



THE UNIVERSITY OF BRITISH COLUMBIA

UBC Obstetrics & Gynaecology 21st Annual Academic Day

Wednesday May 5, 2021

Zoom

Abstract Booklet for Paper Presentations

Wednesday May 5

8:00 – 8:30 **Breakout rooms with Sponsors, Poster Breakout Room**

8:30 – 8:35 **Welcome by Dr Janice Kwon**

Chair, Academic Day Scientific Planning Committee

Introduction of Guest Speaker by Dr. Sarah Finlayson

8:35 – 9:30 **2021 Leanne Dahlgren - Scott Memorial Lecture**



Title: “Racism in Medicine”

Keynote Speaker - Dr. Modupe Tunde-Byass, Assistant

Professor University of Toronto

9:30 – 10:05 **Trainee presentations (Paper Session)**

- “Role of ERBB receptor signaling in copy-number high endometrial cancer cell viability, migration, and invasion” - **Arezoo Mehrizi**
- “Improving routine influenza vaccination among women receiving gynecologic oncology surgery at Vancouver General Hospital; a multidisciplinary quality improvement project” - **Dominique Barnes**
- “Temporal Trends in Thyroid – Stimulating Hormone and Effect of Levothyroxine Treatment on Live Birth Rate in the Hypothyroid Recurrent Pregnancy Loss Population” – **Sophie Jansen**
- “Basal cell adhesion molecule: a novel human cytotrophoblast progenitor marker” – **Matthew Shannon**
- “Reproductive outcomes following surgical management for isthmoceles: A systematic review” – **Rahana Harjee**

10:05 – 10:15 **Break**

10:15 – 10:45 **Trainee Presentations (Poster Session)**

10:45 – 11:15 **Trainee Presentations (Paper Session)**

- “The functional effect of ARID1A and PIK3CA mutations on endometrial organoids” - **Forouh Kalantari**
- “Systematic Access to Penicillin Allergy Testing Results in Direct Benefit of Pregnant Women During Labour and Delivery” – **Ethan Zhang**
- “Chronic intervillitis of unknown etiology (CIUE): prevalence, patterns and reproductive outcomes at a tertiary referral institution” – **Natasha Simula**
- “Postpartum thought of infant-related harm and obsessive-compulsive disorder: Prevalence and relation to maternal physical aggression towards the infant” – **Rose Cameron**
- “Modelling inflammation in pregnancy” - **Lauren St-Germain**

11:15 – 11:25 **Break**

11:25 – 11:55 **Trainee Presentations (Poster Session)**

11:55 – 12:25 **Trainee Presentations (Paper Session)**

- “Cannabis use among women with myofascial pelvic pain: A survey” – **Emily Yang**
- “Documenting Perineal and Obstetrical Anal Sphincter Injury Care at Childbirth: A Cross-sectional Study” – **Gurkiran Mann**
- “The expression and role of bone morphogenetic protein 2 at maternal-fetal interface “– **Yuyin Yi**
- “Clinical predictors of poor pain-related outcome after endometriosis surgery” – **Dwayne Tucker**
- “Disease-free survival in patients undergoing fertility sparing surgery for early stage cervical cancer: a single centre case review” – **Marguerite Heyns**
- “Immune Microenvironment in Endometrioid Ovarian Carcinomas and the influence of Molecular Subtyping” – **Karolin Heinze**

12:25 – 12:30 **Closing Remarks by Dr. Gavin Stuart**

Head, Department of Obstetrics and Gynaecology

Role of ERBB receptor signaling in copy-number high endometrial cancer cell viability, migration, and invasion

Arezoo Alemzadeh Mehrizi†; Klausen, Christian; Leung, Peter C. K.

BACKGROUND: Endometrial cancer (EC) is the most common and second most lethal gynecological cancer. Advances in clinicopathologic classification have established four molecular subtypes, of which copy-number high (CNH) tumors have the worst prognosis. The objectives of this study were to: (1) investigate genomic abnormalities in epidermal growth factor (EGF)/ERBB family members and their correlation with survival in EC molecular subtypes, and (2) test the hypothesis that enhanced signaling by ERBB family receptors increases the viability, migration, and invasion of CNHEC cells.

METHODS: cBioPortal was used to study genomic alterations in ECs from The Cancer Genome Atlas. KLE, EFE184 and MFE280 CNH EC cell lines were treated with EGF family ligands targeting different ERBB receptors: Betacellulin, Neuregulin-1 β 1 and Neuregulin-4 (1 or 10ng/mL). MTT assay (24-72hrs) and transwell migration (24hrs) and invasion (48hrs) assays were used to study effects on cell viability, migration and invasion.

RESULTS: Kaplan-Meier analysis showed that tumors with amplification of ERBB2 or ERBB3 had reduced overall survival (Log-rank test $P=0.004647$ and 0.040 , respectively). Elevation of Betacellulin, Neuregulin-3 or Neuregulin-4 mRNA was associated with reduced disease-free survival ($P=0.009244$, 0.0172 and 0.005715). Betacellulin treatment significantly increased the migration and invasion of all three cell lines. Treatment with Neuregulin-4 enhanced EFE184 cell migration and invasion as well as KLE and MFE280 invasion. Neuregulin-1 β 1 increased the invasiveness of all three cell lines and migration of EFE184 and MFE280 cells. Cell viability was not significantly/consistently altered.

CONCLUSIONS: Enhanced ERBB receptor signaling may contribute to poor prognosis of CNH ECs by enhancing cell motility and invasiveness.

Improving routine influenza vaccination among women receiving gynecologic oncology surgery at Vancouver General Hospital; a multidisciplinary quality improvement project

Barnes, Dominique; Jones, Rebecca; Smith, Tara; Jain, Sneha; Chiu, Allison; McGinnis, Justin

BACKGROUND: All patients with solid organ malignancies are recommended to receive influenza vaccination prior to initiating chemotherapy. Baseline survey of new gynecologic oncology patients at the Vancouver BCCA suggested the influenza vaccination rate was 56% in the 2019/2020 season. The aim of this project was to increase the influenza vaccination rate among patients receiving gynecologic oncology surgery at VGH to 80%, by June 2021.

METHODS: We performed an interrupted time series study using structured quality improvement methodology. Three interventions were introduced to address vaccination barriers: an in-house vaccination program using a pre-printed order (PPO) set and both staff and patient education campaigns. Process and outcome data were collected by patient survey and chart audit and analyzed on statistical process control charts.

RESULTS: We identified 229 patients from November 2020-February 2021. The PPO was utilized in 192 patients (84%). Overall, 140 patients (61%) received vaccination throughout the study. Forty-four percent (n=100/229) received influenza vaccination prior to surgery. Twenty-nine percent (n=40/140) of those vaccinated received their vaccine through our inpatient program. The weekly mean vaccination rate saw a 5% absolute increase to 61%. The 80% target was reached for three weeks of study, but was not sustained. Barriers to vaccination included non-use of PPO (n=39, 17%), patient refusal (n=31, 14%), and process issues where vaccines were ordered, but not administered by ward staff (n=20, 9%).

CONCLUSIONS: Creation of in-house vaccination and education programs improved influenza vaccination among gynecologic cancer patients. Further improvement attempts will focus on adherence to PPO use and vaccine administration for eligible patients.

Temporal Trends in Thyroid-Stimulating Hormone and the Effect of Levothyroxine Treatment on Live Birth Rate in the Hypothyroid Recurrent Pregnancy Loss Population

Jansen, Sophie; Bedaiwy, Mohamed

BACKGROUND: Thyroid autoimmunity is a known cause of hypothyroidism. Overt hypothyroidism has been established as a cause of recurrent pregnancy loss (RPL) that is effectively treated with levothyroxine. It is unclear how thyroperoxidase antibody (TPOAb) positivity impacts thyroid stimulating hormone (TSH) levels over time or if subclinical hypothyroidism can be treated with levothyroxine to improve live birth rate (LBR). This study aimed to examine TSH over time for RPL patients with and without TPOAb positivity and to ascertain if levothyroxine treatment improved LBR in patients with borderline subclinical hypothyroidism (borderline-SCH) (TSH 2.5- 4mIU/L) and clinical/subclinical hypothyroidism (TSH >4mIU/L) relative to euthyroid patients (TSH 0.1-2.5mIU/L).

METHODS: A retrospective chart review of 1444 RPL patients seen in a clinic was conducted. Analysis of TSH in pregnancies after initial evaluation across different TPOAb status was performed using mixed-effects linear regression. Across patients with euthyroid status, borderline-SCH, or clinical/subclinical hypothyroidism, LBR was analyzed using Poisson regression.

RESULTS: Temporal analysis of TSH revealed no significant change across TPOAb or treatment status ($p=0.24$) for up to four subsequent pregnancies. A decreased LBR in untreated borderline-SCH relative to euthyroid patients (OR=0.69) and an increased LBR in borderline-SCH and clinical/subclinical hypothyroid when treated with levothyroxine relative to euthyroid patients (OR=1.68) was shown ($p=0.003$).

CONCLUSIONS: In the RPL population, TPOAb should not be used alone to determine whether hypothyroidism will occur or whether levothyroxine treatment will be needed in euthyroid patients. Levothyroxine treatment should continue to be initiated when a TSH >2.5 mIU/L is identified as it correlated to increased LBR.

Basal Cell Adhesion Molecule: A Novel Human Cytotrophoblast Progenitor Marker

Shannon, Matthew; Castellana, Barbara; Baltayeva, Jennet; Wächter, Jasmin; Treissman, Jenna; Le, Hoa; Yoon, Ji Soo; Lynn, Francis; Beristain, Alexander

BACKGROUND: Establishment of the placenta relies on specialized cells called trophoblasts. Trophoblast sub-types exist to facilitate placenta-related processes in pregnancy. However, little is known about the molecular processes controlling human trophoblast stem cell maintenance and development, prompting our laboratory to establish a single-cell RNA sequencing (scRNA-seq) dataset from first trimester placentas. We hypothesize that by applying transcriptomic analyses to this dataset we can identify molecular programs important in trophoblast stem cell establishment and renewal.

METHODS: cDNA libraries from eleven first trimester placentas were generated or collected from ArrayExpress. Data normalization, clustering, and lineage trajectory analyses were performed. 3D human trophoblast organoids were then established and expanded from trophoblast stem cells for flow cytometry, quantitative PCR (qPCR), immunofluorescence (IF), and differentiation assays.

RESULTS: 8 trophoblast clusters were identified, representing cytotrophoblasts (4 clusters), syncytiotrophoblast progenitors (SCTp; 1 cluster), and extravillous trophoblasts (EVT; 3 clusters). A putative cytotrophoblast progenitor (CTBp) population was identified with increased expression of the cell surface glycoprotein Basal Cell Adhesion Molecule (BCAM). Lineage trajectory analyses and qPCR of human trophoblast stem cells demonstrated that BCAM expression decreased with trophoblast differentiation into mature EVT and SCTp. IF of first trimester placental villi and trophoblast organoid cultures validated BCAM expression is specific to CTBs. Finally, organoid establishment following flow sorting of BCAM⁺ and BCAM⁻ CTB populations demonstrated that BCAM⁺ CTBs possess greater capacity for organoid formation/growth.

CONCLUSIONS: We have identified BCAM as a human cytotrophoblast progenitor marker, providing improved methods for isolating and studying the mechanisms regulating human trophoblast stem cells and early placental development.

Reproductive outcomes following surgical management for isthmoceles: A systematic review

Harjee, Rahana; Khinda, Jaskaran; Bedaiwy, Mohamed

BACKGROUND: Recently, a discontinuity in the anterior lower uterine segment has been recognized, which can present as abnormal uterine bleeding, pelvic pain or secondary infertility. This study aims to evaluate the efficacy of surgical management for caesarean scar defect (CSD) repair in patients presenting with secondary infertility.

METHODS: A systematic search was performed in MEDLINE, EMBASE and Cochrane Library databases from inception to May 2020, limited to studies published in English. After the removal of duplicates, 3380 articles were screened for inclusion independently by two authors who assessed for studies which focused on reproductive aged women with a diagnosed scar defect and secondary infertility who underwent any surgical intervention for defect repair with at least one goal being fertility restoration.

RESULTS: 13 studies, comprised of 1 randomized controlled trial (RCT), 6 prospective case series and 6 retrospective case series describing 234 patients who underwent surgical management for CSD and secondary infertility were included. 188 patients were treated by hysteroscopy, 36 by laparoscopy, 7 by laparotomy, and 3 through a vaginal approach. 153/234 patients were able to become pregnant (65.4%). Pregnancy rates in the RCT were 21/28 (75%) for those treated via hysteroscopy compared to 9/28 (32%) for those untreated. Among studies reporting pregnancy outcomes, 101/116 (87.1%) pregnancies resulted in a live birth. The incidence of adverse events was 2%, including risk of reoperation.

CONCLUSIONS: Although further high-quality evidence is needed, this systematic review suggests that surgical management can improve fertility outcomes in appropriately selected patients presenting with CSD-associated secondary infertility.

The functional effect of ARID1A and PIK3CA mutations on endometrial organoids

Forouh, Kalantari; Dawn, Cochrane; Yemin, Wang; Kieran, Campbell; Germain, Ho; Winnie, Yang; Genny, Trigo-Gonzalez; Lien, Hoang; Jessica, McAlpine; David, Huntsman

BACKGROUND: ARID1A a subunit of SWI/SNF chromatin remodeling complex is particularly mutated in gynecologic cancer. Our lab has discovered inactivating mutations of ARID1A, often together with a PIK3CA activating mutation, in about 50% of clear cell ovarian cancer (CCOC). CCOC is strongly associated with endometriosis, the functional endometrium tissue outside of the uterus cavity.

PIK3CA mutation has been identified as an early event in CCOC and other endometrial pathogenesis as well. While loss of Arid1a alone is not sufficient for tumorigenesis in mice, the addition of a Pik3ca H1047R activating mutation initiates tumour development in the ovary and endometrium.

OBJECTIVE: The goal of this project is to use organoid culture of human endometrium to model early events in CCOC tumor initiation. This project will focus on understanding how mutations and extracellular environment converge to initiate oncogenic transformation.

METHODS: Organoid culture was derived from primary normal human endometrial cells in which ARID1A and PIK3CA mutations achieved by lentiviral transduction. The organoids were maintained over many passages and morphology was assessed at each passage. Single cell RNA and ATAC sequencing was performed to compare gene expression profiles between the non infected and mutant organoids.

RESULTS: Double mutant human organoids demonstrate phenotypic differences compared to the non transduced ones. The mutant organoids are larger than the uninfected organoids and at later passage, the organoids manifest CCOC histopathology, including hobnail cells, and positive PAS staining. Gene expression profiles from two experiment demonstrated downregulation of tumor suppressors RBP1 which correlates ATAC-seq data and western blot data from CCOC and endometrial cancer cell lines.

Risk factors for urinary retention after urogynecologic surgery: a retrospective cohort study and prediction model

Zhang, Bei Yuan (Ethan); Wong, Jeffrey Man Hay; Koenig, Nicole; Lee, Terry; Geoffrion, Roxana

BACKGROUND: Postoperative urinary retention (POUR) is a common complication of urogynecological surgery. Our study aimed to identify demographic and peri-operative risk factors to construct a prediction model for POUR in urogynecology.

METHODS: Our retrospective cohort study reviewed all patients undergoing pelvic reconstructive surgeries at our tertiary care center (Jan 1, 2013 - May 1, 2019). Demographic, pre-, intra- and post-operative variables were collected from medical records. The primary outcome was POUR defined as 1) early POUR (E-POUR), failing initial trial of void (TOV) or; 2) late POUR (L-POUR), requiring an indwelling catheter or intermittent catheterization on discharge. Risk factors were identified through univariate and multivariate logistic regression analyses. A clinical prediction model was constructed with the most significant and clinically relevant risk factors.

RESULTS: In 501 women, 182 (36.3%) had E-POUR and 61 of these women (12.2% of the entire cohort) had L-POUR. Multivariate logistic regression revealed preoperative postvoid residual (PVR) over 200 ml (OR 3.17, $p=0.026$), voiding dysfunction symptoms extracted from validated questionnaires (OR 3.00, $p=0.030$), and number of concomitant procedures (OR 1.30 per procedure, $p=0.021$) as significant predictors of E-POUR; preoperative PVR > 200 mL (OR 4.07, $p=0.011$) and anti-incontinence procedure with (OR 3.34, $p=0.023$) and without (OR 2.64, $p=0.019$) concomitant prolapse repair as significant predictors of L-POUR. A prediction model (AUC 0.70) was developed for E-POUR.

CONCLUSIONS: Elevated preoperative PVR is the most significant risk factor for POUR. Alongside other risk factors, our prediction model for POUR can be used for patient counselling and surgical planning in urogynecologic surgery.

Chronic Intervillositis of Unknown Etiology (CIUE): Prevalence, patterns and reproductive outcomes at a tertiary referral institution

Simula, Natasha; Terry, Jefferson; Kent, Nancy; Robertson, Julie; Purkiss, Susan; Bloomenthal, Dena; Williams, Christina; Bedaiwy, Mohamed

BACKGROUND: The objective of this study was to evaluate the incidence of Chronic Intervillositis of Unknown Etiology (CIUE), a rare placental lesion associated with adverse pregnancy outcomes, at our institution and to report on the pregnancy outcomes based on severity of lesions.

METHODS: Retrospective cohort study including 29 889 perinatal specimens from 27 968 patients. The pathology database at our institution was queried for the keywords "intervillositis" and "CIUE" between February 2006 and April 2019. Histology was re-examined using a standardized diagnostic criterion to confirm diagnosis. Cases in which diagnosis was confirmed were categorized as low grade (5–49% intervillous space involvement) or high grade ($\geq 50\%$ involvement).

Interventions and pregnancy outcomes were recorded.

RESULTS: The overall prevalence of CIUE is 0.17% (47 of 27 968 patients), with significantly higher prevalence in 1st trimester products of conception compared with 2nd and 3rd trimester specimens (0.38% vs 0.09%; $p < 0.0001$). A total of 97 specimens were initially diagnosed with chronic intervillositis. 56 out of 97 (57.7%) specimens met our diagnostic criteria for CIUE on review. Pregnancies with confirmed CIUE had significantly higher rates of pregnancy loss compared with pregnancies with chronic intervillositis not meeting our study criteria for CIUE (94% vs 71%; $p = 0.003$). Pregnancy loss between low grade (42.9%; 24 out of 56 cases of CIUE) and high grade (57.1%; 32 out of 56 cases) CIUE were not significantly different.

CONCLUSIONS: CIUE prevalence is low at 0.17%, but it is associated with pregnancy loss, particularly in the first trimester. High grade disease may be associated with worse pregnancy outcomes than low grade disease.

Postpartum thoughts of infant-related harm and obsessive-compulsive disorder: Prevalence and relation to maternal physical aggression towards the infant

Cameron, Rose; Keeney, Cora; Fairbrother, Nichole

BACKGROUND: Unwanted, intrusive thoughts (UITs) of intentional infant-related harm are ubiquitous among new mothers, raise concerns about infant safety and may increase the risk of obsessive-compulsive disorder (OCD). The purpose of this research was to: (a) assess the prevalence and incidence of maternal, perinatal OCD; (b) assess the relation of new mothers' UITs of intentional, infant-related harm and OCD with maternal aggression towards the infant; and (c) document the prevalence of maternal aggression towards the infant.

METHODS: An unselected sample of 763 English-speaking pregnant women and new mothers participated in a longitudinal, province-wide study between their third trimester in pregnancy and six months postpartum. They completed three online questionnaires and interviews (data collected between February 9, 2014 and February 14, 2017) to assess UITs of infant-related harm, OCD, and maternal aggression towards the infant.

RESULTS: Prevalence estimates for the prenatal and postpartum periods were 7.8% and 16.9% respectively. Point prevalence increased through pregnancy to the early postpartum, and declined thereafter. The cumulative incidence of new OCD diagnoses was estimated at 9% by 6-months postpartum. Participants who reported UITs of intentional, infant-related harm were no more likely to report aggression toward their newborn compared with those who did not report this ideation (2.6% versus 3.1%). The same was true for women with and without OCD.

CONCLUSIONS: Study findings indicate that perinatal OCD is more common than previously believed, and UITs of intentional, infant-related harm and OCD are not associated with an increased risk of infant harm. Findings provide critical and reassuring information regarding perinatal OCD, new mothers' UITs of intentional harm, and infant safety.

Modelling low, moderate, and high grades of inflammation in mice to examine the impact on pregnancy outcome and uterine immune cell biology

St-Germain, Lauren; Castellana, Barbara; Baltayeva, Jennet; Beristain, Alexander

BACKGROUND: Inflammation in pregnancy impacts maternal-fetal tolerance and placentation. To gain insight into uterine processes affected, we generated mouse models of inflammation (induced by bacterial endotoxin lipopolysaccharide; LPS) in early pregnancy.

METHODS: Following pregnancy establishment, different doses (25, 50, 200 µg/Kg) of LPS were administered intraperitoneally on embryonic day (E)7.5 to initiate low, moderate, and high grades of inflammation. Level of inflammation was characterized by white blood cell count ratios and levels of serum IL-1 β , TNF- α , and IL-6 before and after injection. We assessed effects of LPS on fetal viability and uterine artery remodeling (E9.5); uterine immune cell phenotypes (E7.5, E9.5); pregnancy outcomes (fetal/placental weight, litter size, viability) and placental morphology (E17.5). For all time-points and conditions, at least six mice (n=6) were examined.

RESULTS: Compared to saline controls, increasing grades of LPS led to stepwise increases in serum pro-inflammatory cytokines and altered white blood cell count ratios. Implantation site resorption frequency rose from ~3% (saline) to 22%, 59%, and 82% following low-, moderate-, and high-dose LPS. Within viable implantation sites, there was no statistical difference in fetal/placental measurements at E17.5, though fetal weight, fetal length, and placental diameter trended on being less/smaller in LPS-exposed pregnancies. Within viable implantation sites, low- and moderate-dose LPS led to enhanced uterine artery remodelling, alterations in uterine natural killer and myeloid subtype frequencies, and increased uterine immune cell expression of granzyme, TNF- α , and IFN- γ .

CONCLUSIONS: This work highlights uterine immune cell changes resulting from LPS-induced inflammation and provides insight into how aberrant inflammation contributes to impaired pregnancy outcomes.

Cannabis use among women with myofascial pelvic pain: A survey

Yang, Emily; Girard, Anna; Gong, Merry; Koenig, Nicole; Barr, Alasdair; Brotto, Lori; Lee, Terry; Yong, Paul; Geoffrion, Roxana

BACKGROUND: Recreational cannabis use increased among women with pelvic pain after legalization in Canada. We investigated patterns of cannabis use and willingness to use in women with pelvic myofascial pain.

METHODS: We conducted a descriptive study at two tertiary care gynecologic clinics. Women with a diagnosis of pelvic floor muscle spasm on pelvic examination completed a survey including demographics, main pain diagnosis, pain characteristics, recreational and pharmacologic interventions, the Screener and Opioid Assessment for Patients with Pain (SOAPP) questionnaire, and details of cannabis use.

RESULTS: Of 545 survey invitations we received 135 completed surveys (response rate 25%). Mean age was 38.2 (range 20-73), 60% were college graduates and unemployment rate was 10%. Endometriosis was the main diagnosis (71.9%). More than half (52.6%) used anti-inflammatories and 17% used opioids for pelvic pain. There were 77 cannabis users (57%) and 58 non-users (43%). Among users, most (79.2%) used it for pelvic pain specifically and because conventional treatments did not work. They used it mostly daily and preferred to smoke it. Most women rated cannabis positively for effects on pelvic pain and quality of life. Non-users needed more information and were fearful of unwanted side effects. SOAPP scores were low in both groups (mean 3.6 in users vs 2.6 in non-users, $p=0.004$). Approximately 3 of 4 users and non-users were willing to try a vaginal cannabis insert.

CONCLUSIONS: Women using cannabis for pelvic pain with a myofascial component rate its efficacy highly. Both users and non-users would try cannabis as a vaginal insert for pain relief.

Documenting Perineal and Obstetrical Anal Sphincter Injury Care at Childbirth: A Cross-sectional Study

Mann, Gurkiran; Gong, Merry; Koenig, Nicole; Geoffrion, Roxana

BACKGROUND: Obstetrical anal sphincter injuries (OASIS) after vaginal delivery cause significant maternal morbidity. In 2015, national OASIS-focused clinical practice guidelines were released after considerable variations in management were revealed across Canada. This study evaluates whether maternity care providers document guideline-based recommendations for the prevention and care of OASIS for their labour and delivery patients.

METHODS: Through a cross-sectional study, we aimed for a convenience sample of 60 primiparous women over the age of 19 with equal representation of patients who sustained severe (third- and fourth-degree) and minimal (intact or first-degree) tears during vaginal birth. We reviewed medical charts for patient demographics, delivery details, and guideline-endorsed OASIS preventative and management methods.

Descriptive statistics were used when appropriate.

RESULTS: We enrolled 73 women in total. Thirty-four participants sustained an OASIS and 39 had minimal tears. Fetal head control and perineal support during delivery for OASIS prevention were documented in 1 out of 73 patients, while perineal massage and warm compress were not documented. Post-delivery rectal exam was documented for 30% (22/73) of all patients and 62% (21/34) of patients with OASIS. Post-void residual was not documented. Among patients with OASIS, 65% (22/34) received intravenous antibiotics, 88% (30/34) received laxatives, and 100% received nonsteroidal anti-inflammatory medications. Sixty-eight percent (23/34) of patients recalled being informed about their OASIS and 47% (16/34) recalled being referred to pelvic physiotherapy.

CONCLUSIONS: Perineal care practices, as outlined by the national OASIS guideline, were incompletely documented in our study. This may represent partial guideline adherence or suboptimal medical record-keeping.

The expression and role of bone morphogenetic protein 2 at maternal-fetal interface

Yi, Yuyin; Zhu, Hua; Klausen, Christian; Inkster, Amy; Leung, Peter C. K

BACKGROUND: Many pregnancy disorders, including early-onset preeclampsia (EOPET), are associated with abnormal placental trophoblast invasion during early placenta development. Bone morphogenetic protein 2 (BMP2) belongs to the transforming growth factor- β (TGF- β) superfamily and has been shown to promote human trophoblast invasion in vitro. However, the expression of BMP2 in the placenta and molecular mechanisms of how BMP2 regulates trophoblast function remain unclear.

METHODS: Multiple publicly available microarray and RNA-seq datasets were analyzed for the expression of BMP2 in EOPET and gestation-age-matched non-preeclamptic control placentas. The placental expression of BMP2 was evaluated using RNAscope in situ hybridization. The effect of the BMP2 on human first-trimester primary trophoblasts was explored by RNA-seq analysis.

RESULTS: BMP2 levels were significantly reduced in placenta samples from EOPET pregnancies compared with control pregnancies. RNAscope data showed that BMP2 was localized in all subtypes of trophoblasts as well as in decidua. RNA-seq analysis on control and BMP2-treated primary human trophoblast cells (n=5) identified 431 BMP2 target genes with a false discovery rate < 0.05. Gene Ontology analysis demonstrated that BMP2 enhances trophoblast invasion by regulating a network of cellular adhesion and extracellular matrix genes (e.g., AMIGO2). Furthermore, we discovered the transcription factor SOX4 as a direct BMP2 target in trophoblasts. Importantly, SOX4 can transcriptionally regulate the SOX4-dependent BMP2 targets by binding to the enhancers, thereby promoting BMP2-induced trophoblast invasion.

CONCLUSIONS: Collectively, this study elucidates the novel mechanism of BMP2 action in the first-trimester maternal-fetal interface and highlights BMP2 as a potential etiologic factor in EOPET.

Clinical predictors of poor pain-related outcome after endometriosis surgery

Tucker, Dwayne; Yong, Paul

BACKGROUND: Endometriosis causes chronic pain in ~1 million reproductive-aged women in Canada. Though surgical treatment is effective, pain recurs in some women, and there is currently no way to predict surgical success. We hypothesize that a model including proxies for central sensitization can predict post-surgical outcomes. This study aimed to generate a clinical model to predict a poor pain-related surgical outcome in endometriosis.

METHODS: The study utilized prospective registry data from a tertiary centre for endometriosis/pelvic pain. Included were new /referrals (December 2013- June 2018) with suspected/diagnosed endometriosis, >50 years old, had surgery at our centre and completed the Endometriosis Health Profile (EHP-30) questionnaires at baseline and follow-up (1-2 years). Poor outcome was defined as a follow-up score $\geq 60\%$ on the EHP-30 pain subscale. Multivariable logistic regression with eight candidate predictors was performed using the stepwise backward elimination approach (LR-test). Model performance was determined using discrimination ($AUC \geq 0.7$), calibration (Hosmer & Lemeshow test, p -value > 0.05), sensitivity and specificity.

RESULTS: In a cohort of 481 (events=78), poor outcome was predicted by fertility-sparing surgery (compared to hysterectomy), and baseline painful bladder syndrome, pelvic floor myalgia, and the pain catastrophizing scale. The model had good performance ($AUC=0.792$; $CI:0.735, 0.849$; Hosmer & Lemeshow test: $p=0.084$; sensitivity= 73%; specificity= 70%) at an optimum cutoff of 0.15. The presence of myofascial pain and pain catastrophizing in the model supports our hypothesis that central sensitization is a predictor of poorer outcomes.

CONCLUSIONS: The initial model showed that pre-operative clinical factors could provide information to aid surgical decision-making in endometriosis.

Disease-free survival in patients undergoing fertility sparing surgery for early stage cervical cancer: a single centre case review

Heyns, Marguerite; Lee, Murette; May, Taymaa; Nica, Andra

BACKGROUND: Radical trachelectomy (RT) is an acceptable alternative to radical hysterectomy (RH) in select women with early stage cervical cancer who wish preserve fertility. RT has been shown in several studies to provide comparable recurrence rates to RH [1,2]. Currently in Canada, vaginal, laparoscopic, and robotic RTs are offered at several centres, with each centre offering a single approach. In 2018 a large multicenter randomized control trial demonstrated significantly lower rates of disease free survival in women who underwent abdominal radical hysterectomies (ARH) compared to those who underwent robotic or laparoscopic radical hysterectomy, 96.5% versus 86.0% [3]. To date no similar comparison in outcomes of vaginal versus laparoscopic or robotic RTs have occurred. Due to the low numbers of women who undergo RT versus RH, a prospective randomized control trial would not be feasible. The results presented are part of an ongoing multicentre retrospective review to evaluate oncologic outcomes after vaginal RT, versus robotic or laparoscopic RT.

METHODS: A retrospective cohort study of all women treated with vaginal RT for early stage cervical cancer between January 2006 and December 2017, at a single cancer centre, evaluating for a primary outcome of disease-free survival at 4 years. ORMIS gynecological procedure codes were used to identify patients, outcome data was gathered through electronic chart review.

RESULTS: A cohort of 30 patients were identified and reviewed. The rate of disease-free survival at 4 years was 96.7%.

CONCLUSIONS: Vaginal trachelectomy has a similar rate of disease-free survival to open radical hysterectomy.

Immune Microenvironment in Endometrioid Ovarian Carcinomas and the influence of Molecular Subtyping

Heinze, Karolin; Krämer, Pauline; Cairns, Evan; Feil, Lukas; Thornton, Shelby; Gibson-Wright, Bronwyn; Milne, Katy; Leung, Samuel; Chui, Derek; Ramus, Susan; Pearce, C. Leigh; Staebler, Annette; Brucker, Sara; Köbel, Martin; Kommoss, Stefan; Talhouk, Aline; Nelson, Brad; Anglesio, Michael

BACKGROUND: Endometrioid ovarian carcinoma (ENOC) arise through malignant transformation of endometriosis epithelium driven by molecular alterations influencing endometriotic and subsequent tumor microenvironments. The presence of tumor infiltrating lymphocytes (TIL), especially CD8+ cells, can be prognostic in cancer. While the immune tumor-microenvironment (iTME) of high-grade serous ovarian carcinomas (HGSOC) has been studied in great detail, little is known about the iTME of ENOC. We recently established four prognostic molecular subtypes of ENOC, so-named POLEmut (favourable outcome), MMRd (intermediate outcome), p53abn (poor outcome) and a final intermediate outcome group with no specific molecular profile (NSMP). ENOC subtypes are distinct from other ovarian carcinomas but are highly similar to endometrial carcinomas (EC) classified with the same parameters.

METHODS: We evaluated the iTME in ENOC molecular subtype, comparing them to endometrial carcinomas. T-cell lineages (CD3/CD8 and CD25/FoxP3/CD8), B-cell lineages (CD79a/CD20), and macrophages (CD68/PDL1) were quantified by multiplex immunofluorescence.

RESULTS: Our subset of 210 ENOC cases was representative of ENOC populations with expected outcomes in each subtype. Multiplex iTME evaluation revealed high levels of immune infiltration in MMRd and POLEmut subset, similar to trends observed previously for EC. Like EC and unlike HGSOC, stratification into TIL low and TIL high ENOC was not prognostic ($p=0.377$).

CONCLUSIONS: Overall, these findings accentuate the similarity between ENOC and EC and provide further support for histotype-stratified research and clinical prioritization of ovarian cancers. While immune infiltration was elevated in ENOC subtypes with predominantly more favorable outcomes, immune infiltration did not add prognostic value beyond that associated with molecular subtype.

Keynote Speaker



Dr Modupe Tunde-Byass is a Fellow of the Royal College of Obstetricians and Gynecologists of Canada and the UK. She obtained her medical degree from the University of Ibadan in 1987. She completed her OBGYN training (with special interest in Fetal Medicine from Harris Birthright center, London) in the UK and Canada. She has been an active staff at NYGH since 2004. Dr. Tunde-Byass has held major administrative positions e.g Residency site coordinator and Interim Chief of OBGYN at NYGH. She is involved in key quality initiatives at the local and provincial levels. She was the Co-chair for the Quality Standard on Increasing access to Vaginal Birth after Cesarean section and an expert panel member for early pregnancy complications and loss (Joint projects of PCMCH and HQO). She has received numerous teachings and innovation awards. She is involved in medical education. Her research interest is in early pregnancy complications and decreasing CS rate by increasing access to trial of labour after Caesarean section. She has presented some of her research at international conferences and has publications in peer review journals.

Dr. Tunde-Byass is the President of the Black Physicians of Canada. She is involved with Equity, Diversity and Inclusivity with particular focus on Anti-Black Racism.