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1103

乳癌診斷後的生育保存
Fertility Preservation After Breast Cancer Diagnosis

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論文發表方式：
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論文歸類：
生殖內分泌

Background
Breast cancer treatment, especially most common used cyclophosphamide regimen, was found with significant impact on ovarian reserve. There has been a trend of early onset breast cancer within the world lately; furthermore, according to Taiwan CDC statistic, the onset age of breast cancer patient is much younger than Western countries in their productive years. With the improvement of breast cancer treatment, long term life quality and oncofertility had come into light within these survivors.

Case presentation:
We presented 3 cases with different breast cancer hormone receptors, thus various anticancer treatment. Their fertility preservation methods were adapted accordingly. All the cases chose oocyte/embryo cryopreservation as the main strategy. The first case received GnRH antagonist protocol for ovarian stimulation, laparoscopic oocyte pick-up and had 12 oocytes putting into cryopreservation. The second case opted for progestin-prime ovarian stimulation protocol, ultrasound-guided ovum pick-up (OPU) and had 24 oocytes in stored. The third case received GnRH antagonist protocol, after OPU and had 6 embryos stored. She had 2 embryos transferred and gave birth to a healthy twin.

Conclusion:
We review the current early-stage breast cancer anticancer treatment influence on fertility as cyclophosphamide drastically decreasing ovarian reserve and endocrine therapy with tamoxifen taking up fertility period of the women. Main stream fertility preservation options are oocyte/ embryo cryopreservation, and we ought to present it to all patients. Ovarian tissue cryopreservation is introduced and practiced in Europe and is no longer considered experimental. Complimentary gonadotropin-releasing hormone agonist could be given to woman under the age of 45. Last of all, pregnancy after breast cancer treatment was found no impact on disease survival rate.

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1265

經陰道超音波引導取卵後大量腹腔出血的非手術治療 — 病例報告

Non-surgical management of massive intra-abdominal bleeding following transvaginal ultrasound-guided oocyte retrieval — A case report

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生殖內分泌

Transvaginal ultrasonography guided oocyte retrieval (TVOR) is a common procedure in assisted reproductive technology. While generally safe, complications such as intra-abdominal bleeding can rarely occur. We present a case report detailing the non-surgical management strategies employed in a 32-year-old female patient who experienced intra-abdominal bleeding post TVOR. Following the procedure, the patient developed acute abdominal pain and signs of hypovolemic shock. Immediate assessment and intervention were crucial. A multidisciplinary team promptly conducted a thorough evaluation, including imaging studies confirming the presence of intra-abdominal bleeding. The patient underwent angiography which revealed an extravasation of iliac artery branch. Effective management involved hemostasis through transcatheter arterial embolization and hemodynamic stabilization with intravenous fluids and blood products. Post-procedure care included close monitoring, pain management, and prevention of complications. Preventive measures discussed include careful patient selection, thorough preoperative evaluation, and utilizing proper ultrasound technique during oocyte retrieval to minimize the risk of vascular injury. This report emphasizes the importance of prompt recognition and swift intervention in managing intra-abdominal bleeding post TVOR. Implementing preventive strategies and maintaining vigilance during the procedure can minimize the risk of such rare but potentially serious complications, ensuring safer outcomes for patients undergoing assisted reproductive techniques

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卵巢反應不良者新鮮與冷凍胚胎移植的統合分析：評估臨床結果和 IVF 成功率
Clinical Outcomes in Poor Ovarian Responders: A Meta-Analysis of Fresh vs. Frozen Embryo Transfer in IVF

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論文發表方式：
口頭報告

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生殖內分泌

Methods:
We conducted a meticulous systematic review and meta-analysis of retrospective studies. Electronic databases including PubMed, Embase, and the Cochrane Library were systematically queried until 2023, employing keywords such as "poor ovarian response," "fresh embryo transfer," "elective frozen embryo transfer," and "IVF." Eligible studies, directly comparing frozen embryo transfer (FET) to fresh embryo transfer (ET), were identified and included in our analysis. The primary endpoint of interest was the live birth rate (LBR) per cycle, serving as a key indicator of treatment success. Secondary outcomes encompassed the implantation rate, clinical pregnancy rate, and miscarriage rate.

Results:
We incorporated data from eight studies, encompassing 754 participants in the frozen embryo transfer (FET) group and 1527 in the fresh embryo transfer (ET) group. Our analysis revealed no statistically significant difference in the live birth rates between the two groups (odds ratio [OR] = 1.2, [0.93, 1.55]). Remarkably, both the FET and fresh ET groups demonstrated comparable outcomes.

Conslusion:
Even though the success rates were similar in both group, using fresh embryos might be a better choice for poor ovarian responders. It's less expensive because there's no cost for freezing, and it might help people start their pregnancy journey sooner. This means people have a choice, and it's important to think about what's best for them and what they prefer when deciding how to use embryos to help them have a baby.

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抗磷脂症候群的懷孕婦女使用奎寧合併阿斯匹靈及肝素是否會促進懷孕結果
Aspirin plus heparin and /or adding hydroxychloroquine for improving pregnancy outcomes in women with persistent antiphospholipid antibodies

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論文歸類：
生殖內分泌

Background
Antiphospholipid syndrome (APS) is an autoimmune disease characterized by obstetrical complications , and there is no consensus on the treatment of this disease. Long-term anticoagulation is recommended in most cases in patients with thrombotic APS. The current standard prevention of obstetric complications in patients with antiphospholipid antibody syndrome (APS) is the use of combination low-dose aspirin and low molecular weight heparin. However, 20-30% of women still experience refractory obstetrical APS. Recent retrospective studies showed a beneficial effect of hydroxychloroquine (HCQ) in APS due to its anti- inflammatory, immunomodulatory and antithrombotic properties.
Methods
The data were retrieved from the Cochrane Library, PubMed, EMBASE, and Web of Science databases. We collected data on randomized controlled trials/ retrospective studies of HCQ combined aspirin with LMWH in the treatment of pregnant women with APS. The risk ratio (RR) and its 95% confidence interval (CI) were determined using Review Manager.
Results
This study aimed to evaluate whether hydroxychloroquine combined asprin with low-molecular-weight heparin (LMWH) can improve the live birth rate in antiphospholipid syndrome. In this study, we reviewed 141 articles, one randomized controlled trial and two retrospective studies were included, comprising a total of 535 patients. The live birth rate in pregnant women with APS was higher on administration of hydroxychloroquine combined asprin with LMWH than with aspirin plus LMWH (RR=1.36, 95% CI=1.05–1.76, P < .001).
Conclusions
The results showed that the combination of HCQ with aspirin and LMWH could significantly improve the live birth rate of the fetus in women with APS.

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利用縮時攝影培養技術分析具不同粒線體 DNA 含量囊胚之胚胎特徵

The embryonic characteristics of biopsied blastocysts stratified based on their mitochondrial DNA copy numbers are revealed by using time-lapse monitoring

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Background:
The levels of mitochondrial DNA (mtDNA) in the trophectodermal cells of biopsied blastocysts have been suggested to be associated with their developmental potential in patients undergoing in vitro fertilization (IVF). However, the current studies present different opinions regarding the use of mtDNA levels as a reliable biomarker for predicting IVF outcomes.

Methods:
The aim of this retrospective study was to analyze mtDNA levels in the trophectodermal cells of 515 biopsied blastocysts derived from IVF patients. This analysis was done using time-lapse (TL) monitoring and next-generation sequencing (NGS)-based preimplantation genetic tests for aneuploidy (PGT-A) from September 2021 to September 2022. The embryonic morphokinetics and morphology were evaluated using all recorded images at 118 hours post-insemination (hpi). The blastocysts with a morphology greater than 4CC on day 5 or day 6 were selected for TE biopsy and PGT-A. The statistical analysis was performed using generalized estimating equations (GEE), Pearson's chi-squared test, or Kruskal-Wallis test. Statistical significance was indicated at $p < 0.05$ in all analyses.

Results:
To compare the differences in embryonic characteristics between blastocysts with low or high mitoscores, the blastocysts were divided into quartiles based on their mitoscores. Regarding morphokinetic characteristics, there were no significant differences in most developmental kinetics and observed cleavage dysmorphisms. However, blastocysts in mitoscore group 1 had a longer t3 (median 14.4 hours post insemination [hpi]) compared to blastocysts in mitoscore group 2 (median 13.8 hpi) and an extended second cell cycle (t3–t2) [CC2] (median 11.7 hours [h]) compared to blastocysts in mitoscore group 2 (median 11.3 h) and 4 (median 11.4 h) ($P < 0.05$). Moreover, the results demonstrated that blastocysts in mitoscore group 4 had a lower euploid rate (22.6%) and a higher aneuploid rate (59.1%) compared to other mitoscore groups (39.6%–41.9% and 32.1%–43.2%) ($p < 0.05$). The rate of whole-chromosomal alterations in mitoscore group 4 (63.4%) was higher than in mitoscore groups 1 (47.3%) and 2 (40.1%) ($p < 0.05$). The multivariate logistic regression model was used to analyze the associations between mitoscore and the euploidy of elective blastocysts. The backward elimination procedure identified female age, TE quality, and ICM quality as confounding variables ($p < 0.2$). After adjusting for these confounders, the mitoscore remained negatively associated with the probability of euploidy (adjusted odds ratio = 0.599, 95% confidence interval: 0.422–0.850; $p = 0.004$).

Conclusion:
This study demonstrates that the morphological and morphokinetic characteristics of biopsied blastocysts with different mitoscores are similar. However, there seems to be a negative association between the mitoscore and the probability of being euploid.

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雙酚 A 誘發的子宮內膜異位基質細胞上皮-間質轉化有助於子宮內膜異位症的進展

The potential role of bisphenol A-induced endometriotic stromal cell epithelial-mesenchymal transition in the progression of endometriosis

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論文發表方式：
口頭報告

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生殖內分泌

Introduction
Endometriosis, an estrogen-dependent benign gynecological disease associated with pain and infertility, is common in reproductive-aged women and seriously affects their quality of life. Although various pathogenic theories have been proposed, the origin and pathogenesis of endometriosis remains unclear. Epithelial-mesenchymal transition (EMT) is a process in which epithelial cells lose polarity and cell-to-cell contacts, acquiring the migratory and invasive abilities of mesenchymal cells. These changes are thought to be prerequisites for the initial formation of endometriotic lesions. Numerous studies have shown that endocrine disrupting chemicals (EDCs) could mimic the effects of natural estrogen in the body and have been implicated as one of the factors in the increasing incidence of several diseases, including endometriosis. Bisphenol A (BPA), an estrogen-like EDC, is one of the most widely produced chemicals in the world. Whether BPA could induce EMT in endometriosis remains unclear; as such, this study mainly serves to explore the effects of BPA on the EMT of endometriotic stromal cells.

Materials and methods
Endometriotic stromal cells isolated from human ovarian endometrioma (hOVEN-SCs) were used in this study. Gene expression was analyzed using RT-PCR. Protein expression was performed using western blot analysis. Cell migration and invasion were measured by transwell chamber assay.

Results
In our previous study, using Illumina whole genome expression technology, we found that BPA could increase 36 gene expression changes more than tenfold in hOVEN-SCs, including transcription factor Snail. It is a strong repressor of E-cadherin transcription and a well-known inducer of EMT. Our present study revealed that BPA-induced EMT of hOVEN-SCs was characterized by acquiring mesenchymal spindle-like morphology, in addition to the upregulation of vimentin and downregulation of E-cadherin. Silencing of Snail by small interfering RNAs attenuated BPA-induced downregulation of E-cadherin and upregulation of vimentin in hOVEN-SCs, suggesting that Snail plays a crucial role in BPA-induced EMT. Furthermore, our results found that hOVEN-SCs express estrogen receptor α (ERα) and a G protein-coupled estrogen receptor (GPER); BPA treatment could increase the expression of ERα and GPER. However, only ERα antagonist ICI 182,780—but not GPER antagonist G15—was able to abolish BPA-induced Snail upregulation. These results indicated that BPA-induced EMT in hOVEN-SCs operate through the ERα/Snail pathway.

Conclusion
In summary, we hope to further understand the mechanism of EDCs on the progression of endometriosis through this research model.

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褪黑激素調節 IL-1β 在顆粒細胞中誘發的細胞發炎激素表現和細胞凋亡
Melatonin modulates IL-1β-induced inflammatory cytokine expression and apoptosis in human granulosa cells

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生殖內分泌

Introduction
Melatonin, mainly released from the pineal gland and produced in the reproductive organs and cells, plays important roles in the retardation of ageing processes and antioxidant/anti-inflammatory functions. Melatonin serves as a key mediator in the reproductive system by regulating steroidogenesis, folliculogenesis and oocyte maturation, thereby affecting reproductive disorders and pregnancy outcomes. Granulosa cells (GCs) surround the oocyte, which play an important role in regulating oocyte maturation. Interleukin 1β (IL-1β) is an immediate early pro-inflammatory cytokine that regulates the production of several other inflammatory mediators, such as cyclooxygenase 2 (COX)-2 and IL-8. Many studies have found that dysregulation of IL-1β signaling may contribute to female reproductive disorders. This study used human GCs as a model to evaluate the protective effect of melatonin on IL-1β-induced toxicity in GCs.

Materials and methods
The GCs were collected from patients undergoing IVF procedures after controlled ovarian stimulation. Reverse transcription-polymerase chain reaction (RT-PCR) and western blot analysis were used to detect the specific mRNA and protein levels, respectively. Results shown were obtained from at least three separate experiments.

Results
In our previous study, we demonstrated that melatonin significantly reduced IL-1β and prostaglandin E2 production in bisphenol A-induced GCs. In this study, our results showed that IL-1β adversely affected the viability of GCs, increased the expression of apoptosis rate genes (caspase-3), and downregulated the expression of follicle-stimulating hormone (FSH), whereas the administration of melatonin ameliorated these toxic effects. We further revealed that IL-1β exposure upregulates the expression of inflammatory cytokines in GCs, including COX-2 and IL-8. Next, we analyzed the effect of melatonin on IL-1β-induced inflammatory cytokine expression in GCs. The results showed that the melatonin significantly reduced IL-8 and COX-2 expression in IL-1β-induced GCs in a dose-dependent manner. Taken together, our results found that melatonin protects GCs from the adverse effects of IL-1β by ameliorating hormonal dysfunction and inflammation.

Conclusion

This study reveals the mechanism of action of IL-1β and melatonin in GCs and provides important insights into the role of melatonin in improving the quality of GCs.

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子宮內膜微小核糖核酸調控成功著床機制之探討
Study on the mechanism of endometrial microRNAs regulating successful implantation

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生殖內分泌

Objective:
Embryo implantation failure is a critical issue in infertility treatment. In addition to high-quality embryos and an optimal endometrium, effective communication between the two plays an important role in successful implantation. The signaling pathways involved in implantation include various genes and genetic modifiers, including microRNA. Through different expression levels, microRNA regulates the expression of downstream genes and thus affects whether the embryo implantation is successful or not. The purpose of this study was to understand which miRNAs may influence embryo implantation and to evaluate possible mechanisms using systems biology analysis.
Material and methods:
A prospective study was composed of 83 women who had undergone in vitro fertilization (IVF) in combination with preimplantation genetic testing for aneuploidies (PGT-A) in Lee Women's Hospital from November 2018 to October 2021 (IRB：CS18191). Total RNA was extracted from the endometrial tissue of all participants, and microRNA expression profiles were determined by microRNA array. The study cohort was categorized into two groups: non-pregnancies (n=19) and successful pregnancies (n=64). Statistical analyses were employed to identify significant differences in microRNA expression between the two groups. KEGG pathway and Gene Ontology (GO) term enrichment analyses were performed to elucidate the potential functional roles of microRNAs.
Results:
In comparison to the non-pregnant group, the expression levels of hsa-miR-1972, hsa-let-7f-5p, hsa-miR-486-5p, hsa-miR-663a, and hsa-miR-30a-5p in the endometrial tissue of the pregnant group showed significant changes. These microRNAs have the potential to influence pregnancy outcomes by modulating multiple processes, including the Hippo signaling pathway, FoxO signaling pathway, thyroid hormone signaling pathway, p53 signaling pathway, and adhesive junction pathway.
Conclusions:
The findings from this study provide valuable insights into the intricate mechanisms of embryo implantation, emphasizing the potential significance of microRNAs in this critical process. In the future, personalized treatments targeting microRNAs can be developed to improve pregnancy rates in infertile women.