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子宫内腔容受性超声评估指标与冻融囊胚移植临床妊娠的相关性分析

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【摘要】 目的 探索冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期子宫内腔容受性超声评估指标是否与囊胚移植临床妊娠结局相关。方法 采用回顾性病例对照研究, 收集 2021 年 11 月至 2024 年 10 月于四川省妇幼保健院生殖医学中心进行 FET 治疗的患者临床资料, 在肌内注射黄体酮的第 6 天解冻移植 1~2 枚囊胚, 移植前行子宫内腔容受性超声评估。按照是否临床妊娠分为两组: 临床妊娠组 204 例, 未妊娠组 222 例。子宫内腔容受性超声评估指标包括解剖学参数, 如子宫内腔厚度、体积、内腔蠕动波方向; 血流参数, 如子宫内腔血管化指数 (vascularization index, VI)、血流指数 (flow index, FI)、血管化血流指数 (vascularization flow index, VFI), 子宫内腔及内腔下血管血流分级, 子宫动脉搏动指数 (pulsatility index, PI)、阻力指数 (resistance index, RI)、收缩期峰值流速/舒张期峰值流速 (peak systolic velocity/end-diastolic velocity, S/D)。比较两组患者超声子宫内腔容受性指标检测值, 并校正影响妊娠结局的混杂因素后进行多因素 logistic 回归分析。结果 临床妊娠组子宫内腔厚度 [0.88 (0.70, 1.00) cm] 明显高于未妊娠组 [0.80 (0.70, 1.00) cm, $P=0.032$], 内腔 FI [23.57 (21.30, 26.79)] 明显低于未妊娠组 [24.64 (21.78, 28.11)], $P=0.048$ 。临床妊娠组与未妊娠组的子宫内腔体积、波动方向构成比、VI、VFI, 子宫内腔及内腔下血管血流分级构成比, 双侧子宫动脉 PI、RI、S/D 差异均无统计学意义 (均 $P>0.05$)。多因素 logistic 回归分析显示, 子宫内腔厚度与临床妊娠呈正相关 ($OR=3.95$, 95% CI : 1.10~14.23, $P=0.036$), FI 与临床妊娠呈负相关 ($OR=0.96$, 95% CI : 0.92~0.99, $P=0.012$)。结论 FET 日子宫内腔厚度、FI 是临床妊娠的可能影响因素。

【关键词】 胚胎植入; 超声检查; 妊娠结局; 体外受精; 子宫内腔容受性

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Analysis of the correlation between ultrasound assessment indicators for endometrial receptivity and clinical pregnancy outcome of frozen-thawed blastocyst transfer

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【Abstract】 Objective To analyze the correlation between ultrasound indicators of endometrial receptivity and clinical pregnancy of blastocyst transfer in frozen-thawed embryo transfer (FET) cycles. **Methods** This was a retrospective case-control study. From November 2021 to October 2024, the patients undergoing FET were enrolled at the Reproductive Medicine Center of Sichuan Provincial Maternity and Child Health Care Hospital. On the 6th day of progesterone injection, one or two blastocysts were thawed and transferred. The patients were divided into clinical pregnancy group ($n=204$) and non-pregnancy group ($n=222$). Before FET, transvaginal ultrasound evaluation of endometrial receptivity was conducted. The indicators included anatomical parameters such as endometrial thickness, volume, and direction of peristalsis; blood flow parameters, such as endometrial vascularization index (VI), flow index (FI), vascularization flow index (VFI), and blood flow grading, uterine artery pulsatility index (PI), resistance index (RI) and peak systolic velocity/end-diastolic velocity (S/D). Ultrasound indicators between the two groups were compared. Multiple logistic regression analysis was carried out after adjusting for mixed factors which may affect the outcome of pregnancy. **Results** Compared with the non-pregnancy group, the clinical pregnancy group had a significantly higher endometrial thickness [0.88 (0.70, 1.00) cm vs. 0.80 (0.70, 1.00) cm, $P=0.032$] and lower FI [23.57 (21.30, 26.79) vs. 24.64 (21.78, 28.11), $P=0.048$]. No statistically significant differences were detected in endometrial volume, proportion of peristalsis direction patterns, VI, VFI, proportion of endometrial/subendometrial vascular blood flow grading, PI, RI, and S/D of bilateral uterine arteries between the two groups (all $P>0.05$). Multiple logistic regression analysis indicated a positive correlation between endometrial thickness and clinical pregnancy ($OR=3.95$, 95% CI : 1.10–14.23, $P=0.036$), and a negative correlation between FI and clinical pregnancy ($OR=0.96$, 95% CI : 0.92–0.99, $P=0.012$). **Conclusion** The endometrial thickness and FI on the day of FET may affect clinical pregnancy.

【Key words】 Embryo implantation; Ultrasonography; Pregnancy outcome; Fertilization *in vitro*; Endometrial receptivity

Fund program: Key Project of the Maternal and Child Health Medical Science and Technology Innovation Program of Sichuan Provincial (22FXZD01); Research Program of Sichuan Medical Association (S22015); Research Program of Chengdu Municipal Health Commission (2022155); National Center for Women and Children's Health, NHC, PRC "Maternal and Infants Nutrition and Health Research Program" (2023FYH012); General Program of Natural Science Foundation of Sichuan Provincial (2024NSFSC0695)

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基于机器学习构建多囊卵巢综合征患者首次冻融胚胎移植周期活产结局的预测模型

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【摘要】 目的 构建多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者首次冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期活产结局的预测模型。方法 采用回顾性病例对照研究, 纳入 2021 年 1 月至 2024 年 12 月在北京大学第三医院妇产科生殖医学中心首次行 FET 的 1 756 例 PCOS 患者, 其中活产组 715 例, 非活产组 1 041 例, 基于机器学习模型分析内分泌、代谢及炎症指标等对活产结局的影响。数据预处理后按 7:3 分为训练集与测试集, 构建逻辑回归、随机森林、极端梯度提升树、支持向量机和神经网络 5 种机器学习模型, 通过多指标及受试者工作特征曲线评估性能, 用夏普利加性解释值分析特征重要性。结果 基线分析显示, 活产组与非活产组在年龄、体质指数 (body mass index, BMI)、脂质代谢及胚胎相关因素等方面差异均有统计学意义 (均 $P < 0.05$)。各模型的曲线下面积 (area under the curve, AUC) 位于 0.725~0.745 之间, 其中, 逻辑回归表现整体最优 (AUC=0.745), 支持向量机准确度 (70.97%) 和特异度 (0.779) 最高。特征重要性分析表明, 移植胚胎数量与类型是核心预测因子, 血糖代谢异常、

BMI $\geq$ 28.0 kg/m²与活产结局呈负相关。结论 本研究构建的机器学习预测模型可有效评估 PCOS 患者首次 FET 的活产率，明确了移植胚胎特征及可干预代谢因素对妊娠结局的影响，为临床制定个体化助孕策略提供可靠工具。

【关键词】 多囊卵巢综合征； 冻融胚胎移植； 活产预测； 机器学习模型； 代谢状态

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A predictive model for the live birth outcome of the first frozen-thawed embryo transfer cycle in patients with polycystic ovary syndrome based on machine learning

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【Abstract】 Objective To construct a predictive model for live birth outcomes in the first frozen-thawed embryo transfer (FET) cycle of patients with polycystic ovary syndrome (PCOS). **Methods** A retrospective case-control study was adopted. A total of 1 756 PCOS patients who underwent their first FET from January 2021 to December 2024 were included. Among them, there were 715 cases in the live birth group and 1 041 cases in the non-live birth group. The impact of endocrine, metabolic, and inflammatory indicators on live birth outcomes was analyzed using machine learning models. After data preprocessing, the data were divided into a training set and a test set at a ratio of 7 : 3. Five machine learning models (logistic regression, random forest, extreme gradient boosting, support vector machine and neural network) were constructed, and their performance was evaluated through multiple indicators and receiver operating characteristic curves. The feature importance was analyzed using Shapley additive explanation values. **Results** Baseline analysis showed significant differences between the live birth group and the non-live birth group in terms of age, body mass index (BMI), glucose and lipid metabolism, and embryo-related factors (all $P<0.05$). The area under the curve (AUC) of each model ranged from 0.725 to 0.745. Among them, logistic regression performed the best overall (AUC=0.745), and support vector machine had the highest accuracy (70.97%) and specificity (0.779). Feature importance analysis indicated that the number and type of transferred embryos were the core predictors, and abnormal glucose metabolism and BMI $\geq$ 28.0 kg/m² were negatively correlated with live birth outcomes. **Conclusion** The machine learning predictive model constructed in this study can effectively evaluate the live birth rate of the first FET in PCOS patients, clarifying the impact of transferred embryo characteristics and modifiable metabolic factors on pregnancy outcomes, and offers a reliable tool for clinical individualization of assisted reproductive strategies.

【Key words】 Polycystic ovary syndrome; Frozen-thawed embryo transfer; Live birth prediction; Machine learning model; Metabolic status

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首个 IVF/ICSI 完整周期累积活产率预测模型的研究

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【摘要】 目的 探索构建首个体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 完整周期内治疗前、治疗期内、妊娠早期 3 种情景下的个体累积活产率 (cumulative live birth rate, CLBR) 的预测模型。方法 采用回顾性队列研究, 分析 2019 年 1 月至 2022 年 12 月在烟台山医院生殖医学中心首个完整 IVF/ICSI 周期记录, 以及 2023 年 1 月 1 日至 2023 年 12 月 31 日与这些周期相关的冻胚移植数据, 以确保在一个完整周期内对所有胚胎移植进行至少 1 年的随访。主要结局指标是 CLBR, 以活产结局分组。根据 3 种临床不同情景, 全子集回归筛选预测变量, 用以估计在第 1 个完整 IVF/ICSI 周期中首次活产的个体化 CLBR。第一种模型使用开始治疗前的患者信息; 第二种模型基于第一次 IVF/ICSI 治疗期间收集的增量信息; 第三种模型是整合妊娠早期 β -人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 水平数据, logistic 回归预测活产。从区分度、校准度和临床决策三个方面对模型性能进行评价。使用曲线下面积 (area under the curve, AUC) 评估判别性, 使用校准曲线和 Brier 评分评估校准度, 使用临床决策曲线评价临床获益, Nomogram 可视化预测个体活产概率。结果 本研究共纳入 1 010 例女性的首个完整治疗周期信息, 其中 563 例 (55.74%) 患者在周期内获得活产。治疗前模型关键活产预测变量包括女方年龄、体质量指数 (body mass index, BMI)、基础窦卵泡计数, 模型 AUC 为 0.723 (95% CI: 0.691~0.754), 内部交叉验证后 AUC 为 0.715, Brier 评分为 0.212。治疗后活产预测变量包括女方年龄、BMI、可利用胚胎数、首次移植类型和移植次数, 模型 AUC 为 0.854 (95% CI: 0.831~0.877), 内部交叉验证后 AUC 为 0.818, Brier 评分为 0.179。妊娠早期活产预测变量包括女方年龄、移植周期类型、移植胚胎质量、阶段和数量、初始 β -hCG 等效检测天数和水平, 模型 AUC 为 0.879 (95% CI: 0.852~0.907), 内部交叉验证后 AUC 为 0.870, Brier 评分为 0.122。结论 构建的首个完整周期个体 CLBR 预测模型, 区分度与校准度俱佳, 可在治疗前、后及妊娠早期为 IVF 患者预后概率咨询中提供明确的临床净获益。

【关键词】 体外受精； 累积活产； 预测学习模型； 人绒毛膜促性腺激素

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Research on predictive models for estimating cumulative live birth rates in the initial complete IVF/ICSI cycle

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【Abstract】 Objective To establish and evaluate predictive model for individual cumulative live birth rate (CLBR) across three clinically relevant scenarios including before treatment, after treatment, and during the first trimester within a single complete *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycle. **Methods** This retrospective cohort study analyzed the clinical data of 1 010 infertile couples (non-donor cycles) who initiated their first IVF/ICSI treatment, either fresh or frozen cycles, at Reproductive Medicine Center, Yantaishan Hospital from January 2019 to December 2022, as well as the clinical data of frozen-thawed embryo transfer in related cycles from January 1, 2023 to December 31, 2023, to ensure that all embryo transfers were followed up for at least one year in a complete cycle. The primary outcome measure was the CLBR, with patients grouped according to the final live birth outcome. Predictor variables were selected via all-subset regression under three clinical contexts to estimate individualized cumulative probabilities of achieving the first live birth within the initial complete IVF/ICSI cycle. The first model used patient's information available before the treatment initiates; the second model included additional information collected during the first IVF/ICSI treatment cycle; in the third model, β -human chorionic gonadotropin (hCG) levels in the first-trimester were additionally included; logistic regression was applied in all models to predict live birth outcomes. Model performance was evaluated in terms of discrimination, calibration, and clinical utility. Discrimination was assessed using the area under the curve (AUC). Calibration was evaluated using calibration curves and the Brier score. Clinical benefit was assessed using decision curve analysis. A nomogram was used to visualize the individualized live birth probability. **Results** The study included 1 010 female patients with data on their first complete IVF cycle. Of these, 563 (55.74%) patients achieved a live birth within the first cycle. The key pre-treatment predictors of live birth included female partner's age, body mass index (BMI), antral follicle count. The model achieved an AUC of 0.723 (95% *CI*: 0.691–0.754), after internal cross-validation, the AUC remained 0.715, and the Brier score was 0.212. The predictive variables for live birth in the post-treatment model included the female partner's age, BMI, the number of available embryos, the first transfer type, and the number of transfers, with a model AUC of 0.854 (95% *CI*: 0.831–0.877), after internal cross-validation, the AUC remained 0.818, and the Brier score was 0.179. The predictive variables for live birth in the first trimester included female partner's age, type of embryo transfer cycle, embryonic quality,

stage and number of transferred embryos, equivalent days to β -hCG testing, and initial β -hCG level. The model achieved an AUC of 0.879 (95 % CI: 0.852–0.907). After internal cross-validation, the AUC was 0.870 and the Brier score was 0.122.

Conclusion The first complete cycle, individual-level CLBR prediction model we developed demonstrates both excellent discrimination and calibration, offering a clear clinical net benefit for counselling IVF patients on their probability of success at pretreatment, post-treatment, and early pregnancy stages.

【 Key words 】 Fertilization *in vitro*; Cumulative live birth; Predictive learning models; Human chorionic gonadotropin

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实验研究

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荭草苷在人类精子冷冻保存中的抗氧化保护效果研究

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【摘要】 目的 探讨在精子冷冻保护剂中添加不同浓度荭草苷 (orientin, ORI) 后对人精子冷冻保护效果的影响。方法 选取 2024 年 1 月至 2025 年 1 月来自安徽医科大学第一附属医院人类精子库的 105 例男性志愿者精液样本。每例精液样本平均分为 5 份, 其中 1 份作为冷冻前新鲜样本进行活力检测, 剩余 4 份按照冷冻保护剂中添加 ORI 浓度的不同分为对照组 (不含有 ORI)、 10^{-6} mol/L ORI 组、 10^{-7} mol/L ORI 组和 10^{-8} mol/L ORI 组。精液与精子冷冻保护剂按 2:1 混合, 冷冻保存 2 周后进行复苏实验。使用计算机辅助精液分析系统评估精子的运动活力 [前向运动精子百分率 (progressive motility, PR)、曲线速度 (curvilinear velocity, VCL)、直线速度 (sperm linear velocity, VSL)、平均路径速度 (average path velocity, VAP)] ; 采用伊红-苯胺黑染色法分析精子存活率; 使用精子 DNA 碎片指数 (DNA fragmentation index, DFI) 评估精子 DNA 的完整性; 使用 JC-1 法检测各组精子线粒体膜电位 (mitochondrial membrane potential, MMP) 水平; 利用 DHE 探针检测各组精子活性氧 (reactive oxygen species, ROS) 水平; 使

用透射电子显微镜观察精子超微结构变化。结果 冷冻复苏后各组精子的运动活力指标 (PR、VCL、VSL、VAP) 低于冷冻前新鲜样本, 各实验组精子运动活力指标的下降幅度均低于对照组幅度 (均 $P<0.008$), 其中 10^{-8} mol/L ORI 组下降幅度最低。与对照组 ($48.28\pm6.47\%$) 和 10^{-6} mol/L ORI 组 ($49.32\pm6.14\%$) 相比, 10^{-7} mol/L ORI 组 ($56.20\pm6.65\%$) 和 10^{-8} mol/L ORI 组 ($57.08\pm6.64\%$) 精子存活率显著升高 (均 $P<0.008$)。在精子 MMP 水平方面, 10^{-6} mol/L ORI 组 ($40.39\pm4.80\%$)、 10^{-7} mol/L ORI 组 ($42.44\pm5.80\%$) 和 10^{-8} mol/L ORI 组 ($44.52\pm4.78\%$) 均显著高于对照组 ($37.82\pm5.50\%$, 均 $P<0.008$)。 10^{-8} mol/L ORI 组精子 ROS 含量 ($35.81\pm15.49\%$) 较对照组 ($43.91\pm14.44\%$) 显著降低 ($P<0.008$); 与对照组 ($12.11\pm2.64\%$) 相比, 10^{-8} mol/L ORI 组 ($10.94\pm2.55\%$) 的精子 DFI 明显降低 ($P<0.008$)。透射电子显微镜结果显示, 10^{-8} mol/L ORI 组精子保持较好的质膜和线粒体结构, 而对照组则出现质膜破裂和线粒体肿胀等损伤。结论 ORI 对精子冷冻保存具有显著的保护作用, 能够降低氧化应激损伤, 增强冷冻后精子的线粒体功能, 提高精子运动能力和存活率, 尤其在 10^{-8} mol/L 时效果最佳, 可以改善冷冻复苏后的精子质量。

【关键词】 莼草苷; 抗氧化剂; 精子冷冻; DNA 损伤; 线粒体膜电位

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Study on the antioxidant protective effect of orientin in human sperm cryopreservation

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【 Abstract 】 **Objective** To explore the effect of adding different concentrations of Orientin (ORI) to sperm cryopreservation protectants on the cryopreservation protection of human sperm. **Methods** A total of 105 semen samples were collected from male volunteers at the Human Sperm Bank of the First Affiliated Hospital of Anhui Medical University between January 2024 and January 2025. Each semen sample was equally divided into 5 aliquots, one aliquot was used as a fresh pre-freezing sample for motility assessment, and the remaining 4 aliquots were divided into four groups based on the concentration of ORI added to the cryoprotectant, namely control group (without ORI), 10^{-6} mol/L ORI group, 10^{-7} mol/L ORI group, and 10^{-8} mol/L ORI group. Semen was mixed with cryoprotectant at a 2 : 1 ratio and cryopreserved for 2 weeks prior to thawing experiments. The computer-assisted semen analysis system was used to evaluate the motile activity of sperm, including the progressive motility (PR), curvilinear velocity (VCL), sperm linear velocity (VSL) and average path velocity (VAP). Eosin-Nigrosin staining

method was adopted to assess sperm viability. The integrity of sperm DNA was evaluated using the sperm DNA fragmentation index (DFI). The levels of mitochondrial membrane potential (MMP) in sperm of each group were detected by the JC-1 method. The levels of reactive oxygen species (ROS) in sperm of each group were detected by using DHE probes. The ultrastructural changes of sperm were observed by transmission electron microscopy. **Result** By comparing the differences in motion parameters between each frozen group and the fresh sample group, the sperm motility parameters (PR, VCL, VSL, VAP) of frozen samples was lower than that of fresh samples. The decline of sperm motility parameters (PR, VCL, VSL, VAP) in each experimental group was lower than that in control group (all $P<0.008$); among them, the 10^{-8} mol/L ORI group showed the smallest decrease. Compared with control group ($48.28\%\pm6.47\%$) and the 10^{-6} mol/L ORI group ($49.32\%\pm6.14\%$), the sperm survival rates in the 10^{-7} mol/L ORI group ($56.20\%\pm6.65\%$) and 10^{-8} mol/L ORI group ($57.08\%\pm6.64\%$) were significantly increased (all $P<0.008$). In terms of sperm MMP levels, the MMP levels in the 10^{-6} mol/L ORI group ($40.39\%\pm4.80\%$), 10^{-7} mol/L ORI group ($42.44\%\pm5.80\%$) and 10^{-8} mol/L ORI group ($44.52\%\pm4.78\%$) were all significantly higher than that in control group ($37.82\%\pm5.50\%$, all $P<0.008$). The ROS detection results showed that the sperm ROS content in the 10^{-8} mol/L ORI group ($35.81\%\pm15.49\%$) was significantly lower than that in control group ($43.91\%\pm14.44\%$, $P<0.008$). Compared with control group ($12.11\%\pm2.64\%$), the sperm DFI in the 10^{-8} mol/L ORI group ($10.94\%\pm2.55\%$) was significantly decreased ($P<0.008$). The transmission electron microscopy results demonstrated that sperm in the 10^{-8} mol/L ORI group maintained intact plasma membrane and mitochondrial structures, whereas control group exhibited structural damages such as plasma membrane rupture and mitochondrial swelling. **Conclusion** ORI has a significant protective effect on sperm cryopreservation. It can reduce oxidative stress damage, enhance mitochondrial function of frozen sperm, improve sperm motility and survival rate, especially at 10^{-8} mol/L, and can improve the quality of sperm after cryopreservation and thawing.

【 Key words 】 Orientin; Antioxidant; Sperm freezing; DNA damage; Mitochondrial membrane potential

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不孕女性体外受精-胚胎移植后早期流产风险预测模型的系统评价

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【摘要】 目的 系统检索、评价不孕女性体外受精-胚胎移植(*in vitro* fertilization and embryo transfer, IVF-ET)后早期流产的风险预测模型, 为临床实践提供参考。方法 系统检索PubMed、Embase、Web of Science、Cochrane Library、中国知网、万方数据库、维普期刊库和中国生物医学文献数据库中相关文献, 检索时限为建库至2025年7月。2名研究者独立提取文献内容、评价模型性能。结果 共纳入14项研究(28个模型), 其中10项研究报告的受试者工作特征曲线下面积为0.63~0.97, 合并后曲线下面积为0.791。最常见的预测因子为母体年龄、移植日子宫内膜厚度。所有研究适用性均较好, 但均存在高偏倚风险, 主要来自研究对象与统计分析领域。Meta分析显示异质性较高($I^2=97.74\%$, $P<0.001$), 主要来源是不孕病因为病因明确、结局预测时间为移植后28 d。结论 不孕女性IVF-ET后早期流产的风险预测模型尚处于发展阶段, 后续需要参考相关指南, 完善研究设计并标准化模型构建, 开发本土化不孕女性IVF-ET后早期流产最优风险预测模型, 以尽早识别、预防早期流产。

【关键词】 不孕; 体外受精; 胚胎移植; 自然流产; 系统评价; Meta分析; 预测模型

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Systematic review of the risk prediction models for early miscarriage in infertile women undergoing *in vitro* fertilization and embryo transfer

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【Abstract】 Objective To systematically search and evaluate the risk prediction models for early miscarriage in infertile women undergoing *in vitro* fertilization and embryo transfer (IVF-ET), providing references for clinical practice. **Methods** Relevant literature was systematically retrieved from PubMed,

Embase, Web of Science, Cochrane Library, CNKI, Wanfang Database, VIP Journal Database and China Biology Medicine Database from the establishment of the databases to July 2025. Two researchers independently extracted the content of the literature and evaluated the performance of the models. **Results** A total of 14 studies (28 models) were included. Among them, 10 studies reported the area under the receiver operating characteristic curve ranging from 0.63 to 0.97, and the combined area under the curve was 0.791. The most common predictors were maternal age and endometrial thickness on the day of transfer. All studies had good applicability, but all had a high risk of bias, mainly coming from the research subjects and the statistical analysis field. The meta-analysis showed high heterogeneity ($I^2=97.74\%$, $P<0.001$), mainly due to the fact that the causes of infertility were clearly defined and the outcome prediction time was 28 d after transfer. **Conclusion** The risk prediction models for early miscarriage in infertile women undergoing IVF-ET are still in the development stage. Subsequently, it is necessary to refer to relevant guidelines, improve the research design and standardize the model construction, and develop the optimal risk prediction model for early miscarriage in infertile women undergoing IVF-ET to identify and prevent early miscarriage as early as possible.

【Key words】 Infertility; Fertilization *in vitro*; Embryo transfer; Abortion, spontaneous; Systematic review; Meta-analysis; Prediction model

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·临床报道·

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体外受精/卵胞质内单精子注射-胚胎移植周期 中阴道微生物群特征的前瞻性队列研究

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【摘要】 目的 探讨不孕患者在体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer, IVF/ICSI-ET) 促排卵治疗期间的阴道微生物群特征。方法 本研究为前瞻性队列研究, 收集 2019 年 7 月至 2019 年 12 月在中山大学孙逸仙纪念医院妇产科生殖中心 45 例首次接受 IVF/ICSI-ET 的患者资料, 促排卵采用促性腺激素释放激素 (gonadotropin-releasing hormone, GnRH) 激动剂黄体期长方案和 GnRH 拮抗剂方案。在 IVF-ET 过程中多个时点采集阴道样本, 根据采集时间分为促排卵早期组 (记为 B 组)、促排卵晚期组 (记为 G 组)、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日组 (罗红霉素预防性使用前, 记为 H 组)、取卵日组 (记为 O 组) 和胚胎移植日组 (记为 E 组), 比较不同组间阴道微生物群特征及其与临床干预的关系。最终分析时根据新鲜胚胎移植后妊娠结局, 分为妊娠组 ($n=22$) 和非妊娠组 ($n=7$), 比较两组患者阴道微生物群的差异。结果 各组间门水平和种水平优势菌群的相对丰度总体无明显差异。在 IVF/ICSI-ET 周期的不同时间点 (B/G/H/O), 阴道微生物群的 α 多样性差异均有统计学意义 (均 $P<0.05$)。对所有组进行无加权 UniFrac 和 Jaccard 距离的主坐标分析和 Adonis 分析, 结果显示有轻微的分离趋势。在门水平上, 所有组中具有显著差异的物种是 *Parcubacteria* ($P=0.013$) 和 *Deinococcus-Thermus* ($P=0.016$)。预防性抗生素使用前后, H 组与 O 组之间的 α 多样性分析未发现显著差异 ($P>0.05$)。预防性抗生素使用及阴道冲洗前后, H 组与 E 组之间在 Observed、Chao1、ACE 和 Coverage 多样性方面差异均有统计学意义 ($P=0.004$ 、 $P=0.001$ 、 $P=0.002$ 、 $P=0.002$), O 组与 E 组之间差异均有统计学意义 ($P=0.002$ 、 $P=0.006$ 、 $P=0.005$ 、 $P=0.005$)。hCG 注射日阴道微生物群在妊娠组和非妊娠组指标分析显示, OTU3 (乳酸菌) 和 OTU22 (*Ureaplasma*) 在妊娠患者中的相对丰度显著更高, 并且具有更高的指标值。结论 在 IVF/ICSI-ET 的卵巢刺激期间, 阴道微生物群的多样性相对稳定。预防性口服抗生素干预对阴道微生物群特征没有影响。阴道冲洗显著改变了阴道微生物群。hCG 注射日的阴道细菌群落可能与妊娠结局相关。

【关键词】 微生物群; 体外受精; 胚胎移植; 抗生素; 阴道冲洗

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Vaginal microbiota profile during *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer cycles: a prospective cohort study

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【 Abstract 】 **Objective** To investigate the characteristics of vaginal microbiota in infertile patients undergoing controlled ovarian stimulation (COS) for *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET). **Methods** This prospective cohort study enrolled 45 women receiving their first IVF/ICSI-ET cycle at the Reproductive Center, Department of Gynecology and Obstetrics of Sun Yat-sen Memorial Hospital from July to December 2019. COS was performed with either gonadotropin-releasing hormone (GnRH)-agonist long-luteal or GnRH-antagonist protocols. Vaginal swabs were

serially collected and grouped by sampling time: early COS (B), late COS (G), human chorionic gonadotropin (hCG)-trigger day (before prophylactic use of roxithromycin, H), oocyte-retrieval day (O), and embryo-transfer day (E). Vaginal microbiota profiles were compared among groups and in relation to clinical interventions. Patients were further stratified into clinical pregnancy group ($n=22$) and non-pregnancy group ($n=7$) after fresh embryo transfer and microbiota differences between the two groups were finally analyzed. **Results** There were no significant overall differences in the relative abundances of dominant microbiota at the phylum and species levels among the groups. At different time points of IVF/ICSI-ET cycle (B/G/H/O), the α diversity of vaginal microflora was statistically significant (all $P<0.05$). Principal-coordinate analysis (unweighted UniFrac and Jaccard distances) with Adonis testing showed only a slight separation trend. At the phylum level, *Parcubacteria* ($P=0.013$) and *Deinococcus-Thermus* ($P=0.016$) were significantly different among groups. α -diversity was comparable between group H and group O before and after the use of prophylactic antibiotic ($P>0.05$), whereas significant differences in Observed, Chao1, ACE and Coverage indices were detected between group H and group E ($P=0.004$, $P=0.001$, $P=0.002$, $P=0.002$) and group O and group E ($P=0.002$, $P=0.006$, $P=0.005$, $P=0.005$) before and after the use of prophylactic antibiotic and vaginal irrigation. Indicator-species analysis of vaginal microbiota characteristics of pregnant and non-pregnant groups on the day of hCG injection revealed that OTU3 (*Lactobacillus*) and OTU22 (*Ureaplasma*) were significantly more abundant and had higher indicator values in women who achieved clinical pregnancy. **Conclusion** Vaginal microbial diversity remains relatively stable during COS for IVF/ICSI-ET. Prophylactic oral antibiotics did not appreciably alter vaginal microbiota signatures, whereas vaginal flushing induced significant shifts. The vaginal bacterial community on the day of hCG administration may be associated with subsequent pregnancy outcome.

【Key words】 Microbiota; Fertilization *in vitro*; Embryo transfer; Antibiotic; Vaginal flushing

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·临床报道·

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无创胚胎染色体筛选技术结合形态学评级优选 胚胎的移植顺序

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【摘要】 目的 探讨无创胚胎染色体筛选 (noninvasive chromosomal screening, NICS) 结合形态学优选胚胎对不孕患者妊娠结局的影响, 给胚胎的移植顺序提供参考。方法 本研究为回顾性队列研究, 纳入 2019 年 1 月至 2024 年 12 月至河北生殖妇产医院生殖医学科就诊, 并接受胚胎 NICS 检测后进行单囊胚移植的患者的资料。沿用人工智能 (artificial intelligence, AI) 评级优选胚胎的思路, 按照整倍体概率由高到低把胚胎评为 A、B、C 级胚胎, 并根据移植胚胎的评级分为 A 组、B 组、C 组, 统计分析三组之间的临床妊娠率、早期流产率、持续妊娠率及活产率。再把 NICS 评级结合胚胎形态学评级优、中、差进一步分组, 分析各组间临床妊娠率、早期流产率、持续妊娠率及活产率的趋势。结果 共纳入 298 例患者, 移植 A、B、C 级胚胎的患者数分别为 163、57 和 78 例。A、B、C 三组的早期流产率 [18.81% (19/101)、18.75% (6/32)、40.54% (15/37), $P=0.022$]、持续妊娠率 [50.31% (82/163)、45.61% (26/57)、28.21% (22/78), $P=0.005$] 和活产率 [49.08% (80/163)、42.11% (24/57)、26.92% (21/78), $P=0.005$], 组间比较差异均有统计学意义。其中 A 组的持续妊娠率和活产率均高于 C 组 (均 $P=0.001$), 早期流产率低于 C 组 ($P=0.009$)。NICS 评级结合形态学优、中、差分成 9 组, 活产率在 9 组之间存在线性趋势 ($P<0.001$)。Pearson 检验显示活产率随着 NICS 和形态学评级的降低而降低 ($R=0.220$, $P<0.001$)。结论 经 NICS-AI 评级系统评分后的胚胎, 优先移植 NICS-AI 评级为 A, 形态学评级为优+中的胚胎; 其次移植 NICS-AI 评级为 B, 形态学评级为优的胚胎。移植 NICS-AI 评级为 C, 无论形态学评级为何等级的胚胎均需患者充分知情, 告知风险以决定是否移植。

【关键词】 单囊胚移植; 无创胚胎染色体筛选; 活产率; 形态学评级; 移植顺序

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Noninvasive chromosomal screening technology combined with morphological rating for optimal embryo transfer sequence

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【Abstract】 Objective To analyze the differences in pregnancy outcomes among patients after noninvasive chromosomal screening (NICS) testing combined with morphological selection of embryos, guiding the order of embryo transfer in infertile populations. **Methods** This study was a retrospective cohort study that analyzed patients who visited the Department of Reproductive Medicine of Hebei Maternity Hospital between January 2019 and December 2024, underwent NICS testing of embryos, and subsequently underwent single blastocyst transfer.

Following the NICS-artificial intelligence (AI) rating-based selection approach, embryos with higher euploid probabilities [rated A (group A), B (group B), and C (group C)] were transferred sequentially. The clinical pregnancy rate, the ongoing pregnancy rate, and the live birth rate were statistically compared among the three groups. Further stratification based on morphological grading (excellent, moderate, poor) was performed to compare the clinical pregnancy rate, the ongoing pregnancy rate, and the live birth rate among the three groups. **Results** A total of 298 patients who underwent embryo transfer based on NICS-AI ratings were included, with 163, 57 and 78 patients receiving grade A, B, and C embryos, respectively. The early miscarriage rates [18.81% (19/101), 18.75% (6/32), 40.54% (15/37), $P=0.022$], the ongoing pregnancy rates [50.31% (82/163), 45.61% (26/57), 28.21% (22/78), $P=0.005$], and the live birth rates [49.08% (80/163), 42.11% (24/57), 26.92% (21/78), $P=0.005$] differed significantly among groups A, B and C. Specifically, group A showed higher ongoing pregnancy rates and live birth rates, and lower early miscarriage rates compared with group C ($P=0.001$, $P=0.001$, $P=0.009$). When NICS ratings were combined with morphology categories (excellent, moderate, poor) to form nine groups, a linear trend in live birth rates was observed across the nine groups ($P<0.001$). Pearson correlation test further demonstrated that live birth rates decreased with declining NICS and morphology ratings ($R=0.220$, $P<0.001$). **Conclusion** Based on the NICS-AI rating system, embryos with grade A and excellent or moderate morphological rating should be prioritized for transfer. Embryos with grade B and excellent morphological rating should be considered next. For embryos with grade C, regardless of morphological rating, patients should be fully informed of the risks to decide whether to proceed with transfer.

【 Key words 】 Single blastocyst transfer; Noninvasive chromosomal screening; Live birth rate; Morphological rating; Transfer order

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·现场调查·

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妊娠丢失患者及其配偶创伤后应激障碍症状的网络分析及性别差异研究

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【摘要】 目的 探索妊娠丢失患者及其配偶创伤后应激障碍 (post-traumatic stress disorder, PTSD) 的核心症状及网络结构在不同性别间的差异, 为精准干预与护理提供理论依据。**方法** 采用横断面研究, 便利取样法选取 2023 年 8 月至 2024 年 6 月在郑州大学第一附属医院产科就诊的 422 对妊娠丢失患者及其配偶作为调查对象, 采用一般资料调查问卷、PTSD 量表 (平民版) 进行问卷调查。应用 R 软件进行 PTSD 症状网络分析, 包括网络关系分析、核心症状分析、网络结构的准确性和稳定性分析、桥梁分析及性别差异分析。**结果** 妊娠丢失患者及其配偶网络总强度分别为 83.36 和 79.73。妊娠丢失患者 PTSD 症状网络分析显示, 症状“回避与创伤相关的想法与感觉 (AV6)”和“回避联想起创伤事件的活动与事情 (AV7)”相关性最强, 偏相关系数为 0.516; “与创伤相关的情感反应 (RE4)”是核心症状; “因创伤引发的生理反应 (RE5)”是桥梁症状; “难以集中注意力 (HA15)”的预期影响最高。配偶症状网络分析显示, “回避与创伤相关的想法与感觉 (AV6)”和“回避联想起创伤事件的活动与事情 (AV7)”相关性最强, 偏相关系数为 0.564; “难以集中注意力 (HA15)”是核心症状和桥梁症状; “过度警觉 (HA16)”的预期影响最高。性别特征分析结果显示, 患者和配偶组间网络结构 ($M=0.240$, $P=0.143$) 和组间全局预期影响 ($S=0.165$, $P=0.068$) 均无显著性别差异 (均 $P>0.05$)。**结论** 妊娠丢失患者 PTSD 症状网络的核心症状为“与创伤相关的情感反应 (RE4)”, 配偶核心症状为“难以集中注意力 (HA15)”, 妊娠丢失患者及其配偶 PTSD 症状网络无显著性别差异。临床可关注妊娠丢失患者及其配偶 PTSD 的症状网络核心症状, 以此作为干预靶点, 促进其心理健康状况的改善。

【关键词】 创伤后应激障碍; 性别特征; 妊娠丢失; 症状; 网络分析; 核心症状

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A network analysis of posttraumatic stress disorder symptoms and gender differences in patients with pregnancy loss and their spouses

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【Abstract】 Objective To examine the core symptoms of post-traumatic stress disorder (PTSD) in patients with pregnancy loss and their spouses, alongside gender-specific variations in network structure, aiming to furnish a theoretical foundation for targeted interventions and nursing practices. **Methods** A cross-sectional study was conducted, and a convenience sample of 422 pairs of patients with pregnancy loss and their spouses who attended the Department of Obstetrics of the First Affiliated Hospital of Zhengzhou University from August 2023 to June 2024 were enrolled as participants. Questionnaire surveys were performed using a general information questionnaire and the PTSD checklist-civilian version. R software was applied to conduct network analysis of PTSD symptoms, including network relationship analysis, core symptom analysis, analysis of the accuracy and stability of network structure, bridge analysis, and gender differences analysis. **Results** The total network strengths of patients with pregnancy loss and their spouses were 83.36 and 79.73, respectively. Network analysis of PTSD symptoms in patients with pregnancy loss showed that the strongest relationship existed between the symptoms "avoiding thoughts and feelings related to the trauma (AV6)" and "avoiding activities and things that remind one of the trauma (AV7)", exhibited a partial correlation coefficient of 0.516; "trauma-related emotional reactions (RE4)" was the core symptom; "trauma-induced physiological reactions (RE5)" was the bridge symptom; and "difficulty concentrating (HA15)" had the highest expected influence. Network analysis of symptoms in spouses revealed that the strongest relationship was between "avoiding thoughts and feelings related to the trauma (AV6)" and "avoiding activities and things that remind one of the trauma (AV7)", exhibited a partial correlation coefficient of 0.564; "difficulty concentrating (HA15)" was both the core symptom and the bridge symptom; and "hypervigilance (HA16)" had the highest expected influence. Results of gender characteristics analysis showed that there were no significant gender differences in network structure network invariance test ($M=0.240$, $P=0.143$) and global expected influence invariance test ($S=0.165$, $P=0.068$) between the patient group and the spouse group (all $P>0.05$). **Conclusion** The core symptom of the PTSD symptom network in patients with pregnancy loss is "trauma-related emotional reactions (RE4)", while the core symptom in their spouses is "difficulty concentrating (HA15)". There are no significant gender differences in the PTSD symptom networks between patients with pregnancy loss and their spouses. Clinically, attention may be paid to the core symptoms of the PTSD symptom networks in both patients with pregnancy loss and their spouses, which can be used as intervention targets to promote the improvement of their mental health.

【 Key words 】 Post-traumatic stress disorder; Gender characteristics; Pregnancy loss; Symptoms; Network analysis; Core symptom

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基于潜在类别分析的辅助生殖人群饮食相关行为与抑郁症状的关联研究

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【摘要】 目的 探讨饮食相关行为潜在类别与行辅助生殖技术 (assisted reproductive technology, ART) 治疗的患者抑郁症状之间的关联, 为辅助生殖人群饮食行为干预和心理健康促进提供参考依据。方法 选取 2022 年 7 月至 10 月在安徽医科大学第一附属医院生殖医学中心就诊的 1 026 例行 ART 治疗的患者进行横断面调查。采用自编一般资料调查表、自编饮食行为调查表和抑郁筛查自评量表收集 and 评估研究对象的人口统计学信息、饮食信息和抑郁自评状况, 并完成身体测量。使用潜在类别分析模型对饮食相关行为进行潜在类别分组, 应用多因素 logistic 回归分析饮食相关行为潜在类别与抑郁症状的关联。结果 辅助生殖人群抑郁症状检出率为 51.56% (529/1 026), 其中女性检出率 [55.32% (338/611)] 高于男性 [46.02% (191/415)], 差异有统计学意义 ($P=0.003$)。根据模型适配结果饮食相关行为可以分为 3 个潜在类别, 分别为行为高危组 [8.3% (85/1 026)]、行为强化组 [25.5% (262/1 026)]、行为健康组 [66.2% (679/1 026)]。logistic 回归结果显示, 以行为健康组为参照组, 在调整人口学特征后, 行为高危组中辅助生殖人群抑郁症状检出风险是行为健康组的 1.983 倍 (95% CI: 1.169~3.364, $P=0.011$), 行为强化组与行为健康组的抑郁症状检出风险差异无统计学意义 ($P=0.947$)。性别分层分析结果显示, 该关联存在性别差异, 在调整混杂因素后, 男性行为高危组的风险仍升高 ($OR=2.792$, 95% CI: 1.229~6.341, $P=0.014$), 而女性中差异无统计学意义 ($P=0.122$)。结论 辅助生殖人群抑郁症状检出率高, 女性患者高于男性。不良饮食行为可能是抑郁症状发生的危险因素, 但相对男性而言, 女性饮食行为与抑郁的独立关联强度较弱。

【关键词】 抑郁; 饮食行为; 生殖技术, 辅助; 不孕不育; 潜在类别分析

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A study of the association between diet-related behaviors and depressive symptoms in patients undergoing assisted reproductive technology based on latent class analysis

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【Abstract】 Objective To explore the association between latent classes of diet-related behaviors and depressive symptoms in patients undergoing assisted reproductive technology (ART), and to provide a reference for dietary behavioral interventions and mental health promotion among ART patients. **Methods** A cross-sectional survey was conducted among 1 026 ART patients attending the Centre for Reproductive Medicine of the First Affiliated Hospital of Anhui Medical University between July and October 2022. Demographic information, dietary information and depression self-assessment status were collected and assessed using a self-administered general information questionnaire, a self-administered dietary behavior questionnaire and the Patient Health Questionnaire-9. Physical measurements were also completed. A latent class analysis model was used to fit diet-related behaviors latent class, and multivariable logistic regression analysis was applied to analyze the association between diet-related behaviors and depressive symptoms. **Results** The detection rate of depressive symptoms in ART patients was 51.56% (529/1 026), with a higher detection rate in females [55.32% (338/611)] than in males [46.02% (191/415)], and the difference was statistically significant ($P=0.003$). Based on the model fitting results, latent class analysis classified diet-related behaviors into three groups, namely, high-risk behavior group [8.3% (85/1 026)], behavior reinforcement group [25.5% (262/1 026)] and healthy behavior group [66.2% (679/1 026)]. Logistic regression analysis results showed that, with the healthy behavior group as the reference group, after adjusting for demographic characteristics, the risk of detecting depressive symptoms in the high-risk behavior group was 1.983 times higher than that in the healthy behavior group (95% *CI*: 1.169–3.364, $P=0.011$), and there was no significant difference in the risk of detecting depressive symptoms between the behavior reinforcement group and healthy behavior group ($P=0.947$). The results of the gender-stratified analysis indicated that the association exhibited gender differences. The adjusted model showed that the risk remained significantly elevated in the male high-risk behavior group ($OR=2.792$, 95% *CI*: 1.229–6.341, $P=0.014$), whereas no significant association was observed among females ($P=0.122$). **Conclusions** The detection rate of depressive symptoms in ART patients is high, and females are higher than males. Poor dietary behaviors may be a risk factor for the development of depressive symptoms, however, compared with males, the independent association between dietary behavior and depression is weaker in females.

【Key words】 Depression; Feeding behavior; Reproductive technology, assisted; Infertility; Latent class analysis

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专家视角

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辅助生殖技术中孕激素用于黄体支持的现状与展望

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【摘要】 黄体支持是辅助生殖技术 (assisted reproductive technology, ART) 流程中保障并优化妊娠结局的关键环节。本文旨在系统性地综述孕激素在 ART 黄体支持中的应用现状与未来展望。孕酮具有促进子宫内膜向分泌期转化、诱导内膜容受、保持子宫静息以及调节妊娠免疫等多重生理作用, 为促进胚胎着床和维持早期妊娠提供了必要保障。在 ART 周期中, 因卵巢刺激、取卵或生殖障碍患者潜在因素, 普遍存在黄体功能不足的现象, 外源性孕激素补充已成为 ART 实践的标准步骤。本文详细比较了不同孕激素制剂的特点和临床应用: 注射剂型能提供稳定、可监测的全身血药浓度, 在无自身黄体功能的激素替代周期中具有优势; 阴道给药有良好的子宫首过效应且免注射易操作, 被患者广泛选择; 口服地屈孕酮经多项大型随机对照试验研究亦被证实为一种效果相当的替代方案, 临床应用日益普及。当前, 黄体支持正从统一化、标准化, 转向重视个体化、精准化。基于生物标志物和疾病特征的精准管理模式探索以及长效靶向剂型的创新, 为未来黄体支持的持续优化提供了发展方向。

【关键词】 生殖技术, 辅助; 黄体支持; 孕激素; 精准医学

Current status and prospects of progestogens for luteal phase support in assisted reproductive technology

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【Abstract】 Luteal phase support is a crucial step in assisted reproductive technology (ART) procedures to ensure and optimize pregnancy outcomes. This article aims to systematically review the current status and future prospects of the application of progestogens for luteal phase support in ART. Progesterone plays multiple physiological roles, including promoting endometrial transformation to the secretory phase, inducing endometrial receptivity, maintaining uterine quiescence, and modulating pregnancy immunity, all of which provide necessary guarantees for embryo implantation and early pregnancy maintenance. In ART cycles, luteal phase deficiency is common due to ovarian stimulation, oocyte retrieval, or underlying factors in patients with reproductive disorders, making exogenous progestogen supplementation a standard practice in ART. This article details the characteristics and clinical applications of different progestogen formulations: injectable formulations provide stable, monitorable systemic drug concentrations, offering advantages in hormone replacement therapy cycles where intrinsic luteal function is absent; vaginal administration has a favorable uterine first-pass effect and is easy to administer without injection, making it a popular choice among patients; oral dydrogesterone, validated by multiple large-scale randomized controlled trials, has also been confirmed as an equally effective alternative, with its clinical application becoming increasingly widespread. Currently, luteal phase support is transitioning from standardized uniformity to an emphasis on individualized precision. The exploration of biomarker-based precise management models and innovations in long-acting, targeted formulations offer directions for the continuous optimization of future luteal phase support.

【Key words】 Reproductive techniques, assisted; Luteal phase support; Progestogen; Precision medicine

综述

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胚胎植入前遗传学检测人群的产前诊断策略

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【摘要】 胚胎植入前遗传学检测 (preimplantation genetic testing, PGT) 在生殖医学领域中的应用越来越广泛，它通过筛选不携带致病基因的胚胎进行移植，从而降低子代遗传疾病风险和不良妊娠结局的发生。但由于 PGT 的对象仅为配子或植入前胚胎的单个或数个细胞，存在遗传检测的局限性，因此，妊娠后针对胎儿的遗传学产前检测仍然十分重要。本综述结合国内外相关领域进展和专家共识，系统探讨 PGT 助孕成功后的产前筛查和产前诊断方法，为 PGT 人群妊娠后的管理提供诊疗思路和策略。

【关键词】 产前诊断； 胚胎植入前遗传学检测； 无创产前筛查； 体外受精； 胚胎移植

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Strategies for prenatal diagnosis in preimplantation genetic testing populations

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【Abstract】 Preimplantation genetic testing (PGT) is increasingly being used in the field of reproductive medicine. It involves screening embryos that do not carry disease-causing genes before implantation, thereby reducing the risk of genetic diseases in offspring and adverse pregnancy outcomes. However, since PGT targets only single or a few cells from gametes or preimplantation embryos, there are limitations to genetic testing. Therefore, genetic prenatal testing for the fetus remains crucial. This review systematically explores prenatal screening and diagnosis methods following successful PGT-assisted conception, drawing on recent advancements and expert consensus from both domestic and international sources, to provide diagnostic and therapeutic strategies for managing pregnancies in PGT populations.

【Key words】 Prenatal diagnosis; Preimplantation genetic testing; Non-invasive prenatal testing; Fertilization *in vitro*; Embryo transfer

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神经内分泌-免疫轴在母-胎界面节律调控中的新进展

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【摘要】 妊娠的成功有赖于母-胎界面在免疫耐受、代谢适应与内分泌调节上的精确时序协同。昼夜节律作为机体的核心时间参照系统, 可通过褪黑素、糖皮质激素及 5-羟色胺等神经内分泌信号调控母-胎界面的免疫表型与代谢状态; 与此同时, 免疫细胞分泌的细胞因子亦可反向作用于神经内分泌通路, 由此构成生物钟-神经内分泌-免疫代谢轴”的双向调控网络。现有研究提示, 现代生活方式所致的昼夜节律紊乱可能打破这一平衡, 与子痫前期、胎儿生长受限及早产等妊娠并发症的风险升高存在关联。尽管运动和限时进食等干预显示出恢复节律同步的潜力, 但其对已发生的表观遗传重编程的逆转作用仍有待验证。近年来, 组蛋白单胺化作为一种新型表观遗传修饰引起关注, 该修饰可将单胺类神经递质与染色质重塑直接相连, 并呈现独特的节律性特征, 被认为有望成为连接节律失衡、免疫代谢异常与妊娠并发症的关键表观遗传桥梁。本文系统梳理了该领域的研究进展, 并探讨其潜在的转化价值。

【关键词】 昼夜节律; 妊娠并发症; 表观遗传; 组蛋白单胺化; 母-胎界面; 免疫代谢; 神经内分泌调节

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Recent advances in the neuroendocrine-immune axis in rhythmic regulation at the maternal-fetal interface

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【 Abstract 】 Successful pregnancy depends on the precise temporal coordination of immune tolerance, metabolic adaptation, and endocrine regulation at the maternal-fetal interface. Circadian rhythm, serving as the body's core temporal reference system, modulates the immune phenotype and metabolic status of the maternal-fetal interface through neuroendocrine signals such as melatonin, glucocorticoids, and serotonin. Concurrently, cytokines secreted by immune cells can reciprocally act on neuroendocrine pathways, thereby forming a bidirectional regulatory network known as the "circadian clock-neuroendocrine-immunometabolic axis". Current evidence suggests that circadian disruption induced by modern lifestyles may disturb this balance and is associated with an increased risk of pregnancy complications, including preeclampsia, fetal growth restriction, and preterm birth. Although interventions such as exercise and time-restricted eating have shown potential for restoring circadian synchrony, their capacity to reverse established epigenetic reprogramming remains to be validated. In recent years, histone monoaminylation has emerged as a novel epigenetic modification that directly links monoamine neurotransmitters to chromatin remodeling and exhibits distinctive rhythmic characteristics. This modification is considered as a promising epigenetic bridge connecting circadian dysregulation, immunometabolic imbalance, and pregnancy complications. This review systematically summarizes recent advances in this field and discusses its translational potential for pregnancy health management.

【 Key words 】 Circadian rhythm; Pregnancy complications; Epigenetics; Histone monoaminylation; Maternal-fetal interface; Immune metabolism; Neuroendocrine regulation

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