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· 规范与标准 ·

复发性流产合并风湿免疫病免疫抑制剂应 用中国专家共识

复发性流产合并风湿免疫病免疫抑制剂应用中国专家共识编写组

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【摘要】 风湿免疫病是导致复发性流产 (recurrent spontaneous abortion, RSA) 等妊娠并
发症的最常见原因。免疫抑制剂在 RSA 合并风湿免疫病患者的防治方面疗效肯定, 但由于缺乏相应
的规范, 过度治疗、超适应证使用等现象普遍存在。为了进一步规范免疫抑制剂的应用, 风湿免疫
学、妇产科学、生殖免疫学及生殖医学专家共同讨论, 根据 RSA 合并常见风湿免疫病的防治现状、
结合国内外最新的研究证据和进展, 制定本共识, 旨在为临床医师在临床实践中做出合理决策提供
参考。

【关键词】 免疫抑制剂; 复发性流产; 风湿免疫病; 共识

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Chinese experts consensus on application of immunosuppressants in recurrent spontaneous abortion complicated with rheumatic diseases

*Chinese Experts Consensus Group on Application of Immunosuppressants in Recurrent Spontaneous
Abortion Complicated with Rheumatic Diseases*

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【Abstract】 Rheumatic diseases are the most common cause of pregnancy complications such
as recurrent spontaneous abortion (RSA). Immunosuppressants have a positive effect in the
prevention and treatment of RSA patients with rheumatic disease. However, due to the lack of
standard, the phenomena of overtreatment and the use of off-label are common. In order to further
standardize the application of immunosuppressants, the experts in rheumatology, obstetrics and
gynecology, reproductive immunology and reproductive medicine were organized for a joint
discussion. According to the current situation of prevention and treatment of RSA complicated with
common rheumatic diseases, combined with the latest research evidence and progress, this
consensus was formulated, which aims to provide reference for clinicians to make reasonable
decisions in clinical practice.

【Key words】 Immunosuppressants ; Recurrent spontaneous abortion ; Rheumatic
diseases ; Consensus

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· 临床研究 ·

双侧输卵管切除术对控制性卵巢刺激周期卵巢反应的影响

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【摘要】 目的 探讨双侧输卵管切除术对输卵管积水患者控制性卵巢刺激(controlled ovarian stimulation, COS)周期卵巢反应的影响。方法 纳入2010年1月至2017年11月期间因输卵管积水于北京大学第三医院行双侧输卵管切除术、术前及术后均进行COS并且间隔小于1年的患者作为研究组;以年龄1:2匹配选择因单纯男方因素不孕同期行COS的患者作为对照组。回顾性分析研究组输卵管切除术后与术前的卵巢储备及COS卵巢反应以及研究组术后与对照组相比COS卵巢反应的差异。结果 132名患者纳入研究组,264名纳入对照组。研究组术后与术前相比,基础卵泡刺激素(FSH)水平 $[(6.76 \pm 2.15) \text{ IU/L}$ 比 $(6.62 \pm 2.03) \text{ IU/L}$, $P=0.589$]、基础雌二醇水平 $[(160.77 \pm 66.20) \text{ pmol/L}$ 比 $(161.58 \pm 66.42) \text{ pmol/L}$, $P=0.922$]、窦卵泡计数 $(9.36 \pm 4.28$ 比 10.27 ± 5.01 , $P=0.135)$ 差异均无统计学意义;COS中获卵数 $(11.18 \pm 7.43$ 比 11.68 ± 6.20 , $P=0.278)$ 、可移植胚胎数 $(4.82 \pm 4.14$ 比 5.14 ± 3.55 , $P=0.166)$ 差异均无统计学意义。研究组术后与对照组年龄、基础FSH值、雌二醇水平、窦卵泡计数差异均无统计学意义($P>0.05$);两组间促性腺激素(Gn)刺激时间、Gn使用总量、获卵数、可移植胚胎数差异均无统计学意义($P>0.05$)。结论 对于卵巢储备正常的女性,谨慎的双侧输卵管切除术并不降低卵巢储备和COS周期的卵巢反应。

【关键词】 输卵管切除术; 输卵管积水; 控制性卵巢刺激; 卵巢储备; 受精, 体外; 胚胎移植

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Impact of bilateral salpingectomy on ovarian response in controlled ovarian stimulation cycle

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【 Abstract 】 Objective To investigate the effect of bilateral salpingectomy on ovarian response in controlled ovarian stimulation (COS) cycles of women with hydrosalpinx. **Methods** Women with hydrosalpinx who underwent bilateral salpingectomy and COS before and after salpingectomy within 1 year between Jan. 2010 and Nov. 2017 in Peking University Third Hospital were included in study group. Women with male factor infertility who received COS at the same period and matched with age according to the ratio of 1:2 were included in control group. A retrospective analysis of ovarian reserve and COS before and after salpingectomy in study group and between the two groups was performed. **Results** A total of 132 patients were recruited in study group and 264 patients in control group. Compared between after and before salpingectomy in study group, there were no significant differences in basal serum follicle-stimulating hormone (FSH) level $[(6.76 \pm 2.15) \text{ IU/L vs. } (6.62 \pm 2.03) \text{ IU/L}, P=0.589]$, estradiol level $[(160.77 \pm 66.20) \text{ pmol/L vs. } (161.58 \pm 66.42) \text{ pmol/L}, P=0.922]$, antral follicle count (AFC) $(9.36 \pm 4.28 \text{ vs. } 10.27 \pm 5.01, P=0.135)$, the number of oocytes retrieved $(11.18 \pm 7.43 \text{ vs. } 11.68 \pm 6.20, P=0.278)$ and viable embryos $(4.82 \pm 4.14 \text{ vs. } 5.14 \pm 3.55, P=0.166)$. Between study group and control group, there were no differences in age, basal FSH, estradiol level, AFC, duration and dosage of gonadotropin (Gn) used, number of oocytes collected and transferable embryos ($P>0.05$). **Conclusion** Careful bilateral salpingectomy does not decrease ovarian reserve and response in COS cycles of women with normal ovarian reserve.

【 Key words 】 Salpingectomy ; Hydrosalpinx ; Controlled ovarian stimulation ; Ovarian reserve ; Fertilization *in vitro* ; Embryo transfer

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· 临床研究 ·

启动促性腺激素前不同预处理对 POSEIDON 预期卵巢低反应患者临床结局的影响

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【摘要】 目的 分析启动促性腺激素(Gn)前不同预处理对 POSEIDON 预期卵巢低反应(POR)患者体外受精(IVF)结局的影响，探索改善 POR 患者临床结局的策略。**方法** 回顾性分析 2016 年 1 月至 2018 年 5 月期间就诊于北京大学第三医院妇产科生殖医学中心接受体外受精-胚胎移植(IVF-ET)的 POSEIDON 预期 POR 患者 364 个周期[促性腺激素释放激素(GnRH)超短激动剂/拮抗剂方案]的临床资料，按照启动 Gn 前的预处理情况分为短效口服避孕药(OCP)组(A 组， $n=167$)、戊酸雌二醇组(B 组， $n=56$)和未处理组(C 组， $n=141$)，比较 3 组患者的一般资料、促排卵周期指标、实验室情况及临床妊娠率等。**结果** A 组年龄 $[(34.8 \pm 4.9) \text{ 岁}]$ 明显小于 B 组 $[(38.0 \pm 4.9) \text{ 岁}]$ 和 C 组

[(37.9±4.7) 岁] ($P<0.001$) , B 组 体 质 量 指 数 (BMI) [(21.9±3.1) kg/m²] 明 显 小 于 A 组 [(23.5±3.6) kg/m²] 和 C 组 [(23.2±3.1) kg/m²] ($P=0.014$) , 窦 卵 泡 计 数 (AFC) A 组 (2.4±2.0) 、 B 组 (4.1±1.9) 、 C 组 (3.5±2.0) 间 比 较 差 异 有 统 计 学 意 义 ($P<0.001$) , A 组 排 卵 障 碍 的 比 例 (32.9%) 明 显 高 于 B 组 (10.7%) 和 C 组 (11.3%) ($P<0.001$) , C 组 IVF 周 期 数 (3.0±1.7) 明 显 大 于 A 组 (2.5±1.5) ($P=0.017$) ; 3 组 间 不 孕 类 型 、 不 孕 年 限 、 基 础 卵 泡 刺 激 素 (FSH) 、 抗 苗 勒 管 激 素 (AMH) 值 比 较 差 异 均 无 统 计 学 意 义 (P 均 >0.05) 。 人 绒 毛 膜 促 性 腺 激 素 (hCG) 注 射 日 内 膜 厚 度 A 组 [(9.4±1.9) mm] 小 于 B 组 [(10.6±1.5) mm] 和 C 组 [(10.1±2.0) mm] ($P<0.001$) , 受 精 率 A 组 (77.1%) 、 B 组 (77.6%) 明 显 高 于 C 组 (71.3%) ($P=0.041$) ; 3 组 间 Gn 使 用 量 、 Gn 使 用 时 间 、 获 卵 数 、 卵 胞 质 内 单 精 子 注 射 (ICSI) 率 、 卵 裂 率 、 优 质 胚 胎 率 、 可 移 植 胚 胎 数 及 优 质 胚 胎 数 组 间 比 较 差 异 均 无 明 显 统 计 学 意 义 ($P>0.05$) 。 着 床 率 及 临 床 妊 娠 率 A 组 (26.2%、36.1%) 和 B 组 (26.8%、42.0%) 明 显 高 于 C 组 (14.5%、21.2%) (P 均 $=0.014$) ; 胚 胎 移 植 周 期 、 移 植 胚 胎 数 、 囊 胚 移 植 周 期 比 例 、 流 产 率 和 周 期 取 消 率 组 间 比 较 差 异 均 无 统 计 学 意 义 (P 均 >0.05) 。 结 论 启 动 Gn 前 给 予 OCP 或 黄 体 期 戊 酸 雌 二 醇 预 处 理 均 可 提 高 POSEIDON 预 期 POR 患 者 的 临 床 结 局 。 OCP 预 治 疗 适 用 于 排 卵 障 碍 的 POR 患 者 , 而 黄 体 期 戊 酸 雌 二 醇 预 治 疗 适 用 于 有 排 卵 的 POR 患 者 。

【关键词】 促性腺激素释放激素； 超短激动剂； 拮抗剂； 预处理； 卵巢低反应

Effects of different pretreatments prior to gonadotropin stimulation on the clinical outcomes of POSEIDON expected poor ovarian response patients

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【Abstract】 **Objective** To analyze the effect of different pretreatments on the *in vitro* fertilization (IVF) outcome of expected poor ovarian response (POR) patients according to POSEIDON criteria, and explore the appropriate treatment for POR patients. **Methods** A retrospective analysis of the clinical data of 364 cycles of expected POR patients who received *in vitro* fertilization-embryo transfer (IVF-ET) in the Center of Reproductive Medicine, Department of Obstetrics & Gynecology , Peking University Third Hospital from January 2016 to May 2018 was performed. According to the pretreatment prior to gonadotropin (Gn) stimulation, the cycles were divided into oral contraceptive (OCP) group (group A, $n=167$), estradiol valerate group (group B, $n=56$) and no pretreatment group (group C, $n=141$). The clinical data, ovarian stimulation indexes, laboratory status and the clinical pregnancy rate were compared among the three groups. **Results** The age of patients in group A [(34.8±4.9) years] was significantly younger than that of group B [(38.0±4.9) years] and group C [(37.9±4.7) years] ($P<0.001$). The body mass index (BMI) of group B [(21.9±3.1) kg/m²] was significantly lower than that of group A [(23.5±3.6) kg/m²] and group C [(23.2±3.1) kg/m²] ($P=0.014$). There were significant differences in the antral follicle count (AFC) among group A (2.4±2.0), group B (4.1±1.9) and group C (3.5±2.0) ($P<0.001$). The proportion of anovulation in group A (32.9%) was significantly higher than that in group B (10.7%) and group C (11.3%) ($P<0.001$). The number of IVF cycles in group C (3.0±1.7) was higher than that in group A (2.5±1.5) ($P=0.017$) . There was no significant difference in type of infertility, duration of infertility, basal follicle-stimulating hormone (FSH) and anti-Müllerian hormone (AMH) among the three groups ($P>0.05$). The endometrial thickness on the day of human chorionic gonadotropin (hCG) injection in group A [(9.4±1.9) mm] was thinner than that in group B [(10.6±1.5) mm] and group C [(10.1±2.0) mm] ($P<0.001$). The fertilization rate of group A (77.1%) and group B (77.6%) was significantly higher than that of group C (71.3%) ($P=0.041$). There were no significant differences in Gn used dosage, duration of Gn stimulation, number of eggs obtained, intracytoplasmic sperm injection (ICSI) proportion, cleavage rate, number of embryos available for transfer and number of high-quality embryos among the three groups ($P>0.05$). The implantation rate and the clinical pregnancy rate in group A (26.2%, 36.1%) and group B (26.8%, 42.0%) were significantly higher than those in group C (14.5%, 21.2%) ($P=0.014$). There were no significant differences in embryo transfer cycle, number of embryos transferred, proportion of blastocyst transfer cycle, abortion rate and cycle cancellation rate among the three groups ($P>0.05$). **Conclusion** Pretreatment with OCP or estradiol valerate in luteal phase prior to Gn stimulation can improve the clinical outcomes of patients with expected POR. OCP pretreatment is suitable for POR patients with ovulation disorder, while estradiol pretreatment in luteal phase is suitable for POR patients with ovulation.

【Key words】 Gonadotropin-releasing hormone; Ultrashort gonadotropin-releasing hormone agonist; Gonadotropin-releasing hormone antagonist; Pretreatment ; Poor ovarian response

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· 临床研究 ·

间苯三酚对体外受精-胚胎移植结局的影响

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【摘要】 目的 探究间苯三酚对体外受精-胚胎移植(IVF-ET)结局的影响。方法 回顾性分析 2015 年 1 月 1 日至 2018 年 11 月 30 日期间在郑州大学第二附属医院生殖医学部行 IVF-ET 治疗的 4289 例不孕患者的临床资料。根据妊娠结局分为妊娠组及非妊娠组，分析影响患者妊娠结局的危险因素。再根据移植前用药情况将患者分为未接受药物治疗组(A 组)、术前静脉滴注阿托西班组(B 组)、术前联合术中注射阿托西班组(C 组)、术中静脉滴注间苯三酚组(D 组)，比较四组患者的一般情况、妊娠结局，以及治疗期间及治疗后不良反应发生情况。结果 年龄、优质胚胎数及移植前用药方式是影响 IVF-ET 患者妊娠结局的独立因素($P=0.031$ 、 $P=0.039$ 、 $P=0.020$)。D 组患者胚胎种植率、生化妊娠率及临床妊娠率均明显高于 A 组(P 均 <0.001)、B 组(P 均 <0.001)及 C 组($P<0.001$ ， $P<0.001$ ， $P=0.001$)；其异位妊娠率明显低于 A 组、B 组及 C 组(P 均 <0.001)；流产率低于 A 组($P<0.001$)。治疗期间及治疗后，4 组患者均未见不适主诉及过敏反应，所有出生婴儿均无出生缺陷。结论 用药方式是影响 IVF-ET 患者妊娠结局的独立因素，术中静脉注射间苯三酚可明显提升 IVF-ET 患者胚胎种植率及妊娠率，并降低其流产率。

【关键词】 受精，体外； 胚胎移植； 间苯三酚； 妊娠结局

Effects of phloroglucinol on transfer outcome of *in vitro* fertilization-embryo transfer

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【Abstract】 **Objective** To explore the effects of phloroglucinol on transfer outcome of *in vitro* fertilization-embryo transfer (IVF-ET). **Methods** Retrospective analysis of 4289 cases of infertility patients treated with IVF-ET in the Department of Reproductive Medicine, the Second Affiliated Hospital of Zhengzhou University from January 1, 2015 to November 30, 2018 was performed. According to the pregnancy outcome, all patients were divided into pregnancy group and non-pregnancy group to analyze the risk factors affecting the pregnancy outcome. According to medication before transfer, all patients were divided into no medication group (group A), preoperative intravenous infusion of atosiban group (group B), preoperative and intraoperative

injection of atosiban group (group C) and interoperative intravenous infusion of phloroglucinol group (group D). The pregnancy outcomes, occurrence of adverse reactions during and after treatment were compared among the four groups. **Results** Age, number of high-quality embryos, and medication methods before transfer were independent factors influencing pregnancy outcomes in patients undergoing IVF-ET ($P=0.031$, $P=0.039$, $P=0.020$). The embryo implantation rate, the biochemical pregnancy rate and the clinical pregnancy rate of group D were significantly higher than those in group A (all $P<0.001$), group B (all $P<0.001$) and group C ($P<0.001$, $P<0.001$, $P=0.001$), while the ectopic pregnancy rate was significantly lower than that in group A, group B and group C (all $P<0.001$). The abortion rate in group D was lower than that in group A ($P<0.001$). During treatment period and after treatment, there were no discomfort complains and allergic reactions in the four groups. There were no birth defects in all born babies. **Conclusion** The medication method is an independent factor influencing pregnancy outcomes of patients undergoing IVF-ET. Intraoperative intravenous infusion of phloroglucinol can significantly increase embryo implantation rate and pregnancy rate of IVF-ET patients, and reduce their abortion rate.

【Key words】 Fertilization *in vitro* ; Embryo transfer ; Phloroglucinol ; Pregnancy outcome

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· 临床研究 ·

第3日4~5-细胞I~III级胚胎囊胚培养的价值评估

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【摘要】 目的 探讨第3日(D3)4~5-细胞I、II及III级胚胎(4/I~5/III)囊胚的形成及移植对体外受精-胚胎移植(IVF-ET)临床结局的影响。方法 回顾性分析2016年1月至2019年2月期间在解放军联勤保障部队第901医院采用IVF-ET助孕患者共884个周期的临床资料。比较4/I~5/III组间囊胚形成差异；根据囊胚移植周期中D3卵裂胚的情况，将4/I~5/III胚胎来源的164个囊胚移植周期设为A组，247个优质胚胎来源的囊胚移植周期设为B组，比较两组间的临床结局并分析4/I~5/III组间不同细胞数和评级对临床妊娠率及流产率的影响。结果 4/I组的优质囊胚率(5.6%)高于4/II组(1.8%)($P=0.003$)及4/III组(0.6%)($P<0.001$)；5/I组优质囊胚率(8.3%)分别高于4/II组、4/III组及5/III组(1.6%)(P 均 <0.001)；5/II组优质囊胚率(8.4%)高于4/III组($P<0.001$)。A组与B组在获卵数、成熟卵数、受精率、卵裂率、移植胚胎数、移植优质囊胚比、临床妊娠率、流产率、种植率及持续妊娠率差异均无统计学意义($P>0.05$)；A组D3优质胚胎率显著低于B组($P<0.001$)；A组平均移植周期次数高于B组($P=0.034$)；4-细胞和5-细胞来源的囊胚移植临床妊娠率分别为51.6%和50.0%，流产率分别为15.2%和26.8%；I+II级与III级胚胎来源的囊胚移植临床妊娠率分别为53.6%和41.2%，流产率分

别为 22.4%和 21.4%，组间差异均无统计学意义 ($P>0.05$)。结论 4/I~5/III 来源的囊胚能够获得与优质卵裂胚来源囊胚相近的临床结局；在 4/I~5/III 组间，细胞数和评级不会影响其囊胚的临床妊娠率及流产率，但 5-细胞胚胎的囊胚形成率高于 4-细胞胚胎。

【关键词】 囊胚形成； 卵裂胚； 低质量胚胎； 临床结局； 受精，体外； 胚胎移植

Value evaluation of blastocyst derived from 4-5-cell grade I to III embryos on day 3

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【Abstract】 **Objective** To investigate the effects of blastulation and transferred blastocyst derived from the 4-5-cell grade I to III (4/I-5/III) embryos on day 3 on clinical outcomes of *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** A total of 884 IVF cycles with blastocyst culture in the 901st Hospital of the Joint Logistics Support Force of PLA from January 2016 to February 2019 were retrospectively analyzed. The blastocyst formation status was compared among the 4/I-5/III embryos. Blastocyst derived from 4/I-5/III embryos in transfer cycle was served as group A ($n=164$), blastocyst derived from good-quality cleavage stage embryos (7/I-10/II) in transfer cycle was served as group B ($n=247$) according to quality of cleavage stage embryos on day 3. The clinical outcomes were compared between the two groups. The effects of different blastomere number and grade on clinical pregnancy rate and spontaneous abortion rate were evaluated among the 4/I-5/III embryos. **Results** Good-quality blastulation rate for 4/I, 4/II, 4/III, 5/I, 5/II and 5/III were 5.6%, 1.8%, 0.6%, 8.3%, 8.4% and 1.6%, respectively. The differences reached statistical significances ($P<0.05$). There were no significant differences in number of oocytes retrieved, number of mature oocytes, fertilization rate, cleavage rate, number of transferred embryos, percentage of good-quality blastocyst transfer cycles, clinical pregnancy rate, spontaneous abortion rate, implantation rate and ongoing pregnancy rate between group A and group B ($P>0.05$), group A had higher number of embryo transfer cycles ($P=0.034$) and lower good-quality embryo rate on day 3 ($P<0.001$). There were no significant differences in clinical pregnancy rate and spontaneous abortion rate between transferred blastocyst derived from the 4-cell and 5-cell embryo (51.6% vs. 50.0% ; 15.2% vs. 26.8%, respectively). There were no significant differences in clinical pregnancy rate and spontaneous abortion rate between transferred blastocyst derived from grade I+II and grade III (4/I-5/III) (53.6% vs. 41.2% ; 22.4% vs. 21.4%, respectively). **Conclusion** Blastocyst derived from 4/I-5/III embryos and good cleavage stage embryos both are similar clinical outcomes in blastocyst transfer cycles, there are no effects of blastomere number and grade on clinical pregnancy rate and abortion rate in blastocyst transfer cycles, but blastulation rate derived from 5-cell embryo was significantly higher than that of 4-cell embryo.

【Key words】 Blastulation ; Cleavage stage embryos ; Poor quality embryo ; Clinical outcomes ; Fertilization *in vitro* ; Embryo transfer

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· 临床研究 ·

整倍体单囊胚冷冻移植临床结局影响因素分析

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【摘要】 目的 筛选影响整倍体单囊胚移植成功率的关键因素。方法 本项回顾性研究纳入 2014 年 1 月至 2018 年 1 月期间在上海集爱遗传与不育诊疗中心进行胚胎植入前遗传学检测 (PGT) 的冷冻整倍体单囊胚移植周期共 956 个的患者临床资料。按照移植结局, 将患者分为妊娠组 ($n=509$) 及未妊娠组 ($n=447$), 比较两组间的临床资料, 筛选出对移植妊娠率产生影响的关键因素; 同时, 进一步将妊娠组患者分为活产亚组和流产亚组, 对比两亚组间的临床资料并利用 logistic 回归筛选对流产造成影响的显著性因素。结果 妊娠组较未妊娠组, 移植时子宫内膜厚度显著增厚 [$9(8, 10)$ mm 比 $8(8, 10)$ mm] ($P=0.006$); 质量良好的囊胚相对于质量较差的囊胚临床妊娠率 (59.2%比 46.3%) 及活产率 (50.2% 比 37.7%) 显著上升 ($P=0.001$)。此外, 活产亚组与流产亚组相比, 囊胚发育时间为流产相关风险因素, OR 值为 0.536 (95% $CI=0.309\sim0.929$)。结论 在整倍体单囊胚移植冷冻周期中, 较厚的子宫内膜、发育较快以及级别较高的囊胚是种植成功的关键因素。维持后期妊娠的过程中, 发育较快的囊胚 (第 5 日) 活产率更高, 流产率更低。

【关键词】 胚胎移植; 妊娠结局; 整倍体囊胚; 囊胚质量; 囊胚发育

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Analysis of the factors influencing the clinical outcome of frozen euploid single blastocyst transfer

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【Abstract】 Objective To find out the key factors that affect the clinical outcome of euploid single blastocyst transfer. **Methods** This retrospective study included 956 patients' clinical data of frozen euploid single blastocyst transfer cycles for preimplantation genetic testing (PGT) in Shanghai Ji Ai Genetics and IVF Institute from January 2014 to January 2018. According to the outcome of transplantation, the patients were divided into pregnancy group ($n=509$) and non-pregnancy group ($n=447$), and the clinical data between the two groups were compared to screen out the key factors affecting the pregnancy rate of transplantation; at the same time, the pregnancy group was further divided into live birth subgroup and miscarriage subgroup, and the clinical data between the two subgroups were compared and the significant factors affecting the abortion were screened by logistic regression. **Results** The endometrial thickness of pregnancy group was significantly thicker than that of non-pregnancy group [$9(8,10)$ mm vs. $8(8,10)$ mm] ($P=0.006$); the clinical pregnancy rate and the live birth rate of blastocyst with good quality were significantly higher than those with poor quality (59.2% vs. 46.3%, 50.2% vs. 37.7%) ($P=0.001$). In addition, compared with miscarriage subgroup, blastocyst development time was a risk factor of abortion, and the OR value was 0.536 (95% $CI=0.309-0.929$). **Conclusion** In the frozen embryo transfer cycles of single euploid blastocyst, the thicker endometrium, the faster development and the higher score of blastocyst are the key factors for the success of the implantation. In the process of maintaining the late pregnancy, the faster development of blastocyst (D5) has a higher live birth rate and a lower miscarriage rate.

【Key words】 Embryo transfer; Pregnancy outcome; Euploid blastocyst; Blastocyst quality; Blastocyst forming time

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· 临床研究 ·

加速康复外科在子宫内膜异位性疾病患者中的应用研究

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【摘要】 目的 分析加速康复外科(enhanced recovery after surgery, ERAS)临床路径在子宫内膜异位性疾病患者中应用的安全性及有效性。方法 采用病例对照研究方法分析 2017 年 8 月 1 日至 2018 年 8 月 31 日期间于中国医科大学附属盛京医院住院行手术治疗的子宫内膜异位性疾病患者。进入 ERAS 路径的 183 名患者为 ERAS 组, 传统路径的 255 名患者为对照组, 分析两组手术后的康复情况。结果 共纳入 438 例患者。ERAS 组患者手术后排气时间 $[(37.57 \pm 12.10) \text{ h}]$ 早于对照组 $[(47.28 \pm 17.36) \text{ h}]$, $P < 0.001$; ERAS 组手术后疼痛评分(手术后第 1 日晨 8 时: 2.86 ± 0.89 , 手术后第 2 日晨 8 时: 1.99 ± 0.73) 低于对照组(手术后第 1 日晨 8 时: 2.96 ± 0.92 , 手术后第 2 日晨 8 时: 2.41 ± 0.82), P 均 < 0.001 ; ERAS 组手术后较手术前血液中 D-二聚体升高倍数 $[1.67 (0.68, 3.04)]$ 低于对照组 $[3.17 (1.55, 5.72)]$, $P < 0.001$; ERAS 组手术后住院时间 $[(5.20 \pm 1.07) \text{ d}]$ 短于对照组 $[(5.52 \pm 1.46) \text{ d}]$, $P = 0.009$ 。结论 ERAS 路径的应用可缩短子宫内膜异位性疾病患者手术后排气时间, 减轻手术后疼痛, 改善手术后血液高凝状态以及减少住院时间; ERAS 在子宫内膜异位性疾病患者中的应用安全可行且有效。

【关键词】 加速康复外科; 子宫内膜异位性疾病; 疼痛; 肠道功能

Study on the application of enhanced recovery after surgery in patients with endometriosis and adenomyosis

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【Abstract】 **Objective** To study the safety and effect of enhanced recovery after surgery (ERAS) in patients with endometriosis and adenomyosis. **Methods** Totally 483 patients with endometriosis and adenomyosis who were admitted to Shengjing Hospital of China Medical University from August 1, 2017 to August 31, 2018 were included. Totally 183 patients underwent ERAS (ERAS group) and 255 patients underwent conventional pathway (control group) were enrolled. Perioperative intestinal function, pain score, inflammatory index, postoperative complications and length of hospital stay were analyzed. **Results** Compared with control group,

the time of postoperative exhaust in ERAS group was earlier [(37.57±12.10) h vs. (47.28±17.36) h, $P<0.001$]. Postoperative pain score was decreased [8 : 00 am at postoperative day 1 (2.86±0.89 vs. 2.96±0.92); 8 : 00 am at postoperative day 2 (1.99±0.73 vs. 2.41±0.82), all $P<0.001$]. The increase of D-dimer in blood after surgery was lower [1.67(0.68, 3.04) vs. 3.17(1.55, 5.72), $P<0.001$]. Postoperative hospital stay was shorter [(5.20±1.07) d vs. (5.52±1.46) d, $P=0.009$]. **Conclusion** The application of ERAS path in patients with endometriosis and adenomyosis can shorten the postoperative exhaust time, reduce the postoperative pain, improve the postoperative hypercoagulability of blood and reduce the length of hospital stay. ERAS is safe, feasible and effective in patients with endometriosis and adenomyosis.

【Key words】 Enhanced recovery after surgery ; Endometriosis and adenomyosis ; Pain ; Intestinal function

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· 临床报道 ·

胚胎植入前遗传学检测在染色体结构异常不孕夫妇治疗中的应用

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【摘要】 目的 探讨胚胎植入前遗传学检测(preimplantation genetic testing, PGT)在染色体结构异常不孕夫妇治疗中的应用，为 PGT 技术的推广与应用提供参考。方法 回顾性分析 2017 年 6 月至 2019 年 7 月期间由于染色体结构异常到新疆佳音医院接受 PGT 患者的临床资料，按异常类型分为相互易位、罗氏易位和倒位 3 组。卵胞质内单精子显微注射(ICSI)受精后选择培养至囊胚期胚胎进行外滋养层细胞活检及胚胎细胞染色体高通量测序，挑选检测结果正常的胚胎行单囊胚解冻移植。并对患者的一般资料、促排卵和胚胎培养情况、囊胚活检检测序列结果以及移植后的妊娠结局进行组间比较。结果 51 例患者共完成了 67 个 PGT 周期，总计对 189 枚囊胚进行了 PGT。3 组间的复合异常胚胎比率与非整倍体胚胎比率差异均有统计学意义(P 均 <0.001)，其他数据差异无统计学意义($P>0.05$)。33 个完成移植的周期中有 16 个成功妊娠，妊娠率为 48.5%，且有 7 例已顺利分娩获得健康子代。结论 PGT 的临床应用能够有效改善染色体结构异常夫妇的生育情况，不同结构携带者的胚胎异常类型比例存在差异，可作为遗传咨询参考。

【关键词】 胚胎植入前遗传学检测； 染色体结构异常； 高通量测序

Application of preimplantation genetic testing in treatment of infertile couples with abnormal chromosome structure

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【Abstract】 Objective To explore the application of preimplantation genetic testing (PGT) in the treatment of infertile couples with abnormal chromosome structure, and provide a reference for the promotion and application of PGT technology. **Methods** The clinical data of the first batch of patients who received PGT due to chromosomal structural abnormalities in Xinjiang JIAYIN Reproductive Medicine Center from June 2017 to July 2019 were retrospectively analyzed. According to the abnormal type, the patients were divided into three groups: mutual translocation, Roche translocation and inversion. After intracytoplasmic sperm injection (ICSI), the available blastocysts were selected for external trophoblast cell biopsy and next generation sequencing analysis of chromosome of embryonic cells. Embryos with normal detection results were selected for single blastocyst thawing and transplantation. The patient's general information, ovulation induction and embryo culture, blastocyst biopsy results and pregnancy outcome after transplantation were compared among the three groups. **Results** A total of 51 patients completed 67 PGT cycles, a total of 189 blastocysts were genetically detected. There were significant differences among the three groups in the ratio of complex abnormal embryos and aneuploidy embryos (all $P<0.001$), but no significant differences were observed in other data ($P>0.05$). There were 16 successful pregnancies out of 33 successful transplant cycles, with a pregnancy rate of 48.5%, and 7 patients had successfully given birth to healthy babies. **Conclusion** The clinical application of PGT can effectively improve the fertility of couples with abnormal chromosome structure, and the proportion of embryo abnormalities of different types of carriers is different, which can be used as a genetic reference.

【Key words】 Preimplantation genetic testing ; Chromosome structure abnormality ; Next generation sequencing

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· 临床报道 ·

中山市育龄期多囊卵巢综合征患者管理体系的建立对妊娠结局的影响

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【摘要】 目的 探讨育龄期多囊卵巢综合征(PCOS)患者管理体系的建立对妊娠结局的影响。**方法** 回顾性分析 2016 年 6 月至 2018 年 5 月期间在中山市博爱医院生殖中心就诊的 1203 名 20~45 岁多囊卵巢综合征(PCOS)患者,愿意纳入长期管理系统的有 755 名(研究组),进行基础血压及体质量控制、血清指标监测,建立 PCOS 管理微信平台等方法对其进行科普教育。同期 448 位 PCOS 患者未纳入长期管理系统(对照组),进行妊娠情况的追踪。结果 研究组总的妊娠率为 25.74% (148/575),高于对照组的 18.13% (62/342),差异有统计学意义($P=0.010$)。研究组总流产率为 14.19% (21/148),低于对照组的 22.58% (14/62),但差异无统计学意义($P=0.199$)。

结论 对育龄期 PCOS 患者进行综合管理,提高公众对 PCOS 作为慢性病的认知和接受度,提高 PCOS 患者的依从性,能改善 PCOS 患者妊娠结局。

【关键词】 妊娠; 多囊卵巢综合征; 流产; 生殖

基金项目:中山市重大科技项目(2016B1007)

Effect of management system on pregnancy outcome in patients with polycystic ovary syndrome of childbearing age in Zhongshan City

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【Abstract】 **Objective** To investigate the effect of management system on pregnancy outcome in patients with polycystic ovary syndrome (PCOS) of childbearing age. **Methods** A total of 1203 patients with PCOS aged 20–45 years were collected in Reproductive Center of Zhongshan Boai Hospital from June 2016 to May 2018. Totally 755 who would like to be included in the long term management system were collected as study group and received basic blood pressure and weight control and serum monitoring, scientific education was performed through WeChat platform established for PCOS management and other methods. Other 448 patients with PCOS were not included in the long-term management system (control group), and their pregnancy outcomes were followed up. **Results** The total pregnancy rate of study group was higher than that of control group (25.74% vs. 18.13%, $P=0.010$), and the total abortion rate of study group was lower than that of control group (14.19% vs. 22.58%, $P=0.199$). **Conclusion** Comprehensive management of PCOS patients of childbearing age can improve the public's cognition and acceptance of PCOS as a chronic disease, improve the compliance and pregnancy outcome of PCOS patients.

【Key words】 Pregnancy ; Polycystic ovary syndrome ; Abortion ; Reproduction

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·综述·

基于博洛尼亚标准的POSEIDON分层在卵巢低反应临床诊疗中的应用价值

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【摘要】 卵巢低反应 (poor ovarian response, POR) 极大地限制了辅助生殖技术的成功, 准确预测 POR 的发生、制定个体化治疗方案在临床诊疗中具有重要意义。POR 博洛尼亚标准在临床应用中显示出将异质性人群归于一组讨论的不足, POSEIDON (Patient-Oriented Strategies Encompassing Individualized Oocyte Number) 团队在此基础上全面考虑年龄、卵巢储备参数及此前对卵巢刺激的反应性三方面因素对辅助生殖结局的影响, 提出了更为细致的分类。本文着重探讨 POSEIDON 分层特点及其临床应用价值, 以期 POSEIDON 分层在该病的应用提供依据。

【关键词】 卵巢低反应; 博洛尼亚标准; POSEIDON; 分层; 临床诊疗

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Application value of POSEIDON stratification based on Bologna criteria in clinical interviewing of poor ovarian response

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【Abstract】 Poor ovarian response (POR) greatly limits the success of assisted reproductive technology (ART), so it is of great significance to accurately predict the occurrence of POR and formulate individualized treatment programs in clinical diagnosis and treatment. The Bologna criteria showed the deficiency in the discussion of grouping heterogeneous population together in clinical application. Based on this, POSEIDON team comprehensively considered the influence of age, ovarian reserve parameters and previous responsiveness to ovarian stimulation on the outcome of ART and proposed a more detailed classification. This paper focuses on the characteristics of POSEIDON stratification and its clinical application value in order to provide reference for the application of POSEIDON stratification in this disease.

【Key words】 Poor ovarian response; Bologna criteria; POSEIDON; Stratification; Clinical interviewing

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· 综述 ·

APE1 的 DNA 修复作用在早发性卵巢功能不全的遗传学病因中的研究

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【摘要】 近年来许多研究提示 DNA 损伤与卵巢储备功能下降和早发性卵巢功能不全 (premature ovarian insufficiency, POI) 密切相关。影响 DNA 损伤修复的基因众多, 关键修复基因及其转录蛋白的异常或可导致 POI 的发生。目前已有越来越多可诱发 POI 的 DNA 损伤修复相关

基因突变被发现, 其中, 人脱嘌呤/脱嘧啶核酸内切酶 1(Apurinic/Apyrimidinic endonuclease 1, APE1/APEX1), 也称氧化还原因子 1(Redox factor-1, Ref-1), 是一种由 *APEX1* 基因转录的 DNA 损伤修复途径中的关键酶, 并同时具有氧化应激、转录因子调控等多功能酶活性, 因其与肿瘤发生、发展及预后的密切关系成为近年来的研究热点。尽管已有研究报道, 部分 *APEX1* 基因突变会影响细胞周期甚至配子发育, 但其与 POI 发生的直接联系仍未得到证明。本文综述了 DNA 损伤修复、卵巢功能及 *APE1* 基因的关系, 为 POI 的病因学解析及治疗提供新的思考方向。

【关键词】 人脱嘌呤/脱嘧啶核酸内切酶 1; DNA 损伤修复; 早发性卵巢功能不全

Role of DNA repair disorder of APE1 in the genetic etiology of premature ovarian insufficiency

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【Abstract】 Recent researches have pointed out that DNA damage is tightly bound up with the decline of ovarian reserve and the disease we called premature ovarian insufficiency (POI). Many genes affect the DNA damage and repair, and the abnormality of critical genes and the transcribed proteins may lead to the occurrence of POI. At present, more and more DNA damage repair related gene mutations have been found to induce POI, among which Apurinic/Apyrimidinic endonuclease 1 (APE1), or Redox factor-1 (Ref-1), is an essential enzyme in DNA damage repair transcribed by gene *APEX1*, which is also a type of biomacromolecule with multifunction enzymic activities in oxidative stress reaction and transcription factor regulation. It takes the recent research highland owing to the close relationship with the tumorigenesis and prognosis. Although some kinds of *APEX1* mutations have been reported to affect cell cycle and even gamete development, the direct association with POI has not been demonstrated. This paper reviews the relationship between DNA damage repair, ovarian function, and APE1, cultivating new research potentials for the etiological resolve and treatment of POI.

【Key words】 Apurinic/Apyrimidinic endonuclease 1; DNA damage repair; Premature ovarian insufficiency

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·综述·

生物钟基因影响妊娠的研究进展

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【摘要】 生物钟在所有生物体内普遍存在。转录翻译振荡环路机制是哺乳动物中生物钟进行精密调控的主要途径, 其核心部分主要由 Clock、Bmal1、PER 及 CRY 等组成。随着对生物钟基因研究的不断深入, 研究表明生物钟可能参与排卵、胚胎着床、蜕膜化、维持妊娠等一系列过程, 妊娠

后母体生物钟基因会发生相应的改变以适应妊娠过程。然而一旦发生异常改变,可能会导致流产以及出现妊娠并发症。

【关键词】 生物钟; 妊娠; 自然流产; 妊娠并发症

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Research progress on biological clock genes during pregnancy

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【Abstract】 Biological clock exists universally in all organisms. The mechanism of transcriptional translational oscillator loop is the main way of precise regulation of biological clock in mammals. The main part is made up of Clock, Bmal1, PER, CRY and so on. With the deep research of biological clock genes, it is found that the biological clock may be involved in a series of processes such as ovulation, embryo implantation, decidualization, and the maintenance of pregnancy. After pregnancy, the maternal biological clock genes will have corresponding changes to adapt to the pregnancy process. However, abnormal changes of biological clock may lead to pregnancy loss and pregnancy complications.

【Key words】 Biological clocks; Pregnancy; Spontaneous abortion; Pregnancy complications

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·综述·

沉默信息调节因子1在卵子发生中的作用

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【摘要】 沉默信息调节因子2蛋白(Sirtuin)家族是一类依赖于烟酰胺烟嘌呤二核苷酸(NAD^+)的去乙酰化酶,家族成员沉默信息调节因子2(SIR2)最早被发现于酵母中。因哺乳动物体内的沉默信息调节因子(SIRT)1与其同源性最高,目前研究最为深入。SIRT1广泛存在于哺乳动物体内,参与机体多种病理生理过程,如DNA损伤修复、炎症反应及氧化应激等。近年来研究发现SIRT1可能通过多种途径参与卵子发生过程,故本文拟对SIRT1在卵子发生中发挥的作用及可能的机制作一综述,为相关疾病治疗提供新思路。

【关键词】 沉默信息调节因子1; 卵子发生; 机制; 不孕症

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Role of silencing information regulator 1 in the oogenesis

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【Abstract】 Sirtuin family is a type of acetylase dependent on the nicotinethorin (NAD⁺). The family member SIR2 was first discovered in yeast, and because the silencing information regulator 1 (SIRT1) in the mammal has the highest homology with it, for which SIRT1 was thoroughly researched. SIRT1 is widely distributed in mammals and participated in varying physiological processes, such as DNA damage repair, inflammatory response and oxidative stress. In recent years, it has been found that it may participate in the process of oogenesis through diverse ways. Therefore this paper intends to review the role and possible mechanism of SIRT1 in the oogenesis, and provide new ideas for the treatment of related diseases.

【Key words】 Silencing information regulator 1 ; Oogenesis ; Mechanism ; Infertility

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· 综述 ·

糖皮质激素对子代卵巢发育影响及其宫内编程机制

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【摘要】 孕期的各种应激刺激及临床上地塞米松等药物的广泛使用是导致胎儿暴露于内、外源性糖皮质激素的重要原因。女性(雌性)卵巢功能异常甚至疾病状态具有宫内起源，而糖皮质激素可能参与编程子代卵巢功能发育损伤甚至多代的功能异常。本综述结合临床和实验室的研究进展，系统概述内、外源性糖皮质激素导致子代卵巢发育损伤及其多代遗传的现象，并初步探讨其宫内编程机制。

【关键词】 孕期糖皮质激素暴露； 卵巢发育； 宫内编程

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Effects of glucocorticoids on ovarian development of offspring and its intrauterine programming mechanism

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【Abstract】 During pregnancy, stress stimulation and the widespread use of drugs (such as dexamethasone) are the important causes of fetus exposed to endogenous and exogenous glucocorticoids. Ovarian dysfunction and some reproductive endocrine disorders have intrauterine origin. And the abnormal ovarian functional development in offspring could be programmed by glucocorticoids, which even has multigenerational effects. This article systematically reviews the damage of ovarian development and multigenerational phenotype of offspring caused by endogenous and exogenous glucocorticoids, as well as summarizing the potential intrauterine mechanism according to clinical and laboratory studies.

【Key words】 Prenatal glucocorticoids exposure ; Ovarian development ; Intrauterine mechanism

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· 综述 ·

关于高龄女性助孕技术移植胚胎数目的伦理思考

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【摘要】 “全面二孩”政策带来了高龄助孕妇女增多，许多医学问题及伦理冲突凸现，妇幼健康和优生优育面临着巨大的挑战。如何在遵循有利于患者及保护后代等伦理原则下帮助高龄妇女实现再生育愿望是需要我们高度重视的问题。一次移植多枚胚胎是导致多胎妊娠的独立因素。然而目前国内尚无实施单胚胎移植的严格规定。鉴于多胎妊娠导致的一系列母婴危害，本文针对高龄女性移植胚胎数目的伦理思考进行阐述。

【关键词】 移植胚胎数目； 高龄； 母婴安全； 伦理

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Ethical thinking on the number of embryos transferred for women with advanced age

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【 Abstract 】 The “universal two-child” policy has brought an increase in the number of pregnant women with advanced age. Many medical problems and ethical conflicts have emerged, and maternal-child health and prenatal and postnatal care are facing great challenges. How to help elderly women realize their reproductive aspiration according to the ethical principle of “safety of mothers and health of children” is a problem that needs our great attention. The transfer of multiple embryos at a time is an independent factor leading to multiple pregnancies. However, there are no strict regulations on single embryo transfer in China. In view of a series of maternal and infant hazards caused by multiple pregnancies, this paper elaborates on the ethics of assisted pregnancy in elderly women with the number of embryos transferred.

【 Key words 】 Number of embryos transferred ; Advanced age ; Security of mothers and infants ; Ethics

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