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·MDT 专家视角专栏·

## 子宫腺肌病与流产

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**【摘要】** 子宫腺肌病是常见的妇科疾病, 30~45 岁经产妇多发。子宫腺肌病相关的流产等生育问题受到关注。本文综述了子宫腺肌病与流产的相关性、病理机制及临床处理。

**【关键词】** 子宫腺肌病; 流产; 病理机制; 临床处理

### Adenomyosis and miscarriage

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**【Abstract】** Adenomyosis is a common gynecological disease, and it is more common in multiparous women aged 30-45 years. Fertility problems such as adenomyosis-related miscarriage are of concern. This article reviewed the correlation, pathological mechanism and clinical management of adenomyosis related miscarriage.

**【Key words】** Adenomyosis; Miscarriage; Pathological mechanism; Clinical management

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·MDT 专家视角专栏·

# 行辅助生殖技术助孕的子宫腺肌病孕产妇的产科管理

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**【摘要】** 子宫腺肌病是妇科良性疾病, 却是导致育龄期妇女不孕及发生不良妊娠结局的重要原因之一。已有部分研究报道了妊娠合并子宫腺肌病可导致早产等不良妊娠结局的发生, 但目前妊娠合并子宫腺肌病孕妇的产科管理仍未引起足够的重视。本文聚焦子宫腺肌病并发不孕患者通过辅助生殖技术妊娠后的围产期管理难点(高危产科), 包括子宫腺肌病对妊娠不良结局的原因及影响, 风险因素的评估, 建立妊娠风险评分系统(量表)或风险预测模型等问题做综述。

**【关键词】** 子宫腺肌病; 不孕症; 孕期管理

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## Obstetric management of pregnant women with adenomyosis undergoing assisted reproductive technology

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**【Abstract】** Adenomyosis is a benign gynecological disease, but it is one of the important causes of infertility and adverse pregnancy outcomes in women of childbearing age. Some studies have reported that pregnancy with adenomyosis can lead to premature delivery and other adverse pregnancy outcomes, but the obstetric management of pregnant women with adenomyosis has not attracted enough attention at present. This paper reviewed the obstetric management difficulty (high-risk obstetric) of pregnant women with adenomyosis after conception of assisted reproduction for infertility, including the causes and effects of adenomyosis on adverse pregnant outcomes, the risk factors of adenomyosis, and evaluation and establish of pregnancy risk scoring system (scale) or risk prediction model.

**【Key words】** Adenomyosis; Infertility; Pregnancy management

**Fund program:** General Project of Chongqing Natural Science Foundation (cstc2021jcyj-msxmX0206)

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# 低预后人群拮抗剂方案中不同扳机时机对临床结局的影响

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**【摘要】** 目的 探讨在拮抗剂方案中, 低预后人群选择不同扳机时机对临床结局产生的影响。方法 筛选 2017 年 1 月至 2019 年 6 月期间在河南省人民医院生殖中心进行拮抗剂方案助孕的波塞冬标准下的低预后患者资料共 1613 个周期进行回顾性队列研究, 根据不同扳机时机分为 3 组, 按照常规标准扳机为正常组 (961 个周期), 提前 1d 扳机为提前组 (359 个周期), 推迟 1d 扳机为推迟组 (293 个周期)。通过单因素分析、多元 logistics 回归分析等方法比较不同扳机时机对累积妊娠率、累积活产率等临床结局的影响。结果 三组患者鲜胚移植妊娠率分别为提前组 35.77% (44/123)、正常组 39.16% (150/383)、推迟组 34.01% (50/147)。三组患者累积妊娠率和累积活产率由低到高依次为提前组、正常组、推迟组, 组间比较差异均有统计学意义 [累积妊娠率为 33.18% (72/217)、42.33% (276/652)、45.27% (91/201),  $P=0.024$ ; 累积活产率为 22.97% (48/209)、31.96% (201/629)、35.90% (70/159),  $P=0.012$ ]。经过多元 logistics 回归调整混杂因素后, 结果显示提前和推迟扳机与正常扳机相比, 对临床结局的影响无统计学意义 [推迟组的鲜胚移植妊娠率  $OR$  (95%  $CI$ ) = 0.69 (0.44~1.09),  $P=0.114$ ; 累积妊娠率  $OR$  (95%  $CI$ ) = 0.77 (0.51~1.16),  $P=0.214$ ; 累积活产率  $OR$  (95%  $CI$ ) = 0.83 (0.54~1.29),  $P=0.418$ ; 提前组的鲜胚移植妊娠率  $OR$  (95%  $CI$ ) = 0.98 (0.60~1.60),  $P=0.934$ ; 累积妊娠率  $OR$  (95%  $CI$ ) = 0.87 (0.58~1.30),  $P=0.513$ ; 累积活产率  $OR$  (95%  $CI$ ) = 0.86 (0.54~1.35),  $P=0.515$ ]。结论 波塞冬低预后人群在拮抗剂方案中按照常规标准进行扳机可获得理想的临床结局, 可以综合考虑患者的个体情况进行扳机。

**【关键词】** 累积活产率; 累积妊娠率; 低预后; 拮抗剂; 扳机时机  
基金项目: 2020 年辅助生殖中青年医生研究项目

**Effect of trigger timing on clinical outcomes of low prognosis patients with gonadotropin-releasing hormone antagonist**

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**【Abstract】 Objective** To investigate the effect of altering trigger timing on clinical outcomes of low prognosis patients with gonadotropin-releasing hormone (GnRH) antagonist. **Methods** A retrospective cohort study was conducted on 1613 cycles of low prognosis patients based on POSEIDON criteria undergoing *in vitro* fertilization-embryo transfer (IVF-ET) with GnRH antagonist protocol between January 2017 to June 2019 in Reproductive Medicine Center, Henan Provincial People's Hospital. Patients were divided into 3 groups depending on different trigger timing criteria (conventional trigger group,  $n=961$ ; advanced trigger group,  $n=359$ ; delayed trigger group,  $n=293$ ). Univariate analysis and multivariate logistic regression analysis were used to analyze the effect of trigger timing on clinical outcomes such as cumulative pregnancy rate (CPR) and cumulative live birth rate (CLBR) among different groups. **Results** The clinical pregnancy rate of fresh cycle in advanced trigger group, conventional trigger group, delayed trigger group were 35.77% (44/123), 39.16% (150/383), 34.01% (50/147), respectively. CPR and CLBR ranked from low to high in order of advanced trigger group, conventional trigger group and delayed trigger group [CPR: 33.18% (72/217) vs. 42.23% (276/652) vs. 45.27% (91/201),  $P=0.024$ ; CLBR: 22.97% (48/209) vs. 31.96% (201/629) vs. 35.90% (70/159),  $P=0.012$ ]. The result of multivariate logistics regression analysis showed that there were no significant differences on clinical pregnancy rate, CPR and CLBR among three groups [delayed trigger group: the clinical pregnancy rate in fresh cycle  $OR(95\% CI)=0.69(0.44-1.09)$ ,  $P=0.114$ ; CPR  $OR(95\% CI)=0.77 (0.51-1.16)$ ,  $P=0.214$ ; CLBR  $OR(95\% CI)=0.83(0.54-1.29)$ ,  $P=0.418$ ; advanced trigger group: the clinical pregnancy rate in fresh cycle  $OR(95\% CI)=0.98(0.60-1.60)$ ,  $P=0.934$ ; CPR  $OR(95\% CI)=0.87(0.58-1.30)$ ,  $P=0.513$ ; CLBR  $OR(95\% CI)=0.86(0.54-1.35)$ ,  $P=0.515$ ]. **Conclusion** Conventional trigger could obtain the ideal clinical outcomes in low prognosis patients based on POSIDON criteria with GnRH antagonist. Different trigger timing may enable the flexibility of cycle scheduling.

**【Key words】** Cumulative live birth rate; Cumulative pregnancy rate; Low prognosis; Gonadotropin-releasing hormone antagonist; Trigger timing

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·临床研究·



# 多囊卵巢综合征对新鲜胚胎移植周期中单胎出生婴儿体质量的影响

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**【摘要】** 目的 探讨新鲜胚胎移植周期中多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者出生婴儿体质量情况及其影响因素。方法 回顾性队列研究 2014 年 1 月至 2019 年 12 月期间在郑州大学第一附属医院生殖医学中心行体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 助孕并有单胎活产的 5087 例患者的临床资料。患者根据不孕原因分为 PCOS 组 ( $n=1095$ ) 和非 PCOS 组 (记为对照组,  $n=3992$ ), 比较两组一般情况及出生婴儿体质量差异, logistic 回归分析影响婴儿出生体质量的因素。结果 第 3 日 (day 3, D3) 胚胎移植 PCOS 组临床妊娠率 [69.0% (1248/1808)]、种植率 [49.0% (1742/3555)] 均高于对照组 [59.1% (5661/9572)、42.0% (7577/18 040), 均  $P<0.001$ ], 而活产率 [37.0% (670/1810)] 低于对照组 [49.0% (4697/9585),  $P<0.001$ ]。第 5 日 (day 5, D5) 囊胚移植 PCOS 组种植率 [63.1% (500/793)]、活产率 [54.0% (425/787)] 高于对照组 [59.0% (1066/1806),  $P=0.042$ ; 48.0% (876/1825),  $P=0.013$ ]。D5 囊胚移植 PCOS 组婴儿出生体质量 [ $(3\ 459.76\pm527.11)$  g]、超重儿比例 [14.35% (61/425)] 高于对照组 [ $(3\ 391.61\pm521.38)$  g,  $P=0.028$ ; 8.22% (72/876),  $P<0.001$ ] 和 D3 胚胎移植 PCOS 组 [ $(3\ 389.24\pm555.06)$  g,  $P=0.018$ ; 9.25% (62/670),  $P=0.009$ ], 但低体质量儿比例 [2.35% (10/425)] 低于 D5 囊胚移植对照组 [4.91% (43/876),  $P=0.029$ ] 和 D3 胚胎移植 PCOS 组 [4.78% (32/670),  $P=0.042$ ]; logistic 回归分析显示女方体质量指数 (body mass index, BMI) 影响 D5 囊胚移植的出生婴儿体质量 ( $OR=1.12$ , 95%  $CI=0.052\sim0.175$ ,  $P<0.001$ ); 移植胚胎的发育时间影响 PCOS 患者的出生婴儿体质量 ( $OR=1.52$ , 95%  $CI=0.019\sim0.819$ ,  $P=0.040$ )。结论 PCOS 患者 D5 囊胚移植可获得更高的活产率和更低低出生体质量儿比例, 对 PCOS 患者建议新鲜周期进行囊胚移植。

**【关键词】** 多囊卵巢综合征; 出生婴儿体质量; 新鲜移植; 单囊胚移植

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## Effect of polycystic ovary syndrome on body weight of singleton infants in fresh embryo transfer cycle

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**【Abstract】 Objective** To explore the newborn birth weight and its influencing factors of polycystic ovary syndrome (PCOS) patients during fresh embryo transfer cycle. **Methods** In this retrospective cohort study, the clinical data of 5087 patients with singleton live births who underwent *in vitro* fertilization and embryo transfer (IVF-ET) in the Reproductive Medicine Center of the First Affiliated Hospital of Zhengzhou University from January 2014 to December 2019 were analyzed. The patients were categorized into PCOS group ( $n=1095$ ) and non-PCOS group (referred to as control group,  $n=3992$ ) according to the cause of infertility. The general conditions and birth weight of the two groups were compared, and logistic regression analysis was performed to identify the factors affecting birth weight. **Results** For embryo transfer on the 3rd day (day 3, D3), the clinical pregnancy rate [69.0% (1248/1808)] and the implantation rate [49.0% (1742/3555)] in PCOS group were higher than those in control group [59.1% (5661/9572) and 42.0% (7577/18 040), all  $P<0.001$ ], while the live birth rate [37.0% (670/1810)] was lower than that in control group [49.0% (4697/9585),  $P<0.001$ ]. For blastocyst transfer on the 5th day (day 5, D5), the implantation rate [63.1% (500/793)] and the live birth rate [54.0% (425/787)] in PCOS group were higher than those of control group [59.0% (1066/1806),  $P=0.042$ ; 48.0% (876/1825),  $P=0.013$ ]. The birth weight of the infants [(3 459.76 $\pm$ 527.11) g] and the proportion of overweight infants [14.35% (61/425)] in PCOS group of D5 blastocyst transfer were higher than those in control group [(3 391.61 $\pm$ 521.38) g,  $P=0.028$ ; 8.22% (72/876),  $P<0.001$ ] and PCOS group of D3 embryo transfer [(3 389.24 $\pm$ 555.06) g,  $P=0.018$ ; 9.25% (62/670),  $P=0.009$ ], but the proportion of low weight infants [2.35% (10/425)] was lower than that in control group of the D5 blastocyst transfer [4.91% (43/876),  $P=0.029$ ] and PCOS group of D3 embryo transfer [4.78% (32/670),  $P=0.042$ ]. Logistic regression analysis showed that the level of female body mass index (BMI) affects the birth weight of D5 blastocyst transfer ( $OR=1.12$ , 95%  $CI=0.052-0.175$ ,  $P<0.001$ ). Developmental timing of transferred embryos affects birth weight in PCOS patients ( $OR=1.52$ , 95%  $CI=0.019-0.819$ ,  $P=0.040$ ). **Conclusion** For PCOS patients, choosing D5 blastocyst transfer can obtain a higher rate of live birth and a lower proportion of low birth weight infants. It is recommended that blastocyst transfer be performed for PCOS patients in fresh cycle.

**【 Key words 】** Polycystic ovary syndrome; Birth weight; Fresh transplantation; Single blastocyst transfer

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# 应用赠卵与自卵行 ICSI-FET 助孕的围产期结局的比较分析

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**【摘要】** 目的 比较不孕女性应用赠卵与自卵行卵胞质内单精子注射-冻融胚胎移植 (intracytoplasmic sperm injection and frozen-thawed embryo transfer, ICSI-FET) 助孕治疗的围产期结局。方法 回顾性队列研究分析 2016 年 6 月至 2020 年 1 月期间在郑州大学第三附属医院生殖医学中心行 ICSI-FET 并临床妊娠的患者的临床资料。纳入应用赠卵的 73 例患者 (受卵组) 和同期应用自卵的 550 例患者 (自卵组), 利用倾向性评分匹配 (propensity score matching, PSM) 对其匹配得到受卵组 47 例和自卵组 131 例, 比较两组患者基线数据和围产期结局的差异, 应用多因素 logistic 回归与线性回归分析影响其围产期结局的危险因素。结果 受卵组的双侧窦卵泡计数 ( $3.08 \pm 4.78$ ) 和基础雌二醇水平 [ $(71.55 \pm 45.29)$  pmol/L] 均显著低于自卵组 [ $14.95 \pm 6.42$ , ( $132.84 \pm 74.89$ ) pmol/L, 均  $P < 0.001$ ]。受卵组单胎活产的新生儿出生体质量 [ $(2\ 916.48 \pm 537.55)$  g] 低于自卵组 [ $(3\ 326.67 \pm 503.43)$  g], 差异有统计学意义 ( $P < 0.001$ )。受卵组和自卵组相比, 早产率 [21.28% (10/47) 比 16.03% (21/131),  $P = 0.416$ ] 和妊娠期高血压疾病发生率 [12.77% (6/47) 比 7.63% (10/131),  $P = 0.448$ ] 均有升高趋势, 但差异均无统计学意义。赠卵 ICSI-FET 降低了单胎的新生儿出生体质量 (MD = -388.225, 95% CI = -625.914 ~ -150.537,  $P = 0.002$ )。结论 赠卵 ICSI-FET 围产期结局相对安全, 但其单胎活产的新生儿出生体质量低于自卵 ICSI-FET。

**【关键词】** 精子注射, 细胞质内; 冻融胚胎移植; 赠卵; 自卵; 围产期结局

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**Comparative analysis of perinatal outcome of intracytoplasmic sperm injection and frozen-thawed embryo transfer between donor and autologous oocytes**

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**【 Abstract 】 Objective** To investigate the obstetric outcomes of intracytoplasmic sperm injection and frozen-thawed embryo transfer (ICSI-FET) between donor and autologous oocytes. **Methods** A retrospective cohort study was conducted to analyze the clinical data of pregnant patients who underwent ICSI-FET in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from June 2016 to January 2020. Totally 73 patients with donor oocytes, and 550 patients who used autologous oocytes in the same period, and the patients were matched at 1 : 3 with propensity score matching (PSM), then there were 47 patients in donor group and 131 patients in autologous group. The general conditions and obstetric outcomes were compared among donor group and autologous group. Multivariate logistic regression and linear regression were applied to analyze the factors affecting perinatal complications. **Results** The bilateral antral follicle count ( $3.08 \pm 4.78$ ) and basal estradiol level [ $(71.55 \pm 45.29)$  pmol/L] in donor group were significantly lower than those in autologous group [ $14.95 \pm 6.42$ , ( $132.84 \pm 74.89$ ) pmol/L, all  $P < 0.001$ ]. The birth weight of singleton in donor group [ $(2\ 916.48 \pm 537.55)$  g] was lower than that in autologous group [ $(3\ 326.67 \pm 503.43)$  g], and there was significant difference ( $P < 0.001$ ). There were no significant differences in premature birth rate [21.28% (10/47) vs. 16.03% (21/131),  $P = 0.416$ ] and incidence of hypertensive disorder complicating pregnancy [12.77% (6/47) vs. 7.63% (10/131),  $P = 0.448$ ] between donor group and autologous group, but both of them had an increasing trend in donor group. Oocyte-donated ICSI-FET reduced the birth weight of singleton (MD=-388.225, 95% CI=-625.914--150.537,  $P = 0.002$ ). **Conclusion** The perinatal outcome of oocyte-donated ICSI-FET is relatively safe, but the birth weight of singleton is lower than that of self-oocyte ICSI-FET.

**【 Key words 】** Sperm injection, intracytoplasmic; Frozen-thawed embryo transfer; Oocyte donation; Autologous oocyte; Perinatal outcome

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·临床研究·

# 反复种植失败患者后续助孕周期结局及影响因素分析

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**【摘要】** 目的 探讨反复种植失败 (recurrent implantation failure, RIF) 患者后续多周期助孕结局及影响因素。方法 病例对照研究分析 2016 年 1 月至 2019 年 6 月期间在郑州大学第一附属医院生殖医学中心接受胚胎移植助孕, 诊断为 RIF 且行后续助孕治疗的 640 例患者的临床资料。主要结局指标为活产率和诊断 RIF 至获得妊娠的间隔时间。结果 RIF 患者后续助孕治疗的第一周期、第二周期、第三周期及以上的活产率、生化妊娠率、临床妊娠率及流产率差异均无统计学意义 (均  $P>0.05$ ) ; 344 例实现活产的 RIF 患者获得妊娠的间隔时间为 5.00 (3.13, 8.52) 个月。采用多因素回归分析校正混杂因素后, 囊胚移植的累积活产率较卵裂期胚胎移植显著增加 [ $P=0.002$ ,  $RR$  (95%  $CI$ ) =1.492 (1.158~1.923)] ; 年龄 $<35$  岁患者的累积活产率较高龄 ( $\geq 35$  岁) 患者明显增加 [ $P=0.013$ ,  $RR$  (95%  $CI$ ) =0.694 (0.521~0.925)] ; 胚胎移植日子宫内膜厚度 $\geq 8$  mm 患者的累积活产率较 $<8$  mm 患者显著增加 [ $P=0.016$ ,  $RR$  (95%  $CI$ ) =1.943 (1.132~3.335)] ; 仅 1 次 RIF 周期生化妊娠史患者的累积活产率较 0 次患者 [ $P=0.001$ ,  $RR$  (95%  $CI$ ) =0.625 (0.474~0.825)] 或 2 次及以上患者 [ $P=0.003$ ,  $RR$  (95%  $CI$ ) =0.414 (0.233~0.736)] 显著增加。结论 移植胚胎类型、年龄、胚胎移植日子宫内膜厚度及 RIF 周期生化妊娠史是影响 RIF 患者后续累积活产率的独立因素, 应尽可能选择囊胚移植、通过合理的周期管理尽快行助孕治疗, 仅 1 次 RIF 周期生化妊娠史可能预示着更优良的 RIF 后续周期的活产结局。

**【关键词】** 反复种植失败; 胚胎移植; 妊娠结局; 生化妊娠史

## Analysis of the subsequent assisted pregnancy outcomes and the influencing factors of recurrent implantation failure

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**【Abstract】 Objective** To analyze the subsequent assisted pregnancy outcomes of recurrent implantation failure (RIF) and find out the key influencing factors. **Methods** A case-control study was conducted to analyze the clinical data of 640 patients who received embryo transfer assisted fertility in the Center for

Reproductive Medicine of the First Affiliated Hospital of Zhengzhou University from January 2016 to June 2019 and were diagnosed with RIF and received subsequent assisted fertility treatment. The main outcome measures were the live birth rate and the time to pregnancy after diagnosis of RIF. **Results** The live birth rate, the biochemical pregnancy rate, the clinical pregnancy rate and the abortion rate of the first cycle, the second cycle, the third and above cycle after a diagnosis of RIF were not significantly different (all  $P>0.05$ ). The time to pregnancy after diagnosis of RIF of 344 patients who achieved live births was 5.00(3.13, 8.52) months. After adjusting for confounding factors by using multivariate logistic regression, the results showed that the cumulative live birth probability of blastocyst transfer was significantly higher than that of cleavage embryo transfer [ $P=0.002$ ,  $RR$  (95%  $CI$ )=1.492(1.158–1.923)]; the cumulative live birth probability of patients less than 35 years old was significantly higher than older patients ( $\geq 35$  years old)[ $P=0.013$ ,  $RR$  (95%  $CI$ )=0.694(0.521–0.925)]; the cumulative live birth probability of patients with endometrial thickness  $\geq 8$  mm on the embryo transfer day was significantly higher than that of patients with endometrial thickness  $< 8$  mm [ $P=0.016$ ,  $RR$  (95%  $CI$ )=1.943(1.132–3.335)]; compared with patients with 0 [ $P=0.001$ ,  $RR$  (95%  $CI$ )=0.625(0.474–0.825)] or 2 and more [ $P=0.003$ ,  $RR$  (95%  $CI$ )=0.414(0.233–0.736)] biochemical pregnancy in the RIF cycles, the cumulative live birth probability of patients with history of only 1 biochemical pregnancy in the RIF cycles was significantly higher. **Conclusion** The type of embryos transferred, age, endometrial thickness on the embryo transfer day and the history of biochemical pregnancy in the RIF cycles are independent factors for subsequent cumulative live birth probability in RIF patients. Blastocyst transfer should be selected as much as possible, and fertility treatment should be performed as soon as possible through reasonable cycle management, the history of only 1 biochemical pregnancy in the RIF cycles heralds a better live birth outcome in the subsequent cycles of RIF.

**【Key words】** Recurrent implantation failure; Embryo transfer; Pregnancy outcomes; History of biochemical pregnancy

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·临床研究·

## 影响宫腔内人工授精活产率的临床因素分析

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**【摘要】** 目的 探讨与宫腔内人工授精 (intrauterine insemination, IUI) 的活产率相关的临床影响因素。方法 采用回顾性队列研究, 收集 2015 年 1 月至 2018 年 12 月期间于北京大学第三医院妇产科生殖医学中心行 IUI 治疗的 9077 例患者共 15 740 个周期的临床资料。分析年龄、不孕年限、不孕类型、不孕因素、周期方案、周期次数、授精时机、处理后前向运动精子浓度、排卵数等方面对活产率的影响。分析促排卵周期中不同排卵数的活产率的差异。结果 共纳入 15 740 个 IUI 周期, 临床妊娠率为 11.3% (1784/15 740), 活产率为 8.5% (1339/15 740)。在单因素分析中: 年龄因素中 <30 岁活产率 [10.62% (462/4349)] 与 0~35 岁及 >35 岁的活产率 [8.27% (748/9048)、5.51% (129/2343)] 差异有统计学意义 ( $P<0.001$ ); 不孕因素中女性因素在 IUI 治疗后活产率 [11.51% (357/3101)], 与男性因素、双方因素及不明原因的活产率 [8.14% (337/4142)、8.09% (216/2670)、7.36% (429/5829)] 差异有统计学意义 ( $P<0.001$ ); 周期方案中促排卵周期活产率 [10.19% (850/8343)] 与自然周期 [6.61% (489/7397)] 活产率差异有统计学意义 ( $P<0.001$ ); 排卵个数组中排卵数  $\geq 3$  时活产率 [11.80% (19/161)], 与排卵数为 1 及 2 的活产率 [8.31% (1233/14 837)、11.73% (87/742)] 差异有统计学意义 ( $P<0.001$ )。在不同的不孕类型、授精时机、处理后前向运动精子浓度、不孕年限、授精次数等方面差异均无统计学意义 (均  $P>0.05$ )。多因素分析显示: 年龄 ( $OR=0.766$ , 95%  $CI=0.700\sim0.838$ )、不孕因素 (男方因素  $OR=0.762$ , 95%  $CI=0.649\sim0.893$ ; 双方因素  $OR=0.759$ , 95%  $CI=0.634\sim0.909$ ; 不明原因  $OR=0.708$ , 95%  $CI=0.608\sim0.824$ )、周期方案 ( $OR=1.421$ , 95%  $CI=1.260\sim1.604$ )、排卵数 ( $OR=1.206$ , 95%  $CI=1.018\sim1.430$ ) 是 IUI 活产率的独立影响因素。促排卵周期中不同排卵数的活产率差异比较, 排卵数为 2 的活产率 [13.45% (83/617)] 高于排卵数为 1 及 3 以上的活产率 [9.89% (750/7582)、11.81% (17/144)],  $P=0.016$ 。结论 女方年龄、不孕因素、周期方案、排卵数是 IUI 活产率的独立影响因素。女方年龄在 30 岁以下、周期方案为促排卵周期、促排卵周期中排卵数为 2 时活产率最高。

**【关键词】** 授精, 人工 (丈夫供体); 不育, 女性; 活产率

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## Analysis of clinical factors affecting the live birth rate of intrauterine insemination

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**【Abstract】 Objective** To explore the clinical factors related to the live birth rate of intrauterine insemination (IUI). **Methods** A retrospective cohort study was conducted in 9077 patients treated with IUI for 15 740 cycles in Center of Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital from January 2015 to December 2018. The effects of female age, duration of infertility, types of infertility, factors of infertility, protocols and times of cycles, time of insemination, forward motile sperm concentration after treatment and the number of broken eggs on the live birth rate were analyzed. The difference of live birth rate of different number of broken eggs in ovulation induction cycle was analyzed. **Results** A total of 1784 clinical pregnancy cycles were obtained in 15 740 IUI cycles, with a clinical pregnancy rate of 11.3% (1784/15 740) and a live birth rate of 8.5% (1339/15 740). In univariate analysis, among the age factors, the live birth rate of different aged patients was significantly different [ $<30$  years old 10.62% (462/4349), 30–35 years old 8.27% (748/9048),  $>35$  years old 5.51% (129/2343),  $P<0.001$ ]. Among the factors of infertility, the live birth rate of the female factors [11.51% (357/3101)] was significantly different from the male factors [8.14% (337/4142)], the bilateral factors [8.09% (216/2670)] and the unexplained factors [7.36% (429/5829)] after IUI treatment ( $P<0.001$ ). The live birth rate in the ovulation induction cycle [10.19% (850/8343)] was different from that in the natural cycle [6.61% (489/7397),  $P<0.001$ ]. In the No.of oocytes ovulated group, the live birth rate when the number of ovulation was  $\geq 3$  [11.80% (19/161)] was significantly different from that in the groups with ovulation number of 1 and 2 [8.31% (1233/14 837), 11.73% (87/742),  $P<0.001$ ]. There were no significant differences in different types of infertility, time of insemination, forward motile sperm concentration after treatment, duration of infertility and time of insemination. Multivariate analysis showed that female age ( $OR=0.766$ , 95%  $CI=0.700-0.838$ ), factors of infertility (male factor  $OR=0.762$ , 95%  $CI=0.649-0.893$ , bilateral factors  $OR=0.759$ , 95%  $CI=0.634-0.909$  and unexplained factors  $OR=0.708$ , 95%  $CI=0.608-0.824$ ), protocols ( $OR=1.421$ , 95%  $CI=1.260-1.604$ ) and the number of broken eggs ( $OR=1.206$ , 95%  $CI=1.018-1.430$ ) were independent factors affecting the live birth rate of IUI. Compared with the difference of the live birth rate of different number of broken eggs in the ovulation induction cycle, the live birth rate of the ovulation number of 2 [13.45% (83/617)] was higher than that of 1 or more than 3 ovulations [9.89% (750/7582), 11.81% (17/144),  $P=0.016$ ]. **Conclusion** The female age, the type of infertility, the different protocols and the number of broken eggs are the independent factors affecting the live birth rate of IUI. The female age  $<30$  years old, ovulation induction cycle, and the number of broken eggs  $\geq 3$  are independent factors of live birth rate in IUI patients. In the ovulation induction cycle, the live birth rate was the highest when the number of broken eggs was 2.



**【Key words】** Insemination, artificial, homologous; Infertility, female; Live birth rate

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·实验研究·

# 多囊卵巢综合征的 circRNA-miRNA-mRNA 调控网络生物信息学分析及其验证

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**【摘要】** 目的 通过构建多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者卵丘颗粒细胞的环状 RNA (circular RNA, circRNA)-微小 RNA (microRNA, miRNA)-信使 RNA (messenger RNA, mRNA) 调控网络, 并进行临床标本验证, 以探寻 PCOS 发病机制并提供诊疗靶点。方法 使用 R 软件分析来自基因表达图谱 (gene expression omnibus, GEO) 数据库的数据, 得到差异表达的 circRNA、miRNA、mRNA; 使用 CircInteractome、Starbase 数据库, 预测构建 circRNA-miRNA-mRNA 调控网络。回顾性研究收集 2018 年 1 月至 2018 年 12 月期间于郑州大学第二附属医院生殖医学部就诊的 PCOS 患者 (记为 PCOS 组,  $n=40$ ) 和因男方或者输卵管因素治疗的患者 (记为对照组,  $n=20$ ) 的卵丘颗粒细胞, 提取 RNA 后进行实时荧光定量 PCR (real time quantitative PCR, RT-qPCR) 验证。结果 筛选出 278 个差异表达 mRNA、23 个差异 miRNA 和 2402 个差异 circRNA ( $P<0.05$  和  $|\log_2FC|>0.8$ ); 构建 256 条 circRNA-miRNA-mRNA 调控网络, 包含 13 个 mRNA、2 个 miRNA 和 40 个 circRNA; 临床验证后提示, 妊娠相关血浆蛋白 A (pregnancy-associated plasma protein A, PAPP-A)、hsa-miR-127-3p、hsa\_circ\_0086809/hsa\_circ\_0063556 及其调控网络与 PCOS 相关 ( $P=0.004$ 、 $P=0.002$ 、 $P=0.014$ 、 $P=0.003$ )。结论 卵丘颗粒细胞中 PAPP-A、hsa-miR-127-3p、hsa\_circ\_0086809/hsa\_circ\_0063556 的表达水平及其调控网络与 PCOS 发生相关。

【关键词】 多囊卵巢综合征； 卵丘颗粒细胞； 基因表达图谱

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## Bioinformatic analysis and verification of circRNA-miRNA-mRNA regulatory network in polycystic ovary syndrome

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**【Abstract】 Objective** To identify the differentially expressed genes, construct circular RNA-microRNA-messenger RNA (circRNA-miRNA-mRNA) regulatory network, and detect the differentially expressed genes with the clinical samples from patients with polycystic ovary syndrome (PCOS) for further investigating of the mechanisms of pathogenesis and providing novel biomarkers for PCOS, to further explore the pathogenesis of PCOS and provide therapeutic targets. **Methods** The software 'R' was used to analyze the data from gene expression omnibus (GEO). The differentially expressed genes (mRNA, miRNA and circRNA) were identified, and the mRNA-miRNA-circRNA regulatory network was predicted by CircInteractome and Starbase database. The retrospective study was performed based on the PCOS patients in the Department of Reproductive Medicine, the Second Affiliated Hospital of Zhengzhou University during January to December in 2018. The cumulus cells were collected from the PCOS (named PCOS group,  $n=40$ ) and healthy women (named control group,  $n=20$ ). Reverse transcription real time quantitative PCR (RT-qPCR) was performed to further detect and verify the differentially expressed genes and the network. **Results** Analysis from GEO database identified the differentially expressed genes including 278 mRNAs, 23 miRNAs and 2402 circRNAs in PCOS group compared with non-PCOS group ( $P<0.05$  and  $|\log_2FC|>0.8$ ); 256 mRNA-miRNA-circRNA regulatory networks were established with the differentially expressed genes including 13 mRNAs, 2 miRNAs and 40 circRNAs from the database analysis. The verification with the clinical samples finally revealed the regulatory networks of mRNA pregnancy-associated plasma protein A (PAPPA)-miRNA (hsa-miR-127-3p)-circRNA (hsa\_circ\_0086809/hsa\_circ\_0063556) were associated with PCOS ( $P=0.004$ ,  $P=0.002$ ,  $P=0.014$ ,  $P=0.003$ ). **Conclusion** The expressions of mRNA (PAPPA), miRNA (hsa-miR-127-3p) and circRNA (hsa\_circ\_0086809/hsa\_circ\_0063556) in the cumulus cells and their regulatory networks were associated with PCOS.

**【Key words】** Polycystic ovary syndrome; Cumulus cells; Gene expression omnibus

**Fund program:** Medical Science and Technology Program of Henan Province (LHGJ20200421, LHGJ20190318)

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循证医学

# GnRH 激动剂长方案与 GnRH 拮抗剂方案用于中国不孕患者有效性和安全性比较的系统评价和 meta 分析

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**【摘要】** 目的 系统比较促性腺激素释放激素（gonadotropin-releasing hormone, GnRH）激动剂长方案与 GnRH 拮抗剂方案应用于中国不孕患者辅助生殖治疗中的有效性及安全性，为临床实践提供科学参考。方法 计算机检索 PubMed、EMBASE、CENTRAL、CBM、CNKI 和 Wanfang Data 数据库，检索时限均为建库至 2019 年 6 月，纳入相关随机对照试验（randomized controlled trial, RCT）。由两名经方法学培训的研究者独立完成文献筛选、偏倚风险评价及数据提取后，采用 RevMan5.3 软件进行 meta 分析。结果 共纳入 14 项 RCT，共 2335 例中国不孕患者，年龄为 29.0~38.9 岁，不孕年限为 3.8~6.8 年。纳入研究偏倚风险为中到高。在中国不孕患者中，应用 GnRH 激动剂长方案与 GnRH 拮抗剂方案相比获卵数更多（MD=0.60，95% CI=0.07~1.13， $P=0.030$ ）。而两种方案的  $M_{II}$  卵率（ $RR=1.03$ ，95% CI=0.99~1.07）、受精率（ $RR=1.02$ ，95% CI=0.99~1.05）、可移植胚胎数（MD=-0.05，95% CI=-0.15~0.04）、优质胚胎率（MD=-0.17，95% CI=-0.66~0.33）、种植率（ $RR=0.96$ ，95% CI=0.80~1.15）和临床妊娠率（ $RR=1.07$ ，95% CI=0.93~1.22）差异均无统计学意义（均  $P>0.05$ ）。在安全性方面，应用两种方案的周期取消率（ $RR=1.74$ ，95% CI=0.98~3.10）和流产率（ $RR=1.08$ ，95% CI=0.68~1.72）差异均无统计学意义（均  $P>0.05$ ），但 GnRH 激动剂长方案的卵巢过度刺激综合征发生率高于 GnRH 拮抗剂方案（ $RR=2.77$ ，95% CI=1.59~4.81， $P<0.001$ ）。结论 在中国不孕患者中，与 GnRH 拮抗剂方案相比，应用 GnRH 激动剂长方案可能增加获卵数，增加卵巢过度刺激综合征发生风险。而在  $M_{II}$  卵率、受精率、可移植胚胎数、优质胚胎率、种植率、临床妊娠率、周期取消率和流产率上，尚不能认为两种促排卵方案存在差异。

【关键词】 控制性卵巢刺激； 促性腺激素释放激素激动剂； 促性腺激素释放激素拮抗剂； 中国不孕患者； 有效性； 安全性； 系统评价； Meta分析

# Comparison of effectiveness and safety of GnRH agonist long protocol with GnRH antagonist protocol in Chinese infertile women: a systematic review and meta-analysis

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**【Abstract】 Objective** To systematically compare the effectiveness and safety of gonadotropin-releasing hormone (GnRH) agonist long protocol and GnRH antagonist protocol in Chinese infertile women, thus providing scientific support for clinical practice. **Methods** We systematically searched PubMed, EMBASE, CENTRAL, CBM, CNKI and Wanfang Data for eligible randomized controlled trials from inception to June 2019. Two well-trained reviewers who had full understanding of the study protocol conducted the literature screening, risk of bias assessment and data extraction independently. Meta analyses were conducted by RevMan5.3 software. **Results** Totally 14 randomized controlled trials were identified for analysis, including 2335 Chinese infertile women patients, with age ranged from 29.0 to 38.9 years and 3.8–6.8 years duration of infertility. Bias risk of included studies was moderate to high. Meta analyses suggested that in Chinese infertile women, compared with GnRH antagonist protocol, application of GnRH agonist long protocol increased the number of retrieved oocytes ( $MD=0.60$ , 95%  $CI=0.07-1.13$ ,  $P=0.030$ ), but there were no significant differences between the two protocols when referred to  $M_{II}$  oocyte rate ( $RR=1.03$ , 95%  $CI=0.99-1.07$ ), fertilization rate ( $RR=1.02$ , 95%  $CI=0.99-1.05$ ), number of embryos transferred ( $MD=-0.05$ , 95%  $CI=-0.15-0.04$ ), good-quality embryo rate obtained ( $MD=-0.17$ , 95%  $CI=-0.66-0.33$ ), implantation rate ( $RR=0.96$ , 95%  $CI=0.80-1.15$ ) and clinical pregnancy rate ( $RR=1.07$ , 95%  $CI=0.93-1.22$ ). As for safety evaluation, there were no significant differences between the two protocols in cancellation rate ( $RR=1.74$ , 95%  $CI=0.98-3.10$ ) and abortion rate ( $RR=1.08$ , 95%  $CI=0.68-1.72$ ), while the ovarian hyperstimulation syndrome (OHSS) rate of GnRH agonist long protocol was significantly higher than that of GnRH antagonist protocol ( $RR=2.77$ , 95%  $CI=1.59-4.81$ ,  $P<0.001$ ). **Conclusion** Current available evidence showed that in Chinese infertile women, application of GnRH agonist long protocol may result in more retrieved oocytes and higher OHSS risk than GnRH antagonist protocol, while there were no significant differences between the two protocols in  $M_{II}$  oocyte rate, fertilization rate, number of embryos transferred, good-quality embryo rate, implantation rate, clinical pregnancy rate, cancellation rate and abortion rate.

**【Key words】** Controlled ovarian stimulation; Gonadotropin-releasing hormone agonist; Gonadotropin-releasing hormone antagonist; Chinese infertile women; Effectiveness; Safety; Systematic review; Meta-analysis

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·临床报道·

## 既往 TORCH 感染对 IVF/ICSI-ET 妊娠结局影响的临床分析

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**【摘要】** 目的 探讨既往 TORCH 感染对体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer, IVF/ICSI-ET) 妊娠结局的影响。方法 回顾性队列研究分析 2016 年 5 月至 2018 年 5 月期间在中国人民解放军空军军医大学第二附属医院妇产科生殖医学中心进行 IVF/ICSI-ET 治疗的不孕女性患者, 分别采用酶联免疫吸附剂测定 (enzyme-linked immunosorbent assay, ELISA) 法检测血清中巨细胞病毒 (cytomegalovirus, CMV)、单纯疱疹病毒 (herpes simplex virus, HSV)、风疹病毒 (rubella virus, RV) 和弓形虫 (toxoplasma, TOX) 的 IgG、IgM 抗体水平, 若 IgM 阴性、IgG 阳性的患者可以列为既往感染阳性组 [即 IgM (-)、IgG (+)], 若 IgM 阴性、IgG 阴性列为阴性对照组 [即 IgM (-)、IgG (-)], 分别比较 CMV 阳性组 1984 例和阴性组 421 例、HSV 阳性组 1535 例和阴性组 344 例、RV 阳性组 1795 例和阴性组 261 例、TOX 阳性组 75 例和阴性组 211 例的临床一般情况与 IVF/ICSI-ET 治疗周期结局。结果 CMV、HSV、RV、TOX 阳性组与其阴性组间患者的年龄、体质量指数 (body mass index, BMI)、不孕年限、基础卵泡刺激素 (follicle-stimulating hormone, FSH) 及抗苗勒管激素 (anti-Müllerian hormone, AMH) 水平差异均无统计学意义 (均  $P>0.05$ )。CMV、HSV、RV 阳性组的获卵数 ( $9.68\pm4.33$ 、 $10.04\pm3.99$ 、 $10.41\pm4.33$ )、受精率 [82.01% (1627/1984)、82.74% (1270/1535)、82.95% (1489/1795)]、临床妊娠率 [53.20% (1055/1984)、51.66% (793/1535)、52.98% (951/1795)] 和活产率 [50.25% (997/1984)、38.96% (598/1535)、40.33% (724/1795)] 均显著低于阴性组 [ $10.18\pm4.41$ 、 $10.58\pm3.54$ 、 $11.08\pm3.90$ ,  $P$  分别为 0.032、0.021、0.018; 86.46% (364/421)、87.21% (300/344)、88.12% (230/261),  $P$  分别为 0.028、0.043、0.035; 58.4% (246/421)、58.14% (200/344)、60.54% (158/261),  $P$  分别为 0.049、0.030、0.022; 55.58% (234/421)、46.51% (160/344)、47.89%

(125/261),  $P$  分别为 0.047、0.010、0.021], 差异均有统计学意义; 生化妊娠率 [9.47% (188/1984)、9.12% (140/1535)、10.53% (189/1795)] 和流产率 [10.48% (208/1984)、9.97% (153/1535)、10.97% (197/1795)] 均显著高于阴性组 [6.18% (26/421)、5.81% (20/344)、6.51% (17/261)], 分别为 0.031、0.047、0.044; 7.13% (30/421)、6.10% (21/344)、6.51% (17/261),  $P$  分别为 0.036、0.026、0.027], 差异均有统计学意义。而 TOX 阳性组较阴性组获卵数、受精率、临床妊娠率和活产率差异均无统计学意义 (均  $P>0.05$ )。结论 既往 CMV、HSV、RV 感染与患者行 IVF/ICSI-ET 治疗的获卵数、受精率、临床妊娠率和活产率降低有关。既往 CMV、HSV、RV 感染与生化妊娠率和流产率增高有关。而既往 TOX 感染对 IVF/ICSI-ET 妊娠结局无影响。

【关键词】 受精, 体外; 精子注射, 细胞质内; 胚胎移植; 妊娠结局; TORCH; 既往感染

### Clinical analysis for pregnancy outcome of previous TORCH infection patients evolved with *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer

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【Abstract】 **Objective** To investigate the influence of previous TORCH infection on pregnancy outcome of *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET). **Methods** A retrospective cohort study was carried out for infertile female patients who underwent IVF/ICSI-ET treatment from May 2016 to May 2018 at Department of Obstetrics and Gynecology, Reproductive Medicine Center, the Second Affiliated Hospital, Air Force Military Medical University. IgM and IgG in serum have been detected for cytomegalovirus (CMV), herpes simplex virus (HSV), rubella virus (RV) and Toxoplasma (TOX) by enzyme-linked immunosorbent assay (ELISA). Patients with IgM negative and IgG positive [IgM(-), IgG(+)] were assigned as the previous infection, while IgM-negative and IgG-negative [IgM(-), IgG(-)] were assigned as negative control. Four groups of CMV [1984 IgG(+) cases vs. 421 IgG(-) cases], HSV [1535 IgG(+) cases vs. 344 IgG(-) cases], RV [1795 IgG(+) cases vs. 261 IgG(-) cases] and TOX [75 IgG(+) cases vs. 2111 IgG(-) cases] were investigated for general data and pregnancy outcome of IVF/ICSI-ET. **Results** There were no significant differences between previous infection and negative control at age, body mass index (BMI), infertility duration, basal follicle-stimulating hormone (FSH) and anti-Müllerian hormone (AMH) levels among four groups (all  $P>0.05$ ). The number of oocytes retrieved ( $9.68\pm4.33$ ,  $10.04\pm3.99$ ,  $10.41\pm4.33$ ), fertilization rate [82.01% (1627/1984), 82.74% (1270/1535), 82.95% (1489/1795)], clinical pregnancy rate [53.20% (1055/1984), 51.66% (793/1535), 52.98% (951/1795)] and live birth rate [50.25% (997/1984), 38.96% (598/1535), 40.33% (724/1795)] in CMV, HSV, and RV IgG positive groups were significantly lower than those in the negative control [ $10.18\pm4.41$ ,  $10.58\pm3.54$ ,  $11.08\pm3.90$ ,

$P=0.032$ ,  $P=0.021$ ,  $P=0.018$ ; 86.46% (364/421), 87.21% (300/344), 88.12% (230/261),  $P=0.028$ ,  $P=0.043$ ,  $P=0.035$ ; 58.4% (246/421), 58.14% (200/344), 60.54% (158/261),  $P=0.049$ ,  $P=0.030$ ,  $P=0.022$ ; 55.58% (234/421), 46.51% (160/344), 47.89% (125/261),  $P=0.047$ ,  $P=0.010$ ,  $P=0.021$ ]. However, the biochemical pregnancy rate [9.47% (188/1984), 9.12% (140/1535), 10.53% (189/1795)] and the miscarriage rate [10.48% (208/1984), 9.97% (153/1535), 10.97% (197/1795)] in CMV, HSV, and RV IgG positive groups were higher than those in the negative group [6.18% (26/421), 5.81% (20/344), 6.51% (17/261),  $P=0.031$ ,  $P=0.047$ ,  $P=0.044$ ; 7.13% (30/421), 6.10% (21/344), 6.51% (17/261),  $P=0.036$ ,  $P=0.026$ ,  $P=0.027$ ]. There were no significant differences in the number of oocyte retrieved, fertilization rate, clinical pregnancy rate and live birth rate between the TOX IgG positive group and the negative control (all  $P>0.05$ ). **Conclusion** Previous infections of CMV, HSV and RV may be the reason for the fewer number of oocyte retrieved and lower fertilization rate, clinical pregnancy rate and live birth rate for patients undergoing IVF/ICSI-ET treatment. Previous infections of CMV, HSV and RV cause the higher biochemical pregnancy rate and miscarriage rate. The previous TOX infection has no infection on IVF/ICSI-ET pregnancy outcome.

**【Key words】** Fertilization, *in vitro*; Sperm injection, intracytoplasmic; Embryo transfer; Pregnancy outcome; TORCH; Previous infection

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·专家视角·

## 反复着床失败患者种植窗研究新进展

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**【摘要】** 反复着床失败影响了辅助生殖技术成功率的进一步提高, 其中胚胎因素扮演了至关重要的角色, 但子宫内膜因素可能也是不可忽略的一个方面。目前关于子宫内膜种植窗异步及子宫内膜功能缺陷的研究不断涌现, 但结果的准确性、可信性以及临床结局改善的作用都值得商榷。随着相关技术的不断进步, 设计合理的实验研究, 得出可靠的结果, 并与临床结局相结合, 可能有助于提高反复着床失败患者的妊娠率。

**【关键词】** 反复着床失败; 受精, 体外; 胚胎移植; 种植窗; 子宫内膜容受性

## Advances in the window of implantation in patients with repeated implantation failure

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**【Abstract】** Repeated implantation failure (RIF) affects the improvement of the success rate of assisted reproductive technology. Embryo factors play a crucial role in it, but causes of endometrial origin may also be an aspect that cannot be ignored. Studies on asynchronous window of implantation and endometrial functional defects have continued to emerge in recent years. However, the accuracy, credibility and effect of the results on the improvement of clinical outcomes are questionable. Along with the advance of related technologies, experiments should be well-designed in order to achieve reliable results, which should be verified by clinical outcomes. This kind of studies may help increase pregnancy rates in patients with RIF.

**【Key words】** Repeated implantation failure; Fertilization, *in vitro*; Embryo transfer; Window of implantation; Endometrial receptivity

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·综述·

## 剖宫产术后远期并发症及其对辅助生殖妊娠结局影响的研究进展

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**【摘要】** 国内生育政策的放开使备孕二胎、三胎的人数剧增, 其中剖宫产术后接受辅助生殖技术 (assisted reproductive technology, ART) 助孕的患者显著增多, 剖宫产术后对 ART 助孕妊娠结局的影响尚无统一论。本文就剖宫产术后远期并发症及其对 ART 周期妊娠结局影响的进展进行总结, 为临床医生提供更为全面、客观的参考。



【关键词】 辅助生殖； 妊娠结局； 多胎妊娠； 剖宫产术后切口憩室；  
继发不孕

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## Research progress of long-term complications after cesarean section and its effect on the outcome of assisted reproductive pregnancy

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【Abstract】 The loosening of China's one-child policy has led to a dramatic  
increase in the number of people preparing to have the second or third child. The  
number of patients receiving assisted reproductive technology (ART) after cesarean  
section increased significantly. There is no uniform conclusion on the effect of  
cesarean section on the pregnancy outcome in the ART. In this paper, the long-term  
complications after cesarean section and their impact on the pregnancy outcome in  
the ART cycle are summarized, so as to provide a more comprehensive and objective  
reference for clinicians to manage.

【Key words】 Assisted reproductive; Pregnancy outcome; Multiple  
pregnancies; Cesarean scar defect; Secondary infertility

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·综述·

## 母-胎界面微环境在复发性流产中的研究进展

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**【摘要】** 复发性流产 (recurrent spontaneous abortion, RSA) 是育龄期女性常见不良妊娠结局, 其病因复杂, 至今尚不明确。其中, 母-胎界面微环境在维持妊娠方面发挥着关键作用。母-胎界面微环境主要包括滋养层细胞、蜕膜基质细胞和免疫细胞, 而这些细胞数量或功能异常可能会诱发母-胎界面微环境的改变, 如螺旋动脉重塑障碍、蜕膜化异常等, 从而导致 RSA。本文围绕这三种主要细胞在 RSA 发生中的作用和机制进行综述。

**【关键词】** 复发性流产; 母-胎界面; 免疫细胞; 滋养层细胞; 蜕膜基质细胞

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## **Research progress of maternal-fetal interface microenvironment in recurrent abortion**

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**【Abstract】** Recurrent spontaneous abortion (RSA) is a common adverse pregnancy outcome in women of childbearing age and its etiology is complex and still not clear. The maternal-fetal interface microenvironment plays a key role in maintaining pregnancy. There are trophoblast cells, decidual stromal cells and immune cells in the maternal-fetal interface microenvironment. The abnormal number or function of these cells may induce changes in the microenvironment of maternal-fetal interface, such as spiral artery remodeling disorder and abnormal decidualization, which may lead to RSA. This review discusses the role and mechanism of these three main cells in RSA.

**【Key words】** Recurrent spontaneous abortion; Maternal-fetal interface; Immune cells; Trophoblast cell; Decidual stromal cells

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## 富血小板血浆促进组织再生修复机制及其在子宫内膜再生修复的新探索

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**【摘要】** 富血小板血浆 (platelet-rich plasma, PRP) 是富含血小板的血浆浓缩物, 是近年来组织再生修复领域的研究热点。PRP 可释放大量的生物活性因子, 能够有效促进组织的再生修复。宫腔粘连 (intrauterine adhesion, IUA) 是由于子宫内膜基底层受损导致的子宫内膜损伤性疾病, 可引起月经异常、不孕及反复流产等, 严重危害育龄妇女的生殖和生理功能, 而且现有治疗措施无法确切实现子宫内膜的再生修复。因此, 近年来的研究对 PRP 在 IUA 子宫内膜再生修复中的作用进行新探索, 显示 PRP 可有效促进子宫内膜的再生修复。本文将从 PRP 促进组织再生修复的机制、应用现状及其在 IUA 子宫内膜再生修复领域的研究进展等进行综述。

**【关键词】** 富血小板血浆; 组织再生修复; 宫腔粘连; 子宫内膜再生  
基金项目: 国家重点研发计划项目 (2018YFC1004803)

### **Mechanism of platelet-rich plasma in promoting tissue regeneration and repair and its new exploration in endometrial regeneration and repair**

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**【Abstract】** Platelet-rich plasma (PRP) is a concentrate of plasma rich in platelets, has become a hot spot in the field of tissue regeneration and repair. It releases a large number of bioactive factors, and may promote tissue regeneration

and repair effectively. Intrauterine adhesion (IUA) is a disease caused by the damage of endometrial basal layer, which may lead to abnormal menstruation, infertility and recurrent miscarriages. It may seriously damage the reproductive and physiological functions in women of reproductive age. However, the existing treatment for IUA may not realize the regeneration and repair of endometrium successfully. Hence, several studies have explored the effects of PRP in endometrial regeneration and repair of IUA, and found that PRP could effectively promote the regeneration and repair of endometrium. Thus, the aim of this study is to review the mechanisms of PRP in accelerating tissue regeneration and repair, current application status, and research progress of PRP in endometrial regeneration of IUA.

**【 Key words 】** Platelet-rich plasma; Tissue regeneration and repair; Intrauterine adhesion; Endometrial regeneration

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·综述·

## 卵母细胞线粒体功能的研究进展

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**【摘要】** 线粒体是卵母细胞中数量最丰富的细胞器。线粒体功能是决定卵母细胞质量的关键因素, 而卵母细胞质量直接影响受精成败和胚胎发育的结局。线粒体是功能复杂的细胞器, 除能量供应外还参与胞质内蛋白质稳态和细胞内信号通路转导等多个生物学过程。随着辅助生殖技术的不断发展, 线粒体在卵子成熟及老化、早期胚胎发育等过程中的研究也越来越广泛。本文将阐述卵母细胞线粒体在卵子发生中的功能和变化, 并探讨线粒体替代治疗在线粒体疾病治疗中的潜在应用。

**【关键词】** 卵母细胞, 成熟; 线粒体; 老化, 卵母细胞; 线粒体替代治疗

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**Research progresses in the functions of oocyte mitochondria**

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**【Abstract】** Mitochondria are the most abundant organelles in oocytes. Successful fertilization and embryo development are heavily dependent upon inherent qualities of the oocytes, and thus reliant upon mitochondrial function of oocyte maturation. In addition to energy supply, mitochondria are multifunctional organelles that involved in many biological processes such as protein homeostasis in the cytoplasm and intracellular signaling pathways. With the development of assisted reproductive technology, more and more researches focus on the function of mitochondria on oocytes maturation, aging and pre-implantation embryonic development. In this review, we discuss the functions and changes of mitochondria during oogenesis, focusing on the consideration for therapeutic applications of mitochondrial replacement therapy in the treatment of mitochondrial diseases.

**【Key words】** Oocyte, maturation; Mitochondria; Aging, oocyte; Mitochondrial replacement therapy

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·综述·

## PCOS 患者糖脂代谢特点及其相关细胞因子参与卵泡发育的研究现状

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**【摘要】** 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是常见的女性内分泌、代谢紊乱性疾病, 其糖脂代谢异常与生殖功能障碍密切相关。卵巢是能

量代谢活跃的器官，颗粒细胞的增殖，卵母细胞的发育成熟及排卵，都是耗能的过程，需要足够的能量供应。糖、脂类在颗粒细胞中被分解，通过缝隙连接为卵母细胞发育提供能量。PCOS 患者糖脂代谢异常表现在卵巢颗粒细胞和卵泡液中信号分子及细胞因子、卵泡液中代谢产物的变化，影响卵泡发育及卵母细胞质量。本文就 PCOS 患者糖脂代谢特点及与糖脂代谢相关的细胞因子对卵泡发育和卵母细胞质量的影响进行综述，为临床提供参考。

【关键词】 多囊卵巢综合征； 糖脂； 代谢； 细胞因子； 卵母细胞生长/发育

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# Characteristics of glucose and lipid metabolism and the relationship between cytokines related to glucose and lipid metabolism and follicular development in PCOS patients

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【Abstract】 Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder of females. The abnormality of glucose and lipid metabolism is closely related to reproductive dysfunction. The ovary is an organ with active energy metabolism. The proliferation of granulosa cells, the maturation and ovulation of oocytes are all energy-consuming processes and require sufficient energy supply. Sugars and lipids are decomposed in granulosa cells and provide energy for oocyte development through gap junctions. Abnormal glucose and lipid metabolism in PCOS patients is manifested in the changes of signal molecules and cytokines in ovarian granulosa cells and follicular fluid, and the changes of metabolites in follicular fluid, which affect follicular development and oocyte quality. This article reviewed the characteristics of glucose and lipid metabolism and the relationship between cytokines associated with glucose and lipid metabolism and the development and quality of follicular in PCOS patients, contributing to provide reference for clinic.

【Key words】 Polycystic ovary syndrome; Glycolipids; Metabolism; Cell factor; Oocytes growth/development

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# 环状 RNA 参与精子发生的研究进展

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**【摘要】** 精子发生对成年雄性动物完成生育功能来说至关重要, 这一复杂的生理过程需要相关基因适时适度的表达, 大量的表观遗传调控因子参与其中, 包括明星分子环状 RNA。环状 RNA 具有表达丰富、进化保守、细胞或组织特异性以及更高的抗外切酶或核糖核酸酶降解能力等多种特征。它可以调控亲本基因的表达, 作为 mRNA 陷阱、miRNA 或蛋白质的海绵体来发挥作用, 也可以通过结合 RNA 结合蛋白来参与精子的发生过程, 包括生殖干细胞的形成、精子的形成、精浆的组成及睾丸组织的形成。本文就目前环状 RNA 参与精子发生的研究进展进行综述。

**【关键词】** 环状 RNA; 精子发生; 生殖干细胞; 弱精子症; Y 染色体性别决定基因

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## Research advances on circular RNAs involved in spermatogenesis

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**【Abstract】** Spermatogenesis is crucial for adult male animals to complete the reproductive function. This complex physiological process requires the timely and appropriate expression of related genes. A large number of epigenetic regulators are involved, including the star molecule circular RNAs (circRNAs). circRNAs are characterized by rich expression, conservative evolution, cell or tissue specificity, and higher ability to resist exonuclease or ribonuclease degradation. It can regulate the expression of parental genes and act as mRNA trap, miRNA or spongy body of protein. Furthermore, it can also participate in the spermatogenesis process by binding RNA-binding proteins, such as the formation of germ stem cells, sperm formation, spermatid composition and testicular tissue formation. We reviewed the progress of circRNAs in spermatogenesis in recent researches.

**【Key words】** Circular RNA; Spermatogenesis; Reproductive stem cell; Asthenozoospermia; Sex-determining region of Y chromosome

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·综述·

## 时差成像技术在临床应用中的进展

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**【摘要】** 随着对体外胚胎形态学参数、时差动力学参数的认知, 时差成像技术 (time-lapse technology, TLT) 已经进入了一个快速发展的阶段。TLT 能实时连续记录胚胎从受精、卵裂、囊胚形成的各项细节图像并发现传统观察胚胎技术不能发现的细节, 为胚胎筛选提供依据。此外, TLT 还能在临床应用、实验室质量控制中发挥作用。与此同时, TLT 在体外胚胎发育分析、人工智能开发中也存在问题, 本文将对其进行探讨。

**【关键词】** 时差成像技术; 临床应用; 胚胎发育; 人工智能

### Recent advances in time-lapse technology in clinical application

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**【Abstract】** Time-lapse technology (TLT) has entered a stage of rapid development with the recognition of morphological parameters and kinetic parameters of embryos *in vitro*. TLT can continuously record the detailed images of embryo from fertilization, cleavage and blastocyst formation and find the details that traditional observation embryo technology cannot find, providing the basis for embryo screening. In addition, TLT can also play a role in clinical applications and quality control of laboratory. At the same time, TLT also has some problems in *in*



*vitro* embryo development analysis and artificial intelligence development, which will be discussed in this paper.

**【 Key words 】** Time-lapse technology; Clinical application; Embryo development; Artificial intelligence