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2期　2023年2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

编　辑
中华生殖与避孕杂志
编辑委员会
200237,上海市老沪闵路779号
电话:(021)64438169
传真:(021)64438975
Email:randc@sibpt.com
http://zhszybyzz.yiigle.com

总编辑
乔　杰

编辑部主任
王　健

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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本期责任编委　李蓉　孙宁霞　　**本期责任编辑**　王李艳　　**本期责任排版**　年丽红

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

Monthly Established in December 1980 Volume 43, Number 2 February 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

Editor-in-Chief
Qiao Jie

Managing Director
Wang Jian

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.cn101441-20230113-00027
收稿日期　2023-01-13　本文编辑　李天琦

引用本文：新型冠状病毒感染"乙类乙管"措施下人类辅助生殖技术管理建议专家组. 新型冠状病毒感染"乙类乙管"措施下人类辅助生殖技术管理的建议（第一版）[J]. 中华生殖与避孕杂志, 2023, 43(2): 109-111. DOI: 10.3760/cma.j.cn101441-20230113-00027.

·专家建议·

新型冠状病毒感染"乙类乙管"措施下人类辅助生殖技术管理的建议（第一版）

新型冠状病毒感染"乙类乙管"措施下人类辅助生殖技术管理建议专家组

通信作者：陈子江，Email：chenzijiang@hotmail.com，电话：+86-531-85651189；颜军昊，Email：yyy306@126.com，电话：+86-531-85651190

【摘要】　面对新型冠状病毒的快速传播与新型冠状病毒感染"乙类乙管"的措施调整，人类辅助生殖机构在执行新的防控政策和规范的诊疗方面存在困惑。为规范辅助生殖技术诊疗、保障患者安全与利益，结合临床，专家组针对疫情下辅助生殖助孕治疗过程中的常见问题给出了建议。

【关键词】　新型冠状病毒；　生殖技术，辅助；　乙类乙管

Recommendations on the management of assisted reproductive technology under the Class B infectious disease policy for COVID-19 (first edition)

Recommendation Experts Group on the Management of Assisted Reproductive Technology Under the Class B Infectious Disease Policy for COVID-19
Corresponding authors: Chen Zijiang, Email: chenzijiang@hotmail.com, Tel: +86-531-85651189; Yan Junhao, Email: yyy306@126.com, Tel: +86-531-85651190

【Abstract】　In the face of the rapid spread of COVID-19 and the country's decision to downgrade COVID-19 management to Class B, human assisted reproductive institutions should adjust and optimize the preventive and control policies. Standardization of assisted reproductive technology (ART) and interest of patients are both challenged by the new situation. The experts provided suggestions for the common problems emerging under new epidemic situation during clinical practice of assisted reproductive institutions.

【Key words】 COVID-19; Reproductive technology, assisted; Class B infectious disease

DOI:10.3760/cma.j.cn101441-20230113-00001
收稿日期 2023-01-13 本文编辑 王李艳
引用本文：孙宁霞，李蓉. 生育力保存专栏导读[J]. 中华生殖与避孕杂志，2023，43(2)：112. DOI: 10.3760/cma.j.cn101441-20230113-00001.

·生育力保存专栏·

生育力保存专栏导读

当前全球生育率下降的问题备受关注。特别在过去的 20 年中，人们逐渐认识到肿瘤及其他严重疾病的治疗对生育力丧失有着重要影响，而年轻肿瘤患者治疗后长期生存，使得生育力保存的需求日益增加。同时卵母细胞冷冻、卵巢组织冷冻保存及自体移植等技术日臻完善，生育力保存领域已取得了巨大的进步。国际生育力保存学会（International Society for Fertility Preservation，ISFP）、欧洲人类生殖和胚胎学学会（the European Society of Human Reproduction and Embryology，ESHRE）以及美国临床肿瘤学会（American Society of Clinical Oncology，ASCO）等相继颁布了有关女性生育力保存的建议和指南。近年来我国也相继发表了生育力保存领域的专家共识，但生育力保存仍是一项长期而具有挑战性的工作。

当前女性生育力保存的主要技术包括胚胎冷冻、卵母细胞冷冻及卵巢组织冷冻等，其中胚胎冷冻技术已有近 40 年历史，已得到广泛的应用，成为临床最常用的生育力保存方法。而目前受到关注较多的是成熟卵母细胞冷冻及卵巢组织冷冻技术。卵巢组织冷冻技术在美国等一些国家已经不再作为实验性技术开展。未成熟卵的体外成熟（*in vitro* maturation，IVM）技术作为实验性技术也有一定范围的应用。另外生育力保存的前沿技术，如人造卵巢技术、卵泡体外发育、干细胞技术等，也为生育力保存开辟了新的方法和途径。

尽管各类生育力保存临床技术发展迅猛，但仍缺少临床结局的大规模数据，因此亟须评估其证据基础、制定临床指南，以协助医疗人员安全有效地开展诊疗活动。同时，无论一项新兴技术多么有应用前景，在其应用于临床治疗之前，都需要进行严格的临床试验，确保达到国际公认的标准以及论证其有效性和安全性。

本期生育力保存专栏是由《中华生殖与避孕杂志》与中国妇幼保健协会生育力保存专委会联合举办，在李文主委和责任编委的精心组织下，邀请了生殖领域及生育力保存领域专家就女性生育力保存现状与进展，乳腺癌、卵巢癌及淋巴瘤患者生育力保存临床实践，卵巢组织冷冻移植技术、腹腔镜术中取卵技术以及未成熟卵 IVM 技术在生育力保存中的应用等方

面进行了充分的探讨，旨在为生育力保存的标准化、规范化开展提供更多的循证医学证据和经验。

“奋楫笃行，臻于至善”，相信在各位同行的不断努力下，中国生育力保存技术将不断蓬勃发展，为更多的患者带来幸福和希望！

如有不妥之处，敬请各位同仁批评指正！

专栏责任编委：孙宁霞（海军军医大学第二附属医院）
李　蓉（北京大学第三医院）

生育力保存专栏·

DOI：10.3760/cma.j.cn101441-20221222-00585
收稿日期　2022-12-23　本文编辑　王李艳
引用本文：中国医师协会生殖医学专业委员会，中国临床肿瘤学会淋巴瘤专家委员会，中国医疗保健国际交流促进会生殖医学分会，等. 淋巴瘤患者生育力保存临床实践中国专家共识[J]. 中华生殖与避孕杂志, 2023, 43(2): 113-122. DOI: 10.3760/cma.j.cn101441-20221222-00585.

淋巴瘤患者生育力保存临床实践中国专家共识

中国医师协会生殖医学专业委员会　中国临床肿瘤学会淋巴瘤专家委员会　中国医疗保健国际交流促进会生殖医学分会　中国抗癌协会小儿肿瘤专业委员会

通信作者：严杰，Email：yanjiebjmu@bjmu.edu.cn；段彦龙，Email：duanyanlong@hotmail.com；宋玉琴，Email：songyuqin622@163.com；乔杰，Email：jie.qiao@263.net

【摘要】 近年来随着淋巴瘤患者治疗后生存率上升，越来越多的淋巴瘤存活者面临治愈后所带来的生育力下降问题。为保存淋巴瘤患者生育力，提升患者生存质量，根据现有的科学研究及临床实践，结合最新指南和专家意见制定本共识，涵盖淋巴瘤疾病对生育力的影响、患者生育力保存方案的选择等内容，为血液科及生殖医学专科医生提供淋巴瘤患者生育力保存临床指导策略，以更有效地解决淋巴瘤患者（包括未成年患者）的生殖健康需求。

【关键词】 生育力保存；　淋巴瘤；　早发性卵巢功能不全；　专家共识
基金项目：国家重点研发计划（2022YFC2703000、2022YFC2702502）

Chinese expert consensus on clinical practice of fertility preservation in lymphoma patients

Chinese Association of Reproductive Medicine, Union for China Lymphoma Investigator at Chinese Society of Clinical Oncology, Reproductive Medicine Branch of China International Exchange and Promotive Association for Medical and Health Care, Children's Cancer Group, Chinese Anti-Cancer Association

Corresponding authors: Yan Jie, Email: yanjiebjmu@bjmu.edu.cn; Duan Yanlong, Email: duanyanlong@hotmail.com; Song Yuqin, Email: songyuqin622@163.com; Qiao Jie, Email: jie.qiao@263.net

【Abstract】 In recent years, as the survival rate of lymphoma patients has increased, more and more lymphoma survivors are facing fertility problems caused by lymphoma treatment. In order to preserve the fertility of lymphoma patients and improve the quality of life of patients post recovery, this consensus is formulated based on current literature and clinical practice, referring to the latest guidelines and expert advises. This consensus includes the impact of lymphoma on fertility, the selection of fertility preservation options for lymphoma patients, etc. It provides hematological and reproductive professionals with the optimal clinical guideline and strategy regarding fertility preservation options for lymphoma patients, so as to address the demand for reproductive health of lymphoma patients (including minors) more effectively.

【Key words】 Fertility preservation; Lymphoma; Premature ovarian insufficiency; Expert consensus

Fund program: National Key Research and Development Program of China (2022YFC2703000, 2022YFC2702502)

DOI：10.3760/cma.j.cn101441-20220930-00425

收稿日期　2022-10-01　本文编辑　王李艳

引用本文：孙翟，李文. 女性生育力保存现状与进展[J]. 中华生殖与避孕杂志，2023，43(2)：123-128. DOI: 10.3760/cma.j.cn101441-20220930-00425.

·生育力保存专栏·

女性生育力保存现状与进展

孙翟　李文

上海交通大学医学院附属国际和平妇幼保健院生殖医学中心，上海 200030

通信作者：李文，Email：liwen@shsmu.edu.cn，电话：+86-13601858540

【摘要】 当前我国乃至全球均面临人口出生率下降的严峻现状。年龄增长、疾病本身或放化疗等均可能造成女性生育力不可逆下降甚至丧失， 因此开展生育

力保存对于恢复女性生殖功能、孕育健康子代以及保障人口数量和国家发展有着重要意义。本文对女性生育力保存的适应证、临床应用和局限性以及新兴技术研究进展等进行全面梳理和分析，展望了女性生育力保存领域未来研究的重点和方向，为相关专业人员的临床实践和科学研究提供重要参考。

【关键词】 生育力保存； 胚胎冷冻； 卵子冷冻； 卵巢组织冷冻； 卵泡发育； 人工卵巢

基金项目：国家重点研发计划（2018YFC10010202）；国家自然科学基金（82071605、81873821）

Status and progress of fertility preservation in women

Sun Di, Li Wen

Center for Reproductive Medicine, International Peace Maternal and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200030, China

Corresponding author: Li Wen, Email: liwen@shsmu.edu.cn, Tel: +86-13601858540

【Abstract】 At present, the birth rate is declining sharply in China and around the world. It takes irreversible damage to female fertility due to aging, diseases, radiotherapy and chemotherapy. Therefore, fertility preservation (FP) is of great significance for retaining female reproductive function for livebirth and safeguarding the national population and development. This review states the indications, clinical applications and limitations of different technologies for female FP comprehensively, as well as the emerging research progress in this field. Also, we suggest the direction of future research and provide the reference for clinical practice and scientific research of female FP.

【Key words】 Fertility preservation; Embryo cryopreservation; Oocyte cryopreservation; Ovarian tissue cryopreservation; Follicle development; Artificial ovary

Fund program: National Key R&D Program of China (2018YFC10010202); National Natural Science Foundation of China (82071605, 81873821)

DOI：10.3760/cma.j.cn101441-20220626-00276

收稿日期 2022-06-28 本文编辑 王李艳

引用本文：郭梦溪, 陈小君, 吴丹丹, 等. 年轻未婚乳腺癌患者生育力保存临床实践[J]. 中华生殖与避孕杂志, 2023, 43(2): 129-133. DOI: 10.3760/cma.j.cn101441-20220626-00276.

·生育力保存专栏·

年轻未婚乳腺癌患者生育力保存临床实践

郭梦溪 陈小君 吴丹丹 王旻 王丽 李文

上海交通大学医学院国际和平妇幼保健院生殖医学中心，上海 200030

通信作者：李文，Email：liwen@shsmu.edu.cn，电话：+86-13601858540

【摘要】 目的　探讨我国年轻未婚女性乳腺癌患者生育力保存的临床实践情况。方法　回顾性分析 2019 年 1 月至 2020 年 12 月期间在上海交通大学医学院国际和平妇幼保健院生殖医学中心因乳腺癌行生育力保存的 13 例未婚女性患者的临床数据。结果　患者年龄为（31.00±3.98）岁，9 例采用卵泡期来曲唑+促性腺激素（gonadotropin，Gn）的卵巢刺激方案，3 例采用黄体期来曲唑+Gn 的卵巢刺激方案，1 例采用自然周期方案。其中 11 例患者完成了生育力保存周期，Gn 使用总量为（1 865.91±501.03） U，扳机日雌二醇为（1 223.85±709.75） ng/L，冷冻卵母细胞（9.91±4.41）枚，冷冻方式均为玻璃化冷冻。结论　来曲唑+Gn 的卵巢刺激后卵母细胞玻璃化冷冻是年轻未婚女性乳腺癌患者首选的生育力保存方案，但增进医生及患者对生育力保存的认知、促进临床科室间的沟通以及推广生育力保存临床实践仍待加强。

【关键词】 乳腺肿瘤；　生育力保存；　卵母细胞；　玻璃化冷冻；　单身

基金项目：上海地方高水平高校创新团队（SHSMU-ZDCX20212200）；宁夏重点研发计划（2019BFG02007）；国家自然科学基金面上项目（82071605、81873821）

Clinical practice of fertility preservation in young unmarried breast cancer patients

Guo Mengxi, Chen Xiaojun, Wu Dandan, Wang Min, Wang Li, Li Wen

Reproductive Medical Center, International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China

Corresponding author: Li Wen, Email: liwen@shsmu.edu.cn, Tel: +86-13601858540

【**Abstract**】 **Objective** To analyze the clinical practice of fertility preservation in unmarried young female breast cancer patients in China. **Methods** This was a retrospective study of 13 unmarried female patients who underwent fertility preservation due to breast cancer in the Reproductive Medicine Center of International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University School of Medicine from January 2019 to December 2020. **Results** The age of the patients was (31.00±3.98) years old. Nine patients used follicular phase letrozole (LE)+gonadotropin (Gn) ovarian stimulation protocol, 3 patients used luteal phase LE+Gn stimulation protocol, and 1 patient used natural cycle protocol. Eleven patients completed the fertility preservation procedure, with a total Gn used dosage of (1 865.91±501.03) U, estradiol level at trigger of (1 223.85±709.75) ng/L, and 9.91±4.41 frozen oocytes. All of them used vitrification freezing. **Conclusion** Oocyte vitrification frozen after LE+Gn ovarian stimulation is the preferred solution in young unmarried breast cancer patients for fertility preservation. However, promoting the awareness of fertility preservation, improving communication between clinical departments, and increasing clinical practice still need to be promoted.

【**Key words**】 Breast neoplasms; Fertility preservation; Oocyte; Vitrification; Single person

Fund program: Innovative Research Team of High-level Local Universities in Shanghai (SHSMU-ZDCX20212200); Key R&D Program of Ningxia Province (2019BFG02007); General Program of National Natural Science Foundation of China (82071605, 81873821)

DOI：10.3760/cma.j.cn101441-20221213-00562
收稿日期　2022-12-15　本文编辑　宋培培
引用本文：宋雪凌, 严杰, 张文, 等. 腹腔镜卵巢组织切除术中获取未成熟卵在生育力保存中的应用[J]. 中华生殖与避孕杂志, 2023, 43(2): 134-139. DOI: 10.3760/cma.j.cn101441-20221213-00562.

·生育力保存专栏·

腹腔镜卵巢组织切除术中获取未成熟卵在生育力保存中的应用

宋雪凌　严杰　张文　杨硕　张佳佳　杨蕊　杨艳　马彩虹　李蓉　乔杰
北京大学第三医院妇产科生殖医学中心　国家妇产疾病临床医学研究中心（北京大学第三医院）　辅助生殖教育部重点实验室（北京大学）　北京市生殖内分泌与辅助生殖技术重点实验室　中国医学科学院卵成熟障碍创新单元，北京 100191

通信作者：乔杰，Email：jie.qiao@263.net，电话：+86-10-82266849

【摘要】 目的　探索女性肿瘤患者在腹腔镜卵巢皮质切除术中获取未成熟卵体外成熟后（*in vitro* maturation，IVM）冷冻卵母细胞保存生育力的可行性及有效性。方法　回顾分析 2015 年 11 月至 2022 年 4 月期间于北京大学第三医院妇产科生殖医学中心行腹腔镜下卵巢皮质切除术的 22 例肿瘤患者的一般资料、手术方法及术后随访资料。研究组纳入腹腔镜术中同时获取未成熟卵 IVM 的患者（*n*=14）；对照组纳入仅行皮质切除的患者（*n*=8）。分析两组患者的手术时间、出血量、冻存皮质数量等数据，评估该方法的应用价值及安全性。研究组根据取卵方式不同分为两个亚组，经阴道取卵亚组（*n*=10）及经腹腔镜取卵亚组（*n*=4），分析两亚组患者的手术时间、获卵数、冻存皮质数量等数据，评估不同获卵方式的效率。全部 22 例患者术后每年进行随访，询问肿瘤治疗情况、月经情况，条件允许者返院复查盆腔超声、性激素水平测定，记录这些患者肿瘤治疗后的卵巢功能并予以适应证范围内的激素替代治疗（hormone replacement therapy，HRT）。结果　研究组和对照组患者年龄、患病时间、抗苗勒管激素（anti-Müllerian hormone， AMH）水平、冻存皮质数量之间差异均无统计学意义（均 *P*>0.05），但研究组的基础窦卵泡数（19.71±6.04）、手术时间［（68.07±17.35） min］、出血量［（9.0（5.0，10.5） mL］高于对照组［9.25±3.15，*P*<0.001；（44.25±16.97） min，*P*=0.005；3.5（2.0，5.0） mL，*P*=0.001］，差异均具有统计学意义。14 例取卵患者中，经阴道取卵亚

组的获卵数［15.5 （11.0，21.0）个］及年龄［（27.00±2.94）岁］显著高于经腹腔镜取卵亚组［4.0 （0.8，10.3）个，*P*=0.028；（15.75±2.22）岁，*P*<0.001］，两亚组间患者窦卵泡数、手术时间、冻存皮质数量差异均无统计学意义（均 *P*>0.05）。接受造血干细胞移植（hematopoietic stem cell transplantation，HSCT）的 7 例患者出仓后均出现闭经，疾病缓解后予以 HRT，身体发育及生活质量得以维持及改善。结论　年轻肿瘤患者在进行卵巢皮质切除术时同时获取未成熟卵 IVM 后冻存可增加生育力保存的机会；经阴道获取未成熟卵的效率更高；HSCT 治疗后闭经率高，HRT 可以提高患者生活质量。

【关键词】　激素替代疗法；　生育力保存；　体外成熟；　卵巢皮质切除

基金项目：国家重点研发计划（2022YFC2703000）；中国医学科学院医学与健康科技创新工程项目（2019-I2M-5-001）

Application of immature oocytes collection during laparoscopic ovarian tissue resection in fertility preservation

Song Xueling, Yan Jie, Zhang Wen, Yang Shuo, Zhang Jiajia, Yang Rui, Yang Yan, Ma Caihong, Li Rong,

Qiao Jie

Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, National Clinical Research Center for Obstetrics and Gynecology (Peking University Third Hospital), Key Laboratory of Assisted Reproduction (Peking University), Ministry of Education/Beijing Key Laboratory of Reproductive Endocrinology and Assisted Reproductive Technology/Research Units of Comprehensive Diagnosis and Treatment of Oocyte Maturation Arrest, Chinese Academy of Medical Sciences, Beijing 100191, China

Corresponding author: Qiao Jie, Email: jie.qiao@263.net, Tel: +86-10-82266849

【**Abstract**】　**Objective**　To explore the feasibility and effective methods of obtaining immature oocytes during laparoscopic ovarian tissue resection in female tumor patients, aiming at oocytes freezing matured *in vitro* for fertility preservation. **Methods**　Retrospective analysis was made on the general data, surgical methods and postoperative follow-up data of 22 tumor patients who underwent laparoscopic ovarian tissue resection at the Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital from November 2015 to April 2022. The study group included 14 patients who simultaneously obtained *in vitro* maturation (IVM) of immature eggs during laparoscopy. Control group included 8 patients who only underwent cortical resection. The operation time, the amount of bleeding, the number of frozen cortex and other data of the two groups were analyzed to evaluate the application value and safety of this method. Furtherly, the study group was divided into two subgroups, the transvaginal egg retrieval subgroup (10 patients) and the translaparoscopic egg retrieval subgroup (4 patients), according to the method of different methods used for egg retrieval. The time of surgery, the number of eggs obtained and the number of frozen cortices were analyzed in both subgroups to evaluate the efficiency of the different methods of egg retrieval. All 22 patients were followed up annually after surgery, analyzing the information of tumor treatment, menstrual status, and if possible, pelvic ultrasound

and sex hormone levels, recording ovarian function after tumor treatment in these patients and providing hormone replacement therapy (HRT) within the indications. **Results** There were no statistically significant differences between the study group and control group in terms of age, duration of disease, anti-Müllerian hormone (AMH) level, and the number of frozen cortices. But the number of basal sinus follicles (19.71±6.04), procedure time [(68.07±17.35) min], and bleeding volume [9.0 (5.0,10.5) mL] in the study group were higher than those in control group with statistically significant differences [9.25±3.15, *P*<0.001; (44.25±16.97) min, *P*=0.005; 3.5 (2.0, 5.0) mL, *P*=0.001]. In the transvaginal egg retrieval subgroup, the number of oocytes obtained [15.5 (11.0, 21.0)] and age [(27.00±2.94) years] were significantly higher than those in the translaparoscopic egg retrieval subgroup [4.0 (0.8, 10.3), *P*=0.028;(15.75±2.22) years, *P*<0.001], while no statistically significant differences were observed between the two subgroups in the number of sinus follicles, time to surgery, and number of frozen cortices. All 7 patients who underwent hematopoietic stem cell transplantation (HSCT) had amenorrhea after discharge, and were given HRT after disease remission, and their physical development and quality of life were maintained and improved. **Conclusion** Young oncology patients who underwent ovarian cortical resection with simultaneous acquisition of immature eggs, *in vitro* matured oocytes freezing increased the chance of fertility preservation. The efficiency of transvaginal acquisition of immature oocytes was higher; the rate of amenorrhea after HSCT was high, and HRT could improve the quality of life of patients.

【Key words】 Hormone replacement therapy; Fertility preservation; *In vitro* maturation; Ovarian tissue resection

Fund program: National Key Research and Development Program of China (2022YFC2703000); CAMS Innovation Fund for Medical Sciences (2019-I2M-5-001)

DOI：10.3760/cma.j.cn101441-20221011-00446
收稿日期　2022-10-11　本文编辑　王李艳
引用本文：赵伟娥, 孙鹏, 陈攀宇, 等. 卵巢组织卵母细胞体外成熟在恶性肿瘤患者生育力保存中的应用[J]. 中华生殖与避孕杂志, 2023, 43(2): 140-144. DOI: 10.3760/cma.j.cn101441-20221011-00446.

·生育力保存专栏·

卵巢组织卵母细胞体外成熟在恶性肿瘤患者生育力保存中的应用

赵伟娥　孙鹏　陈攀宇　李永芳　李晶洁　曾海涛　方丛　梁晓燕

中山大学附属第六医院生殖医学研究中心，　广州 510000

通信作者：梁晓燕，Email：liangxy2@mail.sysu.edu.cn，电话：+86-13500015058

【摘要】 目的 探讨卵巢组织卵母细胞体外成熟（ovarian tissue oocyte-*in vitro* maturation， OTO-IVM）在肿瘤患者中的临床效果与应用前景。方法 回顾性分析 2017 年 3 月至 2022 年 8 月期间于中山大学附属第六医院生殖医学研究中心行卵巢组织冷冻（ovarian tissue cryopreservation， OTC）并同时行 OTO-IVM 的 27 例肿瘤患者的临床资料。分析总结 OTO-IVM 的临床结局，包括成熟卵母细胞数、成熟率、成熟时间；IVM 来源成熟卵母细胞的受精率、卵裂率和胚胎发育情况；探讨卵巢组织获取前短期使用促性腺激素（gonadotropin， Gn）在 OTO-IVM 中的应用。结果 81.48%（22/27）的患者至少有 1 枚卵母细胞成熟，成熟卵母细胞中位数为 3.00 （1.50，7.00）枚，成熟率为 38.81%（104/268）。4.85%（13/268）的卵母细胞在 24 h 内成熟，14.93%（40/268）在 24~36 h 之间成熟，16.79%（45/268）在 36~48 h 之间成熟，仅有 2.24%（6/268）卵母细胞在 48 h 后成熟。4 例患者的 41 枚卵母细胞行卵胞质内单精子注射（intracytoplasmic sperm injection， ICSI）授精，受精率为 85.37%（35/41），卵裂率为 94.29%（33/35），可利用胚胎率为 54.29%（19/35），优质胚胎率为 34.29%（12/35）。术前短暂使用 Gn 患者的 IVM 率 63.16%（48/76）显著高于未使用者[29.17%（56/192）， P<0.001]。结论 OTO-IVM 可获得一定数量的卵母细胞与胚胎，可作为肿瘤患者生育力保存的补充方法。卵巢组织获取前短暂使用 Gn 可提高卵母细胞成熟率，由于样本量尚少，但还需要进一步研究，验证 Gn 在 OTO-IVM 中的应用价值。

【关键词】 卵母细胞； 体外成熟； 恶性肿瘤； 生育力保存； 卵巢组织冷冻

基金项目：国家重点研发计划（2021YFC2700400）

Feasibility analysis and application of ovarian tissue oocyte-*in vitro* maturation in the patients with malignant tumors undergoing fertility preservation

Zhao Weie, Sun Peng, Chen Panyu, Li Yongfang, Li Jingjie, Zeng Haitao, Fang Cong, Liang Xiaoyan

Reproductive Medicine Research Center, the Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510000, China

Corresponding author: Liang Xiaoyan, Email: liangxy2@mail.sysu.edu.cn, Tel: +86-13500015058

【Abstract】 Objective To explore the prospects of ovarian tissue oocyte-*in vitro* maturation (OTO-IVM) in fertility preservation for patients with malignancy. **Methods** OTO-IVM outcomes from 27 malignant tumor patients who underwent fertility preservation in Reproductive Medicine Research Center of the Sixth Affiliated Hospital of Sun Yat-Sen University from March 2017 to August 2022 were analyzed, including the number of mature oocytes (M_{II} oocytes), maturation rate, and maturation time. The fertilization rate, the cleavage rate, and the embryonic development potential of IVM-derived M_{II} were also analyzed. Further, the short-

term use of gonadotropin (Gn) in OTO-IVM before ovarian tissue acquisition was initially explored. **Results** After OTO-IVM, 81.48% (22/27) of patients had at least one M_{II} oocyte, with a mean number of M_{II} oocytes of 3.00 (1.50, 7.00) and a maturation rate of 38.81%. About 4.85% (13/268) of oocytes matured within 24 h; 14.93% (40/268) matured between 24 h and 36 h; 16.79% (45/268) matured between 36 h and 48 h, and only 2.24% (6/268) matured after 48 h. A total of 41 M_{II} oocytes from 4 patients were fertilized by intracytoplasmic sperm injection (ICSI), with a fertilization rate of 85.37% (35/41), cleavage rate of 94.29% (33/35), variable embryo rate of 54.29% (19/35), and high-quality embryo rate of 34.29% (12/35). The IVM rate was significantly higher in patients who used Gn than in those who did not [63.16% (48/76) *vs.* 29.17% (56/192), $P<0.001$]. **Conclusion** OTO-IVM can be used as a complementary method for fertility preservation in oncology patients and obtain a certain number of oocytes and embryos. Short-term use of Gn before ovarian tissue acquisition can improve oocyte maturation rate, but further studies are needed to verify the value of Gn in OTO-IVM.

【Key words】 Oocytes; *In vitro* maturation; Malignant tumors; Fertility preservation; Ovarian tissue cryopreservation

Fund program: National Key Research and Development Program of China (2021YFC2700400)

DOI：10.3760/cma.j.cn101441-20221009-00440
收稿日期 2022-10-09 本文编辑 孙敏
引用本文：彭瑞瑞, 董冉, 李淼, 等. 妇科手术过程中取卵行生育力保存的初步研究[J]. 中华生殖与避孕杂志, 2023, 43(2): 145-149. DOI: 10.3760/cma.j.cn101441-20221009-00440.

·生育力保存专栏·

妇科手术过程中取卵行生育力保存的初步研究

彭瑞瑞 董冉 李淼 张帅 韩婷 黄玉真 李梅
山东大学生殖医学研究中心（山东大学附属生殖医院） 生殖内分泌教育部重点实验室（山东大学） 山东省生殖医学重点实验室 山东省生殖健康临床医学研究中心 山东省生殖健康技术创新中心 国家辅助生殖与优生工程技术研究中心，济南 250012

通信作者：李梅，Email：lee_mei@163.com，电话：+86-531-85651273

【摘要】 目的 探讨妇科手术过程中取卵行生育力保存的方法，为不宜经阴道取卵行生育力保存的患者提供实验依据。方法 研究对象为 2020 年 4 月至 6 月期间于山东大学附属生殖医院拟行腹腔镜手术的多囊卵巢综合征（polycystic ovary syndrome，PCOS）患者和妇科手术中拟行生育力保存的肿瘤患者。本研究为回顾性研究，经患者知情同意后对 23 例拟行输卵管手术的 PCOS 不孕症患者进行卵巢

表面小卵泡穿刺取卵，获卵后送入辅助生殖实验室进行体外培养，获得优质胚胎冷冻保存。对拟行生育力保存的 6 例肿瘤患者妇科手术同时卵巢表面卵泡穿刺进行卵子体外培养。根据获卵、成熟、受精及胚胎培养等指标评价妇科手术过程中取卵的可行性。结果　对于 PCOS 患者，腹腔镜引导下卵巢表面卵泡穿刺的每周期获卵率为 52.17% （12/23），获卵患者的获卵数为（2.00±1.48）枚，其中可培养卵数为（1.50±1.00）枚，卵子成熟率为 22.22% （4/18），受精 2 枚，卵裂 1 枚。拟行生育力保存的肿瘤患者妇科手术每周期获卵率为 100.00% （6/6），获卵数为（3.00±1.27）枚，卵子成熟率为 38.46% （5/13），受精 3 枚，1 枚发育至囊胚，3 例获得可冷冻卵子或胚胎。结论　对于不适合经阴道取卵行生育力保存的患者，妇科手术过程中取卵可以获得可利用卵子。

【关键词】 腹腔镜手术； 肿瘤； 妇科手术； 卵泡穿刺； 卵子体外成熟； 生育力保存

基金项目：国家重点研发计划（2022YFC2704404、2022YFC2703000）；国家自然科学基金（82171842）

Preliminary study of fertility preservation by oocytes retrieval during gynecological operation

Peng Ruirui, Dong Ran, Li Miao, Zhang Shuai, Han Ting, Huang Yuzhen, Li Mei

Center for Reproductive Medicine, Shandong University (Affiliated Reproductive Hospital of Shandong University); Key Laboratory of Reproductive Endocrinology of Ministry of Education,Shandong University; Shandong Key Laboratory of Reproductive Medicine; Shandong Provincial Clinical Research Center for Reproductive Health; Shandong Technology Innovation Center for Reproductive Health;National Research Center for Assisted Reproductive Technology and Reproductive Genetics, Shandong University, Jinan 250012, China

Corresponding author: Li Mei, Email: lee_mei@163.com, Tel: +86-531-85651273

【Abstract】 Objective To find a method for fertility preservation through oocytes retrieval during gynecological operation and provide an experimental basis for patients who are not suitable for fertility preservation by transvaginal oocyte retrieval. **Methods** The objects of the study were patients with polycystic ovary syndrome (PCOS) who underwent laparoscopic surgery in the Affiliated Reproductive Hospital of Shandong University from April to June 2020 and patients with tumors who underwent fertility preservation during gynecological surgery. This was a retrospective study. Totally 23 patients with PCOS infertility who were to undergo laparoscopy surgery underwent ovarian surface follicle puncture for oocyte retrieval, and the oocytes were obtained and sent to the assisted reproduction laboratory for *in vitro* culture, and mature oocytes were inseminated by intracytoplasmic sperm injection (ICSI), and high-quality embryos were obtained for cryopreservation. Gynecological surgery and ovarian surface follicle puncture were performed for oocytes retrieval in tumor patients (n=6) with fertility preservation. The feasibility of simultaneous gynecological surgery with oocytes retrieved was evaluated according to the indexes of the number of oocytes retrieval, maturation, fertilization and embryo culture. **Results** In PCOS patients, oocytes retrieved rate was 52.17% (12/23) per cycle. The number of oocytes retrieved was 2.00±1.48,

among which the number of culturable oocytes was 1.50±1.00. The oocyte maturation rate was 22.22% (4/18). Two oocytes got fertilization and one zygote got cleavage. In contrast, the fertility-preserving oncology patients undergoing gynecologic surgery had a 100.00% (6/6) oocytes retrieved rate per cycle, with 3.00±1.27 oocytes retrieved. Oocyte maturation rate was 38.46% (5/13). Three oocytes got fertilization and one blastocyst formed. Three patients got oocytes or embryos cryopreservation. **Conclusion** For patients who are not suitable for transvaginal oocyte retrieval for fertility preservation, follicle puncture during the gynecologic operation can yield available oocytes.

【Key words】 Laparoscopy; Neoplasms; Gynecological operation; Follicle puncture; Oocyte *in vitro* maturation; Fertility preservation

Fund program: National Key Research and Development Program (2022YFC2704404, 2022YFC2703000); National Natural Science Foundation of China (82171842)

DOI：10.3760/cma.j.cn101441-20221212-00559

收稿日期 2022-12-13 本文编辑 孙敏

引用本文：许大兵，章翊，顾佳怡，等. 卵巢组织玻璃化冷冻移植效果及体外受精结局的动物实验研究[J]. 中华生殖与避孕杂志, 2023, 43(2): 150-157. DOI: 10.3760/cma.j.cn101441-20221212-00559.

·生育力保存专栏·

卵巢组织玻璃化冷冻移植效果及体外受精结局的动物实验研究

许大兵 章翊 顾佳怡 王亮 孙宁霞

海军军医大学第二附属医院生殖医学中心，上海 200003

通信作者：孙宁霞，Email：suesunchzh@126.com，电话：+86-21-81886715

【摘要】 目的 探讨玻璃化冷冻和组织移植对小鼠卵巢组织的影响。方法 将雌性 ICR 小鼠分为 3 组：正常对照组（卵母细胞体外培养及受精，*n*=9）、新鲜移植组（卵巢组织移植后卵母细胞体外培养及受精，*n*=9）、冷冻移植组（卵巢组织玻璃化冷冻复苏-移植、卵母细胞体外培养及受精，*n*=9）。同时，为了更为直接地说明玻璃化冷冻对于卵泡数量的影响和卵巢移植后内分泌功能的改变情况，本研究还设置了冷冻复苏组（卵巢组织玻璃化冷冻复苏，*n*=6）和卵巢去势组（卵巢组织切除，*n*=6）。卵巢组织移植 3 周后，通过苏木精-伊红（hematoxylin-eosin，HE）染色计算各组小鼠的卵泡数量、CD31 免疫组织化学染色观察卵巢组织新生血管形成、Masson 染色观察卵巢组织纤维化、酶联免疫吸附法（enzyme-linked

immunosorbent assay， ELISA）检测血清性激素水平，并统计获卵数、体外受精数量和形成囊胚数量。结果　新鲜移植组和冷冻移植组小鼠的卵巢组织中总卵泡数量均较正常对照组明显减少（均 *P*<0.001），且都明显少于冷冻复苏组（均 *P*<0.001）；新鲜移植组小鼠卵巢组织 CD31 阳性率明显高于正常对照组（*P*=0.044），冷冻移植组小鼠高于正常对照组，但差异无统计学意义（*P*=0.162）；新鲜移植组和冷冻移植组小鼠卵巢组织纤维化面积百分率均明显高于正常对照组（*P*=0.004；*P*=0.005）；新鲜移植组和冷冻移植组小鼠血清雌二醇水平均明显低于正常对照组（*P*=0.005； *P*=0.001），但明显高于卵巢去势组（*P*=0.011； *P*=0.035），血清卵泡刺激素（follicle-stimulating hormone， FSH）水平均明显高于正常对照组（*P*=0.040； *P*=0.012），但明显低于卵巢去势组（*P*=0.001； *P*=0.004）；新鲜移植组和冷冻移植组小鼠的获卵数均较正常对照组明显减少（均 *P*<0.001），新鲜移植组小鼠的获卵数高于冷冻移植组，但差异无统计学意义（*P*=0.272）；新鲜移植组和冷冻移植组卵母细胞的体外受精数量和囊胚数均明显低于正常对照组（均 *P*<0.001）。新鲜移植组和冷冻移植组小鼠在总卵泡数量、CD31 阳性率、纤维化面积百分率、血清雌二醇和 FSH 水平、受精数和形成囊胚数上差异均无统计学意义（均 *P*>0.05）。结论　小鼠卵巢组织在接受玻璃化冷冻复苏-移植后能够恢复卵泡生长、内分泌功能以及生育功能，证实利用玻璃化冷冻技术进行卵巢组织冻存可以作为女性生育力保存的一个有效手段。玻璃化冷冻和组织移植均会造成卵巢组织中的卵泡损失并影响生育能力，移植后阶段是卵巢组织冷冻复苏-移植过程中卵泡损失的主要阶段，组织移植是影响卵巢组织冷冻复苏-移植效果的主要因素。

【关键词】 受精，体外； 生育力保存； 卵巢组织玻璃化冷冻保存； 卵巢组织移植

Experimental animal studies on the effect of ovarian tissue vitrification-thawed-transplantation and *in vitro* fertilization outcome

Xu Dabing, Zhang Yi, Gu Jiayi, Wang Liang, Sun Ningxia

Department of Reproductive Medicine, the Second Affiliated Hospital of Naval Medical University, Shanghai 200003, China

Corresponding author: Sun Ningxia, Email: suesunchzh@126.com, Tel: +86-21-81886715

【Abstract】 **Objective** To investigate the effects of vitrification and transplantation on mouse ovarian tissues. **Methods** Female ICR mice were divided into three groups: fresh-control group (*in vitro* oocyte maturation and fertilization, *n*=9), fresh-transplanted group (ovarian tissue transplantation, *in vitro* oocyte maturation and fertilization, *n*=9), frozen-transplanted group (ovarian tissue vitrification-thawed-transplantation, *in vitro* oocyte maturation and fertilization, *n*=9). Additionally, frozen-thawed group (ovarian tissue vitrification-thawed, *n*=6) and ovariectomy group (ovariectomy, *n*=6) were also set up, to more directly explain the effects of vitrification and freezing on the number of follicles and the changes of endocrine function after ovarian transplantation. We determined the number of follicles by hematoxylin-eosin (HE) staining, neovascularization by CD31 immunohistochemical staining, tissue fibrosis by Masson staining, and serum sex hormone levels by enzyme-linked immunosorbent assay (ELISA) three weeks following ovarian tissue transplantation. In addition, we counted the number of

oocytes obtained, oocytes *in vitro* fertilized, as well as blastocysts. **Results** The number of total follicles in both the fresh-transplanted group and the frozen-transplanted group significantly decreased compared with the fresh-control group (all $P<0.001$) and the frozen-thawed group (all $P<0.001$). The CD31-positive rate of ovarian tissues in the fresh-transplanted group was significantly higher than that in the fresh-control group ($P=0.044$). Although the CD31-positive rate was higher in the frozen-transplanted group than in the fresh-control group, there was no statistical distinction ($P=0.162$). The fibrosis area percentage of ovarian tissues in both the fresh-transplanted group and the frozen-transplanted group increased significantly compared with the fresh-control group ($P=0.004$; $P=0.005$). Serum estradiol level in the fresh-transplanted group and the frozen-transplanted group was significantly lower than that in fresh-control group ($P=0.005$; $P=0.001$), significantly higher than that in the ovariectomy group ($P=0.011$; $P=0.035$). Serum follicle-stimulating hormone (FSH) level in the fresh-transplanted group and the frozen-transplanted group was significantly higher than that in the fresh-control group ($P=0.040$; $P=0.012$), significantly lower than that in the ovariectomy group ($P=0.001$; $P=0.004$). In comparison to the fresh-control group, the number of oocytes retrieved in the fresh-transplanted group and the frozen-transplanted group decreased significantly (all $P<0.001$). Furthermore, the number of oocytes retrieved in the fresh-transplanted group was higher than that in the frozen-transplanted group, and yet there was no statistical difference ($P=0.272$). And the number of oocytes *in vitro* fertilized and blastocysts in the fresh-transplanted group and the frozen-transplanted group were significantly lower than those in the fresh-control group (all $P<0.001$). The number of total follicles, CD31-positive rate, fibrosis area rate, serum estradiol, and FSH levels, the number of oocytes *in vitro* fertilized and blastocysts were no substantially distinction between the fresh-transplanted group and the frozen-transplanted group (all $P>0.05$). **Conclusion** After ovarian tissue vitrification-thawed and transplantation, follicular growth, endocrine function, and fertility were restored in the mouse model, confirming that ovarian tissue vitrification is an effective method for female fertility preservation. Both vitrification and transplantation could cause follicles to be lost and fertility to decrease. And post-transplantation stage is the primary stage of follicle loss during ovarian tissue frozen-thawed-transplantation, and transplantation is the predominant factor affecting the effectiveness of ovarian tissue frozen-thawed-transplantation.

【Key words】 Fertilization *in vitro*; Fertility preservation; Ovarian tissue vitrification; Ovarian tissue transplantation

DOI：10.3760/cma.j.cn101441-20221214-00563

收稿日期　2022-12-15　本文编辑　宋培培

引用本文：刘艳丽，申峻涵，邝义会，等. 复发性交界性卵巢肿瘤患者双附件切除后完成活产 1 例病例报道[J]. 中华生殖与避孕杂志, 2023, 43(2): 158-163. DOI: 10.3760/cma.j.cn101441-20221214-00563.

复发性交界性卵巢肿瘤患者双附件切除后完成活产 1 例病例报道

刘艳丽[1]　申峻涵[1]　邝义会[1]　李嘉恒[1]　杜姗姗[1]　李静[1]　郜翔[2]

管一春[1]

[1]郑州大学第三附属医院生殖中心，郑州 450000；[2]郑州大学第三附属医院妇产科，郑州 450000

通信作者：管一春，Email：lisamayguan@126.com

【摘要】 目的　探讨复发性交界性卵巢肿瘤患者保留生育力的手术方法和辅助生殖技术助孕策略。方法　回顾性分析 1 例复发性交界性卵巢肿瘤患者的病例资料。该患者因双侧卵巢复发性交界性肿瘤，多次入院治疗行右附件切除术和左附件囊肿剥除术。患者未避孕 3 年未孕，考虑该患者强烈的生育需求，采用微刺激方案进行促排卵治疗，辅助生殖技术助孕过程中左侧卵巢肿瘤显著增大，随后行腹腔镜下左附件切除术，选取健康的卵巢皮质冷冻保存，以保留生育能力。结果　患者共经历了 5 次控制性促排卵，形成了 7 枚可利用胚胎。患者于第 3 次冻胚周期移植获得成功妊娠，并分娩一活婴。患者尚有 2 枚胚胎和 3 片卵巢组织冻存。结论　年轻且有生育需求的交界性卵巢肿瘤患者，可实施保留生育能力的手术和辅助生殖技术助孕，虽在一定程度上可能会导致疾病复发风险提高，但并不影响患者的生存质量，且使得患者的生育愿望得到实现。

【关键词】 卵巢肿瘤；　低温保存；　生育力保存；　交界性卵巢肿瘤；　胚胎冷冻；　卵巢组织冷冻

基金项目：河南省医学科技攻关计划联合共建项目（2018020181）；河南省科技攻关项目（222102310329）；河南省中青年卫生健康科技创新领军人才培养项目（YXKC2021020）；国家卫生健康委科学研究基金河南省医学科技攻关计划省部共建项目（SBGJ202102180）；国家重点研发计划 （2021YFC2700602）

A case report of completed live birth after bilateral adnexal resection for patients with recurrent borderline ovarian tumors

Liu Yanli[1], Shen Junhan[1], Kuang Yihui[1], Li Jiaheng[1], Du Shanshan[1], Li Jing[1], Gao Xiang[2], Guan Yichun[1]

[1] Reproductive Center of the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450000, China; [2] Department of Obstetrics and Gynecology, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450000, China

Corresponding author: Guan Yichun, Email: lisamayguan@126.com

【Abstract】 **Objective** To explore surgical approaches to preserve fertility and assisted reproductive technology strategies for pregnancy in patients

with recurrent borderline ovarian tumors. **Methods** A case of recurrent borderline ovarian tumor was retrospectively analyzed. The patient was admitted several times and underwent right adnexectomy and cysts debulking in the left ovary for recurrent borderline tumors. The patient was infertile for 3 years without contraception. Considering the patient's strong desire for childbearing, ovulation treatment was performed with a microstimulation protocol. The left ovarian tumor enlarged significantly during the process of assisted reproductive technology for pregnancy assistance, left oophorectomy was carried by laparoscopic and healthy ovarian cortex was frozen to preserve fertility. **Results** The patient underwent 5 times of controlled ovulation cycles, acquired 7 available embryos. The patient had a successful pregnancy and delivered a live baby on the third frozen embryo cycle transfer. The patient still had 2 embryos and 3 pieces of ovarian tissue frozen. **Conclusion** Patients with borderline ovarian tumors who are young and have fertility needs can undergo fertility preserving surgery and assisted reproductive technology to help them get pregnant, which may lead to a higher risk of disease recurrence to a certain extent, but it does not affect the quality of patients' survival and allows the patient to achieve her fertility aspirations.

【Key words】 Ovarian Neoplasms; Cryopreservation; Fertility preservation; Borderline ovarian tumors; Embryo cryopreservation; Ovarian tissue cryopreservation

Fund Program: Henan Province Medical Science and Technology Research Program Joint Construction Project (2018020181);Henan Provincial Science and Technology Tackling Project (222102310329); Henan Young and Middle-aged Health Science and Technology Innovation Leading Talent Training Project (YXKC2021020); National Health Commission Scientific Research Foundation Henan Medical Science and Technology Research Program Provincial Joint Construction Project (SBGJ202102180); National Key R&D Program (2021YFC2700602)

DOI：10.3760/cma.j.cn101441-20230106-00015

收稿日期 2023-01-06 本文编辑 王李艳

引用本文：范咏琪，杨丹丹，曹云霞，等. 褪黑素在卵母细胞冷冻保存中的应用研究进展[J]. 中华生殖与避孕杂志, 2023, 43(2): 164-168. DOI: 10.3760/cma.j.cn101441-20230106-00015.

·生育力保存专栏·

褪黑素在卵母细胞冷冻保存中的应用研究进展

范咏琪 杨丹丹 曹云霞 章志国

安徽医科大学第一附属医院妇产科生殖中心，合肥 230032

通信作者：章志国，Email：zzg_100@163.com，电话：+86-18155106683

【摘要】 在卵母细胞低温保存过程中，冷冻保护剂的高毒性及其高渗透性，常造成卵母细胞内的氧化-抗氧化系统失衡，特别是细胞内活性氧含量的增加。褪黑素作为一种有效的抗氧化剂及自由基清除剂，能通过影响能量代谢和细胞信号转导，显著降低卵细胞内活性氧水平，保护线粒体功能，同时也发挥清除细胞内自由基的作用，实现冻融过程中抑制细胞内氧化应激水平，进而减轻卵母细胞在冷冻保存过程中的低温损伤，最终提高冷冻卵子的囊胚形成率及胚胎移植后的临床妊娠率。褪黑素应用于卵母细胞冷冻对于女性生育力保存研究具有积极意义。本文就褪黑素在卵母细胞冷冻过程中的进展进行综述。

【关键词】 褪黑素； 卵母细胞； 冷冻保存

基金项目：国家重大研发计划（2022YFC2703000）；国家自然科学基金（82071724）

Research progress on the application of melatonin in oocyte cryopreservation

Fan Yongqi, Yang Dandan, Cao Yunxia, Zhang Zhiguo

Reproductive Medicine Center, Department of Obstetrics and Gynecology, the First Affiliated Hospital of Anhui Medical University, Hefei 230032, China

Corresponding author: Zhang Zhiguo, Email: zzg_100@163.com, Tel: +86-18155106683

【Abstract】 During cryopreservation of oocytes, the high toxicity and high permeability of cryoprotectants often result in the imbalance of oxidant-antioxidant system in oocytes especially the increase of intracellular reactive oxygen species (ROS) content. As an effective antioxidant and free radical scavenger, melatonin can significantly reduce the level of ROS in oocytes by affecting energy metabolism and signal transduction, and protect mitochondrial function. At the same time, it also plays the role of scavenging free radicals in oocytes, and realizes the suppression of intracellular oxidative stress levels during freezing-thawing process, thereby reducing the cryoinjury of oocytes during cryopreservation, ultimately, improving the blastocyst formation rate of frozen-thawed oocytes and the clinical pregnancy rate after embryo transfer. The application of melatonin in oocyte cryopreservation has a positive significance for the research of female fertility preservation. This article reviews the progress of melatonin in oocyte freezing.

【Key words】 Melatonin; Oocyte; Cryopreservation

Fund program: National Key Research and Development Program of China (2022YFC2703000); National Natural Science Foundation of China (82071724)

DOI：10.3760/cma.j.cn101441-20211108-00494

收稿日期 2021-11-11 本文编辑 王李艳

引用本文：孙亚婷，王佳，李晓霞，等. 超长方案常规体外受精多精受精发生的影响因素分析[J]. 中华生殖与避孕杂志, 2023, 43(2): 169-175. DOI: 10.3760/cma.j.cn101441-20211108-00494.

超长方案常规体外受精多精受精发生的影响因素分析

孙亚婷　王佳　李晓霞　朱爱珍

山西省运城市中心医院生殖医学科，运城 044000

通信作者：朱爱珍，Email： zhuaizhen8768@163.com， Tel： +86-13835968768

【摘要】 目的　探讨超长方案常规体外受精（*in vitro* fertilization，IVF）多精受精发生的影响因素。方法　本研究为回顾性病例对照分析。选择 2018 年 10 月至 2021 年 8 月期间在山西省运城市中心医院生殖医学科采用超长方案行常规 IVF 的 316 例患者，按照本周期多精受精的发生与否分成正常受精组和多精受精组。分别统计两组患者的一般情况和临床助孕情况。将单因素分析中 *P*<0.15 的相关因素纳入 logistic 回归模型进行多因素分析。结果　316 个 IVF 周期的多精受精周期发生率为 71.84%（227/316）。正常受精组和多精受精组的女方年龄、不孕年限、原发不孕占比、不孕因素、体质量指数（body mass index， BMI）、基础卵泡刺激素（follicle-stimulating hormone，FSH）水平和基础抗苗勒管激素（anti-Müllerian hormone，AMH）水平差异均无统计学意义（均 *P*>0.05）。正常受精组和多精受精组的促性腺激素（gonadotropin，Gn）启动剂量、Gn 总剂量、Gn 使用时间和人绒毛膜促性腺激素（human chorionic gonadotropin，hCG）注射日孕酮差异均无统计学意义（均 *P*>0.05）；多精受精组直径≥14 mm 的卵泡数［（13.66±4.51）个］、hCG 注射日雌二醇［17 247.49±9 450.74） pmol/L］和获卵数［（17.48±7.37）个］明显高于正常受精组［（11.78±3.54）个，*P*<0.001；（14 135.29±7 369.84） pmol/L，*P*=0.002；（13.01±6.17）个，*P*<0.001］；多精受精组的 hCG 注射日黄体生成素（luteinizing hormone，LH）水平［（0.79±0.51） U/L］明显低于正常受精组［（1.02±0.78） U/L，*P*=0.014］。logistic 回归结果显示：直径≥14 mm 卵泡数、hCG 注射日雌二醇和 hCG 注射日孕酮未能进入回归方程（分别为 *OR*=1.063、*OR*=1.676 和 *OR*=1.078，均 *P*>0.05）；hCG 注射日 LH 和获卵数与多精受精的发生相关（分别为 *OR*=1.900，*P*=0.028 和 *OR*=2.539，*P*=0.003）。结论　超长方案常规 IVF 多精受精周期发生率偏高；与其多精受精的发生有显著相关性的指标有直径≥14 mm 卵泡数、hCG 注射日雌二醇、hCG 注射日 LH 和获卵数；hCG 注射日 LH 偏低和获卵数较多是超长方案常规 IVF 多精受精发生的独立危险因素，其中获卵数对多精受精发生的影响最大。

【关键词】 受精，体外； 多精受精； 影响因素； 超长方案

基金项目：山西省卫生健康委科研课题（2022054）

Influencing factors of polyspermy during conventional *in vitro* fertilization in super-long protocol

Sun Yating, Wang Jia, Li Xiaoxia, Zhu Aizhen

Department of Reproductive Medicine, Yuncheng Central Hospital of Shanxi Province, Yuncheng 044000, China

Corresponding author: Zhu Aizhen, Email: zhuaizhen8768@163.com, Tel: +86-13835968768

【**Abstract**】 **Objective** To investigate influencing factors of polyspermy during conventional *in vitro* fertilization (IVF) in super-long protocol. **Methods** This study was a retrospective case-control analysis. From October 2018 to August 2021, 316 patients who underwent conventional IVF using super-long protocol in the Department of Reproductive Medicine, Yuncheng Central Hospital of Shanxi Province were selected and divided into normal fertilization group and polyspermy fertilization group according to polyspermy fertilization incidence in this cycle. The general data and clinical assisted pregnancy data in the two groups were analyzed. The correlation factors of $P<0.15$ in the single factor analysis were included in logistic regression model for multivariate analysis. **Results** There were 227 polyspermy fertilization cycles out of 316 IVF cycles, and the incidence of polyspermy fertilization was 71.84%. There were no significant differences in female age, infertility duration, primary infertility ratio, infertility factors, body mass index (BMI), basal follicle-stimulating hormone (FSH) level and basal anti-Müllerian hormone (AMH) level between normal fertilization group and polyspermy fertilization group (all $P>0.05$). There were no significant differences in gonadotropin (Gn) initiation dosage, total dosage and duration of Gn used, and progesterone (P) on human chorionic gonadotropin (hCG) injection day between normal fertilization group and polyspermy fertilization group (all $P>0.05$). The number of follicles with a diameter of ≥14 mm, estradiol (E_2) on hCG injection day and the number of retrieved oocytes in polyspermy fertilization group were significantly higher than those in normal fertilization group [13.66±4.51 *vs*. 11.78±3.54, $P<0.001$; (17 247.49±9 450.74) pmol/L *vs*. (14 135.29±7 369.84) pmol/L, $P=0.002$; 17.48±7.37 *vs*. 13.01±6.17, $P<0.001$]. Luteinizing hormone (LH) level on hCG injection day in polyspermy fertilization group was significantly lower than that in normal fertilization group [(0.79±0.51) U/L *vs*. (1.02±0.78) U/L, $P=0.014$]. Logistic regression results showed that the number of follicles with a diameter of ≥14 mm, E_2 and P level on hCG injection day could not enter the regression equation ($OR=1.063$, $OR=1.676$ and $OR=1.078$, respectively, all $P>0.05$); LH level on hCG injection day and the number of retrieved oocytes were correlated with polyspermy ($OR=1.900$, $P=0.028$; $OR=2.539$, $P=0.003$). **Conclusion** The incidence of polyspermy fertilization cycle during conventional IVF in super-long protocol was high. The number of follicles with a diameter of ≥14 mm, E_2 and LH levels on hCG injection day and the number of retrieved oocytes were significantly correlated with the occurrence of polyspermy. Lower LH level on hCG injection day and larger number of retrieved oocytes were independent risk factors of conventional IVF polyspermy fertilization in super-long protocol, and the number of retrieved oocytes had the greater influence on polyspermy fertilization.

【**Key words**】 Fertilization *in vitro*; Polyspermy; Influencing factors; Super-long protocol

Fund program: Scientific Research Project of Shanxi Provincial Health Commission(2022054)

DOI： 10.3760/cma.j.cn101441-20211110-00498
收稿日期 2021-12-26 本文编辑 李天琦
引用本文：张玉瑢, 杨云, 李蓉, 等. 可溶性 CD36 与多囊卵巢综合征及代谢风险因素的相关性[J]. 中华生殖与避孕杂志, 2023, 43(2): 176-183. DOI: 10.3760/cma.j.cn101441-20211110-00498.

·临床研究·

可溶性 CD36 与多囊卵巢综合征及代谢风险因素的相关性

张玉瑢 杨云 李蓉 赵越

北京大学第三医院妇产科生殖医学中心，北京 100191

通信作者：赵越，Email：zhaoyue0630@163.com，电话：+86-10-82266590

【摘要】 目的 研究血清中可溶性 CD36（soluble CD36，sCD36）与多囊卵巢综合征（polycystic ovary syndrome，PCOS）及其代谢风险因素的相关性。方法 本研究采用病例对照研究，回顾性选择 2015 年 4 月至 2015 年 7 月期间在北京大学第三医院妇产科生殖医学中心接受体外受精-胚胎移植的 PCOS 患者（PCOS 组，*n*=110）和同期、年龄匹配的单纯因男性因素或输卵管因素不孕人群（对照组，*n*=108），收集受试者的一般资料、临床数据，采用酶联免疫吸附法测定血清中 sCD36 水平，并对 sCD36 及临床指标间的相关性进行分析，运用 logistic 回归和受试者工作特征（receiver operating characteristic，ROC）曲线判定 sCD36 对 PCOS 的诊断价值，进一步在 PCOS 组内根据体质量指数、血压、稳态模型胰岛素抵抗（insulin resistance，IR）指数和血脂分代谢亚组比较 sCD36 水平，分析 sCD36 在 PCOS 不同代谢类型中的作用。结果 PCOS 组血清 sCD36 水平为 1.27 μg/L，显著高于对照组（0.84 μg/L，*P*<0.001）；PCOS 组内，sCD36 水平与黄体生成素（*β*=9.537，*P*=0.012）、黄体生成素/卵泡刺激素（*β*=85.374，*P*=0.011）、雄烯二酮（*β*=10.449，*P*=0.028）、0.5 h 胰岛素（*β*=1.260，*P*=0.015）、1 h 胰岛素（*β*=1.213，*P*=0.014）之间存在线性正相关。sCD36 诊断 PCOS 的 ROC 曲线下面积为 0.827，并且其诊断灵敏度（84.54%）、约登指数（0.56）均高于雄烯二酮（65.10%、0.45）和睾酮（58.72%、0.40）。PCOS 合并 IR 亚组中，sCD36 水平显著高于 PCOS 不合并 IR 亚组且 sCD36 与 PCOS 患者中 IR 风险相关（*OR*=1.010，95% *CI*：1.004~1.017，*P*=0.002）。结论 PCOS 患者血清中 sCD36 水平具有良好的 PCOS 诊断效能，可作为 PCOS 发生风险预测标志物，并且与 PCOS 中 IR 相关。

【关键词】 多囊卵巢综合征； 可溶性 CD36； 代谢； 炎症； 胰岛素抵抗

基金项目：国家自然科学基金（81471427）；中国医学科学院医学与健康科技创新工程项目（2019-I2M-5-001）

Correlation of soluble CD36 with polycystic ovary syndrome and metabolic risk factors

Zhang Yurong, Yang Yun, Li Rong, Zhao Yue

Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Zhao Yue, Email: zhaoyue0630@163.com, Tel: +86-10-82266590

【Abstract】 Objective To analyze the correlation of soluble CD36 (sCD36) in serum with polycystic ovary syndrome (PCOS) and metabolic risk factors. **Methods** PCOS group (*n*=110) and the age matched patients with infertility due to male or tubal factors alone (*n*=108) who underwent *in vitro* fertilization-embryo transfer at the Center for Reproductive Medicine, Department of Obstetrics and Gynecology of Peking University Third Hospital from April 2015 to July 2015 were selected in this retrospective case-control study. General information and clinical data were collected, and serum sCD36 level was detected by enzyme-linked immunosorbent assay. Correlation analysis was used to determine the relationship between sCD36 and clinical indices. Logistic analysis and receiver operating characteristic (ROC) curve were used to determine the diagnostic value of sCD36 for PCOS. PCOS group was divided into subgroups based on body mass index, blood pressure, homeostasis model assessment for insulin resistance (IR) and serum lipids. And sCD36 level was compared between metabolic subgroups in patients with PCOS to analyze the role of sCD36 in different metabolic types of PCOS. **Results** In patients with PCOS, sCD36 level was 1.27 μg/L, which was significantly increased compared with 0.84 μg/L of control group (*P*<0.001). And in PCOS group, luteinizing hormone (*β*=9.537, *P*=0.012), luteinizing hormone/follicle-stimulating hormone (*β*=85.374, *P*=0.011), androstenedione (*β*=10.449, *P*=0.028), 0.5 h insulin (*β*=1.260, *P*=0.015) and 1 h insulin (*β*=1.213, *P*=0.014) showed positive linear correlation with sCD36 (all *P*<0.05). As for the diagnostic value of sCD36 for PCOS, the area under the curve of ROC was 0.827, meanwhile, the specificity (84.54%) and Youden index (0.56) of sCD36 were higher than those of androstenedione (65.10%, 0.45) and testosterone (58.72%, 0.40). In the subgroup of PCOS with IR, the level of sCD36 was significantly higher than that of the non-IR subgroup, and sCD36 was correlated with IR in patients with PCOS (*OR*=1.010, 95% *CI*:1.004–1.017, *P*=0.002). **Conclusion** The level of serum sCD36 has predictive value for PCOS. sCD36 can be used as a marker to predict the risk of PCOS and is related to IR in patients with PCOS.

【Key words】 Polycystic ovary syndrome; Soluble CD36; Metabolism; Inflammation; Insulin resistance

Fund program: National Natural Science Foundation of China (81471427); CAMS Innovation Fund for Medical Sciences (2019-I2M-5-001)

DOI：10.3760/cma.j.cn101441-20211201-00533
收稿日期　2021-12-03　本文编辑　宋培培
引用本文：马晓晨，祁玉娟，刘颖，等. 白细胞介素-22 在多囊卵巢综合征大鼠胰岛素抵抗中的作用机制[J]. 中华生殖与避孕杂志, 2023, 43(2): 184-190. DOI: 10.3760/cma.j.cn101441-20211201-00533.

·实验研究·

白细胞介素-22 在多囊卵巢综合征大鼠胰岛素抵抗中的作用机制

马晓晨[1]　祁玉娟[2]　刘颖[2]　孙芳[3]　严晓南[2]　张蓓[3]

[1]徐州医科大学徐州临床学院，徐州 221009；[2]徐州市中心医院生殖医学中心，徐州 221009；[3]徐州医科大学徐州临床学院妇产科，徐州 221009

通信作者：严晓南，Email：yanxiaonan@126.com，电话：+86-516-83956352；张蓓，Email:bettyzhang10@163.com，电话：+86-516-83956855

【摘要】 目的 研究胰腺白细胞介素-22（interleukin-22，IL-22）信号通路在多囊卵巢综合征（polycystic ovary syndrome，PCOS）大鼠胰岛素抵抗（insulin resistance，IR）中的作用机制。方法 选取 21 d 的 SD 大鼠按照计算机随机生成数字的方式分为对照组和 PCOS 组，每组各 10 只。PCOS 组大鼠皮下埋置双氢睾酮（dihydrotestosterone，DHT）硅胶缓释管 90 d。测定大鼠体质量，检测腹腔葡萄糖耐量试验（intraperitoneal glucose tolerance test，IPGTT）、胰岛素耐量试验（intraperitoneal insulin tolerance test，IPITT），酶联免疫吸附法（enzyme-linked immunosorbent assay，ELISA）检测血清 IL-22 和空腹胰岛素（fasting insulin，FINS），计算胰岛素稳态指数（homeostasis model assessment of insulin resistance，HOMA-IR），免疫荧光染色观察胰岛 β 细胞中 IL-22 受体 1（interleukin-22 receptor 1，IL-22R1）的定位与差异性表达，蛋白印迹法检测大鼠胰腺组织 IL-22、酪氨酸蛋白激酶 1（Janus kinase 1，JAK1）、信号转导与转录激活因子 3（signal transducer and activator of transcription 3，STAT3）蛋白表达水平。结果 PCOS 组体质量［（420.50+10.26） g］明显高于对照组［（314.40+6.54） g，*P*=0.003］，血清 IL-22 浓度［（9.86±1.41） ng/L］低于对照组［（16.07±4.68） ng/L，*P*=0.038］，PCOS 组 FINS［（17.97±2.86） mU/L］、HOMA-IR （4.46±0.80）明显高于对照

组［（13.05±2.12） mU/L，*P*=0.001；2.99±0.61，*P*=0.001］。PCOS 组 IPGTT 30 min、60 min、90 min 血糖［（15.58±1.86） mmol/L、（10.71±2.07） mmol/L、（7.47±1.36） mmol/L］均明显高于对照组［（12.54±1.60） mmol/L，*P*=0.010；（8.33±1.02） mmol/L，*P*=0.026；（6.28±0.72） mmol/L，*P*=0.013］；PCOS 组的糖耐量曲线下面积[area under curve，AUC;（1 248.71±164.23）mmol/（L • min）]明显大于对照组［（1 007.29±102.29） mmol/（L • min），*P*=0.010］。PCOS 组 IPITT 60 min、90 min、120 min 血糖[（3.12±0.28）mmol/L、（2.62±0.17）mmol/L、（2.28±0.25） mmol/L］均明显高于对照组［（2.60±0.28） mmol/L，*P*=0.031；（2.10±0.33） mmol/L，*P*=0.026；（1.90±0.24） mmol/L，*P*=0.033］；PCOS 组胰岛素耐量 AUC［（414.60±23.06） mmol/（L • min）］明显大于对照组［（359.40±39.95） mmol/（L • min），*P*=0.044］。免疫荧光染色显示，IL-22R1 与 INS 在胰岛 β 细胞内共表达，PCOS 组大鼠 IL-22R1 表达（48.26±3.83）较对照组（63.44±2.66）显著降低（*P*=0.031）。PCOS 组大鼠胰腺内 IL-22、p-STAT3 蛋白表达水平（0.82±0.09、0.77±0.09）较对照组明显下降（1.01±0.06，*P*=0.025；1.01±0.07，*P*=0.015）。结论　在 PCOS 大鼠胰腺中，IL-22 通过影响 STAT3 信号通路活化，降低 p-STAT3 水平，参与 IR 的发生。

【关键词】　多囊卵巢综合征；　胰岛素抵抗；　白细胞介素-22；　胰岛 β 细胞

基金项目：国家自然科学基金（81571405）；江苏省自然科学基金（BK20161169）

Mechanism of interleukin-22 regulating insulin resistance in polycystic ovary syndrome rats

Ma Xiaochen[1], Qi Yujuan[2], Liu Ying[2], Sun Fang[3], Yan Xiaonan[2], Zhang Bei[3]

[1] Xuzhou Clinical School of Xuzhou Medical University, Xuzhou 221009, China; [2] Clinical Center of Reproductive Medicine, Xuzhou Central Hospital, Xuzhou 221009, China; [3] Department of Obstetrics and Gynecology, Xuzhou Clinical School of Xuzhou Medical University, Xuzhou 221009, China

Corresponding authors: Yan Xiaonan, Email: yanxiaonan@126.com, Tel: +86-516-83956352; Zhang Bei,Email: bettyzhang10@163.com, Tel: +86-516-83956855

【 Abstract 】 **Objective** To evaluate the mechanism of pancreatic interleukin-22 (IL-22) signaling pathway regulating insulin resistance (IR) in polycystic ovary syndrome (PCOS) rats. **Methods** Postnatal 21 d SD rats were divided into control group and PCOS group with 10 rats in each group based on numbers randomly generated by computer. PCOS rats implanted with a silastic tube filled with dihydrotestosterone (DHT) at dosage of 7.5 mg. Their body weight was monitored weekly. At the end of the experiment, the intraperitoneal glucose tolerance test (IPGTT) and intraperitoneal insulin test (IPITT) were conducted, the serum IL-22 and fasting insulin (FINS) were monitored through the enzyme-linked immunosorbent assay (ELISA), and homeostasis model assessment of insulin resistance (HOMA-IR) was calculated. The location and differential expression of the interleukin-22 receptor 1 (IL-22R1) in pancreatic β cells were observed by immunofluorescence staining, and the expressions of the IL-22, Janus kinase 1 (JAK1), signal transducer and activator of transcription 3 (STAT3) proteins were detected by Western blotting. **Results** Compared with control group, the body

weight was increased [(420.50±10.26) g *vs.* (314.40±6.54) g, *P*=0.003] and the serum level of IL-22 in PCOS group was decreased [(9.86±1.41) ng/L *vs.* (16.07±4.68) ng/L, *P*=0.038]. The levels of FINS and HOMA-IR were higher in PCOS group than in control group [(17.97±2.86) mU/L *vs.* (13.05±2.12) mU/L, *P*=0.001; 4.46±0.80 *vs.* 2.99±0.61, *P*=0.001]. The glucose levels in IPGTT test were significantly elevated in PCOS group in 30 min, 60 min and 90 min compared with control group [(15.58±1.86) mmol/L *vs.* (12.54±1.60) mmol/L, *P*=0.010;(10.71±2.07) mmol/L *vs.* (8.33±1.02) mmol/L, *P*=0.026; (7.47±1.36) mmol/L *vs.* (6.28±0.72) mmol/L, *P*=0.013], as well as the area under curve (AUC) [(1 248.71±164.23) mmol/(L·min) *vs.* (1 007.29±102.29) mmol/(L·min), *P*=0.010]. Following IPITT, compared with control group, PCOS group showed significantly higher 60 min [(3.12±0.28) mmol/L *vs.* (2.60±0.28) mmol/L, *P*=0.031], 90 min [(2.62±0.17) mmol/L *vs.* (2.10±0.33) mmol/L, *P*=0.026] and 120 min glucose level [(2.28±0.25) mmol/L *vs.* (1.90±0.24) mmol/L, *P*=0.033], as well as the AUC [(414.60±23.06) mmol/(L·min) *vs.* (359.40±39.95) mmol/(L·min), *P*=0.044]. The immunofluorescence results suggested that IL-22R1 and INS were colocalized in pancreatic β cells and the expression of IL-22R1 was lower in PCOS group than in control group (48.26±3.83 *vs.* 63.44±2.66, *P*=0.031). Further, the levels of pancreatic IL-22 and p-STAT3 protein were significantly lower in PCOS group than in control group (0.82±0.09 *vs.* 1.01±0.06, *P*=0.025; 0.77±0.09 *vs.* 1.01±0.07, *P*=0.015). **Conclusion** Our results demonstrated that the abnormality of IL-22 may result in IR through attenuating the activation of STAT3 signaling pathway and decreasing the level of p-STAT3 in the pancreatic tissue of PCOS rats.

【Key words】 Polycystic ovary syndrome; Insulin resistance; Interleukin-22; Pancreatic β cells

Fund program: National Natural Science Foundation of China (81571405); Natural Science Foundation of Jiangsu Province (BK20161169)

DOI：10.3760/cma.j.cn101441-20220730-00319
收稿日期 2022-08-01 本文编辑 孙敏
引用本文：邓凤, 杨硕, 宋雪凌, 等. 辅助生殖技术助孕中卵巢扭转的临床特点与诊治——十年病例分析[J]. 中华生殖与避孕杂志, 2023, 43(2): 191-197. DOI: 10.3760/cma.j.cn101441-20220730-00319.

·临床报道·

辅助生殖技术助孕中卵巢扭转的临床特点与诊治——十年病例分析

邓凤 杨硕 宋雪凌 杨艳 张佳佳 杨蕊 马彩虹 李蓉 乔杰

北京大学第三医院妇产科生殖医学中心，北京 100191

通信作者：李蓉，Email：roseli001@sina.com，电话：+86-10-82266836

【摘要】 目的 探讨体外受精-胚胎移植（*in vitro* fertilization and embryo transfer， IVF-ET）技术助孕中卵巢扭转的临床特点及可能影响治疗结局的因素。方法 回顾性描述分析 2010 年 1 月至 2019 年 12 月期间北京大学第三医院妇产科生殖医学中心 IVF-ET 助孕过程中发生卵巢扭转并行手术治疗患者的临床特点、周期特征、诊治过程，随访治疗及妊娠结局，分析其影响因素。结果 研究时间段内有控制性卵巢刺激（controlled ovarian stimulation，COS）周期 141 539 个和冻融胚胎移植（frozen-thawed embryo transfer， FET）周期 75 585 个，共计 50 例患者诊断卵巢扭转并于本院行手术治疗，90.0%发生在 COS 周期（39 例新鲜胚胎移植周期、6 例全胚冷冻周期），10.0%（5/50）发生在 FET 周期（自然周期/促排卵周期内膜准备）。86.0% （43/50）的患者发生在 IVF 助孕获得妊娠后，且 81.4%（35/43）发生在早期妊娠期间。仅 34.0%（17/50）的患者存在明确诱因，98.0%（49/50）的患者以腹痛为首发症状，所有患者均有下腹及附件区压痛的体征。术前超声检查提示扭转侧卵巢直径为（78.17±15.98） mm，对侧卵巢直径为（48.69±15.96） mm，双侧卵巢差值为（30.13±19.69） mm（−3.5~80.0 mm）。76.2% （32/42）的扭转侧卵巢超声可见血流信号。50 例患者均行手术治疗，术前诊断与手术确诊的符合率为 96%。术中发现 22 例（44%）扭转卵巢呈紫黑色，其中 16 例行腹腔镜/开腹患侧附件切除；34 例（68%）行患侧卵巢复位。附件切除组的卵巢扭转度数[（727.50±206.54）°]比卵巢复位组[（477.35±262.92）°，*P*=0.002]高；两组在发病到手术的时长、卵巢血流信号缺失率方面差异均无统计学意义（均 *P*>0.05）。44 例胚胎移植周期患者，84.1%（37/44）获得活产，1 例未孕，6 例自然流产。不良妊娠结局组与活产组在卵巢扭转发生的时间、手术方式、发病到手术的时长等方面差异均无统计学意义（均 *P*>0.05）。结论 IVF-ET 助孕患者卵巢扭转多发生于新鲜胚胎移植后的妊娠早期；以腹痛为主要表现，超声检查见患侧卵巢较对侧差异性增大有提示作用，探及卵巢血流信号并不能除外卵巢扭转。积极手术有助于明确诊断、保护生育力；对于扭转时间长、卵巢血流信号缺失、卵巢呈紫黑色的患者也有保留患侧卵巢的机会。卵巢扭转患者手术治疗后妊娠结局满意。

【关键词】 卵巢扭转； 受精，体外； 胚胎移植； 妊娠结局； 手术治疗

基金项目： 国家自然科学基金（82201806）

Clinical characteristics, diagnosis and treatment of ovarian torsion in assisted reproductive technology: cases analysis for ten years

Deng Feng, Yang Shuo, Song Xueling, Yang Yan, Zhang Jiajia, Yang Rui, Ma Caihong, Li Rong, Qiao Jie

Center of Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Li Rong, Email: roseli001@sina.com, Tel: +86-10-82266836

【Abstract】 Objective To explore the characteristics of ovarian torsion in *in vitro* fertilization-embryo transfer (IVF-ET) cycles and identify factors that may affect the outcome. **Methods** Patients who underwent surgery for ovarian torsion during IVF treatment in the Center of Reproductive Medicine, Department of

Obstetrics and Gynecology, Peking University Third Hospital from January 2010 to December 2019 were included. The general information, IVF cycle characteristics, and intraoperative findings of patients were retrospectively analyzed. The diagnosis and treatment process were summarized. The pregnancy outcomes were followed up, and the possible influencing factors were analyzed. **Results** There were 141 539 cycles of controlled ovarian stimulation (COS) and 75 585 cycles of frozen-thawed embryo transfer (FET) during the study period. A total of 50 patients were diagnosed with ovarian torsion and treated surgically, 90.0% of them occurred in the COS cycles (39 cases in fresh embryo transfer cycles and 6 cases in embryo freezing cycles), and 10.0% (5/50) occurred in the FET cycles (endometrial preparation in natural cycles or ovulation induction cycles). About 86.0% (43/50) of the patients occurred during pregnancy assisted with IVF-ET and 81.4% (35/43) occurred in the first trimester of pregnancy. All patients except one had abdominal pain as the first symptom, only 34.0% (17/50) of the patients had definite inducements, and all patients had signs of tenderness in the lower abdomen and adnexal area. Preoperative ultrasound examination showed that the average diameter of the torsional ovaries was (78.17±15.98) mm, compared with (48.69±15.96) mm in the controls, with an average difference of (30.13±19.69) mm (−3.5−80.0 mm). About 76.2% (32/42) of the torsional ovaries showed blood flow signals by color doppler ultrasound. All patients underwent surgery, and the coincidence rate between the preoperative diagnosis and the surgical diagnosis was 96%. Totally 22 torsional ovaries (44%) were found to be purplish-black, of which 16 cases underwent adnexectomy by laparoscopy or laparotomy. Totally 34 cases (68%) underwent ovarian detorsion. The average torsional degree of ovaries in the adnexectomy group was higher than that in the ovarian detorsion group [(727.50±206.54)° *vs*. (477.35±262.92)°, P=0.002]. There were no statistical differences between the two groups in the duration from onset to operation and the ratio of ovarian blood signal deficiency (all P>0.05). Among 44 patients with the embryo transfer, 84.1% (37/44) of patients obtained live birth, 1 case had implantation failure, and 6 cases had a spontaneous abortion. Patients with an adverse pregnancy outcome and patients with a live birth did not have significantly different ovarian torsion time, surgical methods, the duration from onset to operation, and other factors. **Conclusion** Ovarian torsion in patients with IVF-ET treatment mostly occurs in the first trimester of pregnancy after fresh embryo transfer. Abdominal pain accompanied by differential enlargement of bilateral ovaries may suggest the possibility of ovarian torsion. We are unable to rule out ovarian torsion by observation of ovarian blood flow with color Doppler ultrasound. Active surgery was helpful to make a clear diagnosis and protect the fertility of patients. Patients with long torsional durations, purplish-black ovaries, or ovarian blood deficiency still have the opportunity to retain the torsional ovary. The pregnancy outcome of patients with ovarian torsion was satisfactory after surgical treatment.

【Key words】 Ovarian torsion; Fertilization *in vitro*; Embryo transfer; Pregnancy outcome; Surgical treatment

Fund program: National Natural Science Foundation of China (82201806)

DOI：10.3760/cma.j.cn101441-20210202-00059
收稿日期　2021-08-23　本文编辑　孙敏
引用本文：冯科，曲晓伟，夏彦清，等. *DNAH1* 基因突变引起精子鞭毛多发形态异常的不育患者辅助生殖助孕结局分析[J]. 中华生殖与避孕杂志, 2023, 43(2): 198-203. DOI: 10.3760/cma.j.cn101441-20210202-00059.

·临床报道·

DNAH1 基因突变引起精子鞭毛多发形态异常的不育患者辅助生殖助孕结局分析

冯科　曲晓伟　夏彦清　万锋　王雪　陈圆辉　张翠莲　郭海彬
河南省人民医院生殖中心　郑州大学人民医院　河南省生殖医学工程国际联合实验室，郑州 450003

通信作者：郭海彬，Email：13673631683@163.com，电话：+86-13673631683

【摘要】 目的　探讨 *DNAH1* 基因突变引起的精子鞭毛多发形态异常（multiple morphological abnormalities of the sperm flagella，MMAF）不育患者行卵胞质内单精子注射（intracytoplasmic sperm injection，ICSI）助孕后的临床结局。方法　回顾性队列研究分析 2018 年 2 月至 2020 年 1 月期间在河南省人民医院生殖中心就诊的 39 例 MMAF 不育患者的临床资料和基因检测结果，12 例由 *DNAH1* 突变引起的 MMAF 患者为 *DNAH1* 阳性组，27 例未提示 *DNAH1* 突变的 MMAF 患者为 *DNAH1* 阴性组，选择同一时期男女双方年龄匹配进行 ICSI 助孕治疗的 100 例精子形态正常的男性不育症患者作为对照组，观察并分析 3 组不育夫妇进行辅助生殖助孕的治疗结局。结果　39 例 MMAF 患者均行全外显子组测序检测，其中 12 例患者检测到 *DNAH1* 基因突变，分别为 10 例复合杂合突变和 2 例纯合突变，另 27 例患者未检测到目前已知的引起 MMAF 的基因突变。3 组患者夫妇均行 ICSI 助孕治疗，*DNAH1* 阳性组、*DNAH1* 阴性组和对照组在获卵数和 M_{II} 卵子数上的差异均有统计学意义［（17.08±5.32）枚、（9.59±3.98）枚和（10.44±6.33）枚，*P*=0.001；（14.58±5.18）枚、（6.78±3.38）枚和（8.32±5.31）枚，*P*<0.001］，在胚胎种植率、临床妊娠率、早期流产率和活产率上的差异均无统计学意义（均 *P*>0.05）。12 例由 *DNAH1* 突变引起的不育患者夫妇共接受 12 个取卵周期，形成第 3 天胚胎 79 枚，首次新鲜胚胎或复融胚胎移植共 12 次，获得 10 个亲生子代。结论　对于由 *DNAH1* 基因突变引起的 MMAF 患者，ICSI 助孕可以帮助其生育亲生子代，且有较高的临床妊娠率和活产率。

【关键词】 不育，男性；　畸形精子症；　精子注射，细胞质内；　突变；　精子鞭毛多发形态异常；　全外显子组测序；　*DNAH1* 基因

基金项目：河南省医学科技攻关计划省部共建项目（SBGJ202001002、SBGJ202002003）

Analysis of assisted reproduction outcomes for infertility patients with multiple morphological abnormalities of the sperm flagella caused by *DNAH*1 gene mutation

Feng Ke, Qu Xiaowei, Xia Yanqing, Wan Feng, Wang Xue, Chen Yuanhui, Zhang Cuilian, Guo Haibin

Center for Reproductive Medicine, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, Henan Joint International Research Laboratory of Reproductive Bioengineering, Zhengzhou 450003, China

Corresponding author: Guo Haibin, Email: 13673631683@163.com, Tel: +86-13673631683

【**Abstract**】 **Objective** To investigate the clinical outcomes of infertility patients with multiple morphological abnormalities of the sperm flagella (MMAF) caused by *DNAH*1 gene mutation after intracytoplasmic sperm injection (ICSI). **Methods** A retrospective cohort study analyzed the clinical data and genetic test results of 39 MMAF infertility patients who were treated in the Center for Reproductive Medicine of Henan Provincial People's Hospital from February 2018 to January 2020. Twelve MMAF patients caused by *DNAH*1 mutations were acted as *DNAH*1 positive group and 27 MMAF patients with no *DNAH*1 mutations were acted as *DNAH*1 negative group. Totally 100 cases of infertility patients with normal sperm morphology and their spouses who were age-matched by both men and women for ICSI during the same period were selected as control group. The outcomes of assisted pregnancy treatment in the three groups were analyzed. **Results** All 39 MMAF patients underwent whole-exome sequencing. Among them, 12 patients had *DNAH*1 gene mutations, 10 cases of compound heterozygous mutations and 2 cases of homozygous mutations, and the other 27 cases were not detected the currently known *DNAH*1 mutations. The patients of three groups were treated with ICSI, and the differences in the number of oocytes obtained and the number of M_{II} oocytes in the *DNAH*1 gene positive group, *DNAH*1 gene negative group and control group were statistically significant (17.08±5.32, 9.59±3.98, 10.44±6.33, P=0.001; 14.58±5.18, 6.78±3.38, 8.32±5.31, P<0.001). There were no statistically significant differences in the embryo implantation rate, the clinical pregnancy rate, the embryo miscarriage rate and the live birth rate (all P>0.05). Among them, 12 couples of male infertility caused by *DNAH*1 mutation received a total of 12 cycles of oocyte extraction, forming 79 day 3 embryos, 12 times of the first fresh or frozen embryo transplantation, and 10 biological offspring were obtained. **Conclusion** For patients with MMAF caused by *DNAH*1 gene mutation, ICSI can help them to give birth to their own offspring, and has a higher clinical pregnancy rate and live birth rate.

【**Key words**】 Infertility, male; Teratozoospermia; Sperm injections, intracytoplasmic; Mutation; Multiple morphological abnormalities of the sperm flagella; Whole-exome sequencing; *DNAH*1 gene

Fund program: Henan Province Medical Science and Technology Research Plan Joint Provincial and Ministry Project (SBGJ202001002, SBGJ202002003)

DOI：10.3760/cma.j.cn101441-20210930-00445

收稿日期　2021-10-09　本文编辑　王李艳
引用本文：陈娜，李晶宇，崔琳琳. 辅助生殖技术单卵双胎风险因素研究进展[J]. 中华生殖与避孕杂志, 2023, 43(2): 204-208. DOI: 10.3760/cma.j.cn101441-20210930-00445.

·综述·

辅助生殖技术单卵双胎风险因素研究进展

陈娜　李晶宇　崔琳琳
山东大学生殖医学研究中心（山东大学第二医院）　生殖内分泌教育部重点实验室　山东省生殖医学重点实验室　山东省生殖健康临床医学研究中心　国家辅助生殖与优生工程技术研究中心，济南 250012

通信作者：崔琳琳，Email：fdclear3@126.com，电话：+86-15628796080

【摘要】 自 20 世纪 70 年代以来伴随着辅助生殖技术的飞速发展，多胎妊娠发生率明显增加，其所带来的孕期和产后母婴并发症也受到了公众的广泛关注。相关研究提示辅助生殖后代单卵双胎发生率高于自然妊娠，这不仅增加了新生儿相关不良结局的风险，甚至对子代远期健康都存在深远影响。本文对有关辅助生殖子代单卵双胎发生率和诱导排卵、卵子及胚胎操作、体外培养等因素对单卵双胎发生率的影响的相关文献进行了综述，以期深入探讨相关风险因素和可能的机制，为临床减少单卵双胎的发生提供潜在干预靶点。

【关键词】 双胎，单卵；　生殖技术，辅助；　受精，体外；　囊胚移植；　内细胞团

Research progress on risk factors of monozygotic twins in assisted reproductive technology

Chen Na, Li Jingyu, Cui Linlin
Center for Reproductive Medicine, the Second Hospital, Cheeloo College of Medicine, Shandong University; Key Laboratory of Reproductive Endocrinology of Ministry of Education, Shandong University; Shandong Key Laboratory of Reproductive Medicine; Shandong Provincial Clinical Research Center for Reproductive Health; National Research Center for Assisted Reproductive Technology and Reproductive Genetics, Shandong University, Jinan 250012, China
Corresponding author: Cui Linlin, Email: fdclear3@126.com, Tel: +86-15628796080

【Abstract】 With the rapid development of assisted reproductive technology since the 1970s, the incidence of multiple pregnancies has increased significantly, and the maternal and infant complications during pregnancy and postpartum caused by multiple pregnancies have received extensive public attention. Relevant investigations showed that the rate of monozygotic twins after assisted reproductive technology was higher than that of natural pregnancy, which not only increase the

risk of neonatal related adverse outcomes, but also has a far-reaching impact on the long-term health of offspring. In order to understand the related risk factors and potential mechanisms of monozygotic twins after assisted reproductive technology better and provide intervention target for reducing the rate of monozygotic twins in clinic, we sorted out papers about the rate of monozygotic twins in assisted reproductive technology offspring and the effects of factors such as ovulation induction, ovum and embryo manipulation, and *in vitro* culture on the incidence of monozygotic twins.

【Key words】 Twins, monozygotic; Reproductive technology, assisted; Fertilization *in vitro*; Blastocyst transfer; Inner cell mass

DOI：10.3760/cma.j.cn101441-20211221-00564
收稿日期 2021-12-24 本文编辑 王李艳
引用本文：鹿潇柳, 相珊, 连方, 等. 肠道菌群与胰岛素抵抗型多囊卵巢综合征的研究进展[J]. 中华生殖与避孕杂志, 2023, 43(2): 209-212. DOI: 10.3760/cma.j.cn101441-20211221-00564.

·综述·

肠道菌群与胰岛素抵抗型多囊卵巢综合征的研究进展

鹿潇柳[1] 相珊[1] 连方[2] 魏超峰[1] 辛欣[1]

[1]山东中医药大学第一临床医学院，济南 250011；[2]山东中医药大学附属医院中西医结合生殖与遗传中心，济南 250014

通信作者：连方，Email：f_lian@163.com，电话：+86-13706403122

【摘要】 多囊卵巢综合征（polycystic ovary syndrome， PCOS）是一种常见的妇科内分泌疾病，多伴有月经紊乱、肥胖、无排卵等，且50%~70%伴有胰岛素抵抗（insulin resistance， IR），其发病机制尚不清楚。肠道菌群是人体肠道内可作为环境因素参与疾病发生、发展的微生态系统。目前多项研究表明，肠道菌群与PCOS的发生密切相关。本文通过总结肠道菌群与IR型PCOS（IR-PCOS）的相关性研究，综述肠道菌群通过低度炎症、氧化应激、DNA甲基化和糖脂代谢等多条途径在IR-PCOS中的作用机制，为临床上的诊疗提供新思路。

【关键词】 多囊卵巢综合征； 胰岛素抵抗； 肠道菌群

基金项目：国家自然科学基金面上项目（8217152039）；中国博士后科学基金资助项目（2021M702044）

Progress in the study of gut microbiota and insulin resistant-polycystic ovary syndrome

Lu Xiaoliu[1], Xiang Shan[1], Lian Fang[2], Wei Chaofeng[1], Xin Xin[1]

[1] The First Clinical Medical College of Shandong University of Traditional Chinese Medicine, Jinan 250011, China; [2] Reproduction and Genetic Center, Shandong University of Traditional Chinese Medicine Affiliated Hospital Integrated Traditional Chinese and Western Medicine, Jinan 250014, China

Corresponding author: Lian Fang, Email: f_lian@163.com, Tel: +86-13706403122

【Abstract】 Polycystic ovary syndrome (PCOS) is a common gynecological endocrine disease, mostly associated with menstrual disorders, obesity, anovulation, etc., and 50%–70% with insulin resistance (IR), its pathogenesis is still unclear. Gut microbiota is a microecosystem involved in the occurrence and development of diseases as an environmental factor. A number of studies have shown that gut microbiota is closely related to the occurrence of PCOS. This paper summarizes the correlation between gut microbiota and IR-PCOS, and summarizes the mechanism of gut microbiota in IR-PCOS through low-grade inflammation, oxidative stress, DNA methylation and glucolipid metabolism, so as to provide new ideas for clinical diagnosis and treatment.

【Key words】 Polycystic ovary syndrome; Insulin resistance; Gut microbiota

Fund program: General Program of National Natural Science Foundation of China (8217152039); China Postdoctoral Science Foundation (2021M702044)

DOI：10.3760/cma.j.cn101441-20220516-00214

收稿日期　2022-05-26　本文编辑　王李艳

引用本文：楚婷，翟军. 子宫内膜非典型增生和早期子宫内膜癌不孕患者辅助生殖技术助孕的研究进展[J]. 中华生殖与避孕杂志, 2023, 43(2): 213-217. DOI: 10.3760/cma.j.cn101441-20220516-00214.

·综述·

子宫内膜非典型增生和早期子宫内膜癌不孕患者辅助生殖技术助孕的研究进展

楚婷　翟军

郑州大学第一附属医院生殖医学中心　河南省妇科疾病（生殖医学）临床医学研究中心，郑州 450052

通信作者：翟军，Email：bestzhai2005@163.com，电话：+86-13838292725

【摘要】 近年来，子宫内膜非典型增生和早期子宫内膜癌在年轻女性中的发生率呈现持续升高的趋势。对于这些患者的治疗往往是子宫切除术，但这种治疗方式使患者在治愈疾病的同时永久丧失了生育能力。在这些年轻患者中，很多尚有生育需求，保留生育功能的治疗为这些患者带来了生育的希望。本文将根据既往文献，对子宫内膜非典型增生和早期子宫内膜癌患者保留生育功能治疗后进行辅助生殖技术助孕的相关研究进展进行综述。

【关键词】 子宫内膜增生； 生殖技术，辅助； 子宫内膜肿瘤； 生育力保存

基金项目：国家自然科学基金面上项目（82071649）；河南省高校重点科研项目（22A320025）

Research progress of assisted reproductive technology in infertility patients with atypical endometrial hyperplasia and early endometrial cancer

Chu Ting, Zhai Jun

Center for Reproductive Medicine of the First Affiliated Hospital of Zhengzhou University, Henan Provincial Obstetrical and Gynecological Diseases (Reproductive Medicine) Clinical Research Center, Zhengzhou 450052, China

Corresponding author: Zhai Jun, Email: bestzhai2005@163.com, Tel: +86-13838292725

【 Abstract 】 In recent years, the incidence of atypical endometrial hyperplasia and early endometrial cancer in young women has shown a continuous increasing trend. The treatment for these patients is often hysterectomy, but this treatment modality makes patients permanently lose fertility while curing diseases. Among these young patients, many still have fertility needs. And fertility-preserving treatment brings hope for fertility to these patients. The article reviews the relevant research progress of assisted reproductive technology after fertility-preserving treatment in patients with atypical endometrial hyperplasia and early endometrial cancer according to the previous literatures.

【Key words】 Endometrial hyperplasia; Reproductive technology, assisted; Endometrial tumor; Fertility preservation

Fund program: General Program of National Natural Science Foundation of China (82071649); Key Scientific Research Projects of Higher Education Institutions in Henan Province (22A320025)