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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

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目 次

述 评

人工智能与辅助生殖1
乔杰

ART与AI专栏

从实验室到临床:AMH和抑制素B在女性生殖健康的
变革力量5
徐慧玉 李蓉
人工智能在辅助生殖控制性卵巢刺激应用的研究进展14
朱洁茹 欧建平
人工智能在男科实验诊断中的应用进展19
王家雄 商学军
人工智能在胚胎评估中的应用与进展26
王珊珊 孙海翔
以人工智能预测人类胚胎整倍性为例讨论算法解释性的意义31
张孝东 王浩 郭小妮 韩伟 韩树标 黄国宁

临床研究

宫血宁胶囊减少人工流产术后出血的有效性与安全性的
多中心随机双盲研究39
滕莉荣 李春颖 彭萍 赵淑萍 顾向应 郑晓霞 江静
倪亚莉 王敏 汪邦兰 任琛琛 单莉 林青 刘欣燕
宫腔粘连分离术后首个FET周期活产结局的临床影响
因素分析:一项真实世界研究45
汪晨 彭扬琴 陈辉 板得莹 李元 龚斐 林戈
胚胎冷冻时限对行FET助孕患者妊娠及产科结局影响59
陈海霞 匡拓 李芳 张静 穆晓环 吕永焕 田文艳
宋学茹 白晓红
ICSI退化对同胞卵母细胞正常受精后发育潜能及临床
结局的影响67
郑爱燕 孟庆霞 蒲艳 廖桂芝 李培培 丁洁

综 述

LncRNA在多囊卵巢综合征中的双重调控机制、临床价值
及中医药干预研究现状77
刘保松 李彩霞 孙莹莹 张小方 彭孟凡

自噬在女性生殖障碍性疾病中的研究进展·····	85
付胜蓝 李稳安 侯志金 孟昱时	
卵母细胞成熟及其受精过程关键基因的研究进展·····	90
陈佳瑶 张志平 王诗敏 朱鹏飞 武学清	
睾丸类器官培养技术的进展·····	96
黄明昊 杜国尧 吴登龙 乐威	
早发性卵巢功能不全小鼠模型的建立 ·····	103
熊湘蕾 司曼飞 刘梦宇 齐新宇	
《中华生殖与避孕杂志》第三届编辑委员会成员名单·····	18
《中华生殖与避孕杂志》第三届通讯编辑委员会成员名单·····	25
《中华生殖与避孕杂志》稿约 ·····	封三
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Editing

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Tel: 0086-21-64438169
Fax: 0086-21-64438975
Email: rande@sibpt.com
http://zhszybyzz.yiigle.com

Editor-in-Chief

Qiao Jie

Managing Director

Wang Jian

Publishing

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CONTENTS IN BRIEF

Editorial

Artificial intelligence and assisted reproductive technologies1
Qiao Jie

ART and AI Column

From bench to bedside: the transformative power of AMH and inhibin B in reproductive health of women5
Xu Huiyu, Li Rong

Research progress on the application of artificial intelligence in controlled ovarian stimulation14
Zhu Jieru, Ou Jianping

Advances in the application of artificial intelligence in experimental diagnosis in andrology19
Wang Jiexiong, Shang Xuejun

Applications and advances of artificial intelligence in embryo evaluation26
Wang Shanshan, Sun Haixiang

Clinical implications of algorithmic interpretations of artificial intelligence in human embryo ploidy prediction31
Zhang Xiaodong, Wang Hao, Guo Xiaoni, Han Wei, Han Shubiao, Huang Guoning

Clinical Studies

A multicenter, randomized, double-blind clinical trial on the efficacy and safety of Gongxuening Capsule in reducing postoperative bleeding after induced abortion39
Teng Lirong, Li Chunying, Peng Ping, Zhao Shuping, Gu Xiangying, Zheng Xiaoxia, Jiang Jing, Ni Yali, Wang Min, Wang Banglan, Ren Chenchen, Shan Li, Lin Qing, Liu Xinyan

Analysis of clinical factors affecting live birth outcomes in the first FET cycle after intrauterine adhesion separation: a real-world study45
Wang Chen, Peng Yangqin, Chen Hui, Ban Deying, Li Yuan, Gong Fei, Lin Ge

Effect of embryo cryostorage duration on pregnancy and obstetric outcomes in patients undergoing FET assisted reproduction59
Chen Haixia, Kuang Tuo, Li Fang, Zhang Jing, Mu Xiaohuan, Lyu Yonghuan, Tian Wenyan, Song Xueru, Bai Xiaohong

Effect of oocyte degeneration after ICSI on the developmental potential and clinical outcomes of sibling oocytes67
Zheng Aiyun, Meng Qingxia, Pu Yan, Liao Guizhi, Li Peipei, Ding Jie

Reviews

Dual regulation mechanism, clinical value of lncRNA in PCOS and intervention role of Traditional Chinese Medicine77
Liu Baosong, Li Caixia, Sun Yingying, Zhang Xiaofang, Peng Mengfan

Research progress of autophagy in female reproductive disorders	85
<i>Fu Shenglan, Li Wenan, Hou Zhijin, Meng Yushi</i>	
Progress on key genes in oocyte maturation and its fertilization process	90
<i>Chen Jiayao, Zhang Zhiping, Wang Shimin, Zhu Pengfei, Wu Xueqing</i>	
Advances in testicular organoid culture technology	96
<i>Huang Minghao, Du Guoyao, Wu Denglong, Le Wei</i>	
Establishment of premature ovarian insufficiency mouse model	103
<i>Xiong Xianglei, Si Manfei, Liu Mengyu, Qi Xinyu</i>	

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人工智能与辅助生殖

乔杰

北京大学第三医院妇产科生殖医学中心 女性生育力促进全国重

点实验室 国家妇产疾病临床医学研究中心, 北京 100191

Email: jie.qiao@263.net

【摘要】 将人工智能 (artificial intelligence, AI) 整合到人类辅助生殖技术 (assisted reproductive technology, ART) 中, 将是现代医学最具前景的进步之一。ART 包括体外受精、卵胞质内单精子注射、胚胎植入前遗传学检测和胚胎冷冻等, 传统上需要依赖于临床医生和胚胎学家的专业知识。考虑到这些技术的复杂性, 以及不可完全避免的固有主观性, 加之临床对更高成功率需求的不断增长, 研究人员和临床医生近年来不断在探索 AI 驱动的解决方案。AI 能够处理大量数据、识别模式和进行预测分析, 有可能彻底改变人类生殖医学的各个方面——从初始诊断到治疗计划制定, 再到胚胎选择和妊娠监测等。本述评探讨了 AI 在 ART 中的应用现状, 阐述了目前主要进展、挑战, 并对未来发展前景进行展望。

【关键词】 人工智能; 生殖技术, 辅助; 变革; 伦理; 监管

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Artificial intelligence and assisted reproductive technology

Qiao Jie

Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital; State Key Laboratory of Female Fertility Promotion; National Clinical Research Center for Obstetrics and Gynecology, Beijing 100191, China

Email: jie.qiao@263.net

【 Abstract 】 The integration of artificial intelligence (AI) into human assisted reproductive technology (ART) represents one of the most promising advancements in modern medicine. ART, which include *in vitro* fertilization,

intracytoplasmic sperm injection, preimplantation genetic testing and embryo freezing, have traditionally relied on the expertise of clinicians and embryologists. The inherent subjectivity and complexity of these processes, coupled with the ever-increasing demand for higher success rates, have prompted researchers and clinicians to explore AI-driven solutions. AI, with its capacity to process vast amounts of data, recognize patterns, and make predictive analyses, offers the potential to revolutionize every aspect of human reproduction, from initial diagnosis and treatment planning to embryo selection and pregnancy monitoring. This summary explores the current landscape of AI applications in ART, reviewing key advancements, challenges, and future prospects.

【 Key words 】 Artificial intelligence; Reproductive technology, assisted; Transformation; Ethics; Supervise

Fund program: Beijing Research Ward Excellence Program (BRWEP2024W0940901001); National Natural Science Foundation of China (82288102)

ART 与 AI 专栏

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从实验室到临床: AMH 和抑制素 B 在女性生殖健康的变革力量

徐慧玉 李蓉

女性生育力促进全国重点实验室 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@bjmu.edu.cn, 电话: +86-10-82265051

【摘要】 抗苗勒管激素 (anti-Müllerian hormone, AMH) 因其稳定的分泌模式, 已成为评估卵巢储备的可靠指标。与此同时, 抑制素 B 在卵泡中期 (月经第 7 天左右) 达到高峰, 并通过与卵泡刺激素的相互调节, 为实时监控卵巢功能提供了独特的洞察。本文深入探讨了 AMH 和抑制素 B 在评估卵巢储备及整体生殖健康中

的关键作用，还讨论了将 AMH 和抑制素 B 与其他临床指标结合，并整合到人工智能工具中的重要性。这种集成技术不仅显著提高了诊断精度，还优化了个性化治疗策略，并推动了卵巢功能评估的准确性和便捷性。此外，本文还展望了这些生物标志物在未来临床实践中的应用前景，强调了其在推动生殖健康管理领域创新和数据驱动应用中的核心作用。

【关键词】 抗苗勒管激素； 抑制素 B； 卵巢储备； 生殖健康； 生物标志物； 人工智能驱动诊断工具； 个性化医疗

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From bench to bedside: the transformative power of AMH and inhibin B in reproductive health of women

Xu Huiyu, Li Rong

State Key Laboratory of Female Fertility Promotion; Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Li Rong, Email: roseli001@bjmu.edu.cn, Tel: +86-10-82265051

【Abstract】 Anti-Müllerian hormone (AMH), known for its stable secretion patterns, has become a reliable indicator for evaluating ovarian reserve. Concurrently, inhibin B peaks around the seventh day of the menstrual cycle during the mid-follicular phase and provides unique insights into real-time ovarian function through its regulatory interactions with follicle-stimulating hormone. This article delves deeply into the crucial roles of AMH and inhibin B in assessing ovarian reserve and overall reproductive health. The article also discusses the importance of integrating AMH and inhibin B with other clinical indicators into artificial intelligence tools. This integration significantly enhances diagnostic precision, optimizes personalized treatment strategies, and advances the accuracy and convenience of ovarian function assessments. Furthermore, the article forecasts the future clinical applications of these biomarkers, emphasizing their central role in driving innovation and data-driven applications in reproductive health management.

【 Key words 】 Anti-Müllerian hormone; Inhibin B; Ovarian reserve; Reproductive health; Biomarkers; AI-driven diagnostic tool; Personalized medicine

Fund program: National Key Research and Development Program of China (2023YFC2705500, 2023YFC2705501, 2023YFC2705504); Innovation & Transfer Fund of Peking University Third Hospital (BYSYZHHC2023102, BYSYZHQB2020102)

·ART 与 AI 专栏·

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人工智能在辅助生殖控制性卵巢刺激应用的研究进展

朱洁茹 欧建平

中山大学附属第三医院生殖医学中心, 广州 510630

通信作者: 欧建平, Email: oujp3@mail.sysu.edu.cn, 电话:
+86-20-85256037

【摘要】 近年来, 人工智能 (artificial intelligence, AI) 技术在医疗健康领域取得了广泛应用, 尤其在疾病诊断与治疗决策方面带来了颠覆性变革。辅助生殖技术 (assisted reproductive technology, ART) 作为治疗不孕不育的重要方法, 亦受益于 AI 技术的融入, 特别是其核心环节——控制性卵巢刺激 (controlled ovarian stimulation, COS) 的智能化发展。传统 COS 方案的选择与调整高度依赖医生的经验与主观判断, 存在不确定性; 而 AI 技术通过深度学习患者的人口统计学特征、生殖内分泌水平及超声监测结果等多维度数据, 为 COS 提供了精准的个性化优化与动态调整方案。具体而言, AI 模型能够精确计算 COS 起始剂量、智能监测卵泡发育过程、实时预测最佳排卵触发时机, 从而显著提升诊疗效率, 减轻医生工作负担, 并为患者提供更为个体化、精准化的治疗方案。本文对 AI 在 COS 中促性腺激素起始剂量个体化优化、卵泡发育智能监测、卵巢反应性评估及最佳排卵触发时机预测四个方面的最新研究进展进行综述, 旨在为 AI 在辅助生殖超促排卵中的临床实践提供有价值的参考。

【关键词】 人工智能; 机器学习; 生殖技术, 辅助; 控制性卵巢刺激; 不孕

Research progress on the application of artificial intelligence in controlled ovarian stimulation

Zhu Jieru, Ou Jianping

Center for Reproductive Medicine, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, China

Corresponding author: Ou Jianping, Email: oujp3@mail.sysu.edu.cn, Tel: +86-20-85256037

【Abstract】 In recent years, artificial intelligence (AI) technology has seen widespread application in the field of healthcare, particularly revolutionizing disease diagnosis and treatment decisions. Assisted reproductive technology (ART), a crucial method for treating infertility, has also benefited from the integration of

AI, especially in the intelligent development of its core process--controlled ovarian stimulation (COS). Traditional COS protocols heavily relied on the experience and subjective judgment of physicians, leading to uncertainties. However, AI technology leverages deep learning to analyze multi-dimensional data, including patients' demographic characteristics, reproductive endocrine levels, and ultrasound monitoring results, to provide precise, personalized optimization and dynamic adjustments for COS. Specifically, AI models can accurately calculate the initial COS dosage, intelligently monitor follicular development, and predict the optimal timing for ovulation triggering in real-time, significantly enhancing diagnostic and treatment efficiency, reducing the workload of physicians, and offering more individualized and precise treatment plans for patients. This article reviews the latest research progress in AI applications for individualized optimization of initial gonadotropin dosage during COS, intelligent follicular monitoring, assessment of ovarian responsiveness, and prediction of the optimal timing for ovulation triggering, aiming to provide valuable insights for the clinical practice of AI in assisted reproductive hyperstimulation.

【 Key words 】 Artificial intelligence; Machine learning; Reproductive technology, assisted; Controlled ovarian stimulation; Infertility

·ART 与 AI 专栏·

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人工智能在男科实验诊断中的应用进展

王家雄¹ 商学军²

¹南京医科大学附属苏州医院 苏州市立医院生殖与遗传中心, 苏州

215002; ²南京大学医学院附属金陵医院 东部战区总医院泌尿外科,

南京 210002

通信作者: 商学军, Email: shangxj98@sina.com, 电话:

+86-13813905418

【摘要】 随着计算机硬件的突破和软件工程的进步，人工智能在包括医学领域的多个领域产生了深远影响。在男科实验研究领域，已有研究尝试利用人工智能模型进行精子质量检测，包括精液常规、精子形态和精子 DNA 完整性等。此外，人工智能也开始在其他男科检测领域，如病理学、影像学和遗传学检测中发挥作用。本文旨在对人工智能在男科实验诊断方面的研究进展进行综述，探讨当前人工智能检测的不足和开发中所面临的瓶颈问题，为未来人工智能在男科诊疗体系中的进一步应用提供参考。

【关键词】 人工智能； 男科； 临床检验； 深度学习

Advances in the application of artificial intelligence in experimental diagnosis in andrology

Wang Jiaxiong¹, Shang Xuejun²

¹ Center for Reproduction and Genetics, the Affiliated Suzhou Hospital of Nanjing Medical University; Suzhou Municipal Hospital, Suzhou 215002, China; ² Department of Urology, Jinling Hospital Affiliated to Nanjing University School of Medicine; General Hospital of Eastern Theater Command, Nanjing 210002, China

Corresponding author: Shang Xuejun, Email: shangxj98@sina.com, Tel: +86-13813905418

【 Abstract 】 With the breakthroughs in computer hardware and the advancement of software engineering, artificial intelligence (AI) has exerted a profound impact across various domains, including the medical field. In the realm of urological experimental research, studies have endeavored to employ AI models for the assessment of sperm quality, encompassing routine semen analysis, sperm morphology, and sperm DNA integrity testing. Moreover, AI is beginning to play a role in other urological diagnostic areas, such as pathology, radiology, and genetic testing. The purpose of this article is to summarize the research progress in AI applications within urological laboratory diagnostics, to discuss the current limitations and bottlenecks in AI detection, and to provide a reference for the further application of AI in the urological diagnostic and treatment framework.

【 Key words 】 Artificial intelligence; Andrology; Clinical laboratory; Deep learning

·ART 与 AI 专栏·

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人工智能在胚胎评估中的应用与进展

王珊珊 孙海翔

南京大学医学院附属鼓楼医院生殖医学和妇产医学中心, 南京
210008

通信作者: 孙海翔, Email: stevensunz@163.com, 电话:
+86-25-68183322

【摘要】 随着人工智能 (artificial intelligence, AI) 技术的快速发展, 其在胚胎评估方面的应用日益广泛。本文回顾了近年来 AI 在胚胎评估中的主要进展, 包括图像识别、胚胎质量评估和结局预测等。AI 模型可以有效分析大规模胚胎图像数据, 识别形态学特征, 从而提高评估的准确性和效率。此外, AI 还能够整合图像与临床数据, 提供个体化的胚胎评估策略。尽管 AI 在胚胎评估中展现出良好前景, 但仍面临模型可解释性及临床应用标准化等挑战。未来研究需深入探讨 AI 在胚胎评估中的应用潜力, 以推动生殖医学的发展与创新。

【关键词】 人工智能; 胚胎评估; 深度学习

Applications and advances of artificial intelligence in embryo evaluation

Wang Shanshan, Sun Haixiang

Center for Reproductive Medicine and Obstetrics and Gynecology, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing 210008, China.

Corresponding author: Sun Haixiang, Email: stevensunz@163.com, Tel: +86-25-68183322

【 Abstract 】 With the rapid development of artificial intelligence (AI) technology, its application in embryo evaluation is becoming more and more extensive. This article reviews the main progress of AI in embryo evaluation in recent years, including image recognition, embryo quality evaluation and outcome prediction. AI models can effectively analyze large-scale embryo image data and identify morphological features, thereby improving the accuracy and efficiency of evaluation. In addition, AI can also integrate images and clinical data to provide individualized embryo evaluation strategies. While AI shows promising potential in embryo evaluation, challenges remain in model interpretability and clinical application standardization. Future study needs to explore the application potential of AI in embryo evaluation in depth to promote the development and innovation of reproductive medicine.

【Key words】 Artificial intelligence; Embryo evaluation; Deep learning

·ART 与 AI 专栏·

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以人工智能预测人类胚胎整倍性为例讨论算法解释性的意义

张孝东¹ 王浩² 郭小妮¹ 韩伟¹ 韩树标¹ 黄国宁¹

¹重庆市妇幼保健院 重庆医科大学附属妇女儿童医院生殖医学中

心, 重庆 400010; ²中国食品药品检定研究院医疗器械检定所, 北

京 102629

通信作者: 黄国宁, Email: Gnhuang217@sina.com, 电话:

+86-23-63846879

【摘要】 人工智能 (artificial intelligence, AI) 技术有望辅助医生提升胚胎评估的准确性和效率。然而, 胚胎发育是一个连续的动态过程, 什么时段比较有意义? 还是整个发育过程都需要考虑? 部分研究团队采用静态图像分析丢失诸多重要信息; 另一部分团队利用算法驱动的“黑盒”模型计算胚胎发育视频, 解释性有限。机器学习及深度学习由于固有的复杂性易被滥用, 为了更精准地应用 AI, 本文以 AI 预测人类胚胎整倍性为例讨论算法解释性的意义及临床价值。

【关键词】 人工智能; 胚胎; 机器学习; 深度学习; 黑盒; 整倍性

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Clinical implications of algorithmic interpretations of artificial intelligence in human embryo ploidy prediction

Zhang Xiaodong¹, Wang Hao², Guo Xiaoni¹, Han Wei¹, Han Shubiao¹, Huang Guoning¹

¹ IVF Clinical Center, Chongqing Maternal and Child Healthcare Hospital; Affiliated Women's and Children's Hospital of Chongqing Medical University, Chongqing 400010, China; ²Institute for Medical Device Control, National Institutes for Food and Drug Control, Beijing 102629, China

Corresponding author: Huang Guoning, Email: Gnhuang217@sina.com, Tel: +86-23-63846879

【Abstract】 Artificial intelligence (AI) technology is expected to assist physicians in improving the accuracy and efficiency of embryo assessment. However, embryo development is a continuous and dynamic process, when is

meaningful or the whole development process need to be considered? Some research teams use static image analysis, which loses much important information, and others utilize algorithm-driven applications of "black-box" models to analyse embryo videos, which have limited their interpretability or explainability. Machine learning or deep learning is prone to abused due to its inherent complexity, and in order to apply AI more accurately, this paper discusses the clinical implications of algorithmic interpretations of AI in human embryo ploidy prediction.

【 Key words 】 Artificial intelligence; Embryo; Machine learning; Deep learning; Black-box; Ploidy

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宫血宁胶囊减少人工流产术后出血的有效性与安全性的多中心随机双盲研究

滕莉荣¹ 李春颖¹ 彭萍¹ 赵淑萍² 顾向应³ 郑晓霞⁴ 江静⁵

倪亚莉⁶ 王敏⁷ 汪邦兰⁸ 任琛琛⁹ 单莉¹⁰ 林青¹¹ 刘欣燕¹

¹中国医学科学院北京协和医院妇产科学系产科中心, 北京 100730;

²青岛大学附属妇女儿童医院妇科, 青岛 266034; ³天津医科大学总

医院妇产科, 天津 300052; ⁴济南市妇幼保健院妇科, 济南 250001;

⁵河北医科大学第二医院妇产科, 石家庄 050000; ⁶甘肃省妇幼保健院

生殖医学中心, 兰州 730050; ⁷大连市妇女儿童医疗中心(集团)

计划生育科, 大连 116011; ⁸安徽省妇女儿童医学中心门诊手术室, 合肥 230001; ⁹郑州大学第三附属医院妇科, 郑州 450052; ¹⁰西北妇女儿童医院妇科, 西安 710061; ¹¹首都医科大学附属北京友谊医院妇产科, 北京 100050

通信作者: 刘欣燕, Email: liuxymeng@163.com, 电话: +86-10-69156208

【摘要】 目的 评价宫血宁胶囊在减少人工流产后出血的有效性和安全性。方法 采用多中心随机双盲研究。11家分中心于2022年5月31日至2023年3月31日期间纳入484例宫内早孕接受负压电吸人工流产术的患者, 1:1按照中心区组随机方式分配到对照组和研究组。对照组术后口服安慰剂9d, 研究组术后口服宫血宁胶囊9d, 观察比较两组术后受试者阴道出血量、阴道出血时间、子宫内膜厚度、月经复潮时间及并发症等情况。结果 ①研究入组受试者484例, 完成研究472例。450例受试者纳入有效性分析集, 对照组224例, 研究组226例; 468例受试者纳入安全性分析集, 对照组236例, 研究组232例, 两组受试者一般资料具有可比性(均 $P>0.05$)。②研究组阴道出血量为 (13.30 ± 12.14) mL, 对照组阴道出血量为 (19.00 ± 17.67) mL, 组间差异有统计学意义($P<0.001$)。研究组出血天数小于4d的受试者比例[29.65% (67/226)]高于对照组[19.20% (43/224), $P=0.010$]。③月经复潮时间、子宫内膜厚度两组间差异均无统计学意义(均 $P>0.05$)。④研究组有3例受试者发生非疗效相关并发症, 对照组有11例受试者发生, 研究组非疗效相关并发症发生率[1.29% (3/232)]低于对照组[4.66% (11/236)], 差异有统计学意义($P=0.033$)。结论 人工流产后女性使用宫血宁胶囊治疗, 可明显减少阴道出血量, 且安全性良好, 易为受试者接受。

【关键词】 流产, 人工; 多中心研究; 随机对照试验; 宫血宁胶囊; 双盲

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A multicenter, randomized, double-blind clinical trial on the efficacy and safety of Gongxuening Capsule in reducing postoperative bleeding after induced abortion

Teng Lirong¹, Li Chunying¹, Peng Ping¹, Zhao Shuping², Gu Xiangying³, Zheng Xiaoxia⁴, Jiang Jing⁵, Ni Yali⁶, Wang Min⁷, Wang Banglan⁸, Ren Chenchen⁹, Shan Li¹⁰, Lin Qing¹¹, Liu Xinyan¹

¹ Obstetrics Center, Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China; ² Gynecology, Women and Children's Hospital, Qingdao University, Qingdao 266034, China; ³ Department of Gynecology and Obstetrics, Tianjin Medical University General Hospital, Tianjin 300052, China; ⁴ Department of Gynecology, Jinan Maternity and

Child Care Hospital, Jinan 250001, China; ⁵ Department of Gynecology and Obstetrics, the Second Hospital of Hebei Medical University, Shijiazhuang 050000, China; ⁶ Reproductive Medicine Center, Gansu Provincial Maternity and Child-care Hospital, Lanzhou 730050, China; ⁷ Family Planning Department, Dalian Women and Children's Medical Group, Dalian 116011, China; ⁸ Outpatient Operating Room, Anhui Women and Children's Medical Center, Hefei 230001, China; ⁹ Department of Gynecology, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China; ¹⁰ Department of Gynecology, Northwest Women's and Children's Hospital, Xi'an 710061, China; ¹¹ Department of Obstetrics and Gynecology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China

corresponding author: Corresponding author: Liu Xinyan, Email: liuxymeng@163.com, Tel: +86-10-69156208

【Abstract】 Objective To assess the efficacy and safety of Gongxuening Capsules in reducing post-abortion bleeding following artificial abortion. **Methods** A multicenter, randomized, double-blind study was conducted. From May 31, 2022 to March 31, 2023, 484 women who underwent vacuum aspiration abortion for early intrauterine pregnancy were enrolled in 11 centers and randomly assigned to control group and the study group at a 1 : 1 ratio using a center-block randomization method. Control group were administered a placebo of Gongxuening Capsules for 9 d, while the study group received the actual Gongxuening Capsules for the same duration. The outcomes measured included vaginal bleeding volume, duration of vaginal bleeding, endometrial thickness, time to menstrual recovery, and complications. **Results** 1) A total of 484 subjects were enrolled, and 472 completed the study. Totally 450 subjects were included in the efficacy analysis set, with 224 in control group and 226 in the study group; 468 subjects were included in the safety analysis set, with 236 in control group and 232 in the study group. The baseline characteristics of the two groups were comparable (all $P>0.05$). 2) The vaginal bleeding volume was lower in the study group [(13.30±12.14) mL] than in control group [(19.00±17.67) mL, $P<0.001$]. The proportion of subjects in the study group with bleeding days less than 4 d [29.65% (67/226)] was higher than that in control group [19.20% (43/224), $P=0.010$]. 3) No significant differences were observed between the two groups in terms of time to menstrual recovery and endometrial thickness (all $P>0.05$). 4) In the study group, 3 subjects experienced non-therapeutic-related complications, while 11 subjects in control group. The incidence of complications was lower in the study group [1.29% (3/232)] than in control group [4.66% (11/236), $P=0.033$]. **Conclusion** The administration of Gongxuening Capsules to women following artificial abortion significantly reduced vaginal bleeding volume and was associated with good safety, with the treatment being well-tolerated by the subjects.

【Key words】 Abortion, induced; Multicenter study; Randomized controlled trial; Gongxuening Capsules; Double-blind

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宫腔粘连分离术后首个 FET 周期活产结局的临床影响因素分析: 一项真实世界研究

汪晨¹ 彭扬琴² 陈辉³ 板得莹³ 李元³ 龚斐³ 林戈³

¹中南大学基础医学院 生殖与干细胞工程研究所, 长沙 410013; ²

湖南省生殖与遗传临床医学研究中心 中信湘雅生殖与遗传专科医院

院科研部, 长沙 410221; ³湖南省生殖与遗传临床医学研究中心 中

信湘雅生殖与遗传专科医院生殖中心, 长沙 410221

汪晨和彭扬琴对本文有同等贡献

通信作者: 林戈, Email: linggf@hotmail.com, 电话:

+86-13187057355

【摘要】 目的 探讨宫腔粘连分离术后首个冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期活产结局的临床影响因素。方法 采用回顾性病例对照研究, 分析 2019 年 1 月至 2022 年 6 月期间在中信湘雅生殖与遗传专科医院生殖中心行 FET 的宫腔粘连患者临床资料 ($n=6154$)。根据患者宫腔粘连的严重程度分为轻度粘连 ($n=172$)、中度粘连 ($n=5723$) 和重度粘连 ($n=259$), 并按照 FET 结局分为活产组与未活产组。通过多因素 logistic 回归对影响活产的危险因素和保护因素进行分析。结果 ①在轻度粘连患者中, 未找到影响活产率的独立因素。②在中度粘连患者中, 影响活产的保护因素包括继发不孕 ($OR=1.39$, 95% CI : 1.07~1.80, $P=0.015$)、术中同时行子宫内膜息肉 ($OR=1.38$, 95% CI : 1.05~1.83, $P=0.023$)、移植优质胚胎数 (1 枚胚胎 $OR=1.58$, 95% CI : 1.37~1.82, $P<0.001$; 2 枚胚胎 $OR=2.55$, 95% CI : 1.80~3.64, $P<0.001$)、移植 2 枚胚胎 ($OR=1.77$, 95%

CI: 1.48~2.12, $P<0.001$)、移植胚胎类型(囊胚 $OR=4.93$, 95% CI: 3.68~6.63, $P<0.001$; 囊胚+卵裂期胚 $OR=1.90$, 95% CI: 1.11~3.21, $P=0.021$)、植入前遗传学检测胚胎($OR=1.42$, 95% CI: 1.19~1.69, $P<0.001$)、移植前内膜厚度($OR=1.11$, 95% CI: 1.07~1.15, $P<0.001$)；影响活产的危险因素包括女方年龄($OR=0.94$, 95% CI: 0.92~0.96, $P<0.001$)、男方因素不孕($OR=0.83$, 95% CI: 0.71~0.96, $P=0.011$)、合并反复植入失败($OR=0.60$, 95% CI: 0.42~0.87, $P=0.007$)、合并单角子宫/双子宫($OR=0.25$, 95% CI: 0.06~0.79, $P=0.033$)、宫腔粘连评分($OR=0.94$, 95% CI: 0.89~0.98, $P=0.010$)、既往宫腔粘连分离手术次数($OR=0.83$, 95% CI: 0.77~0.90, $P<0.001$)、周期方案(降调节人工周期 $OR=0.56$, 95% CI: 0.45~0.69, $P<0.001$; 人工周期 $OR=0.62$, 95% CI: 0.51~0.76, $P<0.001$)。③在重度粘连患者中,影响活产的危险因素为人工周期($OR=0.25$, 95% CI: 0.07~0.80, $P=0.027$)。结论 影响宫腔粘连分离术后首个 FET 周期活产结局的临床因素在不同严重程度的粘连患者中结果不同。在中度粘连患者中,有 17 个临床指标影响活产率。在重度粘连患者中,人工周期是影响活产率的独立因素。

【关键词】 不孕症； 宫腔粘连； 生殖技术, 辅助； 冻融胚胎移植； 活产率

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Analysis of clinical factors affecting live birth outcomes in the first FET cycle after intrauterine adhesion separation: a real-world study

Wang Chen¹, Peng Yangqin², Chen Hui³, Ban Deying³, Li Yuan³, Gong Fei³, Lin Ge³

¹ Institute of Reproductive and Stem Cell Engineering, NHC Key Laboratory of Human Stem Cell and Reproductive Engineering; School of Basic Medical Sciences, Central South University, Changsha 410013, China; ² Department of Science and Research, Reproductive and Genetic Hospital of CITIC-XIANGYA; Clinical Research Center for Reproduction and Genetics in Hunan Province, Changsha 410221, China; ³ Reproductive Center, Reproductive and Genetic Hospital of CITIC-XIANGYA; Clinical Research Center for Reproduction and Genetics in Hunan Province, Changsha 410221, China

Wang Chen and Peng Yangqin contributed equally to the article

Corresponding author: Lin Ge, Email: linggf@hotmail.com, Tel: +86-13187057355

【Abstract】 **Objective** To investigate the independent clinical factors of live birth rate of the first frozen-thawed embryo transfer (FET) cycle after transcervical resection of adhesion (TCRA). **Methods** A retrospective case-control study was conducted to analyze the clinical data of patients with intrauterine adhesion (IUA) who received FET in Reproductive Center of Reproductive and Genetic Hospital of CITIC-XIANGYA from January 2019 to June 2022 ($n=6\ 154$). According to the severity of intrauterine adhesions in patients, they were classified into mild adhesions ($n=172$), moderate adhesions ($n=5\ 723$), and severe adhesions ($n=259$). Based on the FET outcome, the patients were divided into live birth group and non-live birth group. The risk factors and protective factors of live birth were analyzed by multivariate logistic regression. **Results** 1) No independent factor of live birth was found in the mild IUA group. 2) In the moderate IUA group, the protective factors of live birth included secondary

infertility ($OR=1.39$, 95% CI : 1.07–1.80, $P=0.015$), hysteroscopic polypectomy ($OR=1.38$, 95% CI : 1.05–1.83, $P=0.023$), No. of high-quality embryos transferred (one embryo: $OR=1.58$, 95% CI : 1.37–1.82, $P<0.001$; two embryos: $OR=2.55$, 95% CI : 1.80–3.64, $P<0.001$), two embryos transferred ($OR=1.77$, 95% CI : 1.48–2.12, $P<0.001$), embryo stage (blastocyst transferred, $OR=4.93$, 95% CI : 3.68–6.63, $P<0.001$; blastocyst+cleavage transferred $OR=1.90$, 95% CI : 1.11–3.21, $P=0.021$), preimplantation genetic testing embryo ($OR=1.42$, 95% CI : 1.19–1.69, $P<0.001$), endometrial thickness before transplantation ($OR=1.11$, 95% CI : 1.07–1.15, $P<0.001$). Risk factors of live birth included female age ($OR=0.94$, 95% CI : 0.92–0.96, $P<0.001$), infertility due to male factor ($OR=0.83$, 95% CI : 0.71–0.96, $P=0.011$), combined repeated implantation failure ($OR=0.60$, 95% CI : 0.42–0.87, $P=0.007$), combined unicornuate uterus/uterus didelphys ($OR=0.25$, 95% CI : 0.06–0.79, $P=0.033$), American Fertility Society score ($OR=0.94$, 95% CI : 0.89–0.98, $P=0.010$), No. of TCRA ($OR=0.83$, 95% CI : 0.77–0.90, $P<0.001$), gonadotropin-releasing hormone agonists down-regulation combined with artificial cycle ($OR=0.56$, 95% CI : 0.45–0.69, $P<0.001$), artificial cycle ($OR=0.62$, 95% CI : 0.51–0.76, $P<0.001$). 3) In the severe IUA group, the risk factor of live birth was artificial cycle ($OR=0.25$, 95% CI : 0.07–0.80, $P=0.027$). **Conclusion** The clinical factors that affect the live birth outcome of the first FET cycle after TCRA have different results in patients with different degrees of adhesion. In patients with moderate adhesions, there are 17 clinical indicators that affect the live birth rate. In patients with severe adhesions, the artificial cycle is an independent factor affecting the live birth rate.

【Key words】 Infertility; Intrauterine adhesion; Reproductive technology, assisted; Frozen-thawed embryo transfer; Live birth rate

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胚胎冷冻时限对行 FET 助孕患者妊娠及产科结局影响

陈海霞 匡拓 李芳 张静 穆晓环 吕永焕 田文艳 宋学茹

白晓红

天津医科大学总医院妇产科生殖医学中心 天津市女性生殖健康与

优生重点实验室, 天津 300052

通信作者: 白晓红, Email: bxhjj@163.com, 电话: +86-13821343592

【摘要】 目的 分析胚胎冷冻时限对冻融胚胎移植后患者的临床妊娠及产科结局的影响。方法 采用回顾性队列研究, 分析 2016 年 1 月至 2020 年 12 月期间在天津医科大学总医院妇产科生殖医学中心接受冻融胚胎移植的不孕症患者 2 662 例, 根据胚胎冷冻时限的不同分为 A 组 (≤ 1 年, $n=2 115$)、B 组 (>1 年且 ≤ 3 年, $n=319$)、C 组 (>3 年且 ≤ 6 年, $n=174$)、D 组 (>6 年, $n=54$)。使用倾向性匹配 (propensity score matching, PSM) 法按 1:3 的比例根据 D 组匹配其他 3 组的取卵年龄基线数据后, 比较不同冷冻时限的胚胎解冻移植后临床结局及产科结局。最后通过多因素 logistic 回归分析取卵年龄、移植年龄、胚胎冻存时限、内膜准备方案、子宫内膜厚度、移植胚胎数、移植的优质胚胎数对移植后临床结局及活产的影响。结果 ①在 PSM 前, 四组间取卵年龄、解冻年龄、胚胎冷冻时限差异均有统计学意义 (均 $P<0.001$)。②在 PSM 后, 取卵年龄基线特征在各组间达到平衡。各组间移植胚胎数、优质胚胎数、移植胚胎期、内膜准备方案差异均无统计学意义 (均 $P>0.05$)。D 组的临床妊娠率 [37.04% (20/54)]、活产率 [33.33% (18/54)] 均低于 A 组 [51.57% (82/159)、40.88% (65/159)]、B 组 [50.00% (65/130)、40.77% (53/130)] 和 C 组 [49.59% (61/123)、39.02% (48/123)], 但 4 组间比较差异均无统计学意义 ($P=0.310$ 、 $P=0.781$)。在新生儿男女婴比例、分娩孕周、出生体质量、早产率、低体质量儿出生率、巨大儿出生率、出生缺陷率、胎膜早破率方面 4 组间差异均无统计学意义 (均 $P>0.05$)。③多因素 logistic 回归分析显示, 移植优质胚胎数是影响临床妊娠结局 (PSM 前: $OR=2.614$, 95% $CI: 2.168\sim 3.151$, $P<0.001$; PSM 后: $OR=1.984$, 95% $CI: 1.406\sim 2.800$, $P<0.001$) 和活产 (PSM 前: $OR=2.708$, 95% $CI: 2.198\sim 3.336$, $P<0.001$; PSM 后: $OR=2.122$, 95% $CI: 1.474\sim 3.053$, $P<0.001$) 的显著因素。胚胎冷冻时限不影响临床妊娠结局和活产 (均 $P>0.05$)。结论 胚胎冷冻时限不影响解冻胚胎移植周期的临床结局及活产, 未来仍需要大样本数据支持该结论。

【关键词】 活产; 冷冻时限; 临床妊娠; 产科结局

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Effect of embryo cryostorage duration on pregnancy and obstetric outcomes in patients undergoing FET assisted reproduction

Chen Haixia, Kuang Tuo, Li Fang, Zhang Jing, Mu Xiaohuan, Lyu Yonghuan, Tian Wenyan, Song Xueru, Bai Xiaohong

Reproductive Medicine Center, Department of Gynecology and Obstetrics, Tianjin Medical University General Hospital; Tianjin Key Laboratory of Female Reproductive Health and Eugenics, Tianjin 300052, China

Corresponding author: Bai Xiaohong, Email: bxhjj@163.com, Tel: +86-13821343592

【 Abstract 】 Objective To investigate the effect of the embryo cryopreservation duration on pregnancy and obstetric outcome. **Methods** A retrospective cohort study of 2 662 frozen-thawed embryo transfer (FET) cycles was conducted in the Reproductive Medicine Center, Department of Obstetrics and Gynecology, Tianjin Medical University General Hospital from January 2016 to December 2020. According to embryo cryopreservation duration, the patients were divided into group A (≤ 1 year, $n=2 115$), group B (>1 years and ≤ 3 years, $n=319$), group C (>3 years and ≤ 6 years, $n=174$), and group D (>6 years, $n=54$). We used the propensity score matching (PSM) to match the baseline data of oocyte retrieval age of the other three groups according to group D at a ratio of 1 : 3. Clinical and obstetric outcomes were compared among the four groups. Multiple logistic regression analysis was used to analyze the effect of oocyte retrieval age, embryo transfer age, the duration of embryo cryopreservation, endometrial preparation scheme, endometrial thickness, the number of transferred embryos and the number of high-quality embryos on pregnancy and live birth outcome. **Results** 1) Before PSM, there were significant differences in the maternal age at oocyte retrieval and embryo transfer and duration of embryo cryopreservation among the four groups (all $P < 0.001$). 2) After PSM, the baseline characteristics of oocyte retrieval age reached a balance among the four groups. There were no statistical differences in the number of embryos transfer, the number of high-quality embryos, the transferred embryo stage, the endometrial regimen among the groups (all $P > 0.05$). The clinical pregnancy rate [37.04% (20/54)] and the live birth rate [33.33% (18/54)] in group D were lower than those in group A [51.57% (82/159), 40.88% (65/159)], group B [50.00% (65/130), 40.77% (53/130)] and group C [49.59% (61/123), 39.02% (48/123)], but the difference was not statistically significant between the four groups ($P=0.310$, $P=0.781$). There were no statistical differences among the four groups in the ratio of male to female newborns, gestational age, birth weight, preterm delivery rate, low birth weight rate, macrosomia rate, birth defects, and premature rupture of membranes (all $P > 0.05$). 3) Multiple logistic regression analysis showed that the number of high-quality embryos transferred affected the clinical pregnancy outcome (before PSM, $OR=2.614$, 95% CI : 2.168–3.151, $P < 0.001$; after PSM, $OR=1.984$, 95% CI : 1.406–2.800, $P < 0.001$) and live birth (before PSM, $OR=2.708$, 95% CI : 2.198–3.336, $P < 0.001$; after PSM, $OR=2.122$, 95% CI : 1.474–3.053, $P < 0.001$). The duration of embryo cryopreservation does not affect the clinical outcome and live birth (all $P > 0.05$). **Conclusion** The duration of embryo cryopreservation does not affect the clinical outcome and live birth, but large sample data are still needed to support this conclusion in the future.

【 Key words 】 Live birth; Duration of embryo cryopreservation; Clinical pregnancy; Obstetric outcome

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临床研究

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ICSI 退化对同胞卵母细胞正常受精后发育潜能及临床结局的影响

郑爱燕 孟庆霞 蒲艳 廖桂芝 李培培 丁洁

南京医科大学附属苏州医院 苏州市立医院生殖与遗传中心 南

京医科大学姑苏学院, 苏州 215002

通信作者: 丁洁, Email: dj95028@163.com, 电话: +86-512-62362184

【摘要】 目的 探讨卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 后发生的卵母细胞退化现象对患者同胞卵母细胞正常受精后的胚胎发育潜能及临床治疗结局的影响。方法 采用回顾性队列研究, 分析 2019 年 1 月至 2023 年 6 月期间在苏州市立医院生殖与遗传中心行 ICSI, 且使用时差培养箱培养的患者临床资料, 共收集到 242 个周期 3 119 枚卵母细胞, 信息收集截至 2024 年 2 月 5 日最后 1 例纳入统计的患者分娩。按 ICSI 后是否发生卵母细胞退化为退化组 (140 个周期) 和对照组 (102 个周期), 比较两组胚胎的生长发育情况及移植后的临床结局, 并进一步分析两组胚胎形态动力学参数之间的差异。结果 两组的女方年龄、不孕年限、体质量指数、基础卵泡刺激素、基础黄体生成素、基础雌二醇、窦卵泡计数、抗苗勒管激素、不孕因素及精液来源组间差异均无统计学意义 (均 $P>0.05$)。退化组人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日雌二醇水平 [2 513.00 (1 842.20, 3 638.50) ng/L]、获卵数 [(13.56±4.80) 枚] 和成熟卵率 [84.35% (1 601/1 898)] 显著高于对照组 [2 270.50 (1 472.00, 3 044.20) ng/L, $P=0.019$; (11.97±4.71) 枚, $P=0.011$; 81.08% (990/1 221), $P=0.017$], 但其正常受精率 [69.33% (1 103/1 591)]、第 3 天 (day 3, D3) 优质胚胎率 [57.85% (634/1 096)]、囊胚形成率 [50.87% (469/922)] 以及胚胎利用率 [58.30% (643/1 103)] 均显著低于对照组 [85.56% (847/990), $P<0.001$; 65.72% (556/846), $P<0.001$; 61.26% (446/728), $P<0.001$];

66.12% (560/847) , $P<0.001$] 。进一步分析显示,退化组的 D3 低细胞数 (<7) 胚胎比例 [33.76% (370/1 096)] 和 D3 高碎片率 (碎片率 $\geq 50\%$ 、碎片率 20%~50%) 胚胎比例 [10.01% (109/1 089) 、18.64% (203/1 089)] 显著高于对照组 [27.19% (230/846) , $P=0.002$; 6.06% (51/841) , $P=0.002$; 14.15% (119/841) , $P=0.009$], 异常分裂 DC1 和 CC 的发生率 [5.98% (66/1 103) 、2.45% (27/1 103)] 亦显著高于对照组 [2.48% (21/847) , $P<0.001$; 0.94% (8/847) , $P=0.013$] 。而对于可利用胚胎而言,退化组的 tPNf [22.82 (21.13, 24.84) h] 、t2 [25.37 (23.62, 27.37) h] 、t3 [35.64 (33.10, 38.03) h] 、t4 [36.85 (34.70, 39.52) h] 的发生显著早于对照组 [23.04 (21.76, 25.41) h, $P=0.001$; 25.91 (24.15, 28.05) h, $P=0.001$; 36.16 (33.11, 38.81) h, $P=0.040$; 37.39 (35.11, 40.27) h, $P=0.026$] , t5、cc2、cc3 和 s2 则在两组间差异均无统计学意义 (均 $P>0.05$) 。对两组患者进行第一次新鲜或者冻融胚胎移植后显示,两组的临床妊娠率、种植率、早期流产率、活产率、新生儿出生性别比、早产率、低出生体重儿率和出生缺陷率之间差异均无统计学意义 (均 $P>0.05$) 。ICSI 后是否发生卵母细胞退化不是 ICSI 周期种植率、早期流产率和活产率的独立影响因素,移植胚胎数目是其种植率和活产率的独立影响因素 ($OR=2.806$, 95% CI : 1.179~6.677, $P=0.020$; $OR=2.622$, 95% CI : 1.129~6.090, $P=0.025$) 。结论 ICSI 后卵母细胞退化对其同胞卵母细胞正常受精后的整体发育潜能存在一定影响,并在一定程度上扰乱了胚胎发育形态动力学,但并不影响其形成的最可利用胚胎移植后的妊娠结局和新生儿出生结局。

【关键词】 卵母细胞; 细胞膜; 胚胎发育; 延时成像; 精子注射, 细胞质内

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Effect of oocyte degeneration after ICSI on the developmental potential and clinical outcomes of sibling oocytes

Zheng Aiyun, Meng Qingxia, Pu Yan, Liao Guizhi, Li Peipei, Ding Jie

Reproductive and Genetic Center, the Affiliated Suzhou Hospital of Nanjing Medical University; Suzhou Municipal Hospital; Gusu School, Nanjing Medical University, Suzhou 215002, China

Corresponding author: Ding Jie, Email: dj95028@163.com, Tel: +86-512-62362184

【Abstract】 **Objective** To compare the embryo development potential and clinical outcomes between the patients with and without oocyte degeneration. **Methods** This retrospective cohort study included a total of 242 cycles underwent ICSI that cultured in time-lapse incubator from January 2019 to June 2023 at the Reproductive and Genetic Center of Suzhou Municipal Hospital and all 3 119 oocytes were evaluated. Data collection continued to February 5th,2024 until the last birthing of the study. Patients were divided into degenerated group (140 cycles) and control group (102 cycles) according to whether oocyte degenerated after ICSI. Then the embryo developmental potential and clinical outcomes were compared. Furthermore, we also investigated whether embryo morphokinetics could be different between the two groups. **Results** Female age, duration of infertility, body mass index, basal follicle stimulating hormone, basal luteinizing hormone, basal estrogen (E_2), antral follicle count, anti-Müllerian hormone, factors

of infertility and source of semen were similar between the two groups ($P>0.05$). E₂ on human chorionic gonadotropin triggered day [2 513.00 (1 842.20, 3 638.50) ng/L], number of oocytes retrieved (13.56±4.80) and oocyte maturation rate [84.35% (1 601/1 898)] were significantly higher in degenerated group than those in control group [2 270.50 (1 472.00, 3 044.20) ng/L, $P=0.019$; 11.97±4.71, $P=0.011$; 81.08% (990/1 221), $P=0.017$], while normal fertilization rate [69.33% (1 103/1 591)], day 3 (D3) good-quality embryos [57.85% (634/1 096)], blastocyst formation rate [50.87% (469/922)] and embryo utilized rate [58.30% (643/1 103)] were significantly lower in degenerated group than those in control group [85.56% (847/990), $P<0.001$; 65.72% (556/846), $P<0.001$; 61.26% (446/728), $P<0.001$; 66.12% (560/847), $P<0.001$]. In addition, the proportion of low cell number (<7) of D3 embryos [33.76% (370/1 096)] and high fragmentation (fragmentation $\geq 50\%$, fragmentation 20%–50%) of D3 embryos [10.01% (109/1 089), 18.64% (203/1 089)] in degenerated group were significantly higher than those in control group [27.19% (230/846), $P=0.002$; 6.06% (51/841), $P=0.002$; 14.15% (119/841), $P=0.009$], and so were the incidence of DC1 and CC [5.98% (66/1 103) vs. 2.48% (21/847), $P<0.001$; 2.45% (27/1 103) vs. 0.94% (8/847), $P=0.013$]. As regard to the utilized embryos, there were no significant differences in t₅, cc₂, cc₃ and s₂ ($P>0.05$), but tPnf [22.82(21.13, 24.84) h], t₂ [25.37 (23.62, 27.37) h], t₃ [35.64 (33.10, 38.03) h] and t₄ [36.85 (34.70, 39.52) h] in degenerated group were significantly earlier than those in control group [23.04 (21.76, 25.41) h, $P=0.001$; 25.91 (24.15, 28.05) h, $P=0.001$; 36.16 (33.11, 38.81) h, $P=0.040$; 37.39 (35.11, 40.27) h, $P=0.026$]. Further more, after the first transfer of fresh or frozen embryos, there were no significant differences in clinical pregnancy rate, implantation rate, early abortion rate, live birth rate, sex ratio, preterm birth rate, low birth weight rate and birth defect rate between the two groups (all $P>0.05$). ICSI degeneration was not an independent factor of implantation rate, early abortion rate and live birth rate after ICSI treatment, but number of embryos transferred was an independent factor of implantation rate and live birth rate after ICSI treatment ($OR=2.806$, 95% CI : 1.179–6.677, $P=0.020$; $OR=2.622$, 95% CI : 1.129–6.090, $P=0.025$). **Conclusion** The presence of oocyte degeneration after ICSI may affect the overall developmental potential of its sibling oocytes and may also disturb the morphokinetics of the embryos, however the pregnancy outcomes and neonatal birth outcomes may not be affected if transfer the best embryo in the first fresh or frozen cycle.

【Key words】 Oocyte; Cell membrane; Embryonic development; Time-lapse imaging; Sperm injections, intracytoplasmic

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LncRNA 在多囊卵巢综合征中的双重调控机制、临床价值及中医药干预研究现状

刘保松¹ 李彩霞² 孙莹莹³ 张小方³ 彭孟凡³

¹驻马店市中医院药学部, 驻马店 463000; ²新乡医学院第一附属医院

药学部, 新乡 453100; ³黄淮学院医学院, 驻马店 463000

通信作者: 彭孟凡, Email: pengmengfanfan@163.com, 电话: +86-13903822476

【摘要】 多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 是育龄女性常见生殖内分泌紊乱性疾病, 并可引起代谢紊乱、心血管疾病、卵巢癌和子宫癌等并发症, 严重危及机体健康。我国已成为 PCOS 患病率增长最快的国家之一, 但其发病机制复杂, 导致临床表现高度异质性, 难以彻底治愈。因此, 明确 PCOS 潜在发病机制对于临床早期筛查、诊断、治疗和预后等均具有重要意义。近年研究表明, 长链非编码 RNA (long noncoding RNA, lncRNA) 在 PCOS 发病中扮演着双重角色, 是潜在的预测病情发展的新型生物标志物和干预靶点。中医药多成分、多靶点和多途径的作用特点与 lncRNA 种类多样、角色双重和作用部位广泛的生物学特性相符。但是, 关于 lncRNA 介导 PCOS 的研究及中医药如何通过调控 lncRNA 改善 PCOS 发病的研究较为零散, 不利于其临床价值的肯定。基于此, 文章就 lncRNA 在 PCOS 发病机制中的双重调控作用、临床价值及中医药干预研究现状进行系统综述, 旨在明确 lncRNA 如何影响 PCOS 的发生与发展及潜在治疗策略, 以期为 PCOS 的临床防治提供新思路。

【关键词】 多囊卵巢综合征; 长链非编码 RNA; 生物标志物; 中医药
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Dual regulation mechanism, clinical value of lncRNA in PCOS and intervention role of Traditional Chinese Medicine

Liu Baosong¹, Li Caixia², Sun Yingying³, Zhang Xiaofang³, Peng Mengfan³

¹ Department of Pharmacy, Zhumadian Traditional Chinese Medicine Hospital, Zhumadian 463000, China; ² Department of Pharmacy, the First Affiliated Hospital of Xinxiang Medical University, Xinxiang 453100, China; ³ Faculty of Medicine, HuangHuai University, Zhumadian 463000, China

Corresponding author: Peng Mengfan, Email: pengmengfanfan@163.com, Tel: +86-13903822476

【Abstract】 Polycystic ovary syndrome (PCOS) is a common reproductive endocrine disorder in women of childbearing age, which can cause metabolic disorders, cardiovascular disease, ovarian cancer, uterine cancer and other complications, seriously endangering the health of the body. China has become one of the countries with the fastest increasing prevalence of PCOS, but its complex pathogenesis leads to highly heterogeneous clinical manifestations, making it difficult to completely cure. Therefore, clarifying the potential pathogenesis of PCOS is of great significance for early clinical screening, diagnosis, treatment, and prognosis. Recent studies have shown that long noncoding RNA (lncRNA) plays a dual role in the pathogenesis of PCOS and is a potential novel biomarker and intervention target. The characteristics of multi-component, multi-target, and multi-pathway action in Traditional Chinese Medicine (TCM) are consistent with the biological properties of lncRNA, which have diverse types, dual roles, and diverse locations. However, research on lncRNA mediated PCOS and how TCM can improve PCOS by regulating lncRNA is relatively scattered, which is not conducive to the recognition of its clinical value. Therefore, this article provides a systematic review of the dual regulatory mechanism, clinical value, and TCM intervention research of lncRNA in the occurrence and development of PCOS, aiming to clarify how lncRNA affects the occurrence and development of PCOS and potential treatment strategies, in order to provide new ideas for the clinical prevention and treatment of PCOS.

【 Key words 】 Polycystic ovary syndrome; Long noncoding RNA; Biomarkers; Traditional Chinese Medicine

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综述

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自噬在女性生殖障碍性疾病中的研究进展

付胜蓝 李稳安 侯志金 孟昱时

昆明医科大学第二附属医院生殖医学科, 昆明 650101

通信作者: 孟昱时, Email: mengyushi0102@163.com

【摘要】 近年来,越来越多的研究表明自噬与女性生殖过程密切相关。自噬是真核生物中广泛存在且高度保守的降解系统,可以在缺氧、饥饿、缺乏营养或极端 pH 值等条件下启动。在生殖健康方面,自噬可以通过清除受损细胞器,调节细胞生长代谢从而改善生殖功能障碍,适当的自噬调控有助于提高卵母细胞质量、延缓卵巢的衰老、精细调控子宫内膜的生长,确保胚胎成功着床,但自噬通路的异常可能会造成盆腔炎症性细胞因子激活、子宫内膜容受性降低、卵泡发育异常以及滋养细胞的侵袭能力减弱等问题,从而导致子宫内膜异位症、慢性子宫内膜炎、多囊卵巢综合征、早发性卵巢功能不全、复发性流产等生殖障碍性疾病的发生、发展。本文综述自噬在女性生殖相关疾病中的作用机制以及治疗靶点,为改善女性生殖健康提供临床思路及诊疗策略。

【关键词】 自噬; 子宫内膜异位症; 多囊卵巢综合征; Beclin-1 蛋白; 微管相关蛋白 1 轻链 3; 慢性子宫内膜炎; 复发性流产; 生殖障碍性疾病

Research progress of autophagy in female reproductive disorders

Fu Shenglan, Li Wenan, Hou Zhijin, Meng Yushi

Department of Reproductive Medicine, the Second Affiliated Hospital of Kunming Medical University, Kunming 650101, China

Corresponding author: Meng Yushi, Email: mengyushi0102@163.com

【 Abstract 】 In recent years, more and more studies have shown that autophagy is closely related to female reproductive process. Autophagy is a widespread and highly conserved degradation system in eukaryotes that can be activated under conditions such as hypoxia, starvation, lack of nutrients, or extreme pH. In terms of reproductive health, autophagy can improve reproductive dysfunction by removing damaged organelles and regulating cell growth and metabolism. Appropriate regulation of autophagy helps to improve oocyte quality, delay ovarian aging, fine-regulate endometrial growth, and ensure successful implantation of embryos. However, the abnormality of autophagy pathway may cause problems such as activation of pelvic inflammatory cytokines, reduced endometrial receptivity, abnormal follicle development, and weakened invasion ability of trophoblast cells, thus leading to the occurrence and development of reproductive disorders such as endometriosis, chronic endometritis, polycystic ovary syndrome, early-onset ovarian insufficiency, and recurrent spontaneous abortion. This article reviews the mechanism and therapeutic targets of autophagy

in female reproductive diseases, providing clinical ideas and diagnosis and treatment strategies for improving female reproductive health.

【 Key words 】 Autophagy; Endometriosis; Polycystic ovary syndrome; Beclin-1 protein; Microtubule-associated protein 1 light chain 3; Chronic endometritis; Recurrent abortion; Reproductive disorders

综述

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卵母细胞成熟及其受精过程关键基因的研究进展

陈佳瑶¹ 张志平² 王诗敏¹ 朱鹏飞² 武学清²

¹山西医科大学临床学科建设中心, 太原 030001; ²山西省儿童医院

山西省妇幼保健院生殖医学中心, 太原 030013

通信作者: 武学清, Email: xueqingwu416@126.com, 电话:
+86-351-3360725

【摘要】 卵母细胞成熟障碍和受精失败是由多种因素引起的, 包括染色体异常和卵母细胞质量不佳等复杂因素。随着高通量测序技术的广泛应用, 越来越多的基因突变被发现与不孕患者的卵母细胞成熟及受精过程有关。本文总结并讨论了11个有关卵母细胞成熟和受精相关的女性关键基因 (*TRIP13*、*TBPL2*、*LHX8*、*PATL2*、*TUBB8*、*CDC20*、*WEE2*、*ZP*、*ASTL*、*JUNO*和*CD9*), 为研究卵母细胞成熟阻滞和受精失败相关疾病的预防和开发靶向治疗提供基础。

【关键词】 受精; 卵母细胞成熟; 基因突变

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Progress on key genes in oocyte maturation and its fertilization process

Chen Jiayao¹, Zhang Zhiping², Wang Shimin¹, Zhu Pengfei², Wu Xueqing²

¹ Center for Clinical Discipline Construction, Shanxi Medical University, Taiyuan 030001, China; ² Center of Reproductive Medicine, Children's Hospital of Shanxi; Women Health Center of Shanxi, Taiyuan 030013, China
Corresponding author: Wu Xueqing, Email: xueqingwu416@126.com, Tel: +86-351-3360725

【Abstract】 Oocyte maturation disorders and fertilization failures are caused by a variety of factors, including complex factors such as chromosomal abnormalities and poor oocyte quality. With the widespread use of high-throughput sequencing technology, more and more genetic mutations have been found to be associated with oocyte maturation and fertilization process in infertile patients. This paper summarizes and discusses 11 key genes (*TRIP13*, *TBPL2*, *LHX8*, *PATL2*, *TUBB8*, *CDC20*, *WEE2*, *ZP*, *ASTL*, *JUNO* and *CD9*) related to oocyte maturation and fertilization-related disorders in females, providing a basis for research on the prevention of diseases associated with oocyte maturation blockage and fertilization failure and the development of targeted therapies.

【Key words】 Fertilization; Oocyte maturation; Gene mutation

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睾丸类器官培养技术的进展

黄明昊¹ 杜国尧¹ 吴登龙² 乐威²

¹同济大学医学院, 上海 200092; ²同济大学附属同济医院泌尿外科,
上海 200065

通信作者: 乐威, Email: Lewei0411@163.com

【摘要】 随着男性生殖系统疾病和生育障碍发病率的增加, 男性不育的诊治及生育力保存成为需要临床克服的难题。类器官是一种利用成体干细胞或胚胎干细胞在体外不同微环境中培养的细胞产物, 具备和天然组织类似的组织解剖和生理功

能。近年来，睾丸类器官在体外诱导精子增殖、分化等方面的技术有所突破，为解决上述问题提供了新的思路。本文对常见的睾丸类器官技术（微孔培养法、微流体培养法、三层梯度系统、气-液平面培养法、细胞外基质水凝胶支架、悬滴培养法、3D 打印技术）进行了简要介绍，包括技术特点、研究情况和技术瓶颈等，并简要概述了部分常见的类器官培养液在睾丸类器官领域应用的特点和应用情况。

【关键词】 睾丸； 类器官； 生物支架； 3D 培养

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Advances in testicular organoid culture technology

Huang Minghao¹, Du Guoyao¹, Wu Denglong², Le Wei²

¹Tongji University School of Medicine, Shanghai 200092, China; ²Department of Urology, Tongji Hospital of Tongji University, Shanghai 200065, China

Corresponding author: Le Wei, Email: Lewei0411@163.com

【Abstract】 With the increasing incidence of male reproductive system diseases and reproductive dysfunctions, diagnosis and treatment of male infertility and fertility preservation have become clinical challenges to be overcome. Organoids, a kind of cell product cultured *in vitro* under different microenvironments by using adult stem cells or embryonic stem cell, can possess histological anatomy and physiological function that are similar to natural tissues. In recent years, technological breakthroughs have been made in testicular organoids in terms of sperm proliferation and differentiation induced *in vitro*, providing a new idea for solving the above problems. This article briefly introduces common testicular organoid techniques (micropore culture, microfluidics culture method, three-layer gradient system, air-liquid interface culture, extracellular matrix hydrogel scaffold, hanging drop cultures, and 3D printing technology, etc.), including technical features, research conditions, technical bottlenecks and summarizes the application characteristics and situations of some ordinary organoid culture solutions in the field of testicular organoids as well.

【Key words】 Testis; Organoid; Biological scaffold; 3D culture

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早发性卵巢功能不全小鼠模型的建立

熊湘蕾 司曼飞 刘梦宇 齐新宇

北京大学第三医院妇产科 女性生育力促进全国重点实验室 国

家妇产疾病临床医学研究中心, 北京 100191

通信作者: 齐新宇, Email: cicyqixinyu@163.com, 电话:

+86-10-82266591

【摘要】 早发性卵巢功能不全 (premature ovarian insufficiency, POI) 是指女性在 40 岁以前出现卵巢功能减退的临床综合征, 使年轻女性出现生育力减退、激素水平降低等生殖衰老表现, 严重影响女性的身心健康和生活质量。POI 的发病机制尚不明确, 存在很大的未知空间, 利用动物模型深入探索其病因和机制具有重要的临床意义, 可以帮助提前识别和规避危险因素, 并制定针对性的预防和治疗策略。本文通过对不同 POI 小鼠模型的分析研究, 可以为 POI 的基础研究提供参考依据, 为提升育龄女性的生育力提供新的思路。

【关键词】 早发性卵巢功能不全; 小鼠模型; 基因; 代谢

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Establishment of premature ovarian insufficiency mouse model

Xiong Xianglei, Si Manfei, Liu Mengyu, Qi Xinyu

Department of Obstetrics and Gynecology, Peking University Third Hospital; State Key Laboratory of Female Fertility Promotion; National Clinical Research Center for Obstetrical and Gynecological Diseases, Beijing 100191, China

Corresponding author: Qi Xinyu, Email: cicyqixinyu@163.com, Tel: +86-10-82266591

【Abstract】 Premature ovarian insufficiency (POI) leads to reproductive aging in young women, such as reduced fertility and reduced hormone levels, which seriously affects women's physical and mental health and quality of life. The pathogenesis of POI is still unclear, and there is a large unknown space. In-depth exploration of its etiology and mechanism using animal models has important clinical significance, which can help identify and avoid risk factors in advance, and formulate targeted prevention and treatment strategies. Through the analysis and study of different POI mouse models, this paper can provide a reference for the basic research of POI and a new idea for improving the fertility of women of childbearing age.

【Key words】 Premature ovarian insufficiency; Mouse model; Genes; Metabolism

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