUMP であった。完全切除は不能で化学療法に施行したが再発後1年で死亡。症例2, 89歳。20数年前に多発性子宮筋腫の診断で、他院にて腹式子宮全摘術施行。術後病理診断は平滑筋腫とのことであった。今回右側腹部に20cmの充実性腫瘍を認め、開腹手術施行。腫瘍は周辺臓器に浸潤しており切除不能であった。組織診断は STUMP であった。緩和ケアに移行し、3か月で死亡。【結論】初回手術時には平滑筋腫と診断されたものの、悪性の経過をたどる STUMP として再発した症例を経験した。高齢者で手術適応になるほどのサイズの子宮平滑筋腫瘍に関しては、病理結果が良性であっても定期フォローの必要性を考慮するべきと思われる。

P-66-3 高齢女性に生じた子宮捻転の一例

市立伊丹病院

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【緒言】子宮捻転は子宮が長軸を中心に45度以上回転したものと定義され、妊娠中や閉経後に生じたものなど、様々な症例報告がされている。今回、我々は40年以上前から子宮筋腫を指摘されていた高齢女性に生じた子宮捻転を経験したので報告する。【症例】81歳 G3P1。腹痛のため当院救急外来に救急車搬送。腹部 CT 検査で13cm 大の石灰化子宮筋腫を認めたが、その他に明らかな異常所見なく、腹痛の原因は特定できなかった。症状改善し帰宅するも、腹痛再燃のため同日夜間に受診され婦人科紹介となった。子宮は過新生児頭大に腫大しており、経腔超音波で子宮筋腫の後方に長径7cm 大の腫瘍およびダグラス窩に腹水貯留を認め卵巣腫瘍の可能性を疑った。症状が判然とせず、緊急性は乏しいと判断し翌日再診を指示し帰宅。翌日診察時、下腹部に圧痛および反跳痛の所見あり、血液検査で Hb7.6g/dl と貧血を認めた。CT および MRI 所見より子宮捻転による腹腔内出血を疑い、同日緊急開腹手術を行った。子宮底部付近より発育する漿膜下筋腫で、子宮は内子宮口を起点に反時計回りに360度捻転して子宮捻転と診断。子宮および右付属器はうっ血し暗紫色に色調変化し、腹腔内には約600mlの血性腹水が貯留していた。腹式単純子宮全摘および両側付属器切除術を実施。摘出子宮重量は1140g、子宮筋腫は石灰化のため割を入れることができなかった。術後に RBC4 単位輸血。術後経過に異常なく、術後7日目退院となった。【結語】高齢者は自覚症状が乏しく、評価が困難であるため緊急疾患を見逃す可能性がある。子宮捻転は稀な疾患であるが、急性腹症の鑑別疾患として考慮する必要があると考えた。

P-66-4 子宮ポリープ状異形腺筋腫、子宮内膜症に対してレルゴリクス開始後腸管子宮内膜症による腸閉塞が顕在化し外科的治療を要した1例

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腸管子宮内膜症では子宮内膜様組織が腸管に発生しており、子宮内膜症全体の12%程度に存在するとされるが、高度な腸管狭窄をきたすことは稀である。今回、子宮ポリープ状異形腺筋腫(APAM)および子宮内膜症に対する薬物治療中に腸管子宮内膜症による腸閉塞を発生し、外科的治療を要した1例を経験したので報告する。症例は0経妊。40歳時に月経困難症、拳児希望を主訴に当院を受診。左内膜症性嚢胞、3cm大APAMを認め、腹腔鏡下卵巣腫瘍摘出術を行い経過観察していた。今回、48歳時にAPAMの増大および月経困難症・過多月経が増悪したため、レルゴリクスを開始し子宮摘出を予定した。レルゴリクス開始から2週間後に食事摂取不良、嘔吐のため緊急受診、CT検査でS状結腸を閉塞起点とする腸閉塞とAPAMの急速増大を認めた。イレウス管により腸管減圧するも排便は得られず、緊急開腹したところ、子宮は手拳大に腫大し、内膜症性嚢胞はS状結腸と強く癒着を形成していた。ダグラス窩は完全閉鎖し、内膜症性嚢胞の癒着と異なる部位でS状結腸に高度な狭窄および全周性硬結を認めた。子宮全摘術、両側付属器摘出術、高位前方切除術を施行し、病理組織学的所見よりAPAM、両側子宮内膜症性嚢胞、腸管子宮内膜症と診断した。現時点で腹部症状なく経過している。GnRHアゴニストであるレルゴリクスはGnRHと競合することでゴナトロピン分泌を抑制し低エストロゲン状態を作る。これにより子宮内膜症組織の萎縮が期待できるが、本症例はレルゴリクス開始から間もなく腸閉塞を発生した。レルゴリクスの効果により子宮内膜症病変が萎縮し硬結をきたしたことがS状結腸狭窄のきっかけとなった可能性を考えた。

P-66-5 卵巣子宮内膜症性嚢胞の破裂を契機に正常血糖ケトアシドーシスを発症した一例

田附興風会医学研究所北野病院

横田美緒、小園祐喜、井関莉花、阿部秋子、大月美輝、林しほり、山内綱大、奥田亜紀子、関山健太郎、吉岡弓子、樋口壽宏

【緒言】卵巣子宮内膜症性嚢胞の破裂は急性腹症症状を呈するが、全身状態の増悪に至ることは少ない。今回我々は、糖尿病合併症例で敗血症との鑑別に苦慮した卵巣子宮内膜症性嚢胞破裂の症例を経験した。【症例】48歳、既婚未妊、高血圧、糖尿病、子宮筋腫核出術の既往あり。X年6月突然の上腹部痛と嘔吐を主訴に他院救急外来を受診し、右卵巣腫大を指摘されて当院産婦人科を紹介受診した。内診及び経陰超音波にて右付属器に緊満感を欠く嚢胞性腫瘤を認め、骨盤MRIにより右卵巣子宮内膜症性嚢胞の破裂後と診断した。ジェノゲスト内服による保存治療の方針としたが、同年9月に上腹部痛が再燃し当院救急外来を受診。造影CTで右卵巣腫瘤の再増大及び腹水貯留を認め、腫瘤再破綻と診断した。一旦帰宅としたが、翌日に嘔吐で再度救急外来を受診。白血球21400/μL、CRP50.47mg/dL、血糖230mg/dL、血液ガス分析pH7.11、塩基過剰-21.0であり代謝性アシドーシスの所見であった。腫瘤破綻に関連した敗血症と診断し、同日緊急開腹手術を施行。右卵巣は直径10cmに腫大し、腹腔内に茶褐色腹水の貯留を認めた。腫瘤は周囲の消化管と広範囲に癒着していたが剝離は比較的容易だった。右付属器切除術及び腹腔内ドレーン留置を施行し、術後はノルアドレナリン、炭酸水素ナトリウム及びインスリンによる全身管理を行いアシドーシスと炎症反応は著明に改善した。【考察】病歴再聴取で選択的SGLT2阻害薬の内服が判明し、卵巣腫瘤破綻による腹膜炎症状下での同薬服用による正常血糖ケトアシドーシスの可能性が考えられた。【結語】婦人科救急疾患の治療において内科合併症治療の影響を常に念頭におく必要性が再認識された。

P-66-6 慢性に貯留した大量血性腹水に対し審査腹腔鏡を行い子宮内膜症と診断した1例

名古屋市立大附属東部医療センター

佐藤 玲、倉本泰葉、近藤好美、石橋朋佳、倉兼さとみ、関宏一郎、小島和寿、村上 勇、中山健太郎

【症例】初診時34歳、0妊、23歳時に左卵巣内膜症性嚢胞に対して開腹嚢胞摘出の既往あり。下腹痛で前医受診し、右卵巣腫瘍と子宮筋腫を指摘され、精査加療目的で当院紹介受診した。骨盤MRI検査の結果、右卵巣は漿液性嚢胞または機能性嚢胞の診断で経過観察とし、縮小を確認後半年毎にフォローした。右卵巣、筋腫ともに著変なく約7年が経過した。経過観察中の経陰超音波検査で右卵巣軽度腫大と腹水増加を認め精査すると、MRI検査で骨盤内に悪性所見を認めなかったが、CA125は89.2U/ml、CA19-9は71.9U/mlと上昇していた。上下部消化管内視鏡検査で悪性腫瘍がないことを確認後ダグラス窩穿刺を行い、採取した赤色腹水から少数の異型細胞が検出されたため、悪性疾患を疑い審査腹腔鏡を計画した。腹腔内には血性腹水が4500ml貯留しており、右付属器は回盲部との強固な癒着で視認できず、左卵管も癒着のため不明瞭、左卵巣は正常だった。術中迅速診断で右付属器周囲表面組織が腺癌疑いとされ、右卵管摘出と子宮内膜搔爬を追加して手術終了とした。全検体の最終病理結果は子宮内膜症だった。術後腸閉塞となり再度腹水貯留を認めたが補液の影響で矛盾しないと判断し、腫瘍マーカーは正常化、骨盤MRI再検で悪性腫瘍を疑う所見は認めず、子宮内膜症として薬物治療を開始した。GnRHアゴニスト4クール施行後にジェノゲストを内服し、現在まで腹水減少を維持したまま経過している。【結語】大量血性腹水を契機に子宮内膜症と診断した症例を経験した。子宮内膜症が原因で大量の血性腹水を呈する症例は稀であり診断に難渋することが多いが、腹腔鏡下手術は悪性疾患との鑑別も含め、診断に有用であると考えられた。

P-66-7 採卵後に内膜症性嚢胞の感染から直腸穿通を来した1例

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【緒言】採卵後の骨盤内感染症は0.3%と報告されているが、卵巣子宮内膜症性嚢胞の存在は感染のリスク因子である。今回、採卵後に卵巣子宮内膜症性嚢胞が感染を来し直腸へ穿通した症例を経験した。【症例】41歳、0妊。2型糖尿病と20代で内膜症性嚢胞核出術の既往があった。39歳時に挙児希望のため当科を初診し、両側に4cm大の卵巣子宮内膜症性嚢胞と子宮筋腫を認めたため、手術療法後にARTを行う方針となった。審査腹腔鏡を行ったが、癒着が高度であったため根治的な手術は臨めず、腫瘍内容を吸引しアルコール固定術を行い終了した。術後ARTを開始したところ、採卵後に発熱と腹痛を生じ、10cm大の膿瘍を左付属器に認めた。入院による抗菌薬治療を行い軽快し、その後もART治療を実施したものの卵胞発育が得られず不妊治療を終了した。4か月後の膿瘍のフォローで、血便と左付属器膿瘍の増大を認めたため造影MRI検査を実施したところ、付属器膿瘍の直腸穿通が疑われ、下部消化管内視鏡検査では直腸へ浸潤する圧排性病変を認めた。同部位の生検では悪性腫瘍は認めず、子宮内膜症様組織であった。両側尿管ステント留置の後に開腹子宮全摘術、両側付属器切除術、低位前方切除術を施行した。病理組織学的検査では左卵巣の内膜類似腺管構造が直腸粘膜を置換して増殖し粘膜表面に露出していたことから子宮内膜症性病変が直腸穿通を来した直腸内膜症の診断となった。感染を背景とした高度な癒着のため侵襲度の高い手術ではあったが術後経過は良好で、現在はホルモン補充療法を施行中である。【結語】感染要因を持つ患者に対するART治療は術後感染性合併症の注意を要する。

P-66-8 閉経後に起こった巨大粘膜下筋腫を伴う子宮捻転の1例

兵庫県立淡路医療センター

園田あゆみ, 鷲尾佳一, 海府 葉, 真鍋 仁, 伏見菖子, 西野由香里, 金山智子, 西島光浩

【緒言】子宮捻転は非常に稀な疾患である。捻転が起こった場合、様々な症状を来した時にはショック状態に至ることもあるため、速やかに手術を施行し捻転を解除することが求められる。今回、術前に画像検査で巨大粘膜下筋腫を伴う子宮捻転を診断し、手術を安全に遂行できた1例を経験したので報告する。【症例】75歳2経産。2か月前、巨大子宮筋腫に伴う脳塞栓症を発症し当院内科受診し、直接経口抗凝固薬(DOAC)を開始された。失語症、右片麻痺に対してリハビリテーション病院へ転院となっていたが、1か月後、突然の腹部痛、その後ショックバイタルとなり当院へ搬送となった。診察にて臍上に左方偏位した子宮を触知した。血液検査では白血球数上昇、腎機能低下、Lactate上昇を認めた。腹部単純CT検査、骨盤部単純MRI検査にてwhirl signを認め、粘膜下筋腫を伴う子宮捻転の診断となり緊急手術を施行した。成人頭大に腫大した子宮は暗赤色に変色し、両側付属器を巻き込み子宮頸部に尾側から見て時計回りに2回転半捻転していた。捻転を解除し、膈上部切断術・両側付属器摘出術を施行した。術後の経過は良好であり、術後19日目に転院となった。【考察】子宮捻転を超音波検査のみで診断することはしばしば困難である。今回の症例では、単純CT検査、単純MRI検査を撮影し子宮頸部にwhirl signを認め、子宮捻転を診断することができた。巨大子宮筋腫や付属器腫瘍の保存的加療を行っている場合に認める急性腹症は、子宮捻転の可能性を考慮する必要がある。【結語】術前に画像検査で巨大粘膜下筋腫を伴う子宮捻転を診断し、手術を安全に遂行できた1例を経験した。

P-66-9 若年性嚢胞性腺筋症に対して腹腔鏡下手術を施行した1例

一宮市立市民病院

久保裕子

【緒言】若年性嚢胞性腺筋症は極めて稀な子宮の嚢胞性疾患であり、腫瘍径に関わらず激しい月経困難症を呈することがある。今回我々は、激しい月経痛を呈する若年性嚢胞性腺筋症に対して腹腔鏡下手術を施行し月経痛の著明な改善が得られた1例を経験したので報告する。【症例】19歳、0妊0産。2022年9月に月経困難症のため前医受診し、超低用量ピルの内服を開始したが改善なく、精査のため当院紹介受診となった。骨盤部MRIで子宮体部筋層内に2cm大の境界明瞭な結節の内部にT1強調像高信号を認めた。以上より若年性嚢胞性腺筋症による子宮筋層内出血が原因と判断し、2023年7月に腹腔鏡下腺筋症核出術を予定した。腹腔内を観察すると、子宮体部右側前面に径2cm程度の膨隆する結節を認めた。結節の周囲にバソプレシンを局注し電気メスで切開し結節を切除した。結節性病変と子宮筋層の境界の判別が困難であったためダグラス窩に生理食塩水を貯留し、経直腸超音波検査で病変が摘出できたことを確認し、切除面を縫合し終了した。病理組織学的所見で切除した結節は術前診断と相違なく腺筋症であった。術後1か月で月経発来し、手術前の激しい月経痛は改善された。【考察】本症例では手術中に超音波検査を併用することで病変を完全に切除できた。また、手術後に月経痛の著明な改善を認め、低侵襲である腹腔鏡下手術が有効であった。

P-66-10 ロボット支援腹腔鏡下子宮全摘術の際に、自然発生の parasitic myoma 形成の途中過程を捉えたと考えられた 1 例

愛仁会千船病院

柴田直輝, 城 道久, 大木規義, 村越 誉, 吉田茂樹

【緒言】異所性子宮筋腫 (parasitic myoma, 以下 PM) は子宮と離れた位置で栄養血管を獲得し発育する筋腫である。子宮筋腫核出術後に発生する医原性 PM の他に自然発生の PM も報告されているがその機序は未だ十分に明らかでは無い。今回多発子宮筋腫に対する腹腔鏡下子宮全摘術の際に後腹膜に癒着した有茎性漿膜下筋腫を認め、術後の病理診断で茎に平滑筋細胞を認めず、PM の発生過程を捉えたと考えられる 1 例を経験した。【症例】51 歳, 1 妊 1 産。器質性月経困難症を伴う多発子宮筋腫に対してロボット支援腹腔鏡下子宮全摘術を実施した。腹腔内を観察すると多数の有茎性漿膜下筋腫を認めた。子宮体部前壁右側から有茎性に発生する 3cm 大の子宮筋腫の腫瘤が膀胱子宮窩腹膜の右側に強固に癒着していた。当初は有茎性漿膜下筋腫が後腹膜に癒着したものと判断した。まず茎をバツセルシーラーでシール切離した。筋腫は後腹膜との癒着が強く、膀胱や外腸骨血管に注意しながらモノポーラーで脂肪組織を筋腫に付ける形で摘出した。子宮全摘術は合併症無く、定型的に実施した。手術時間は 2 時間 27 分、出血量は少量であった。病理診断で後腹膜に癒着した腫瘍は硝子化した平滑筋腫と診断した。茎に平滑筋細胞は認めず、脂肪組織・細血管・疎性結合組織のみで構成されていた。以上より有茎性漿膜下筋腫が後腹膜に癒着後、茎が変性していずれは PM になる途中過程を見たと判断した。【結論】自然発生の PM の中には、有茎性漿膜下筋腫が後腹膜に癒着し茎が変性・自然破綻し形成される例があると考えられた。

P-66-11 頸部筋腫により自然に挙上し尿管と離れた基韧带血管の先行処理後に筋腫核出を行い、安全に全腹腔鏡下子宮全摘術を実施した子宮頸部筋腫の 2 例

愛仁会千船病院

小島 怜, 城 道久, 大木規義, 村越 誉, 吉田茂樹

【緒言】子宮頸部筋腫は子宮動静脈・尿管等の組織を偏移させ、TLH の難易度は高い。膀胱子宮韧带前処理は手技が困難で、筋腫核出の出血が問題となる。今回、頸部筋腫により自然に挙上し尿管と離れた基韧带血管の先行処理後に筋腫核出を行い、安全に TLH を実施した 2 例を経験した。【症例】【症例 1】49 歳, 2 妊 2 産。過多月経を伴う 88×87mm の後壁頸部筋腫に対し TLH を実施した。後腹膜を展開すると左側は通常通り展開できたが、右側は頸部筋腫のため視野不良で子宮動脈本幹の処理は実施せず。右基韧带血管が頸部筋腫により腹側へ偏移し尿管から確実に離れた状態で子宮本体に近い部位をバイポーラで焼灼し左側も基韧带血管を処理すると、子宮全体の血流が不良となった。頸部筋腫を核出するも出血はほぼなく、改めて尿管を確認した後基韧带を通常的位置で処理し TLH を完遂した。手術時間は 6 時間 22 分、出血量は 200ml、子宮は 494g であった。【症例 2】52 歳, 3 妊 1 産。過多月経を伴う 77×66mm の左側壁発生の頸部筋腫を指摘。レルゴリクスで筋腫が 44×40 mm に縮小した状態で TLH を実施した。右側は通常の手順で基韧带血管を処理した。左側は症例 1 と同様に頸部筋腫で腹側に偏移した基韧带血管を尿管から明らかに離れた位置で焼灼し凝固した。子宮血流が減少した状態で筋腫核出後に、通常の TLH を実施した。手術時間は 6 時間 9 分、出血量は 183ml、子宮は 255g であった。【結論】頸部筋腫により基韧带血管が腹側に尿管から離れるように偏移する。その基韧带血管を子宮本体に近い部位で凝固することで、子宮血流を遮断の上で筋腫核出をして安全に TLH が可能である。

P-66-12 腹腔鏡手術予定の子宮筋腫に対し GnRH アンタゴニストを投与後、開腹手術を選択した 2 例

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【緒言】子宮筋腫に対し術前に GnRH アンタゴニスト投与すると、貧血の改善や筋腫の縮小により待機的に腹腔鏡手術が可能となることが期待できる。今回、我々は腹腔鏡手術予定で術前に GnRH アンタゴニストを投与したが、臨床所見により開腹手術を選択した 2 例を経験したので報告する。【症例】症例 1 は 39 歳, 3 妊 3 産。過多月経と貧血を主訴に前医受診となった。超音波検査で 40mm の粘膜炎下筋腫を認め、子宮内黄体ホルモン放出システム (IUS) を挿入されたが、性器出血時に自然脱落した。当院紹介受診となり、腹腔鏡下単純子宮全摘術 (TLH) を行う方針でレルゴリクスの内服を開始した。内服後腫瘍の縮小を認めたが、骨盤部造影 MRI で子宮肉腫を否定できず、腹式単純子宮全摘術を施行した。病理診断は、低悪性度子宮内膜間質肉腫であった。症例 2 は 43 歳, 3 妊 1 産。多発子宮筋腫と過多月経に対する手術目的に当院を紹介受診となった。前医で IUS を挿入されていたが、筋腫は増大傾向で性器出血も持続していたため IUS を抜き、TLH を行う方針でレルゴリクスの内服を開始した。内服開始 12 日目に大量性器出血を認め緊急入院となった。貧血と凝固機能異常に対し RBC 輸血と FFP 輸血および止血剤を投与し一時的に性器出血の減少を認めたが、入院 5 日目に再度大量性器出血があり、緊急で腹式単純子宮全摘術を行った。病理診断の結果は子宮平滑筋腫であり、大量性器出血の原因は不明であった。【考察・結語】子宮筋腫に対する腹腔鏡手術療法の術前投薬として GnRH アンタゴニストは有用であるが、投与後に術式の変更が必要な症例もあり、文献的考察を加えて報告する。

P-66-13 帝王切開術後の子宮腺筋症の変性に対してMRIが診断に有用だった1例

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【緒言】子宮腺筋症合併妊娠は様々な周産期合併症をきたすハイリスク妊娠である。子宮腺筋症合併妊娠に対する帝王切開術後に著明な炎症反応上昇を認め、MRIで子宮腺筋症の変性と診断した症例について報告する。【症例】44歳、1妊0産。妊娠初期に妊娠反応を確認し、近医で子宮内の胎嚢を確認されたが、24週まで医療機関を受診していなかった。28週6日の3回目の医療機関受診時に子宮収縮と子宮頸管長短縮を認め、切迫早産と診断され当院へ搬送された。搬送時の超音波検査で子宮筋層の肥厚を認め、子宮腺筋症合併妊娠と診断した。入院後、塩酸リトドリン点滴と安静で治療開始し、29週3日に血圧上昇に対しカルシウム拮抗薬内服を開始した。33週5日に妊娠高血圧腎症が増悪したため緊急帝王切開術を行った。術後5日目にWBC33600/ul, CRP22mg/dlと上昇したが、子宮創部感染や発熱、子宮の圧痛、帯下の臭異、プロカリスチンなど感染を示す所見は認めなかった。MRIでも膿瘍や子宮感染の所見は認めず、子宮筋層の出血性変化を伴う変性所見を認めたため、子宮腺筋症の変性に伴う炎症反応の上昇と判断した。抗菌薬の投与は行わず、術後7日目にWBC10500/ul, CRP5.76mg/dlへと改善を認め、術後9日目に退院した。【考察】帝王切開術後の血液検査で炎症反応上昇を認めた場合、術後の感染を疑うことが多く、無症状でも抗菌薬投与が行われがちである。本症例ではMRIが術後感染と子宮腺筋症変性の鑑別に有用であった。【結語】帝王切開術後に子宮腺筋症が著明な炎症反応上昇を伴う変性をきたす場合がある。MRIが感染と変性の鑑別に有用であり、不要な抗菌薬投与を避けることができる可能性がある。

P-67-1 効果的な卵巣組織移植を志向した移植手技に関する基礎的検討

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【目的】卵巣移植術後の卵巣機能温存のために有効な手術手技を探索することを目的として、移植片の卵巣への固定時の縫合糸の径と回数に焦点を当てた検証を行った。【方法】Wistar系8週齢ラットの卵巣に2週齢ラットの卵巣を同所性移植した。移植方法は、卵巣のう内に挿入する方法(A群)、6-0 Vicrylで1針縫合する方法(B群)、10-0 Vicrylで1針縫合する方法(C群)、10-0 Vicrylで3針縫合する方法(D群)とした。移植から2週間後に卵巣を摘出し、移植卵巣のHE染色とIHCによる組織学的検証ならびにreal time PCRによる遺伝子発現を比較した。なお、当学動物実験委員会の承認を得て、倫理規定を順守して行われた。【成績】生着率は、A群で62.5%、B群で100%、C群で91.7%、D群で100%であり、縫合群で有意に生着率が高かった。一方、原始卵胞数はA群で1044.2±49.4個、B群で722.3±82.0個、C群で481.3±122.6個、D群で330.8±41.6個(全てmean±SE)で、D群で有意に低値であった。また、胞状卵胞数はA群で有意に高値であった。遺伝子発現では、D群でTNF α の発現が有意に高く、GDF9ならびにFSHRの発現が有意に低下した。IL-6, CD31, VEGFAおよびVEGFレセプターの発現には有意差は認められなかった。HE染色での組織学的評価では、縫合部周囲にリンパ球浸潤と肉芽組織が認められた。IHCによるFSHRの発現は、縫合に伴って低下した。【結論】無縫合の同所性移植に比べ、卵巣への直接縫合は移植片の生着率を向上させたが、縫合回数を増やすことで原始卵胞数が減少した。卵巣組織移植は、移植片の生着のために最適な径の縫合糸を用いて、卵巣機能を維持するために最小限の縫合回数で行うことが重要である。

P-67-2 微小残存病変(MRD)マウスモデルを用いた卵巣移植実現可能性の検証

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【目的】抗がん剤治療後の若年がん患者における卵巣組織の凍結保存と移植は、妊孕性を温存するための現実的な選択肢となっているが、凍結保存した卵巣組織に悪性細胞が存在するリスクと移植後の再発リスクを考慮する必要がある。そこで本研究は、卵巣組織凍結の対象となる疾患の中でもとくに若年層で罹患率が高い白血病を研究対象として、卵巣内の微小残存病変(MRD)をマウスモデルで正確に評価することを目的とした。【方法】卵巣MRD白血病モデルマウスは、GFP遺伝子を導入したマウス由来白血病細胞株(EL4-GFP)の腹腔内投与により作製した。今回は、卵巣内に浸潤する白血病細胞数をコントロールすることが可能かについて細胞投与後から卵巣採取までの時間を検討した。採取した卵巣のゲノムを抽出しqPCRにより白血病細胞数を測定した。【成績】これまでに作製したEL4-GFP細胞の5つのクローンを投与し、1週間あるいは2週間後に卵巣を採取してqPCRにより卵巣内に浸潤したEL4-GFP細胞数を検討した。その結果、卵巣へ浸潤するEL4-GFP細胞数には細胞クローンごとの差、個体差、さらには卵巣の左右差が存在していた。しかしその中でも#3のクローンを投与後1週間の卵巣では浸潤細胞数の割合が比較的安定しており(0.13-1%)、卵巣1個あたり平均して約5000個のEL4-GFP細胞が含まれていた。【結論】本研究により卵巣に浸潤する白血病細胞数はある程度制御可能であることが示された。今後はさらに卵巣MRDを正確に評価し、原疾患の最小伝播細胞数を特定することにより白血病患者の妊孕性回復に対して大きく貢献できるものとする。

P-67-3 閉経前乳がん患者に対する GnRH アゴニスト製剤中断/終了後の月経再開時期に関する検討

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【目的】閉経前乳癌のホルモン療法では tamoxifen に加えて GnRH アゴニスト (GnRHa) 製剤がしばしば併用され、近年では長期徐放製剤を用いることが多くなっている。一方、がん治療と妊孕性を両立させるがん・生殖医療が注目されている。そこで、GnRHa 製剤を中断した後の卵巣機能や月経再開時期について検討した。【方法】ホルモン療法として GnRHa 製剤を用いてこれを中断ないし終了した閉経前乳癌症例で、第二子希望による二回の休止症例を含む 23 症例 (25 周期) を対象とした。最後に投与した製剤の種類、投与後の血中ホルモン濃度、月経再開時期を診療録から後方視的に調査した。【成績】最後に投与した製剤をリュープロレリン 1 か月 (L1)、3 か月 (L3)、6 か月製剤 (L6)、ゴセレリン 1 か月 (G1)、3 か月製剤 (G3) として比較検討した。1 か月製剤 (L1, G1 群) では最終投与日から 196 ± 76 日で、3 か月製剤 (L3, G3 群) では 247 ± 91 日で、6 か月製剤 (L6 群) では 322 ± 124 日で月経が再開した。血中ホルモン濃度を測定した症例では、添付文書上の薬効持続期間を超えて血中ゴナドトロピンが抑制されていた。月経再開時期に影響を与える要因について多変量解析を行ったが、年齢、AMH、GnRHa 投与期間、化学療法の有無は有意な因子で無かった。【結論】GnRHa 製剤の薬効持続期間、休止後の月経再開時期は個人差が極めて大きかった。閉経前乳癌患者がホルモン療法を中断して妊娠・出産を目指すことは近年増加傾向であるため、産婦人科医と乳癌治療医が連携してホルモン療法の内容を最適化し、可及的に短い中断期間で妊娠・出産を目指すことが今後求められていくと思われる。

P-67-4 当院での妊孕性温存を目的とした卵巣組織凍結の現状と融解卵巣組織移植の実施例

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【目的】小児・若年女性がん患者に対する、妊孕性温存目的の卵巣組織凍結件数は増加しており、臨床成績の検討が必要である。【方法】当院で 2018 年 2 月から 2023 年 6 月までに妊孕性温存目的の卵巣組織凍結を行った患者 33 例を検討し、融解卵巣組織移植を行った症例について報告する。【成績】初診時年齢は平均 18.8 歳 (4.37 歳)、うち 15 歳未満の小児症例は 14 例であった。院内紹介が 18 例、他院紹介が 15 例であった。原疾患は血液・造血器疾患 16 例、骨軟部腫瘍 7 例、乳腺腫瘍 6 例、肺・縦隔腫瘍 2 例、その他 2 例であった。凍結希望から手術までの平均日数は 11.8 日 (2.52 日) で、凍結切片数は平均 14 片 (2.25 片) であった。全例で摘出標本に明らかな悪性所見は認めなかった。IVM 施行 12 例のうち、獲得未熟卵数は平均 6.3 個 (2.20 個)、IVM 後の成熟卵数は平均 3.1 個 (0.10 個) であった。移植症例は初診時年齢 34 歳、G0、原疾患は下肢粘液型脂肪肉腫。術前化学療法で Doxorubicin+Ifosfamide 投与のため、妊孕性温存目的に卵巣組織凍結を希望。初診日から 5 日後に腹腔鏡下右卵巣摘出術を施行し、組織片 12 片を凍結、未熟卵 2 個を獲得後、IVM によって成熟卵 2 個を凍結した。術後半年で当科に再度受診し、IVF の方針で卵巣刺激を 6 周期行ったが胚凍結に至らないため、腹腔鏡下卵巣移植術を施行。移植後は 2 周期タイミング治療後に ARTへ Step up となり、4 周期目で胚盤胞 1 個 (Day6:3AB) の凍結に至った。ホルモン補充周期での融解胚移植を行ったが、妊娠判定陰性であり、現在も ART 継続中である。【結論】現時点において全例で原疾患治療の遅延なく、卵巣組織凍結を行うことができている。今後は卵巣組織移植後の成績についても集計していく。

P-67-5 AYA サポートチームと協働した妊孕性温存体制の構築

鹿の門病院

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【目的】がん診療において「がん診療連携拠点病院等の整備に関する指針」の改訂により、就学、就労、アピアランスケア等と並び妊孕性温存に対応できる多職種からなる AYA 世代支援チームの設置が推奨された。当院における AYA サポート体制の一環として AYA サポートチームと協働した妊孕性温存体制の構築を報告する。【方法】地域がん診療連携拠点病院である当院のがん総合診療部がん診療推進委員会の AYA サポートチームと当科の生殖チームが協働して妊孕性温存体制を構築した。【成績】1) AYA サポートチームの組織化と連動し、相談フローシートに妊孕性温存を設けて支援体制を組織化した。2) 既存のがん・生殖カンファレンスに加えて、妊孕性温存や卵巣過剰刺激症候群のフォローなどの支援が継続してできるよう、外来、病棟、外来化学療法室、放射線治療部のスタッフ、AYA サポートチームメンバー等が、前方視的な AYA ケースカンファレンスおよび倫理カンファレンスを実施した。また実施にあたってはミニレクチャー併用した。3) AYA サポートに関する院内の意識を向上させるために全職員を対象として月 1 回開催される AYA セミナーにおいて妊孕性温存をテーマとした。4) がん・生殖医療外来の受診者のみならず、AYA サポートチームが調査している外来・入院の AYA 症例に対する妊孕性温存を検討した。5) AYA サポートチームの広報活動において、妊孕性温存の情報も同時に提供した。【結論】がん・生殖医療における妊孕性温存においては、院内のがん診療の一環としての組織的な支援が望ましく、AYA サポートチームと協働した妊孕性温存体制の構築が望ましいと考えられる。

P-67-6 当院における医学的適応による女性の妊孕性温存の現状

浜松医大

松本雅子, 田村直顕, 伊東宏晃

【目的】当院では、2014年から医学的適応による妊孕性温存を実施している。約10年間の妊孕性温存外来の実績を調査し報告する。【方法】2014年9月～2023年3月の間に、医学的適応による妊孕性温存を目的に生殖外来を受診した女性を対象とした。診療録から後方視的に原疾患、未受精卵または胚凍結実施の有無、治療後の妊娠中の有無について調査した。【成績】対象症例は61例（乳がん32例、血液疾患16例、骨肉腫・Ewing肉腫3例、免疫疾患2例、副腎がん2例、婦人科がん4例、甲状腺癌1例、卵黄嚢腫瘍1例）であった。そのうち妊孕性温存療法を希望したのは42例で、未受精卵凍結は26例（乳がん14例、血液疾患7例、副腎がん2例、婦人科がん2例、甲状腺癌1例）、受精卵凍結は12例（乳がん10例、婦人科がん2例）、卵巣刺激を実施したが凍結に至らなかった症例は4例（乳がん1例、血液疾患2例、骨肉腫・Ewing肉腫1例）であった。妊孕性温存療法を希望しなかったのは19例（乳がん7例、血液疾患7例、骨肉腫・Ewing肉腫2例、免疫疾患2例、卵黄嚢腫瘍1例）であった。凍結していた受精卵を使用し妊娠した症例は4例（乳がん3例、婦人科がん1例）、凍結していた未受精卵または受精卵を使用せず自然妊娠した症例は6例（乳がん2例、血液疾患1例、副腎がん1例、婦人科がん1例、甲状腺癌1例）であった。未受精卵を使用しなかった症例はなかった。【結論】適応疾患は乳がんが最も多かった。受精卵の使用率は33%で、移植した症例全例が妊娠に至った。未受精卵の使用率は0%であり、年齢や疾患を抱えての婚姻の難しさなど影響していると推察される。未受精卵を使用した妊娠に関しては、今後に期待したい。

P-67-7 当院リプロダクションセンターにおけるCAYAがん患者の生殖医療診療の現状

獨協医大埼玉医療センターリプロダクションセンター

池永晃大, 杉本公平, 正木希世, 大久保美紀, 竹川悠起子, 岡田 弘

【目的】妊孕性温存に対する社会的関心が高まりつつあり、その一方で妊孕性温存を行わなかった症例については多くの議論がなされていない。AYA世代に小児期のがん経験を加えたCAYAがんサバイバーに対する妊孕性温存療法を含めた生殖医療全般について議論をしていく必要があると考えられる。CAYAがん患者に対する妊孕性温存療法を含めた生殖医療の現状について調査し、今後の検討すべき課題を抽出する。【方法】2020年4月より当院リプロダクションセンターで診療したCAYAがん患者49例を対象とした。患者の初診時年齢、がん種などの背景、受診目的、妊孕性温存療法の有無とその転帰、不妊治療の結果、カウンセリング施行状況などを調査した。【成績】受診患者の平均年齢は33歳、妊孕性温存の相談で来院した患者41例（そのうち温存術施行30例、未施行11例）、がん経験後不妊治療患者5例でPOI例を含めた2例が妊娠・出産に至っていた。卵巣予備能確認などが3例であった。妊孕性温存後、胚移植を施行した症例は1例であった。【結論】当センターを受診したCAYAがん患者の8割以上が妊孕性温存の相談が目的であった。妊孕性温存未施行が27%であり、妊孕性温存術施行するもできなかった1例を含めると約3割が妊孕性温存を行わなかった。一方でがん経験後に不妊治療を施行した5例では、POI症例1例を含む2例が生児獲得に至っていた。妊孕性温存療法は普及が進みつつあるが、妊孕性温存をできなかった、あるいは選択しなかった患者の不妊治療転帰などを調査し、そのライフコース選択を支えるための支援のあり方を長期的に検討することが課題と考えられた。

P-67-8 術中迅速病理診断を併用し体外で採卵した右卵巣への大腸癌転移疑いの一例

熊本大

中村美和, 佐々木瑠美, 今村裕子, 井上尚美, 大場 隆, 近藤英治

【緒言】他臓器癌の卵巣転移が認められた場合の付属器切除ならびに妊孕性温存に関する適切な方法は定められていない。今回我々は、挙児希望のある大腸癌右卵巣転移疑いの症例に対し、両側付属器摘出の上で採卵を実施した1例を報告する。【症例】症例は35歳、2妊2産の女性で離婚歴がある。34歳時に大腸癌IVa期（肝転移）の診断で腹腔鏡下S状結腸切除術及び肝部分切除術、化学療法を受け、術後6か月に肝転移に対して腹腔鏡下肝部分切除術を受けた。初回術後10か月のPET-CT検査で肝転移及び正常大の右卵巣に長径2cmのFDGの異常集積が認められたため当院消化器外科より紹介され、骨盤造影MRI検査でも右卵巣転移が強く疑われた。外科と合同での手術の方針とし、ロボット支援下腹腔鏡下肝部分切除術に続いて腹腔鏡下両側付属器摘出術を計画した。患者の妊孕性温存の希望が強く術中採卵を行う方針とし、術前15日よりhMG製剤とGnRHアンタゴニストを用いてランダムスタート法で調節卵巣刺激を開始した。右卵巣からの腹腔鏡下採卵は腫瘍細胞を拡散させる危険性が高いと判断し、当院病理部と協議の上、右付属器摘出後直ちに体外で採卵を行った後に術中迅速病理診断へ提出した。大腸癌の右卵巣転移を確認した上で左付属器摘出術を行い、右卵巣同様に体外で採卵し、合計19個の未受精卵を採取し凍結した。最終病理診断で右卵巣のみに転移が認められた。【結語】本症例では他科との連携の下、術中迅速病理診断を組み合わせた術式を選択しすることで播種の危険を避けつつ十分な採卵数が確保できた。術中迅速病理診断を組み合わせた付属器摘出後の採卵は転移性卵巣腫瘍症例に対する妊孕性温存の一方策となると考えられる。

P-67-9 当院における妊孕性温存症例の治療背景とその転帰

徳島大

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【目的】近年 AYA 世代のがん患者に対する妊孕性温存が広く実施されているが、地域の施設間での連携が重要である。当院における妊孕性温存の実施状況を振り返るとともに徳島県の施設連携の課題点について検討した。【成績】2007年1月から2022年12月までの間に合計60例に対し妊孕性温存カウンセリングが実施された。紹介元の内訳として院内紹介が50例、他施設からの紹介が10例、疾患内訳として乳癌が37例、血液疾患が15例、その他疾患が8例であった。受診時期の内訳として乳癌は化学療法・ホルモン療法前が31例、ホルモン療法中・化学療法後が6例、血液疾患は化学療法前が6例、化学療法中が9例、その他疾患は化学療法前8例であった。カウンセリングの結果、合計48例が妊孕性温存の実施を希望した。乳癌は27例に妊孕性温存が実施され、うち4例が分娩に至り、3例は現在妊娠中である。血液疾患は11例に妊孕性温存が実施され、うち1例はその後妊娠・分娩に至った。その他疾患6例は全例に妊孕性温存が実施され、うち3例は妊娠・分娩に至った。12例はカウンセリング後妊孕性温存を試みず、その理由として希望なしが9例、閉経が1例、適応外が1例、転居が1例であった。【結論】当院でカウンセリングを実施した症例の80%に妊孕性温存が試みられ、このうち92%に胚・卵子凍結が実施された。当院では妊孕性温存に関する診療科間の連携が確立しており、胚・卵子凍結に至った症例が多いと考えられる。一方、他のがん診療施設からの紹介は少なく今後は他施設への周知徹底が課題である。また、凍結胚・凍結卵子の多くは未使用の状態であり、凍結保存管理体制の維持、患者への継続的なカウンセリングが重要と考えられる。

P-68-1 周産期における自書式問診票を用いた児童虐待スクリーニング

トヨタ記念病院

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【目的】児童虐待件数は年々増加し、その予防、早期介入は行政において重要な課題であると考えられる。しかし有用なスクリーニング方法はなく、効果的なハイリスク群の抽出は行えていないのが現状である。今回我々は行政と連携し、既存の自書式問診票を用いて児童虐待の発生リスクについて検討した。【方法】2019年4月1日から2021年3月31日の間で行政機関に訪問介入の依頼のあった症例を対象とした。初回訪問時にエジンバラ産後うつ質問票 (EPDS) と赤ちゃんへの気持ち質問票 (MIBS-J) を用いて妊産婦の3、4か月児健康診察時点での虐待の有無を自書式で評価が可能であった症例について後方視的に検討を行った。各質問票および質問項目と虐待との関連について、多変量解析を用いて後方視的に検討した。【成績】1,790例の介入依頼の内、解析対象となったのは1,404例で、身体的虐待を29例 (2.1%) に認めた。身体的虐待の有無に関して EPDS の ROC 曲線の AUC は 0.72、感度 0.76、特異度 0.65 であり、MIBS-J の AUC は 0.70、感度 0.52、特異度 0.84 であった。また各質問項目と身体的虐待発生リスクに関して、MIBS-J の「赤ちゃんに対して何も特別な気持ちがわからない」、「赤ちゃんに対して怒りがこみ上げる」、「こんな子でなかったらなあと思う」の adjusted Odds Ratio はそれぞれ 4.88 (95% 信頼区間 2.55-9.34)、5.72 (95% 信頼区間 3.27-10.0)、6.41 (95% 信頼区間 3.30-12.5) であった。【結論】問診表の合計点だけでなく各質問項目の評価を行うことにより、効果的な虐待リスクの抽出からリスクの層別化を行うことができると考える。

P-68-2 音声とディープラーニングを用いた妊娠中の精神障害の検出

岡山大

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【目的】本研究は、画像分類モデルを用いて妊婦の発声パターンを検出し、妊娠中に合併している精神障害を特定することを目的とした。【方法】産後1か月健診に参加した204人の妊婦を対象に実施された。面接時に社会人口統計学的データとエジンバラ産後うつ病評価尺度 (EPDS) スコア、対象者の音声を記録した。音声サンプルは、環境ノイズや他人の音声を除去するためにクリーニングされ、その後セグメント化されてメルスペクトログラムに変換された。トレーニングデータに対してデータ拡張を行い、ImageNet で訓練された Efficientformer V2 を用いて転移学習を行った。ハイパーパラメータは Optuna を用いて最適化され、セグメントごとの判定結果をアンサンブルし最終的な予測とした。Primary outcome は音声による予測の G 平均とした。【成績】204人の妊婦のうち、データ不足のため32人が除外され、172人が解析に組み込まれた。参加者は3つのグループに分けられた：トレーニング用97人、検証用32人、テスト用43人。平均音声持続時間は約35.9秒であった。セグメントデータは、トレーニング用2,942セグメント、検証用197セグメント、テスト用323セグメントであった。データ拡張後、トレーニングセグメント数は14,170に増加した。学習の結果、アンサンブル後の音声による予測は G-mean 0.81、Accuracy 0.70、Recall 0.82、ROC-AUC 0.82 であった。音声による検出は感度を、EPDS による検出は特異度を重視する傾向が見られた。EPDS との比較の結果、ROC-AUC について有意差は認められなかった ($p = 0.759$)。【結論】妊娠中の精神障害を検出するための音声と人工知能は、より良いスクリーニング方法を提供する可能性がある。

P-68-3 当院における妊娠中のエジンバラ産後うつ病質問票の有用性の検討

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【目的】エジンバラ産後うつ病質問票（以下 EPDS）は、産後うつ病の評価に有用であるとされる。しかし、現在妊娠中に産後うつ病の予測し得るような基準値やその他のスケールはない。今回、社会的ハイリスク妊婦に対し妊娠中からの EPDS の評価が産後うつ病リスクの予測に有用かどうかを検討したので報告する。【方法】2022年1月-12月に当院で分娩した妊婦に対し、初診時、産後2週間健診および1か月健診時に EPDS を用いて評価を行った。その後、初診時の EPDS を独立変数、2週間健診および1か月健診で産後うつ病のリスクが高い（EPDS > 9 点）ことを目的変数として検定を行い AUC およびカットオフ値を算出した。さらに、社会的ハイリスク群において同様に検定を行った。【成績】対象となった妊婦は 115 人（うち社会的ハイリスク 54 人）であった。分娩時年齢（平均）は 29.0 歳、分娩週数（平均）は 38.9 週であった。初診時、2週間健診、1か月健診の EPDS の平均（社会的ハイリスク）は各々 5.9 (8.09) 点、3.59 (5.34) 点、2.89 (4.21) 点であった。全体の初診時 EPDS 検査の AUC（カットオフ値）は 2週間健診および1か月健診でそれぞれ 0.774 (6.5 点)、0.767 (6.5 点) であった。また社会的ハイリスク群においてはそれぞれ 0.722 (8.5 点)、0.722 (7.5 点) であった。【結論】本検討において、妊娠中の EPDS は産後うつ病リスクの予測に有用であった。特に社会的ハイリスク群は全ての時期において EPDS が高く、妊娠中に EPDS が高値の妊婦を抽出することで、妊娠中から早期に精神的なサポートなどの介入ができると考えられた。

P-68-4 総合周産期母子医療センターにおける NICU 入室の有無と産後健診時エジンバラ産後うつ病質問票（EPDS）の検討

獨協医大

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【目的】妊産婦の産後支援とメンタルヘルスケアの必要性が周知され、産後2週および4週でエジンバラ産後うつ病質問票（EPDS）による評価を行っている。当院産科では小児科医、看護師、精神科医、ソーシャルワーカー、地域の保健師らと連携しながら支援を継続している。今回、本院倫理委員会の承認のもと、児が NICU 管理となった産婦の EPDS の推移について検討した。【方法】2022年4月から2023年3月に総合周産期母子医療センターで分娩し EPDS を2回施行した 409 名を対象とし、精神疾患合併例は除外した。児が NICU に入室した初産婦（A1 群, n=71）および経産婦（A2, n=55）、児が産科管理の初産婦（B1, n=113）および経産婦（B2, n=170）の4群で、EPDS の変化を後方視的に抽出し、比較、検討した。【成績】①ハイリスクとされる EPDS が9点以上の人数は、産後2週において A1 (n=12), A2 (n=7), B1 (n=18), B2 (n=11) であり NICU 入室の有無にかかわらず初産婦が多かった。②2週目の B2 の平均値は他の3群よりも有意に低く、また A1, B1 は差が無く、初産婦における EPDS 高値が再度確認された。③4週目の点数を2週目と比較すると、A1, A2, B1 群で有意に減少しており、また A2 群の点は B2 群との間に差は認められなかった。さらに A1, B1 においても有意に低下していることから支援・介入が有効であると推察された。【結論】初産は産後うつ病のハイリスクであり、また NICU への入室は経産婦の EPDS 増悪と関連した。一方、4週目の健診時の EPDS の低下から産後2週目の EPDS 聴取と育児支援等の介入は、スクリーニングおよびリスク軽減に有用であると推測した。

P-68-5 医療保護入院を要した精神疾患合併妊娠の3症例

大阪公立大

柴田 悟

【緒言】医療保護入院は精神保健指定医の診察が必須であり、緊急時の対応が困難な場合が多い。今回、当院神経精神科での医療保護入院を必要とした精神疾患合併妊娠の3例を報告する。【症例1】30歳。1妊0産。妊娠前に統合失調症の診断を受けたが、通院を自己中断していた。近医で帝王切開術後より精神症状増悪のため当院へ搬送となった。夜間のため医療保護入院の対応が困難であり、一時的に産科病棟に収容、搬送6日目に医療保護入院となった。抗精神薬により症状は徐々に改善、術後39日目に任意入院となった。【症例2】27歳。2妊0産。近医で妊娠40週に経膈分娩、産褥1日目より不眠、希死念慮が強く、当院へ搬送となった。神経精神科医により双極性障害と診断されたが神経精神科病棟での収容が困難であったため産科病棟へ入院後、翌日に医療保護入院となった。抗精神薬により精神症状は徐々に軽快し、第15病日に任意入院となった。【症例3】26歳。1妊0産。妊娠前より不安神経症の診断で当院神経精神科に通院していた。妊娠39週に経膈分娩、産後6日目に産科病棟で自殺企図があった。夜間のため、翌日に医療保護入院となった。抗うつ薬によって症状は徐々に改善し希死念慮も消失したことから自宅退院となった。【結論】精神疾患合併妊娠では妊娠中および産褥期に精神疾患が増悪することがある。医療保護入院は精神保健指定医による診察が必須であり、入院手続きも煩雑であるため、夜間や休日での緊急入院は困難である。今回提示した3例はいずれも神経精神科での受入が出来ず産科病棟で管理せざるを得なかった。これら症例に対応するため、精神疾患合併妊娠婦の入院体制の構築が重要である。

P-68-6 国内における COVID-19 胎盤の解析

日本大微生物学分野

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【目的】新型コロナウイルス感染症 (COVID-19) の子宮内感染は稀であるが、しばしば胎盤から SARS-CoV-2 が検出されることが報告されている。国内の COVID-19 レジストリ登録症例の中で、胎盤の提供に同意された症例の胎盤を解析した。【方法】各医療施設から提供された胎盤の凍結検体、ホルマリン固定検体などを解析に用いた。検体は感染性物質の輸送規則に則って輸送した。検体より核酸を抽出し、SARS-CoV-2 の定量的 RT-PCR を行った。SARS-CoV-2 抗原の免疫組織化学、in situ hybridization (ISH) を行った。ウイルスが検出された凍結胎盤検体からウイルスを分離し、次世代シーケンサーで解析した。【成績】分娩時 COVID-19 発症中の 23 例、妊娠中 COVID-既往あり分娩時陰性の 6 例、計 29 例の胎盤を解析した。分娩時に COVID-19 発症中 23 例のうち 10 例 (43.4%) の胎盤から SARS-CoV-2 のウイルスゲノムが検出された。ウイルス陽性胎盤の免疫組織化学および ISH では syncytiotrophoblast に陽性シグナルを認めた。ウイルス陽性胎盤凍結検体からは感染性を有するウイルスが分離され、次世代シーケンサー解析にて SARS-CoV-2 と同定された。母体の重症度と胎盤のウイルス検出には相関が見られなかった。胎児への垂直感染例はなかった。分娩時陰性の 6 例の胎盤からはウイルスは検出されなかった。【結論】SARS-CoV-2 の子宮内感染は非常に稀であるにもかかわらず、胎盤には一定の割合でウイルスが感染していることが示された。胎盤に局在するウイルスは感染性を有している場合があるので、分娩後の胎盤の取り扱いには注意が必要である。

P-68-7 MATISSE 国際共同試験の日本部分集団における母子免疫による 2 価 RSV 安定化融合前 F タンパク質サブユニットワクチン (RSVpreF) の安全性および有効性

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【目的】第 3 相、無作為化、プラセボ対照、二重盲検、国際共同治験 (ClinicalTrials.gov number NCT04424316) に日本で組入れられた治験参加者における RSVpreF の安全性及び有効性の記述評価【方法】妊娠 24-36 週の 49 歳以下の妊婦を RSVpreF 群又はプラセボ群に 1:1 に無作為割付けし、生まれた乳児の生後 180 日以内に発現した医療機関受診に至る RSV 陽性重症下気道感染症 (RSV-MA-sLRTI) 及び下気道感染症 (RSV-MA-LRTI) に対するワクチン有効性 (VE) を評価【成績】主要解析時点で、日本部分集団に含まれたワクチン接種完了の妊婦は RSVpreF 群 230 例、プラセボ群 232 例、生まれた乳児は各 218 例及び 216 例だった。日本部分集団の乳児の生後 180 日までの全ての評価時点で RSV-MA-sLRTI (生後 180 日時点で RSVpreF 群 1 例、プラセボ群 4 例) 及び RSV-MA-LRTI (生後 180 日時点で RSVpreF 群 1 例、プラセボ群 8 例) の症例数はプラセボ群と比べて RSVpreF 群で少なかった。生後 180 日時点の VE は、RSV-MA-sLRTI で 75.1% [95% 信頼区間 (CI) : -151.5%, 99.5%], RSV-MA-LRTI で 87.6% (95% CI : 7.2%, 99.7%) だった。RSVpreF 群とプラセボ群との間で安全性の結果に臨床的に重要な差は認められず、母親及び乳児の全集団の安全性結果と概ね同様だった。【結論】日本部分集団でも有効性は全集団の結果と一貫し、母親及び乳児参加者に対して RSVpreF の忍容性は良好だった。

P-68-8 分娩前の腔分泌物培養でウレアプラズマが検出された妊婦の分娩転帰

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【目的】分娩前の腔分泌物培養でウレアプラズマが検出された正期産妊婦の分娩転帰を明らかにすることを目的とした。【方法】2021 年 9 月から 2023 年 8 月に当院で経陰分娩予定であった単胎妊婦を対象とした後方視的コホート研究である。妊娠 35~36 週で腔分泌物培養検査を施行し、ウレアプラズマが検出された症例を U 群、検出されなかった症例を N 群として分娩転帰を検討した。早産症例は除外した。本研究は当院倫理委員会の承認のもと行われた。【成績】全分娩症例 1347 例のうち、経陰分娩予定は 998 例であった。U 群 (n=173) と N 群 (n=825) の背景では、分娩時年齢 (中央値 [最小値-最大値]: 33 [20-42] vs 34 [19-46]), 経妊回数 (1 [1-9] vs 2 [1-7]), 未経産婦 (63.3% vs 50.6%) で差を認めた。分娩転帰では、分娩週数 (39+2 [37+0-41+6] vs 39+5 [37+0-41+6]), 前期破水 (19.7% vs 9.7%) に差を認めた。臨床的絨毛膜羊膜炎 (2.3% vs 1.9%), Apgar Score (5 分値) <7 (2.3% vs 0.7%), NICU 入院 (8.1% vs 8.1%) に差はなかった。多変量解析では前期破水が抽出された。【結論】腔分泌物培養でウレアプラズマが検出された妊婦では前期破水が多いが、それ以外の分娩転帰との関連はないという結果であった。ウレアプラズマは絨毛膜羊膜炎や前期破水の羊水中で高率に検出されると報告されているが、今回の検証では腔内のウレアプラズマと絨毛膜羊膜炎の関連は見られなかった。妊娠後期のウレアプラズマのスクリーニングは分娩、新生児予後の観点からは有用性を見出すことができなかったことから、分娩前のウレアプラズマ検出を目的としたスクリーニングは不要である可能性が示唆された。

P-68-9 帝王切開後、経産分娩後の感染症で、検査科との連携によって *Mycoplasma hominis* が同定され治療し得た2例

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Mycoplasma hominis は、 β ラクトム系抗菌薬に抵抗性を示す泌尿生殖器に常在する菌である。今回、*M. hominis* が同定された2症例を経験したため報告する。症例1は31歳1妊0産。妊娠糖尿病インスリン使用患者。妊娠39週、分娩停止の適応で緊急帝王切開を行なった。術後7日目の採血でWBC 15230/ μ L、CPR 19.85 mg/dLと炎症反応の上昇を認め、創部感染と診断し、Ceftriaxone および Metronidazole の投与および創部洗浄を開始した。術後11日目、炎症反応の改善が乏しく、子宮切開創前面に6cmの膿瘍形成を認めたためドレナージを行なった。穿刺液は培養48時間以降に、微小コロニーの発育を認め、*M. hominis* 感染症を疑い Doxycycline の投与を行い、術後17日目に退院となった。症例2は35歳1妊0産。妊娠38週、前期破水のため誘発分娩を行い経産分娩となった。産後3日目に38度の発熱および会陰の創部離開を認めた。創部感染及び子宮内膜炎を疑い、Cefmetazole での治療を開始したが、炎症反応の改善が乏しく、血液培養および創部培養から微小コロニーの発育を認め、産後9日目に Ampicilin・Gentamicin・Clindamycin へ抗生剤を変更し、産後14日目に退院となった。両症例とも、質量分析にて推定菌種 *M. hominis* と同定された。症例1のみ16SrRNA解析でも *M. hominis* と同定した。当院では2021年夏に、グラム染色で菌体を認めず、白血球が2+以上かつ48時間培養で菌の発育がなかった場合は培養を延長する運用を開始した。導入後は3例で *M. hominis* が検出された。 β ラクトム系抗菌薬を使用しても効果が乏しい場合は、検査科と情報を共有し *M. hominis* 感染症を念頭に置いて Clindamycin や Doxycycline を用いて治療する必要がある。

P-68-10 帝王切開後に発症した、診断に苦慮した創部感染と合併した可能性のある壊疽性膿皮症の1例

鳥取県立中央病院

圓井孝志、山根恵美子、上垣 崇、野中道子、竹中泰子、高橋弘幸

壊疽性膿皮症は炎症反応の上昇と発熱、創部の潰瘍を伴い、抗生剤治療やデブリードマンでは軽快しないため創部感染と診断に難渋する。症例は30歳、女性。妊娠38週0日骨盤位のため選択的帝王切開術を施行した。術後3日に発熱と炎症反応の上昇を認め、広域抗生剤を開始した。術後7日に腹部の創部より多量の排膿を認めたため、デブリードマンを行ったが改善を認めなかった。術後11日目に子宮切開創に膿瘍、腹膜炎を疑う所見を認めたため、Open Abdominal Management 管理とし、腹腔内洗浄を複数回行った。術後14日より、陰圧閉鎖療法を行い、全身状態と創部状態に改善を認めた。壊疽性膿皮症の所見とも矛盾なく、術後18日よりブレドニゾロンを開始した。炎症反応は改善し、術後35日目に全層植皮術を行い、術後45日に陰圧閉鎖療法を終了とした。複数回の創部の洗浄とステロイド投与が奏効したことから、壊疽性膿皮症と創部感染が合併した可能性を考える。壊疽性膿皮症は慢性に経過し、繰り返す蚕蝕性の皮膚潰瘍を特徴とする好中球性皮膚症と位置付けられている。炎症性腸疾患や関節リウマチなど基礎疾患を伴うことが多い。しかし、妊娠に伴う好中球増加は壊疽性膿皮症が誘発されている準備状態であると推測されている。基礎疾患がなくても、帝王切開後に壊疽性膿皮症が誘発されることが報告されている。帝王切開術後の創部合併症に対して、壊疽性膿皮症も可能性も考慮しつつ、診療にあたる必要があると考える。

P-68-11 敗血症を伴った流死産の3症例

愛媛県立中央病院

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【緒言】敗血症治療を必要とした、経過の異なる流死産の3症例を経験したので報告する。【症例1】35歳、G4P3。過多月経と発熱、頭痛、関節痛にて当科受診した。血清HCG 1655 mIU/mL、超音波所見から進行流産と診断した。翌日再診し、頭痛増悪と嘔吐、右肩痛を認め、血圧76/50 mmHg、脈拍95回/分、体温38.0℃、呼吸23回/分、WBC 3950/ μ L、Hb 13.9 g/dL、Plt 8.0万/ μ L、CRP 21.7 mg/dL、髄液検査と頭部CT検査では異常なかった。腔分泌物培養と血液培養からGASが検出され、敗血症と診断し治療を開始した。【症例2】40歳、G9P4。妊娠20週4日、39℃の発熱と右腰背部痛にて前医を受診し、子宮内胎児死亡のため緊急搬送となった。血圧73/34 mmHg、脈拍113回/分、体温36.7℃、呼吸20回/分、WBC 1740/ μ L、Hb 12.8 g/dL、Plt 24.4万/ μ L、CRP 3.9 mg/dLであり、敗血症を疑い治療を開始、同日死産となった。腔分泌物培養からE.coliが検出され、血液培養は陰性であった。【症例3】33歳、G2P2。妊娠22週6日、破水感にて前医を受診し、腔内に胎児娩出され死産し、胎盤遺残で出血が2000gを超え緊急搬送となった。血圧70/50 mmHg、脈拍110回/分、体温36.5℃、呼吸20回/分、WBC 32270/ μ L、Hb 8.8 g/dL、Plt 10.0万/ μ L、CRP 10.1 mg/dL、胎盤を用手排出し、輸血とSBT/ABPC投与を行った。しかし血圧77/52 mmHg、脈拍110回/分、体温36.6℃、呼吸23回/分と改善せず、前医で39℃発熱の情報があり、敗血症と診断し治療を開始した。腔分泌物培養からGBSが検出され、血液培養は陰性であった。【結語】感染が原因の流死産においては、敗血症を伴い全身管理が必要になる場合があり、迅速な診断が重要である。

P-69-1 臍帯血バンク臍帯血採取施設における新型コロナ感染以前と新型コロナ禍の比較

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【目的】非血縁者間造血幹細胞移植には骨髓移植, 臍帯血移植, 末梢血幹細胞移植があり, 臍帯血移植は1997年から実施されている。2016年より骨髓移植を上回り, 特に新型コロナ禍, すでに保管されている臍帯血の需要は高まっている。臍帯血採取は産科施設でしか採取できない。新型コロナ感染以前と新型コロナ禍での臍帯血採取について比較し, より多くの質の良い臍帯血を採取し登録公開するための課題を考えた。【方法】当院では2001.4より臍帯血を採取している。2020.1新型コロナ感染が発症してからの2020.4~2023.3 (B群)とそれ以前2017.4~2020.3 (A群)について当院での臍帯血採取状況, 臍帯血バンクでの受入状況, 臍帯血移植数について検討した。【成績】日本の臍帯血公開数は現在約1万件である。当院での分娩数A: 5191, B: 4884。臍帯血受入数A: 2393, B: 2449。調整数A: 445, B: 422。日本赤十字社関東甲信越さい帯血バンク全体では臍帯血受入数A: 10991, B: 12050。調整数A: 2320, B: 1949であった。分娩数は全国でコロナ禍減少しており, 当院でもB群で減少しているが, 臍帯血受入数は当院もバンクもB群で微増していた。調整数は当院もバンクもB群で減少しており, 特に2022年の減少が目立った。【結論】新型コロナ感染が引き金となって日本全体の出生数が100万人から77万人と大きく減少している。分娩数が減少すれば, 当然臍帯血採取数も減少する。しかし, 臍帯血の需要は拡大している。造血幹細胞提供支援施設が開催した研修会の実施, 臍帯血採取施設の拡大, 臍帯血献血の一般向け周知, リクルート, 臍帯血採取スタッフの技術向上, モチベーションアップ等今後に向けて改善する必要があると考えた。

P-69-2 RPOC に対するレルゴリクスの有効性

杏林大

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【目的】RPOC (retained products of conception) の治療法は, 確立されていない。子宮鏡手術や子宮内容除去術は術中大量出血の危険があり, 優位性も示されていない。また, 子宮動脈塞栓術は次回妊娠に危惧がある。今回, 我々は出血が持続するRPOC例にレルゴリクス (gonadotropin-releasing hormone agonist) を投与し, 有効性を検討した。【方法】RPOCを認め, 2022年以降に十分な説明後レルゴリクス40mg/日を内服した4例 (R群)と, 2015年から2022年に保存的治療のみ行った5例 (C群)及び侵襲的治療を行った4例 (I群)について後方視的に検討した。【成績】先行妊娠の週数の中央値はR群9週, C群21週, I群19週 (以下同順に記載)であり, RPOC診断時に全例性器出血を認めた。子宮内残存組織の長径の中央値は29mm, 19mm, 19mm, 介入 (レルゴリクス内服開始または侵襲的治療日)までの日数の中央値はR群8日, I群22日であった。止血までの日数は中央値でR群は介入後43日, C群は診断後48日, I群は介入後21日要した。子宮内残存組織の消失の中央値はR群は介入後51日, C群は診断後48日, I群は介入後19日であった。レルゴリクス内服中に侵襲的治療を要した例はなく, 1例で内服終了後に妊娠成立し, 良好に経過している。【結論】今回の検討では, レルゴリクス投与群で子宮内残存組織が大きい傾向にあるにもかかわらず, 止血及び残存組織消失までの日数は保存的治療群に比し短縮傾向にあり, RPOCの非侵襲的治療としてレルゴリクス投与が考慮されると思われた。一方, 止血が優先される例は, 侵襲的治療の優位性が示唆された。今後症例を集積し, 母体背景と病型を鑑みたRPOC治療戦略を構築していきたい。

P-69-3 NRFSにより緊急帝王切開術を実施し生児を得た Massive perivillous fibrin deposition の1例

高知医療センター

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【緒言】Massive perivillous fibrin deposition (MPVFD) は絨毛間腔にフィブリンが沈着し, 絨毛の壊死や変性をきたすものである。頻度は0.03~0.5%と稀であるが, 胎児発育不全 (FGR) や胎児機能不全 (NRFS), 時に子宮内胎児死亡 (IUFD) を起こすことがある。今回, 交通事故を契機に入院となり, 胎児機能不全のために緊急帝王切開術を実施して生児を得たMPVFDの1例を経験したので報告する。【症例】30歳2妊1産。当院で妊娠初期より管理していたが, 経過は良好であった。妊娠27週4日の定期的妊婦健診では異常を認めなかった。妊娠27週5日から胎動減少を自覚しており, 妊娠27週6日に交通事故を契機に当科を受診した。経腹超音波検査上, 明らかな胎盤肥厚や後血腫などは認めなかったが, 胎児心拍数陣痛図にて遅発一過性徐脈を認めたため, 入院管理とした。その後, 経時的に胎児血流の悪化認め, また, 遅発一過性徐脈も繰り返すため胎児機能不全 (NRFS) として, 妊娠28週0日に緊急帝王切開術を実施した。児は1076gの男児でApgar score: 4点 (1分値) / 6点 (5分値), 臍帯動脈血ガスpH: 7.131であった。術中所見では明らかな常位胎盤早期剝離を示唆する所見は認めなかった。胎盤は母体面がびまん性に白色調を認め, 非常に硬い印象であった。胎盤病理検査ではMPVFDと診断された。母体の術後経過は良好であり, 術後4日目に退院となった。【考察】MPVFDは13~50%でIUFDを起こすとの報告もあり, 胎動減少時や胎児 well-being の評価が必要な場合には胎盤異常も念頭に診察を行う必要があると考えられた。

P-69-4 胎児発育不全の一因として胎盤限局性モザイクが考えられた一例

長崎大

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【症例】43歳, 6妊2産(経産分娩2回, 自然流産3回)。自然妊娠し, 初期から近医産婦人科で妊娠管理されていた。妊娠16週3日の妊婦健診で大腿骨長が $-2.8 \sim -3.0SD$ と短縮を認め, その他の長幹骨も $-2.0SD$ から正常下限範囲であり系統疾患の可能性が疑われたため, 精査と今後の妊娠管理のため当科へ紹介された。当科受診時の超音波検査でも長幹骨長は同様の所見であり, 染色体異常の可能性を疑い, 羊水染色体検査(Gバンド分析およびFISH法)を施行したが結果は正常核型であった。妊娠26週で胎児MRI検査を施行したが, FL短縮以外の異常所見は認めなかった。また妊娠31週で胎児の骨評価目的に胎児3D-CT検査を施行したが, 骨系統疾患は否定的であった。胎盤の超音波検査所見およびMRIでは胎盤の肥厚と絨毛膜下血腫が疑われ, 骨系統疾患ではなく胎盤機能不全による胎児発育不全と考えた。妊娠36週4日より頻回な胎児一過性徐脈を認めるようになり, 妊娠36週5日に胎児機能不全の診断で緊急帝王切開術を施行した。児は $1,600g$ ($-3.2SD$, SGA)の女児でありApgar Scoreは8点/9点(1分/5分)であった。臍帯は卵膜付着であり, 胎児機能不全の原因と考えられた。胎盤病理学的検査では胎盤の絨毛膜下血腫と梗塞を認めた。胎盤の染色体検査で $47,XX,+10$ [22], $46,XX$ [18], 臍帯血染色体検査では正常女児の核型であったため, 胎盤限局性モザイクと診断した。【まとめ】骨系統疾患が疑われ, 精査の結果胎児発育不全と診断した。絨毛膜下血腫および臍帯卵膜付着が胎児発育不全の原因と考えられたが, 同時に胎盤限局性モザイクを認めた。

P-69-5 MRIが妊娠後期における臍帯の走行および付着部評価に有用であった2症例

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臍帯卵膜付着は, 胎児発育不全, 胎児機能不全, 緊急帝王切開などのリスクが上がると思われ, 近年臍帯付着部を評価する機会が増えている。臍帯付着部評価は, 妊娠初期から中期においては超音波で比較的容易に可能とされているが, 妊娠週数経過とともに胎児の陰影が増強し評価困難になっていく。今回われわれは, 妊娠後期での臍帯付着部および臍帯走行評価にMRIが有用であった2症例を経験したので報告する。症例142歳, 初産婦。他院で妊娠初期に卵膜付着を指摘。妊娠23週に当院初診。胎盤は前壁付着。臍帯付着部は後壁卵膜を疑うが, 確定できずMRIを撮像した。臍帯動脈は卵膜内を前壁胎盤から後壁に向かって走行, 後壁卵膜からの卵膜付着を認めた。妊娠39週5日に帝王切開施行し, 肉眼的にもMRI所見に一致した卵膜付着を認めた。症例219歳, 初産婦。他院で2絨毛膜2羊膜双胎の管理をされ, 頸管長短縮を認めたため切迫早産で妊娠28週に当院紹介初診。前医より卵膜付着が疑われていた。胎盤は後壁, 臍帯は前壁下部の卵膜付着が疑われたが, 臍帯走行が不明瞭であったためMRIを撮像した。胎盤は後壁付着, 先進児の臍帯は子宮下部前壁の卵膜付着が疑われた。同部位で臍帯動脈は, 臍帯動脈1本と臍帯動脈2本に別れ, 後者は子宮壁から遊離した隔壁構造内を走行していた。妊娠32週0日に子宮収縮抑制困難となり緊急帝王切開術を施行。帝王切開時, 子宮筋層切開部のごく近傍の卵膜内を走行する臍帯が透見された。臍帯は卵膜付着で, MRIと同様の所見であった。結論MRIにより超音波で評価困難な妊娠後期の臍帯付着部や臍帯走行の正確な評価をおこない, 安全に周産期管理を行うことができる。

P-69-6 MRIを用いた新しい低置胎盤の診断法について

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【目的】低置胎盤は, 分娩時大量出血の原因となる可能性があり分娩方法の選択にも関与するため, その診断はより正確に行われる必要がある。診断は主に経産超音波検査でなされるが, 特に側壁付着の低置胎盤では, 距離の測定が難しく, 多くが見逃されている可能性がある。今回, MRIを用いた新しい測定方法を考案したので報告する。【方法】内子宮口に接する平面0を想定, この平面に直交し, 内子宮口を通る直線をLとする。直線Lを含み直線Lを軸に15度ずつ回転して得られる平面群 α で子宮を撮影した。平面群 α は計12枚の画像よりなり, 子宮壁は内子宮口より花弁状に立ち上がり描出され, その子宮壁の内側に付着して胎盤が確認できる。この撮像法をPlacenta previa procedure (PPP)と命名した。このうち内子宮口付近に胎盤が確認できる画像を選択し, 胎盤下縁から内子宮口までの距離を測定した。【成績】この撮像法を用いた低置胎盤症例を, 前壁付着胎盤で1例, 後壁付着胎盤で2例, 側方付着胎盤で1例経験した。前壁付着の症例では, 診断自体は通常の横断面, 矢状面でも可能であったが, 空間的広がりを見視化することで, 帝王切開の際の切開ラインの決定に寄与した。また, 側方付着の症例では, 経産超音波や通常の基本断面のみで撮影したMRIでは測定できなかった内子宮口と胎盤下縁までの距離を測定することができ, 分娩様式の選択に際して重要な決定材料となった。【結論】MRIでは指定した平面での断面像を得ることが比較的容易であり, 今回考案した測定法は, 特に側方付着の低置胎盤症例の診断に有効であると考えられる。今後さらに症例を集積し, PPPを用いた胎盤の位置測定法の有用性について検討する必要がある。

P-69-7 一児胎児発育不全の原因として分娩後に胎児血管血栓症が判明した一絨毛膜二羊膜双胎の一例

宮崎大

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【緒言】胎児血管血栓症は一絨毛膜双胎で多く、しばしば臍帯異常を伴う。妊娠中の診断は困難で胎盤病理で初めて診断される例も多い。今回、妊娠中期から一児胎児発育不全と同児の血流異常を認め、妊娠29週頃より単一臍帯動脈となり、妊娠30週に胎児心拍数異常のため緊急帝王切開を施行し、胎盤病理で患児側に胎児血管血栓症を認めた症例を経験したので報告する。【症例】30歳、G1P0、不妊治療後妊娠。妊娠10週に一絨毛膜二羊膜双胎のため当院初診、妊娠15週より羊水量差を認め入院となった。smaller児は発育緩慢で次第に臍帯動脈血流波形異常を認め、妊娠19週に同児の羊水過少、一児胎児発育不全から胎児鏡下胎盤吻合血管レーザー凝固術(fetoscopic laser photocoagulation: FLP)の適応と判断し、妊娠25週FLP目的に他院受診、同日入院となった。他院でも適応を満たしていたが本人希望で実施せず、妊娠29週5日状態著変なく当院転院となった。smaller児は推定体重500g(-4.0SD)ほどで、これ以上の妊娠延長は胎児死亡のリスクが高いと判断、リンデロン投与後に分娩の方針とした。リンデロン投与後、妊娠30週3日同児の胎児心拍数異常を認め緊急帝王切開となった。第1子は1052g(small for dates: SFD)、女児、Apgar score: 3/6、UA-pH: 7.320、第2子は747g(SFD)、女児、Apgar score: 2/4、UA-pH: 7.012であった。第2子はNICU入室後の頭部エコーで出血性脳梗塞を疑う所見を認めた。胎盤は第2子側で臍帯卵膜付着と過短臍帯に加え、胎児血管に広範囲の石灰化を伴う壁血栓を認め、本例は慢性的な胎児血管灌流異常による胎児発育不全と思われた。【結語】臍帯異常を伴う一絨毛膜双胎は胎児血管血栓症に注意が必要である。

P-69-8 子宮底部横切開による帝王切開5例の検討

旭川医大

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【背景】胎盤や臍帯血管が子宮体下部前壁に付着している症例の帝王切開では、通常の子宮体下部横切開では胎盤への切り込みを回避できない場合がある。この際、当院では子宮底部横切開を選択している。今回我々は、子宮底部横切開を要した選択帝王切開5例を経験したので報告する。【症例】症例1は29歳、2妊0産。辺縁前置胎盤、前置血管に対して妊娠36週1日に選択帝王切開を施行した。術中出血は2445mLだった。症例2は38歳、3妊0産。辺縁前置胎盤に対して妊娠36週0日に選択帝王切開を施行した。術中出血は1324mLだった。症例3は35歳、4妊3産(うち帝王切開1回、癒着胎盤3回)。低置胎盤、癒着胎盤疑いに対して妊娠37週2日に選択帝王切開を施行した。胎盤は自然剥離せず癒着胎盤が強く疑われ、一期的に子宮全摘術を行った。帝王切開術中に内腸骨動脈バルーンを留置し、児娩出後に血流遮断して子宮を摘出した。術中出血は1256mLだった。症例4は41歳、1妊0産。前置血管に対して妊娠35週0日に選択帝王切開を施行した。術中出血は834mLだった。症例5は33歳、3妊1産(経陰分娩1回)。全前置胎盤に対して妊娠37週2日に選択帝王切開を施行した。底部横切開創からの強出血がみられた。子宮収縮も不良であり、子宮腔内バルーン留置など止血処置をしたが産科DICとなった。子宮摘出はせず閉腹したが性器出血が持続し、手術室で子宮動脈塞栓を行った。術中出血は4947mLだった。【結語】胎盤や前置血管が子宮体下部横切開の切開予定部位上に存在する症例に対して、子宮底部横切開を行うことで、これらへの切り込みを回避することができた。

P-69-9 COVID-19感染18日後に子宮内胎児死亡し、胎盤病理で胎児血管灌流不全(FVM; fetal vascular malperfusion)を認めた一例

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29歳。G2P1。X-18日にCOVID-19感染しその後自然軽快した。X日(妊娠34週5日)、胎動減少を主訴に前医を受診し、CTGでFHR190bpmの高度頻脈を認めた。経腹超音波断層法で心機能低下を疑われ精査目的に当院へ母体搬送となった。当院搬送後CTG装着し、基線再変動はminimalでFHR180bpmであった。経腹超音波断層法で羊水過少を認めたが、心拡大はなく、胎児水腫は認めなかった。臍帯動脈拡張期血流は保たれていた。帝王切開のためCTGを外し、母体移動した5分後にCTGを再装着したところ胎児心拍の停止を確認した。X+2に経陰的に死胎児娩出した。児は、体重2540g、身長46cm、外性器は女児で、外表奇形は認めなかった。胎盤娩出後に表面を擦過しPCR検査を実施したが、SARS-CoV-2は検出されなかった。原因究明目的に母体採血を行い、AFP: 148(妊婦正常値: 300-800 ng/ml)、Hb-F: 0.3%で母児間輸血症候群は認めず、母体の凝固異常、内分泌異常は認めなかった。抗SS-A抗体と抗核抗体が陽性であり、内科へ紹介し精査中。TORCH症候群は認めなかった。胎盤病理検査では、剖面はびまん性に蒼白であった。組織学的には、幹絨毛血管の狭窄・閉塞、末梢絨毛では血管の虚脱、絨毛間質血管核崩壊像を認め、胎児血管灌流不全(FVM)の像であった。絨毛に炎症所見はなく、CAMは否定的であった。COVID-19の免疫染色を行うも、優位な所見は得られなかった。SARS-CoV-2による急性胎盤感染は、組織球性絨毛間質炎、線維周囲沈着、および栄養膜壊死等の特徴的な所見がみられるが、その後は持続的感染しにくいことが知られている。非急性期には局所の免疫応答として、母体血管還流不全(MVM)や胎FVMを発症するとの報告がある。今回子宮内胎児死亡となった病態として、FVMが考えられた。

P-69-10 頻回に分娩後異常出血を来す明らかな遺残胎盤のないRPOC (Retained products of conception) で過大着床部が認められた1例

市立奈良病院

原田直哉, 延原一郎, 春田典子, 東浦友美, 藤井 肇, 赤坂往倫範

【緒言】以前われわれは、間欠的に致死的な分娩後異常出血 (PPH) を繰り返す症例を経験し、子宮摘出により子宮筋層には過大着床部 (EPS) が認められた症例を報告した。その後の更なる組織学的な検討により retained products of conception (RPOC) も認められたため、追加の報告を行う。【症例】34歳、凍結胚細胞移植により第2子を妊娠し、39週に吸引分娩で出産となったが、PPHとなり(出血量: 2500mL) 輸血をおこなった (MAP6U, FFP6U)。産褥7日目に特記すべき異常所見なく退院したが、14日目に自宅で多量の出血をきたし救急車で来院した。子宮頸管後唇で動脈性に噴出していた部分を数か所縫合し (3000mL) 輸血した (MAP10U, FFP8U)。直後の造影CTでは子宮体部後壁筋層の血流が著明で、早期に濃染される2cmほどの隆起性病変も認めたが、extravasationは無かった。16日目に再出血を来し (200mL) 造影CTで今度は子宮腔内に著明な extravasation を認めたため、子宮動脈塞栓術による止血を行い輸血した (MAP2U, FFP4U)。17日目の造影MRIで子宮腔内に明らかな胎盤遺残を認めなかったが、本人の強い希望もあり根治目的で21日目に子宮を摘出した。摘出後の肉眼検査でも子宮腔内に明らかな胎盤遺残を認めなかったが、病理学的に子宮筋層部にはEPSを、脱着膜部にRPOCを認めた。【結語・考察】画像検査や摘出標本の肉眼的所見にて子宮腔内に明らかな遺残胎盤が無くても、詳細な病理学的検索でRPOCが認められる場合がある。従来、EPSは着床部位の中間型栄養膜細胞の子宮筋層にまでおよぶ浸潤性変化であるが非腫瘍性変化であり病的意義は乏しいと考えられてきたが、われわれはRPOCの発症にEPSが関与しているのではと考えている。

P-69-11 血腫形成を伴った胎盤遺残の一例

飯塚病院

徳永奈穂

【緒言】胎盤遺残は Retained products of conception (以下 RPOC) の主要原因である。遺残胎盤からの出血により、子宮口より下垂する血腫形成を認めたため、診断に苦慮した症例を報告する。【症例】31歳、G4P2。妊娠40週1日に前医で自然頭位経膣分娩となり経過良好で自宅退院した。産褥23日目に下腹部痛と性器出血があり、前医に救急搬送され、入院となった。前医入院時は腫瘤形成なく、子宮口からの持続出血があり、子宮復古不全の診断で子宮収縮薬投与を開始されたものの、性器出血は持続した。2日間でHb 11.6 g/dl から 5.7 g/dl に低下し、産褥25日目に当院に救急搬送となった。当院での診察では子宮口から突出する表面平滑で暗赤色の手拳大腫瘤があり、出血が持続していた。高度貧血を伴っており輸血を開始した。造影MRI検査では腫瘤は造影されず、子宮内に血管外漏出像があり、胎盤遺残の所見を疑った。両側子宮動脈塞栓術を施行し、出血コントロールを得た。産褥26日目に全身麻酔下で腫瘤除去及び子宮鏡下の胎盤遺残除去を行った。術後経過は良好であり、術後3日目に退院となった。病理検査では腫瘤は血腫の診断で、内部に炎症細胞の浸潤、石灰化を伴う絨毛組織や脱着膜組織を認めた。子宮内容物は胎盤遺残に矛盾しない所見であった。【考察】後期分娩後異常出血の最多の原因はRPOCである。今回の症例は、産後出血が卵膜に包まれていたことから産褥23日目に性器出血として顕在化したと考えられた。RPOCによる産後出血の症例が過去にも報告されており文献的な考察も含め本症例について考察する。

P-69-12 急激な経過を辿ったが、児を救命し得た壊死性臍帯炎の1例

新潟市民病院

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【緒言】今回、急激な経過を辿ったが、児を救命し得た壊死性臍帯炎の1例を経験したので文献的考察を加えて報告する。【症例】35歳の初産婦。他院で妊娠管理中、妊娠30週4日に性器出血あり入院。炎症反応上昇あり、塩酸リトドリンと抗生剤点滴が投与された。妊娠31週5日、前期破水し子宮収縮増強したため当院へ母体搬送となる。当院到着後、すぐに児は高度遷延徐脈となり、超緊急帝王切開術で1833gの女児を娩出したが、児心拍は聴取されず、気管挿管や胸骨圧迫などの蘇生で、出生後7分30秒に児心音をわずかに聴取、14分30秒で児心拍が再開した。児は当院NICU入院管理となる。臍帯は児の臍輪部で狭小化、血種あり、全長に渡り臍帯静脈壁の白色肥厚を認めた。胎盤病理では高度の絨毛膜羊膜炎と臍帯炎があり、特に臍帯静脈周囲の炎症が高度で石灰化を認め、壊死性臍帯炎の診断であった。術後、母体の経過は問題なく、第7日目に退院。児は神経学的異常を認めず、第5生日に抜管でき、第47日目に退院。1歳8か月時点で、頭部MRIの異常なく、発達・知能検査は正常である。【考察】壊死性臍帯炎は臍帯の慢性的、重度な炎症であり、いくつかの病原性感染因子の報告があるが、本症例では不明であった。超音波検査では臍帯血管に沿った石灰化が特徴的だが、急激な経過のため出生前に確認は出来ず、分娩後に肉眼的、病理組織学的に確認された。【結語】壊死性臍帯炎は稀ではあるが、早産や子宮内胎児発育遅延のみならず、胎児機能不全や子宮内胎児死亡など重篤な状態の原因となりうるため、超音波検査での臍帯の精査は重要であり、異常を認めた場合、厳重な管理が必要と考えられた。

P-70-1 性暴力被害者へ必要なケアを実現するために～国境なき医師団が行う性暴力被害者への医療サービスについて～

国境なき医師団助産師
國吉悠貴

【目的】性暴力は性に対する人権侵害である。その被害は性別や年齢に関係なく、何百万人もの性暴力被害者（以下、被害者）の人生を残酷に破壊する。しかし、特に国境なき医師団（MSF）が活動する低・中所得国においては、性暴力が医療上の緊急事態であるにもかかわらず、被害者に対する医療サービスが不足していたり、必要なケアへのアクセスが制限されていることが深刻な問題となっている。【成績】【方法】2022年、MSFは3万9900人以上の被害者を診療した。その数は2016年の1万3800件から3倍近く増加している。MSFのプロジェクトでは、特に性暴力発生率の高い国において、性暴力被害にあった後のHIVや性感染症の予防、緊急避妊薬の投薬のため72時間以内に医療を提供できるよう努めている。もちろんその中には身体的損傷の治療も含まれ、また心理的サポートも重要なケアの一部である。被害者は被害にあった後、恐怖、偏見、自己嫌悪など多くの精神的苦痛や心的外傷によりその後の人生において長期間（もしくは一生）苦しみ続ける。それらの精神的苦痛を抱える被害者達に寄り添うために、心理士によるカウンセリングを継続的に行っている。今回はMSFが行う性暴力ケアサービスの三つの柱、すなわち、(1)性感染症と妊娠の予防と身体的損傷の治療、(2)心のケア、(3)社会的ケア、について、またそのような情報をどのように地域住民や近隣の公共機関に周知してもらい必要な医療サービスへのアクセスを可能にしているのかを報告していく。【結論】被害者の人生に深刻な影響をもたらす性暴力に対して、包括的かつ継続的なケアが必要である。

P-70-2 月経前症候群の重症度に伴う皮脂中 mRNA 発現変化の解析～客観的指標の確立に向けて～

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【目的】月経前症候群（PMS）は、多様な精神・身体症状により女性のQOLに悪影響を及ぼすことが知られているが、診断の補助となるような客観的指標が存在しないため、本人および医師が病状を正確に把握することが難しいという課題がある。我々はこれまでに非侵襲的に採取可能な皮膚表面の皮脂中にヒト mRNA 分子が存在する事を見出し、皮脂中 mRNA の網羅的発現解析により、mRNA の月経周期に伴う発現変動を観察できる可能性を示してきた。そこで今回、PMS の重症度を知る為の客観的指標として皮脂中 mRNA が有用であるか可能性検証を行った。【方法】健康女性を対象に、PMS 症状の重症度を知る為の目録である Daily Records of Severity of Problems (DRSP) を用いた症状記録と黄体期に顔全面から皮脂採取を行い、医師の診断結果を基に対象者を無症状群と PMS 有症群に分け、皮脂中 mRNA の網羅的発現解析を実施した。【成績】次世代シーケンサーから得られた皮脂中 mRNA 発現情報と DRSP score との相関解析を実施したところ、DRSP score と相関関係にある遺伝子が165種抽出された（Spearman 順位相関係数 > 0.35）。それら遺伝子群に対しエンリッチメント解析を実施したところ、PMS の病態と密接に関連する成長ホルモンや酸化ストレス、免疫応答（炎症）などの生物学的機能に紐づく遺伝子が豊富に含まれていることが明らかになった。【結論】DRSP score と相関する遺伝子群が PMS の病態と密接に関連する機能をもっていたことから、皮脂中 mRNA の発現情報は PMS の重症度を簡便かつ非侵襲的に知る客観的な指標になる可能性が示唆された。

P-70-3 わが国における DV・性暴力被害者に対する医療的支援に関する全国調査

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河野美江¹、渥美治世²、種部恭子³、安達知子⁴、京 哲⁵

【目的】わが国の産婦人科医師における「DV・性暴力被害者に対する診察」ならびに「こども、男性、性的マイノリティの性暴力被害者に対する医療支援」について現状を明らかにする。【方法】2022年12月から2023年1月、全国の医療機関に勤務する産婦人科医師16,500名にアンケート調査を行った。1,387名から返信があり、有効回答の1,158名を対象とした（有効回答率83.5%）。【成績】対象のうち母体保護法指定医は67.7%で、患者が人工妊娠中絶、緊急避妊薬処方、性感染症検査を希望した場合に性暴力があったことを確認している割合はそれぞれ、72.9%、62.3%、50.7%であった。DV・性暴力被害が疑われる患者の診察に携わったことがある割合は76.5%で、性暴力の定義は90.5%、ワンストップ支援センターは73.8%で認知されていた。こども、男性、性的マイノリティの性暴力被害を学ぶ機会があった割合はそれぞれ42.3%、25.8%、19.2%と少なかったが、その内訳でそれぞれ50-60%を占めたのが学会講演であった。なお、実際に診察した割合はそれぞれ25.7%、1.6%、1.7%であった。【結論】回答した産婦人科医師は3/4以上が女性被害者の診療に携わっており、DV・性暴力被害が疑われる患者への対応に注力している一方、回答率の低さに課題があると考えられた。こども、男性、性的マイノリティの被害への学習の機会や支援割合は低く、これらの対象が速やかに受診できる、あるいは受診先から連携できる診療科の確保、体制整備やマニュアル作りは急務であり、医学部や学会で性暴力被害者支援に関する教育が行われるよう働きかけが必要と考えられた。

P-70-4 機能性保温素材衣料による月経痛和痛と温熱性愁訴の軽減

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【目的】月経痛の治療には、主に薬物治療が用いられているが、消化器症状や血栓症などの副作用の問題もあり、必ずしも好まれてはいない。非薬物的な月経痛の和痛法にカイロなどで40℃程度の下腹部加温する理学的方法もあるが、発熱材料を用いるため、特に環境温の高い季節には適用に困難がある。ところで、近年、身体からの蒸散成分を吸着熱に変える技術(蓄熱保温法)が開発され、同技術を用いた高機能衣料が市井に広まりつつあるが、これらを月経痛和痛に試みた報告はない。高機能素材を用いた月経痛和痛のために、主として腰背部から下腹部を穏やかに蓄熱保温する衣類を新たに作成し、それらによる月経痛の和痛や過強な冷房による温熱的愁訴に対する軽減効果を検討した。【方法】検討は夏季昼間時間帯に実施した。倫理委員会審査・認可の下、下腹部全体をマイルドに加温するショーツ、またはショーツパンツを作成して被験者に着用させ、4～5時間の通常の日常行動をとらせた。対象は21～35歳の女性18名である。高機能衣料の着用のある場合とない場合の月経痛の程度、温熱的不快感の程度を4段階評価させた。【成績】被験者18名中、11名が7時間以上、高機能素材のショーツを着用できた。高機能素材衣料による過強な熱感(暑すぎ)を訴える被験者はなかった。月経痛の程度は、温熱素材の不使用時に比して、57%の被験者で月経痛和痛が得られた。過強な冷房への温熱的不快感は、91%の被験者で軽減が得られた。【結論】高機能素材を用いた衣類の着用によって、月経痛が軽減し、温熱的不快感が軽減した。蓄熱保温作用を持つ高機能衣料材料による下腹部保温は、月経痛や冷えの改善方法として有用である。

P-70-5 当院で経験した月経血流出障害を伴う女性生殖器形態異常に対する検討

弘前大
内田苑佳, 福原理恵, 横田 恵, 横山良仁

【目的】月経血流出障害を伴う女性生殖器形態異常では、初経後早期から腹痛や月経困難症を生じることが多く、適切な治療を要する。しかし治療方法や術後管理について、日常臨床において迷うことが少なくない。今回我々は、当院で経験した月経血流出障害を伴う女性生殖器形態異常について、手術方法や術後管理、予後について検討し報告する。【方法】2010年から2023年までの間に当院で月経血流出障害を伴う女性生殖器形態異常と診断した10例を後方視的に検討した。【成績】初診時の平均年齢は14.0歳(11-24歳)で、全例で下腹部痛や月経困難症などの症状がみられた。疾患の内訳は膣欠損が5例、OHVIRA症候群が3例、Wunderlich症候群が1例、非交通性副角子宮を伴う単角子宮が1例であった。経腹・経直腸超音波検査、MRI検査、症例に応じてvaginostomyも行い診断し、全例で月経血流出路作成のため手術を施行した。手術アプローチは腹腔鏡+経膣が5例、経膣が4例、腹腔鏡+経膣から術中に開腹へ移行したものが1例であった。症例に応じて、術中に超音波検査や子宮鏡検査も併用した。腹腔内観察を行った6例中4例で子宮内膜症の合併を認めた。術後は月経痛や子宮内膜症再発の有無についてフォローを行い、手術時に子宮内膜症を合併していた4例中1例で子宮内膜症の再発を認めた。【結論】月経血流出障害を伴う女性生殖器形態異常では子宮内膜症の合併率が高く、手術時に腹腔内観察を行うことは子宮内膜症の評価および治療も同時に施行できるため有用である可能性がある。また術後は月経痛や子宮内膜症再発に注意し、長期的にフォローをする必要がある。

P-70-6 日本語版のPMS/PMDD尺度の検討

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【目的】PMS/PMDDはQOLを低下させる有症女性の重大な健康課題の一つであり、医療につながる手前の未病状態から治療に難渋する重症状態まで広範囲のスペクトラムを形成する病態である。近年それらに対する医療以外のヘルスケアサービスも多数提供され、これらの有効性を測る上で重症度などを評価するツールが必要である。今回、PMS/PMDDを対象とした日本語の既存の尺度についてレビューを行い、各尺度の目的や計量心理学的特徴などを整理する。【方法】データベース(医中誌web, Pubmed)を1960年～2023年の期間で検索し、PMS/PMDDを対象とした日本語版の尺度を収集した。日本語か英語で本文が入手できる文献のレビューを行い、下位尺度の概要と、信頼性・妥当性の検討の有無について評価した。【成績】該当する尺度は29種あった。信頼性の検討が行われているものが12種、妥当性の検討が行われているものが11種、信頼性・妥当性ともに評価されているものが10種であった。PMS/PMDDの尺度はその記録の方法から、毎日記録を行う「日々記録型」と、記憶している月経前の症状を1回の質問で問う「記憶型」に分類される。日々記録型で信頼性・妥当性がともに検討されているものは3種、記憶型で信頼性・妥当性が検討されているものは7種存在した。尺度の目的としては、スクリーニング・診断・重症度・生活への影響度の評価などがあった。【結論】現時点ではPMS/PMDDの評価をする尺度は統一も確立もされていない。PMS/PMDDの現状把握や介入の効果判定のためには、その目的や対象に応じた適切な評価ツールが求められるので、尺度の確立に向けてさらなる検討が必要である。

P-70-7 閉経前乳がん患者の治療にともなう QOL 変化について

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【目的】乳がんは日本人女性の9人に1人と罹患数が多く、乳がんサバイバー人口も増加している。婦人科医がサバイバーシップとしてヘルスケアに携わる機会が多いが、本邦における閉経前初期乳がん患者のQOLデータは存在しない。本研究の目的は、閉経前乳がん患者の治療によるQOLを明らかにすることである。【方法】当院婦人科と乳腺外科が共同で行う「閉経前乳がん患者のcancer treatment induced bone loss: CTIBLとQOLの観察研究」で同意の得られた初期治療を開始する乳がん患者28人を対象に、治療開始前から6か月ごと2年間、調査を行った。QOLの指標にはEuro Qol 5-dimensions 5-levels: EQ-5D-5Lの日本語版タリフで換算したものを使用し、エストロゲン欠落によるQOLは簡略更年期指数 (simple menopause index: SMI) で評価した。血液学的データはFSH, LH, エストラジオール (E2) を測定した。経時変化はANOVAで統計解析を行った。本研究は当院の倫理委員会で承認を受けている。(承認No.B191200055)【成績】治療開始時EQ-5D-5Lは0.8659±0.7617, 6か月後0.8338±0.136と低下し、12か月でも0.8339±0.1347と変わらず、18か月で0.9100±0.0503, 24か月で0.9032±0.0359と上昇した。血管運動神経症状のSMIは経時的に悪化し治療開始後18か月で有意に上昇した($p=0.02$)。FSHは治療開始時に比べ6か月で有意に上昇し($p=0.002$)、12か月、18か月では減少した。E2はばらつきが大きかった。【結論】閉経前乳がん患者では治療開始後6か月から12か月のQOL低下が強くみられ、その後改善する。ただし、エストロゲン欠乏症状としての血管運動神経症状は持続的に悪化しており適切な対処を要すると考えられた。

P-70-8 性犯罪・性暴力被害者のためのワンストップ支援センターの活動

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【目的】性犯罪・性暴力被害者のためのワンストップ支援センターは性暴力被害者に、被害直後から回復まで継続して総合的な支援(医学的、心理学的、社会的、法的支援など)を可能な限り一か所で提供する。これにより被害者の心身の負担を軽減して回復を図り、警察への届出の促進、被害の潜在化防止を目的としている。当センターは救命救急センターを有する総合病院に設置された病院拠点型のワンストップ支援センターで、24時間365日体制を取っている。2016年1月5日開設から2023年3月31日までの活動内容を報告する。【方法】開設から2023年3月31日までの延べ利用者数は電話相談11307件、来所相談3340件、診察1001件、新規受付実人数2396名、新規来所実人数1057名であった。性暴力被害の実態を後方視的に検討する。【成績】2016年に開設後、相談件数も新規受付者数も年々増加していたが、COVID-19が流行し始めた2020年は減少し、2021年以降は再度増加している。2022年度は新規受付者が521名、新規来所者が198名だった。新規来所者198名のうち18歳未満が20.2%、被害から72時間以内の急性期に来所した人が44.4%であった。見知らぬ人からの被害は12.0%のみ、加害者は知人や親族が83.3%を占めた。SNSが関係する被害は年々増加し、2022年度は31件だった。また2022年6月から施行されたAV出演被害防止・救済法に関連する被害は2件だった。受診経路は警察からの紹介が26.3%、診察費用は、警察介入での公費負担が55.7%だった。【結論】性暴力被害者の人権が守られ、希望する対応、治療や支援がスムーズに受けられるよう今後も活動を続けていきたい。

P-70-9 当院における子宮頸がんワクチン接種状況とその傾向

関東中央病院

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【目的】2022年4月から子宮頸がん予防ワクチン(以下HPVワクチン)定期接種の積極的勧奨がようやく再開され、勧奨差し控えにより接種機会を逃していた世代への無料でのキャッチアップ接種も開始された。これを受け、近隣の医療機関からの紹介患者を診ることが多い当院のような総合病院でもHPVワクチン接種希望者は増加した。当院での接種希望者の傾向を分析する。【方法】積極的勧奨が中止された2013年から2023年8月までに当院にてHPVワクチン接種を開始した13歳から27歳までの132人を対象とした。【成績】2020年に国がHPVワクチン接種に関する情報提供を勧告し2021年春に当院のある自治体で対象者に情報提供のリーフレットが配布されたのをうけ、それまで年に数人程度で推移していた接種希望者は増加し2021年1月から2022年3月までで32人だった。積極的勧奨再開後の2022年4月から2023年8月にかけては85人だった(定期接種27人, キャッチアップ58人)。2021年1月以降積極的勧奨再開までをA群、積極的勧奨再開後の定期接種をB群、キャッチアップをC群として分析したところ、受診のきっかけはA群とB群では母親が当科通院中の方が2割近くを占め多く、C群では本人が当科通院中の方が半数近くを占めた。接種中断はA群0人、B群2人、C群4人だった。【結論】当院での接種者は本人または家族が受診の際に医療者から接種を勧められ、相談する機会があった方が大多数であった。一度中断されていたワクチンの接種率を向上させるにはまずその存在を知ってもらうこと、正しい知識を得て接種への不安をなくしてもらうことが必要であり、検診や受診の機会を逃さず医療者側から積極的な呼びかけを続ける必要性を強く感じた。

P-70-10 人工妊娠中絶における経口法手術法選択実施後の満足度について

定生会谷口病院

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【目的】世界標準である経口中絶薬が使用可能となり人工妊娠中絶に選択が出来るようになった。SRHRの観点から安全に使用できる方法を示して選択できることは重要。今回我々は手術法(MVA)と内服法それぞれ選択した方法に満足だったかどうか、問題と感じたことを聴取しまとめたので報告する。【方法】2023年7月1日より8月31日までに人工妊娠中絶を希望されて来院された19例の患者に手術法と経口法について説明、自身で方法を選択していただいた。手術法は静脈麻酔下にMVAを用いて施行内服法はミフェプリストン服用後36~48時間でミソプロストールを服用した。12時間を超える場合はMVAにて人工妊娠中絶を行った。終了後にアンケート調査を行った。【成績】来院19例中15例が内服法を選択された。内服法の情報はSNSが9例来院して初めて知った4例であった。選択した理由は内服法では合併症は少ない9例、次回の妊娠を考えて2例、麻酔が怖い2例、処置に向き合えと思った1例であった。手術法を選択した理由は時間が読める3例、新しい方法は不安がある1例であった。内服法に関しては2剤目投与から娩出までの時間は3時間44分で1例24時間を越え手術法に移行した。大量出血になったものは無く痛みのために追加の鎮痛薬投与を行った例は9例、吐き気であつた例1例であった。また内服法では排出物を見てあつたかと答えたものが3例あつた。今回の選択に関しては内服法では手術法に移行した1例をのぞき手術法も含めて納得していると答えた。【結論】自身が選択した方法についてどちらの方法を選んででも不満は少なかった。排出物を見る可能性が内服法にはあり、事前の説明と処置後のケアが必要だと感じた。

P-70-11 遺伝性乳癌卵巣癌に対するリスク低減卵管卵巣摘出術後の女性ヘルスケア

岡山大

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【目的】遺伝性乳癌卵巣癌(Hereditary Breast and Ovarian Cancer: HBOC)では、卵巣癌未発症者の場合、リスク低減卵管卵巣摘出術(risk reducing salpingo oophorectomy: RRSO)が唯一の卵巣癌予防法であり、35~40歳で出産完了時に行うことが推奨されている。至適時期にRRSOを行うことは、外科的閉経を招き女性ヘルスケアに影響を与える。今回我々は、当院でRRSOを行った患者の現状と今後のヘルスケアにおけるマネジメントについて検討し、課題を抽出した。【方法】2016年4月~2023年9月の期間に95例のHBOCと診断された患者のうち66例にRRSOが施行された。66例の臨床情報(年齢, BMI, 乳癌既往や治療内容, BRCA1/2変異, 術前の閉経の有無, 術後更年期症状の有無, 骨密度測定および治療)を診療録より後方視的に検討した。【成績】RRSO実施時の年齢中央値49.8歳(38-71歳)であった。21/66例(31.8%)で何らかの女性ヘルスケアに対する医学的管理が行われた。7例では、RRSO以前に乳癌治療により早発閉経をきたしていた。RRSO術後の更年期症状は、術前閉経患者6/48例(12.5%), 術前未閉経患者の8/18例(44.4%)に認めた。更年期症状に対して8例で漢方やサプリメントなどの非ホルモン療法が行われ、HRTを行った症例は2例であった。また、術後骨粗鬆症の有無を確認するため15例で骨密度測定が行われ、4例が骨粗鬆症のため薬物療法が開始された。この4例はいずれも乳癌治療により50歳未満で閉経をきたしていた。【結論】RRSO後の患者への女性ヘルスケアが十分に提供されていないことが明らかになった。閉経の有無に関わらず、適切な女性ヘルスケアの提供が必要と考えられ、そのためのシステム作りが今後の課題である。

P-70-12 プレコンセプションケアの普及のために~フェムテックの活用

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【目的】プレコンセプションケアの普及は、女性に将来の生活や健康に向き合う機会を与えるものであるが、若年成人女性に広く届ける時期と方法が課題である。今回女性に早期に的確にプレコンセプションケアを届ける方法としてQRコードよりスマートフォンで問診・アドバイスを受けられるフェムテックを作成し、付設したアンケートによりその有効性を検討した。【方法】対象は18歳以上の女性とし、企業の健康管理室などを通して本フェムテックを利用してもらいアンケートの結果を集計した。アクセスされた女性は260名であり、そのうち18-39歳までの220人について検討した。月経関連症状や、乳がん・子宮がん、肥満・痩せ他数項目について問診し、その回答にあてはまるアドバイスを認めるように設定し、子宮内膜症、子宮筋腫、低用量ピル、乳がん・子宮がん他についての説明項目も設置した。【成績】アンケートの結果、このフェムテックはわかりやすかった89.0%、参考になった90.2%、自身の健康に当てはまる点があった72.0%、また医療機関を早めに受診したい17.4%、いずれ受診したい54.9%という結果であった。【結論】QRコードよりスマートフォンで見える問診・アドバイズツールは若年成人女性にとって受け入れやすい方法であり、有効なプレコンセプションケア普及のツールであると考えられた。多くの女性が自身に当てはまる健康問題に気づき、医療機関受診の足がかりとなることも証明された。企業の健康管理室、学校のなどでQRコード付きパンフレットを配布することにより若年成人女性に広くプレコンセプションケアを広める事ができ、多くの女性の将来への健康管理に役立つものとする。

P-70-13 帝王切開術後鎮痛法としての transversus abdominis plane block の有効性についての後方視的検討

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【目的】帝王切開の術後鎮痛強化は、深部静脈血栓症 (deep vein thrombosis, DVT) の予防のみならず、早期離床、母子関係の構築、産後うつ予防にも重要である。今回、腹横筋膜ブロック (transversus abdominis plane block, TAPB) の有効性について後方視的検討を行い報告する。【方法】2022年8月から2023年8月までの1年間に、帝王切開術を実施した85症例を対象に術後アンケート numerical rating scale (NRS) を実施し、術後補助鎮痛剤の投与回数、手術終了から初回鎮痛剤投与までの時間について検討・解析した。帝王切開の麻酔は手術室麻酔科医に一任した。補助鎮痛は産婦の鎮痛希望時に使用し、鎮痛剤の選択は助産師に一任した。【成績】脊椎麻酔において同様の投薬のある症例で TAPB を実施した 19 症例 (TAPB (+)) 及び実施していない 20 症例 (TAPB (-)) を比較した。患者背景には有意差認めず。TAPB (+) 群及び TAPB (-) 群の手術終了から初回鎮痛剤投与までの時間はそれぞれ 506 ± 74 min 及び 282 ± 57 min で、TAPB (+) 群は有意に延長した。補助鎮痛剤の投与回数はそれぞれ 1.0 ± 0.2 回及び 2.3 ± 0.2 回で TAPB (+) 群は有意に少なかった。帰室から 1, 2, 4, 6 時間及び翌朝の NRS はいずれも TAPB (+) 群は有意に低かった。両群の麻酔時間に有意差はなく、TAPB の有害事象は認めなかった。【結論】TAPB はより良好な術後鎮痛を得られることが示唆される。術後鎮痛強化により、早期離床や早期新生児ケア、DVT 及び産後うつ予防に期待できる。鎮痛剤リクエスト回数が少ないため、術後管理スタッフや医師の負担も軽減できる。今後も症例を蓄積し TAPB の効果、他の鎮痛剤の効果・副作用への影響についても検討する必要がある。

P-70-14 当院におけるレボノルゲストレル放出システムの使用例の検討

山形大

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【目的】レボノルゲストレル放出子宮内システム (LNG-IUS) は子宮内局所の黄体ホルモン分泌促進作用を示し、本邦では 2007 年に避妊薬として承認、2014 年に過多月経・月経困難症の適応で保険収載された。諸外国でのデータは多くあるが、本邦でのデータは限られている。当院で LNG-IUS を使用した症例について、合併症や脱落率、脱落を予見出来る因子があるかを明らかにすることを目的とした。【方法】当院において 2014 年～2022 年に LNG-IUS を挿入したすべての患者を対象とした。診療録を用いて後方的にデータを抽出し解析を行った。繰り返し挿入している患者は初回挿入のみを解析対象とした。【成績】対象症例は 55 例、年齢の中央値は 40 歳 [11-47]、LNG-IUS 留置期間の平均は 691.4 日 [8-2072] であった。出産歴は経産婦が 35 例 (63.4%)、未産が 20 例 (36%) であった。適応は避妊目的が 9 例 (16%)、過多月経・月経困難症が 46 例 (84%) であった。自然脱落・途中抜去が 23 例 (41%) であった。合併症は筋層内迷入が 1 例、骨盤内炎症性疾患、子宮穿孔、異所性妊娠は認めなかった。脱落/抜去群と脱落なし群と比較すると、腺筋症が脱落群で有意に多かった。年齢、肥満、妊娠歴、筋腫、内膜症、挿入前のホルモン治療の有無、内膜干渉病変の有無は有意差を認めなかった。子宮筋層の厚みは脱落/抜去群で厚い傾向があったが、統計学的有意差は認めなかった。IUS 留置期間は腺筋症、挿入前に不正出血があると有意に短い結果であった。脱落群と脱落なし群では挿入後の不正出血期間に有意差を認めなかった。【結論】既報と比較すると脱落・抜去例が多くあった。腺筋症があり、不正出血がある症例は LNG-IUS の脱落のリスク因子であった。

P-70-15 ジェノゲストを内服している子宮内膜症患者における、FSH 値による中止タイミングの検討

愛知医大

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【目的】子宮内膜症の治療では反復手術を最大限に回避するため、薬物療法を閉経まで継続し、コントロールが不良な場合は手術療法が勧められている。薬物療法には Gn-RH アゴニスト・アンタゴニストによる偽閉経療法と LEP (low dose estrogen progestin) ・ジェノゲスト (DNG) による治療があるが、LEP は 50 歳か閉経のいずれかで中断する必要があるため周閉経期では最終的には DNG に移行している症例が多い。偽閉経療法では下垂体の FSH を強く抑制するため、FSH 値による卵巣機能低下の評価は困難であるが、DNG では FSH の抑制作用はないため、FSH 値が参考できる可能性がある。既報告では FSH : 40mIU/ml 以上で感度 41.2% 特異度 95.5%、FSH : 56mIU/ml 以上で感度 58.8% 特異度 68.1%、FSH : 100mIU/ml 以上で感度 100.0% 特異度 22.7% とされている。【方法】今回、当院女性ヘルスケア外来で 5 年以上 DNG 2mg/日を内服中の子宮内膜症患者で、糖尿病や高血圧、腺筋症、境界悪性等を除外した 8 例において、DNG 内服中の FSH 値、E2 値を経時的に評価した。E2 の測定感度は 20pg/ml のものを用いた。【成績】DNG 療法を続けている内膜症患者の平均年齢は 50.8 歳であった。平均内服期間は 6.2 年であった。47 歳と 54 歳の症例で FSH が 100mIU/ml 以上となり自然閉経した。50 歳と 52 歳の症例では、FSH が 1 回のみ 40mIU/ml 以上になったがその後低下し、40mIU/ml 未満を推移した。その他 48 歳・50 歳・53 歳・53 歳の症例では FSH が 40mIU/ml 未満を、E2 は 30pg/ml 前後を推移しており現在も DNG を続行している。【結論】DNG は FSH 値に大きな影響はないため、FSH 値が上昇すれば治療中であっても閉経と判断し、治療を中止することができると報告されているが、実際は症例により変動が大きいと考える。

P-71-1 子宮体癌における術前 MRI 画像を用いた脈管侵襲予測モデルの構築

広島大

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【目的】子宮体癌の治療では再発リスク因子によって術式や術後療法を選択するが、脈管侵襲の有無は術後病理組織診断で評価するため、術前画像による判断が困難である。近年、多量の画像データと臨床情報を活用して、治療後の再発や転移を予測する Radiomics 研究が行われている。本研究で、Radiomics 解析により術前 MRI 画像を用いた脈管侵襲予測モデルを構築したので報告する。【方法】2014年から2020年に当院で子宮体癌に対して子宮全摘出術手術を施行した153症例を対象に脈管侵襲予測モデルを構築した。術前の MRI 画像 (T1, T2 強調画像) に対して子宮体部を CTV とし関心領域 (ROI) を作成し、加えて CTV 内部や周辺領域を含めた ROI など合計5種類を作成し画像特徴量を Radiomics 解析で抽出した。モデル構築に、LASSO 回帰による次元削減を行い、オーバーサンプリング手法である SMOTE によるデータ不均衡補正を行った。【成績】脈管侵襲モデルの作成において、LASSO 回帰により16個 (T1 強調: 7個, T2 強調: 9個) の特徴量が選択され、子宮体部だけでなく、腫瘍領域に近い限局した領域や子宮体部周辺からも予測因子が選択されていた。SMOTE を用いた脈管侵襲予測モデルの平均精度、感度、特異度はそれぞれ 83.8%, 83.1%, 84.6% であり、平均 AUC は 0.88 であった。【結論】本研究では、SMOTE を用いた子宮体癌の脈管侵襲予測精度および感度が高率であり、術前 MRI 画像からの予測モデルの有用性が示唆された。今後、多施設での検証や生物学的特徴との関連を解析することで、治療選択に貢献できる可能性が期待される。

P-71-2 子宮体癌における三次リンパ球構造 (TLS) の空間的分布と免疫チェックポイント阻害剤 (ICI) の治療効果

京都大

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【目的】三次リンパ系構造 (TLS) は、いくつかの癌種において予後や免疫チェックポイント阻害薬 (ICI) の治療効果に関連することが知られているが、子宮体癌における ICI の臨床的有用性と TLS に関するエビデンスはない。【方法】我々は、転移学習 DeepLabV3 を用いて人工知能 (AI) ベースの TLS 検出プログラムを開発し、258人の子宮体癌患者の腫瘍サンプル 958 タイルにおける TLS の空間解析を行った。そして、この AI ベースのプログラムを応用して、TLS の空間的分布と、子宮体癌患者の予後や免疫チェックポイント阻害薬の抗腫瘍効果との関係を評価した。【成績】まず、腫瘍検体中の TLS を自動認識するプログラムを作成し、トレーニングデータで 96%、評価データで 92% の精度一致率を得た。104例の子宮内膜癌患者において、81例 (78%) で TLS が検出され、腫瘍境界線から 500um 以上の位置に TLS がある患者 (extra-TLSs) は良好な無増悪生存と密接に関連していたが ($P < 0.004$)、腫瘍境界線から 500um 未満の位置に TLS がある患者 (peri-TLSs) は関連が見られなかった。また、ICI 治療を受けた12人の子宮体癌症例のうち、extra-TLSs を有する5人中4人が臨床的奏効 (奏効率 80% : 完全奏効2人, 部分奏効2人) を示したが、peri-TLSs を有する症例では7人中1人だけが奏効率 14% (部分奏功1人) を示した。【結論】TLS の空間的分布は局所免疫状態と密接に関連している可能性がある。TLS は進行子宮体癌における ICI の抗腫瘍バイオマーカーの一つである可能性がある。

P-71-3 子宮体癌におけるコピー数多型異常は相同組換え修復欠損を予測する藤田医大¹, 藤田医大先端ゲノム医療科²市川亮子¹, 小谷燦瑠古¹, 成宮由貴¹, 高田恭平¹, 小林 新¹, 大脇晶子¹, 伊藤真友子¹, 野村弘行¹, 須藤 保²

【目的】相同組換え修復欠損 (HRD) は PARP 阻害薬の効果を予測する重要な分子遺伝学的異常である。今回子宮体癌において、HRD を有する子宮体癌の臨床的背景と分子遺伝学的特徴を検討した。【方法】当施設にて診断および治療を行った子宮体癌 41 例に対し、同意を取得した上で、摘出腫瘍のパラフィン包埋組織より DNA を抽出し次世代シーケンサーを用いたがん遺伝子パネル解析 (PlessisionRapid) を行った。また、当該症例の臨床情報を診療録より後方視的に収集した。【成績】対象の症例の年齢中央値は 59 (34-87) 歳、進行期分類 (FIGO2008) は I 期 26 例, II 期 5 例, III 期 7 例, IV 期 3 例であった。組織学的分類は、類内膜癌 G1/2 が 27 例, 類内膜癌 G3 が 3 例, 漿液性癌 3 例, 脱分化癌 2 例, 明細胞癌 1 例, 混合癌 1 例, 癌肉腫 4 例であった。TCGA による分子遺伝学的分類は、POLE-ultermutant 1 例, MMR-deficient 9 例, p53-mutant 6 例, NSMP 25 例であった。そのうち HRD を認めた症例は 7 例であり、癌肉腫が 3 例, 漿液性癌, 脱分化癌, 類内膜癌 G3, 類内膜癌 G1 がそれぞれ 1 例であった。コピー数多型異常 (CNA) は 18 例に認め、copy number-high 16 例, copy number-low 10 例 (重複あり) で、CNA と HRD に明らかな相関を認めた ($r=0.91$)。【結論】子宮体癌における HRD はエストロゲン非依存性腫瘍に多く認め、CNA が HRD の予測因子となる可能性が示唆された。

P-71-4 演題取り下げ

P-71-5 がん遺伝子パネル検査 (CGP) で診断され、pembrolizumab で寛解したリンチ症候群子宮体癌の一例

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子宮頸部腺癌の診断で治療開始しCGPを契機にリンチ症候群と診断され、pembrolizumabで寛解後に子宮体癌と診断された症例を経験したので報告する。【症例】30代, 0妊0産, 悪臭帯下, 下腿浮腫, 腔内腫瘍, 性器出血による出血性ショックのため当院に搬送された。骨盤MRIで腔内占拠する10cm大子宮頸部腫瘍を認めた。子宮内膜のjunctional zoneは保たれていた。CT検査で傍大動脈リンパ節腫大, 肺転移を認め, 組織生検では低分化腺癌の診断であった。子宮頸癌IVB期と診断し手術摘出を目的として術前動脈注化学療法を実施するもDVT増悪のため中止し, 全腹部CCRT及びTC療法に変更した。TC療法6サイクル直後に原発腫瘍が増大したため, 腫瘍組織のCGPを提出した。腫瘍感染による敗血症を発症しICU治療後にショック状態は離脱したが局所感染は残りPS3で家族にBSCの説明をした。CGPの結果, MSI-H, TMB 64 Muts/Mb, MSH2変異(生殖細胞及び体細胞変異疑い)より十分なIC後にpembrolizumabを投与した。腫瘍は縮小しMRI検査で子宮体下部にも病変を認めた。病理標本を見直すと類内膜癌様の所見がありp16免疫染色が一部で陰性であった。診断を子宮体癌に変更した。その後完全寛解し1型糖尿病の発症に対してインスリン治療を併用しながら約3年間治療継続している。また, 遺伝カウンセリングを経て生殖細胞系列MSH2変異を診断した。【結語】若年子宮頸部腺癌では体下部発生子宮体癌やリンチ症候群を鑑別に挙げる必要がある。リンチ症候群はICIsで寛解が得られ診断の意義は大きい。

P-71-6 サイクリンA2を標的とした新規抗腫瘍薬の子宮内膜癌に対する効果の検討

信州大

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【目的】我々は子宮内膜癌において, サイクリンA2(cycA2)の過剰発現が予後不良因子であることやシスプラチン(CDDP)耐性に関与することを見出したため, これを標的とする抑制剤の開発を試みた。低分子化合物ライブラリーからcycA2発現抑制活性を有する化合物Xを同定し, さらに化合物Xの構造を改変して10倍の活性を有する化合物X1を合成した。本研究では化合物X1の抗腫瘍効果を検討した。【方法】内膜癌細胞に化合物X1を添加し細胞生存率をWST-1 assayで評価した。Ishikawa細胞のマウス皮下移植腫瘍に, 化合物X1の腹腔内, 局所投与を行い, 抗腫瘍能を評価した。Doxycycline(DOX)投与によるPtenとArid1aを子宮内膜特異的にノックアウトすることで, 子宮内膜癌を発症するマウスモデルを用い, 化合物X1の抗腫瘍能を評価した。4週間のDOX投与から1週後と3週後に子宮腔内に化合物X1の局所投与を行い, 3週と5週後に片側ずつ子宮角を摘出し, 病理像を観察した。【成績】化合物X1添加により, 細胞生存率はコントロールと比較してIshikawa:46%, HHUA:18%, KLE:46%, HEC1B:10%に低下した。マウス皮下移植モデルにおいて化合物X1の腹腔内投与で化合物X1の腫瘍縮小率は33%とコントロールに対し有意差を認めた(P=0.03)。また, マウス皮下移植腫瘍への化合物X1の局注では腫瘍が消失した。子宮内膜癌発癌モデルマウスの各子宮角では, 投与後3週では癌組織の遺残を認めたが, 5週間後には異型内膜増殖症, あるいは正常内膜のみであった。また, 化合物X1による体重減少, 臓器障害は認められなかった。【結論】化合物X1は子宮内膜癌に対する新規分子標的治療薬として有望であると考えられた。

P-71-7 子宮体癌においてLICAMが予後不良因子となりうる機序に関する検討北海道大¹, 北海道大医学研究院統合病理学教室²黒須博之^{1,2}, 朝野拓史¹, 櫻井愛美¹, 松宮寛子¹, 山崎博之¹, 遠藤大介¹, 井平 圭¹, 三田村卓¹, 金野陽輔¹, 谷口浩二², 渡利英道¹

【目的】膜貫通型糖タンパク質であるL1 cell adhesion molecule (LICAM) の高発現は多くのがんにおいて予後不良と関連しているとされており、子宮体癌においても全生存期間の短縮、再発リスク上昇、高頻度のリンパ節転移、遠隔転移に関与していると報告されている。しかしながらその分子機構は明らかとなっておらず、LICAMの発現がどのような影響を及ぼすかを解明するために本研究を計画した。【方法】複数の子宮体癌細胞株に対して、LICAMの過剰発現もしくはshRNAによるknockdownを行い、樹立したLICAM過剰発現細胞株やknockdown細胞株を用いて、遺伝子発現解析や増殖能、apoptosis等の評価を行うとともに、Western blottingや免疫蛍光染色によりLICAMの発現や局在についての評価を行った。【成績】免疫蛍光染色により、LICAMの発現局在が細胞株によって異なることが明らかとなった。LICAM knockdownにより、WST-1を用いたcell proliferation Assayでは、有意な細胞増殖の低下を認め、細胞形態の変化も見られた。一方でflow cytometryでの評価でLICAM knockdownによるapoptosisの増加は確認されなかった。qPCRにてIL6 mRNAの発現が低下することが確認され、STAT3のリン酸化にも影響を及ぼす可能性が示唆された。【結論】LICAMは子宮体癌において増殖能に関与する可能性が示唆された。機能解析をさらに進めてその分子生物学的機序に迫りたいと考えている。

P-72-1 日本におけるHPVワクチンの効果とHPV感染型変移への影響；多施設合同調査 (J-HERS 2021)

金沢医大

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【目的】日本人に対する2価・4価HPV感染予防ワクチンの効果とHPV型変移への影響を調査した。【方法】全国11施設において16-39歳の日本人女性1529人のHPVワクチン接種歴情報を収集し、子宮頸部擦過細胞液状検体によるHPV型判定及び子宮頸部細胞診異常の有無を調査した (J-HERS2021)。また本結果と年齢一致させたHPVワクチン定期接種開始前の調査 (J-HERS2011) 結果を比較した。【成績】対象者の2価・4価ワクチン接種率は約2割であり、22-27歳の対象者が最も高い接種率 (約5割) であった。ワクチン接種群は非接種群に比べ、細胞診HSIL以上の異常 (HSIL+) 発生率とHPV16, 18感染率は有意に低かった。一方、いくつかのHPV型は逆に増加した。10年前のJHERS2011との比較では、LSIL/ASCH (P<0.0001), HSIL (P=0.0006) とも発生率は有意に低下し、HPV16/18型陽性HSILの発生はなかった。すべてのHSILとHPV16/18陽性HSILの防御率はそれぞれ72%, 100%であった。HPV16, 18感染のみならずHPV16近縁型の感染率も有意に低下したが、この比較では他のHPV型の増加はなかった。【結論】日本で開始されたHPVワクチン接種によって、HPV16, 18感染のみならず、これらに近いHPV型の感染防止 (交差予防効果) も示唆され、その結果子宮頸部高度病変は予想値以上に減少した。2価, 4価ワクチンであっても中高年生への接種は、若年子宮頸癌の撲滅に寄与すると思われる。

P-72-2 子宮頸部胃型腺癌のオルガノイド培養技術を用いた動物実験モデルの樹立

信州大

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【目的】子宮頸部胃型腺癌 (GAS) は、治療抵抗性で予後不良であるが、利用可能な細胞株などの実験モデルが存在しないため、治療薬の研究は進んでいない。オルガノイド培養は、高い樹立効率や腫瘍細胞の不均一性の保持などの利点から、患者由来がんモデルとして注目されている。我々はこれまでに安定的に長期の継代培養可能なGASの患者由来オルガノイド (PDO) を2系統 (G-PDO-1, G-PDO-2) で樹立しているが、これらのPDOからオルガノイド由来異種移植腫瘍 (ODX) の作成を試みたので報告する。【方法】2系統のG-PDOを高度の免疫不全マウス (NSGマウス) に皮下移植し、ODX形成の有無を観察した。形成されたODXを摘出し、一部をBALB/cヌードマウスへ継代移植した。摘出したODXのホルマリン固定パラフィン包埋切片を作成し、HE染色、AB-PAS染色、免疫染色 (HIK1083抗体, 抗CLDN18抗体) を実施し、元の腫瘍と比較した。【成績】2系統のG-PDOともNSGマウス皮下に腫瘍形成しているが、G-PDO-1由来のODX (G-ODX-1) は2cmの腫瘍となったため、摘出した。一部をヌードマウス皮下に継代移植したところ、NSG同様に腫瘍の形成・増大を認め、さらにヌードマウス間でも安定して継代が可能であることを確認した。形成されたG-ODX-1はPAS陽性、CLDN18陽性を強発現しており、腫瘍間質が豊富である点など、原発のGASと同様の性質を示した。以上よりGASのODXが樹立できたと判断した。G-PDO-2由来のODX (G-ODX-2) は増大速度が非常に遅く、現時点で樹立の確認に至っていない。【結論】G-PDO-1由来のG-ODX-1の樹立に成功した。これらを用い、今後GASの生物学的特性や薬剤感受性などの研究に利用する予定である。

P-72-3 全国がん登録との比較からみた、日本産科婦人科学会婦人科腫瘍登録による子宮頸部悪性病変の症例把握状況

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【目的】日本産科婦人科学会婦人科腫瘍登録(学会登録)は登録施設からのがんが登録され、全国がん登録(がん登録)は法律に基づき日本全国のがんが登録される。学会登録はがん登録よりも詳細な治療情報があるが、登録施設が限定され、日本全体のがんをどの程度把握しているか明らかでない。そこで子宮頸部悪性病変についてがん登録と比較し、学会登録がカバーする疾患の割合や特徴を明らかにすることを目的とした。【方法】2019年の学会登録報告と、2016-2019年診断の全国がん登録情報を用い、子宮頸部悪性病変の登録件数を比較し、組織型別に学会登録のカバー率(がん登録数に対する学会登録数)を集計した。また上皮性病変である癌のうちの腺癌の割合を、学会登録とがん登録(2016~2019年の年度別)とで集計した。【成績】2019年の子宮頸部悪性病変は学会登録では23837例、がん登録では35192例で、学会登録カバー率は67.7%であった。浸潤癌でのカバー率は75.4%で、扁平上皮癌76.2%、腺癌75.0%、その他の上皮性悪性腫瘍では76.9%であった。浸潤癌に占める腺癌割合は学会登録では22.7%で、がん登録では2016年の21.8%から漸増し2019年は22.8%であった。上皮内腫瘍でのカバー率は65.8%で、CIN3では69.1%であり、上皮内腺癌とその他の上皮内腫瘍については学会登録にその区分がなく、がん登録ではそれぞれ946例と209例であった【結論】学会登録はがん登録の子宮頸部悪性腫瘍の約7割をカバーしている。学会登録の区分はがん登録での浸潤癌該当疾患をほぼ網羅しているが、登録数は限定され、上皮内腫瘍の網羅的把握はない。細分類や、上皮内腫瘍を含めての罹患状況や比率では、解釈に注意が必要である。

P-72-4 子宮頸癌予後に影響を及ぼす因子の検討

佐賀大
福田亜紗子

【目的】子宮頸癌の発生には、HPVが関与していることは周知の事実である。一方で、子宮頸癌の予後に影響を与える因子は、HPV型、HPV有無、年齢、喫煙、組織型等が検討されているがコンセンサスを得ていない。【方法】2016年から2022年に当院で治療を行った子宮頸癌症例を後ろ向きに検討した。HPV型(16, 18, その他、陰性)、予後(無再発生存、再発/死亡)、年齢(40未満、40から70、70以上の3群又は56未満、56以上の2群)、喫煙、臨床病期、治療内容、組織型、細胞診、検診歴を検討した。【成績】年齢の中央値は56歳。喫煙率は28.0%で若年者に多い傾向を認めた。(40歳未満の喫煙率は50%)HPV陽性率は75.1%で内訳は16型が4割、18型が2割、その他4割であった。既知の報告通り、16型、18型は40歳未満の若年者に多い傾向を認めた。組織型はSCCが73.0%、それ以外が27.0%であった。臨床病期の内訳はI期約40.5%、II~IV期がそれぞれ約20%であった。予後は70%が無再発生存、30%が再発もしくは死亡であった。各因子(年齢、喫煙、HPV、組織型、検診歴、臨床病期)と予後の単変量解析の結果、HPV、組織型、臨床病期で有意差を認めた。さらに、単変量解析で有意差を認めた因子を組み込んでロジスティック回帰分析を行ったところ、HPVの有無に有意差を認め、陰性は陽性と比してオッズ比3.9倍を示した。【結論】本研究では、子宮頸癌の予後に影響を与える因子として、HPV陰性が明らかとなった。

P-72-5 細胞内ヘム生合成の誘導を利用した抗マラリア薬 Artesunate の子宮頸癌治療への応用

岐阜大
上田陽子

【目的】我々は、卵巣がん細胞株CaOV3においてArtesunate(ATS)がフェリチノファジーを介してフェロトローシスを誘導することを見出した。一方、遊離ヘムがATSのフェロトローシス誘導を活性化することが報告された。そこで、今回ヘム前駆体のアミノレブリン酸(ALA)併用によるATSの増感について検討した。【方法】【成績】子宮頸癌細胞HeLaはフェロトローシス感受性細胞HT1080に比べてATS感受性が低かった。HT1080とHeLaにおける各種オルガネラ特異的Fe²⁺検出プローブを用いた蛍光イメージングの結果、HT1080ではATSによりリソソーム、ERでFe²⁺濃度の有意な上昇が認められたが、HeLa細胞ではFe²⁺は誘導されなかった。いずれもALA(1mM)の併用でATSの細胞毒性が有意に増強し、それはヘム合成阻害剤SAの添加でほぼ消失したが、DFOやFer-1では部分的な抑制に留まった。また、遊離ヘム特異的蛍光プローブAc-H-FluNoxにより、HeLa細胞にALAを添加すると徐々に遊離ヘムが増加することが明らかになった。種々の子宮頸癌細胞株HeLa、CaSki、TCS、ME180のうち、CaSkiがATSに強い抵抗性を示した。ALAを併用したところ、CaSki以外の細胞では、ALAを併用でATSの細胞毒性が有意に増感された。また、CaSkiの細胞内グルタチオン含有量は、他の細胞に比べ、数倍多かった。【結論】以上、ATSのフェロトローシス誘導作用には、Fe²⁺よりも遊離ヘムの増強が重要で、ALAによるヘム合成活性化でATSの効果を増感できることがわかった。しかし、CaSki細胞は細胞内GSH濃度が高く、ATSに抵抗性を示し、ALA併用の効果も示さなかった。今後CaSki細胞のATS抵抗性におけるヘム合成系、抗酸化系の関与につき検討する予定である。

P-72-6 子宮頸癌・外陰部癌に対するホウ素中性子補足療法 (BNCT: Boron Neutron Capture Therapy)

大阪医科薬科大

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【目的】ホウ素中性子補足療法 (BNCT: Boron Neutron Capture Therapy) は、中性子とホウ素の核反応を利用したもので、正常細胞にはほとんど損傷を与えず、がん細胞を選択的に破壊する治療法である。BNCT は腫瘍細胞に取り込まれたホウ素と中性子の核反応で発生する細胞の径を越えない高エネルギーにより細胞を破壊することが可能な治療法である。脳神経外科領域や頭頸部癌、悪性黒色腫では臨床応用されてきているが、婦人科癌における BNCT の研究は少ない。今回、子宮頸癌・外陰癌に対する BNCT の抗腫瘍効果に関する基礎的研究を行った。【方法】*In vitro* では子宮頸癌・外陰癌細胞株にホウ素化合物 (BPA: boronophenylalanine) を暴露し、各細胞株のホウ素濃度を測定した。また BPA を暴露後に中性子を照射し、colony forming assay を用いて BNCT の効果を検証した。*In vivo* では子宮頸癌・外陰癌細胞株による皮下腫瘍モデルマウスを用い、BPA の腹腔内投与後に腫瘍および各臓器・血液のホウ素濃度を検証した。BPA の腹腔内投与後に中性子を照射し、BNCT の抗腫瘍効果を検証した。【成績】子宮頸癌・外陰癌細胞株において BPA の暴露によりホウ素の集積を確認できた。BPA 曝露後の子宮頸癌細胞株に中性子を照射することでその抗腫瘍効果を確認できた。皮下腫瘍モデルマウスにおいて BPA の腹腔内投与によりホウ素は腫瘍に選択的に集積しており各臓器・血液への集積は少なかった。また BPA の腹腔内投与後に中性子を照射することで control に比し有意な抗腫瘍効果を確認できた。【結論】子宮頸癌・外陰部癌に対しての BPA 投与後に中性子を照射する BNCT は今後期待できる新たな治療法の一つである。

P-72-7 化学修飾型 microRNA143 リポプレックスの子宮頸癌 PDX への抗腫瘍効果

大阪医科薬科大

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【目的】近年、次世代がん治療として核酸医薬が注目されており、核酸医薬には、siRNA, microRNA(miRNA), アンチセンス, デコイ等があるが、我々は miRNA を用いた核酸治療に注目している。miRNA を的確にターゲット遺伝子に作用させるためには、drug delivery system (DDS) の確立と、核酸修飾が必要である。我々は、化学修飾型 miRNA-143 (CM-miR-143) を開発し、大腸癌・膀胱癌・胃癌などの様々な癌種に対して、その有効性を報告してきた。しかし、子宮頸癌に関しての有効性については未だ知られていない。そのため、今回、我々は子宮頸癌への有効性を明らかにするために、CM-miR-143 の投与と実験を行い、抗腫瘍効果を検証した。【方法】手術検体(正常頸部組織と子宮頸癌組織) (n=16) に対して、RT-PCR 法を行い、組織内の miRNA143 の濃度測定を行った。次に、*in vitro* で、子宮頸癌細胞株 (HeLa・SiHa) に対して、Control, CM-miR-143 をそれぞれリポフェクションして、cell viability を比較検証した。最後に、以前に我々の研究室で樹立した PDX マウスモデル (patient-derived xenograft: PDX) (PMID: 35740635) に対して、control miRNA と CM-miR-143 を DDS である liposome と共に尾静脈投与し、抗腫瘍効果を検証した。【成績】手術検体での正常頸部組織に比べて子宮頸癌組織の miRNA 143 は有意に低下していた。*In vitro* では、HeLa, SiHa とともに、有意に CM-miR-143 投与群で cell viability の低下が確認された。動物実験でも、CM-miR-143 群で、有意に腫瘍増大が抑制され、CM-miR-143 の高い抗腫瘍効果を示唆する結果であった。【結論】子宮頸癌に対して、CM-miR-143 は高い抗腫瘍効果を示した。

P-72-8 TAZ は子宮頸部胃型腺癌の新規治療標的候補となりうる

信州大

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【目的】子宮頸部胃型腺癌 (GAS) は、放射線や化学療法などの既存の治療に抵抗性で予後不良であるため、新規治療法の開発は重要な課題である。Hippo pathway 因子の YAP および TAZ は、活性化すると核内移行により転写因子として細胞増殖やアポトーシス抑制、幹細胞性の維持等に作用し、胃癌など多くの癌で活性化が報告されているが、GAS での YAP/TAZ 発現を検討した報告はない。そこで我々は GAS における YAP/TAZ 発現および治療標的としての可能性を検討した。【方法】当院で手術を行った GAS 16 例と通常型腺癌 (UEA) 13 例における YAP および TAZ の核発現を免疫染色で検討した。また我々が培養細胞として樹立した 2 系統の GAS 患者由来オルガノイド (PDO) を用い、YAP と TAZ の核発現と、YAP/TAZ inhibitor の抗腫瘍効果を検証した。【成績】免疫染色の検討では、UEA では YAP が TAZ と同程度以上に高発現している症例が 85% (11/13 例) であったが、GAS では 69% (11/16 例) で TAZ 優位に核発現が増強していた。同様に 2 系統の PDO でも TAZ 発現が増強していた。また YAP/TAZ 阻害薬 Verteporfin (VP) の添加により、オルガノイドの大きさ、数(密度)とも減少することが観察された。PDO の免疫蛍光染色での検討では、VP 投与によりアポトーシス関連マーカーである Cleaved-Caspase3 の発現増強が認められ、アポトーシスが誘導されていることが明らかとなった。【結論】GAS では TAZ 活性化および核内移行が増殖に重要な役割を持ち、TAZ の pathway が治療標的候補となる可能性が示唆された。

P-72-9 高齢の子宮頸癌患者の治療の動向

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高齢の子宮頸癌患者への医療行為について、その動向を調査した。【目的】DPC (Diagnosis Procedure Combination) データを用いて、子宮頸癌 Ib1 期から IIb 期までを対象とし、各年齢における手術療法、放射線療法、CCRT、化学療法の割合の相違を調査することを目的とした。【方法】2014 年度から 2021 年度までの 8 年間の DPC 対象病院における入院を対象とした。子宮頸癌初発例の入院データより、手術症例は「子宮悪性腫瘍手術」を含む開腹手術例、腹腔鏡下手術例を抽出した。放射線管理料が記載されたものから放射線治療施行例を抽出し、シスプラチンあるいはパクリタキセル、カルボプラチン投与例を抽出して、後方視的に比較した。(倫理委員会承認番号 R2-073)【成績】65 歳以降を 5 歳毎の年齢層に分類し、各医療行為の割合を調べたところ、75 歳以降から放射線単独治療例が有意に増加し、手術例は減少傾向であった。70-74 歳の群よりも、75-79 歳の群のほうが CCRT の割合は高かった。その他の患者背景として、BMI、ADL、退院転帰について比較した。75 歳以降の高齢者は、周術期リスクやシスプラチンによる有害事象を回避するため、放射線治療単独で治療する傾向があるということが示唆された。【結論】子宮頸癌に罹患する高齢の患者だけではなく、今後も高齢のがん治療に対して、実臨床の医療行為に関するエビデンスの蓄積が必要である。特に子宮頸癌治療には手術以外の治療法があり、高齢者に対して適切な治療方針を確立していくことが課題となる。

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P-73-1 病理診断支援人工知能技術を用いて卵巣高異型度漿液性癌の病理組織学的構造から遺伝子相同組み換え修復欠損の有無を判定することに関する検討

防衛医大

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【目的】病理診断支援人工知能技術 (HALO ソフトウェア) を用いて、卵巣高異型度漿液性癌 (HGSC) の病理組織学的構造を記憶させ、その構造の違いから、HRD の有無を判定できるかを検討すること。【方法】2006 年から 2022 年の間に当院で HGSC と診断され、myChoice 診断システムで HRD を調べた症例を対象とし、HRD 群と HRP 群に分けた。各症例の中で、腫瘍量が最も多い HE スライドを 1 枚選択し、デジタルスライド化した。病理診断支援人工知能に、HRD、HRP 群から 3 症例ずつ選び、200 倍視野で最も腫瘍細胞が含まれる領域を選択した。そして、各視野の核、細胞、間質を含めた全体的な構造を、HRD、HRP の腫瘍構造としてそれぞれ HPD 群と HRP 群に分類し記憶させた。残りの症例を上述の方法で学習、記憶させたデータを用いて、腫瘍の全体を病理診断支援人工知能技術に自動判定させた。各症例で HRD 類似構造と判定された面積と HRP 類似構造と判定された面積が自動算出されるので、その値から HRD 面積/(HRD 面積+HRP 面積) を計算した。HRD 面積/(HRD 面積+HRP 面積) とのカットオフ値の算出には ROC 曲線を用いた。【成績】HRD 群 22 症例、HRP 群 10 症例を判定群とした。腫瘍面積比の HRD に対する ROC 曲線の AUC は 0.77、カットオフ値は 31% だった。HRD の診断感度は 59.1%、特異度は 90.0% だった。【結論】病理診断支援人工知能は相同組み換え遺伝子状態の補助診断として有効な可能性がある。

P-73-2 子宮頸部上皮内腫瘍に対するトリクロール酢酸療法の臨床的検討

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【目的】子宮頸部上皮内腫瘍 (CIN) の治療としては通常、頸部円錐切除が施行されている。しかし、術後の合併症として早産率の増加、頸管狭窄などがあり、安易に施行することは控えるべきである。我々は現在、非外科的治療法であるトリクロール酢酸 (TCA) 療法を施行しており、その臨床的検討を行った。TCA 療法は病変に塗布することにより、病変の剥脱を促進させ治療に導く治療法である。【方法】対象は CIN1-3 の 174 例 (CIN1: 9 例, CIN2: 63 例, CIN3: 102 例) であり、CIN1, 2 では 2 年治療しない症例を適応とした。TCA 療法の治療回数、非治療率、再発率、予後因子を分析した。4 週ごとに TCA を病変に塗布し、コルポ診で効果を観察した。細胞診 2 回連続陰性とコルポ診で治療とした。再発は組織診で CIN1 以上とした。TCA 塗布にて最終的に治療しなかった例を非治療とした。予後因子としては CIN の grade 別に子宮頸部病変占拠率 (1/3 未満, 1/3-2/3 未満, 2/3 以上) と治療回数を解析した。【成績】TCA 療法単独の治療率は 92.5% (161/174) であり、7.5% (13/174) が非治療であった。再発率は 7.5% (12/161) であった。CIN1, 2, 3 の平均治療回数は 2.7, 2.8, 3.1 であり、3 つの grade で有意差は認めなかった。CIN の grade 別において治療回数と病変占拠率には有意差は認めなかったが、病変占拠率の高いほど非治療例と再発例が多い傾向がみられた。【結論】TCA 療法の治療率は 92.5% であり、再発率は 7.5% であった。CIN の grade 別の治療回数に有意差は認めなかった。さらに病変占拠率と治療回数にも有意差はなかった。TCA 療法は非外科的治療として有用と思われた。

P-73-3 当施設における婦人科悪性腫瘍に対するがん遺伝子パネル検査の現状と今後の課題

熊本大

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【目的】本邦では、2019年6月よりがん遺伝子パネル検査が保険適用となった。今回われわれは、当科におけるがんゲノム医療の現状を明らかにすることを目的として、本検討を行なった。【方法】2019年1月から2023年8月までに、当科でがん遺伝子パネル検査を実施した婦人科悪性腫瘍48症例を対象として、各症例のがん関連遺伝子異常や解析結果について後方視的な検討を行なった。尚、各症例の特性に応じて、FoundationOne® CDx, FoundationOne® Liquid CDx, TruSight™ Oncology 500, PleSSision®による遺伝子プロファイリングを行なった。【成績】対象となった48例中(子宮体癌15例, 子宮肉腫6例, 子宮頸癌13例, 卵巣癌13例, 外陰癌1例), 治療標的として介入が期待される遺伝子(Actionable 遺伝子)が46例(95.8%)において同定された。その中で、治療に直結する遺伝子(Druggable 遺伝子)は19例(39.6%)に認められた。しかし、現状ではエビデンスレベルが比較的低い研究段階の治験の提案やその選択基準の適合性の問題に加えて、治験実施施設への通院に伴う時間的あるいは経済的負担などの理由で、実際の治療に結びついた症例は2例(4.2%)のみであった。1例は、腫瘍遺伝子変異量(TMB)-highの子宮頸癌に対して免疫チェックポイント阻害剤を使用し、他の1例ではBRCA2遺伝子変異を有する子宮平滑筋肉腫に対して患者申出療養としてPARP阻害剤の投与を行なった。【結論】当施設における婦人科悪性腫瘍に対するがん遺伝子パネル検査に基づいた実際の治療到達率は低い状況であることが明らかにされた。今後、より多くの症例に有望な治療を提供するためには、地域差のないがんゲノム医療の体制を構築していくことが肝要である。

P-73-4 後腹膜多形脂肪肉腫合併妊娠の一例

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症例は31歳2経妊1経産。自然妊娠成立し、妊娠初期より近医にて妊婦健診を施行していた。初診時(妊娠6週時)の両側付属器に異常所見は認めず、妊娠20週、24週時に施行した経陰超音波検査でも骨盤内に異常所見は認めなかった。妊娠30週4日の定期的健診の経陰超音波検査で右下腹部に12cmを超える充実性腫瘤を認め、悪性骨盤内腫瘍の疑いで、妊娠30週6日に当院紹介となった。当院の診察ではダグラス窩に14cm大の充実性の骨盤内腫瘍を認めた。骨盤MRI検査では右卵巣由来の腫瘍性病変が疑われ、診断目的に妊娠32週0日に試験開腹術を施行した。手術時、両側付属器は正常であり、右広間膜から露出した腫瘍から出血していた。広間膜内発育子宮肉腫を疑い、妊娠継続は困難と判断し、緊急帝王切開術を施行し、子宮及び両側付属器摘出術に変更した。兄は1948g Apgar score 2点/6点の女児であった。腫瘍は子宮との連続性に乏しく骨盤底筋に強固に癒着していた。En bloc 摘出は困難で腫瘍摘出後肉眼的腫瘍が残存した。出血量は6400mlであった。術後病理結果より後腹膜多形型脂肪肉腫の結果であったと診断した。がん遺伝子パネル検査では治療に結びつく遺伝子変化を認めず、肉腫に準じて4レジメンを実施したが、いずれもPDとなり術後9か月で緩和ケアへと移行した。

P-73-5 病理診断支援人工知能技術を用いて子宮体部類内膜癌のGrade分類が可能かどうかに関する比較—中間解析—

防衛医大

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【目的】病理診断支援人工知能技術(HALOソフトウェア)を用いて、子宮体部類内膜癌(Endometrial endometrioid carcinoma: EEC) G2とG3が分類可能かを検討すること。【方法】1996年から2015年の間に当院でEECのG2, G3と診断された症例を対象とした。各症例の腫瘍量の多いHEスライドを1枚選びデジタルスライド化した。G2, G3群からそれぞれ3症例ずつ選び、200倍の視野で各症例の最も腫瘍量が多く充実部と腺管部を含む箇所を200倍視野で選択した。更にその視野の中の、各野の核、細胞、間質を含めた全体的な構造を、充実部と腺管部に分類して記憶させた。残りの症例を用い記憶したデータに基づいて腫瘍のGradeを自動判定させた。充実部、腺管部と自動判定された面積から充実部/(充実部+腺管部)を計算し、充実部50%をカットオフ値として診断の感度、特異度を計算した【成績】G2群29症例, G3群12症例を判定群とした。充実部の割合を50%以上とした際のG3の診断感度は100.0%, 特異度は24.1%だった。【結論】病理診断支援人工知能では充実部と腺管部を用いたGradingは困難な可能性がある。今後症例を更に蓄積し、検討していく価値があると考えられる。

P-73-6 婦人科悪性腫瘍治療にどのように生成系 AI (人工知能) を利用できるか?

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【目的】近年, 医療分野のみならず人工知能の活用が広がっている. OpenAI 社が開発した ChatGPT (Generative Pre-trained Transformer) は機械的/網羅的に情報を収集するだけでなく, 人と会話しているかのような出力をすることで医療分野への活用の可能性が高まったと考えられる. 本研究では生成系 AI (Artificial Intelligence) の網羅性と正確性を評価し, 今後の可能性を探ることを目的とした. 【方法】OpenAI 社の ChatGPT 有料版 (GPT-4) を使用し第 112 回-第 117 回医師国家試験 (婦人科腫瘍分野), 2016 年-2022 年の産婦人科専門医試験 (婦人科腫瘍分野), 婦人科悪性腫瘍ガイドラインの CQ を提示し適切な回答が得られるのかを判定した. 【成績】医師国家試験における婦人科腫瘍分野の問題は正解率 100% (15/15) であった. 一方で産婦人科専門医試験は正解率が 50% (44/87) であった. 問題形式としては選択肢から正解を複数選ぶ設問よりも, 1 つを選ぶ設問の方が正解率が低かった. 長文問題で正解率が低いということは無かった. ガイドラインの CQ については元々明確な正解がないものが多く回答の評価は困難であった. 【結論】ChatGPT は 2022 年 1 月までの情報を元に回答するため, 現時点では最新の情報に対応することは難しい. 一方で, 少なくとも婦人科分野については国家試験には十分対応できることが解った. しかし, まだ専門医レベルにはないことも判明した. ガイドラインについては, 現時点では患者が正解を求めるのではなくセカンドオピニオンを求めるために使用することは可能だと判断した. 我々臨床医は, 常に人工知能の発展に気をくばりその最良の使用方法を見つける事でより良い診療に生かしていく努力が必要である.

P-73-7 生成 AI を用いた症例報告データベースの構築

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【目的】臨床に稀な症例を経験した際, 類似の症例を文献から検索するのは手間や時間がかかるため, 要点を絞った症例報告データベースが構築されることが望まれる. 一方で, 症例報告を文献ごとに人力で要点を整理することは現実的に不可能である. そこで, 生成 AI を用いて自動的に要点を作成する手法の妥当性を検討した. 【方法】2023 年 8 月 28 日時点において, Pubmed にて, 「case report gynecology」でヒットする文献 43039 報を調査対象とした. Pubmed API にて PMID から Abstract を抽出したのち, ChatGPT API (OpenAI) を用いて, 症例報告の年齢, 性別, 疾患名, 症例報告となった理由 (他の症例との違い) を抽出した. データベース構築には Claris Filemaker Pro 19 (Claris) 【成績】サンプルとして 100 例を抽出し, 検証を行った. 一例の要約にかかる時間は約 30 秒から 60 秒で, 各種 API の利用許容速度に依存した. 必要なトークン数は平均 696 (最小 359, 最大 1140) であり, 検討時点でのコストは 0.1\$/100 症例であった. 年齢や性別は正確に抽出された. 子宮頸癌などの性別固有の疾患について, 抄録内に性別が記載されていなくても判別可能であった. また, 単に疾患名を抽出するしようとする, 主病名が抽出されてしまい, 症例報告となった状態が抽出できなかった. 一方で, プロンプトを工夫し (プロンプトエンジニアリング), “the main condition or complication discussed” と指示することで, 症例報告の話題にあっていて疾患名が抽出可能であった. 【結論】生成 AI を用いた症例報告データベースの構築は現実的に可能であると考えられた. 特に, 地方部会の症例などの日本の症例を集積することが, 集合知として期待される.

P-74-1 当院における婦人科悪性腫瘍の肺転移再発に対する外科的治療の現状

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【目的】婦人科悪性腫瘍で肺転移再発は予後不良因子として知られている. 当院では oligometastasis の場合に治療目的に, また近年 oligometastasis でなくともがん遺伝子パネル (以下 FICDx) 検査目的に外科的切除を行っている. 今回当院で肺転移再発を認め, 外科的切除した症例を後方視的に検討した. 【方法】過去 7 年間の婦人科悪性腫瘍術後肺転移再発に対し呼吸器外科で治療及び検査目的に手術を実施された 7 例において診療録を元に後方視的に検討した. 【成績】卵巣癌 3 例, 子宮平滑筋肉腫 1 例, 卵管癌 1 例, 子宮体癌 1 例, 陰癌 1 例であった. そのうち検査目的に手術をしたのは卵巣癌 2 例であった. 治療目的に手術した卵巣癌は初回治療から 5 年 (以下 Y) 3 か月 (以下 M) で肺転移再発し, 初回治療から 11Y1M 再発はない. 子宮肉腫は初回治療から 4Y2M で肺転移再発し手術実施, 5Y8M で再々発, FICDx 検査を行い治療選択, 一時的に PR に至るも 7Y9M で DOD に至った. 卵管癌は初回治療から 3Y4M で肺転移再発し, 初回治療から 6Y7M で再々発し治療中である. 子宮体癌は初回治療から 2Y で肺転移再発し, 初回治療から 5Y10M 再発ない. 陰癌は初回治療から 1Y6M で肺転移再発し手術実施, 初回治療から 4Y5M で再々発し治療中である. 検査目的に手術実施した 1 例は FICDx 検査提出し, 1 例は術後早期に PS 低下認め, 検査提出に至らなかった. 【結論】今回の検討では 4 例中 1 例術後再発なく経過し, 2 例は再発, 1 例死亡していた. FICDx 検査は 2 例が治療に繋がったが, もう 1 例は病状進行し BSC となっていた. 今後 FICDx 検査提出目的の手術症例も増加する可能性が考えられ, さらに症例を重ね有効性の検討が必要である.

P-74-2 がん遺伝子パネル検査を実施した遺伝性腫瘍原因遺伝子の VAF と腫瘍含有率の関係兵庫医大¹, 兵庫医大遺伝子医療部²上田友子¹, 鏑本浩志¹, 成田幸代¹, 瀧本裕美¹, 谷口路善¹, 上田真子¹, 澤井英明², 柴原浩章¹

【目的】がん遺伝子パネル検査 (CGP) では、検出された遺伝子変異の癌化への関与の評価が薬剤選択及び2次の所見の取り扱いに重要であるが腫瘍組織を用いた CGP ではしばしば困難となる。【方法】Two hit theory と Loss of Heterozygosity (LOH) に基づき腫瘍変異率 (VAF) と病理判定腫瘍含有率を両軸とするグラフを作成した。2018年から2022年までにCGP及び遺伝学的検査を行った患者の変異遺伝子をグラフにプロットし意義を検討した。【成績】CGPを契機に11名を遺伝性腫瘍と診断した (BRCA1/2 9名, RAD51C 1名, MSH2 1名)。BRCA1/2 の7名及びRAD51C の1名はLOHに一致した。この内BRCA2変異子宮体部漿液性癌の2例あり、1例はPARP阻害剤が奏効した。もう1例は生殖細胞由来とBRCA2のVAFは一致するも、LOHとは一致しなかった。BRCA1変異卵巣癌の1名は初回プラチナ抵抗性、LOH陰性の粘液性癌で、BRCA1変異は未発症常染色体優性癌抑制遺伝子に一致した。MSH2変異子宮体癌は、生殖細胞由来及び体細胞変異の2か所に変異を認め、リンチ症候群と診断し、免疫チェックポイント阻害剤でCR継続中である。非遺伝性と診断された子宮体癌2名の変異遺伝子のうち1名はPOLE変異であり、複数の生殖細胞系列由来であることが推定される病的バリエーション (PGPV) を認め、すべて体細胞変異であった。【結論】グラフは変異遺伝子の意義を可視化し遺伝カウンセリングや治療選択推奨に有益であった。

P-74-3 カルボプラチン過敏性反応例に対する脱感作療法の選択と安全性に関する検討

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【目的】プラチナ製剤は婦人科悪性腫瘍治療におけるkey drugであるが、反復投与により過敏性反応 (HSR: hypersensitivity reaction) をきたすことがあり、他剤への変更や脱感作療法が必要となる。今回われわれは、カルボプラチン (CBDCA) に対しHSRをきたした症例に対する脱感作療法の選択と安全性を検討したので報告する。【方法】2018年3月から2023年8月に、当院でCBDCAに対しHSRを認めた13例 (卵巣癌7例, 腹膜癌1例, 卵管癌1例, 子宮体癌1例, 子宮頸癌3例) に行ったべ21例の脱感作療法について検討を加えた。【成績】CBDCAによる脱感作療法 (CBDCA脱感作療法) は8例、シスプラチン (CDDP) に変更して脱感作療法を行ったもの (CDDP脱感作療法) は13例であった。初回HSRまでの既往CBDCA投与サイクル中央値は、CBDCA脱感作療法群で7 (4-9) サイクルであり、CDDP脱感作療法群では10 (7-22) サイクルであった。初回HSRはCBDCA脱感作療法群でGrade1が1例, Grade2が7例であり、CDDP脱感作療法群でGrade1が3例, Grade2が10例であった。CBDCA脱感作療法でHSRを再発症したものが4例 (50%, 全てGrade2) 認められたのに対し、CDDP脱感作療法ではHSR再発症は認められなかった。CDDP脱感作療法を行った13例において、投与開始後に高度な有害事象を生じた症例は認めず、完遂率は100%であった。【結論】CBDCAにHSRを認めた際のプラチナ製剤再投与方法として、CDDP脱感作療法はHSRの再発症や有害事象の発生リスクが低く、安全性が高いと考えられる。

P-74-4 当院における免疫チェックポイント阻害薬の使用と免疫関連有害事象についての検討

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【目的】免疫チェックポイント阻害薬 (ICI) が様々ながん腫で適応となっているが、ICIでは免疫関連有害事象 (irAE) の発生に注意が必要である。今回、当院におけるICIの使用状況、irAEの発症頻度・発現時期について検討を行った。【方法】対象は、2021年12月から2023年8月にICIを導入した全症例とした。ICIの使用状況、がん腫、レジメン、irAE発症の有無、発症時の初回投与後日数、治療、中止の有無について後方視的に検討した。【成績】当院においてICIは34例に使用されており、ペンブロリズマブ30例 (単独投与2例, 併用投与28例)、セミプリマブ4例であった。irAE発症は67.6% (23/34例) あり、その内訳 (同一患者を含む) は甲状腺機能障害44.1% (15例), 肝機能障害32.4% (11例), 下垂体性副腎障害14.7% (5例), 大腸炎5.9% (2例), 髄膜炎2.9% (1例), ぶどう膜炎2.9% (1例), infusion reaction 2.9% (1例) であった。irAE発症の初回投与後日数の中央値は72 (1-294) 日目であった。irAEにより投与中止となった症例はペンブロリズマブを投与し30日後に髄膜炎を生じた1例であった。【結論】当院におけるirAE発現時期は既報の臨床試験の結果と同様であった。発症頻度はやや高めであったが、既報の臨床試験と比較して症例数が少ないためと考えられる。irAEは様々な時期に発症しうるため、定期的な検査に加え症状発現時の適切な検査が有用である。また、発症時は他科との連携により早急な治療介入が必要であると考えられる。

P-74-5 卵巣成熟奇形腫症例は卵巣固有靭帯が長いために茎捻転しやすい?

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【目的】卵巣成熟奇形腫（以下、奇形腫）は茎捻転しやすいことが知られている。その原因は明らかでないが、我々は奇形腫症例で卵巣固有靭帯が長いために茎捻転しやすいと仮説を立て、手始めに奇形腫例の卵巣固有靭帯の長さを計測したので報告する。【方法】2023年5月から9月にかけて当院で手術を行った片側の奇形腫例7例に対して術前に説明し、術中に卵巣固有靭帯の長さを絹糸で測定し、健側の卵巣固有靭帯の長さと比較した。茎捻転していた場合は解除された状態での計測とし、病理学的に奇形腫でなかったものは除外した。患者背景は年齢、術式、捻転有無、癒着有無、嚢腫サイズ（最大径）を調査した。統計はウィルコクソンの符号順位検定と相関係数を用いた。【成績】患者年齢は平均38.1歳、茎捻転は1例、嚢腫サイズ平均6.4cmであった。卵巣固有靭帯の長さは平均3.8cm（患側）、1.7cm（健側）であった（ $p=0.09$ ）。症例数が少なく有意差はなかったが、奇形腫の卵巣固有靭帯は健側と比較して長い傾向はあった。奇形腫の最大径と、卵巣固有靭帯の長さに関連は認めなかった（ $r=0.30$ ）。過去の報告で奇形腫は小骨盤腔を超えた位置で茎捻転を起こしやすいとされるが、卵巣固有靭帯が長いという報告は現在までない。奇形腫で卵巣固有靭帯が長いメカニズムとして脂肪や毛髪など嚢腫内容物の重さや大きさに伴う引力により後発的に長くなった可能性を考えましたが、腫瘍最大径と卵巣固有靭帯の長さに関連は見られず、そのメカニズムは不明のままである。【結論】奇形腫では卵巣固有靭帯が長いために茎捻転しやすい可能性はあるが、正常例を含めた症例の更なる検討が必要である。

P-74-6 高齢者のがん治療方針に対する医療者バイアスの後方視的検討

京都大

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【目的】高齢者は身体的、精神的、社会的な機能に個人差が大きく、年齢を基準にがん治療方針を決定することは難しい。高齢者総合機能評価が高齢者を多面的に評価する指標となっているが、検査・評価に労力や時間がかかり多忙な臨床現場では使用しにくく、医療者の主観で決定していることも多い。今回、75歳以上の婦人科がん患者に対し、医療者が主観的に標準治療が可能か判断した医療者バイアスについて検討した。【方法】2018年4月から2022年3月に婦人科癌として診断・初回治療を開始した75歳以上の患者のうち手術療法が標準治療となる患者37人の年齢、BMI、血中ヘモグロビン、アルブミン、クレアチニンおよび内服薬に関して、標準治療群と非標準治療群の2群で検討した。【成績】対象は標準治療群19例、非標準治療群18例であった。単変量解析で年齢は非標準治療群で有意に高く（中央値78歳 vs 83歳（ $p<0.01$ ））、BMIおよびヘモグロビン値が標準治療群で有意に高かった（BMI: 22.8kg/m² vs 22.1kg/m²（ $p=0.02$ ）、ヘモグロビン: 12.6g/dL vs 10.9g/dL（ $p<0.01$ ））。86歳以上は全例で非標準治療を行っていた。抗凝固薬や抗血小板薬の使用は差を認めなかった。さらに75歳から79歳に限局した（標準治療群17例、非標準治療群6例）ところ、BMIおよびヘモグロビンは標準治療群で有意に高かった（BMI: 25.2kg/m² vs 19.8kg/m²（ $p=0.03$ ）、ヘモグロビン: 12.6g/dL vs 9.8g/dL（ $p<0.01$ ））。多変量解析では年齢（ $p<0.01$ ）とヘモグロビン値（ $p=0.03$ ）で差を認めた。【結論】医師が主観的な評価で高齢者の治療方針を決める際、年齢が強く影響している。さらに、貧血のある患者が標準治療から除外される傾向にあることが示唆された。

P-74-7 当院における緊急子宮全摘術の後方視的検討

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【目的】当院は24時間体制で緊急手術に対応している。緊急子宮全摘術を後方視的に検討し、今後の緊急子宮全摘術において妥当な術式選択を可能にすることを目的とした。【方法】2012年9月から2023年5月の期間に緊急子宮全摘術を行った39例を対象とし、開腹子宮全摘術（ATH）と腹腔鏡下子宮全摘術（TLH）の治療成績を比較した。【成績】ATHが17例、TLHが22例であった。緊急手術となった原因として、ATH群では腹腔内感染10例（悪性合併3例、他科の術中併診2例）、有症状の悪性3例（卵巣癌1例、重複癌2例）、出血2例（子宮筋腫・腺筋症2例）、筋腫捻転1例、PTHrP産生筋腫による高Ca血症1例であった。TLH群では出血20例（子宮筋腫・腺筋症8例、異所性妊娠6例、胎盤遺残・ポリープ4例、術後合併症1例、帝王切開癒着部症候群1例）、腹腔内感染2例であった。ATH群の平均手術時間は167分（50-301分）、平均出血量は986ml（0-4410ml）、子宮重量中央値342g（54-2800g）、合併症は直腸筋腫損傷の1例であった。TLH群の平均手術時間は114分（66-255分）、平均出血量は158ml（0-1331ml）、子宮重量中央値は160g（45-1329g）で、合併症は高度癒着による開腹手術への移行1例であった。術式別の手術件数の年次推移について偏りはなかった。【結論】当院では感染症例の特に子宮の大きい症例または悪性合併例に対する緊急子宮全摘術は開腹を選択し、出血症例に対しては腹腔鏡下を選択する傾向があった。腹腔鏡下では手術時間や出血量を抑えられ、手術による合併症も認めなかった。緊急時においても子宮、付属器の大きさや悪性所見の有無によっては開腹を選択し、その他は可能な限り腹腔鏡下で施行することが望ましいと考える。

P-75-1 周閉経期以降に腹腔鏡下手術により診断された子宮内膜症女性の臨床的特徴の検討

長崎大

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【目的】性成熟期では子宮内膜症の疼痛や不妊症に対して手術療法を選択するが、周閉経期以降では手術適応や留意点が異なる。今回周閉経期以降で手術療法を選択した子宮内膜症女性の臨床的特徴を検討することを目的とした。【方法】2011年から2022年まで当科で腹腔鏡下に子宮内膜症と診断された45歳以上の症例でrASRM分類で評価された58例を対象とし、それらの臨床背景と手術所見の特徴を後方視的に検討した。【成績】平均年齢49.1±5.9歳、7例は手術時閉経していた。術前診断は、卵巣内膜症性嚢胞45例、子宮筋腫21例、子宮腺筋症11例、子宮頸部異形成3例、その他7例であった(重複を含む)。手術適応は、卵巣嚢胞の増大あるいはマーカー上昇26例、疼痛16例、嚢胞所見+疼痛8例、その他8例であった。付属器に限定(付属器摘除もしくは嚢胞核出)した術式が24例(A群)、子宮の処置(子宮摘出もしくは筋腫核出)を行った例が34例(B群)あった。平均手術時間はA群123±29分、B群233±64分、出血量はA群66±81g、B群193±429gで、rASRM進行期はI期B群のみ2例;II期A群1例、B群2例;III期A群6例、B群10例;IV期A群17例、B群20例であった。術前に子宮内膜症と診断されなかった9例のうち6例はIV期であり、両群とも進行期が重症であれば手術時間が延長し出血量も増加した。術後病理学的に卵巣内膜症性嚢胞と診断した41例のうち、内膜症に併存して類内膜型境界悪性腫瘍および明細胞癌が1例ずつ認められた。【結論】周閉経期以降の子宮内膜症の腹腔鏡下手術では、卵巣内膜症性嚢胞に関する症候が手術適応となることが多く、潜在的な悪性転化に留意する。術前に重症子宮内膜症が予測困難な例もあるため、術中対応への準備は肝要である。

P-75-2 子宮筋腫へのレルゴリクス投与では内腔突出例で出血リスクが高く、投与1か月以内は注意を要する

秋田大

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【目的】経口GnRHアンタゴニスト製剤のレルゴリクスは術前の子宮筋腫の縮小を目的として広く使用されている。GnRHアンタゴニスト製剤と比較しフレアアップはないと言われているが、投与中に性器出血をきたすことがある。当院でのレルゴリクスの使用経験をもとにレルゴリクス投与中の性器出血に関して検討することを目的とした。【方法】2020年2月から2023年2月に当院で子宮全摘術、子宮筋腫核出術の術前にレルゴリクスを投与した243例を後方視的に検討した。FIGO重分類のtype0からtype2(子宮内腔に突出した状態)の筋腫を1つ以上有するものをA群、それ以外をB群とした。【成績】平均年齢は41.2±5.7歳、レルゴリクスの平均投与期間は82.1±42.6日であった。レルゴリクス投与中の性器出血は28.0%(68例)であり、性器出血を認めた割合はA群36.2%(42/114例)、B群15.7%(26/129例)でありA群で有意に高かった(p=0.003)。投与開始から1か月の観察期間において、79.4%(54/68例)が性器出血を認めたが、その85.1%(46/54例)で自然止血が得られた。8.9%(6/68例)は投与後1-2か月に、11.8%(8/68例)は2か月以降に出血がみられた。多量出血のため投与が中止された症例は3例で、全てA群に分類され、うち2例は投与開始後2か月以降に生じていた。【結論】レルゴリクスは子宮内腔に突出する筋腫を持つ症例では性器出血のリスクが有意に高く、特に投与1か月以内での性器出血が多い傾向であった。性器出血はほとんどの症例において自然軽快するが、多量出血するリスクについて注意しながら適切に使用していく必要がある。

P-75-3 当院での卵巣子宮内膜症性嚢胞合併妊娠における妊娠管理の検討

岡山大

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【目的】子宮内膜症は生殖可能年齢の女性において約5~10%、不妊症女性では約5~50%が罹患している。妊娠中に卵巣子宮内膜症性嚢胞を伴う頻度は約0.5%であり、52%で縮小、20%で増大、28%は不変であるとの報告があるが、自然に縮小する可能性もあるため経過観察を行うことが多い。しかし、卵巣子宮内膜症性嚢胞への感染による膿瘍形成、嚢胞破裂による急性腹症のリスクや、悪性腫瘍との鑑別が難しい症例があり、その場合は妊娠中の腹腔鏡下手術や経腔的穿刺など外科的処置が選択されるが、明確な管理指針はない。今回、当院での卵巣子宮内膜症性嚢胞合併妊娠における妊娠管理について報告する。【方法】2008年5月~2023年7月に当院で分娩となった5926例のうち、妊娠成立後の初回診察時に卵巣子宮内膜症性嚢胞を認めた22例について後方視的に検討した。【成績】18例は経過観察され、そのうち1例は妊娠25週に膿瘍形成に起因した急性腹症を認め、保存的治療を行ったが、下腹部痛、切迫早産のため発症から分娩まで入院を要した。4例は妊娠13~16週に外科的処置(腹腔鏡下卵巣子宮内膜症性嚢胞内容除去術2例、経腔的穿刺内容除去術2例)を行った。いずれも妊娠初期の嚢胞径は長径5~11cmであり、子宮増大に伴う疼痛や嚢胞の増大傾向を認めた症例であった。分娩方法は経陰分娩が11例、帝王切開が11例であり、帝王切開術と同時に卵巣子宮内膜症性嚢胞に対し付属器切除術や嚢胞核出術等を行ったのは4例であった。早産は2例、低出生体重児は4例であった。【結論】卵巣子宮内膜症性嚢胞合併妊娠は、嚢胞への感染や破裂による急性腹症のリスクがあり、症例によっては妊娠中の外科的処置が周産期管理上有益である可能性がある。

P-75-4 子宮筋腫核出術における GnRH antagonist 術前投与期間の検討

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【目的】子宮筋腫核出術の際に GnRH antagonist (G) を術前投与する方法は広く用いられている。子宮筋腫術前の G 投与は長期間に及べば副作用が強く表れる。本研究では術前投与期間としてどれくらいが適当かを検討した。【方法】研究開始に先立ち当院倫理委員会にプロトコルを公開し、許可を得た。対象となった症例には十分なインフォームドコンセントを行い同意を得た。過去2年間、当科にて術前に G (40mg/day) を術前1, 2, 4か月間投与し、腹式子宮筋腫核出術を施行した35例を対象とした(1か月:9例, A群, 2か月:14例, B群, 4か月:12例, C群)。これらにつき、以前我々が手術時の新しい客観的評価の指標として導入した、Bleeding Index (BI: 出血量 (g)/摘出物重量 (g)), Operation Index (OI: 手術時間 (分)/摘出物重量 (g)) により、手術時の所見について検討を加えた。【成績】A, B, C 群でそれぞれ、手術時出血量: A: 532.4±124.5, B: 483.2±153.6, C: 453.3±132.4g, 手術時間: A: 95.2±15.0, B: 90.4±22.6, C: 88.3±24.1分といずれも有意差はなかった。より客観的で sensitive と考えられる BI, AI では、BI: A: 2.97±0.85, B: 1.73±0.42, C: 1.63±0.50, OI: A: 0.59±0.05, B: 0.32±0.07, C: 0.33±0.08 と、いずれも A 群で有意に高値を示したが (いずれも p<0.05), B, C 群間では有意差はなかった。【結論】子宮筋腫核出術の G の術前投与期間は、2か月で十分に手術時所見を改善することが明らかとなった。

P-75-5 当院の子宮内膜症手術における妊娠率に関する成績

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【目的】子宮内膜症は生殖可能年齢の女性の10%に発症し、不妊症や骨盤痛の原因となり女性のQOLを大きく下げる疾患である。重症の子宮内膜症や深部子宮内膜症に対して手術を行うことにより妊孕性の向上があるかどうかについてはまだRCTもなく議論の余地がある。今回、当院の子宮内膜症手術における妊娠率の成績について検討した。【方法】2014年から2018年まで当院で行った子宮内膜症手術のうち、20歳から40歳の腹腔鏡下卵巣子宮内膜症性嚢胞摘出術を後方視的に検討した。深部子宮内膜症病変摘出も同時に行なった症例 (DE group) と卵巣嚢胞摘出術のみを行なった症例 (C group) とを分類した。観察期間を2020年までとして、術後の追跡により挙児を希望した症例の中で妊娠を確認した割合を確認した。手術前の妊娠治療の有無や術中のr-ASRM, EFIなど周術期データと妊娠率を解析した。なお、後方指視的観察研究として施設内の倫理審査承認を得ている。【成績】対象の手術症例は119例であり、その中で2020年までに終診となり追跡できなかった症例、また半年未満の妊娠活動であった症例の48例を除いた、71例が本解析の対象となった。そのうちDE groupは48例で、C groupは23例であった。DE groupのうち43例 (89%), C groupのうち21例 (91%) の妊娠が確認できた。r-ASRM や出血量において両グループに有意差を認めなかった。【結論】本研究の解析において深部子宮内膜症病変摘出も同時に行なった症例のうち89%, 卵巣嚢胞摘出術のみを行なった症例のうち91%の妊娠を確認した。本学会では我々がやっている子宮内膜症手術について、妊娠背景や手術のデータを解析し発表する。

P-75-6 生殖補助医療に関連して急速に増大した子宮内膜症性嚢胞の2例

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子宮内膜症性嚢胞合併不妊症例において、採卵等の処置後に感染を合併したり、不妊治療中に卵巣痛と診断される症例の報告が散見される。今回、生殖補助医療に関連して急速に増大した子宮内膜症性嚢胞の2例を報告する。【症例1】44歳, 0妊0産。原発性不妊症, 子宮筋腫, 子宮内膜ポリープのため、腹式子宮筋腫核出術, 子宮鏡下内膜ポリープ摘出術を受けた後、不妊専門施設を初診。初診時に20mmの左卵巣子宮内膜症性嚢胞を指摘された。卵巣予備能低下のため、初診より2か月後に両側卵巣に多血小板血漿 (PRP) 注入を受けた。1か月後に左卵巣嚢胞が65mmに増大し、精査加療目的に当科紹介となった。PRP注入後に2度の発熱をきたしていた。MRIで卵巣膿瘍を疑う所見を認め、腹腔鏡下左卵巣嚢胞摘出術を施行した。嚢胞内容は黄緑色膿汁様であった。病理所見では、子宮内膜症性嚢胞に炎症所見が強く加わっていた。【症例2】38歳, 2妊2産。続発性不妊症のため前医初診時、23mmの右卵巣子宮内膜症性嚢胞を指摘。初診より2か月後にアンタゴニスト法で採卵、胚盤胞7個凍結した。採卵2か月後に卵巣嚢胞が61mmに増大し、その1か月後には91mmまで増大し、当科紹介となった。初診時、腹部全体の強い痛みを訴え、右卵巣嚢胞は6cmに縮小、骨盤内から上腹部にかけて血性腹水を認め、右卵巣嚢胞破裂の診断で同日腹腔鏡下右卵巣嚢胞摘出術を施行した。病理診断は子宮内膜症性嚢胞であった。子宮内膜症性嚢胞が急速に増大した場合、悪性化の有無を確認するのはもちろんのことだが、採卵後などでは感染の可能性も考慮する必要があり、排卵誘発やエストロゲン補充などによる内膜症増悪についても注意を払う必要があると考えられた。

P-75-7 稀少部位子宮内膜症の6例の臨床的検討

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【緒言】稀少部位子宮内膜症は患者数が少なく治療法に苦慮することが多い。今回我々は6例の稀少部位子宮内膜症を経験したので報告する。【症例】発症部位は帝王切開癒痕部が2例、膀胱、鼠径部、臍部、胸腔がそれぞれ1例ずつであった。診断時の年齢は31歳から45歳(39.8歳±5.67SD)であり、いずれも月経期に出現もしくは増悪する、当該部位に関連した症状を主訴とし、画像検査より稀少部位子宮内膜症が疑われた。病変の大きさはいずれも20mm程度(19.8mm±6.55SD)であり、うち3例(膀胱、臍部、胸腔)は薬物療法で症状が軽快した一方、薬物療法が効果不十分であった3例では外科的治療を行った。外科的治療を行った症例と病変の大きさは、帝王切開癒痕部2例(30mm, 11mm)と右鼠径部(15mm)であり、病理学的診断はいずれも子宮内膜症であった。術後は2例で薬物療法を行い、3例とも再発を認めていない。【考察】稀少部位子宮内膜症と診断した際に、我々の施設では治療の第一選択として薬物療法を行った症例がほとんどであったが、薬物療法のみでは症状が改善せず外科的治療を行った症例では、術後経過良好で術後合併症や再発も認めなかった。【結語】我々の経験した稀少部位子宮内膜症では、症例によって有効である治療が異なり、治療法の選択に関して今後もさらに検討していきたい。稀少部位子宮内膜症はその診断・治療ともに苦慮することが多く、また臓器ごとに症状や治療効果も異なる可能性があることから、個別の取り扱いが必要である。

P-75-8 子宮筋腫、子宮内膜症手術後のLEP製剤使用中に大きくなった子宮筋腫の1例

新生会総合病院高の原中央病院

谷口文章, 奥口聡美, 鈴木聡一郎, 曾山浩明, 吉田剛祥

【緒言】子宮内膜症症例や子宮内膜症の術後症例にLEP製剤がしばしば使用されている。子宮筋腫が併存する症例にも使用されているが、LEP製剤の使用中に子宮筋腫が大きくなったとの報告はほとんどない。今回、子宮内膜症の術後再発予防のためにLEP製剤を使用し、子宮底部が臍の高さまで達した多発子宮筋腫の1症例を報告する。【症例】未婚、未産婦。31歳時に両側内膜症性嚢胞、深部子宮内膜症、子宮筋腫、癒着にて腹腔鏡下卵巣嚢腫摘出術、子宮内膜症病巣除去術、子宮筋腫核出術、癒着剝離術を行った。r-ASRM: Stage IV, 摘出子宮筋腫: 9個, 566g, 出血量: 750mlであり、病理組織診は子宮内膜症、平滑筋腫であった。子宮内膜症再発予防のために、術後1か月よりLEP製剤の定期的投与を行った。内診はあまり希望せず、1回/年で行っていたが、手術後3年10か月の時点で多発子宮筋腫の再発により子宮底部が臍の高さまで達していた。そのためLEP製剤の投与を中止し、Gn-RH antagonistのレルゴリクスを投与した。子宮筋腫は、レルゴリクスに反応して大きく縮小し、腹腔鏡下子宮筋腫核出術を行なった。摘出子宮筋腫: 27個, 134g, 出血量: 340mlであり、子宮内膜症の再発所見は認めなかった。病理組織診は、平滑筋腫であった。再手術1か月後よりProgestin製剤のディナゲストの投与を開始した。【考察・結論】子宮筋腫の症例にLEP製剤を使用しても子宮筋腫は、増大しないのが一般的な報告である。しかし、今回の症例のようにLEP製剤使用中に増大することがあるので、LEP製剤の使用中は、十分な観察が必要と思われる。

P-76-1 当院で経験した胎児甲状腺腫大の二例

市立広島市民病院

岡田秀治, 上野尚子, 徳本佑奈, 坂井裕樹, 築澤良亮, 田中奈緒子, 森川恵司, 植田麻衣子, 関野和, 依光正枝, 石田理, 見玉順一

【背景】今回、異なる機序による胎児甲状腺腫大の二例を経験したので報告する。【症例1】34歳, 1妊0産。31歳時に近医内科にてバセドウ病と診断、挙児希望のためメルカゾール20mgからプロピルチオウラシル(PTU)300mgに変更となった。融解移植にて妊娠成立、近医にて妊婦健診を開始した。妊娠22週, FT4低下のため200mgに減量された。妊娠27週, 羊水過多, 切迫早産にて当科紹介入院となった。胎児甲状腺周囲径67mmと胎児甲状腺腫大を認め、TSHレセプター抗体陰性, FT4低値であり抗甲状腺薬による胎児甲状腺機能低下が疑われ、PTU100mgまで減量した。FT4低値のためPTUに加え、チラージン開始し50μgまで増量した。胎児甲状腺腫大, 羊水過多は徐々に改善し経過、妊娠36週3日NRFSのため超緊急帝王切開で分娩となった(2298g, AS7/9)。出生時、児の甲状腺はやや腫大、大腿骨遠位骨端核を認めず胎児甲状腺機能低下だったと考えられたが、甲状腺機能は既に回復しており治療は要さなかった。【症例2】35歳, 1妊0産。近医にて子宮卵管造影(HSG)後に妊娠成立、妊婦健診開始した。妊娠31週, 羊水過多, 胎児甲状腺腫大が疑われ当科紹介入院となった。胎児甲状腺周囲径は106mmと腫大、母体は軽度の甲状腺機能低下と尿中ヨウ素濃度高値を認め、HSGに伴うヨード過剰が考えられた。妊娠33週よりチラージン50μg内服開始、甲状腺腫大縮小し、羊水過多も改善した。外来管理とし、妊娠38週5日に経陰分娩となった(2955g, AS9/10)。児の甲状腺はやや腫大していたが、甲状腺機能異常はなかった。

P-76-2 帝王切開癒痕部妊娠に対して子宮内容除去術を行い妊孕性温存し得た一例

公立陶生病院

春原真由子, 丹羽優莉, 福田圭祐, 箕田 章, 岸田 薫, 岩田愛美, 宇野あす香, 近藤紳司

帝王切開癒痕部妊娠 (cesarean scar pregnancy : CSP) の頻度は近年上昇しているが, その治療選択肢は多岐にわたる。今回妊娠9週相当のCSPに対して子宮内容除去術により治療を完遂し子宮温存が可能であった症例を経験したので報告する。症例は32歳, 5妊3産, 2回の帝王切開歴があった。不正出血および市販妊娠反応検査薬の陽性反応を主訴に前医を受診し, CSPが疑われ当院紹介受診となった。当院初診時の経陰超音波でも子宮峡部前壁の筋層欠損部に, 膀胱側へ著明に突出する37mm大の胎囊およびその内部にCRL23.6mmの心拍のある胎児を認めた。骨盤部単純MRIでも同様の所見を呈していたが, 胎囊を覆う子宮漿膜面と膀胱壁との境界は明瞭であった。妊娠継続に伴う子宮破裂のリスクが高いと判断し, 患者にICのち子宮温存希望が強かったため, 開腹手術移行の準備下で子宮内容除去術を施行した。経腹超音波ガイド下に頸管を拡張した後, 手動真空吸引法を用いて子宮内容を吸引除去し, 術後は子宮内の血腫形成を経時的に観察し管理した。胎囊に置換するように最大85mm大の血腫が形成されたが, 止血は得られ, 術後1か月程度で子宮形態も妊娠前同様に復し, 輸血などの追加治療はせず子宮温存が可能であった。CSPは増大に伴って, 大量出血や子宮破裂により母体の生命に関わるリスクがあり, 適切な治療選択が重要となる。妊孕性温存希望などの患者背景や妊娠週数, MRI検査を含む画像診断によるリスクの評価など総合的な判断は必要ではあるが, 子宮内容除去術は, 完遂できれば低侵襲な治療選択肢の一つとなり得る。

P-76-3 腹腔鏡下手術で治療し得た腹膜妊娠の1例

愛仁会明石医療センター

夏山貴博, 松岡正造, 北口智美, 江島有香, 林田恭子, 細谷俊光, 宮原義也

【緒言】腹膜妊娠は異所性妊娠の中で約1.0%の頻度で発生する稀な疾患である。術前診断は困難であり, 術中に診断することがほとんどである。今回MRIで術前診断したがメトトレキサート (Methotrexate, 以下MTX) が奏功せず, 腹腔鏡下手術を要した腹膜妊娠の1例を経験したので報告する。【症例】32歳, 2妊2産, 既往歴なし。胚盤胞移植で妊娠。妊娠5週の診察で子宮内に胎囊を認めなかったため, 異所性妊娠の疑いで紹介となった。初診時診察所見で血中hCG値は2269mIU/mLであり, 経陰超音波では子宮, 両側付属器周囲に胎囊を示唆する所見は無かったため, 子宮内容除去術を施行したが, 絨毛成分は認めなかった。術後1日目の血中hCG値は2797mIU/mLと上昇しており, 経陰超音波で右卵管膨大部付近に9mm大の胎囊を認めたため, 精査目的でMRI検査を施行した。膀胱子宮窩右側にT2強調画像高信号を呈する内部不均一な嚢胞性腫瘍を認め, 腹膜妊娠と診断した。患者が薬物治療を希望したため, MTX 50mgを筋注した。MTX投与後5日目の血中hCG値が6318mIU/mLと上昇しており, 経陰超音波で膀胱子宮窩右側に胎囊を認め, 胎囊内に心拍を伴う胎芽を認めたため, 緊急手術とした。術中所見は子宮, 両側付属器は正常であり, 膀胱子宮窩右側に胎囊様腫瘍を認めた。胎囊様腫瘍を回収し, 肉眼的に絨毛を確認した。最終病理所見も絨毛を認めた。腹腔鏡下手術後2週間の血中hCG値も12mIU/mLと低下を認めた。【結語】腹膜妊娠は卵管妊娠と比較して, MTX投与後に手術療法を要した割合が多いとする報告がある。本症例もMTXが奏功せず手術を要した。腹膜妊娠を画像診断で疑った場合はMTXが奏功しない可能性があることを十分に説明する必要がある。

P-76-4 術前にMRIを撮影するも両側卵管妊娠を術前に疑うことのできなかつた2例～MRI画像を振り返る～

倉敷中央病院

西村智樹, 橋本阿実, 原 理恵, 田中 優, 伊藤拓馬, 堀川直城, 清川 晶, 楠本知行, 福原 健, 中堀 隆, 長谷川雅明, 本田徹郎

【緒言】自然妊娠による両側卵管妊娠は1/200,000と報告されており非常に稀な疾患であるが, 排卵誘発剤の使用によりその頻度は上昇するものと思われる。今回, 術前にMRIを撮影するも術前診断に至れなかつた2例を経験した。術前に診断できたかどうかについて振り返る。【症例1】31歳, G2P1。他院にてFSH自己注射によるタイミング法で妊娠反応陽性となった。HCG 4734.8 mIU/mL, 経陰超音波で左付属器領域に血腫およびダグラス窩に高輝度腹水を認め異所性妊娠を疑った。MRIを撮影し左卵管に胎囊構造認め左卵管妊娠と診断, 腹腔鏡下手術を行った。術中に左卵管に加え, 右卵管膨大部にも異所性妊娠を疑う腫大を認めたが未破裂でありこちらは切除せずに手術を終えた。術後の診察で右卵管内に胎児心拍が確認されMTX投与を行い治療した。治療後の子宮卵管造影検査で右卵管の通過性はなくARTにて第2子を出産した。【症例2】26歳, G4P2。自然排卵周期で妊娠反応陽性となった。HCG 4452.4 mIU/mL, 経陰超音波で妊娠部位は同定できず, 腹水もなかった。4日後の診察でHCG 10160.2 mIU/mLと上昇, 超音波所見に変わりなく, 子宮内容除去術を行った。脱膜組織のみであり翌日以降もHCGは上昇したため, MRIを撮影したところ左卵管に胎囊構造を認め腹腔鏡手術を行った。術中に右卵管膨大部にも卵管妊娠と思われる所見を認め, 両側卵管切除を行い, 病理検査で両側卵管妊娠の診断が確定した。【考察】2症例とも後方視的にMRI画像を見直すも術前に指摘されている病変の他に, 対側卵管にも胎囊様構造を認めた。稀な疾患であるが, その可能性を念頭に注意深く画像の読影を行えば術前に診断できた可能性がある。

P-76-5 妊娠25週の腰椎破裂骨折

山形県立中央病院

武士ゆい, 福長健史, 小幡美由紀, 國井勝俊, 丸山真弓, 堤 誠司

【緒言】妊娠中の脊椎骨折の管理には、手術の体位やアプローチ方法、胎児の被曝などの問題がある。今回、妊娠25週の腰椎破裂骨折を経験したので報告する。【症例】31歳、1妊0産、妊娠25週2日に階段を降りるときに転倒し臀部を強打した。そのあとから強い腰痛があり、かかりつけの産科クリニックを受診した。体動が困難な腰痛のため、当院に母体搬送された。来院時、腰部から両腸骨後付近の強い痛みを訴えていた。両下肢に痛覚や触覚の低下は認めなかった。単純X線検査で第1腰椎の破裂骨折を認め、MRIで脊髄の圧迫を認めた。翌日、肛門括約筋の収縮力減弱や左アキレス腱部の痛覚過敏、左鼠径部の痛覚過敏が出現し、緊急手術の方針とした。全身麻酔、腹臥位で、脊椎後方固定術、椎弓切除術、椎弓形成術、骨移植術を施行した。手術時間は3時間48分で出血量は1,158gであった。術後12日で歩行練習を開始し、術後19日で独歩可能となった。術後20日目(妊娠27週5日)に産科に転科し、リハビリを継続した。術後膀胱直腸障害があったが徐々に改善し、術後27日目(妊娠28週5日)に退院した。妊娠38週3日に2,430gの男児を自然分娩した。現在後遺症は認めていない。【考察】妊娠中の脊椎骨折の治療として外科的治療と保存治療がある。外科的治療は手術の体位や出血、麻酔のリスクがあるが、保存治療は長期臥床となるため血栓症のリスクや脊椎変形の原因となる。本症例は神経症状が出現したため手術の方針とした。側臥位での手術は難易度が高いため、腹部の圧迫を極力避けるように固定した腹臥位で行った。【結語】妊娠25週の腰椎破裂骨折を経験した。早期の手術とリハビリにより後遺症なく治療を行うことができた。

P-76-6 完全心脱出を伴う Cantrell 五徴症の一症例

足立病院

市川尚寛, 濱田啓義, 小木曾望, 衛藤美穂, 大坪昌弘, 姜 賢淑, 須藤慎介, 須戸龍男, 山出一郎, 井上卓也, 澤田守男, 畑山 博

【緒言】Cantrell 五徴症は異所性心、腹壁欠損、胸骨下部欠損、横隔膜の前部欠損、心嚢心膜欠損を五徴とする極めて稀な奇形症候群である。我々は完全心脱出、腹壁破裂を伴う五徴症の一例を経験したためここに報告する。【症例】症例は37歳女性1妊0産(今回の妊娠・分娩含む)。当院にて凍結融解胚移植を行い妊娠が成立、妊婦健診を受診していた。本人および夫の希望にて非侵襲的出生前遺伝学的検査(NIPT)を受検し陰性であったが、妊娠16週の妊婦健診にて超音波検査で心臓、腹部臓器が体腔外に脱出していることが指摘された。更なる精査にて、胎児心は胸腔外から脱出、肝臓、胃、下部消化管も腹腔外に脱出しており、これらの所見より Cantrell 五徴症との診断に至った。また心臓には心室中隔欠損および大動脈騎乗が見られ Fallot 四徴症を疑う所見であった。脱出臓器が広範囲に及び、心奇形を合併していることから出生後の修復は不可能で胎外での生存が期待できない状態であることを夫婦に説明した。夫婦の希望として人工妊娠中絶を選択し、妊娠17週に人工死産となった。事前の診断の通り心臓および腹腔内臓器の胎外への脱出が確認された。【結語】Cantrell 五徴症は、異所性心、脱出範囲が軽度である場合などに出生後、外科的修復が行われている症例も存在する。一方で本症例のように広範囲の臓器脱出を伴う症例や重度の先天性心奇形を合併する症例の予後は極めて不良である。特徴的な超音波所見のため診断が難しい疾患ではないが、胎児の状態が母の両親にとって極めて衝撃的であるため、十分な説明とその後のフォローが必要だと考える。key-word: 奇形症候群, Cantrell 五徴症, 出生前診断

P-76-7 流産手術法の違いは絨毛染色体検査の精度に影響するか?

日本医大

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【目的】近年、従来の子宮内容除去術(D&C)に変わり、子宮損傷のリスクが低い手動吸引法(MVA)が流産手術で多く選択されている。当教室は、流産絨毛染色体検査において母体細胞の混入を背景に正常女性核型の比率が高いことを報告してきた。本研究では、流産手術法の違いが絨毛染色体検査の精度に影響するか検討した。【方法】当院で2011年2月から2019年5月に初期流産に対してMVAまたはD&Cを実施し、絨毛検体を染色体検査(G分染法)に提出した症例について後方視的に検討した。母体細胞の混入率は、正常男性核型もしくは異常核型において、正常女性核型が同時に検出された比率として算出した。【成績】MVA群は43例で、内訳は異常核型60.4%(26/43)、母体細胞の混入率22%(7/31)、正常女性核型12例>正常男性核型5例であった。D&C群149例で、内訳は培養不良による解析不可5%(8/149)、異常核型67.1%(100/149)、母体細胞の混入率12%(13/107)、正常女性核型34例>正常男性核型7例であった。本来、正常核型の男女比は同等であることから、正常女性核型と解析された例数から正常男性核型の例数を差し引き、MVA群7例およびD&C群27例ほどが、胎児絨毛の培養不良を背景に母体細胞のみが解析されたものと推定された。解析不可の症例と合わせ、絨毛細胞の培養不良はMVA群16%(7/43)、D&C群23%(35/149)と算出された。いずれも両群で統計学的有意差を認めなかった。【結論】MVAはD&Cと比較し、絨毛細胞の培養不良が少ない一方、母体細胞の混入が多い可能性が示唆された。いずれの方法でも、絨毛細胞の培養不良を背景として母体細胞が解析される可能性があり、正常女性核型の結果に際しては慎重な解釈が求められる。

P-77-1 頸管長をより正確に測定するための工夫—オリブオイルにより、外子宮口を明瞭化できる—

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【目的】頸管長を測定する場合、組織学的内子宮口が閉鎖している場合は、「組織学的内子宮口から外子宮口までの距離を測定すること」となっており、子宮峡部は含めないこととなっている。ここで、測定の誤差の原因として、まず、考えられるのは、「子宮峡部を含めて頸管長を測定してしまう」こと。次には、外子宮口の位置が決めづらい点にある。過去の論文では、外子宮口の位置として、「the location of the triangular area of echo-density」を、また、「子宮腔部の前唇と後唇の交差した部分」と述べているが、実際には、外子宮口がはっきりしない場合が多い。これが、誤った計測の原因の一つとなっていると思われる。今回、「内診の時、腔の狭い症例等で、潤滑をよくするために、従来から使われている医療用のオリブオイルを使用することにより、外子宮口の像が明瞭化できることを見出した」ので、同オイルを使用した場合の頸管長測定データを検討した。【方法】令和5年4月より、妊娠16週から20週の妊婦に、頸管長の測定時、内診時のグローブと超音波プローブカバーに、オリブオイルを塗布し測定した。【成績】令和5年8月7日現在、43例に施行。このうち10例では、外子宮口そのものに、echo-free spaceを認めた。また、10例には、腔門蓋部のecho-rich像を、29例には、腔管のecho-rich像を認めた。これらの所見は、外子宮口の位置決定に寄与した。頸管長の平均値と標準偏差は、 33.5 ± 4.590 mmであった。【結論】経陰超音波施行時、オリブオイルを塗布することにより、外子宮口の像を明瞭化でき、頸管長を、より正確に測定できる方法を考案した。

P-77-2 当院での胎胞脱出症例の検討

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【目的】胎胞脱出は頸管無力症や感染を伴った場合に発症し、流早産となる可能性が高い。当院での胎胞脱出例において生児を得た症例と流死産例を比較し、妊娠継続に関与した因子を予測する。【方法】2013年10月から2023年9月までに当院で管理した胎胞露見・胎胞脱出症例の33例を対象として診断時の母体年齢、妊娠週数、頸管縫縮術の有無、その後の妊娠経過について後方視的に診療録を用いて比較した。【成績】母体搬送および紹介例18例を含む33例を検討した。母体年齢の中央値は30歳(20-35歳)、すべて単胎であった。診断時の妊娠週数は、22週未満が13例、22週以降が20例で平均20.3週であった。治療的縫縮術例は5例あり、すべて25週未満に実施していた。22週未満の13例では縫縮術を1例行ったが、全例が流産となった。22週以降に診断された20例のうち18例が生児を得ており、そのうち4例が縫縮術を実施していた。また、診断時のCRPが2.0 mg/dL以上の症例では、治療的縫縮術を実施せず1週間以内に娩出となっていた。【結論】胎胞脱出症例に対して治療的縫縮術を行うと破水などのリスクがあり、実施については症例毎に判断されるが、実施可能であった症例では妊娠継続が延長できている傾向にあった。よって診断時に感染が疑われない症例では治療的縫縮術を積極的に選択してもよいと考えらる。

P-77-3 子宮頸管無力症に対する子宮頸管縫縮術の治療効果についての検討

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【目的】早産の主な原因の1つに子宮頸管無力症があり、治療かつ早産予防として子宮頸管縫縮術が行われる。当院では、頸管縫縮術としてMcDonald法を主に行っている。縫縮糸の深さが妊娠期間延長に関連するという報告があるが、未だ一定の見解は得られていない。今回当院で直近5年間に子宮頸管縫縮術を行った症例について後方視的に検討を行ったので報告する。【方法】当院にて2018年7月から2023年6月に当院で子宮頸管縫縮術を施行した102例を対象とし、周産期予後については診療録を用いて検討した。【成績】予防的頸管縫縮術(予防群)が50例、治療的頸管縫縮術(治療群)が52例であった。うちShirodkar法は3例で全て治療的頸管縫縮術であった。36週未満で早産とし、予防群では7例(14%)、治療群では15例(28%)が早産であった。妊娠延長期間は予防群で平均19.2(±4.0)週、治療群で13.6(±3.9)週と予防群で有意であった($p < 0.001$)。治療群における検討では、BMI、母体年齢と妊娠延長期間は有意な負の相関を示し、治療前の頸管長、治療後の頸管長、縫縮糸の深さと妊娠延長期間は有意な正の相関を示した。重回帰分析では妊娠延長期間において、BMI($\beta = -1.85$, $p < 0.01$)、縫縮術の施行週数($\beta = -0.62$, $p < 0.001$)、治療後頸管長($\beta = 1.80$, $p < 0.001$)が有意であったが、縫縮糸の深さは有意でなかった。【結論】子宮頸管縫縮術において、縫縮糸の深さについてはその後の妊娠期間に有意な影響を与えないという結果であった。今後もより良い治療のためにデータの蓄積と研究が必要である。

P-77-4 当院における子宮収縮抑制剤の使用法と周産期予後の検証

高知大

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【目的】本邦の切迫早産に対する子宮収縮抑制剤の使用法は施設毎に異なっており、諸外国の管理方針と大きく異なる。当院において、切迫早産の管理方法を変更する前後での周産期予後を評価し、子宮収縮抑制剤の投与方法毎の治療効果を検証した。【方法】2021年4月1日～2023年8月31日の期間に切迫早産の診断で当院に入院した妊婦を対象とし、子宮収縮抑制剤長期使用群（2021年4月1日～2022年3月31日：前期群）と短期使用群（2022年4月1日～2023年8月31日：後期群）に分類した。分娩週数を主要評価項目とし、切迫早産の入院期間、子宮収縮抑制剤点滴の使用量および使用期間、母体合併症、出生児のApgar score、NICUの入院頻度、新生児慢性肺疾患の有無を副次評価項目とした。これらを診療録から後方視的に抽出した。【成績】対象患者数は前期60例、後期61例であった。患者背景は入院時頸管長が後期群で有意に短い以外は有意差を認めなかった。分娩週数の中央値は前期群36.5週、後期群37週と有意差を認めなかった。子宮収縮抑制剤点滴使用期間、リトドリン塩酸塩使用本数の中央値はそれぞれ前期群20.5日・20.8本、後期群4日・0本と後期群で有意に減少した。切迫早産の入院期間、硫酸マグネシウムの使用量、母体合併症（無顆粒球症、横紋筋融解症、肺水腫、肝酵素上昇）や新生児転帰（Apgar score、NICUの入院頻度、新生児慢性肺疾患）においては両群間で有意差を認めなかった。【結論】後期群ではリトドリン塩酸塩点滴使用量は減少し、子宮収縮抑制剤点滴使用期間は短縮したが、周産期予後は変わらなかった。子宮収縮抑制剤の使用法は短期使用に変更することが可能と考える。

P-77-5 絨毛膜羊膜炎を合併し診断が困難であった頸管無力症の一例

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【緒言】子宮頸管無力症は客観的な所見や明確な診断基準が存在しないため診断が困難である。今回、1度目では診断できず、2度の後期流産後に子宮頸管無力症と診断し、3度目の妊娠時に頸管縫縮術を施行することで生児を得た症例を経験したので報告する。【症例】30歳3妊0産。後期流産の既往が2回ある。1度目の妊娠（27歳時）は妊娠17週3日に腔内胎胞脱出、妊娠18週2日に経腔分娩に至った。胎盤病理はCAM stageIIIの診断であり、子宮内感染による後期流産と考えた。1度目の後期流産より1年3か月後、細菌性膣症の治療と乳酸菌製剤によるプロバイオティクスを行いながら2度目の自然妊娠成立したが、18週4日に胎胞形成を認めた。同日マクドナルド頸管縫縮術を行ったが、妊娠20週2日に経腔分娩に至った。胎盤病理はCAM stageIの診断であった。以上の経過より頸管無力症と診断した。2度目の後期流産より1年3か月後に3度目の妊娠成立し、妊娠12週2日にシロッカー法による予防的頸管縫縮術を施行した。妊娠経過は順調であり、妊娠36週6日に縫縮糸を抜糸、妊娠39週0日に3330gの男児を経腔分娩した。【考察】1度目の妊娠は胎盤病理検査から子宮内感染による後期流産を疑い、2度目の妊娠時には予防的頸管縫縮術を行わなかった。絨毛膜羊膜炎を合併すると子宮頸管無力症の診断はさらに困難となる。2度の中期流産を経て本症例は子宮頸管無力症と診断され、予防的頸管縫縮術を施行した3度目の妊娠でようやく生児獲得に至った。詳細な妊娠経過を再度確認し、頸管無力症の鑑別は慎重に検討すべきであると考えられた。

P-77-6 妊娠25週で完全破水したのち妊娠35週まで妊娠継続できた1例

富山県立中央病院

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【緒言】早産期前期破水（pPROM）の多くの症例が破水後1週間以内に分娩に至るとされている。また、pPROMに対する子宮収縮抑制剤の長期投与に、児の予後を改善する効果はみられないとされる報告がある。一方、妊娠中期からのpPROMで、長期間妊娠延長したとする報告は多くない。今回、妊娠25週からのpPROMで妊娠35週まで妊娠延長するに至った一例を経験したので、児の短期予後等を含め報告する。【症例】38歳3妊2産。早産の既往なし。自然妊娠成立し、当科での妊娠管理を継続した。妊娠25週4日に完全破水の診断で入院した。絨毛膜羊膜炎を疑う所見なく、抗菌薬と塩酸リトドリンの投与を開始した。ベタメタゾン12mgを計2回投与した。妊娠27週5日には頻回の子宮収縮を認め、硫酸マグネシウムの併用を開始した。以降は、感染徴候や切迫早産の進行なく経過した。妊娠34週で硫酸マグネシウムは中止し、妊娠35週で塩酸リトドリン点滴も中止した。妊娠35週4日に陣痛発来し、経腔分娩に至った。2583gの女児をApgar 8/8点、臍帯血pH 7.390で娩出した。児はdry lung syndromeの診断で、酸素投与とCPAPによる呼吸補助を必要としたが、日齢1でCPAPは中止し、日齢2には酸素投与も中止した。【考察】妊娠25週からの完全破水で、妊娠35週まで妊娠延長した一例を経験した。児は気管支挿管を必要とせず、日齢2には酸素投与も不要となった。妊娠34週未満のpPROMでは、子宮内感染のリスクが懸念され、ステロイドの効果が出現する48時間の子宮収縮抑制剤を推奨する報告が多い。感染や早産徴候がなく、妊娠延長が可能なお場合、長期間の妊娠延長により児の予後が大きく改善する症例も存在すると考えられる。

P-77-7 当院に母体搬送された胎胞可視 100 例の検討～経腔エコー所見による妊娠延長期間の評価～

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【目的】クスコ腔鏡診にて胎胞が露見する胎胞可視症例では、その多くは近日中の分娩が避けられない。当院では胎胞可視に対し可能であれば McDonald 法による治療的頸管縫縮術 (Mc 縫縮) を行っている。一方で胎胞が大きく頸管縫縮術を施行できない症例も存在する。今回我々は当院に母体搬送となった胎胞可視症例を後方視的に検討した。【方法】2017年11月から2023年3月の期間に胎胞可視で当院に搬送となった100例を対象とした。Mc 縫縮群と非縫縮群の2群に分け、それぞれの妊娠延長期間について検討した。縫縮が困難であった非縫縮群について、搬送時の経腔エコー所見と妊娠延長期間との相関について検討した。本研究では以下の5つの経腔エコーでの指標を用いた。①外子宮口の開大径 ②外子宮口から児先進部までの距離 ③胎胞の最大径 ④子宮頸管後唇の厚み ⑤胎胞の形態：A・B・Cの3つに分類【成績】100例中、Mc 縫縮群は17例、非縫縮群は83例であった。Mc 縫縮群は、9例が満期での出産であり、15例が28日以上妊娠期間延長に成功した。Mc 縫縮群は非縫縮群と比較し有意な妊娠期間延長を認めた。非縫縮群83例中、経腔エコーのデータが利用可能であった75例を検討した。重回帰分析を行うと、胎胞の形態「A」は妊娠期間延長に相関した ($P<0.05$)。7日以内に分娩に至る因子について多変量ロジスティック解析を行うと、外子宮口の開大径は有意なリスク因子であり ($OR=1.07, P=0.026$)、その cutoff は 14.7mm であった。【結論】胎胞可視に対し、可能と思われる症例については縫縮術を積極的に検討すべきと考える。非縫縮群において、胎胞の形態や外子宮口の開大径は妊娠延長期間の予測に役立つ可能性が示唆された。

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