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# 辅助生殖过程中 GnRH 拮抗剂用于卵巢刺激的管理建议: 针对不同卵巢反应人群的获益与风险评估

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**【摘要】** 引言 体外受精治疗周期的控制性卵巢刺激 (controlled ovarian stimulation, COS) 中, 促性腺激素释放激素 (gonadotropin-releasing hormone, GnRH) 拮抗剂被广泛用于预防过早黄素化及确保卵泡同步成熟。欧洲人类生殖与胚胎学会 2020 年指南建议将 GnRH 拮抗剂应用于不同卵巢反应状态患者, 但其具体方

案路径的优化管理仍需深入探讨。方法 本临床实践指南严格遵循世界卫生组织指南制订流程，围绕 GnRH 拮抗剂在 COS 中的应用形成 8 个临床问题。研究团队通过 Cochrane 标准系统评价、分级推荐评估、制订与评价 (Grades of Recommendations, Assessment, Development and Evaluation, GRADE) 证据质量分级系统进行证据综合评价，并运用 GRADE 证据至决策框架形成推荐意见。我们预先设定了各临床问题的重要结局指标，并将着床率、临床妊娠率、活产率及中重度卵巢过度刺激综合征确立为所有临床问题共同的关键结局指标。指南制订全过程严格遵循国际实践指南报告规范及临床指南研究与评估系统。推荐意见 指南制订组最终形成 14 条关于 GnRH 拮抗剂临床应用的推荐意见。总结如下：对于高卵巢反应患者，低把握度证据支持 GnRH 拮抗剂方案的有效性；在卵巢正常反应人群中，极低把握度证据支持口服避孕药或雌激素进行预处理；低把握度证据支持使用固定 GnRH 拮抗剂方案，极低把握度证据支持使用 GnRH 激动剂联合扳机方案。针对使用 GnRH 拮抗剂方案的患者，极低把握度证据提示高卵巢反应患者，以及低把握度证据支持卵巢正常反应患者实施全胚冷冻策略，可规避新鲜周期移植的风险。然而，特定情况下多胚胎新鲜胚胎移植，仍可能具有临床获益。

【关键词】 控制性卵巢刺激； 促性腺激素释放激素拮抗剂； 指南； 体外受精； 预处理； 扳机； 黄体支持

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临床研究

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基于年龄分层的卵巢储备功能减退  
患者临床妊娠结局分析

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【摘要】 目的 探讨不同年龄分层的卵巢功能减退 (diminished ovarian reserve, DOR) 患者的临床妊娠结局和潜在分子代偿机制。方法 采用回顾性队列研究，纳入 2019 年 1 月至 2021 年 12 月于南京大学医学院附属鼓楼医院生殖医学和妇产医学中心接受体外受精/卵胞质内单精子注射-胚胎移植的不孕患者，根据

患者是否患有 DOR 进行分组,按照 1:2 经过基线资料的倾向性评分匹配,收集到 DOR 组 2 286 例和非 DOR 组 4 350 例。采用单因素及多因素 logistic 回归分析临床妊娠的影响因素,并利用广义相加模型分析年龄与临床妊娠率的关系。采用多准则决策流程确定 27 岁为最佳年龄分界点,选取 $\leq 27$  岁 DOR 患者进行妊娠结局相关因素分析。分析 GEO 数据库中第二次减数分裂中期卵母细胞的转录组数据 (GSE87201),根据供者年龄和窦卵泡计数 (antral follicle count, AFC) 分为四组:年轻高卵巢储备组 (年龄 20~22 岁且  $AFC \geq 10$ ,  $n=9$ )、年长高卵巢储备组 (年龄 33~35 岁且  $AFC \geq 10$ ,  $n=9$ )、年轻低卵巢储备组 (年龄 20~22 岁且  $AFC < 10$ ,  $n=8$ ) 和年长低卵巢储备组 (年龄 33~35 岁且  $AFC < 10$ ,  $n=9$ ),比较代偿机制相关基因的表达模式。结果 DOR 组基础抗米勒管激素 (anti-Müllerian hormone, AMH) [0.69 (0.43, 0.94)  $\mu\text{g/L}$ ]、AFC [6 (4, 8)] 和基础睾酮水平 [0.24 (0.15, 0.40)  $\text{nmol/L}$ ] 显著低于非 DOR 组 [3.01 (1.99, 4.72)  $\mu\text{g/L}$ ,  $P < 0.001$ ; 17 (12, 23),  $P < 0.001$ ; 0.32 (0.21, 0.47)  $\text{nmol/L}$ ,  $P < 0.001$ ]。多因素 logistic 回归显示仅女方年龄是临床妊娠的独立预测因素 ( $OR=0.92$ , 95%  $CI$ : 0.89~0.94,  $P < 0.001$ )。 $\leq 27$  岁 DOR 患者临床妊娠率达 53.68% (102/190),且妊娠组总 AFC [7 (5, 10)] 显著高于未妊娠组 [6 (4, 9),  $P=0.040$ ],总睾酮水平 [0.23 (0.14, 0.40)  $\text{nmol/L}$ ] 显著低于未妊娠组 [0.31 (0.20, 0.49)  $\text{nmol/L}$ ,  $P=0.042$ ]。转录组分析显示年轻低卵巢储备患者代偿基因 *RAD51* ( $\log_2FC=0.273$ ,  $P=0.022$ ) 显著上调。结论 DOR 患者具有独特的临床特征,年龄是妊娠结局的最强预测因素,而年轻 DOR 患者的妊娠成功率异质性大,可能受 AFC 和雄激素水平调控。

【关键词】 卵巢储备功能减退; 窦卵泡计数; 妊娠结局预测

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## Analysis of clinical pregnancy outcomes in patients with diminished ovarian reserve based on age stratification

Li Yifan, Kong Na, Shen Xiaoyue, Wang Zhilong, Shi Qingqing, Lu Feifei, Wang Lingjuan, Sun Haixiang

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【Abstract】 **Objective** To explore the clinical pregnancy outcomes and potential molecular compensatory mechanisms of patients with diminished ovarian reserve (DOR) at different age groups. **Methods** A retrospective study integrating clinical cohort and transcriptomic data was conducted, including infertile patients who underwent *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer at the Center for Reproductive Medicine and Obstetrics and Gynecology in Nanjing Drum Tower Hospital affiliated to Nanjing University Medical School from January 2019 to December 2021. The patients were grouped based on whether they had DOR. Using propensity score matching with a 1:2 ratio, 2 286 cases were collected from the DOR group and 4 350 cases from the non-DOR group. Univariate and multivariate logistic regression analyses were used to identify factors influencing clinical pregnancy, and a generalized additive model

was applied to analyze the relationship between age and clinical pregnancy rate. The multi-criteria decision-making process was used to determine 27 years old as the optimal age cut-off point. Patients aged  $\leq 27$  years with DOR were selected for analysis of factors related to pregnancy outcomes. The transcriptome data of oocyte cells at the metaphase of the second meiotic division in the GEO database (GSE87201) were analyzed. According to the donor's age and antral follicle count (AFC), they were divided into four groups: young high ovarian reserve group (age 20–22 years old and  $\text{AFC} \geq 10$ ,  $n=9$ ), old high ovarian reserve group (age 33–35 years old and  $\text{AFC} \geq 10$ ,  $n=9$ ), young low ovarian reserve group (age 20–22 years old and  $\text{AFC} < 10$ ,  $n=8$ ), and old low ovarian reserve group (age 33–35 years old and  $\text{AFC} < 10$ ,  $n=9$ ). The expression patterns of genes related to compensatory mechanisms were compared. **Results** The DOR group showed significantly lower basal anti-Müllerian hormone (AMH) [0.69 (0.43, 0.94)  $\mu\text{g/L}$ ], AFC [6 (4, 8)], and basal total testosterone levels [0.24 (0.15, 0.40)  $\text{nmol/L}$ ] compared with the non-DOR group [3.01 (1.99, 4.72)  $\mu\text{g/L}$ ,  $P < 0.001$ ; 17 (12, 23),  $P < 0.001$ ]; 0.32 (0.21, 0.47)  $\text{nmol/L}$ ,  $P < 0.001$ ]. Multivariate logistic regression identified female age as the only independent predictor of clinical pregnancy outcomes ( $OR=0.92$ , 95%  $CI$ : 0.89–0.94,  $P < 0.001$ ). The clinical pregnancy rate of DOR patients aged  $\leq 27$  years was 53.68% (102/190). In DOR patients aged  $\leq 27$  years, the pregnancy group had significantly higher AFC [7 (5, 10)], and lower testosterone levels [0.23 (0.14, 0.40)  $\text{nmol/L}$ ] compared with the unpregnancy group [6 (4, 9),  $P=0.040$ ; 0.31 (0.20, 0.49)  $\text{nmol/L}$ ,  $P=0.042$ ]. Transcriptomic analysis revealed upregulation of *RAD51* ( $\log_2FC=0.273$ ,  $P=0.022$ ) in young low ovarian reserve patients. **Conclusion** DOR patients exhibit unique clinical characteristics, with age being the strongest predictor of pregnancy outcomes. However, young DOR patients demonstrate significant heterogeneity in pregnancy success rates, which may be influenced by AFC and androgen levels.

**【Key words】** Diminished ovarian reserve; Antral follicle count; Pregnancy outcome prediction

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## ·临床研究·

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# 上海市浦东新区围孕期空气污染物暴露与妊娠期糖尿病风险的关联研究

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**【摘要】** 目的 评估上海市浦东新区孕妇围孕期空气污染物暴露水平, 分析其与妊娠期糖尿病(gestational diabetes mellitus, GDM)的关联, 并精准锁定污染物暴露的关键时间窗口。方法 本研究为前瞻性队列研究, 对象为2023年1月至2024年6月上海市浦东新区妇幼保健院产科门诊建卡的571名孕妇, 采用国际妊娠合并糖尿病研究组推荐的诊断标准对GDM进行筛查和诊断。根据孕妇居住地址和空间网格化空气污染物数据集获取孕前3个月至孕期6个月每天细颗粒物(PM<sub>2.5</sub>)、可吸入颗粒物(PM<sub>10</sub>)、二氧化硫(SO<sub>2</sub>)、二氧化氮(NO<sub>2</sub>)和一氧化碳(CO)浓度, 计算不同窗口期的日均污染物浓度。采用logistic回归建立单污染、双污染模型分析GDM与孕前期、孕早期和孕中期污染物暴露之间的关联; 通过非线性分布滞后模型(distributed lag non-linear models, DLNM)分析不同孕月污染物暴露对GDM的影响。结果 GDM发病率为22.8%(130/571)。与健康孕妇相比, GDM孕妇高龄组占比更大[31~35岁, 33.8%(44/130)比27.7%(122/440); >35岁, 9.2%(12/130)比5.0%(22/440)], 孕前超重及肥胖比例更高[35.2%(45/128)比21.2%(93/439)], 孕早期空腹血糖水平[(4.8±0.5) mmol/L比(4.6±0.4) mmol/L]、糖化血红蛋白A1c(5.5%±0.5%比5.4%±0.3%)更高, 差异均具有统计学意义(P=0.034、P=0.002、P<0.001、P=0.002)。PM<sub>2.5</sub>、PM<sub>10</sub>、SO<sub>2</sub>、NO<sub>2</sub>和CO的日均暴露中位数(第25百分位数, 第75百分位数)分别为28.23(24.58, 32.63) μg/m<sup>3</sup>、50.60(46.59, 53.68) μg/m<sup>3</sup>、6.85(6.52, 7.13) μg/m<sup>3</sup>、28.24(24.55, 32.63) μg/m<sup>3</sup>和0.65(0.62, 0.69) mg/m<sup>3</sup>。无论是单污染模型还是双污染模型, 均未发现孕前期、孕早期及孕中期空气污染物暴露与GDM存在显著关联。然而基于月暴露的DLNM分析显示, 孕期第2、第6个月的空气污染物暴露与GDM发生风险显著相关, 其中第2个月的NO<sub>2</sub>、第6个月的PM<sub>2.5</sub>和第6个月的NO<sub>2</sub>每增加一个四分位距暴露, GDM的OR分别为1.33(95%CI: 1.01~1.74)、1.48(95%CI: 1.03~2.12)和1.47(95%CI: 1.03~2.11)。结论 上海市浦东新区孕妇在孕期第2个月的NO<sub>2</sub>暴露、第6个月的PM<sub>2.5</sub>和NO<sub>2</sub>暴露与GDM风险呈正相关; 依因果时序推断, 孕期第2个月可能是空气污染物影响上海市浦东新区孕妇糖代谢的敏感窗口期。

**【关键词】** 空气污染物; 队列研究; 妊娠期糖尿病; 非线性分布滞后模型

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## Peri-pregnancy air pollution exposure and risk of gestational diabetes mellitus in Pudong New Area, Shanghai

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**【Abstract】 Objective** To assess peri-pregnancy exposure to ambient air pollutants among pregnant women in Pudong New Area, Shanghai, quantify its relationship with gestational diabetes mellitus (GDM), and precisely identify the critical exposure window that associated with GDM risk. **Methods** This prospective cohort study enrolled 571 pregnant women who registered at the Obstetric Outpatient Department, Maternal and Child Health Hospital of Pudong New Area in Shanghai between January 2023 and June 2024. Screening and diagnosis of GDM were conducted in accordance with the diagnostic criteria recommended by the International Association of Diabetes in Pregnancy Study Groups. The daily concentrations of fine particulate matter (PM<sub>2.5</sub>), inhalable particulate matter (PM<sub>10</sub>), sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>), and carbon monoxide (CO) from 3 months before pregnancy to 6 months during pregnancy were obtained based on the residential address of pregnant women and the spatial grid-based air pollutant dataset, and the average daily pollutant concentrations in different window periods were calculated. Logistic regression was used to build single- and co-pollution models, examining the association between GDM and pollutant exposure during pre-conception, first-trimester and second-trimester periods. Distributed lag non-linear models (DLNM) were further applied to analyze the effects of pollutant exposure at different gestational months on GDM. **Results** The incidence rate of GDM was 22.8% (130/571). Compared with healthy controls, women who developed GDM had a higher proportion in the older age groups [31–35 years old: 33.8% (44/130) vs. 27.7% (122/440); >35 years old: 9.2% (12/130) vs. 5.0% (22/440)], had a higher proportion of overweight and obesity before pregnancy [35.2% (45/128) vs. 21.2% (93/439)], and exhibited elevated first trimester FBG [(4.8±0.5) mmol/L vs. (4.6±0.4) mmol/L] and HbA1c (5.5%±0.5% vs. 5.4%±0.3%), and all the differences were statistically significant ( $P=0.034$ ,  $P=0.002$ ,  $P<0.001$ ,  $P=0.002$ ). The median (25th percentile, 75th percentile) daily average exposures of air PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and CO were 28.23 (24.58, 32.63) µg/m<sup>3</sup>, 50.60 (46.59, 53.68) µg/m<sup>3</sup>, 6.85 (6.52, 7.13) µg/m<sup>3</sup>, 28.24 (24.55, 32.63) µg/m<sup>3</sup> and 0.65 (0.62, 0.69) mg/m<sup>3</sup>, respectively. Neither the single-pollution model nor the co-pollution model showed any significant association between air pollutant exposure during the pre-conception, first-trimester, or second-trimester periods and risk of GDM. However, the DLNM analysis based on monthly exposure indicated that the air pollutant exposure

during the 2nd and 6th months of pregnancy was significantly associated with the risk of GDM. An interquartile range increase in NO<sub>2</sub> during 2nd gestational month was associated with a 1.33-fold higher GDM risk (95% *CI*: 1.01–1.74); in 6th gestational month, equivalent increments in PM<sub>2.5</sub> and NO<sub>2</sub> raised the risk 1.48-fold (95% *CI*: 1.03–2.12), and 1.47-fold (95% *CI*: 1.03–2.11), respectively. **Conclusion** Exposure to NO<sub>2</sub> during the 2nd gestational months and exposure to PM<sub>2.5</sub> and NO<sub>2</sub> during the 6th gestational months are positively correlated with the risk of GDM among pregnant women in Pudong New Area, Shanghai. Based on the causal sequence, the 2nd month of pregnancy may be a key sensitive window for air pollutants to affect the glucose metabolism of pregnant women in this population.

**【Key words】** Air pollutants; Cohort study; Gestational diabetes mellitus; Distributed lag non-linear model

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·流行病学研究·

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# 1994—2023 年中国孕产妇疾病发病和死亡趋势分析

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**【摘要】** 目的 分析 1994—2023 年中国孕产妇疾病发病与死亡趋势, 为孕产妇疾病防控策略提供科学依据。方法 基于全球疾病负担研究 2023 数据库的 1994—2023 年中国孕产妇相关数据, 采用 Joinpoint 回归分析孕产妇疾病发病率和死亡率趋势, 运用年龄-时期-队列模型 (age-period-cohort model, APC) 评估年龄、时期和队列效应; 同时比较不同年龄组的死亡数与孕产妇死亡率 (maternal mortality ratio, MMR), 并分析主要病因的标化发病率和标化死亡率变化及排名。结果 1994—2023 年, 中国孕产妇疾病粗发病率、粗死亡率、标化发病率和标化死亡率平均年度变化百分比分别为-3.35%、-10.92%、-1.88%和-9.57%。APC 模型结果显示, 孕产妇疾病发病率在 25~29 岁达到高峰, 死亡率在 20~24 岁达到高峰。发病率的时期和队列率比 (rate ratio, *RR*) 整体均呈上升趋势, 死亡率的时期和队列 *RR* 均呈下降趋势。与 1994 年相比, 2023 年各年龄组孕产妇疾病死亡数均明显下降, 其中 30~34 岁年龄组死亡数最高; MMR 整体明显降低, 但仍在 50~54

岁年龄组最高,且10~14岁年龄组也表现出相对较高水平;主要病因分析显示,孕产妇高血压发病率仍居首位,首位死因转为间接孕产妇死亡,其中只有人类免疫缺陷病毒导致孕产妇死亡上升了28.90%,其他均下降。结论 近30年来,中国孕产妇疾病防控取得明显进展,其发病率和死亡率总体下降,然而,近些年发病风险在缓慢上升。应重点关注20~34岁孕产妇人群,同时加强对极端年龄妊娠,如 $\leq 14$ 岁及 $\geq 50$ 岁的风险管理,强化高风险人群个体防护、生殖健康教育及高危妊娠管理。

【关键词】 孕产期并发症; 发病率; 死亡率; Joinpoint 回归; 年龄-时期-队列模型

## Analysis of trends in maternal disorders morbidity and mortality in China from 1994 to 2023

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**【 Abstract 】 Objective** To analyze the trends in maternal disease incidence and mortality in China from 1994 to 2023, providing scientific evidence for maternal disease prevention and control strategies. **Methods** Maternal health data for China from 1994 to 2023 were obtained from the Global Burden of Disease 2023 database. Joinpoint regression was used to assess trends in incidence and mortality rates, and age-period-cohort model (APC) was applied to evaluate age, period, and cohort effects. Number of deaths and maternal mortality ratio (MMR) were compared across age groups, and changes and rankings in age-standardized incidence and mortality rates by major causes were analyzed. **Results** From 1994 to 2023, the average annual percentage change in crude incidence, crude mortality, age-standardized incidence, and age-standardized mortality rates were -3.35%, -10.92%, -1.88% and -9.57%, respectively. The APC model showed that maternal disease incidence rate peaked at ages 25-29 years and mortality rate peaked at ages 20-24 years. Overall, the period and cohort rate ratio (RR) of incidence showed an increasing trend, while those for mortality declined. Compared with 1994, the number of maternal deaths due to maternal diseases decreased markedly across all age groups in 2023, with the highest number observed in the 30-34 years age group. The MMR decreased overall, but remained highest in the 50-54 years age group, while relatively higher MMR was also observed in the 10-14 years age group. Among major causes, maternal hypertensive disorders remained the leading cause of incidence, while indirect maternal causes became the leading cause of death, only maternal deaths due to human immunodeficiency virus exhibited an increase of 28.90%, while all other causes declined over the study period. **Conclusion** Over the past 30 years, substantial progress has been made in the prevention and control of maternal diseases in China, with overall declines in both incidence and mortality. However, the risk of incidence has shown a gradual increase in recent years. Greater attention should be given to women aged 20-34 years, while strengthened risk management is also needed for pregnancies at

extreme maternal ages, such as  $\leq 14$  years and  $\geq 50$  years. In addition, individual protection for high-risk groups, reproductive health education, and the management of high-risk pregnancies should be reinforced.

【Key words】 Pregnancy complications; Morbidity; Mortality; Joinpoint regression; Age-period-cohort model

## 临床报道

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# 多囊卵巢综合征患者睡眠时型与激素水平及精神状态的相关性研究

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【摘要】 目的 研究多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者睡眠时型与激素水平及焦虑抑郁的关系。方法 本研究为横断面研究, 采用便利抽样法, 选取 2024 年 7 月至 2025 年 6 月就诊于安徽医科大学第一附属医院生殖中心门诊的 140 例 PCOS 患者为 PCOS 组, 同期因输卵管因素或男方因素就诊的 116 例月经规律的非 PCOS 女性为对照组; 测定两组患者的身高、体质量、腰围; 观察并记录多毛及痤疮情况, 测定激素 [如卵泡刺激素 (follicle-stimulating hormone, FSH)、黄体生成素 (luteinizing hormone, LH)、雌二醇、睾酮、催乳素] 及糖脂代谢水平等; 计算稳态模型评估胰岛素抵抗指数 (homeostasis model assessment-insulin resistance index); 使用清晨型与夜晚型量表 (mornings-evenings questionnaire, MEQ) 评估睡眠时型, 匹兹堡睡眠质量指数 (Pittsburgh sleep quality index, PSQI) 量表获得睡眠质量信息, 医院焦虑抑郁量表 (hospital anxiety and depression scale, HADS) 评估焦虑抑郁情况, 用 1:1 的倾向性评分匹配 (propensity score matching, PSM) 方法匹配两组年龄、体质量指数 (body mass index, BMI)、腰围和月经情况, 以纠正混杂因素的影响, 并通过逐步线性回归分析 MEQ、PSQI 量表评分与性激素水平、糖代谢及焦虑抑郁的相关性。结果 PSM 后最终纳入 PCOS 组与对照组均 85 例, 两组 BMI、腰围差异均无统计学意义 (均  $P > 0.05$ )。PCOS 组患者的睡眠时型夜晚型占比 17.6% (15/85), 中间型占比 71.8% (61/85), 清晨型占比 10.6% (9/85), MEQ 评分 [ (47.60 ± 7.15) 分] 较对照组 [ (52.60 ± 7.89) 分] 低 ( $P < 0.001$ ); PCOS 组

睡眠障碍者(PSQI $\geq 7$ 分)占比48.2%(41/85),对照组睡眠障碍者占比31.5%(22/85),PCOS组PSQI总得分[6.00(5.00,7.00)分]显著高于对照组[5.00(3.00,7.00)分, $P<0.001$ ]。逐步线性回归分析显示PCOS组MEQ评分与睾酮水平、LH/FSH比值、HADS抑郁得分及HOMA-IR呈负相关( $\beta=-0.343, P<0.001$ ;  $\beta=-0.285, P=0.002$ ;  $\beta=-0.270, P=0.002$ ;  $\beta=-0.296, P=0.003$ ),与BMI呈正相关( $\beta=0.242, P=0.017$ );PSQI评分与HOMA-IR、HADS抑郁得分及LH/FSH比值呈正相关( $\beta=0.330, P=0.001$ ;  $\beta=0.220, P=0.029$ ;  $\beta=0.205, P=0.037$ )。结论 与非PCOS女性相比,PCOS患者睡眠时型更倾向于夜晚型,睡眠质量更差;睡眠时型与血清睾酮、LH水平、LH/FSH比值、HOMA-IR、BMI及抑郁状态有关。

【关键词】 多囊卵巢综合征; 昼夜节律; 睡眠时型; 睡眠质量; 胰岛素抵抗; 性激素; 焦虑; 抑郁

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### Associations study of sleep chronotype with hormone levels and mental state in patients with polycystic ovary syndrome

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【Abstract】 **Objective** To investigate the relationship between sleep chronotype, sex hormones, anxiety and depression in patients with polycystic ovary syndrome (PCOS). **Methods** This cross-sectional study employed convenience sampling to select 140 PCOS patients who visited the Reproductive Center Outpatient Clinic at the First Affiliated Hospital of Anhui Medical University from July 2024 to June 2025 as the PCOS group, and 116 non-PCOS women with regular menstrual cycles seeking treatment due to tubal or male factors during the same period as control group. For both groups, height, body weight, and waist circumference were measured; the presence of hirsutism and acne was observed and recorded; and hormone levels [including follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, testosterone, and prolactin] and glucose/lipid metabolism parameters were measured. The homeostasis model assessment-insulin resistance index (HOMA-IR) was calculated. The morningness-eveningness questionnaire (MEQ) was used to assess sleep chronotype, the Pittsburgh sleep quality index (PSQI) was used to obtain sleep quality information, and the hospital anxiety and depression scale (HADS) was used to evaluate anxiety and depression. A 1 : 1 propensity score matching (PSM) method was employed to match the two groups for age, body mass index (BMI), waist circumference, and menstrual status, thereby correcting for confounding factors. The correlations between MEQ/PSQI scores and sex hormone levels, glucose metabolism, as well as anxiety and depression were analyzed. **Results** After PSM, 85 cases were ultimately included in both the PCOS group and control group. BMI and waist circumference were not significantly different between the

two groups (both  $P>0.05$ ). Among the 85 PCOS patients, the proportions of evening sleep chronotypes were 17.6% (15/85), intermediate sleep chronotypes were 71.8% (61/85), and morning sleep chronotypes were 10.6% (9/85), respectively. The MEQ score ( $47.60\pm7.15$ ) in the PCOS group was significantly lower than that in control group ( $52.60\pm7.89$ ,  $P<0.001$ ). The proportion of patients with sleep disturbance ( $PSQI\geq 7$ ) was 48.2% (41/85) in the PCOS group and 31.5% (22/85) in control group. The total PSQI score in the PCOS group [6.00 (5.00, 7.00)] was significantly higher than that in control group [5.00 (3.00, 7.00),  $P<0.001$ ]. Stepwise linear regression analysis revealed that MEQ scores in the PCOS group were negatively correlated with testosterone levels ( $\beta=-0.343$ ,  $P<0.001$ ), LH/FSH ratio ( $\beta=-0.285$ ,  $P=0.002$ ), HADS depression scores ( $\beta=-0.270$ ,  $P=0.002$ ), and HOMA-IR ( $\beta=-0.296$ ,  $P=0.003$ ), while positively correlated with BMI ( $\beta=0.242$ ,  $P=0.017$ ). PSQI scores were positively correlated with HOMA-IR ( $\beta=0.330$ ,  $P=0.001$ ), HADS depression scores ( $\beta=0.220$ ,  $P=0.029$ ), and LH/FSH ratio ( $\beta=0.205$ ,  $P=0.037$ ). **Conclusion** Compared with non-PCOS women, patients in the PCOS group were more inclined to have an evening chronotype and poorer sleep quality. Sleep chronotype was associated with serum testosterone, LH levels, LH/FSH ratio, HOMA-IR, BMI, and depressive state.

**【 Key words 】** Polycystic ovary syndrome; Circadian rhythm; Sleep chronotype; Sleep quality; Insulin resistance; Sex hormones; Anxiety; Depression

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·临床报道·

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# 早孕不完全性药物流产清宫风险预测模型的构建与评价

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**【摘要】** 目的 探索构建早孕不完全性药物流产清宫机器学习 (machine learning, ML) 预测模型并进行预测效果评估。方法 本研究为回顾性队列研究, 收集 2023 年 1 月至 2024 年 6 月期间在杭州市妇产科医院计划生育科行早孕药物流产对象的临床资料 411 例, 其中非手术治疗组 300 例, 手术清宫组 111 例。分析不完全性药物流产的相关因素, 采用 logistic 回归、K 近邻、支持向量分类器、随机森林 (random forest, RF)、极端梯度提升 (extreme gradient boosting, XGBoost)、轻量级梯度提升机 (light gradient boosting machine, LightGBM)、梯度提升决策树 (gradient boosting decision tree, GBDT) 7 种 ML 方法构建不完全性药物流产清宫全变量和简约预测模型并评估和比较其预测效果。结果 采用不同 ML 方法构建的不完全性药物流产清宫全模型预测受试者工作特征曲线下面积 (area under the curve, AUC) 介于 0.696~0.790 之间, 其中 RF、GBDT、XGBoost、LightGBM 四种模型的 AUC 均值略高 (0.77~0.79 之间), 准确率在 0.75~0.79。分析结果提示, 药物流产后第一次复查血人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG)、孕妇体质量指数、第一次复查残留物直径、超声阻力指数 (resistance index, RI) 以及孕妇年龄等 5 个指标对不完全性药物流产清宫风险预测贡献度最大。纳入这 5 个变量构建不完全性药物流产清宫简约预测模型, 其 AUC 是全变量模型的 96.5%~99.9%。结论 ML 预测模型能较好预测不完全性药物流产清宫发生风险。包含流产后第一次复查血  $\beta$ -hCG、残留物直径、超声 RI 以及孕妇体质量指数和年龄等 5 个指标的简约预测模型可基本替代全变量模型, 且具有相似的预测效能, 具有较高的应用价值。

**【关键词】** 早孕; 不完全性药物流产; 预测模型; 应用价值

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## Development and validation of a machine learning model for predicting incomplete medication abortion requiring uterine curettage in early pregnancy

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**【Abstract】 Objective** To develop and validate machine learning (ML) models for predicting the risk of incomplete medication abortion requiring uterine curettage during early pregnancy. **Methods** A retrospective cohort study was conducted to collect the clinical data of 411 patients who underwent first-trimester medication abortion at the Family Planning Department of Hangzhou Maternity and Child Health Care Hospital from January 2023 to June 2024, including 300 cases in the non-surgical treatment group and 111 cases in the surgical curettage group. Factors associated with incomplete medication abortion were analyzed, and 7 ML algorithms such as logistic regression, KNeighbors, support vector classifier, random forest (RF), extreme gradient boosting (XGBoost),

light gradient boosting machine (LightGBM) and gradient boosting decision tree (GBDT), were adopted to construct full-predictor models and parsimonious prediction models for uterine curettage due to incomplete medication abortion. The predictive efficacy of the models was evaluated and compared by the area under the receiver operating characteristic curve (AUC). **Results** The AUC of the full-predictor models constructed by different ML methods ranged from 0.696 to 0.790, among them, the average AUC of RF, GBDT, XGBoost and LightGBM models was slightly higher (between 0.77 and 0.79), and the accuracy was between 0.75 and 0.79. The analysis identified five predictors with the highest contribution to the risk prediction of uterine curettage for incomplete medication abortion, namely serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) level at the first post-abortion follow-up, maternal body mass index (BMI), diameter of retained products of conception on the first follow-up ultrasonography, ultrasonic resistance index (RI), and maternal age. The parsimonious model incorporating these five variables achieved an AUC accounting for 96.5% to 99.9% of that of the full-predictor models. **Conclusion** ML models have good performance in predicting the risk of uterine curettage due to incomplete medication abortion during early pregnancy. The parsimonious model based on five key indicators, such as serum  $\beta$ -hCG level at the first post-abortion follow-up, diameter of retained products of conception, ultrasonic RI, maternal BMI and maternal age, can basically replace the full-predictor models with similar predictive efficacy, and thus has high clinical application value.

**【Key words】** Early pregnancy; Incomplete medication abortion; Prediction model; Application value

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循证医学

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## 集合培养与单胚胎培养对胚胎发育和临床结局影响的 meta 分析

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**【摘要】** 目的 比较微滴培养中集合培养模式与单胚胎培养模式对胚胎发育和临床结局的影响, 为辅助生殖技术中的胚胎培养决策提供科学依据。方法 检索 PubMed、Cochrane Library、Embase、Web of Science、中国生物医学文献数据库、中国知网、维普中文科技期刊数据库及万方数据库, 纳入比较集合培养与单胚胎培养的随机对照试验和回顾性队列研究。检索时限均从建库至 2025 年 11 月 7 日。结局指标包括卵裂率、第 3 天优质胚胎率、囊胚形成率、临床妊娠率、着床率和活产率。采用 R 软件 meta 程序包进行 meta 分析。结果 共纳入 8 项原始研究, 包括 29 134 枚胚胎。Meta 分析结果显示, 与单胚胎培养相比, 集合培养的卵裂率 ( $OR=1.24$ , 95%  $CI$ : 0.88~1.75,  $P=0.21$ )、第 3 天优质胚胎率 ( $OR=1.03$ , 95%  $CI$ : 0.94~1.12,  $P=0.54$ )、囊胚形成率 ( $OR=0.92$ , 95%  $CI$ : 0.79~1.06,  $P=0.25$ )、临床妊娠率 ( $OR=1.10$ , 95%  $CI$ : 0.90~1.34,  $P=0.35$ ) 和着床率 ( $OR=1.00$ , 95%  $CI$ : 0.86~1.15,  $P=0.98$ ) 差异均无统计学意义。集合培养的活产率虽高于单胚胎培养 ( $OR=1.49$ , 95%  $CI$ : 1.05~2.12,  $P=0.03$ ), 但纳入研究仅 2 篇, 若以活产胎儿数/移植胚胎数校正后, 则差异无统计学意义 ( $OR=1.30$ , 95%  $CI$ : 0.99~1.71,  $P=0.06$ )。结论 除活产率证据尚不确定外, 集合培养模式与单胚胎培养模式在卵裂率、第 3 天优质胚胎率、囊胚形成率、临床妊娠率及着床率上相当, 但该结论的普适性仍需更多高质量研究加以验证。

**【关键词】** Meta 分析; 胚胎培养; 微滴培养; 集合培养  
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## Meta-analysis of the effects of group culture versus single embryo culture on embryo development and clinical outcomes

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**【Abstract】 Objective** To compare the effects of group culture and single embryo culture in microdroplet systems on embryo development and clinical outcomes, providing scientific evidence for embryo culture decisions in assisted reproductive technology. **Methods** We searched PubMed, Cochrane Library, Embase, Web of Science, CBM, CNKI, VIP and Wanfang Data for randomized controlled trials and retrospective cohort studies comparing group culture with single embryo culture. The search period spanned from the inception of each database to November 7, 2025. Outcome measures included cleavage rate, day 3 high-quality embryo rate, blastocyst formation rate, clinical pregnancy rate, implantation rate, and live birth rate. Meta-analysis was performed using the meta package in R software. **Results** A total of 8 original studies involving 29 134 embryos were included. Meta-analysis revealed no significant differences between group culture and single embryo culture in cleavage rate ( $OR=1.24$ , 95%  $CI$ : 0.88–1.75,  $P=0.21$ ), day 3 high-quality embryo rate ( $OR=1.03$ , 95%  $CI$ : 0.94–1.12,  $P=0.54$ ), blastocyst formation rate ( $OR=0.92$ , 95%  $CI$ : 0.79–1.06,  $P=0.25$ ), clinical pregnancy rate ( $OR=1.10$ , 95%  $CI$ : 0.90–1.34,  $P=0.35$ ), or implantation rate ( $OR=1.00$ , 95%  $CI$ : 0.86–1.15,  $P=0.98$ ). Although group culture showed a higher live birth rate than single embryo culture ( $OR=1.49$ , 95%  $CI$ : 1.05–2.12,  $P=0.03$ ), this

finding was based on only two studies. After adjusting for the number of live births per embryo transferred, the difference became statistically non-significant ( $OR=1.30$ , 95%  $CI$ : 0.99–1.71,  $P=0.06$ ). **Conclusion** Except for the uncertain evidence regarding live birth rates, the cleavage rate, day 3 high-quality embryo rate, blastocyst formation rate, clinical pregnancy rate, and implantation rate are comparable between group culture and single embryo culture modes. However, the generalizability of this conclusion still requires further validation through more robust evidence from high-quality studies.

**【Key words】** Meta-analysis; Embryo culture; Microdroplet culture; Group culture

**Fund program:** Gansu Provincial Health Industry Scientific Research Program (GSWSKY2023-43)

## 生殖医学伦理

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# 儿童与青少年生育力保存: 技术前沿、伦理困境与我国临床实践

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**【摘要】** 随着儿童及青少年恶性肿瘤生存率显著提升, 性腺毒性治疗导致的生育力损伤已成为癌症幸存者的长期困扰。生育力保存 (fertility preservation, FP) 是应对这一困扰的重要手段。由于儿童性腺尚未成熟, 常规的精子或卵母细胞冷冻方法不适用, 卵巢组织冷冻 (ovarian tissue cryopreservation, OTC) 与“实验性”的睾丸组织冷冻 (testicular tissue cryopreservation, TTC) 成为其主要甚至唯一的选择。本文回顾了儿童与青少年 OTC 和 TTC 的技术前沿与存在问题, 探讨了其背后复杂的伦理困境, 包括知情同意、最佳利益原则、实验性技术应用及社会公平, 针对当前中国面临的问题, 提出构建以标准化的多学科协作模式为核心、完善的政策框架为支撑的 FP 体系。

**【关键词】** 生育力保存; 肿瘤生育学; 儿童; 青少年; 卵巢组织冷冻; 睾丸组织冷冻; 多学科协作

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## Fertility preservation in children and adolescents: technological frontiers, ethical dilemmas and clinical practice in China

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**【Abstract】** Recent years have seen a remarkable improvement in the survival rates of children and adolescents with malignancies. Consequently, fertility impairment resulting from gonadotoxic treatments has emerged as a long-term concern for cancer survivors. Fertility preservation (FP) represents a crucial strategy to mitigate this challenge. Given the immaturity of gonads in pediatric patients, conventional methods such as sperm or oocyte cryopreservation are often unsuitable. This makes ovarian tissue cryopreservation (OTC) and the still-experimental testicular tissue cryopreservation (TTC) the primary, and sometimes sole, available options. This article reviews the technological frontiers and existing problems of OTC and TTC for children and adolescents. It delves into the ethical dilemmas underlying these practices, including informed consent, the principle of the child's best interests, the application of experimental technologies, and social equity. Focusing on the practice in China, we highlight obstacles and propose the establishment of a comprehensive FP system, centered on a standardized multidisciplinary team model, and supported by comprehensive policy frameworks.

**【Key words】** Fertility preservation; Oncofertility; Children; Adolescents; Ovarian tissue cryopreservation; Testicular tissue cryopreservation; Multidisciplinary team

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## 生殖医学伦理

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## 时差成像技术在人类辅助生殖医疗中的伦理挑战与治理路径

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**【摘要】** 在人类辅助生殖技术中, 胚胎选择是提升妊娠率的关键环节。时差成像技术 (time-lapse imaging, TLI) 可在不干扰胚胎体外培养环境的前提下, 持续记录胚胎发育的过程, 实现动态监测。结合形态动力学算法, TLI 系统能够依据胚胎的发育特征和时间进行潜能的预测, 并支持远程查看、视频生成, 不仅有助于优化胚胎选择流程与临床决策, 亦被患者视为记录生育过程的纪念。然而, 尽管 TLI 技术具有一定潜力和便利性, 在带来技术优化的同时, 也引发一系列尚待回应的伦理挑战, 包括其提升妊娠率的循证依据不足、商业化推广过程中的资源分配不均与经济负担增加、医患沟通与知情同意的问题, 以及与人工智能结合后数据采集、使用及隐私保护的风险。本文主要聚焦于 TLI 技术的有效性、商业化趋势、患者自主权及数据治理四个方面, 并据此提出相关伦理治理建议, 以期推动 TLI 技术在生殖医学中的规范应用, 平衡好技术创新与伦理责任。

**【关键词】** 时差成像; 生殖技术, 辅助; 胚胎选择; 科技伦理治理  
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## **Ethical challenges and governance pathways of time-lapse imaging technology in human assisted reproductive medicine**

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**【Abstract】** In human assisted reproductive technology, embryo selection is essential for improving pregnancy rates. Time-lapse imaging (TLI) enables continuous monitoring of embryo development without disturbing the culture environment. Combined with morphokinetic algorithms, TLI can predict embryo potential based on developmental characteristics and timing, and supports remote viewing and video generation. It is not only helpful to optimize the embryo selection process and clinical decision-making but also regarded by patients as a way to record the reproductive process. However, while TLI offers certain potential and convenience, technological advances in this area also raise a range of ethical challenges that must be addressed. These include limited evidence for its efficacy in improving pregnancy outcomes, unequal resource distribution and financial burdens linked to commercialization, issues in clinician-patient communication and informed consent, and risks related to data collection, usage, and privacy when integrated with artificial intelligence. This paper examines TLI's effectiveness, commercialization, patient autonomy, and data governance, and proposes ethical governance strategies to guide its regulated application in reproductive medicine, balancing technological innovation with ethical responsibility.

**【Key words】** Time-lapse imaging; Reproductive technology, assisted; Embryo selection; Ethical governance of technology

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## 综述

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## 社会支持对育龄期多囊卵巢综合征患者的影响

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**【摘要】** 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是育龄期女性最常见的内分泌代谢紊乱疾病, 表现为月经紊乱、糖脂代谢异常、生育障碍及焦虑抑郁等, 形成生殖代谢异常与心理应激之间的双向恶性循环, 严重影响女性的心理、生殖健康和生活质量。研究表明, 受地区、经济及文化等因素影响, 育龄期 PCOS 女性在生育管理 (如生活方式调整、药物干预等) 方面存在诸多问题, 包括认知不足、焦虑抑郁情绪及治疗依从性差等。社会支持作为 PCOS 整体治疗策略的重要组成部分, 不仅有助于缓解患者的心理压力、提高治疗依从性, 还可协同其他治疗方式增强疗效, 进而改善亲密关系和生育结局。因此, 加强医疗干预并构建全方位的社会支持体系显得尤为迫切。本综述通过系统梳理相关文献, 聚焦当前育龄期 PCOS 女性社会支持干预策略, 分析现有研究的不足, 旨在为优化患者诊疗过程中的社会支持提供理论依据。

**【关键词】** 多囊卵巢综合征; 社会支持; 育龄期; 研究进展

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### Impact of social support on women with polycystic ovary syndrome in the reproductive age

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**【 Abstract 】** Polycystic ovary syndrome (PCOS) is the predominant endocrine and metabolic disorder among women of reproductive age, characterized by menstrual irregularities, abnormal glucose and lipid metabolism,

fertility issues, and anxiety and depression. This condition establishes a bidirectional detrimental loop between disrupted reproductive function and mental well-being, significantly impacting women's psychological and reproductive health as well as their overall quality of life. Research indicates that women with PCOS encounter challenges in fertility management, such as inadequate awareness, anxiety, depression, and poor adherence to treatment, influenced by geographical, economic, and cultural factors. Social support plays a pivotal role in the comprehensive management of PCOS, contributing not only to alleviating psychological strain and enhancing treatment compliance, but also synergizing with other therapeutic approaches to improve treatment outcomes, intimate relationships, and fertility prospects. There is an urgent need to bolster medical interventions and establish a holistic social support framework. This review critically examines the current literature, with a specific focus on social support interventions for women with PCOS of reproductive age, identifying gaps in existing research. The aim is to offer a theoretical foundation for optimizing social support provision during patient diagnosis and treatment.

**【Key words】** Polycystic ovary syndrome; Social support; Reproductive age; Research advances

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## 子宫内膜异位症致早发性卵巢功能不全的机制进展

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**【摘要】** 子宫内膜异位症 (endometriosis, EMS) 是育龄期女性常见疾病, 其导致早发性卵巢功能不全 (premature ovarian insufficiency, POI) 的机制复杂。近年来的研究显示 EMS 通过局部解剖学改变与异位内膜细胞侵袭、免疫逃逸与炎症微环境、血管生成与缺氧微环境、表观遗传学改变、代谢紊乱与激素调控异

常等多个机制共同作用，导致 POI 的发生发展。本文将对以上几个方面进行综述，  
以为 EMS 导致 POI 的发病机制的研究提供新线索，为疾病精准诊疗提供新思路。

【关键词】 子宫内膜异位症； 早发性卵巢功能不全； 免疫逃逸； 表观遗传学； 炎症微环境

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**Advances in the mechanisms of endometriosis-induced premature ovarian insufficiency**

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【 Abstract 】 Endometriosis (EMS) is a common disease in women of reproductive age, and its role in the development of premature ovarian insufficiency (POI) involves a complex interplay of mechanisms. Recent studies have shown that EMS contributes to the development and progression of POI through multiple interconnected mechanisms, including local anatomical alterations and ectopic endometrial cell invasion, immune evasion and inflammatory microenvironment, angiogenesis and hypoxic microenvironment, epigenetic changes, as well as metabolic disorders and abnormal hormonal regulation. Therefore, this article aims to summarize the above aspects, offering new insights into the pathogenesis of POI caused by EMS and suggesting novel strategies for the precise diagnosis and treatment of the disease.

【 Key words 】 Endometriosis; Premature ovarian insufficiency; Immune escape; Epigenetics; Inflammatory microenvironment

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综述

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**卵巢内注射富血小板血浆治疗卵巢储备功能减退的临床应用及机制研究进展**

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**【摘要】** 卵巢储备功能减退 (diminished ovarian reserve, DOR) 患者生育能力降低, 自然受孕困难, 临床上常依赖辅助生殖技术助孕。然而此类患者常合并卵巢低反应等, 导致辅助助孕结局不佳。因此, 改善 DOR 患者的卵巢功能及生育结局仍是亟待解决的临床挑战。富血小板血浆 (platelet-rich plasma, PRP) 富含多种生物活性因子, 作为一种新兴的再生医学疗法, 卵巢内注射 PRP 有望改善卵巢储备功能, 并可能提高助孕妊娠率与活产率, 日益受到研究者关注。本文将从卵巢内注射 PRP 治疗 DOR 的机制及临床应用、PRP 治疗的局限性与安全性等方面展开论述, 客观评价其临床疗效, 评估其在 DOR 患者治疗中的应用前景。

**【关键词】** 富血小板血浆; 卵巢储备功能减退; 生育能力低下; 临床应用

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## Progress in the mechanism and clinical application of intra-ovarian injection of platelet-rich plasma in the treatment of diminished ovarian reserve

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**【Abstract】** Patients with diminished ovarian reserve (DOR) experience reduced fertility and face significant challenges in achieving natural conception, making them clinically dependent on assisted reproductive technology for assistance. However, such patients frequently exhibit poor ovarian response, which negatively impacts assisted reproductive pregnancy outcomes. Consequently, enhancing ovarian reserve and improving reproductive outcomes in DOR patients remain pressing clinical challenges. Platelet-rich plasma (PRP), rich in various biological factors, represents an emerging regenerative therapy. Intra-ovarian injection of PRP has been investigated as a potential intervention to improve ovarian reserve function. This approach may enhance the success rate of assisted reproductive technology, including clinical pregnancy rate and live birth rate, and has consequently garnered increasing attention from researchers. This article reviews the latest progress in the mechanism, clinical application, limitations and safety of intra-ovarian injection of PRP, to objectively assess its clinical merit and the future prospects.

**【Key words】** Platelet-rich plasma; Diminished ovarian reserve; Subfertility; Clinical application

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