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收稿日期　2023-02-17　本文编辑　李天琦
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·临床研究·

女性体质量指数对宫腔内人工授精妊娠结局的影响：一项单中心大样本队列研究

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【摘要】 目的　探讨在宫腔内人工授精（intrauterine insemination， IUI）助孕技术过程中，女性体质量指数（body mass index， BMI）对妊娠结局的影响。方法　回顾性队列研究分析 2010 年 1 月至 2021 年 12 月期间于郑州大学第一附属医院生殖医学中心就诊，并首次进行 IUI 助孕的 21 137 例患者，包括夫精人工授精（artificial insemination by husband， AIH）和供精人工授精（artificial insemination by donor， AID）周期。根据临床妊娠与否，分成妊娠组和非妊娠组。首先比较临床妊娠组和非临床妊娠组的基线资料，然后根据女性 BMI，将患者分为 4 组，A 组：BMI≤18.5 kg/m^2（偏瘦），B 组：18.6~23.9 kg/m^2（正常体质量），C 组：24.0~27.9 kg/m^2（超重），D 组：BMI≥28 kg/m^2（肥胖），比较组间基本资料和妊娠结局；采用多因素 logistic 回归分析 BMI 对临床妊娠率和早期流产率的影响。结果　在所有 IUI 助孕周期中，妊娠组患者的 BMI［（24.58±3.52） kg/m^2］和非妊娠组［（23.35±4.20） kg/m^2］差异有统计学意义（*P*<0.001）。在 AIH 助孕周期中，C 组和 D 组患者的临床妊娠率［18.21%（877/4 815），17.12%（222/1 297）］和早期流产率［17.10%（150/877），21.62%（48/222）］高于 A 组［11.24%（130/1 157），10.77%（14/130）］和 B 组［13.40%（1 229/9 174），15.30%（188/1 229）］，4 组间比较差异均有统计学意义（*P*=0.012， *P*=0.003）。经过多因素 logistic 回归分析，BMI 高低对临床妊娠率无显著影响，但肥胖显著增加早期流产的风险（*OR*=1.63，95% *CI*：1.25~1.95， *P*=0.003）。在 AID 助孕周期中，不同 BMI 人群的妊娠结局差异无统计学意义，肥胖是早期流产的危险因素（*OR*=1.58，95% *CI*：1.14~1.87，*P*=0.016）。结论　女性 BMI 并不影响 AIH 和 AID 周期的临床妊娠率，但肥胖显著增加早期流产的风险。

【关键词】 体质量指数； 妊娠结局； 宫腔内人工授精； 夫精人工授精；供精人工授精

基金项目：国家自然科学基金青年科学基金 （81801448）

Impact of female body mass index on clinical outcomes in patients treated with intrauterine insemination: a single-center cohort study

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【Abstract】 Objective To explore the impact of female body mass index (BMI) on clinical outcomes in patients treated with intrauterine insemination (IUI). **Methods** This study was a retrospective cohort study. A total of 21 137 patients who visited the Reproductive Medical Center, the First Affiliated Hospital of Zhengzhou University from January 2010 to December 2021 were recruited. The patients underwent the first IUI cycles, including artificial insemination by husband (AIH) and artificial insemination by donor (AID). According to clinical pregnancy or not, it is divided into pregnancy group and non-pregnancy group. The basic parameters between clinical pregnancy group and non-clinical pregnancy group were compared. According to the BMI, patients were divided into 4 groups, group A: BMI≤18.5 kg/m^2, group B: 18.6–23.9 kg/m^2, group C: 24.0–27.9 kg/m^2 and group D: BMI≥28.0 kg/m^2. Patients' basic parameters and clinical outcomes were compared among the four groups. Multivariate logistic regression analysis was used to explore the impact of BMI on pregnancy outcomes. **Results** In all IUI cycles, BMI was significantly different between pregnant patients and non-pregnant patients [(24.58±3.52) kg/m^2 *vs.* (23.35±4.20) kg/m^2, P<0.001]. In AIH cycles, clinical pregnancy rate [18.21% (877/4 815), 17.12% (222/1 297)] and early spontaneous miscarriage rate [17.10% (150/877), 21.62% (48/222)] were significantly higher in patients of group C and group D than in group A [11.24% (130/1 157), 10.77% (14/130)] and group B [13.40% (1 229/9 174), 15.30% (188/1 229)]. The differences among the 4 groups were statistically significant (P=0.012, P=0.003). However, BMI was not associated with clinical pregnancy rate in multivariate logistic analysis, but obesity was a predictor for early spontaneous miscarriage (OR=1.63, 95% CI: 1.25–1.95, P=0.003). In AID cycles, pregnancy outcomes were comparable among the four BMI groups. Obesity significantly increased early spontaneous miscarriage rate (OR=1.58, 95% CI: 1.14–1.87, P=0.016). **Conclusion** Female BMI is not associated with clinical outcomes in IUI cycles. Obesity is a predictor for early spontaneous miscarriage in both AIH and AID cycles.

【 Key words 】 Body mass index; Pregnancy outcome; Intrauterine insemination; Artificial insemination by husband; Artificial insemination by donor

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·临床研究·

GnRH-a 降调节人工周期方案对不明原因反复种植失败患者妊娠结局的影响

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袁彩霞和胡凯伦对本文有同等贡献

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【摘要】　目的　探讨促性腺激素释放激素激动剂（gonadotropin-releasing hormone agonist，GnRH-a）降调节人工周期（artificial cycle，AC）方案对不明原因反复种植失败患者妊娠结局的影响。方法　回顾性队列研究分析 2018 年 1 月至 2019 年 12 月期间北京大学第三医院生殖医学中心行冻融胚胎移植的不明原因反复种植失败患者的 1 285 个周期临床资料。按照子宫内膜准备方案的不同分成 2 组，GnRH-a 垂体降调节 AC 组（记为 GnRH-a+AC 组，411 个周期）和 AC 组（874 个周期）。比较 2 组患者的一般临床资料、周期特点和临床结局，采用多因素 logistic 回归分析临床妊娠和活产的影响因素。结果　2 组中一般资料比较差异均无统计学意义（均 *P*>0.05）。GnRH-a+AC 组患者内膜转化日子宫内膜厚度［（10.26±1.73）mm］比 AC 组［（9.66±1.54） mm］厚，差异有统计学意义（*P*=0.002）。GnRH-a+AC 组的临床妊娠率［42.58%（175/411）］、胚胎种植率［32.52%（200/615）］均高于 AC 组［35.59%（311/874），*P*=0.016；27.20%（346/1272），*P*=0.017］，差异均有统计学意义；GnRH-a+AC 组活产率［33.57%（138/411）］有增高趋势，但与 AC 组［28.73%（251/874）］相比，差异无统计学意义（*P*>0.05）。多因素 logistic 回归结果显示，临床妊娠率与年龄、体质量指数（body mass index， BMI）呈负相关（*OR*=0.953，95% *CI*：0.924~0.982；*OR*=0.959，95% *CI*：0.926~0.994），与 GnRH-a 方案呈正相关（*OR*=1.329，95% *CI*：1.039~1.699）；活产率仅与年龄、BMI 呈负相关（*OR*=0.947，95% *CI*：0.917~0.977；*OR*=0.963，95% *CI*：0.927~0.999），方案选择并未成为其影响因素（*P*>0.05）。子宫内膜厚度≥7 mm 不是临床妊娠率

和活产率的影响因素（均 *P*>0.05）。结论　对于不明原因反复种植失败患者，GnRH-a 降调节联合 AC 方案可显著增加子宫内膜厚度，改善患者的子宫内膜容受性，提高患者胚胎种植率和临床妊娠率，但在活产率方面虽有升高趋势但尚无统计学意义，仍需大样本量进一步研究。

【关键词】　妊娠结局；　反复种植失败；　冻融胚胎移植；　降调节人工周期方案；　人工周期方案

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Effect of GnRH-a down-regulation combined with artificial cycle protocol on pregnancy outcomes in patients with unexplained repeated implantation failure

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【Abstract】　Objective　To investigate the effect of gonadotropin-releasing hormone agonist (GnRH-a) down-regulation combined with artificial cycle (AC) protocol on pregnancy outcomes in patients with unexplained repeated implantation failure (RIF). **Methods**　The clinical data of 1 285 frozen-thawed cycles of unexplained RIF patients who underwent frozen-thawed embryo transfer from January 2018 to December 2019 in the Reproductive Medical Center of Peking University Third Hospital were retrospectively analyzed. They were divided into two groups according to different endometrial preparation protocols: GnRH-a down-regulation combined with AC protocol group (named GnRH-a+AC group, 411 cycles) and AC group (874 cycles). The general clinical data, cycle characteristics and clinical outcomes between the two groups were compared. Multiple logistic regression analysis was used to analyze the influencing factors of clinical pregnancy and live birth. **Results**　There was no significant difference in the general data between the two groups (*P*>0.05). The endometrial thickness of GnRH-a+AC group [(10.26±1.73) mm] was thicker than that of AC group [(9.66±1.54) mm], and the difference was statistically significant (*P*=0.002). The clinical pregnancy rate [42.58% (175/411)] and the embryo implantation rate [32.52% (200/615)] of GnRH-a+AC group were higher than those of AC group [35.59% (311/874), *P*=0.016; 27.20% (346/1 271), *P*=0.017], and the differences were statistically significant. The live birth rate of GnRH-a+AC group [33.57% (138/411)] showed an increasing tendency, but there was no significant difference compared with AC group [28.73% (251/874), *P*>0.05]. The multivariate logistic regression analysis showed that the clinical pregnancy rate was negatively correlated with age and body mass index (BMI; *OR*=0.953, 95% *CI*: 0.924–0.982; *OR*=0.959, 95% *CI*: 0.926–0.994), and positively correlated with GnRH-a protocol (*OR*=1.329, 95% *CI:* 1.039–1.699); the live birth rate was only negatively correlated with age and BMI (*OR*=0.947, 95% *CI*: 0.917–0.977; *OR*=0.963, 95% *CI*:

0.927–0.998) and GnRH-a protocol was not an influencing factor (*P*>0.05). Endometrial thickness ≥7 mm was not the influencing factor of clinical pregnancy rate and live birth rate (all *P*>0.05). **Conclusion** For RIF patients, GnRH-a down-regulation combined with AC protocol can significantly increase endometrial thickness, improve endometrial receptivity and clinical pregnancy rate, but there is no statistical significance in the live birth rate, which still needs to be further studied in large scale.

【Key words】 Pregnancy outcome; Repeated implantation failure; Frozen-thawed embryo transfer; GnRH-a down-regulation; Artificial cycle

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·临床研究·

滋养外胚层细胞活检对冻胚移植后妊娠早期血清 β-hCG 水平及围产期结局的影响：一项倾向评分匹配研究

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【摘要】 目的 探讨胚胎植入前遗传学检测（preimplantation genetic testing，PGT）中滋养外胚层细胞活检对冻融胚胎移植后妊娠早期血清 β-人绒毛膜促性腺激素（β-human chorionic gonadotropin，β-hCG）水平及围产期结局的影响。方法 回顾性队列研究分析 2017 年 1 月至 2021 年 12 月期间于郑州大学第三附属医院生殖中心行冻融胚胎移植患者的临床资料，根据患者助孕方式分为两组：PGT 组 308 例和卵胞质内单精子注射（intracytoplasmic sperm injection，ICSI）组 802 例。经

1∶2 倾向评分匹配后，得到 PGT 组 300 例和 ICSI 组 571 例。比较匹配前后两组患者一般资料、胚胎移植后第 14 天血清 β-hCG 水平及围产期结局，采用多因素线性回归校正混杂因素后，分析滋养外胚层细胞活检对冻胚移植后妊娠早期血清 β-hCG 水平及围产期结局的影响。结果　匹配前 PGT 组女方年龄［（31.2±4.1）岁］明显高于 ICSI 组［（30.4±4.3）岁，*P*=0.007］，PGT 组抗苗勒管激素水平［（4.38±3.62）μg/L］及移植日内膜厚度［（9.1±1.6） mm］明显小于 ICSI 组［（4.87±3.78）μg/L，*P*=0.049；（9.6±1.6） mm，*P*<0.001］；匹配后两组患者一般资料差异均无统计学意义（均 *P*>0.05）。匹配前后两组患者临床妊娠患者、早期流产患者及活产患者的胚胎移植后第 14 天血清 β-hCG 水平差异均无统计学意义（均 *P*>0.05）；匹配前后两组生化妊娠率、临床妊娠率、早期流产率及活产率差异均无统计学意义（均 *P*>0.05）。经多因素线性回归分析显示，是否行 PGT 对血清 β-hCG 水平没有影响（*P*=0.494），女方体质量指数及移植囊胚类型对 β-hCG 水平有影响（均 *P*<0.001）。两组妊娠期高血压疾病发生率、妊娠期糖尿病发生率、妊娠期甲状腺功能减退发生率、胎膜早破发生率、前置胎盘发生率、剖宫产率、早产率、低出生体质量儿率、巨大儿率、性别比、新生儿出生体质量、新生儿身长与新生儿出生缺陷率差异均无统计学意义（均 *P*>0.05）。结论　冻融胚胎移植前行滋养外胚层细胞活检不影响妊娠早期血清 β-hCG 水平，PGT 不增加母婴不良并发症发生风险。

【关键词】　β-人绒毛膜促性腺激素；　胚胎植入前遗传学检测；　滋养外胚层细胞活检；　冻融胚胎移植；　围产期结局

Effects of blastocysts trophoectoderm biopsy on serum β-hCG levels of early pregnancy and perinatal outcomes in frozen embryo transplantation: a propensity score matching research

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【Abstract】　Objective　To investigate the effect of trophoectoderm biopsy of blastocysts on serum β-human chorionic gonadotropin (β-hCG) in early pregnancy and perinatal outcome after frozen-thawed embryo transfer (FET) in the preimplantation genetic testing (PGT). **Methods**　It was a retrospective cohort study. Patients who underwent FET in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2017 to December 2021 were recruited. The patients were divided into two groups according to the progestation method: 308 patients underwent trophoectoderm biopsy (PGT group) and 802 patients underwent intracytoplasmic sperm injection (ICSI group). The patients were matched at 1∶2 with propensity score matching (PSM), then there were 300 patients in PGT group and 571 patients in ICSI group. The general conditions and perinatal outcomes were compared among PGT group and ICSI group before and after PSM. Multivariate linear regression was applied to analyze the effect of trophoectoderm biopsy to serum β-hCG level by day 14 after embryo transfer. **Results**　Before PSM, the female age in PGT group was significantly higher than that in ICSI group [(31.2±4.1) years *vs.* (30.4±4.3) years, *P*=0.007]. The anti-Müllerian

hormone levels [(4.38±3.62) μg/L *vs.* (4.87±3.78) μg/L, *P*=0.049] and endometrial thickness on the day of embryo transfer [(9.1±1.6) mm *vs.* (9.6±1.6) mm, *P*<0.001] were lower in PGT group than in ICSI group. There was no significant difference in the general data between the two groups after PSM (all *P*>0.05). Before and after PSM, there was no significant difference in serum β-hCG level on day 14 after embryo transfer between PGT and ICSI groups of the all patients, clinical pregnancy patients, early abortion patients and live birth patients (all *P*>0.05). There were no significant differences in biochemical pregnancy rate, clinical pregnancy rate, early abortion rate and live birth rate between the two groups before and after matching (all *P*>0.05). Multivariate linear regression analysis showed that whether or not PGT was performed had no effect on serum β-hCG levels (*P*=0.494), and female body mass index and type of blastocyst transferred had an effect on β-hCG levels (all *P*<0.001). There were no significant differences in the incidences of hypertensive disorder complicating pregnancy, gestational diabetes, hypothyroidism during pregnancy, premature rupture of membranes, placenta previa between the two groups (all *P*>0.05). The cesarean section rate, premature delivery rate, low birth weight rate, macrogenesis rate, sex ratio, neonatal body mass, neonatal length and neonatal birth defects rate were not significantly different between the two groups (all *P*>0.05). **Conclusion** Trophoectoderm biopsy of blastocysts before FET does not affect serum β-hCG level in early pregnancy, and does not increase the risk of maternal and infant adverse complications.

【Key words】 β-human chorionic gonadotropin; Preimplantation genetic testing; Trophoectoderm biopsy; Frozen-thawed embryo transfer; Perinatal outcome

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·临床研究·

卵裂期胚胎与囊胚移植的妊娠结局和围产期结局的比较

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【摘要】 目的 比较卵裂期胚胎和囊胚移植的妊娠结局和围产期结局，探讨不孕患者胚胎移植的最佳策略。方法 本回顾性队列研究分析了 2021 年 1 月至 2022 年 12 月期间就诊于山西医科大学第五临床医学院、第一临床医学院和晋中婴泰妇产医院生殖医学科接受体外受精/卵胞质内单精子注射的患者资料，分为卵裂期胚胎移植组（记为 D3 组，*n*=2 827）和囊胚移植组（记为 D5 组，*n*=1 253）。主要观察指标为大于胎龄儿（large for gestational age，LGA）、早产，次要观察指标为多胎妊娠、分娩孕周、新生儿性别和体质量等。采用单因素及多因素二元 logistic 回归统计分析移植胚胎类型与不良结局的相关性。结果 D5 组的临床妊娠率［64.5%（808/1 253）］、活产率［55.5%（696/1 253）］、种植率［46.0%（1 026/2 230）］、多胎妊娠率［22.6%（183/808）］、男婴占比［58.6%（515/879）］、单胎 LGA 率［19.8%（103/520）］和单胎早产率［21.7%（113/520）］比 D3 组显著升高［54.3%（1 535/2 827），*P*<0.001；48.2%（1 362/2 827），*P*<0.001；36.7%（1 962/5 346），*P*<0.001；19.0%（291/1 535），*P*=0.026；49.7%（822/1 653），*P*=0.001；7.5%（80/1 071），*P*<0.001；17.2%（184/1 071），*P*=0.029］。D5 组在冷冻周期中的单胎 LGA 率［24.8%（72/290）］和新鲜周期中的单胎 LGA 率［13.5%（31/230）］均较 D3 组［8.8%（36/409），*P*<0.001；6.6%（44/662），*P*=0.002］显著升高。D5 组男婴发生 LGA［24.8%（82/330）］和女婴发生 LGA［11.1%（21/190）］的风险均显著高于 D3 组［9.1%（54/592），a*OR*=2.95，95% *CI*：2.01~4.33，*P*<0.001；5.4%（26/479），a*OR*=2.04，95% *CI*：1.10~3.77，*P*=0.024］。结论 囊胚移植的 LGA 和早产的发生风险高于卵裂期胚胎移植，临床实践中应结合患者自身条件及胚胎情况选择胚胎移植方式。

【关键词】 早产； 卵裂期胚胎移植； 囊胚移植； 大于胎龄儿； 临床结局

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Comparison of pregnancy and perinatal outcomes between cleavage-stage embryo transfer and blastocyst-stage embryo transfer

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【**Abstract**】 **Objective** To compare the pregnancy and perinatal outcomes following cleavage-stage embryo transfer and blastocyst-stage embryo transfer, and to explore the best strategy of embryo transfer for infertile patients. **Methods** In this retrospective cohort study, data of patients who underwent *in vitro* fertilization/intracytoplasmic sperm injection from January 2021 to December 2022 in Reproductive Medicine Department of the Fifth Hospital and the First Hospital of Shanxi Medical University and Jinzhong Yingtai Women's and Children's Hospital were collected. Patients were divided into cleavage-stage embryo transfer group (named D3 group, *n*=2 827) and blastocyst-stage embryo transfer group (named D5 group, *n*=1 253). The main observation indicators were large for gestational age (LGA) and preterm birth (PTB). The secondary observation indicators were multiple pregnancy, gestational age, birth weight and newborn gender. Univariate and multivariate logistic regression were applied to analyze the correlation between embryo transfer type and adverse outcomes. **Results** Clinical pregnancy rate [64.5% (808/1 253)], live birth rate [55.5% (696/1 253)], implantation rate [46.0% (1 026/2 230)], multiple pregnancy rate [22.6% (183/808)], male newborn rate [58.6% (515/879)], single LGA rate [19.8% (103/520)] and single PTB rate [21.7% (113/520)] in D5 group were significantly higher than those in D3 group [54.3% (1 535/2 827), *P*<0.001; 48.2% (1 362/2 827), *P*<0.001; 36.7% (1 962/5 346), *P*<0.001; 19.0% (291/1 535), *P*=0.026; 49.7% (822/1 653), *P*=0.001; 7.5% (80/1 071), *P*<0.001; 17.2% (184/1 071), *P*=0.029]. LGA rate [24.8% (72/290)] in the single frozen-embryo transfer and LGA rate [13.5% (31/230)] in the single fresh-embryo transfer of D5 group were significantly higher than those of D3 group [8.8% (36/409), *P*<0.001; 6.6% (44/662), *P*=0.002]. LGA in male newborns [24.8% (82/330)] and female newborns [11.1% (21/190)] of D5 group were significantly higher than those of D3 group [9.1% (54/592), a*OR*=2.95, 95% *CI*: 2.01–4.33, *P*<0.001; 5.4% (26/479), a*OR*=2.04, 95% *CI*: 1.10–3.77, *P*=0.024]. **Conclusion** The risk of LGA and premature birth in blastocyst-stage embryo transfer is higher than that in cleavage-stage embryo transfer. In clinical practice, embryo transfer methods should be selected based on the condition of patient and embryo.

【**Key words**】 Preterm birth; Cleavage-stage embryo transfer; Blastocyst-stage embryo transfer; Large for gestational age; Clinical outcomes

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·实验研究·

人类精原细胞分化过程的生物信息学分析

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【摘要】 目的　为了明确精子发生过程中的关键基因和生物学过程，挖掘人类精原细胞（spermatogonia，SPG）分化过程中的差异表达基因（differentially expressed genes，DEGs）及其信号通路，探索精子发生早期的分子机制，增加对SPG 分化过程的分子生物学认识。方法　从公共数据库下载人类未分化精原细胞（undifferentiated spermatogonia，uSPG）和分化精原细胞（differentiating spermatogonia，dSPG）的转录组数据，利用 Hisat2 和 StingTie 筛选 DEGs，并对差异表达基因进行 GO 和 KEGG 功能富集分析。利用 MACS2 软件对 ATAC-seq 数据中开放染色质区域进行富集分析。结果　共筛选出 8 532 个 DEGs，包括 4 127 个上调基因和 4 405 个下调基因，它们通过一些重要的生物学过程，如细胞周期、细胞因子介导的信号通路、有机物代谢过程、细胞运动、甲基化等来调控 SPG 的分化过程。KEGG 富集分析结果表明一些重要信号通路包括 FoxO 信号通路、JAK-STAT 信号通路等在 SPG 分化过程中具有重要作用。GO 富集分析结果显示甲基化在 SPG 分化过程中发挥重要作用，甲基化相关基因表达差异显著。组蛋白甲基化词条相关基因 *TDRD*s 家族显著富集，9 个 *TDRD*s 基因在 dSPG 中表达更加活跃。结论　本研究通过生物信息学分析鉴定了 SPG 分化过程中的差异表达基因，明确了关键基因在转录和染色质水平的差异，为 SPG 分化机制研究奠定了重要的理论基础。

【关键词】 精子发生；　精原细胞；　生物信息学；　不育，男性；　分化

Bioinformatics analysis of human spermatogonia differentiation process

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【**Abstract**】 **Objective** To clarify the key genes and biological processes in spermatogenesis, integrate and analyze the differentially expressed genes (DEGs) and key signaling pathways in the differentiation process of human spermatogonia (SPG), and to explore the early molecular mechanism of spermatogenesis, increase the molecular biology understanding of SPG differentiation process. **Methods** The transcriptome data of human undifferentiated spermatogonia and differentiated spermatogonia (dSPG) were downloaded from the public database. Hisat2 and StingTie were used to screen DEGs. DEGs were analyzed by gene ontology (GO) and Kyoto encyclopedia of genes and genomes (KEGG) functional enrichment analysis. MACS2 software was used to analyze the open chromatin regions (OCRs) in ATAC-seq data. **Results** A total of 8 532 DEGs were screened, including 4 127 up-regulated genes and 4 405 down-regulated genes. They regulate the differentiation of SPG through some important biological processes, such as cell cycle, cytokine-mediated signaling pathways, organic matter metabolism, cell movement, and methylation. KEGG enrichment analysis showed that some important signaling pathways including FoxO signaling pathway and JAK-STAT signaling pathway played an important role in SPG differentiation. GO enrichment analysis showed that methylation played an important role in the differentiation of SPG, and the expression of methylation-related genes was significantly different. The *TDRD*s family was significantly enriched, and 9 *TDRD*s genes were found to be more active in dSPG. **Conclusion** In this study, the differentially expressed genes during SPG differentiation were identified by bioinformatics analysis, and the differences in transcription and chromatin levels of key genes were clarified, which laid an important theoretical foundation for the study of SPG differentiation mechanism.

【**Key words**】 Spermatogenesis; Spermatogonia; Bioinformatics; Infertility, male; Differentiation

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·临床报道·

拮抗剂灵活方案促排卵 LH 提前升高对 IVF/ICSI 鲜胚移植临床结局的影响：一项倾向评分匹配研究

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【摘要】 目的　探讨黄体生成素（luteinizing hormone，LH）提前升高对应用促性腺激素释放激素拮抗剂灵活方案促排卵患者体外受精/卵胞质内单精子注射（*in vitro* fertilization/intracytoplasmic sperm injection，IVF/ICSI）鲜胚移植临床结局的影响。方法　回顾性队列研究分析 2016 年 1 月至 2021 年 9 月期间在郑州大学第三附属医院生殖医学中心采用拮抗剂灵活方案促排卵后行 IVF/ICSI 的卵巢储备功能正常的患者资料。根据添加拮抗剂前 LH 水平将患者分为两组，A 组：LH 提前升高（添加拮抗剂前 LH>10 U/L），共 65 个周期；B 组：添加拮抗剂前 LH≤10 U/L，按照年龄、不孕年限、抗苗勒管激素水平、体质量指数、窦卵泡计数与 A 组进行 1∶3 倾向评分匹配，共 193 个周期。比较两组患者的一般情况、临床资料、胚胎实验室指标及临床结局。结果　两组患者基线特征差异均无统计学意义（均 *P*>0.05）。A、B 两组患者基础 LH 水平、促性腺激素（gonadotropin，Gn）启动剂量、Gn 使用总量、Gn 使用时间、添加拮抗剂时 Gn 使用时间、扳机日雌二醇水平差异均无统计学意义（均 *P*>0.05）。A 组患者添加拮抗剂日 LH 水平［12.2（11.1，17.5）U/L］、雌二醇水平［3 301.0（2 708.0，4 275.0）pmol/L］及卵泡直径［14.0（12.6，15.5） mm］均明显高于 B 组［3.5（2.2，5.2） U/L、2 178.5（1 208.0，3 218.0）pmol/L、13.0（12.0，14.0） mm］，差异均有统计学意义（均 *P*<0.001）。添加拮抗剂后 A 组 LH 水平迅速下降，虽然 A 组添加拮抗剂后 LH 水平［3.4（2.0，5.2）U/L］、扳机日 LH 水平［3.0（1.7，4.7） U/L］仍高于 B 组［2.1（1.5，3.3） U/L，*P*<0.001；2.1（1.4，3.3） U/L，*P*=0.004］，但扳机日孕酮水平与 B 组比较差异无统计学意义（*P*>0.05）。两组患者获卵数、双原核受精率、优质胚胎率、囊胚形成率、移植日内膜厚度、移植胚胎数、移植囊胚占比、种植率差异均无统计学意义（均 *P*>0.05）。两组患者临床妊娠率、早期流产率、活产率差异均无统计学意义（均 *P*>0.05）。结论　卵巢储备功能正常的患者，在应用拮抗剂灵活方案促排卵时 LH 水平提前升高，及时添加拮抗剂后 LH 水平迅速下降，不会导致扳机日孕酮水平的升高，最终不影响 IVF/ICSI 鲜胚移植的临床结局。

【关键词】 卵巢储备功能；　促性腺激素释放激素拮抗剂灵活方案；　黄体生成素；　临床结局

Influence of early elevation of LH with flexible GnRH antagonist protocol on clinical outcomes of IVF/ICSI fresh embryo transfer: a propensity score matching study

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【 Abstract 】 **Objective** To observe the effect of early elevation of luteinizing hormone (LH) with flexible gonadotropin-releasing hormone antagonist (GnRH-A) protocol on pregnancy outcomes of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) fresh embryo transfer. **Methods** A retrospective cohort study was conducted to analyze patients with normal ovarian reserve function who underwent IVF/ICSI with flexible GnRH-A protocol at the Reproductive Medicine Center of the Third Affiliated Hospital of Zhengzhou University from January 2016 to September 2021. According to the level of LH before antagonist addition, the patients were divided into two groups, group A: early elevation of LH (LH >10 U/L before the addition of antagonist, n=65), group B: the patients whose LH≤10 U/L before the addition of antagonist (n=193), which was matched with group A using the 1∶3 propensity score matching by age, duration of infertility, anti-Müllerian hormone, body mass index and antral follicle count. The general conditions, clinical data, embryonic laboratory indicators and clinical outcomes were compared between the two groups. **Results** There were no significant differences in the baseline characteristics between the two groups (all P>0.05). There were no significant differences in basic LH levels, gonadotropin (Gn) initiation dosage, total dosage and duration of Gn used, duration of Gn used when adding antagonists and estradiol (E_2) level on the trigger day between group A and group B (all P>0.05). The LH level [12.2 (11.1, 17.5) U/L], E_2 level [3 301.0 (2 708.0, 4 275.0) pmol/L] and follicle diameter [14.0 (12.6, 15.5) mm] were significantly higher in group A than in group B [3.5 (2.2, 5.2) U/L, 2 178.5 (1 208.0, 3 218.0) pmol/L, 13.0 (12.0, 14.0) mm] when adding antagonist (all P<0.001). The level of LH in group A decreased rapidly after adding antagonist, LH level in group A after antagonist application [3.4 (2.0, 5.2) U/L] and the LH level on the trigger day [3.0 (1.7, 4.7) U/L] were still higher than those in group B [2.1 (1.5, 3.3) U/L, P<0.001; 2.1 (1.4, 3.3) U /L, P=0.004], the level of progesterone on the trigger day was not significantly higher than that in group B (P>0.05). There were no statistically significant differences in the number of oocytes retrieved, two pronuclei fertilization rate, the rate of high-quality embryo, the rate of blastocyst formation, endometrial thickness on the day of transplantation, the number of transferred embryos, the proportion of transferred blastocysts and the implantation rate between the two groups (all P>0.05). The clinical pregnancy rate, the early abortion rate, and the live birth rate were not statistically different between the two groups (all P>0.05). **Conclusion** In patients with normal ovarian reserve, LH level was elevated early with antagonist flexible protocol, and decreased rapidly after the timely addition of antagonist, which did not lead to an increase of progesterone on the trigger day, and ultimately did not affect the clinical outcomes of IVF/ICSI fresh embryo transfer.

【Key words】 Ovarian reserve; Gonadotropin-releasing hormone antagonist flexible protocol; Luteinizing hormone; Clinical outcomes

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·临床报道·

辅助生殖技术受孕双绒毛膜双胎手术减胎与自然减胎活产儿母婴结局分析

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【摘要】 目的　探讨辅助生殖技术（assisted reproductive technology，ART）受孕的双绒毛膜双胎手术减胎与自然减胎活产儿母婴结局间的差异。方法　回顾性队列分析江西省妇幼保健院生殖医学中心 2014 年 3 月至 2021 年 10 月期间共 11 050 个新鲜/冻融周期双胚胎移植后单胎活产周期的临床资料。患者分为手术减胎组（226 例）、自然减胎组（1 506 例），同时以单胎妊娠者为对照组（9 318 例）。采用单因素分析比较 3 组的基本临床资料、母胎并发症及新生儿出生结局的差异，采用多因素 logistic 回归分析影响母婴结局的因素。结果　自然减胎组胎膜早破比例为 1.4%（21/1 506），手术减胎组为 1.3%（3/226），对照组为 0.6%（56/9 318），3 组间差异有统计学意义（*P*=0.003），手术减胎组、自然减胎组早产率[17.3%（39/226）、11.6%（175/1 506）]、极早产率[4.0%（9/226）、1.9%（28/1 506）]、低出生体质量儿占比[15.5%（35/226）、8.6%（129/1 506）]、极低出生体质量儿占比[3.1%（7/226）、1.3%（20/1 506）]、小于胎龄儿发生率[9.3%（21/226）、9.1%（137/1 506）]与对照组[7.7%（721/9 318）、0.9%（86/9 318）、3.9%（367/9 318）、0.5%（45/9 318）、6.0%（560/9 318）]比较，3 组间差异均具有统计学意义（均 *P*<0.001）。手术减胎组早产（a*OR*=2.37，95% *CI*：1.64~3.42，*P*<0.001）、极早产（a*OR*=4.26，95% *CI*：2.02~8.97，*P*=0.001）、低出生体质量（a*OR*=4.35，95% *CI*：2.94~6.44，*P*<0.001）及小于胎龄儿（a*OR*=1.82，95% *CI*：1.14~2.92，*P*=0.013）与自然减胎组（a*OR*=1.54，95% *CI*：1.29~1.84，*P*<0.001；a*OR*=1.95，95% *CI*：1.26~3.01，*P*=0.003；a*OR*=2.26，95% *CI*：1.83~2.79，*P*<0.001；a*OR*=1.60，95% *CI*：1.31~1.95，*P*<0.001）相比风险均更高。3 组出生缺陷率差异无统计学意义（*P*>0.05）。结论　ART 受孕的双绒毛膜双胎手术减胎及自然减胎活产儿的母胎并发症及子代出生缺陷风险与单胎妊娠近似，胎膜早破比例更高，且手术减胎早产及低出生体质量风险高于自然减胎，不提倡依赖手术减胎对 ART 受孕双绒毛膜双胎进行补救。

【关键词】 生殖技术， 辅助； 妊娠减少， 多胎； 手术减胎； 自然减胎； 母婴结局

Analysis of maternal and neonatal outcomes for the living singleton of surgically and spontaneously reduced dichorionic pregnancies following assisted reproductive technology

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【Abstract】 Objective To analyze the difference of maternal and neonatal outcomes for the living infant of surgically and spontaneously reduced dichorionic pregnancies following assisted reproductive technology (ART). **Methods** We used a retrospective cohort study to analyze the clinical data of 11 050 fresh/frozen-thawed double embryos transfer with singleton live birth cycles in the Center for Reproductive Medicine of Jiangxi Maternal and Child Health Hospital from March 2014 to October 2021, including 226 cases in the surgical reduction group, 1 506 cases in the spontaneous reduction group, and 9 318 cases of singleton pregnancy in control group. The basic clinical data, maternal and fetal complications and birth outcomes of the three groups were compared by univariate analysis. Multivariate logistic regression was used to analyze the factors affecting maternal and infant outcomes. **Results** The rate of premature rupture of membranes in the natural fetal reduction group, the surgical reduction group and control group was 1.4% (21/1 506), 1.3% (3/226) and 0.6% (56/9 318), respectively, with a significant difference among the three groups (P=0.003). The differences of the risk of preterm birth, very premature birth, low birth weight, very low birth weight, and small for gestational age among the surgical fetal reduction group [17.3% (39/226), 4.0% (9/226), 15.5% (35/226), 3.1% (7/226), 9.3% (21/226)], the natural fetal reduction group [11.6% (175/1 506), 1.9% (28/1 506), 8.6% (129/1 506), 1.3% (20/1 506), 9.1% (137/1 506)] and control group [7.7% (721/9 318), 0.9% (86/9 318), 3.9% (367/9 318), 0.5% (45/9 318), 6.0% (560/9 318)] were statistically significant (all P<0.001). Compared with the spontaneous reduction group, the surgical reduction group had a higher risk of premature birth [(aOR=2.37, 95% CI: 1.64–3.42, P<0.001) *vs.* (aOR=1.54, 95% CI: 1.29–1.84, P<0.001)], very preterm birth [(aOR=4.26, 95% CI: 2.02–8.97, P=0.001) *vs.* (aOR=1.95, 95% CI: 1.26–3.01, P=0.003)], low birth weight [(aOR=4.35, 95% CI: 2.94–6.44,P<0.001) *vs.* (aOR=2.26, 95% CI: 1.83–2.79, P<0.001)] and small-for-gestational age[(aOR=1.82, 95% CI: 1.14–2.92, P=0.013) *vs.* (aOR=1.60, 95% CI: 1.31–1.95, P<0.001)]. There was no statistical difference in birth defect rate among the three groups (P>0.05). **Conclusion** The risk of maternal and fetal complications and birth defects for the living singletons of surgically and spontaneously reduced dichorionic diamniotic pregnancies were similar to those singleton pregnancies following ART, but the proportion of premature rupture of membranes is higher, and the risk of premature birth and low birth weight of

surgical reduction were higher than that of spontaneous reduction. Surgical reduction is not recommended to use as a rescue measure of dichorionic twins conceived by ART.

【**Key words**】 Reproductive technology, assisted; Pregnancy reduction, multifetal; Surgical reduction; Spontaneous reduction; Maternal and neonatal outcome

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·临床报道·

宫颈鳞状上皮内病变患者行 IVF/ICSI 助孕结局及宫颈局部手术治疗对围产结局的影响

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【摘要】 目的 探讨宫颈鳞状上皮内病变（squamous intraepithelial lesion，SIL）对生育力和体外受精/卵胞质内单精子注射（*in vitro* fertilization/intracytoplasmic sperm injection，IVF/ICSI）的助孕结局影响及宫颈局部手术治疗对围产结局的影响。方法 将 2016 年 1 月至 2020 年 12 月期间在郑州大学第三附属医院生殖中心首次行 IVF/ICSI 的 SIL 患者进行回顾性队列分析，设为 SIL 组（*n*=113）；根据 SIL 组患者年龄、体质量指数、基础卵泡刺激素、窦卵泡计数、取卵时间按 1∶3 标准采用倾向性评分匹配首次行 IVF/ICSI 的无宫颈病变患者，记为对照组（*n*=339）。分析两组患者的基础情况、IVF/ICSI 助孕指标、新鲜周期移植的临床妊娠率、胚胎种植率、累积妊娠率、累积活产率及母婴预后，评估 SIL 患者的助孕结局及宫颈局部手术治疗对围产结局的影响。结果 SIL 组与对照组患者基本情况差异均无统计学意义（均 *P*>0.05）。与对照组相比，SIL 组促性腺激素（gonadotropin，Gn）使用时间、Gn 使用总量、获卵数、受精率、可利用胚胎数、优质胚胎数、可利用囊胚数差异均无统计学意义（均 *P*>0.05）。鲜胚移植周期中 SIL 组移植胚胎数略少于对照组，而临床妊娠率、胚胎种植率略高于对照组，但差异均无统计学意义（均 *P*>0.05）。两组达妊娠时间、累积妊娠率、累积活产率等指标差异均无统计学意义（均 *P*>0.05）；两组分娩方式、分娩孕周、新生儿出生体质

量、妊娠期并发症发生率的差异均无统计学意义（均 *P*>0.05）。79 例获得活产的 SIL 患者根据局部手术治疗的方式分为宫颈锥切亚组、环形电切术亚组和未手术亚组，3 组间分娩方式、分娩孕周、新生儿出生体质量、妊娠期并发症发生率的差异均无统计学意义（均 *P*>0.05）。结论　SIL 不影响患者的生育力及 IVF/ICSI 的助孕结局，且局部手术治疗未增加早产、低出生体质量儿等风险。

【关键词】　宫颈鳞状上皮内病变；　受精，体外；　精子注射，细胞质内；　助孕结局；　局部治疗；　围产结局

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Outcomes of IVF/ICSI assisted pregnancy in patients with squamous intraepithelial lession and obstetric outcomes after local treatment

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【Abstract】 Objective To explore the impact on the fertility and outcomes of females with squamous intraepithelial lesion (SIL) undergoing *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) and obstetric outcomes after local treatment. **Methods** Patients with SIL undergoing IVF/ICSI were set as the SIL group in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2016 to December 2020. While, control group was matched using the propensity scoring method in a 1∶3 ratio in accordance with the age, body mass index, and basic follicle-stimulating hormone, antral follicle count and the oocytes retrieval time. Pregnancy outcomes were compared by analyzing the basic conditions of the two groups, the index of the IVF/ICSI cycles, the clinical pregnancy rate and the implantation rate of the fresh cycles, the cumulative pregnancy rate, the cumulative live birth rate, and obstetric outcomes of patients giving live birth after local treatment were also analyzed. **Results** The demographic characteristics were of no significant differences between the SIL group and control group (all *P*>0.05). As for the IVF/ICSI results, no significant differences were observed in the duration of gonadotropins (Gn) used, total dosage of Gn used, No. of oocytes retrieved, normal fertilization rate, No. of available embryos, No. of high-quality embryos, and No. of blastocyst formation between the two groups (all *P*>0.05). For fresh embryo transfer cycles, the number of transferred embryos was lower, the clinical pregnancy rate and the implantation rate in the SIL group were higher than those in control group, while the differences were not significant (all *P*>0.05). The differences of time to pregnancy,the cumulative pregnancy rate and the cumulative live birth rate between SIL group and control group were not statistically significant (all *P*>0.05). There were no statistically significant differences in delivery methods, gestational age, newborn birth weight, and incidence of pregnancy complications between the two groups (all *P*>0.05). According to local surgical treatment, 79 patients with SIL who achieved live birth

were divided into cold knife conization subgroup, loop electrosurgical excisional procedure subgroup, and no-operation subgroup. There were no statistically significant differences in delivery methods, gestational age, newborn birth weight and incidence of pregnancy complications among the three subgroups (all $P>0.05$). **Conclusion** SIL did not affect fertility of patients or assisted pregnancy outcomes of IVF/ICSI, and local surgical treatment does not increase the risk of preterm birth, low birth weight infants.

【Key words】 Squamous intraepithelial lesions of the cervix; Fertilization *in vitro*; Sperm injections, intracytoplasmic; Pregnancy outcome; Local treatment; Obstetric outcomes

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·临床报道·

用于精子 DNA 碎片指数检测的精液标本处理方式探讨

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【摘要】 目的　探讨不同的精液处理方式对精子 DNA 碎片指数（DNA fragmentation index，DFI）检测结果的影响，评价当前精液处理方式对男性生育力评估的准确性。方法　本研究采用自身配对设计，选取 2021 年 8 月至 2022 年 1 月期间在广西壮族自治区妇幼保健院生殖医学中心行体外受精助孕患者在取卵当日获得的 50 份精液。每一份精液分为 3 组，进行不同方法处理，A 组：精液样本混匀后留取精液原液 50 μL；B 组：密度梯度离心后留取精液与梯度液交界层的精液 50 μL；C 组：密度梯度离心后，吸取精子沉淀团加入含有 1.0 mL 精子洗涤液的试管底部置于培养箱内上游 15 min 后，吸取 50 μL 上游液。精液处理后，进行精液常规检测和精子 DFI 检测。采用 Pearson 进行分析 DFI 和精子不动精子百分率、精子前向运动百分率的相关性。结果　C 组的精子活动率［（96.83±2.28）%］显著高于 A 组［（57.16±11.28）%］和 B 组［（22.54±9.35）%］，组间两两比较和 3 组之间比较差异均有统计学意义（均 $P<0.001$）。B 组的不动精子百分率

[（77.46±9.35）%]、DFI[37.18%（30.41%，47.80%）]高于 C 组[（3.14±2.31）%、0.78%（0.00%，2.07%）]和 A 组[（42.83±11.28）%、22.00%（14.75%，29.25%）]，组间两两比较和 3 组之间比较差异均有统计学意义（均 $P<0.001$）。Pearson 分析结果显示，A 组和 B 组的 DFI 与不动精子百分率呈正相关（$r=0.304$，$P=0.032$；$r=0.612$，$P<0.001$），B 组 DFI 与精子前向运动百分率呈负相关（$r=-0.517$，$P<0.001$）。结论　对于同一份精液，不动精子的 DFI 显著高于活动精子的 DFI。精液原液的 DFI 值因受不动精子的干扰，不能真实反映参与受精的活动精子的 DNA 情况，提示应该选择梯度离心法、上游法或其他方法收集的活动精子进行 DFI 检测，这样更能准确地评估男性生育力。

【关键词】　DNA 碎片指数；　精子活力；　不动精子；　精液处理方法

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Investigating the method of semen treatment for the detection of sperm DNA fragmentation index

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【**Abstract**】　**Objective**　To investigate the effects of different semen sample collection methods on sperm DNA fragmentation index (DFI) test results, then to evaluate the accuracy of the current semen sample collection method in the assessment of male fertility. **Methods**　In this study, 50 semen sample obtained on the day of oocyte retrieval from patients undergoing *in vitro* fertilization at the Reproductive Medical Center in Maternity and Child Health Hospital of Guangxi Zhuang Autonomous Region from August 2021 to January 2022 were collected. For each semen, a small amount of samples were collected in three different retention methods for routine semen and sperm DFI testing. Three different ways of retaining samples were as follows: group A, after mixing of the semen, 50 μL sample was directly collected; group B, after density gradient centrifugation, 50 μL sample was collected at the interface between semen and gradient fluid; group C, after density gradient centrifugation, the sperm pellet was upstream, then 50 μL sample was collected from upstream liquid. After semen treatment, routine semen testing and sperm DFI testing were performed. Pearson was used to analyze the correlation between DFI and the percentage of immobile sperm and the percentage of forward sperm movement. **Results**　The sperm motility rate of group C [(96.83±2.28)%] was significantly higher than that of group A [(57.16±11.28)%, $P<0.001$] and group B [(22.54±9.35)%, $P<0.001$], and there was a statistical difference among the three groups. The immotile sperm rate of group B sample was (77.46±9.35)%, which was significantly higher than that of samples from group C [(3.14±2.31)%, $P<0.001$] and group A [(42.83±11.28)%, $P<0.001$]. There was also a statistical difference in DFI among the three groups ($P<0.001$). The DFI of group B [37.18% (30.41%, 47.80%)] was significantly higher than that of group A [22.00% (14.75%, 29.25%), $P<0.001$]

and group C [0.78% (0.00%, 2.07%), *P*<0.001]. Pearson analysis results showed that the DFI of group A and group B was positively correlated with the percentage of immobile sperm (*r*=0.304, *P*=0.032; *r*=0.612, *P*<0.001), while the DFI of group B was negatively correlated with the percentage of sperm forward movement (*r*=−0.517, *P*<0.001). **Conclusion** For the same semen, the DFI of immotile sperm was significantly higher than that of motile sperm. Therefore, due to the interference of immotile sperm, the DFI value by the current sample retention method cannot accurately reflect the DNA status of active sperm participating in fertilization. This suggests that the samples used for DFI testing should be collected from motile sperm collected by gradient centrifugation, upstream or other methods, which can more accurately assess male fertility.

【Key words】 DNA fragmentation index; Sperm motility; Immotile sperm; Semen treatment

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·个案报道·

体外受精-胚胎移植中第 3 天极低等级胚胎 4 例成功活产病例报道并文献复习

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【摘要】 目的 探讨体外受精-胚胎移植中取卵后移植第 3 天极低等级胚胎的临床价值。方法 回顾性分析 4 例取卵后第 3 天胚胎质量极差且新鲜移植后均成功活产的临床案例，并进行相关文献复习。结果 4 例移植极低等级胚胎 12 d 后血人绒毛膜促性腺激素值显示成功生化妊娠，5 周后 B 超提示均为宫内单胎妊娠，最终 4 名孕妇均成功活产，3 例患者足月产，1 例患者早产，胎儿出生后健康状况良好。结论 通过对 4 例移植第 3 天极低等级胚胎成功活产的分析，建议为少数周期第 3 天所有胚胎质量极差的患者提供新的尝试与选择。

【关键词】 受精； 胚胎移植； 极低等级胚胎； 活产

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Four cases of successful live birth after transferred with extremely low-grade cleavage-stage embryos on day 3 of IVF-ET and literature review

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【**Abstract**】 **Objective** To explore the possible of clinical application value after transferred with day 3 extremely low-grade cleavage-stage embryos during *in vitro* fertilization and embryo transfer. **Methods** The clinical outcomes of four cases with extremely low-grade cleavage-stage embryos on day 3 undergoing IVF-ET were retrospectively analyzed and the related literatures were reviewed. **Results** Four cases successfully got pregnant after 12 days of transplantation of extremely low-grade embryos detected by human chorionic gonadotropin testing, and all of them were intrauterine singleton pregnancies. Finally these four patients had successful live births, and three of them were full-term delivery, one of them was delivery prematurely. All the babies were in the good health. **Conclusion** There is still a degree of successful pregnancy and live birth rate after transferred with day 3 extremely low-grade cleavage-stage embryos. If the quality of all the embryos was extremely low-grade on day 3, we can provide new attempts and choices for the patients who were often giving up embryos transfer.

【**Key words**】 Fertilization; Embryo transfer; Low-grade cleavage-stage; Live birth

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·个案报道·

KRAS 基因突变子宫内膜癌患者高效孕激素治疗后成功助孕 1 例病案报道

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【摘要】 目的　探讨 *KRAS* 基因突变子宫内膜癌患者保留生育功能治疗的疗效及助孕方案的选择。方法　对 1 例 *KRAS* 基因突变子宫内膜癌患者保留生育功能治疗及助孕过程进行报道，并对相关文献进行回顾性分析。结果　患者经高效孕激素及宫腔放置左炔诺孕酮宫内释放系统（levonorgestrel-releasing intrauterine system，LNG-IUS）治疗 20 个月后达到完全缓解，拮抗剂加来曲唑方案促排卵，取出 LNG-IUS 后，降调节后人工周期解冻囊胚移植妊娠并足月分娩一活女婴。结论　*KRAS* 基因突变子宫内膜癌患者经联合治疗可达到完全缓解并生育，但治疗周期长，需严密监测病情变化。

【关键词】 受精，体外；　胚胎移植；　子宫内膜癌；　*KRAS* 基因突变；保留生育功能治疗

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A successful case of assisted pregnancy after highly effective progestogen treatment for endometrial carcinoma patient with *KRAS* gene mutation

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【Abstract】 **Objective** To explore the curative effect of fertility-preserving therapy for endometrial carcinoma patient with *KRAS* gene mutation and the choice of pregnancy-assisting strategy. **Methods** We reported the fertility-preserving treatment and pregnancy-assisted process of a case of endometrial carcinoma patient with *KRAS* gene mutation and analyzed the related literatures. **Results** After 20 months of treatment with highly effective progestogen and intrauterine levonorgestrel-releasing intrauterine system (LNG-IUS), the patient achieved complete remission. Antagonist plus letrozole was used to induce ovulation. After LNG-IUS was taken out, the pregnancy from blastocyst transfer was achieved after downregulation and artificial cycle, and a live baby girl was born at term. **Conclusion** Endometrial carcinoma patient with *KRAS* gene mutation can achieve complete remission and fertility after combined treatment, but the treatment period is long, therefore, it is necessary to closely monitor changes of the disease.

【Key words】 Fertilization *in vitro*; Embryo transfer; Endometrial carcinoma; *KRAS* gene mutation; Fertility-preserving therapy

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·综述·

全球生殖健康理论发展及现状

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【摘要】 生殖健康是人类健康的核心要素，是社会可持续发展的重要支柱。社会、经济和文化等是直接影响生殖健康的决定因素，基于 2030 可持续发展目标，全球应将视角放在更宽广的人类与地球、与自然生态环境的关系上。生殖健康不仅要达到降低死亡率、提高人口出生率及出生人口素质的目的，更要促进人类与资源、环境的可持续发展，是人类健康以及生殖健康的重要内涵。本文通过对生殖健康理论发展和全球生殖健康现状进行系统论述，旨在阐明生殖健康在全民健康中的重要地位和作用，全力推动妇幼健康事业高质量发展。

【关键词】 生殖健康；　性健康；　人口发展；　生殖健康服务

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Development and current status of　reproductive health theory in global

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【Abstract】 Reproductive health is a basic element of human health and an important pillar of social sustainable development. Based on the 2030 sustainable development goal, a global perspective should be given to the broader relationship between human beings and the earth and the natural ecological environment. The purpose of reproductive health is not only to reduce the death rate and improve the quality and the rate of the birth, but also to promote the sustainable development of human beings, resources, and environment. This paper systematically discussed the development of reproductive health theory and the current situation of global reproductive health, in order to clarify the important status and role of reproductive

health in the national health and to promote the high-quality development of maternal and child health.

【**Key words**】 Reproductive health; Sexual health; Population development; Reproductive health services

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·综述·

女性生殖道菌群与异位妊娠相关性的研究进展

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【摘要】 异位妊娠是早孕期常见的不良妊娠结局之一，一般认为与输卵管、子宫内膜、胚胎三者均有相关性，亦受到遗传、环境、免疫、感染等多因素影响。而随着宏基因组测序技术的发展，女性生殖道菌群被证实与内膜容受性的获得、生殖道免疫环境的稳定及炎症调节紧密联系，在早孕期排卵、受精、胚胎运输及着床各个环节均可能发挥重要作用。研究提示菌群异常可能导致不孕、流产、早产等不良妊娠结局，特别是严重危害女性生命安全的异位妊娠，也可能与之具有相关性。本文主要总结女性生殖道菌群与异位妊娠相关性的研究进展，探讨生殖道菌群的正常组成以及菌群失调导致异位妊娠发生的潜在机制，为临床干预提供参考和借鉴。

【关键词】 妊娠， 异位； 生殖道感染； 输卵管； 菌群； 子宫内膜容受性

基金项目：北京市科技计划项目（Z191100006619076）；国家杰出青年科学基金（81925013）

Research progress on the relationship between female reproductive tract microbiota and ectopic pregnancy

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【Abstract】 Ectopic pregnancy is one of the most common adverse pregnancy outcomes during first trimester, and is generally believed to be caused by disorders of the fallopian tube, the endometrium and the embryo, accompanying genetic, environmental, immune, pathogen infection and other endocrine abnormalities. With the development of the macro genome sequencing, the female genital tract flora was confirmed to be closely linked with the establishment of endometrium receptivity, the regulation of genital tract inflammation and maintaining immune environment stability. It also plays an essential role in ovulation, fertilization, embryo transport and implantation. Studies suggested that genital tract dysbiosis might cause adverse pregnancy outcomes such as infertility, miscarriage, preterm birth, and ectopic pregnancy, which severely endanger women's security and safety. It suggests that genital tract microbiota may be associated with impaired functions of the reproductive system that potentially lead to ectopic pregnancy. This article mainly summarizes the research progress of the correlation between female genital tract microbiota and ectopic pregnancy, discusses the normal composition of genital tract microbiota and the potential mechanism of ectopic pregnancy caused by microbiota dysbiosis, so as to provide reference for clinical intervention.

【Key words】 Pregnancy, ectopic; Repoductive tract infections; Fallopian tubes; Microbiota; Endometrium receptivity

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·综述·

铁死亡与女性生殖相关疾病的研究进展

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【摘要】 铁及铁代谢参与调节女性生殖系统的生理功能。必要的铁对女性生殖功能起着积极作用，而铁过载可诱导机体代谢过程发生异常。铁死亡是一种铁依赖性的脂质氧化物代谢障碍，伴随着抗氧化机制失衡及脂质活性氧堆积的细胞死亡方式。研究表明，子宫内膜异位症、多囊卵巢综合征及滋养细胞功能障碍疾病的病理过程中都有着不同程度的铁死亡，并且铁死亡通路及相关基因参与早期胚胎发育、胎盘氧化应激，卵母细胞功能调控等，提示铁代谢及铁死亡关键基因作为潜在治疗靶点的可能性。目前，铁死亡女性生殖系统功能及相关疾病的研究仍不明确，本文就铁死亡及相关机制在女性生殖系统相关疾病中的研究进展进行讨论，以期为临床相关疾病的诊疗提供参考。

【关键词】 铁死亡； 铁代谢； 脂质过氧化； 生殖系统

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Research progress of ferroptosis and female reproductive-related diseases

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【Abstract】 Iron and iron metabolism are involved in regulating the physiological functions of the female reproductive system. Essential iron plays a positive role in female development and reproductive function, while iron overload can induce abnormal metabolic processes in the body. Ferroptosis is a cellular iron-dependent disorder of lipid oxide metabolism, accompanied by oxidative imbalance and accumulation of lipid reactive oxygen species. Studies have shown that ferroptosis occurred in the pathology of endometriosis, polycystic ovary syndrome and trophoblast dysfunction diseases. Besides, the pathways and related genes of ferroptosis are involved in early embryonic development, placental oxidative stress, and regulation of oocyte function, suggesting the possibility of key molecules of iron metabolism and ferroptosis as potential therapeutic targets. The regulation

mechanism for ferroptosis in female reproduction-related diseases is unclear now.This review discussed and summarized the recent research progress of iron overload and ferroptosis in female reproductive system and related diseases, in order to provide reference for clinical treatment of related diseases.

【Key words】 Ferroptosis; Iron metabolism; Lipid peroxides; Reproductive system

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·综述·

卵母细胞线粒体自噬的研究进展

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【摘要】 线粒体作为卵母细胞含量最丰富的细胞器，其数量和质量直接影响卵母细胞质量与发育潜能，从而决定了女性生育的结局。线粒体自噬作为一种细胞内选择性降解功能异常线粒体的大自噬，对卵母细胞内线粒体功能维持和平衡至关重要。近年来，围绕线粒体自噬在卵母细胞内的相关功能与机制研究也逐渐成为女性生殖领域的研究热点。本文综述了线粒体自噬参与卵母细胞成熟、卵母细胞老化，以及线粒体自噬参与药物与环境刺激影响卵母细胞质量，和在辅助生殖技术中的意义，期望有利于深入理解卵母细胞线粒体自噬的生物学意义，为体外或体内改善卵母细胞质量提供帮助。

【关键词】 卵母细胞；　线粒体自噬；　氧化应激

基金项目：贵州医科大学附属医院国家自然科学基金培育项目（gyfynsfc-2021-38）

Research progress on the mitophagy in oocytes

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【Abstract】 Mitochondria are the most abundant organelles in oocytes, and their quantity and quality directly affect the quality and developmental potential of oocytes, thus determining the outcome of female fertility. Mitophagy, as a large autophagy that selectively degrades dysfunctional mitochondria, is crucial for mitochondrial function maintenance and homeostasis in oocytes. In recent years, studies on the functions and mechanisms of mitophagy in oocytes have gradually become a research hotspot in the field of female reproduction. This paper reviews the mitochondrial autophagy in oocyte maturation, oocyte aging, and mitochondria autophagy involving in drugs and environmental stimuli which affects oocyte quality, and its significance in assisted reproductive technology. We expect to benefit for further understanding the biological significance of mitophagy in oocytes, and to inform the improvement of oocyte quality *in vitro* or *in vivo*.

【Key words】 Oocyte; Mitophagy; Oxidative stress

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·综述·

自噬在子宫内膜中的作用及机制研究进展

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【摘要】 自噬是一种维持细胞、组织和生物体稳态的重要代谢过程。在子宫内膜细胞中，自噬通过多种途径参与调节子宫内膜生长和容受性，包括AMPK/TSC/mTOR信号通路、PI3K/AKT/mTOR信号通路，以及ATG4C、ULK4和RB1CC1/FIP200等相关信号通路，这些途径对于维持细胞内环境稳态和女性生殖系

统健康至关重要。同时，自噬异常会导致子宫内膜容受性下降，并与多种内膜相关疾病的发生发展有关，且自噬水平在疾病的不同时期呈现出动态变化。本文对自噬在子宫内膜中的作用及机制进行了综述，且为新药研发和治疗策略提供相关依据，有望为解决子宫内膜疾病的治疗难题提供新思路和方向。

【关键词】 自噬； 子宫内膜容受性； 子宫内膜疾病

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Research progress on the role and mechanism of autophagy in endometrium

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【Abstract】 Autophagy is an important metabolic process that maintains homeostasis of cells, tissues and organisms. In endometrial cells, autophagy is involved in regulating endometrial growth and receptivity through a variety of pathways, including AMPK/TSC/mTOR signaling pathway, PI3K/AKT/mTOR signaling pathway, ATG4C, ULK4, RB1CC1/FIP200 and other related signaling pathways. These pathways are essential for maintaining intracellular environmental homeostasis and the health of the female reproductive system. At the same time, abnormal autophagy can lead to decreased endometrial receptivity and is associated with the occurrence and development of a variety of endometria-related diseases, and the level of autophagy presents dynamic changes in different periods of disease. In this paper, the role and mechanism of autophagy in endometrium were reviewed in order to provide relevant evidence for new drug development and treatment strategies. Deep understanding of the role and mechanism of autophagy in endometrium is expected to provide new ideas and directions for the treatment of endometrial diseases.

【Key words】 Autophagy; Endometrial receptivity; Endometrial disease

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·综述·

泛素蛋白在子宫内膜异位症中作用的研究进展

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【摘要】 子宫内膜异位症为育龄期妇女的多发病和常见疾病，严重影响着患者的生育能力和生活质量。泛素蛋白可广泛地分布于各种细胞中，参与调控细胞周期、信号转导、细胞凋亡、转录调节、炎症反应等许多生理或病理过程。近年研究显示，泛素蛋白参与了子宫内膜异位症的发生与发展，因此本文就不同泛素蛋白在子宫内膜异位症中的作用作一综述。

【关键词】 子宫内膜异位症； E3 泛素连接酶； 去泛素化酶

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Research progress on the role of ubiquitin protein in endometriosis

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【Abstract】 Endometriosis is a common and frequently occurring disease among women of childbearing age, which seriously affects the the patient's fertility and quality of life. Ubiquitin proteins exist widely in all kinds of cells and participate in many physiological or pathological processes, such as cell cycle regulation, transcriptional regulation, signal transduction, inflammatory response, apoptosis. Recent studies have shown that ubiquitin proteins are involved in the origin and development of endometriosis, so this article reviews the roles of different ubiquitin proteins in endometriosis.

【Key words】 Endometriosis; E3 Ubiquitin ligase; Deubiquitinating enzymes

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·管理论坛·

关于胚胎植入前遗传学检测遗传咨询规范化的探讨

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【摘要】 随着分子诊断技术的快速发展和大众优生优育意识的提高，近年来胚胎植入前遗传学检测（preimplantation genetic testing，PGT）技术在临床上得到了广泛应用。PGT 助孕流程中，遗传咨询由始至终贯穿了 PGT 助孕的各个阶段，是 PGT 助孕成功的重要保证。目前在我国，关于 PGT 遗传咨询如何规范地开展缺乏相应的法律法规进行统一规定，也没有全国统一标准的培训体系和认证机构，专家共识和指南也少有涉及。因此，制定切实可行的 PGT 遗传咨询流程和标准十分必要，做到有理可循，有法可依，保障 PGT 过程的顺利实施，最大化降低出生缺陷儿的发生风险。本文从遗传咨询体系的现状和规范化建设两个方面，结合国内外的实际情况以及现有的法律法规，对 PGT 遗传咨询的规范化做了一个全面的梳理和探讨。

【关键词】 胚胎植入前遗传学检测；　遗传咨询；　规范

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Discussion on standardization of genetic counseling of preimplantation genetic testing

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【Abstract】 With the rapid development of molecular diagnostic technology and the increased public awareness of eugenics, preimplantation genetic testing

(PGT) technology has been widely used in clinical practice in recent years. Genetic counseling is provided throughout all stages of PGT and is an important guarantee for carrying on the PGT work smoothly. At present, there is a lack of laws and regulations governing how PGT genetic counseling should be conducted, there is also no nationally standardized training system and certification bodies, and expert consensus and guidelines are also scarce, so it is necessary to develop practical processes and standards for genetic counseling of PGT. Therefore, it is essential to develop practical procedures and standards for genetic counseling of PGT, to ensure the smooth implementation of the PGT process, and to minimize the risk of birth defects. This article makes a comprehensive review and discussion on the standardization of genetic counseling of PGT from the current situation and standardization construction of the genetic counseling system, combined with the actual situation worldwide and existing laws and regulations.

【 Key words 】 Preimplantation genetic testing; Genetic counseling; Standardization

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·管理论坛·

育龄期子宫内膜异位症患者的长期管理

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【摘要】 子宫内膜异位症（endometriosis，EMS）是育龄期女性的常见病，EMS 可能会引起疼痛、不孕及包块等。由于 EMS 影响患者的整个生育期，易复发，难以根治，故应该制定 EMS 患者的长期管理方案，包括药物治疗、手术治疗、辅助生殖技术等。生育需求正是育龄期 EMS 女性的主要需求之一，故临床医生对于育龄期 EMS 女性进行长期随访管理、治疗和咨询的主要目的不仅是治疗 EMS 所引起的疼痛，减少 EMS 复发和进展，更要注意在适当的时候对患者进行生育指导，

在患者合并不孕问题时给予恰当的助孕治疗。本文对育龄期 EMS 患者长期管理方案进行综述。

【关键词】 子宫内膜异位症； 不孕症； 育龄期； 长期管理； 生育指导

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Long-term management of patients with endometriosis in reproductive age

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【 Abstract 】 Endometriosis (EMS) is a common disease in women of reproductive age. EMS may cause pain, infertility and mass. Because EMS affects the entire reproductive period of patients, it is easy to relapse, and difficult to cure. Therefore, a long-term management plan for patients with EMS should be formulated, including medical treatment, surgical treatment, and assisted reproductive technology. Fertility needs are one of the main needs of women with EMS of reproductive age. Therefore, long-term follow-up management is needed for women with EMS of reproductive age. The main purpose of treatment and consultation is to treat the pain caused by EMS and reduce the recurrence and progression of EMS, and give fertility guidance to patients when appropriate, and give appropriate treatment when patients are diagnosed with infertility. This article reviewed the long-term management of EMS patients of reproductive age.

【 Key words 】 Endometriosis; Infertility; Reproductive age; Long-term management; Fertility guidance

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