中华生殖与避孕杂志®

原刊名《生殖与避孕》

CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION

月刊　1980年12月创刊　第43卷　第5期　2023年5月25日出版

主　管
中国科学技术协会

主　办
中华医学会
上海市生物医药技术研究院
复旦大学附属妇产科医院

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中华生殖与避孕杂志
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Email:randc@sibpt.com
http://zhszybyzz.yiigle.com

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出　版
《中华医学杂志》社有限责任公司
100710,北京市东四西大街42号
电话(传真):(010)51322059
Email:office@cmaph.org

广告发布登记号
京东市监广登字20200006号

印　刷
上海船舶设备研究所

发　行
范围:公开
国内:中国邮政集团公司上海分公司
国外:中国国际图书贸易集团责任有限公司
(北京399信箱,100044)
代号BM 389

订　购
全国各地邮政局
邮发代号4-928

邮　购
中华生殖与避孕杂志编辑部
200237,上海市老沪闵路779号
电话:(021)64438169,64438975
Email:randc@sibpt.com

定　价
每期35.00元,全年420.00元

中国标准连续出版物号
ISSN 2096-2916
CN 10-1441/R

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CHINESE JOURNAL OF REPRODUCTION AND CONTRACEPTION (Original title: *Reproduction and Contraception*)

Monthly Established in December 1980 Volume 43, Number 5 May 25, 2023

Responsible Institution
China Association for Science and Technology

Sponsor
Chinese Medical Association, Shanghai Institute for Biomedical and Pharmaceutical Technologies, Obstetrics and Gynecology Hospital of Fudan University

Editing
Editorial Board of Chinese Journal of Reproduction and Contraception
779 Laohumin Road, Shanghai 200237, China
Tel: 0086-21-64438169
Fax: 0086-21-64438975
Email: randc@sibpt.com
http://zhszybyzz.yiigle.com

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Publishing
Chinese Medical Journals Publishing House Co., Ltd.
42 Dongsi Xidajie, Beijing 100710, China
Tel(Fax): 0086-10-51322059
Email: office@cmaph.org

Printing
Shanghai Marine Equipment Research Institute

Overseas Distributor
China International Book Trading Corporation
P.O. Box 399, Beijing 100044, China
Code No.M389

Mail-Order
Editorial Board of Chinese Journal of Reproduction and Contraception
779 Laohumin Road, Shanghai 200237, China
Tel: 0086-21-64438169
Fax: 0086-21-64438975
Email: randc@sibpt.com

CSSN
ISSN 2096-2916
CN 10-1441/R

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DOI：10.3760/cma.j.cn101441-20221230-00600
收稿日期　2022-12-31　本文编辑　孙敏
引用本文：金晨曦，于文澔，张倩，等. 嵌合型胚胎移植妊娠结局的影响因素分析[J]. 中华生殖与避孕杂志, 2023, 43(5): 440-447. DOI: 10.3760/cma.j.cn101441-20221230-00600.

·生殖障碍性疾病遗传学专栏·

嵌合型胚胎移植妊娠结局的影响因素分析

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【摘要】 目的　探讨基于二代测序（next-generation sequencing，NGS）的胚胎植入前遗传学检测（preimplantation genetic testing，PGT）后嵌合型胚胎移植的妊娠结局，及不同嵌合比例、类型对嵌合型胚胎移植结局的影响。方法　回顾性队列研究分析 2018 年 1 月至 2021 年 12 月期间于山东大学生殖医学研究中心接受 PGT 助孕患者的临床资料，共纳入 308 个嵌合型胚胎移植周期（记为嵌合型组）和 904 个整倍体胚胎移植周期（记为整倍体组）。比较嵌合型组和整倍体组的妊娠结局，包括生化妊娠率、临床妊娠率、持续妊娠率、早期流产率、活产率和妊娠并发症发生率。根据嵌合比例将嵌合型组分为低比例嵌合亚组、高比例嵌合亚组，根据嵌合类型将嵌合型组分为片段缺失/重复嵌合亚组、染色体单体/三体嵌合亚组、复杂嵌合亚组，分析不同嵌合比例、类型对嵌合型胚胎移植结局的影响。结果　嵌合型组的持续妊娠率［49.35%（152/308）］及活产率［48.38%（149/308）］均较整倍体组明显降低［58.19%（526/904），*P*=0.020，*OR*=0.924；55.75%（504/904），*P*=0.031，*OR*=0.930］，但两组间妊娠并发症的发生风险差异无统计学意义（*P*>0.05）。高比例嵌合亚组的活产率［35.00%（14/40）］较低比例嵌合亚组显著下降［50.37%（135/268），*P*=0.028，*OR*=0.840］。染色体单体/三体嵌合亚组的生化妊娠率［58.49%（62/106）］、临床妊娠率［49.06%（52/106）］、持续妊娠率［43.40%（46/106）］及活产率［43.40%（46/106）］与整倍体组［70.91%（641/904），*P*=0.020，*OR*=0.891；64.82%（586/904），*P*=0.003，*OR*=0.864；58.19%（526/904），*P*=0.003，*OR*=0.864；55.75%（504/904），*P*=0.008，*OR*=0.868］比较，差异均有统计学意义。片段缺失嵌合胚胎的生化妊娠率［64.47%（49/76）］、临床妊娠率［57.89%（44/76）］、持续妊娠率［47.37%（36/76）］及活产率［46.05%（35/76）］均较片段重复嵌合胚胎［84.13%（53/63），*P*=0.002，*OR*=0.793；77.78%（49/63），*P*=0.006，*OR*=0.814；68.25%（43/69），*P*=0.017，*OR*=0.829；65.08%（41/63），*P*=0.042，*OR*=0.850］显著降低。结论　部分嵌合型胚胎移植后仍能获得健康活产，且不同嵌合比例、类型影响嵌合型胚胎移植的妊娠结局。因此，对于无整倍体胚胎可移植的患者，在临

床遗传咨询中应综合考虑不同嵌合比例、类型推荐嵌合型胚胎的移植顺序，以期得到最优妊娠结局。

【关键词】 妊娠结局； 胚胎植入前遗传学检测； 第二代测序； 嵌合型胚胎； 嵌合比例； 嵌合类型

基金项目：国家重点研发计划（2021YFC2700604）；国家自然科学基金面上项目（82171648）；山东省重点研发计划（2021LCZX02）

Analysis of factors related to pregnancy outcome after mosaic embryo transfer

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【Abstract】 Objective To investigate the pregnancy outcome of mosaic embryo transfer in next-generation sequencing (NGS) based-preimplantation genetic testing (PGT), and the effect of different mosaic ratios and types on the pregnancy outcome. **Methods** This was a retrospective, single-center, cohort study of 308 mosaic embryo transfer cycles (named mosaic group) and 904 euploid embryo transfer cycles (named euploid group) from January 2018 to December 2021 at Center for Reproductive Medicine, Cheeloo College of Medicine. Pregnancy outcomes, including biochemical pregnancy, clinical pregnancy, ongoing pregnancy, early miscarriage, live birth and pregnancy complication rate, were compared between the mosaic and euploid groups. The mosaic group was further divided into low- and high-level mosaicism subgroups according to mosaic ratio, and fragmental deletion/duplication, chromosomal monosomy/trisomy and complex mosaicism subgroups according to the chimerism type, in order to analyze the effects of different mosaic ratios and types on the transfer outcome of mosaic embryos. **Results** Compared with euploid group, the rates of ongoing pregnancy [49.35% (152/308) *vs*. 58.19% (526/904), *P*=0.020, *OR*=0.924] and live birth [48.38% (149/308) *vs*. 55.75% (504/904), *P*=0.031, *OR*=0.930] were significantly lower in mosaic group, but there was no significant difference in the risk of pregnancy complications between the two groups (*P*>0.05). The high-level mosaic subgroup had a significantly lower live birth rate [35.00% (14/40)] compared with low-level mosaic subgroup [50.37% (135/268), *P*=0.028, *OR*=0.840]. The biochemical pregnancy rate [58.49% (62/106) *vs*. 70.91% (641/904), *P*=0.020, *OR*=0.891], the clinical pregnancy rate [49.06% (52/106) *vs*. 64.82% (586/904), *P*=0.003, *OR*=0.864], the ongoing pregnancy rate [43.40% (46/106) *vs*. 58.19% (526/904), *P*=0.003, *OR*=0.864] and the live birth rate [43.40% (46/106) *vs*. 55.75% (504/904), *P*=0.008, *OR*=0.868] of chromosomal monosomy/trisomy mosaic subgroup were significantly lower than those of euploid group. The biochemical pregnancy rate [64.47% (49/76) *vs*. 84.13% (53/63), *P*=0.002, *OR*=0.793], the clinical pregnancy rate [57.89% (44/76) *vs*. 77.78% (49/63), *P*=0.006, *OR*=0.814], the ongoing pregnancy rate [47.37% (36/76) *vs*. 68.25% (43/69), *P*=0.017, *OR*=0.829] and the

live birth rate [46.05% (35/76) *vs*. 65.08% (41/63), *P*=0.042, *OR*=0.850] of fragmental deletion mosaic embryos were significantly lower than those of fragmental duplication mosaic embryos. **Conclusion** Partial mosaic embryo transfer can also achieve healthy live births, and different mosaic ratios and types affect the pregnancy outcomes. Therefore, patients with no available euploid embryos could be counseled about the possibility of transferring a mosaic embryo, taking into consideration the different mosaic ratios and types.

【Key words】 Pregnancy outcome; Preimplantation genetic testing; Next-generation sequencing; Mosaic embryo; Mosaic ratio; Mosaic type

Fund program: National Key R&D Program of China (2021YFC2700604); General Program of National Natural Science Foundation of China (82171648); Key R&D Program of Shandong Province (2021LCZX02)

DOI：10.3760/cma.j.cn101441-20221230-00598
收稿日期 2023-01-29 本文编辑 李天琦
引用本文：李小兰, 梁晓燕. 骨形态发生蛋白 15 基因多态性与早发性卵巢功能不全相关性荟萃分析[J]. 中华生殖与避孕杂志, 2023, 43(5): 448-454. DOI: 10.3760/cma.j.cn101441-20221230-00598.

·生殖障碍性疾病遗传学专栏·

骨形态发生蛋白 15 基因多态性与早发性卵巢功能不全相关性荟萃分析

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【摘要】 目的 探索骨形态发生蛋白 15（bone morphogenetic protein 15，BMP15）基因多态性与早发性卵巢功能不全（premature ovarian insufficiency，POI）的相关性，为 POI 患者遗传咨询提供循证医学证据。方法 运用计算机检索 Pubmed、EMbase、Cochrane Library 及中国期刊全文数据库中关于 *BMP*15 基因多态性及 POI 有关的病例对照研究或队列研究，检索时限是 1950 年 1 月至 2022 年 12 月。由 2 名研究者独立地根据纳入及排除标准进行文献筛选、数据提取及研究质量评价，采用 RevMan5.3 软件进行 meta 分析，*P*<0.05 考虑有统计学意义。结果 最终纳入 17 项研究，共 3 758 例患者，其中 POI 组 1 631 例患者，对照组 2 127 例患者。meta 分析显示，不管是全部地区还是亚洲地区，POI 组患者的 *BMP*15-9C>G、788insTCT 及 852C>T 均与对照组相似，差异均无统计学意义（均 *P*>0.05）。

另外，尽管 POI 组患者的 *BMP*15 443T>C 及 308A>G 多态性与对照组相似，差异均无统计学意义（均 *P*>0.05），但 POI 组 *BMP*15 308A>G 和 443T>C 的纯合突变率较对照组增加。POI 组患者 *BMP*15 538G>A 突变发生率较对照组增加，差异有统计学意义（基因型 AA+AG 与基因型 GG 相比，*OR*=6.48，95% *CI*：2.48~16.92，*P*<0.001；等位基因 A 与等位基因 G 相比，*OR*=7.61，95% *CI*：2.93~19.57，*P*<0.001）。结论　*BMP*15 538G>A 突变与 POI 发病可能相关，携带 *BMP*15 538G>A 突变的人群发生 POI 风险增加。未来仍需要不同种族的大样本量前瞻性队列研究来进一步证实 *BMP*15 基因变异与 POI 之间的关系。

【关键词】　骨形态发生蛋白 15；　meta 分析；　早发性卵巢功能不全

Relationship between polymorphisms of bone morphogenetic protein 15 gene and premature ovarian insufficiency: a meta-analysis update

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【**Abstract**】　**Objective**　To systematically evaluate the relationship between polymorphisms of bone morphogenetic protein 15 (BMP15) gene and premature ovarian insufficiency (POI), and to provide evidence-based medical evidences for genetic counseling of POI patients. **Methods**　Case control studies or cohort studies related to *BMP*15 gene polymorphisms and POI in Pubmed, EMbase, Cochrane Library and Chinese Journal Full Text Database were systematically searched. All articles were published from January 1950 to December 2022. Two researchers independently performed literature screening, data extraction and research quality evaluation. RevMan5.3 software was used for meta-analysis. *P*<0.05 was considered statistically significant. **Results**　The literature search yielded 17 studies with a total of 3 758 patients, including 1 631 patients in POI group and 2 127 patients in control group. Meta-analysis showed that the polymorphisms of *BMP*15-9C>G, 788insTCT and 852C>T in patients with POI were comparable to those in control group (*P*>0.05). In addition, although the polymorphisms of *BMP*15 443T>C and 308A>G in patients with POI were comparable with those in control group (*P*>0.05), the homozygous mutation incidence of *BMP*15 308A>G and 443T>C in patients with POI were higher than those in control group. The incidence of *BMP*15 538G>A mutation in patients with POI was significantly higher than that in control group (genotype AA+AG *vs.* GG, *OR*=6.48, 95% *CI*: 2.48-16.92, *P*<0.001; allele A *vs.* G, *OR*=7.61, 95% *CI*: 2.93-19.57, *P*<0.001). **Conclusion**　The polymorphism of *BMP*15 538G>A may be related to the pathogenesis of POI, and 538G>A carriers may be prone to POI. Further well-designed studies with larger samples are required to confirm the association between *BMP*15 gene variants and POI.

【**Key words**】　Bone morphogenetic protein 15; Meta analysis; Premature ovarian insufficiency

DOI：10.3760/cma.j.cn101441-20221221-00581

收稿日期　2022-12-12　本文编辑　孙敏
引用本文：张旸, 韩烁, 孟文佳, 等. 子宫内膜异位症的遗传学研究进展[J]. 中华生殖与避孕杂志, 2023, 43(5): 455-460. DOI: 10.3760/cma.j.cn101441-20221221-00581.

·生殖障碍性疾病遗传学专栏·

子宫内膜异位症的遗传学研究进展

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【摘要】 子宫内膜异位症是育龄期常见的妇科疾病，表现为痛经、不孕，严重影响女性的身心健康，其发病机制尚未明确。研究表明子宫内膜异位症是多因素病因所致，其中遗传在子宫内膜异位症发病机制中起重要作用。遗传关联研究从功能候选基因到全基因组水平发现了多个与该疾病发生、发展相关的遗传易感性位点。此外，表观遗传学也可能参与了子宫内膜异位症的发生和发展。本文从激素调节、免疫炎症、黏附、侵袭和血管生成等相关的基因入手，总结了与子宫内膜异位症相关的遗传学研究进展。子宫内膜异位症遗传学的研究将有助于理解其发生、发展机制，发现新的治疗靶点，为子宫内膜异位症的诊断、治疗提供理论基础。

【关键词】 子宫内膜异位症； 疾病遗传易感性； 多态性， 单核苷酸；表观遗传学

Advances in genetic research of endometriosis

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【 **Abstract** 】 Endometriosis is a common gynecological disease in childbearing age, manifested as dysmenorrhea and infertility, which seriously affects women's physical and mental health. The pathogenesis of endometriosis is not yet clear. Researches show that endometriosis is caused by multiple factors, among which heredity plays an important role in the pathogenesis of endometriosis. Genetic association research has found many genetic susceptibility sites related to the occurrence and development of the disease from functional candidate genes to the whole genome level. In addition, epigenetics may also be involved in the occurrence and development of endometriosis. This paper summarized the genes related to

hormone regulation, immune inflammation, adhesion, invasion and angiogenesis. The research on genetics of endometriosis will help to understand the occurrence and development mechanism of endometriosis, find new therapeutic targets, and provide theoretical basis for the diagnosis and treatment of endometriosis.

【 **Key words** 】 Endometriosis; Genetic predisposition to disease; Polymorphism, single nucleotide; Epigenetics

DOI：10.3760/cma.j.cn101441-20221206-00546
收稿日期 2022-12-06 本文编辑 王李艳
引用本文：董凡, 陈向锋. 精子形态学异常的遗传学研究及进展[J]. 中华生殖与避孕杂志, 2023, 43(5): 461-467. DOI: 10.3760/cma.j.cn101441-20221206-00546.

·生殖障碍性疾病遗传学专栏·

精子形态学异常的遗传学研究进展

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【摘要】 精子形态学异常和畸形精子症是男性不育的重要原因之一。近年来随着研究的深入，遗传学因素被发现是导致精子形态学异常和畸形精子症的重要病因。本文就近年来精子形态学异常和畸形精子症的遗传学研究进展作一综述，从畸形精子症诊断、基因异常、染色体异常、生殖结局等角度阐释遗传因素与畸形精子症的关系，重点阐述了特殊类型畸形精子症，如圆头精子症、鞭毛多发形态异常等表型相关的基因异常。本文旨在为精子形态学异常及畸形精子症的诊疗和研究提供遗传学角度新的思路。

【关键词】 不育，男性； 畸形精子症； 遗传； 基因； 染色体； 精子形态

Advances in the genetic researches of human sperm morphological abnormality and teratozoospermia

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【 **Abstract** 】 Morphological abnormality of human sperm and teratozoospermia is one of the key causes of male infertility. With the progress of

recent researches, more genetic causes were found to be involved in the pathogenesis of sperm morphological abnormality and teratozoospermia. This review analyzed the advances in genetic researches of human sperm morphological abnormality and teratozoospermia. We summarized the diagnosis of teratozoospermia, teratozoospermia-related genes, chromosomal abnormalities-related teratozoospermia as well as the reproductive outcomes of teratozoospermia. We also emphasized the relationship between genetic abnormalities and some special types of teratozoospermia, such as globozoospermia and multiple morphological abnormalities of the flagella (MMAF). We hope the article could give new genetic insight into the diagnosis, treatment and study of human sperm morphological abnormality and teratozoospermia.

【 Key words 】 Infertility, male; Teratozoospermia; Genetics; Gene; Chromosome; Sperm morphology

DOI：10.3760/cma.j.cn101441-20230228-00072
收稿日期　2023-02-28　本文编辑　宋培培
引用本文：谢冲, 武云浩, 孙斐. 非梗阻性无精子症的遗传学研究进展[J]. 中华生殖与避孕杂志, 2023, 43(5): 468-472. DOI: 10.3760/cma.j.cn101441-20230228-00072.

·生殖障碍性疾病遗传学专栏·

非梗阻性无精子症的遗传学研究进展

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【摘要】 非梗阻性无精子症（non-obstructive azoospermia， NOA）是困扰全世界不育男性的严峻问题，但是目前还不完全清楚其具体的遗传学致病因素。近些年，随着对生物信息学以及基因学研究的不断深入，越来越多的致病基因被发现。针对 NOA 的遗传学研究对象主要包括染色体异常、染色体微缺失、基因突变以及表观遗传修饰等。在本文中，我们对这些发现进行了简单的总结与评估，有助于大家进一步了解关于 NOA 的遗传学研究进展。

【关键词】 不育，男性； 非梗阻性无精子症； 遗传学研究
基金项目：浙江省"尖兵""领雁"研发攻关计划（2023C03035）

Progress in genetic research of non-obstructive azoospermia

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【Abstract】 Non-obstructive azoospermia (NOA) is a serious problem that plagues infertile men all over the world, but its specific genetic pathogenic factors are not completely clear at present. In recent years, with the continuous deepening of research on bioinformatics and genetics, more and more pathogenic genes have been found. The objects of genetic research on NOA mainly include chromosome abnormality, chromosome microdeletion, gene mutations and epigenetic modifications. In this paper, we have made a simple summary and evaluation of these findings, which will help you further understand the progress of genetic research on NOA.

【Key words】 Infertility, male; Non-obstructive azoospermia; Genetic research

Fund program: Top Leading Reaserch and Development Project of Zhejiang Province (2023C03035)

DOI：10.3760/cma.j.cn101441-20220511-00204
收稿日期　2022-05-14　本文编辑　王李艳
引用本文：陈虹, 陈智勤, 孙子莉, 等. 应用 PPOS 与拮抗剂方案的 20~50 岁患者每取卵周期累积活产率比较：一项倾向性评分匹配研究[J]. 中华生殖与避孕杂志, 2023, 43(5): 473-482. DOI: 10.3760/cma.j.cn101441-20220511-00204.

·临床研究·

应用 PPOS 与拮抗剂方案的 20~50 岁患者每取卵周期累积活产率比较：一项倾向性评分匹配研究

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【摘要】 目的 比较拮抗剂方案和高孕激素状态下促排卵（progestin-primed ovarian stimulation，PPOS）方案在20~50岁患者中的每取卵周期累积活产率。方法 回顾性队列研究分析2017年1月至2021年4月期间在同济大学附属上海市第一妇婴保健院生殖医学科接受体外受精/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）助孕并采用拮抗剂方案或PPOS方案的20~50岁不孕症患者3 752例，使用倾向性评分匹配（propensity score matching， PSM）方法按1∶1匹配均衡两组间的变量后，比较两组的基本特征、临床/实验室指标及助孕结局等。通过多因素logistic回归分析对混杂因素进行校正后对比两种促排卵治疗的每取卵周期累积活产率；通过分层分析比较两种促排卵方案在不同类型患者中的临床疗效。结果 匹配后，1 466例患者（每组各733例）纳入分析，两组患者的年龄、体质量指数、不孕类型、不孕病因、不孕年限、取卵次数、基础卵泡刺激素、窦卵泡计数和授精方式构成比等差异均无统计学意义（均*P*>0.05）。拮抗剂方案组扳机日雌二醇水平[1700.30（1011.76，2 580.50）ng/L]及黄体生成素（luteinizing hormone，LH）水平［1.95（1.07，5.27） U/L］显著低于PPOS方案组［2 056.50（884.08，3 601.59） ng/L，*P*=0.010；3.00（1.51，5.00） U/L，*P*<0.001］，差异均有统计学意义。PPOS方案组周期取消率[30.56%（224/733）]显著高于拮抗剂方案组[18.83%（138/733），*P*<0.001]；而获卵数、可利用胚胎数及优质胚胎数与拮抗剂方案组相似（均*P*>0.05）。PPOS方案组的胚胎种植率［16.97%（207/1 220）］、每移植周期临床妊娠率[21.78%（188/863）]、每移植周期持续妊娠率[16.11%（139/863）]和每移植周期活产率[15.06%（130/863）]均明显低于拮抗剂方案组[21.42%（266/1 242），*P*=0.010；27.38%（233/851），*P*=0.012；21.62%（184/851），*P*=0.004；20.80%（177/851），*P*=0.002]；PPOS方案组累积活产率［17.74%（130/733）］显著低于拮抗剂方案组［24.15%（177/733）］，差异有统计学意义（*P*=0.003）。多因素logistics回归分析调整混杂因素后显示卵巢刺激方案为影响每取卵周期累积活产率的独立危险因素（*OR*=1.42，95% *CI*：1.03~1.95，*P*=0.032）。分层分析结果显示，在年龄≤35岁与取卵次数≥2次的人群中，PPOS方案组的累积活产率[21.35%（111/520），7.85%（41/522）］显著低于拮抗剂方案组［28.93% （151/522），*P*=0.005；12.23% （62/507），*P*=0.019］。结论 与PPOS方案相比，拮抗剂方案可改善20~50岁不孕症患者的每取卵周期累积活产率，且在女方年龄≤35岁及非首次取卵的患者中更为显著。

【关键词】 受精，体外； 胚胎移植； 高孕激素状态下促排卵方案； 拮抗剂方案； 累积活产率

基金项目：上海市卫健委临床医学科研专项面上项目（202040127）；上海市卫生和计划生育委员会科研课题面上项目（201540237）

Cumulative live birth rate per oocyte retrieval cycle in patients aged 20–50 years using PPOS versus GnRH antagonist protocol: a propensity score matching study

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【**Abstract**】 **Objective** To compare the cumulative live birth rate (CLBR) per oocyte retrieval cycle between gonadotropin-releasing hormone (GnRH) antagonist protocol and progestin-primed ovarian stimulation (PPOS) protocol in patients aged 20–50 years. **Methods** A retrospective cohort study was conducted to analyze 3 752 infertile patients aged 20–50 years who received *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET). They used either GnRH antagonist protocol or PPOS protocol at the Center of Assisted Reproduction in Shanghai First Maternity and Infant Hospital from January 2017 to April 2021. One to one propensity score matching (PSM) was used to match the population characteristics. Baseline, clinical and laboratory characteristics, as well as pregnancy outcomes were compared between the two groups. The differences of CLBR was analyzed by multivariate logistic regression and subgroup analysis. **Results** After matching, 1 466 patients (733 in each group) were included in the analysis. No significant differences were detected in age, body mass index, infertility type, cause and duration of infertility, number of stimulation cycles, basal follicle-stimulating hormone, number of antral follicles and composition ratio of insemination methods between the two groups (P>0.05). Serum estradiol level [1 700.30 (1 011.76, 2 580.50) ng/L] and luteinizing hormone (LH) level [1.95 (1.07, 5.27) U/L] on trigger day were significantly lower in GnRH antagonist group than in PPOS group [2 056.50 (884.08, 3 601.59) ng/L, P=0.010; 3.00 (1.51, 5.00) U/L, P<0.001]. The cycle cancellation rate of PPOS group [30.56% (224/733)] was significantly higher than that of GnRH antagonist group [18.83% (138/733), P<0.001]. The numbers of oocytes obtained, available embryos and good-quality embryos were similar to those in GnRH antagonist group (all P>0.05). For each embryo transfer cycle, the implantation rate [16.97% (207/1 220) *vs.* 21.42% (266/1 242)], the clinical pregnancy rate [21.78% (188/863) *vs.* 27.38% (233/851)], the onging pregnancy rate [16.11% (139/863) *vs.* 21.62% (184/851)] and the live birth rate [15.06% (130/863) *vs.* 20.80% (177/851)] were significantly lower in PPOS group than in GnRH antagonist group (P=0.010, P=0.012, P=0.004 and P=0.002, respectively). The CLBR of PPOS group was significantly lower than that of GnRH

antagonist group [17.74% (130/733) *vs.* 24.15% (177/733), *P*=0.003]. Multivariate logistic regression analysis showed that ovarian stimulation protocol was an independent risk factor for CLBR [*OR*=1.42, 95% *CI*: 1.03–1.95, *P*=0.032]. The results of subgroup analysis showed that the CLBR of PPOS group was significantly lower than that of GnRH antagonist group in the population aged ≤35 years and underwent non-first IVF/ICSI cycle [21.35% (111/520) *vs.* 28.93% (151/522), *P*=0.005; 7.85% (41/522) *vs.* 12.23% (62/507), *P*=0.019]. **Conclusion** Compared with PPOS regimen, antagonist regimen can improve the CLBR per oocyte cycle in infertile patients aged 20–50 years, and is more significant in women aged ≤35 years and non-first oocyte collection patients.

【Key words】 Fertilization *in vitro*; Embryo transfer; Progestin primed ovarian stimulation protocol; Antagonist protocol; Cumulative live birth rate

Fund program: Special Fund for Clinical Medical Research of Shanghai Municipal Health Commission (202040127); Foundation of Health and Family Planning Commission of Shanghai (201540237)

DOI：10.3760/cma.j.cn101441-20221103-00482
收稿日期 2022-11-07 本文编辑 宋培培
引用本文：李珊, 黄铄, 胡凯伦, 等. 胚胎植入前非整倍体遗传学检测患者血清抗苗勒管激素水平与囊胚整倍体率的相关性研究[J]. 中华生殖与避孕杂志, 2023, 43(5): 483-489. DOI: 10.3760/cma.j.cn101441-20221103-00482.

·临床研究·

胚胎植入前非整倍体遗传学检测患者血清抗苗勒管激素水平与囊胚整倍体率的相关性研究

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【摘要】 目的 分析卵胞质内单精子注射（intracytoplasmic sperm injection，ICSI）后进行胚胎植入前非整倍体遗传学检测（preimplantation genetic testing for aneuploidies，PGT-A）的患者中，其血清抗苗勒管激素（anti-Müllerian hormone，AMH）水平对囊胚整倍体率及整倍体胚胎数量的影响。方法 采用回顾性队列研究，收集 2018 年 1 月 1 日至 2020 年 12 月 31 日期间于北京大学第三医院生殖医学中心行 ICSI 并进行 PGT-A 的 504 例患者的临床资料。根据促排卵治疗前血清 AMH

水平，将研究对象分为低 AMH 组（AMH<1.00 μg/L，85 例）与正常 AMH 组（AMH≥1.00 μg/L，419 例）。采用倾向评分匹配方法，基于年龄、体质量指数（body mass index，BMI）、复发性流产病史、促排卵方案进行 1∶1 匹配（卡钳值=0.02），匹配后比较两组患者（每组各 82 例）的囊胚整倍体率及整倍体囊胚数量。应用受试者工作特征（receiver operator characteristic，ROC）曲线评估 AMH 水平对 PGT-A 周期存在至少一个整倍体胚胎的预测作用。结果　①低 AMH 组胚胎整倍体率［50.0%（0，100.0%）］及整倍体胚胎数［1（0，1）个］显著低于正常 AMH 组［60.0%（33.3%，100.0%），*P*=0.025；1（1，2）个，*P*<0.001］。②匹配后低 AMH 组和正常 AMH 组患者的胚胎整倍体率分别为 50.0%（0，100.0%）、50.0%（19.2%，100.0%），组间差异无统计学意义（*P*=0.265），低 AMH 组患者的整倍体囊胚数［1（0，1）个］低于正常 AMH 组［1（1，2）个，*P*=0.004］，低 AMH 组中至少存在一个整倍体囊胚的周期比例［57.3%（47/82）］显著低于正常 AMH 组［76.8%（63/82），*P*=0.008］。③共 378 个（75.0%）周期得到至少一个可移植整倍体胚胎。AMH 与年龄联合预测存在至少一个整倍体胚胎的曲线下面积（area under the curve，AUC，0.78）较单一指标年龄的 AUC 值更优（0.75，*P*=0.024）。结论　在调整年龄、BMI、复发性流产病史、促排卵方案等因素的影响下，血清 AMH 水平与 PGT-A 囊胚整倍体率无关。年龄结合血清 AMH 可用于预测每促排卵周期存在至少一个整倍体胚胎的可能性。

【关键词】　倾向性评分；　抗苗勒管激素；　非整倍体；　胚胎植入前非整倍体遗传学检测

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）

Relationship between serum anti-Müllerian hormone and rate of euploid blastocysts in patients undergoing preimplantation genetic testing for aneuploidies (PGT-A)

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【Abstract】　**Objective**　To analyze the impact of serum anti-Müllerian hormone (AMH) on the rate and number of euploid blastocysts among women undergoing intracytoplasmic sperm injection (ICSI) and preimplantation genetic testing for aneuploidies (PGT-A). **Methods**　A retrospective cohort study was performed by analyzing clinical data from 504 patients approaching ICSI cycle with PGT-A in Reproductive Medicine Center of Peking University Third Hospital from January 1st 2018 to December 31st 2020. According to serum AMH level measured before ovarian stimulation, subjects were divided into two groups: the low AMH group (AMH<1.00 μg/L, 85 patients) and the normal AMH group (AMH≥1.00 μg/L, 419 patients). Rates and number of euploid blastocysts were compared between the two groups (82 patients per group) after using propensity score matching (PSM) to adjust confounding variables, including age, body mass index (BMI), history of recurrent miscarriage and ovarian stimulation protocols. **Results**　1) The rate and number of euploid blastocysts were significantly lower in the low AMH group [50.0%

(0, 100.0%), 1 (0, 1)] than in the normal AMH group [60.0% (33.3%, 100.0%), *P*=0.025; 1 (1, 2), *P*<0.001]. 2) After PSM, the rate of euploid blastocysts was 50.0% (0, 100.0%) in the low AMH group and 50.0% (19.2%, 100.0%) in the normal AMH group, with no significant difference (*P*=0.265). Patients in the low AMH group had significantly fewer euploid blastocysts [1 (0, 1) *vs.* 1 (1, 2), *P*=0.004] and were less likely to have at least one euploid blastocyst [57.3% (47/82) *vs.* 76.8% (63/82), *P*=0.008]. 3) A total of 378 (75.0%) cycles had at least one euploid embryo. The area under the curve (AUC) value of AMH combined with age in predicting the presence of at least one euploid embryo was better than that of age alone (0.78 *vs.* 0.75, *P*=0.024). **Conclusion** Serum AMH level is not independently associated with the rate of blastocyst euploidy after adjusting for age, BMI, history of recurrent abortion and ovulation induction protocol. AMH combined with age can be used to predict the possibility of having at least one euploid embryo per cycle.

【Key words】 Propensity score; Anti-Müllerian hormone; Aneuploidy; Preimplantation genetic testing for aneuploidies

Fund program: Beijing Municipal Science & Technology Commission (Z191100006619076); National Science Fund for Distinguished Young Scholars (81925013)

DOI：10.3760/cma.j.cn101441-20220110-00011

收稿日期 2022-01-12 本文编辑 孙敏

引用本文：伏静, 杨天颖, 武田宇, 等. 多囊卵巢综合征患者卵泡液的拉曼光谱分析及其对小鼠卵母细胞体外成熟的影响[J]. 中华生殖与避孕杂志, 2023, 43(5): 490-500. DOI: 10.3760/cma.j.cn101441-20220110-00011.

·实验研究·

多囊卵巢综合征患者卵泡液的拉曼光谱分析及其对小鼠卵母细胞体外成熟的影响

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伏静和杨天颖对本文有同等贡献

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【摘要】 目的 探究多囊卵巢综合征（polycystic ovary syndrome，PCOS）患者与非 PCOS 患者卵泡液中的差异性代谢物及其对小鼠卵母细胞体外成熟（*in vitro* maturation，IVM）和体外受精（*in vitro* fertilization，IVF）胚胎发育的影响。方法 本研究的临床资料采取回顾性队列研究的研究方法获取；动物实验采取随机对照试验。收集 2019 年 6 月至 2020 年 6 月期间在上海集爱遗传与不育诊疗中心第一次接受 IVF 或卵胞质内单精子注射（intracytoplasmic sperm injection，ICSI）周期的女性患者的卵泡液。根据是否为 PCOS 患者，分为 PCOS 组（*n*=71）和非 PCOS 组（*n*=70），回顾性分析两组患者的临床资料，并利用深度学习的拉曼光谱分析技术检测两组患者卵泡液的代谢谱差异。后续进行实验性研究，在 PCOS 患者和非 PCOS 患者卵泡液中进行小鼠 GV 期卵母细胞 IVM 培养，收集两组成熟的鼠卵母细胞进行 IVF，进一步探讨卵泡液中差异性代谢物对鼠卵成熟及胚胎发育的影响。结果 PCOS 组患者卵母细胞成熟率［82.19%（886/1 078）］和受精第 3 天的有效胚胎率［51.30%（553/1 078）］显著低于非 PCOS 组［85.85%（625/728），*P*=0.038；53.30%（388/728），*P*=0.042］，两组患者的累积临床妊娠率和累积活产率差异均无统计学意义（均 *P*>0.05）。PCOS 患者和非 PCOS 患者卵泡液之间存在差异性拉曼代谢光谱。两组间特征性拉曼位移主要集中在 600~1 000 cm^{-1}、1 168 cm^{-1}、1 344 cm^{-1}、1 440 cm^{-1}、1 504 cm^{-1}、1 632 cm^{-1}、1 664 cm^{-1}。拉曼特征位移数据库显示，两组卵泡液样本的差异代谢物主要集中蛋白质、脂质、游离核酸、葡萄糖、胆固醇、类胡萝卜素和氨基酸等物质。利用两组卵泡液行鼠卵 IVM，PCOS 卵泡液组的鼠卵 MⅡ率［49.04%（77/157）］较非 PCOS 组更低［65.07%（95/146），*P*=0.005］，利用小鼠 MⅡ卵进行 IVF，PCOS 卵泡液组卵裂率［46.75%（36/77）］显著低于非 PCOS 组［63.16%（60/95），*P*=0.031］，而两组囊胚率差异无统计学意义（*P*>0.05）。结论 PCOS 患者卵泡液存在差异性拉曼代谢光谱，其差异性代谢物可能导致卵母细胞成熟障碍，并进一步影响 IVF 胚胎的发育，拉曼光谱为 PCOS 诊断和代谢组学的差异物分析提供了简便有效的方法。

【关键词】 多囊卵巢综合征； 拉曼光谱； 卵泡液； 代谢组学

基金项目：黄浦区卫健委科研基金面上项目（HKM201933）；上海市卫健委面上项目（201840353）；上海集爱遗传与不育诊疗中心院内基金项目（JA-2018-05）

临床试验注册：美国国家临床试验注册中心，NCT04838535

Raman spectroscopy analysis of follicular fluid from patients with polycystic ovary syndrome and its effect on *in vitro* maturation of mouse oocytes

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【Abstract】 **Objective** To explore the different metabolites in the follicular fluids (FFs) of polycystic ovary syndrome (PCOS) patients and non-PCOS patients and their effects on the maturation of mouse oocytes and the developmental potential of *in vitro* fertilization (IVF) embryos. **Methods** The clinical data were

collected for the retrospective cohort study. Animal experiments were conducted in a randomized controlled trial. This study included PCOS (*n*=71) and non-PCOS (*n*=70) patients who underwent the first IVF or intracytoplasmic sperm injection (ICSI) cycle in Shanghai JIAI Genetics & IVF institute from June 2019 to June 2020. The patients' FFs were collected and the clinical data from these patients were analyzed. Raman spectroscopy analysis technology was used to detect differences in the metabolic spectra of FFs between the two groups. Mouse GV phase oocytes were placed in FFs from PCOS patients and non-PCOS patients for *in vitro* maturation (IVM) culture respectively, then the matured mouse oocytes were collected for IVF. The effects of differential metabolites in FFs on mouse oocyte maturation and embryonic development were further explored. The Raman spectrum was also applied to identify the differences of the IVM spent culture media. **Results** The MⅡ rate [82.19% (886/1 078)] and day 3 available embryo rate [51.30% (553/1 078)] from PCOS group were significantly lower than those of the non-PCOS group [85.85% (625/728), *P*=0.038; 53.30% (388/728), *P*=0.042]. However, there were no significant differences between the two groups in the cumulative clinical pregnancy rate and the cumulative live birth rate (all *P*>0.05). Raman was capable of distinguishing PCOS from non-PCOS FFs. The characteristic Raman displacement difference between the two groups is mainly concentrated in the 600−1 000 cm^{-1}, as well as 1 168 cm^{-1}, 1 344 cm^{-1}, 1 440 cm^{-1}, 1 504 cm^{-1}, 1 632 cm^{-1} and 1 664 cm^{-1}. The Raman characteristic shift database showed that the different metabolites of the two sets of FFs samples were mainly concentrated in protein, lipids, free nucleic acis, glucose, cholesterol, carotenoids, and amino acids. Mouse oocyte IVM results showed that the PCOS-FF group had a lower MⅡ rate [49.04% (77/157)] than that of non-PCOS group [65.07% (95/146), *P*=0.005). IVF results showed the PCOS-FF group had a significantly lower cleavage rate [46.75% (36/77)] than that of non-PCOS group [63.16% (60/95), *P*=0.031], but there was no significant difference in the blastocyst rate between the two groups (*P*>0.05). **Conclusion** Differential metabolites detected by Raman spectrum in the PCOS FFs may cause defected maturation of the oocytes, leading to infertility, and Raman spectroscopy is an effective approach towards PCOS diagnosis and the identification of metabolomics differences.

【Key words】 Polycystic ovary syndrome; Raman spectroscopy; Follicular fluids; Metabolomics

Fund program: Project of Health and Family Planning Commission of Huangpu District (HKM201933); Foundation of Shanghai Municipal Commission of Health and Family Planning (201840353); Shanghai JIAI Genetics and IVF Institute Found (JA-2018-05)

Trial Registraion: ClinicalTrials.gov, NCT04838535

DOI：10.3760/cma.j.cn101441-20220302-00091

收稿日期 2022-03-08 本文编辑 孙敏

引用本文：杜晓果, 宋雪凌, 王丽颖, 等. 输卵管妊娠患侧输卵管切除术患者的助孕策略[J]. 中华生殖与避孕杂志, 2023, 43(5): 501-505. DOI: 10.3760/cma.j.cn101441-20220302-00091.

输卵管妊娠患侧输卵管切除术患者的助孕策略

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【摘要】 目的　探讨输卵管妊娠（tubal pregnancy，TP）患侧输卵管切除患者助孕策略。方法　回顾性队列研究分析 2019 年 1 月 1 日至 2020 年 12 月 31 日期间因 TP 切除患侧输卵管于北京大学第三医院妇产科生殖医学中心行子宫输卵管超声造影（hysterosalpingo contrast sonography，HyCoSy）的患者临床资料。根据患者接受 HyCoSy 时的试孕时间及是否有不孕症/史分为 3 组，A 组：既往无不孕症病史，TP 后试孕<1 年（*n*=33），B 组：既往有不孕症病史，TP 后试孕<1 年（*n*=22），C 组：TP 后试孕≥1 年（*n*=64），分析输卵管通畅度检查及临床结局的影响因素。结果　A、B、C 三组间患者年龄、孕次、重复 TP 史、窦卵泡计数、体外受精（*in vitro* fertilization，IVF）妊娠率、IVF 及自然妊娠再次 TP 发生率、HyCoSy 后至妊娠的时间（time to pregency，TTP）比较差异均无统计学意义（均 *P*>0.05）。C 组输卵管切除术至 HyCoSy 的时间（time to HyCoSy，TTH）［30.0（20.0，42.0）个月］显著大于 A、B 组［13.0（7.5，16.5）个月、8.0（7.0，10.0）个月，*P*<0.001］。A 组通畅型输卵管比例［72.7%（24/33］及自然妊娠率［42.4%（14/33）］显著高于 C 组［43.8%（28/64），*P*=0.025；12.5%（8/64），*P*=0.004］。A 组 IVF 治疗比例［30.3%（10/33）］显著小于 B、C 组［86.4%（19/22）、71.9%（46/64），*P*<0.001］。B 组通畅型输卵管比例及自然妊娠率高于 C 组，差异无统计学意义（*P*>0.05）。自然妊娠所需时间 A 组小于 B、C 组，差异均无统计学意义（均 *P*>0.05）。logistic 回归分析显示不孕（史/症）是输卵管通畅度和妊娠结局的相关影响因素（*OR*=0.366，95% *CI*：0.148~0.904，*P*=0.029；*OR*=8.504，95% *CI*：2.294~31.519，*P*=0.014）。结论　一侧输卵管切除术后，无不孕史患者可积极试孕 6 个月，如未孕可积极行输卵管通畅度评估后决定助孕策略；而已有不孕（史/症）患者建议积极 IVF 助孕，无需进行输卵管通畅性评估。

【关键词】 输卵管妊娠；　输卵管通畅度；　生育策略

基金项目：北京市科技计划（Z191100006619085）；国家自然科学基金（82171632）；国家重点研发计划（2021YFC2700605）

Fertility strategies for patients with salpingectomy on the affected side of tubal pregnancy

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【Abstract】 **Objective** To explore the strategy of pregnancy in patients with tubal pregnancy (TP) undergoing salpingectomy. **Methods** A retrospective cohort study was conducted to analyze the clinical data of patients who underwent hysterosalpingo contrast sonography (HyCoSy) at Reproductive Medicine Center of Peking University Third Hospital from January 1, 2019 to December 31, 2020 due to salpingectomy for TP. Patients were divided into 3 groups according to the time of pregnancy test and infertility history at the time to HyCoSy (TTH), group A: patients with no history of infertility, attempted pregnancy <1 year after TP (*n*=33); group B: patients with history of infertility, attempted pregnancy <1 year after TP (*n*=22); group C: patients attempted pregnancy ≥1 year after TP (*n*=64). The remaining tubal patency and clinical outcome were analyzed. **Results** There were no significant differences in age, number of pregnancies, history of repeated TP (RTP), number of antral follicles, pregnancy rate treated with *in vitro* fertilization (IVF), incidence of RTP in IVF and spontaneous pregnancy, and the time to pregnancy (TTP) from HyCoSy among groups A, B and C (all *P*>0.05). TTH from salpingectomy in group C [30.0 (20.0, 42.0) months] was significantly longer than that in groups A and B [13.0 (7.5, 16.5) months, 8.0 (7.0, 10.0) months, *P*<0.001]. The proportion of unobstructed fallopian tubes and the spontaneous pregnancy rate in group A were significantly higher than those in group C [72.7% (24/33) *vs.* 43.8% (28/64), *P*=0.025; 42.4% (14/33) *vs.* 12.5% (8/64), *P*=0.004], and the IVF treatment rate in group A [30.3% (10/33)] was significantly lower than that in groups B and C [86.4% (19/22), 71.9% (46/64), *P*<0.001]. The proportion of unobstructed fallopian tubes and the spontaneous pregnancy rate in group B were higher than those in group C, and the differences were not statistically significant (all *P*>0.05). The time required for spontaneous pregnancy in group A was less than that in groups B and C, but the difference was not statistically significant (*P*>0.05). Logistic regression analysis showed that infertility (history/symptom) was a related factor of tubal patency and pregnancy outcome (*OR*=0.366, 95% *CI*: 0.148–0.904, *P*=0.029; *OR*=8.504, 95% *CI*: 2.294–31.519, *P*=0.014). **Conclusion** After salpingectomy on one side, patients without infertility (history/symptoms) can actively try to conceive for 6 months, if they are not pregnant, tubal patency test can be actively performed and decide on fertility strategy; for patients with infertility (history/symptom), IVF was recommended actively without tubal patency evaluation.

【Key words】 Tubal pregnancy; Tubal patency; Fertility strategy

Fund program: Beijing Science and Technology Planning Project (Z191100006619085); National Natural Science Foundation of China (82171632); National Key Research and Development Program (2021YFC2700605)

DOI：10.3760/cma.j.cn101441-20230103-00004
收稿日期　2023-01-12　本文编辑　王李艳
引用本文：杨天云，杨清美，姬萌霞，等. 口服地屈孕酮对子宫内膜植入窗期超微结构的影响：一项前瞻性研究[J]. 中华生殖与避孕杂志, 2023, 43(5): 506-512. DOI: 10.3760/cma.j.cn101441-20230103-00004.

·临床报道·

口服地屈孕酮对子宫内膜植入窗期超微结构的影响：一项前瞻性研究

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【摘要】 目的　探讨地屈孕酮（dydrogesterone，DYD）对植入窗期子宫内膜超微结构的影响。方法　前瞻性研究分析 2020 年 7 月至 2022 年 7 月期间于浙江省人民医院生殖医学中心行体外受精-胚胎移植（*in vitro* fertilization and embryo transfer，IVF-ET）并符合纳排标准的患者资料，并对患者的子宫内膜进行扫描与透射电子显微镜检测。对因男性因素行 IVF-ET 的 20 例患者进行自身对照研究，比较自然周期和 DYD 40 mg/d 转化周期植入窗期子宫内膜超微结构的差异。同时采用自身对照研究，筛选原因不明反复种植失败（recurrent implantation failure，RIF）行 IVF-ET 患者（n=43），比较不同剂量 DYD （40 mg/d 与 80 mg/d）转化后内膜超微结构的变化。结果　男性因素不孕患者自然周期与 DYD 转化周期的子宫内膜在转化日的超声厚度测量、回声分型和在植入窗期的胞饮突评分、核仁通道系统（nucleolar channel system，NCS）阳性率、分泌状态评分、线粒体数目和形态评分差异均无统计学意义（均 P>0.05）。RIF 患者 DYD 80 mg/d 组的胞饮突评分（−46.26±19.97）、NCS 阳性率［65.12%（28/43）］和线粒体形态评分［0（0，1）］均显著高于 DYD 40 mg/d 组［−67.62±15.94，P<0.001；39.53%（17/43），P=0.043；0（0，0），P=0.023］，而两组间子宫内膜厚度、回声类型、分泌状态评分及线粒体数目差异均无统计学意义（均 P>0.05）。结论　口服 DYD 转化内膜可以构建与自然周期类似的植入窗期子宫内膜超微结构。80 mg/d DYD 剂量可以改善 RIF 患者子宫内膜的胞饮突成熟度评分、NCS 阳性率和线粒体形态评分。

【关键词】 地屈孕酮；　子宫内膜；　超微结构；　反复种植失败；　植入窗期

基金项目：白求恩·中青年医生优才培养计划（XJ-2019-024）

Effect of oral dydrogesterone on ultrastructure during the window of implantation: a prospective study

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【**Abstract**】 **Objective** To investigate the effect of dydrogesterone (DYD) on the ultrastructure of the endometrium in the window of implantation. **Methods** We prospectively studied endometrium tissues of patients who underwent *in vitro* fertilization and embryo transfer (IVF-ET) from July 2020 to July 2022 at the Center for Reproductive Medicine of Zhejiang Provincial People's Hospital. The ultrastructure of mid-luteal endometrium was examined by scanning electron microscopy and transmission electron microscopy. Firstly, we used self-control study to compare the ultrastructure of endometrium between the natural cycle group and the DYD 40 mg/d group in 20 patients with male factor infertility. Secondly, we used self-control study to compare the ultrastructure of the endometrium between the DYD 40 mg/d group and the DYD 80 mg/d group in 43 patients with recurrent implantation failure (RIF). **Results** There were no significant differences in endometrial thickness, ultrasound grading, positivity rate of nucleolar channel system (NCS), pinopode score and secretor status score, in addition to number and morphology score of mitochondria, between the natural cycle group and the DYD 40 mg/d group (all $P>0.05$). In RIF patients, the DYD 80 mg/d group rendered significantly higher pinopode score (−46.26±19.97), NCS positivity rate [65.12% (28/43)] and mitochondrial morphology score [0 (0, 1)] than those in the DYD 40 mg/d group [−67.62±15.94, $P<0.001$; 39.53% (17/43), $P=0.043$; 0 (0, 0), $P=0.023$], while other characteristics were not significantly different between the two groups (all $P>0.05$). **Conclusion** The ultrastructure of endometrium in DYD supplementation cycle was similar to that in the natural cycle. Increasing the dosage of DYD significantly improved pinopode maturity, NCS positivity rate and mitochondrial morphology of the endometrium in RIF patients.

【**Key words**】 Dydrogesterone; Endometrium; Ultrastructure; Recurrent implantation failure; Window of implantation

Fund program: Bethune Charitable Foundation · Youth Excellence Grant (XJ-2019-024)

DOI：10.3760/cma.j.cn101441-20221222-00583

收稿日期 2022-12-22 本文编辑 宋培培

引用本文：陈立雪, 樊易简, 李蓉, 等. 接受辅助生殖技术治疗人群的新冠疫苗接种情况分析[J]. 中华生殖与避孕杂志, 2023, 43(5): 513-518. DOI: 10.3760/cma.j.cn101441-20221222-00583.

接受辅助生殖技术治疗人群的新冠疫苗接种情况分析

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【摘要】　目的　探讨接种新冠疫苗是否影响辅助生殖技术（assisted reproductive technology，ART）的临床妊娠率。方法　本研究为横断面研究，通过对 2021 年 8 月 1 日至 2022 年 7 月 31 日期间在北京市市属 12 家人类辅助生殖机构接受 ART 治疗的 17 611 个周期的调查，分析患者的接种新冠疫苗情况及 ART 的临床妊娠率。结果　接受 ART 治疗男、女双方的新冠疫苗接种率分别为 58.83%（10 361/17 611）和 41.46%（7 301/17 611）；80.88%（5 864/7 250）的夫妇因担心疫苗的安全性或不良反应没有完成接种。单因素分析与 logistic 多因素分析结果均显示是否接种新冠疫苗不会影响人工授精或体外受精-胚胎移植的临床妊娠率，人工授精双方全程接种的临床妊娠率为 10.74%（100/931），双方均未接种为 11.10%（206/1 856），组间差异无统计学意义（*P*=0.776），校正后的 *OR*=0.96，95% *CI*：0.74~1.24，*P*=0.766。体外受精双方全程接种的临床妊娠率为 41.88%（2 450/5 850），双方均未接种为 40.92%（1 815/4 435），组间差异无统计学意义（*P*=0.330），校正后的 *OR*=1.02，95% *CI*：0.94~1.11，*P*=0.578。结论　接种新冠疫苗不会影响 ART 治疗的妊娠率。有助孕需求的育龄人群疫苗接种率偏低，需要引起广泛关注。

【关键词】　生殖技术，辅助；　新冠疫苗；　疫苗接种率

Analysis of the vaccination of people treated with assisted reproductive technology

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【**Abstract**】 **Objective** To explore whether the vaccination of COVID-19 vaccine affects the clinical pregnancy rate of assisted reproductive technology (ART). **Methods** Based on a cross-sectional design, 17 611 cycles of ART treatment in 12 human-assisted reproductive institutions under Beijing Municipality from August 1, 2021, to July 31, 2022 were investigated, and their vaccination status and clinical pregnancy rate were investigated and analyzed. **Results** The new crown vaccination rates of men and women receiving ART treatment were 58.83% (10 361/17 611) and 41.46% (7 301/17 611), respectively; 80.88% (5 864/7 250) of the couples did not complete the vaccination due to concerns about the safety or adverse reactions of the vaccine. The results of univariate analysis and logistic multivariate analysis showed whether vaccination with the new crown vaccine will not significantly affect the clinical pregnancy rate of artificial insemination or *in vitro* fertilization and embryo transfer (IVF-ET). The clinical pregnancy rate of fully vaccinated under artificial insemination was 10.74% (100/931), which was 11.10% (206/1 856) of both not vaccinated, there was no significant difference (P=0.776), while adjusted OR=0.96, 95% CI: 0.74-1.24, P=0.766. The clinical pregnancy rate of fully vaccinated under IVF-ET was 41.88% (2 450/5 850), both not vaccinated was 40.92% (1 815/4 435), there was no significant difference (P=0.330), while adjusted OR=1.02, 95% CI: 0.94-1.11, P=0.578. **Conclusion** Vaccination against COVID-19 does not affect the clinical pregnancy rate of ART treatments. The low vaccination rate of the childbearing age group who needs to assist in pregnancy needs more attention.

【**Key words**】 Reproductive techniques, assisted; COVID-19 vaccines; Vaccination coverage

DOI：10.3760/cma.j.cn101441-20220307-00102
收稿日期 2022-03-24 本文编辑 宋培培
引用本文：王雨，李志英. 卵巢衰老和盆底功能障碍性疾病的相关性研究进展[J]. 中华生殖与避孕杂志，2023, 43(5): 519-522. DOI: 10.3760/cma.j.cn101441-20220307-00102.

·综述·

卵巢衰老和盆底功能障碍性疾病的相关性研究进展

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【摘要】 盆底功能障碍性疾病（pelvic floor dysfunction，PFD）是女性最常见的疾病之一，随着人口老龄化严重及国家"三孩政策"的放开，发病率呈逐年上升的趋势，不仅影响了患者的身体健康，也严重影响了患者的生活和心理健康。目前PFD 的发病机制不完全明确，绝经是导致 PFD 的主要危险因素之一，卵巢衰老主要表现为绝经，绝经后卵巢功能逐渐衰退，且内分泌水平失调，并影响全身多器官系统，最终导致一系列相关疾病的发生。本文讨论遗传、雌激素及线粒体功能异常、氧化应激等对卵巢及盆底功能的影响，从而寻找出卵巢衰老和 PFD 之间的相关性。

【关键词】 衰老； 盆底功能障碍； 盆腔器官脱垂； 卵巢老化

基金项目：湖北省卫健委联合基金（WJ2019H535）

Research progress on the correlation between ovarian aging and pelvic floor dysfunction

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【Abstract】 Pelvic floor dysfunction (PFD) is one of the most common diseases in women. With the serious aging of the population and the release of the national "three-child policy", the incidence rate is increasing year by year, which not only affects the the patient's physical health also seriously affects the patient's life and mental health. At present, the pathogenesis of PFD is not completely clear. Menopause is one of the main risk factors for PFD. Ovarian aging is mainly manifested in menopause. After menopause, ovarian function gradually declines, and endocrine levels are imbalanced, which affects multiple organ systems throughout the body, eventually leading to a series of related diseases. In this review, we discuss the effects of genetics, estrogen and mitochondrial dysfunction, and oxidative stress on ovarian and pelvic floor function, so as to find out the correlation between ovarian aging and pelvic floor dysfunction.

【Key words】 Aging; Pelvic floor disorders; Pelvic organ prolapse; Ovarian aging

Fund program: Hubei Provincial Health Commission Joint Fund (WJ2019H535)

DOI：10.3760/cma.j.cn101441-20230116-00029

收稿日期 2023-01-19 本文编辑 孙敏

引用本文：陈秀菊，孙宁霞. SARS-CoV-2 对女性生殖健康的研究进展[J]. 中华生殖与避孕杂志, 2023, 43(5): 523-529. DOI: 10.3760/cma.j.cn101441-20230116-00029.

·综述·

SARS-CoV-2 对女性生殖健康的研究进展

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【摘要】 严重急性呼吸综合征冠状病毒 2（severe acute respiratory syndrome corona virus 2，SARS-CoV-2）在全球迅速蔓延并引发了世界大流行。目前 SARS-CoV-2 是否对女性生育力产生潜在不利影响尚不明确，后续需要更多的证据支持。对妊娠合并 SARS-CoV-2 的初步研究显示，SARS-CoV-2 可能会增加子痫前期、早产和胎膜早破的风险，但似乎早期流产风险不高，感染 SARS-CoV-2 是否垂直传播而影响下一代，目前暂不清楚，还需要更多的证据支持。随着 SARS-CoV-2 的流行，SARS-CoV-2 疫苗的研发和临床试验在全球范围内广泛开展，目前研究表明接种 SARS-CoV-2 疫苗可能不会对女性的生殖系统存在不利影响。本文结合近几年来关于 SARS-CoV-2 对女性生殖健康的研究进展进行简要综述。

【关键词】 生育力； 卵巢储备； 妊娠结局； 疫苗接种； SARS-CoV-2

基金项目：国家自然科学基金（82271662、81901482）；军队计生专项研究任务（21JSZ06）

Research progress of SARS-CoV-2 on female reproductive health

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【Abstract】 Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has spread rapidly around the world and triggered a worldwide pandemic. Whether SARS-CoV-2 potentially adversely affects female fertility is unclear now, and more evidence is needed to support the follow-up. Preliminary studies of combined SARS-CoV-2 in pregnancy have found that SARS-CoV-2 may increase the risk of preeclampsia, preterm delivery, and premature rupture of membranes, but does not appear to be associated with a high risk of early miscarriage. Whether SARS-CoV-2 infection will be vertically transmitted and affect the next generation is unclear and requires more evidence supports. With the prevalence of SARS-CoV-2, the development and clinical trials of SARS-CoV-2 vaccine are widely conducted worldwide, and current studies suggest that SARS-CoV-2 vaccination may not have adverse effects on the reproductive system of women. This article briefly reviewed the progress of research on SARS-CoV-2 on female reproductive health in the context of recent years.

【Key words】 Fertility; Ovarian reserve; Pregnancy outcome; Vaccination; SARS-CoV-2

Fund program: National Natural Science Foundation of China (82271662, 81901482); Military Innovation Project Special Project (21JSZ06)

DOI：10.3760/cma.j.cn101441-20221024-00466
收稿日期　2022-10-25　本文编辑　王李艳
引用本文：千日成, 邹荣良, 郭陆萍, 等. 从受精卵到囊胚期胚胎在体外培养发育过程中的乳酸代谢[J]. 中华生殖与避孕杂志, 2023, 43(5): 530-534. DOI: 10.3760/cma.j.cn101441-20221024-00466.

·综述·

从受精卵到囊胚期胚胎在体外培养发育过程中的乳酸代谢

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【摘要】 体外受精-胚胎移植（*in vitro* fertilization and embryo transfer，IVF-ET）是将精子和卵子在体外受精结合，并在体外进行胚胎培养发育至卵裂期或囊胚期胚胎，再移植到子宫内的过程。通常把受精卵到着床前囊胚期的发育过程称之为“胚胎着床前发育”。一般认为，人的胚胎着床前发育是靠卵母细胞蓄积的蛋白和mRNA 发育至 8-细胞期，然后开始激活胚胎自体基因进一步发育到囊胚期。由此可见，IVF 技术治疗不孕不育的重要环节之一是着床前胚胎体外培养。体外培养液的成分会直接影响着床前胚胎发育和临床治疗结局。其中，乳酸可能在受精卵早期分裂发育过程中起了相对重要作用。本文对受精卵到囊胚期胚胎着床前体外培养液的发展过程和培养液中的乳酸成分对胚胎着床前发育的影响进行概述。同时，对培养液中乳酸成分来源的乳酸盐原料进行简单的介绍。

【关键词】 受精卵；　囊胚；　胚胎着床前发育；　胚胎自体基因；　乳酸；　培养液

Lactate metabolism from the development of zygote to blastocyst stage during culture *in vitro*

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【Abstract】 Infertility treatment with *in vitro* fertilization and embryo transfer (IVF-ET) involves several processes such as the production of zygote (fusion of sperm and oocyte), the culturing of embryos (from zygote to blastocyst stage), and embryo transfer to uterus. The development of culturing embryos from zygote to blastocyst stage is typically called "embryo preimplantation development". In human, it has been noted that from zygote to 8-cell stage of embryo development relies on the accumulation of proteins and mRNAs which the oocyte itself has got, and then continues to develop into the blastocyst stage after zygote genome activation (ZGA). Therefore, *in vitro* culture of embryos from zygote to blastocyst stage is relatively important for IVF treatment. The composition of culture media directly affects the development of embryos, and in turn, subsequently affects the outcome of the IVF treatment. Among them, lactate may play an important role in early cleavage of zygote during embryonic development cultured *in vitro*. In this review, we discussed the composition of developed media from zygote to blastocyst stage, dealing especially with the function of lactate in culture for embryonic development. Concurrently, we discussed commercially available materials for the lactate that are used in the making of culture media.

【Key words】 Zygote; Blastocyst; Embryo preimplantation development; Zygote genome activation; Lactate; Culture media

DOI：10.3760/cma.j.cn101441-20221017-00454
收稿日期　2022-10-17　本文编辑　李天琦
引用本文：宋阳阳，郑洁，陈竹. 睾丸和附睾缺氧导致精液质量下降的研究进展[J]. 中华生殖与避孕杂志, 2023, 43(5): 535-540. DOI: 10.3760/cma.j.cn101441-20221017-00454.

·综述·

睾丸和附睾缺氧导致精液质量下降的研究进展

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【摘要】 近年来，男性精液质量逐年下降，影响着全球数以百万的育龄期人群，越来越多的学者开始关注影响精液质量的因素。大量研究证实，睾丸和附睾缺氧会导致精子数量减少、精子活力下降，而精子数量和活力的异常与精子细胞的过度凋亡、生殖内分泌紊乱、机体内活性氧水平过高等密切相关。本文就睾丸和附睾组织缺氧对精液质量的影响及其作用机制进行综述，以期为从事相关研究和临床服务的专业人员提供有益的参考。

【关键词】 缺氧； 精液质量； 精子发生； 精子成熟

基金项目：国家自然科学基金（31701074）

Research progress of declined semen quality caused by hypoxia in testis and epididymis

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【Abstract】 In recent years, the quality of male semen has been declining year by year, affecting millions of people of childbearing potential worldwide.So more and more scholars are paying attention to the factors affecting the quality of semen. Numerous studies have suggested that hypoxia in testis and epididymis could result in decreased number and activity of sperms, which are closely associated with excessive apoptosis of sperm cells, reproductive-endocrine disorders, and excessively high reactive oxygen species in the bodies. This paper reviewed the effects of hypoxia in testis and epididymis on semen quality and its mechanism of action, in an effort to provide useful evidence for the researchers and healthcare practitioners.

【Key words】 Hypoxia; Semen quality; Spermatogenesis; Sperm maturation

Fund program: National Natural Science Foundation of China (31701074)

DOI：10.3760/cma.j.cn101441-20220410-00155

收稿日期 2022-04-14 本文编辑 王李艳

引用本文：杜超，范馨月，侯开波，等. 2006 年至 2020 年抗苗勒管激素相关研究趋势及热点分析[J]. 中华生殖与避孕杂志, 2023, 43(5): 541-547. DOI: 10.3760/cma.j.cn101441-20220410-00155.

·热点追踪·

2006 年至 2020 年抗苗勒管激素相关研究趋势及热点分析

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【摘要】 目的　分析 2006 年至 2020 年抗苗勒管激素相关研究趋势及热点，为今后相关领域研究提供借鉴与参考。方法　基于 PubMed 数据库，检索 2006 年 1 月 1 日至 2020 年 12 月 31 日收录的抗苗勒管激素相关文献，采用文献计量学方法，以每 5 年为时间节点，分析每个阶段与抗苗勒管激素相关的发文趋势、高频主题词/副主题词共现和研究热点，对其发展趋势进行探讨和预测。结果　本文共检索到相关文献 4 276 篇，总发文量呈增长趋势。相关研究热点逐步增多，2005 年至 2010 年的核心研究热点为抗苗勒管激素的生物标志物作用；2011 年至 2015 年、2016 年至 2020 年两个阶段的核心研究热点均为抗苗勒管激素与多囊卵巢综合征。结论　抗苗勒管激素相关研究热点不断拓展与丰富的同时，也存在一定更迭和交替，部分新兴热点仍具有进一步研究的价值和意义。抗苗勒管激素Ⅱ型受体与生育力保存可能成为今后该领域的新兴热点。

【关键词】 抗苗勒管激素；　多囊卵巢综合征；　卵巢反应性；　生育力保存

基金项目：辽宁省科学技术计划课题（2020JH2/10300118）；军委后勤保障部重点项目（16JS014）

Research trends and hotspots of anti-Müllerian hormone from 2006 to 2020

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【**Abstract**】 **Objective** To analyze the research trends and hotspots of anti-Müllerian hormones (AMH) from 2006 to 2020, and to provide reference for future research in related fields. **Methods** Based on the PubMed database, the literatures related to AMH collected from January 1st, 2006 to December 31st, 2020 were retrieved, and the bibliometric method was used to analyze the relationship between each stage and AMH with every 5 years as the time node. The publication trends, high-frequency main MeSH/subheadings co-occurrence and research hotspots related to AMH were discussed and forecasted. **Results** A total of 4 276 related literatures were retrieved in this paper, and the total number of published papers showed an increasing trend. Relevant research hotspots were gradually increasing. The core research from 2005 to 2010 was the biomarker effect of AMH;

from 2011 to 2015 and 2016 to 2020, the core research hotspots were all AMH and polycystic ovary syndrome. **Conclusion** While the research hotspots related to AMH have been continuously expanded and enriched, there are also certain changes and alternations, and some emerging hotspots still have the value and significance of further research. AMH type Ⅱ receptor and fertility preservation may become an emerging hotspot in this field in the future.

【Key words】 Anti-Müllerian hormone; Polycystic ovary syndrome; Ovarian response; Fertility preservation

Fund program: Liaoning Provincial Science and Technology Program Project (2020JH2/10300118); The Key Project of the Logistics Support Department of the Military Commission (16JS014)