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辅助生殖前和期间甲状腺疾病筛查 诊治专家共识

中国优生优育协会生育力保护与修复专业委员会

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【摘要】 甲状腺疾病是造成生育力下降的重要原因之一。生育力低下女性患甲状腺疾病比例逐年增加, 甲状腺功能对男性生殖系统的影响正逐渐引起重视。在行辅助生殖治疗前应对夫妇双方甲状腺功能进行检查, 尤其女方在进行卵巢刺激期间应注意甲状腺功能的变化, 对于甲状腺功能减退者, 需考虑左旋甲状腺素治疗。为了规范筛查和治疗, 参照国内外指南和文献形成本专家共识, 旨在为伴甲状腺疾病或功能异常的不孕不育夫妇提供治疗的辅助生殖科医生、内分泌科医生和妇科医生提供指导。

【关键词】 生殖技术, 辅助; 低生育力; 甲状腺功能减退; 甲状腺自身免疫

实践指南注册: 国际实践指南注册与透明化平台, PREPARE-2023CN379

Expert consensus on thyroid disease screening before and during assisted reproduction

Fertility Protection and Repair Specialized Committee of the Chinese Eugenics and Fertility Association

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【Abstract】 Thyroid disease is one of the significant factors contributing to reduced fertility. The prevalence of thyroid disease in females with reduced fertility is on the rise. The impact of thyroid function on the male reproductive system is gaining attention. Therefore, it is crucial to test the thyroid function of couples before undergoing assisted reproductive technology (ART), especially during ovarian stimulation, and levothyroxine (LT4) therapy should be considered for patients with hypothyroidism. To standardize screening and treatment, this expert consensus is formed with reference to domestic and foreign guidelines and literature, aiming to provide guidance for assisted reproductive surgeons, endocrinologists and gynecologists who provide treatment for infertile couples with thyroid disease or dysfunction.

【 Key words 】 Reproductive technology, assisted; Subfertility; Hypothyroidism; Thyroid autoimmunity

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临床研究

多胎妊娠减胎术临床特征及妊娠结局分析——历时 12 年的队列研究

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【摘要】 目的 分析多胎妊娠减胎术患者的妊娠结局及影响活产的因素, 为减胎策略提供参考依据。方法 回顾性队列研究纳入 2009 年 1 月 1 日至 2020 年 12 月 31 日期间于北京大学第三医院妇产科生殖医学中心进行多绒毛膜性多胎妊娠减胎术的患者, 分析患者临床特征, 随访妊娠结局, 分为活产组 ($n=1\ 555$) 和非活产组 ($n=205$), 并应用多因素 logistic 回归分析影响活产的因素。并进一步亚组分析, 将多胎妊娠分为双绒毛膜双羊膜囊、三胎妊娠、四胎及以上多胎妊娠三组。结果 纳入 1 925 例多胎妊娠减胎病例, 完成妊娠结局随访 1 760 例。数据显示 12 年来减胎多胎类型中双绒毛膜双羊膜囊增多, 经腹减胎比例逐年增加, 年减胎患者活产率波动于 83%~94%。四胎及以上多胎妊娠减胎后活产率 [75.8% (72/95)] 分别低于双绒毛膜双羊膜囊减胎后 [90.0% (796/884), $P<0.001$]、双绒毛膜三羊膜囊减胎后 [89.9% (241/268), $P<0.001$] 和三绒毛膜三羊膜囊减胎后 [86.9% (446/513), $P=0.005$]。经腹部超声引导下减胎术后活产率 [91.4% (655/717)] 分别高于经阴道氯化钾 (KCl) 胎心搏动区注射减胎后活产率 [84.9% (304/358), $P=0.001$] 及经阴道胚胎抽吸减胎后活产率 [87.0% (596/685), $P=0.009$], 经阴道 KCl 胎心搏动区注射减胎与经阴道抽吸减胎活产率差异无统计学意义 ($P=0.351$)。减胎术后保留单胎的患者活产率 [89.7% (1 062/1 184)] 高于保留双胎患者 [85.6% (493/576), $P=0.012$]。在调整了年龄、助孕方式、多胎类型、保留胚胎数等混杂因素后, 中孕期经腹部超声引导下减胎为活产率的保护因素 ($P=0.040$, $OR=1.604$, 95% CI : 1.021~2.519)。结论 随移植策略的改变, 双绒毛膜双羊膜囊妊娠减胎比例增加, 中孕期经腹部超声引导下减胎术的比例增加, 经腹部减胎可能是多胎妊娠减胎术更好的选择; 早孕期经阴道抽吸减胎法与 KCl 胎心搏动区注射法减胎妊娠结局相似; 四胎及以上多胎妊娠减胎后妊娠结局较差, 临床上需严格控制胚胎移植数目, 规范诱导排卵方案。

【关键词】 多胎妊娠; 多胎妊娠减胎术; 经阴道多胎妊娠减胎术; 经腹部多胎妊娠减胎术; 妊娠结局

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Clinical characteristics and pregnancy outcomes of multifetal pregnancy reduction: a 12-year cohort study

Li Li, Li Yanyi, Yang Rui, Fan Mengjie, Yang Shuo, Li Jia, Song Ying, Pan Ningning, Tian Tian, Ma Caihong, Li Rong, Liu Ping, Qiao Jie

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【Abstract】 Objective To analyze the clinical characteristics, pregnancy outcomes and factors affecting live birth of patients undergoing multifetal

pregnancy reduction (MFPR), in order to provide reference for clinical strategies.

Methods A retrospective cohort study was conducted on all patients who underwent multifetal pregnancy reduction among polychorionic multifetal pregnancy patients at the Center for Reproductive Medicine, Department of Obstetrics and Gynecology of Peking University Third Hospital during a period of 12 years from January 1, 2009 to December 31, 2020. The overall and annual clinical characteristics were analyzed, pregnancy outcomes were followed up. Patients were divided into live birth group ($n=1\ 555$) and not live birth group ($n=205$), and factors affecting live birth were analyzed by multivariate logistic. Through further subgroup analysis, multiple pregnancies were divided into three subgroups: dichorionic diamniotic twin, triplet pregnancy, and four or more high sequence multiple pregnancy. **Results** A total of 1 925 patients who underwent MFPR were included, and 1 760 pregnancy outcomes were followed up. In the past 12 years, there had been an increase in dizygotic twins, and the proportion of transabdominal fetal reduction had significantly increased, from 3% in 2009 to 77% in 2020. The annual live birth rate of reduction patients fluctuated between 83% and 94%. The live birth rate of patients with MFPR was related with the type of multiple pregnancies, the method of reducing pregnancies, and the number of retained embryos. The live birth rate of four or more high sequence multiple pregnancies [75.8% (72/95)] was lower than that of dichorionic diamniotic twins [90.0% (796/884), $P<0.001$], the dichorionic diamniotic twins [89.9% (241/268), $P<0.001$], the trichorionic triamniotic triplet pregnancy [86.9% (446/513), $P=0.005$]. The live birth rate of transabdominal fetal reduction [91.4% (655/717)] was higher than that of transvaginal fetal reduction with fetal cardiac activity area injection of KCl [84.9% (304/358), $P=0.001$], and vaginal embryo aspiration [87.0% (596/685), $P=0.009$]. There was no statistically significant difference in the live birth rate between vaginal KCl injection and vaginal aspiration ($P=0.351$). The survival rate of patients with retained singletons [89.7% (1 062/1 184)] was higher than that of patients with retained twins [85.6% (493/576), $P=0.012$]. After adjusting for confounding factors such as age, assisted pregnancy method, type of multiple pregnancies, and number of retained embryos, transabdominal fetal reduction was an independent protective factor for live birth rate ($P=0.040$, $OR=1.604$, 95% CI : 1.021–2.519). **Conclusion** With the change of transplantation strategy, the proportion of dichorionic diamniotic twins increased, and the proportion of transabdominal fetal reduction increased, which pregnancy outcomes might be better. There was no difference in pregnancy outcomes between those who underwent vaginal aspiration and transvaginal fetal reduction with fetal cardiac activity area injection of KCl. The outcomes of four or more high sequence multiple pregnancies were poor, and it was necessary to strictly control the number of embryo transfers and optimize ovulation promotion plans in clinical practice.

【 Key words 】 Multiple pregnancy; Multifetal pregnancy reduction; Transvaginal fetal reduction; Transabdominal fetal reduction; Pregnancy outcome

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临床研究

子宫内膜异位症相关性不孕症患者的胚胎质量及 IVF/ICSI-ET 结局的研究

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【摘要】 目的 探讨子宫内膜异位症 (endometriosis, EMT) 对行体外受精/卵胞质内单精子注射-胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer, IVF/ICSI-ET) 治疗的不孕症患者的卵母细胞、胚胎质量及妊娠与分娩结局的影响。方法 通过回顾性队列研究, 选取于 2016 年 1 月至 2023 年 12 月期间就诊于哈尔滨医科大学附属第一医院生殖医学科行 IVF/ICSI-ET 治疗的 EMT 患者 (383 例, EMT 组) 和单纯输卵管因素的不孕症患者 (1 613 例, 对照组), 采用 1:1 倾向性评分匹配对两组患者的年龄、抗苗勒管激素水平、体质量指数、不孕类型占比、不孕年限、促排卵方案、授精方式、IVF/ICSI 既往周期数进行匹配, 最终纳入 EMT 组 285 例和对照组 285 例, 分析 EMT 对胚胎质量及临床结局的影响。结果 ①两组患者的促性腺激素 (gonadotropin, Gn) 使用时间、Gn 使用总量、Gn 启动剂量、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日雌二醇黄体生成素、孕酮水平的差异均无统计学意义 (均 $P>0.05$)。②EMT 组患者的获卵总数 [(7.48±5.15) 枚]、MII 卵子数

[(6.38±4.61) 枚]、可移植胚胎数 [(4.16±3.16) 枚]、优质胚胎数 [2.00 (0.00, 3.00) 枚]、双原核 (two pronuclei, 2PN) 优质胚胎率 [42.33% (602/1422)] 均低于对照组 [(8.45±4.86) 枚, $P=0.021$; (7.32±4.43) 枚, $P=0.013$; (4.95±3.19) 枚, $P=0.003$; 2.00 (1.00, 4.00) 枚, $P=0.002$; 48.76% (747/1532), $P=0.032$], 差异均有统计学意义。③两组患者新鲜周期移植和新鲜周期全胚冷冻后进行第一次解冻周期移植的临床妊娠率、胚胎种植率、早产率、早期流产率、异位妊娠率、男婴/女婴比例、分娩周数、剖宫产率的差异均无统计学意义 (均 $P>0.05$) , 新鲜周期移植的 EMT 患者活产率 [29.71% (41/138)] 低于对照组 [48.90% (89/182)], $P=0.023$], 差异具有统计学意义。④EMT 不是 IVF/ICSI 治疗的临床妊娠率和活产率的独立影响因素, 年龄、移植胚胎数是 IVF/ICSI 治疗的临床妊娠率和活产率的独立影响因素 ($OR=0.923$, 95% CI : 0.868~0.982, $P=0.011$; $OR=0.890$, 95% CI : 0.832~0.952, $P=0.001$; $OR=2.408$, 95% CI : 1.331~4.356, $P=0.004$; $OR=3.838$, 95% CI : 1.869~7.879, $P<0.001$)。结论 EMT 可能导致进行 IVF/ICSI-ET 治疗的不孕症患者的获卵总数和 MII 卵子数减少, 胚胎质量下降, 但是不影响其临床妊娠结局和分娩结局。

【关键词】 子宫内膜异位症; 不孕症; 胚胎; 临床妊娠率; 活产率; 受精, 体外; 精子注射, 细胞质内; 胚胎移植

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Embryo quality and IVF/ICSI-ET treatment outcomes in patients with endometriosis and infertility

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【Abstract】 **Objective** To investigate the effect of endometriosis (EMT) on oocytes, embryo quality and pregnancy and delivery outcomes in infertility patients treated with *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET). **Methods** A retrospective cohort study was conducted to select the EMT patients (383 cases, EMT group) and the infertility patients with tubal factor (1 613 cases, control group) who underwent IVF/ICSI-ET treatment in the Department of Reproductive Medicine, the First Affiliated Hospital of Harbin Medical University from January 2016 to December 2023. The cases were matched with the number of age, body mass index, anti-Müllerian hormone, proportion of infertility type, duration of infertility, ovulation stimulating therapy, insemination mode, number of previous IVF/ICSI cycles of the two groups by 1 : 1 propensity score matching. Totally 285 patients with EMT and 285 patients in control group were finally included to analyze the effects of EMT on embryo quality and pregnancy outcome. **Results** 1) There were no statistically significant differences in the duration of gonadotropin (Gn) used, the total dosage and the initiating dosage of Gn used, and the levels of estradiol, luteinizing hormone, and

progesterone on the human chorionic gonadotropin (hCG) injection day between the two groups (all $P>0.05$). 2) The total number of oocytes (7.48 ± 5.15), the number of MII oocytes (6.38 ± 4.61), the number of transferable embryos (4.16 ± 3.16), the number of high-quality embryos [2.00 ($0.00, 3.00$)] and the rate of two pronuclei (2PN) high-quality embryos [42.33% ($602/1\ 422$)] in EMT group were all lower than those in control group [$8.45\pm4.86, P=0.021$; $7.32\pm4.43, P=0.013$; $4.95\pm3.19, P=0.003$; 2.00 ($1.00, 4.00$), $P=0.002$; 48.76% ($747/1\ 532$), $P=0.032$], the differences were statistically significant. 3) There were no statistically significant differences in clinical pregnancy rate, embryo implantation rate, premature birth rate, early abortion rate, ectopic pregnancy rate, male/female ratio, number of weeks of delivery and cesarean section rate between the two groups with fresh cycle transplantation and with embryo freezing in fresh cycle and embryo transferred in the first resuscitation cycle (all $P>0.05$), the live birth rate of EMT patients with fresh cycle transplantation [29.71% ($41/138$)] was lower than that of control group [48.90% ($89/182$), $P=0.023$], and the difference was statistically significant. 4) EMT was not an independent factor of clinical pregnancy rate and live birth rate after IVF/ICSI treatment, but age and number of embryos transferred were independent factors of clinical pregnancy rate and live birth rate of IVF/ICSI treatment ($OR=0.923$, 95% CI : $0.868-0.982$, $P=0.011$; $OR=0.890$, 95% CI : $0.832-0.952$, $P=0.001$; $OR=2.408$, 95% CI : $1.331-4.356$, $P=0.004$; $OR=3.838$, 95% CI : $1.869-7.879$, $P<0.001$). **Conclusion** EMT may reduce the number of oocytes and MII oocytes in infertility patients treated with IVF/ICSI-ET, and the quality of embryos in patients with EMT treated with IVF is worse, but it does not affect the clinical pregnancy outcome and delivery outcome in patients with EMT.

【Key words】 Endometriosis; Infertility; Embryo; Clinical pregnancy rate; Live birth rate; Fertilization *in vitro*; Sperm injection, intracytoplasmic; Embryo transfer

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·临床研究·

微环境中肾上腺髓质素水平与多囊卵巢综合征患者卵巢功能及炎症状态相关性研究

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【摘要】 目的 探讨多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者卵泡液肾上腺髓质素 (adrenomedullin, ADM) 的表达水平及其与卵巢功能和炎症的相关性。方法 收集 2023 年 3~12 月于山西省儿童医院(山西省妇幼保健院)生殖医学中心接受体外受精 (*in vitro* fertilization, IVF)/卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 拮抗剂方案来促排卵助孕的不孕夫妻的资料进行队列研究。将 PCOS 患者作为 PCOS 组 ($n=20$), 选择同期单纯因输卵管和/或男方因素行 IVF/ICSI 助孕的患者作为对照组 ($n=20$)。检测并比较两组患者一般临床资料和卵泡液中 ADM、白细胞介素 1β (interleukin 1β , IL- 1β)、IL-18、转化生长因子 β (transforming growth factor β , TGF- β) 的浓度, 并以卵泡液 ADM 浓度为主要研究指标与其他指标进行相关性及多元线性回归分析。同时比较两组患者颗粒细胞 (granulosa cells, GCs) 的 ADM mRNA 表达、细胞周期与凋亡情况。结果 与对照组相比, PCOS 组患者卵泡液及 GCs 中 ADM 表达明显更低 (均 $P<0.001$), 而其睾酮、黄体生成素与卵泡刺激素比值、窦卵泡计数 (antral follicle count, AFC)、获卵数、卵巢敏感指数以及卵泡液 IL- 1β 、IL-18、TGF- β 更高, 且均与 ADM 浓度呈负相关 ($r=-0.37, P=0.019$; $r=-0.32, P=0.047$; $r=-0.50, P<0.001$; $r=-0.38, P=0.017$; $r=-0.38, P=0.016$; $r=-0.44, P=0.005$; $r=-0.37, P=0.018$; $r=-0.54, P<0.001$)。多元线性回归分析表明, AFC、促性腺激素启动剂量、IL- 1β 和 TGF- β 是影响局部 ADM 水平的独立相关因素 ($r=-0.37, P=0.008$; $r=-0.27, P=0.035$; $r=-0.28, P=0.028$; $r=-0.45, P<0.001$)。两组患者 GCs 的周期情况差异无统计学意义 ($P>0.05$), 但 PCOS 组 GCs 凋亡率 (apoptosis rate, AR) 高于对照组 (PCOS 组 AR 中位数=46.07%, 对照组 AR 中位数=28.57%, $n=10$,

$P=0.036$)。结论 PCOS 患者卵泡液中 ADM 表达的降低与卵巢内分泌紊乱、多个囊泡、高卵巢反应性及局部炎症状态有关。

【关键词】 多囊卵巢综合征； 肾上腺髓质素； 卵泡液； 卵巢功能； 炎症

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A study on the correlation between adrenomedullin levels in microenvironment and ovarian function and inflammatory status in patients with polycystic ovary syndrome

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【 Abstract 】 **Objective** To explore the expression levels of adrenomedullin (ADM) in follicular fluid of patients with polycystic ovary syndrome (PCOS) and its correlation with ovarian function and inflammation. **Methods** To conduct a cohort study, the data on infertile couples who received an antagonistic regimen of *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI) to promote ovulation from March to December 2023 at the Reproductive Medicine Center of Shanxi Children's Hospital (Shanxi Maternal and Child Health Hospital) were collected. PCOS patients were selected as the PCOS group, and patients who underwent IVF/ICSI assisted pregnancy solely due to tubal and/or male factors during the same period were selected as control group. The general clinical data of two groups of patients were analyzed, and the expression of ADM, interleukin 1 β (IL-1 β), IL-18, transforming growth factor β (TGF- β) in the follicular fluid were compared between the two groups of patients. And taking the concentration of ADM in follicular fluid as the main research indicator, correlation and multiple linear regression analysis were conducted with other indicators. Simultaneously the ADM mRNA expression, cell cycle and cell apoptosis of granulosa cells were compared between the two groups. **Results** This study included 20 cases in the PCOS group and 20 cases in control group. Compared with control group, the expression of ADM in follicular fluid and granulosa cells of patients with PCOS were significantly lower (both $P<0.001$), while its testosterone, the ratio of luteinizing hormone and follicle-stimulating hormone, antral follicle count (AFC), number of retrieved eggs, ovarian sensitivity index, as well as IL-1 β , IL-18 and TGF- β in follicular fluid were higher and negatively correlated with ADM

($r=-0.37$, $P=0.019$; $r=-0.32$, $P=0.047$; $r=-0.50$, $P<0.001$; $r=-0.38$, $P=0.017$; $r=-0.38$, $P=0.016$; $r=-0.44$, $P=0.005$; $r=-0.37$, $P=0.018$; $r=-0.54$, $P<0.001$). Multiple linear regression showed that AFC, gonadotropin initiation dose, IL-1 β and TGF- β were the independent related factors that affect local ADM levels ($r=-0.37$, $P=0.008$; $r=-0.27$, $P=0.035$; $r=-0.28$, $P=0.028$; $r=-0.45$, $P<0.001$). There was no statistically significant difference in the cell cycle of granulocytes between the two groups ($P>0.05$), but the apoptosis rate (AR) of granulocytes was higher in the PCOS group than in control group (median AR in the PCOS group was 46.07%, median AR in control group was 28.57%, $n=10$, $P=0.036$). **Conclusion** The decreased expression of ADM in follicles of PCOS patients is related to ovarian endocrine disorders, multiple vesicles, high ovarian responsiveness and local inflammatory status.

【Key words】 Polycystic ovary syndrome; Adrenomedullin; Follicular fluid; Ovarian function; Inflammation

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·临床研究·

多囊卵巢综合征合并代谢综合征患者的月经特点及肠道菌群特征分析

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【摘要】 目的 探讨多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者月经异常对于日后合并代谢综合征 (metabolic syndrome, MS) 的预测意义, 并比较合并 MS 患者与不合并者的肠道菌群结构差异。方法 采用病例对照研究的方法选取 2021 年 2 月至 2023 年 12 月期间于复旦大学附属金山医院妇产科门诊就诊的 111 例 PCOS 患者作为研究对象, 根据其是否合并 MS 分为 PCOS 不合并 MS 组 ($n=74$, 记为 NMS 组) 和 PCOS 合并 MS 组 ($n=37$, 记为 MS 组), 收集所有病例的月经相关信息及粪便标本, 分析两组月经特点以及其对 PCOS 合并 MS 的预测意义; 通过 16S rDNA 高通量测序对两组患者的肠道菌群进行对比分析。结果 NMS 组月经初潮正常后异常者月经改变年龄 [(23.47±4.73) 岁]、月经改变发生于初潮后的时间 [(9.85±5.11) 年]、月经改变时长 [(3.43±2.78) 年] 与 MS 组 [(20.71±3.61) 岁, $P=0.020$; (7.04±3.34) 年, $P=0.025$; (7.63±3.47) 年, $P<0.001$] 比较, 差异均有统计学意义。MS 组月经异常率、月经稀发及闭经的比例均高于 NMS 组, 两组间月经模式构成比差异有统计学意义 ($P=0.036$)。初潮 8 年以后两组月经异常率差异均有统计学意义 (均 $P<0.05$), 初潮后 8~13 年 OR 值分别为 2.76 (95% CI: 1.07~7.11)、3.68 (95% CI: 1.28~10.56)、3.27 (95% CI: 1.13~9.41)、3.07 (95% CI: 1.06~8.87)、4.02 (95% CI: 1.16~15.21)、11.57 (95% CI: 1.48~90.49); 月经改变病程 4 年以上两组月经异常率差异亦均有统计学意义 (均 $P<0.05$), 月经改变病程 4~9 年 OR 值分别为 8.89 (95% CI: 2.14~36.99)、11.88 (95% CI: 3.07~46.02)、16.56 (95% CI: 4.15~66.13)、11.25 (95% CI: 2.88~32.95)、7.80 (95% CI: 2.04~29.84)、10.00 (95% CI: 1.91~52.48)。MS 组肠道菌群 α 多样性指数较 NMS 组降低, 但差异无统计学意义 ($P>0.05$); 门水平下, 两组肠道菌群丰度差异有统计学意义 ($P<0.001$), MS 组拟杆菌丰度较 NMS 组低, 两组厚壁菌门丰度相近; 属水平下, 两组肠道菌群丰度差异有统计学意义 ($P<0.001$), MS 组较 NMS 组双歧杆菌属丰度降低, 链球菌属及埃希氏菌属丰度增加。结论 PCOS 患者初潮 8 年以后月经异常对日后合并 MS 具有预测作用, 且其预测效果随年龄上升而增加, 但随月经异常改变病程增加无明显变化。PCOS 合并 MS 患者肠道菌群结构与不合并 MS 者确实存在明显不同。

【关键词】 多囊卵巢综合征; 代谢综合征; 月经; 肠道菌群

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Characterization of menstruation and intestinal flora in patients with polycystic ovary syndrome combined with metabolic syndrome

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【Abstract】 **Objective** To investigate the significance of menstrual abnormalities in polycystic ovary syndrome (PCOS) for the prediction of future combined metabolic syndrome (MS) and compare the differences in intestinal flora structure between patients with MS and those without. **Methods** A case-control study was used to select 111 patients with PCOS who attended the outpatient clinic

of the Department of Obstetrics and Gynecology of Jinshan Hospital affiliated to Fudan University between February 2021 and December 2023, and they were divided into the group of PCOS not combined with MS ($n=74$, recorded as the NMS group) and the group of PCOS combined with MS ($n=37$, recorded as the MS group). The menstrual-related information and stool specimens of all cases were collected to analyze the menstrual characteristics of the two groups and their predictive significance for PCOS combined with MS; and the intestinal flora of the two groups were analyzed by 16S rDNA high-throughput sequencing. **Results** The age of menstrual changes [23.47 ± 4.73 years], time of menstrual changes occurring after menarche [9.85 ± 5.11 years], and duration of menstrual changes [3.43 ± 2.78 years] in the NMS group were statistically significantly different when compared with those in the MS group [20.71 ± 3.61 years, $P=0.020$; 7.04 ± 3.34 years, $P=0.025$; 7.63 ± 3.47 years, $P<0.001$]. The rate of menstrual abnormality, scanty menstruation and amenorrhea were higher in the MS group than in the NMS group, and the difference in the ratio of the composition of the menstrual pattern between the two groups was statistically significant ($P=0.036$). The differences in the rates of menstrual abnormalities 8 years later after menarche between the two groups were statistically significant (all $P<0.05$), and the ORs from 8 to 13 years after menarche were 2.76 (95% CI: 1.07–7.11), 3.68 (95% CI: 1.28–10.56), 3.27 (95% CI: 1.13–9.41), 3.07 (95% CI: 1.06–8.87), 4.20 (95% CI: 1.16–15.21), 11.57 (95% CI: 1.48–90.49), respectively; the difference in the rate of menstrual abnormality between the two groups with menstrual alteration duration of more than 4 years was also statistically significant (all $P<0.05$), and the ORs for menstrual alteration duration of 4–9 years were 8.89 (95% CI: 2.14–36.99), 11.88 (95% CI: 3.07–46.02), 16.56 (95% CI: 4.15–66.13), 11.25 (95% CI: 2.88–32.95), 7.80 (95% CI: 2.04–29.84), and 10.00 (95% CI: 1.91–52.48), respectively. The α -diversity index of intestinal flora was lower in the MS group than in the NMS group, but the difference was not statistically significant ($P>0.05$). At the phylum level, there was a statistically significant difference in the abundance of intestinal flora between the two groups ($P<0.001$), the abundance of *Bacteroidetes* was lower in the MS group than in the NMS group, and the abundance of the *Firmicutes* was similar in the two groups. At the genus level, there was a statistically significant difference in the abundance of intestinal flora between the two groups ($P<0.001$), the abundance of *Bifidobacterium* decreased and the abundance of *Streptococcus* and *Escherichia* increased in the MS group compared with those in the NMS group. **Conclusion** Abnormal menstruation 8 years later after menarche in patients with PCOS is predictive of future MS, and its predictive effect increases with age, but does not change significantly with the duration of disease in abnormal menstruation. The structure of the intestinal flora of patients with MS in PCOS is indeed significantly different from that of those without MS.

【 Key words 】 Polycystic ovary syndrome; Metabolic syndrome; Menstruation; Intestinal flora

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临床报道

亚微型及复发性染色体拷贝数变异在复发性流产中的作用

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【摘要】 目的 探讨复发性流产 (recurrent spontaneous abortion, RSA) 相关的关键的染色体拷贝数变异 (copy number variation, CNV) 区域、候选基因及信号通路。方法 基于 2016 年 1 月至 2022 年 9 月期间于郑州大学第三附属医院检验医学科采用高通量测序技术进行流产组织 CNV 分析的 1 870 例 RSA 患者病例资料进行回顾性队列研究。根据孕妇流产年龄和孕周对病例进行分组, 采用 χ^2 检验或 Fisher 精确概率法分析染色体异常及 CNV 分布情况。通过基因富集分析鉴定 RSA 相关 CNV 内基因功能、信号通路。结果 1 870 例样本检出染色体异常 1 001 例 (53.53%), 其中 93 例 (9.29%) 检出 140 种 CNVs, 亚微型 CNVs (<10 Mb) 34 种, 片段 ≥ 10 Mb CNVs 106 种。在孕早期 RSA (≤ 12 周) 样本中检测到具有统计学差异的亚微型致病性 CNVs 涉及 1p36.33p36.23、2q37.3、4p16.3、22q11.21 ($\chi^2=6.99$, $P=0.008$), 此外, 16p11.2、Xp11.23p11.22 微缺失首次在流产病例中报道。显著复发的大型 CNVs 主要涉及 18q22q23、4p16p15、9p24p22、8p23p22、Xp22.3 区域, 所包含流产候选基因主要集中在 PI3K-Akt 及 JAK-STAT 信号通路。结论 罕见亚微型 CNVs 和复发性大型 CNVs 与孕早期 RSA 相关, GO 和 KEGG 数据库分析发现了潜在的流产候选基因及信号通路, 为 RSA 的遗传学病因提供了新信息。

【关键词】 复发性流产; 高通量测序分析; 拷贝数变异

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Role of subminiature and recurrent chromosome copy number variations in recurrent spontaneous abortion

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【Abstract】 Objective To explore the key copy number variation (CNV) regions, abortion candidate genes and signaling pathways associated with recurrent spontaneous abortion (RSA). **Methods** A retrospective cohort study was conducted based on the data of 1 870 miscarriage cases of RSA patients who received CNV analysis by high-throughput sequencing technology in the Laboratory Medicine Department of the Third Affiliated Hospital of Zhengzhou University from January 2016 to September 2022. These cases were divided into different groups based on the age of miscarriage and gestational age of the pregnant women. Chi-square test or Fisher's exact test was used to analyze the distribution of chromosome abnormalities and CNV. Gene functions and signaling pathways in RSA-related CNV were identified by gene enrichment analysis. **Results** Among the 1 870 tissues, 1 001 (53.53%) cases were detected with chromosomal abnormalities. A total of 140 CNVs were detected in 93 tissues (9.29%), including 34 submicroscopic CNVs (segment<10 Mb) and 106 large CNVs with segment $\geq$ 10 Mb. Submicroscopic pathogenicity CNVs with statistical differences were involved 1p36.33p36.23, 2q37.3, 4p16.3, 22q11.21 ($\chi^2=6.99$, $P=0.008$) in early RSA embryos ($\leq$ 12 weeks). 16p11.2 and Xp11.23p11.22 microdeletion were firstly reported in abortion cases. Significantly recurrent large CNVs were mainly involved 18q22q23 (del/dup), 4p16p15, 9p24p22, 8p23p22, and Xp22.3 regions, and the candidate genes mainly concentrated on PI3K-Akt and JAK-STAT signaling pathway. **Conclusion** Rare submicroscopic CNVs and recurrent large CNVs were associated with RSA in early pregnancy. GO and KEGG database analysis revealed potential abortion candidate genes and signaling pathways, providing new information for the genetic etiology of RSA.

【 Key words 】 Recurrent spontaneous abortion; High-throughput sequencing; Copy number variations

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·临床报道·

超声测量妊娠囊相对大小和血清孕酮水平预测 早期妊娠结局的研究

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【摘要】 目的 探讨妊娠囊相对大小及联合孕酮水平预测早孕妊娠结局的临床价值。方法 回顾性队列研究选取 2020 年 4 月至 2023 年 6 月期间在上海市长宁区妇幼保健院超声医学科接受早孕超声检查的患者, 使用经阴道二维超声测量妊娠囊三径(纵径、横径、前后径)和胚芽长度, 并记录 3 d 内孕酮水平, 随访至妊娠满 12 周。分别根据妊娠囊径线(Hellman 公式)和胚芽长度(Hadlock 公式)计算孕周, 按照孕周相对大小把患者分成妊娠囊偏小组($n=100$)和妊娠囊正常组($n=500$); 比较两组妊娠囊相对大小和孕酮的差异, 对于有统计学意义的指标通过受试者工作特征曲线计算其预测早孕妊娠结局的效能。结果 ①妊娠囊正常组的妊娠囊相对大小(3.24 ± 1.06)与妊娠囊偏小组(1.65 ± 0.56)比较, 差异具有统计学意义($P=0.004$)。超声测量妊娠囊相对大小预测早孕妊娠结局不良的阳性预测值为 97.00% (97/100), 阴性预测值为 94.20% (471/500), 灵敏度为 76.98% (97/126), 特异度为 99.37% (471/474), 总体准确率为 94.67% (568/600)。②妊娠囊正常组孕酮水平为(68.4 ± 37.2) nmol/L, 妊娠囊偏小组孕酮水平为(29.6 ± 11.8) nmol/L, 两组比较差异有统计学意义($P<0.001$)。③受试者工作特征曲线显示妊娠囊相对大小、孕酮水平、妊娠囊相对大小联合孕酮水平预测早期妊娠结局的曲线下面积分别为 0.804、0.818、0.847, 妊娠囊相对大小的预测临界值为 2.40, 孕酮的预测临界值为 37.6 nmol/L。④超声参数妊娠囊相对大小单独预测早期妊娠结局不良的灵敏度为 76.98% (97/126)。孕酮水平单独预测早期妊娠结局不良的灵敏度为 78.57% (99/126)。以妊娠囊相对大小与孕酮水平联合预测早期妊娠结局不良, 则灵敏度提升为 84.92% (107/126)。结论 超声测量和计算妊娠囊相对大小简单易行, 超声参数妊娠囊相对大小对于早孕妊娠结局具有较好的预测价值; 妊娠囊相对大小联合血清孕酮水平的预测效能更佳。

【关键词】 早孕期; 妊娠囊相对大小; 孕酮; 妊娠结局; 预测价值

基金项目: 上海市长宁区医学博士创新人才基地(RCJD2021B09); 上海市长宁区妇科超声重点专科(20231004)

Study of ultrasound measured relative size of gestational sac and serum progesterone levels in predicting first trimester pregnancy outcomes

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【Abstract】 Objective To explore the clinical value of the relative size of gestational sac and serum progesterone levels in predicting early pregnancy outcomes. **Methods** Retrospective cohort study selected patients who underwent early pregnancy ultrasound examination at the Ultrasound Medicine Department of Shanghai Changning Maternity and Infant Health Hospital from April 2020 to June 2023. Transvaginal two-dimensional ultrasound was used to measure the three diameters of the gestational sac (longitudinal diameter, transverse diameter, anterior-posterior diameter) and fetal pole length. Serum progesterone levels were tested in 3 d. All patients were followed up until 12 weeks of gestation to estimate the early pregnancy outcomes. Gestational age was calculated based on the gestational sac diameter line (Hellman's formula) and embryo length (Hadlock's formula), and the patients were divided into the gestational sac deviation group (deviation group, $n=100$) and the gestational sac normal group (normal group, $n=500$) based on the relative size of gestational age. The relative size of the gestational sac and progesterone level were compared between the two groups, and the effectiveness of predicting early pregnancy outcomes for statistically significant indicators was calculated with receiver operating characteristic curve.

Results 1) The relative size of gestational sac in the normal group and the deviation group were 3.24 ± 1.06 and 1.65 ± 0.56 , respectively, and the difference between the two groups was statistically significant ($P=0.004$). The positive predictive value of ultrasound gestational sac size for predicting adverse pregnancy outcome in the first trimester was 97.00% (97/100) and the negative predictive value was 94.2% (471/500). 2) The levels of progesterone in the normal group and the deviation group were (68.4 ± 37.2) nmol/L and (29.6 ± 11.8) nmol/L, respectively, with a statistically significant difference ($P<0.001$). 3) The areas under receiver operating characteristic curves of the relative size of gestational sac, progesterone levels and the both combined in predicting early pregnancy outcomes were 0.804, 0.818 and 0.847, respectively, and the cut-off values of the relative size of pregnancy sac and progesterone was 2.40 and 37.6 nmol/L, respectively. 4) The accuracy of the relative size of gestational sac in predicting adverse outcomes in early pregnancies was 76.98% (97/126). The accuracy of progesterone in predicting adverse outcomes in early pregnancy was 78.57% (99/126). When the both combined, the predicting accuracy was increased to 84.92% (107/126).

Conclusion It is easy to measure and calculate the relative size of pregnancy sac by ultrasound, which provided a good predictive value for the outcomes of early pregnancies. The relative size of pregnancy sac combined with progesterone levels showed better predictive efficacy.

【 Key words 】 Early pregnancy; Relative size of pregnancy sac; Progesterone; Pregnancy outcomes; Predicting value

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·现场调查·

活性 γ 型宫内节育器型号-宫腔深度匹配度与 医学原因终止风险的关联研究

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【摘要】 目的 探讨现行指南或产品说明书推荐活性 γ 型宫内节育器 (intrauterine device, IUD) 型号选择标准是否降低 IUD 医学原因终止风险。方法 基于国家卫生健康委重点实验室开展的避孕药具首诊排查登记项目选取江苏地区 2015 年 1 月至 2020 年 10 月期间月经后放置 IUD 的女性建立观察队列, 按照产品说明书建议的型号选择标准对型号-宫腔深度匹配情况进行分组, 分为匹配组、IUD 偏小组和 IUD 偏大组, 收集活性 γ 型 IUD 放置后的随访信息。采用多因素 Cox 比例风险回归模型分析不同的型号-宫腔深度匹配度与 IUD 医学原因终止风险之间的关联。结果 共纳入 4 631 例研究对象, 其中匹配组 2 331 例, IUD 偏大组 182 例, IUD 偏小组 2 118 例。中位随访 29 个月 (1~65 个月), 研究期间 IUD 医学原因终止 528 例 (11.33%), IUD 非医学原因终止 108 例 (2.32%), 失访 333 例 (7.19%), 其中, 月经异常终止率发生最高。多因素 Cox 回归分析显示, 与匹配组相比, IUD 偏大组和 IUD 偏小组对象总医学原因、意外妊娠、IUD 脱落、IUD 下移、疼痛等相关终止的发生风险差异均无统计学意义 (均 $P>0.05$)。结论 活性 γ 型 IUD 型号与宫腔深度不匹配不增加医学原因终止风险, 在临床实践中可适当放宽活性 γ 型 IUD 的型号选择范围。

【关键词】 活性 γ 型宫内节育器； 型号； 宫腔深度； 医学原因终止
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A study of the association between medicated γ intrauterine device model-cavity depth match degree and the risk of termination for medical reasons

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【Abstract】 Objective To explore whether the size selected criteria for medicated γ intrauterine device (γ -IUD) in current guideline or product manuals can reduce the risk of IUD termination for medical reasons. **Methods** An observation cohort was established by selecting women who had an IUD placed after menstruation between January 2015 and October 2020 in the Jiangsu region based on the contraceptive first diagnosis registration program carried out by the Key Laboratory of the National Health Commission. Then the cohort were divided into the matched group, smaller size group, and larger size group according to the model selection criteria recommended by the product manual for model-uterine cavity depth matching. The follow-up information after the placement of the γ -IUD was collected. Multifactorial Cox proportional risk regression models were used to analyze the association between different model-cavity depth matches and the risk of IUD termination for medical reasons. **Results** A total of 4 631 study participants were included, including 2 331 in the matched group, 182 in the larger size group, and 2 118 in the smaller size group. With a median follow-up of 29 months (1–65 months), 528 (11.33%) IUD terminations were for medical reasons, 108 (2.32%) IUD terminations were for non-medical reasons, and 333 (7.19%) were lost to follow-up during the study period, with the highest rate of termination occurring for menstrual abnormalities. Multifactorial Cox regression analysis showed that there were no statistically significant differences in the risk of termination related to total medical reasons, unintended pregnancy, IUD expulsion, IUD dislocation, and pain in subjects with large IUDs or small IUDs compared with those in the matched group (all $P>0.05$). **Conclusion** The mismatch between γ -IUD model and the depth of the uterine cavity does not increase the risk of IUD termination for medical reasons. In clinical practice, the model selection range of γ -IUD can be appropriately relaxed.

【Key words】 Medicated γ intrauterine device; Size; Depth of uterine cavity; Medical termination

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·临床管理·

生殖联盟转诊机制在辅助生殖助孕患者中的应用效果研究

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【摘要】 目的 探索生殖联盟转诊机制和转诊专职接待护士在辅助生殖助孕患者中的应用效果。方法 回顾性总结 2023 年 3 月至 9 月期间于郑州大学第三附属医院生殖中心转诊+联合促排卵(记为转诊+联合促排卵组)、转诊非联合促排卵(记为转诊非联合促排卵组)和自行来诊(记为对照组)行辅助生殖助孕的患者情况。比较 3 组间来诊次数、促排卵方案及助孕结局等指标。结果 本研究共调查 425 例患者, 其中转诊+联合促排卵组 99 例, 转诊非联合促排卵组 98 例, 对照组 228 例。3 组患者的基线数据差异均无统计学意义(均 $P>0.05$)。在患者来本院就诊的次数上, 转诊+联合促排卵组来院次数为 1.79 ± 1.20 , 转诊非联合促排卵组来院次数为 5.48 ± 2.24 , 对照组来院次数为 5.77 ± 1.72 , 3 组间比较差异有统计学意义($P<0.001$), LSD 多重比较结果显示, 转诊+联合促排卵组与转诊非联合促排卵组、对照组的来院次数差异均存在统计学意义(均 $P<0.001$)。3 组患者促排卵方案、促性腺激素释放激素激动剂使用总量和使用时间、促性腺激素使用总量和使

用时间差异均无统计学意义 (均 $P>0.05$)。3 组间获卵数、双原核数、可利用胚胎数、MII 卵数、优质胚胎数、可移植胚胎数、冷冻胚胎数、囊胚培养数、囊胚形成数、可利用囊胚数差异均无统计学意义 (均 $P>0.05$)。结论 联盟促排卵转诊模式在辅助生殖助孕患者中临床应用效果较好, 可以避免患者两地辗转的辛苦。

【关键词】 辅助生殖; 联盟转诊; 转诊专职护士; 患者满意度

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Application effect of reproductive alliance referral mechanism in patients with assisted reproductive technology

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【Abstract】 **Objective** To explore the application effect of reproductive alliance referral mechanism and referral full-time reception nurses in patients with assisted reproductive technology. **Methods** From March 2023 to September 2023, the demographic data of patients attending the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University were retrospectively summarized. This included patients referred for combined ovarian stimulation, patients referred without combined ovarian stimulation, and a control group consisting of self-visit patients. The number of visits, ovulation induction protocols, and outcomes among the three groups were compared. **Results** The study included a total of 425 patients, comprising 99 patients in combined ovarian stimulation, 98 patients in no combined ovarian stimulation, and 228 patients in control group. The baseline data did not show any significant differences among the three groups (all $P>0.05$). The number of hospital visits was 1.79 ± 1.20 in the referral+ovulation induction group, 5.48 ± 2.24 in the referral non-ovulation induction group, and 5.77 ± 1.72 in control group, with a significant difference among the three groups ($P<0.001$). The results of LSD multiple comparison method revealed statistically significant differences in the number of visits between the referral+combined ovarian stimulation group and the referral non-combined ovarian stimulation group, as well as the control (all $P<0.001$). The protocol, dosage and duration of gonadotropin-releasing hormone agonist used and the duration and dosage of gonadotropin used were no significant differences among the three groups (all $P>0.05$). The numbers of oocytes retrieved, two pronuclei, available embryos, MII, high-quality embryos, transferable embryos, frozen embryos, blastocyst culture, blastocyst formation, and available blastocysts were not significantly different among the three groups (all $P>0.05$). **Conclusion** The alliance ovulation induction referral model demonstrates a favorable clinical application effect in patients undergoing assisted reproduction, alleviating the burden of patients having to visit multiple locations.

【Key words】 Assisted reproduction; Alliance referral; Referral to full-time nurses; Patient satisfaction

Fund program: Henan Provincial Science and Technology Research Joint Project (LHGJ20200429)

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循证医学

初潮年龄与多囊卵巢综合征发病风险相关性的系统评价与 meta 分析

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【摘要】 目的 系统评价初潮年龄与多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 的关系。方法 计算机检索 11 个数据库, 搜集有关初潮年龄和 PCOS 的研究, 检索时限为建库以来到 2023 年 9 月 1 日。由两位评价员独立按纳入标准筛选文献、提取资料后进行 meta 分析。所有统计分析均使用 Stata17.0 软件进行。结果 从检索的 3 107 篇文献中筛选得到 10 篇符合标准的文献, 包含 6 462 个研究对象。meta 分析结果显示, 初潮年龄延迟 PCOS 发病风险是初潮年龄正常 PCOS 发病风险的 1.84 倍 (95% CI: 1.14~2.97), 初潮年龄提前与初潮年龄正常相比, PCOS 发病风险未见统计学意义 ($P>0.05$)。结论 初潮年龄延迟是 PCOS 发生的危险因素。

【关键词】 月经初潮; 多囊卵巢综合征; meta 分析

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Relationship between age at menarche and polycystic ovarian syndrome: a systematic review and meta-analysis

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【 Abstract 】 Objective To systematically evaluate the connection between polycystic ovary syndrome (PCOS) and age at menarche. **Methods** We searched 11 databases from inception to September 1st 2023 to collect studies about the association between age at menarche and PCOS. Two reviewers independently screened literatures, accordance with the inclusion criteria and extracting the data, extracted data and performed meta-analysis by Stata17.0 software. **Results** A total of 10 literatures, including 6 462 subjects, were included at last in the study. A meta-analysis revealed that there was no statistically significant difference in the risk of getting PCOS between early and normal age at menarche, and the risk of PCOS with delayed age at menarche was 1.84 (95% CI: 1.14–2.97) times greater than that with normal age at menarche. **Conclusion** There may be a connection between delayed age at menarche and the development of PCOS.

【Key words】 Menarche; Polycystic ovary syndrome; Meta analysis

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热点追踪

基于 WHO 国际临床试验注册平台的全球多囊卵巢综合征临床研究注册现状分析

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【摘要】 目的 分析多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 相关临床研究在全球范围内的注册特点, 为把握该领域研究的重点及动向提供参考。方法 检索世界卫生组织 (World Health Organization, WHO) 国际临床试验注册平台 (International Clinical Trials Registry Platform, ICTRP) 数据库, 筛选出 PCOS 相关临床研究, 对注册时间、注册平台、国家/地区分布、研究设计和研究内容等方面进行分析。结果 共纳入 PCOS 相关临床研究 1 473 项, 注册数量基本呈逐年上升趋势, 项目开展国家主要分布在亚洲和欧洲。以育龄期 PCOS 女性为研究对象的研究占 96.81% (1 426/1 473), 根据研究主题不同分为不孕症及生育相关主题 ($n=435$) 和生命健康相关主题 ($n=991$) 两组, 二者的研究类型、干预措施、药物干预的种类、观察指标等的差异均具有统计学意义 (均 $P<0.001$), 不孕症及生育相关研究的干预措施以药物干预为主 [70.21% (271/386)], 其中又以促排卵药相关研究最多 [68.27% (185/271)]; 而生命健康相关研究的干预措施则主要为药物和膳食补剂 [74.56% (595/798)], 集中在草药及传统医学 [31.45% (117/372)]、口服降糖药 [27.69% (103/372)] 和口服避孕药 [17.74% (66/372)] 三个方面。结论 PCOS 临床研究热点集中在育龄期女性的生育及生命健康相关主题, 而青少年和绝经后 PCOS 女性及其他研究方向的临床研究数量较少, 仍需进一步关注和探索; 注册临床试验的意识仍需加强, 注册资料的完整性和准确性有待进一步提高。

【关键词】 多囊卵巢综合征; 临床研究; WHO 国际临床试验注册平台; 注册现状

An analysis of the status of clinical trial registration for polycystic ovary syndrome based on WHO International Clinical Trials Registry Platform

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【Abstract】 Objective To analyze the registration characteristics of clinical studies related to polycystic ovary syndrome (PCOS) worldwide and provide a reference for grasping the focus and trend of research in this field. **Methods** The database of World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) was searched to screen out PCOS-related clinical studies, and the registration time, registration platform, regional distribution, study design and study content were analyzed. **Results** A total of 1 473 PCOS-related clinical studies were included, and the number of registrations basically increased year by year. The projects were mainly carried out in Asia and Europe. About 96.81% (1 426/1 473) of the study subjects were PCOS women of reproductive age, and they were divided into two groups according to the different research topics: infertility and fertility-related topic ($n=435$) and life-health-related topic ($n=991$). There were statistically significant differences in the types of studies, interventions, types of intervention drugs and observation indicators between the two groups (all $P<0.001$). The main interventions in fertility-related studies were drug interventions [70.21% (271/386)], among which ovulation-stimulating drugs were the most common [68.27% (185/271)]. The interventions in

life-health-related studies were mainly drugs and dietary supplements [74.56% (595/798)], and mostly in three aspects: herbal and traditional medicine [31.45% (117/372)], oral hypoglycemic agents [27.69% (103/372)] and oral contraceptives [17.74% (66/372)]. **Conclusion** The focus of PCOS-related clinical studies is on fertility and life-health-related topic in women of reproductive age, while clinical studies in adolescent and postmenopausal women with PCOS and other directions is much fewer, which still needs further attention and exploration. Awareness of clinical trials registration needs to be strengthened and the integrity and accuracy of registration information needs to be further improved.

【Key words】 Polycystic ovary syndrome; Clinical trial; WHO International Clinical Trials Registry Platform; Registration status

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综述

剖宫产瘢痕子宫对辅助生殖技术助孕结局影响的研究进展

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【摘要】 由于剖宫产率的增加，继发性不孕的人数增多，从而使剖宫产术后接受辅助生殖技术（assisted reproductive technology, ART）助孕治疗的患者也逐渐增加，但目前关于剖宫产术对 ART 妊娠结局的影响尚存争议。研究显示剖宫产切口瘢痕可能通过改变子宫解剖结构、降低子宫内膜容受性、破坏宫腔微生态环境等影响胚胎着床，从而增加反复种植失败、复发性流产及异位妊娠等风险。瘢痕修补术是改善此类患者助孕结局的有效手段，近年来宫腔灌注、抑制异常宫缩、抗生素治疗等也成为改善宫腔环境的新思路。本文基于剖宫产瘢痕子宫与后续生育力的关系，围绕其影响 ART 妊娠结局的可能机制及处理方案展开综述，为临床工作提供参考。

【关键词】 剖宫产术； 瘢痕； 生殖技术，辅助； 妊娠结局； 继发不孕

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Research progress on the impact of scarred uterus after cesarean section on the pregnancy outcomes of assisted reproductive technology

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【 Abstract 】 Due to the formation of scars in the local uterus during cesarean section, the subsequent natural pregnancy of these patients is affected and they receive assisted reproductive technology (ART) for pregnancy treatment. However, the impact of cesarean section on the pregnancy outcomes of ART is still controversial. Studies have shown that poor scar healing after cesarean section is related to changes in uterine anatomy, weakened endometrial receptivity, and imbalance in uterine microenvironment, which is not conducive to embryo implantation and increases the risk of recurrent implantation failure and recurrent miscarriage. Scar diverticulum repair is an effective method to improve the pregnancy outcomes of patients with scarred uterus. In recent years, uterine perfusion, inhibition of uterine contractions, and the application of antibiotics have also become new ideas to improve the uterine environment. Based on the relationship between cesarean section scarred uterus and subsequent fertility, this article reviews the possible mechanisms and treatment options that affect the pregnancy outcomes of ART, providing clinical evidence for daily practice.

【Key words】 Cesarean section; Cicatrix; Reproductive techniques, assisted; Pregnancy outcome; Secondary infertility

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综述

促性腺激素释放激素激动剂在年轻乳腺癌化疗患者卵巢功能保护中的研究进展

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【摘要】 乳腺癌发病率呈逐年上升趋势, 化疗是延长年轻乳腺癌患者生存时间的有效治疗方式, 同时也会对卵巢造成不可逆损害。近年来, 越来越多的研究聚焦于促性腺激素释放激素激动剂 (gonadotropin-releasing hormone agonist, GnRH-a) 用于保护乳腺癌化疗患者的卵巢功能, 但研究结论尚有争议。本文从化疗对乳腺癌患者卵巢功能的影响, GnRH-a 概述及保护卵巢功能机制, GnRH-a 在乳腺癌患者化疗中卵巢功能保护的临床研究进展及相关问题 4 个方面进行阐述, 以期为临床诊疗和相关研究提供思路。

【关键词】 乳腺肿瘤; 化疗; 生育力保护; 促性腺激素释放激素激动剂

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Advances research of gonadotropin-releasing hormone agonist in the protection of ovarian function in young breast cancer patients undergoing chemotherapy

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【Abstract】 The incidence of breast cancer is on the rise annually, and chemotherapy is potentially effective in prolonging the lifespan of young breast cancer patients which also irreversibly harm the ovaries. Recently, increasingly more studies have focused on the role of gonadotropin-releasing hormone agonist (GnRH-a) for protecting ovarian function in patients undergoing chemotherapy with disputable findings. This review addresses four perspectives including the impact of chemotherapy on ovarian function, the introduction of GnRH-a and the possible mechanism of protecting ovarian function, the advances of clinical research on the ovarian protection by GnRH-a in chemotherapy for patients with breast cancer and other related issues, with the aim of providing thoughts for clinical diagnosis and associated research.

【Key words】 Breast neoplasms; Chemotherapy; Fertility preservation; Gonadotropin-releasing hormone agonist

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综述

宫腔微生物菌群诱导的免疫耐受对生殖结局的影响

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【摘要】 微生物组在人类生殖中的作用已成为“人类的第二基因组”。实际上, 对于生殖过程中微生物组的作用已有比较多的研究, 包括下生殖道和上生殖道, 甚至与配子发生时的相互作用。微生物组不仅在健康和微生态失调引起的病理状态中扮演着关键角色, 也可能在成功受精和健康妊娠中发挥了重要作用。目前, 关于微生物组和人类生殖轴之间关系的研究正引起广泛关注。本文综述了微生物菌群对生殖结局的影响, 及宫腔内的微生物菌群对免疫耐受的影响和可能的机制, 探讨菌群紊乱可能是通过免疫耐受来发挥作用的。这可能对微生态的调节和探索生殖疾病治疗新方法起到指导作用。

【关键词】 宫腔; 微生物群; 免疫耐受; 治疗; 生殖结局

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Impacts of immune tolerance induced by the uterine microbiota on reproductive outcomes

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【Abstract】 The role of microbiota in human reproduction has become the “the second genome of humanity”. In fact, more and more researches have investigated the microbiota in reproduction, including the lower and upper

reproductive tracts, and even the interactions with gametogenesis. The microbiota not only plays a crucial role in the pathological states caused by health and microecological disorders, but may also play an important role in successful fertilization and healthy pregnancy. Currently, researches on the relationship between microbiota and human reproductive axis are attracting widespread attention. This article reviews the impact of microbiota on reproductive outcomes, as well as the impact and possible mechanisms of microbiota in the uterine cavity on immune tolerance. It explores that dysbiosis of microbiota may play a role through immune tolerance. This may play a guiding role in regulating the microecology and exploring new methods for treating reproductive diseases.

【 Key words 】 Uterine; Microbiota; Immune tolerance; Therapy; Reproductive outcomes

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综述

子宫内膜液与子宫内膜容受性的研究进展

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【摘要】 子宫内膜容受性是影响辅助生殖助孕成功率的一个关键环节, 在胚胎着床过程中起着重要作用。如何评估子宫内膜容受性一直是困扰生殖医学界的难题。传统的超声对于内膜的评估缺乏可靠性, 对子宫内膜组织进行子宫内膜微阵列检测可以一定程度上反映子宫是否处于种植窗, 但是因为有创且检查当月无法移植限制了它的应用。子宫内膜液随着月经周期不断变化在一定程度上可反应子宫内膜容受性。随着各种组学技术的发展, 对子宫内膜液的研究有了进一步发展。本文就子宫内膜液作为一种无创的子宫内膜容受性检测媒介的最新研究进展进行了综述。

【关键词】 子宫内膜液; 子宫内膜容受性; 无创诊断; 组学分析

Progress on the relationship between uterine fluid and endometrial receptivity

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【 Abstract 】 A successful pregnancy in patients accepting assisted reproductive technologies needs a good endometrial receptivity. But how to assess endometrial receptivity precisely is a major issue. Evaluating endometrial receptivity through ultrasound is not reliable. The endometrial receptivity array is more accurate to find the window of implantation, but its invasiveness restricts its application. Uterine fluid changes with the menstrual cycle, which can reflect endometrial receptivity to some extent. The development of a wealth of omics technologies promote a further research of uterine fluid. This paper will review latest research progress of uterine fluid as a non-invasive medium for endometrial receptivity detection.

【Key words】 Uterine fluid; Endometrial receptivity; Noninvasive diagnosis; Omics analysis

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综述

生物医学材料联合间充质干细胞治疗在改善薄型子宫内膜中的应用

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【摘要】 子宫内膜损伤修复障碍可能出现薄型子宫内膜, 可危害患者的生育功能, 导致不良的妊娠结果, 增加母婴并发症的发生率。间充质干细胞移植是子宫内膜再生领域的研究热点, 但干细胞在宫腔内定植存活率低是目前亟待解决的关键问题, 极大地限制了干细胞治疗的临床推广。搭载生物医学材料可实现间充质干

细胞高效能的移植转化, 引导子宫内膜细胞的再生, 优化宫腔微环境, 为治疗薄型子宫内膜、改善妊娠结局提供潜在的治疗选择。

【关键词】 间充质干细胞; 薄型子宫内膜; 生物医学材料

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Application of biomedical materials in conjunction with mesenchymal stem cell-based therapy in enhancing thin endometrium

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【Abstract】 Obstruction in repairing endometrial damage may result in thin endometrium, which can impair the patient's reproductive function, worsen pregnancy outcomes, and increase the incidence of maternal and infant complications. In the field of endometrial regeneration, mesenchymal stem cells transplantation is a research hotspot. However, a major obstacle that must be surmounted before stem cell therapy can be widely promoted clinically is the low survival rate of stem cell colonization in the uterine cavity. Mesenchymal stem cells can be transplanted and transformed efficiently, the uterine microenvironment can be optimized, endometrial cell regeneration can be guided, and potential therapeutic options for treating thin endometrium and improving pregnancy outcomes can be provided by applying biomedical materials.

【Key words】 Mesenchymal stem cells; Thin endometrium; Biomedical materials

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综述

非梗阻性无精子症关键基因及表观遗传因素的研究进展

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【摘要】 非梗阻性无精子症 (non-obstructive azoospermia, NOA) 是因精子生成障碍所致的复杂性生殖系统疾病。近年来随着测序技术的广泛应用, 精子发生中一些关键基因被不断挖掘。这些基因中涉及减数分裂前后变化的基因数量最多。表观遗传修饰包括 DNA 甲基化、组蛋白变体参与以及非编码 RNA 调控等。它们在多个层面反映了 NOA 患者的精子发生异常。本文系统地梳理了 NOA 中精子发生关键基因和一些表观遗传因素的最新研究动态, 为 NOA 临床诊断的生物学标志物开发和临床诊疗方案的优化提供新思路。

【关键词】 精子发生; 基因; 减数分裂; 甲基化; 非编码 RNA

Advances of key genes and epigenetic factors during spermatogenesis in non-obstructive azoospermia

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【 Abstract 】 Non-obstructive azoospermia (NOA) is a complex male infertility disease with abnormal spermatogenesis. With the wide application of sequencing technology in recent years, key genes related to spermatogenesis in NOA patients have been continuously mined out. Some epigenetic factors, such as DNA methylation, histone changes and non-coding RNAs are important indicators that reflect to the heterogeneity and complexity of spermatogenesis failure in NOA. This article systematically reviewed the latest studies on the key genes and some epigenetic factors during spermatogenesis of NOA, which may prospectively help to exploit clinical biomarker and to optimize therapeutic proposals.

【 Key words 】 Spermatogenesis; Gene; Meiosis; Methylation; Non-coding RNA

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综述

先天性心脏病相关 *TBX5* 突变的研究进展

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【摘要】 先天性心脏病 (congenital heart diseases, CHDs) 严重影响人类健康, 遗传因素与 CHDs 的发生密切相关。在辅助生育过程中, 利用极体活检、卵裂球活检和囊胚活检等方法, 结合单细胞 DNA 扩增及高通量测序技术, 能够准确检测出着床前胚胎中与单基因遗传疾病相关的致病突变。T 盒转录因子 5 (T-box transcription factor 5, *TBX5*) 是心脏和上肢发育的重要转录因子, 已报道有 227 种 *TBX5* 突变与 CHDs 相关。通过植入前单基因遗传病检测 (preimplantation genetic testing for monogenic disease, PGT-M), 检测胚胎中是否存在 CHDs 相关性 *TBX5* 突变, 对于预防 CHDs 的发生有重要意义。本文系统整理了已报道的 *TBX5* 突变相关信息, 并结合家族性遗传数据、动物模型、诱导多潜能干细胞疾病模型和预测软件, 对 *TBX5* 错义突变进行了综合分析, 以期对 CHDs 相关 *TBX5* 突变的 PGT-M 提供参考。

【关键词】 先天性心脏病; 植入前单基因遗传病检测; *TBX5*; 基因突变

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Research progress on congenital heart disease-related *TBX5* mutations

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【Abstract】 Congenital heart diseases (CHDs) seriously affect human health, and genetic mutation is closely related to the occurrence of CHDs. In the process of assisted reproduction, the use of methods such as polar body biopsy, blastomere biopsy and blastocyst biopsy, combined with single-cell DNA amplification and

high-throughput sequencing technology, can accurately detect pathogenic mutations associated with single-gene genetic diseases in pre-implantation embryos. T-box transcription factor 5 (TBX5) is an important transcription factor for heart and upper limb development. It is reported 227 *TBX5* mutations are related to CHDs. Preimplantation genetic testing for monogenic disease (PGT-M) to detect CHD-related *TBX5* mutations in embryos is of great significance for preventing the occurrence of CHDs. In this review, we systematically summarized the *TBX5* mutation information, and analyzed the deleterious effects of *TBX5* missense mutations based on familial genetic data, animal models, induced pluripotent stem cell disease models and prediction software to provide references for the detection of CHD-related *TBX5* mutations using PGT-M.

【Key words】 Congenital heart disease; Preimplantation genetic testing for monogenic disease; *TBX5*; Gene mutation

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