



不同胰岛素抵抗评估指标与多囊卵巢综合征患者体外受精-胚胎移植结局的相关性研究*

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【摘要】目的 探讨多种胰岛素抵抗(insulin resistance, IR)评估指标与多囊卵巢综合征(polycystic ovary syndrome, PCOS)患者体外受精-胚胎移植(*in vitro* fertilization and embryo transfer, IVF-ET)过程中胚胎质量及妊娠结局的相关性。**方法** 采用回顾性队列设计, 纳入2019年1月-2022年7月期间首次接受体外受精/卵胞质内单精子注射(*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI)治疗的PCOS患者。选取基于空腹状态计算的IR评估指标(HOMA-IR、QUICKI、李光伟指数、Bennett ISI)(以上统称静态IR指标)以及基于口服葡萄糖耐量试验(oral glucose tolerance test, OGTT)计算的IR评估指标(曲线下面积比、Matsuda指数、Gutt指数)(以上统称动态IR指标), 依据中位数分为IR组(即高水平)和非IR组(即低水平), 比较各种IR评估指标水平高低在胚胎质量和妊娠结局的差异。主要结局指标为D3优质胚胎率(简称优胚率)、新鲜周期临床妊娠率、累积妊娠率和累积活产率, 其余为次要结局指标。采用多因素二元logistic回归模型校正因素, 多重比较校正控制假阳性, 分析不同IR评估指标高低水平与胚胎质量及妊娠结局的相关性。**结果** 共纳入571例PCOS患者, 均包含空腹状态的血糖和胰岛素数据, 其中499例具有完整的OGTT数据。主要结局指标: 静态IR指标高低水平与主要结局指标均未呈现统计学关联; 动态IR指标中的Gutt指数高低水平与优胚率有关, 调整后比值比(odds ratio, OR)为0.88[95%置信区间(confidence interval, CI): 0.79 ~ 0.99, $P=0.035$]; Matsuda指数高低水平与累积妊娠率有关, 调整后OR为0.61(95%CI: 0.39 ~ 0.97, $P=0.036$)。次要结局指标: 静态IR指标和动态IR指标未观察到经多重比较校正后仍具有统计学意义的关联。**结论** 基于OGTT的Matsuda指数和Gutt指数较基于空腹的静态指标更敏感地反映了PCOS患者辅助生殖结局的差异, 具有重要的临床应用价值。

【关键词】 多囊卵巢综合征 胰岛素抵抗 OGTT 辅助生殖 胚胎质量 妊娠结局

A Study on the Association Between Various Insulin Resistance Assessment Indices and IVF-ET Outcomes in Patients With Polycystic Ovary Syndrome

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[Abstract] Objective To explore the correlations between various insulin resistance (IR) assessment indicators and embryo quality and pregnancy outcomes during *in vitro* fertilization and embryo transfer (IVF-ET) in patients with polycystic ovary syndrome (PCOS). **Methods** A retrospective cohort design was used, including PCOS patients who received *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatment for the first time from January 2019 to July 2022. Assessment indicators of insulin resistance (IR) based on fasting status (HOMA-IR, QUICKI, Li Guangwei Index, Bennett ISI), collectively referred to as static IR indicators, and assessment indicators based on the oral glucose tolerance test (OGTT) (area under the curve ratio, Matsuda Index, Gutt Index), collectively referred to as dynamic IR

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indicators, were selected. Patients were divided into the IR group (high level) and the non-IR group (low level) according to the median. Differences in the levels of various IR assessment indicators, embryo quality, and pregnancy outcomes were compared. The primary outcome indicators were the D3 high-quality embryo rate (high embryo rate), fresh cycle clinical pregnancy rate, cumulative pregnancy rate, and cumulative live birth rate; other outcomes were considered secondary indicators. A multivariate binary logistic regression model was used to adjust for confounding factors, and multiple comparison correction was applied to control false positives when analyzing the correlation between different levels of IR assessment indicators and embryo quality and pregnancy outcomes. **Results** A total of 571 PCOS patients were included, all of whom had fasting blood glucose and insulin data. Among these, 499 cases had complete OGTT data. Main outcome indicators: There was no statistical correlation between the levels of static IR indicators and the main outcome indicators. The levels of dynamic IR indicators (Gutt index) were associated with the pregnancy rate of good embryos, with an adjusted odds ratio (OR) of 0.88 (95% CI: 0.79-0.99, $P = 0.035$). The levels of the Matsuda index were associated with the cumulative pregnancy rate, with an adjusted OR of 0.61 (95% CI: 0.39-0.97, $P = 0.036$). Secondary outcome indicators: No statistically significant correlations were observed between the static IR indicators and dynamic IR indicators after multiple comparison correction. **Conclusion** The Matsuda index and Gutt index based on OGTT are more sensitive than static fasting indicators in reflecting differences in reproductive outcomes among PCOS patients, and thus have significant clinical value.

[Key words] Polycystic ovary syndrome Insulin resistance OGTT Assisted reproduction
Embryo quality Pregnancy outcome

胰岛素抵抗(insulin resistance, IR)是指机体对胰岛素的敏感性降低,导致葡萄糖摄取和利用效率下降的一种病理状态^[1],主要由胰岛素信号通路异常调控引起^[2]。作为代谢紊乱的重要标志,IR与2型糖尿病、心血管疾病、多囊卵巢综合征(polycystic ovary syndrome, PCOS)等多种疾病密切相关^[1-2]。其中,IR在PCOS患者中的发生率高达70%^[3-4]。

PCOS是育龄期女性最常见的内分泌代谢疾病之一,PCOS患者的临床表现以高雄激素血症、排卵障碍和卵巢多囊样改变为特征^[5],其中约75%的患者因无排卵导致不孕^[6]。生活方式干预和药物诱导排卵为PCOS患者不孕的首选治疗方法^[7],但当未能成功实现妊娠时,体外受精(*in vitro* fertilization, IVF)或胞质内单精子注射(intracytoplasmic sperm injection, ICSI)等辅助生殖技术成为临床上的重要治疗选择^[8]。既往多项研究表明,PCOS患者通过辅助生殖技术通常能够获得较高的活产率,但在辅助生殖治疗及妊娠维持过程中,仍面临卵巢过度刺激、受精率下降、流产等不良结局风险^[9-12]。

作为PCOS患者常见的代谢异常,IR对辅助生殖结局的影响越来越受到重视。然而,关于IR是否显著影响辅助生殖技术后的胚胎质量和妊娠结局,现有研究结果尚不一致^[13-17]。不同研究中所采用的IR评估方法存在较大差异,可能是导致研究结果不一致的重要原因。目前,评估IR的“金标准”是高胰岛素-正常血糖钳夹试验(hyperinsulinemic euglycemic clamp, HEC),该方法可直接测量外周组织对胰岛素的敏感性^[18]。但由于成本高

昂、操作繁琐及检测周期较长等因素^[19],其应用受到了较大限制。因此,目前大多数临床研究采用替代评估方法,包括基于空腹血糖(fasting plasma glucose, FPG)和空腹胰岛素(fasting plasma insulin, FPI)的静态指标(如HOMA-IR)^[20-21]以及基于口服葡萄糖耐量试验(oral glucose tolerance test, OGTT)数据计算的动态指标(如Matsuda指数)^[22]。这些方法广泛用于糖尿病等内分泌疾病的预后评估,但在评估PCOS患者辅助生殖结局中的作用尚不清楚。

本研究旨在系统比较多种IR评估指标与PCOS患者IVF/ICSI过程中胚胎质量及妊娠结局的相关性,以期为临床合理选择IR评估方法、优化辅助生殖策略提供依据。

1 资料与方法

1.1 研究对象

本研究采用回顾性队列设计,纳入研究对象为在2019年1月-2022年7月期间首次接受IVF/ICSI治疗的PCOS患者。分组标准:IR相关评估指标包括静态IR指标和动态IR指标。基于空腹状态计算的IR评估指标(HOMA-IR、QUICKI、李光伟指数、Bennett ISI)统称静态IR指标;基于OGTT计算的IR评估指标(曲线下面积比、Matsuda指数、Gutt指数)统称动态IR指标。这些指标均依据中位数分为IR组(即IR处于高水平,简称高水平)和非IR组(即IR处于低水平,简称低水平):HOMA-IR、曲线下面积比高于中位数者定义为IR组,低于中位数者为非IR组;其余指标低于中位数者定义为IR组,高于中位数者为非IR组。

本研究已获得四川大学华西第二医院伦理委员会批准(批准号2021-033),且免除了书面知情同意。

1.2 纳入排除标准

纳入标准:①因不孕首次接受IVF/ICSI治疗,治疗方案采用促性腺激素释放激素(gonadotropin-releasing hormone, GnRH)拮抗剂进行控制性促排卵(controlled ovarian stimulation, COS)。不孕定义为至少12个月规律未避孕性生活后未成功妊娠。②PCOS的诊断需至少满足以下三项标准中的两项:月经稀发/闭经,临床或生化高雄激素症(改良Ferriman-Gallwey评分 ≥ 5 和/或总睾酮 ≥ 0.40 ng/mL),以及多囊卵巢形态(2~9 mm窦卵泡计数 ≥ 20 或卵巢体积 ≥ 10 cm³超声检查),且排除其他高雄激素症和排卵功能障碍的原因。③所有患者在促排卵治疗前6个月内完成FPG及FPI水平测定或OGTT测定。

排除标准:①合并其他内分泌疾病(如甲状腺疾病、糖尿病)或自身免疫疾病(如系统性红斑狼疮、抗磷脂综合征)等;②染色体异常者;③植入前基因检测周期患者;④临床资料不全者。

1.3 临床资料采集

通过临床病案管理系统回顾性收集PCOS患者的相关信息,包括人口统计学资料:年龄、体质量指数(body mass index, BMI);不孕相关信息及所采用的辅助生殖技术方案;实验室检测指标:窦卵泡数(antral follicle count, AFC),基础激素水平包括雌二醇(estradiol, E2)、孕酮(progesterone, P)、睾酮(testosterone, T)、卵泡刺激素(follicle-stimulating hormone, FSH)、黄体生成素(luteinizing hormone, LH)及抗米勒管激素(anti-Müllerian hormone, AMH);OGTT期间不同时间点的血糖和胰岛素水平;以及扳机日相关激素指标。胚胎学指标包括卵裂期(D3)和囊胚期的胚胎数量和质量相关指标。妊娠结局分别记录新鲜胚胎移植周期和冷冻胚胎移植周期中的临床妊娠、流产及活产情况。

1.4 IVF/ICSI-ET方案

根据PCOS管理指南^[23],患者均采用GnRH拮抗剂方案。于月经周期第2天起予以促性腺激素(Gn)进行促排卵,起始剂量150~300 IU/d;在COS第6天,或当优势卵泡直径达到14 mm,或血清雌二醇达到30 pg/mL时,加用GnRH拮抗剂(0.25 mg/d);当监测到 ≥ 2 个 ≥ 18 mm或 ≥ 3 个 ≥ 17 mm卵泡时,使用尿源性人绒毛膜促性腺激素(human chorionic gonadotropin, hCG)8 000~10 000 IU(根据患者体质量)或重组hCG 250 μ g进行扳机;扳机后36~38 h在阴道超声引导下取卵,根据卵母细胞质量和患者病史选择IVF或ICSI受精。受精后参考人类卵裂期胚

胎及囊胚形态学评价中国专家共识^[24]每日评估胚胎质量,D3优质胚胎进行移植或冷冻,其余继续培养至第五日后移植或冷冻。胚胎移植包括新鲜胚胎移植(embryo transfer, ET)和冷冻胚胎移植(frozen embryo transfer, FET)。ET于取卵后第3日或第5日进行;FET于人工周期内膜准备及孕激素支持后实施。所有患者在移植前均接受黄体支持。ET后2周检测血清 β -hCG,3~4周后经阴道超声确认妊娠。胚胎移植数目依据胚胎质量及患者具体情况决定。

1.5 研究变量

基于胰岛素抵抗评估的专家指导意见^[22],本研究选取多种IR指标作为主要自变量,包括基于FPG和FPI的静态指标和基于OGTT的动态指标。静态指标包括:HOMA-IR、QUICKI、李光伟指数和Bennett ISI。动态指标包括:曲线下面积比、Matsuda指数和Gutt指数。以上各指标具体计算公式见附表1。所有附表见网络资源附件。

1.6 结局变量

本研究的结局指标包括胚胎质量相关指标(D3优质胚胎率、D3可利用胚胎率、囊胚形成率、优质囊胚率、可利用囊胚率)和妊娠结局指标(新鲜周期临床妊娠率、新鲜周期着床率、新鲜周期流产率、新鲜周期活产率、累积活产率、累积妊娠率)。主要结局指标为D3优质胚胎率(简称优胚率)、新鲜周期临床妊娠率、累积妊娠率和累积活产率,其余指标为次要结局指标。胚胎质量评价参考《中国人类卵裂期胚胎及囊胚形态学评价专家共识》^[24]及Gardner和Schoolcraft提出的囊胚分级体系^[25]。此外,根据ESHRE指南^[26]和《胚胎实验室关键指标质控专家共识》^[27]计算结局指标。

1.7 统计学方法

本研究使用R4.3.2软件进行统计分析。连续变量以 $\bar{x} \pm s$ 表示,分类资料以频数(%)描述。

组间差异比较方面,分类变量采用卡方检验或Fisher精确检验,连续变量根据分布情况选择合适方法:若符合正态分布且方差齐性,采用独立样本 t 检验;非正态分布时采用Mann-Whitney U 检验。首先进行未调整的单因素分析(模型1),以胚胎结局和妊娠结局作为因变量(Y),调整协变量(年龄、BMI、不孕年限及AMH)构建模型2;针对新鲜周期结局,除了上述协变量外,还进一步调整移植日型和移植胚胎数量,构建模型3,作为敏感性分析。结果采用比值比(odds ratio, OR)和95%置信区间(confidence interval, CI)表示。此外,本文对促排卵刺激结果以及次要结局进行多重比较校正,分别针对静态指标和动态指标独立进行,在模型2中采用Benjamini-Hochberg方法控制假阳性发现率,以减少第一类错误的

概率, 仅当校正后的 $P<0.05$ 时, 相关性才被认为具有统计学意义。模型3的结果则单独呈现。

2 结果

2.1 PCOS患者基线

本研究共纳入571例患者, 可基于其FPG和FPI数据计算IR相关指标, 其基线特征见附表2。在此基础上, 进一步筛选出其中499例具备完整OGTT过程中多个时间点血糖及胰岛素数据的患者, 计算相应的动态IR指标, 详见附表2。

2.2 不同IR指标水平高低的促排卵刺激指标差异

根据静态及动态IR指标分组标准, 经多重比较校正后, 促排卵刺激相关指标的组间比较结果均整理于附表

3和附表4。其中, 根据静态IR指标分组标准, IR组(高水平)和非IR组(低水平)在仅在总Gn量方面的组间差异有统计学意义($P\text{-adjust}<0.001$); 基于动态IR指标分组标准, IR组(高水平)和非IR组(低水平)在Matsuda指数、Gutt指数、总Gn量的组间差异有统计学意义($P\text{-adjust}<0.001$)。

2.3 不同IR指标水平高低的胚胎质量指标差异

静态IR指标分水平与各项胚胎质量指标无关, 调整相关协变量后结果仍无显著变化, 其中主要结局的结果见表1, 次要结局的结果见附表5。动态IR指标(Matsuda指数或Gutt指数)水平高低与部分胚胎质量结果有关, 其中Gutt指数在调整协变量后与优胚率相关($OR: 0.88, 95\%CI: 0.79 \sim 0.99, P=0.035$), 其余动态指标在多重比较校正后不再有关。其中主要结局指标见表2, 次要结局指标见附表6。

表 1 静态IR指标与胚胎质量的关联 (主要结局)

Table 1 Association between static IR indicators and embryo quality (primary outcomes)

Grouping variable	Outcome variable	Non-IR group (low level)	IR group (high level)	Model 1		Model 2	
				OR (95% CI)	P	OR (95% CI)	P
HOMA-IR	High-quality D3 embryo rate	1 300/3 129 (41.5%)	1 303/3 138 (41.5%)	1.00 (0.90-1.11)	1.000	1.00 (0.89-1.11)	0.938
QUICKI	High-quality D3 embryo rate	1 295/3 112 (41.6%)	1 308/3 155 (41.5%)	0.99 (0.90-1.10)	0.921	0.99 (0.88-1.11)	0.845
Li Guangwei Index	High-quality D3 embryo rate	1 295/3 112 (41.6%)	1 308/3 155 (41.5%)	0.99 (0.90-1.10)	0.921	0.99 (0.88-1.11)	0.845
Bennett ISI	High-quality D3 embryo rate	1 299/3 099 (41.9%)	1 304/3 168 (41.2%)	0.97 (0.88-1.07)	0.561	0.96 (0.86-1.07)	0.459

OR: odds ratio. Model 1 is unadjusted. Model 2 is adjusted for age, BMI, duration of infertility, and AMH.

表 2 动态IR指标与胚胎质量的关联 (主要结局)

Table 2 Association between dynamic IR indicators and embryo quality (primary outcomes)

Grouping variable	Outcome variable	Non-IR group (low level)	IR group (high level)	Model 1		Model 2	
				OR (95% CI)	P	OR (95% CI)	P
AUC ratio	High-quality D3 embryo rate	1 183/2 873 (41.2%)	1 095/2 656 (41.2%)	1.00 (0.90-1.12)	0.991	1.01 (0.90-1.13)	0.877
Matsuda index	High-quality D3 embryo rate	1 159/2 747 (42.2%)	1 119/2 782 (40.2%)	0.92 (0.83-1.03)	0.144	0.89 (0.79-1.00)	0.053
Gutt index	High-quality D3 embryo rate	1 196/2 825 (42.3%)	1 082/2 704 (40.0%)	0.91 (0.82-1.01)	0.084	0.88 (0.79-0.99)	0.035

OR: odds ratio. Model 1 was unadjusted. Model 2 was adjusted for age, BMI, duration of infertility, and AMH. Bold values indicate $P < 0.05$.

2.4 不同IR指标水平高低的妊娠结局指标差异

静态IR指标与妊娠结局指标之间未观察到显著关联, 调整协变量以及进行多重比较校正后结果无变化, 主要结局的结果详见表3, 次要结局的结果见附表7。动态IR指标与新鲜周期的着床率、临床妊娠率、流产率及活产率无关, 调整协变量以及多重比较校正后结果无变化。Matsuda指数、Gutt指数水平高低与累积妊娠率有关, 其中Matsuda指数在调整协变量后关联性仍存在($OR: 0.61, 95\%CI: 0.39 \sim 0.97, P=0.036$), 详见表4, 其余次要结果见附表8。

3 讨论

本研究系统比较了多种静态与动态IR指标在

PCOS患者辅助生殖结局中的表现, 并选取了多个反映辅助生殖全程的结局指标, 全面评估了IR指标与胚胎发育质量及妊娠结局之间的关系; 分析中调整了多种关键协变量, 提高了结果的稳健性。结果显示, 静态IR指标与部分COS指标相关, 但在胚胎质量和妊娠结局方面, IR组与非IR组无显著差异。相比之下, 动态IR指标(Matsuda指数和Gutt指数)不仅与COS指标相关, 还与D3优胚率、D3可用胚胎率、囊胚优胚率及累积妊娠率相关, 部分差异在调整协变量以及多重比较校正后仍然显著, 提示动态指标对反映PCOS患者代谢状态及辅助生殖结局更具敏感性和临床价值。

IR在PCOS相关的生殖障碍中发挥重要作用。IR通过抑制肝脏合成性激素结合球蛋白并增强胰岛素与黄体

表 3 静态IR指标与妊娠结局的关联（主要结局）

Table 3 Association between static IR indicators and pregnancy outcomes (primary outcomes)

Grouping variable	Outcome variable	Non-IR group (low level)	IR group (high level)	Model 1		Model 2		Model 3	
				OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
HOMA-IR	Clinical pregnancy rate	47/230 (20.4%)	48/241 (19.9%)	1.03 (0.64-1.66)	0.980	1.04 (0.64-1.70)	0.865	1.07 (0.65-1.75)	0.789
	Cumulative pregnancy rate	128/211 (60.7%)	127/230 (55.2%)	0.80 (0.54-1.19)	0.289	0.97 (0.63-1.50)	0.895	—	—
	Cumulative live birth rate	109/211 (51.7%)	112/230 (48.7%)	0.89 (0.61-1.29)	0.599	1.02 (0.67-1.56)	0.936	—	—
QUICKI	Clinical pregnancy rate	47/230 (20.4%)	48/241 (19.9%)	1.03 (0.64-1.66)	0.980	1.04 (0.64-1.69)	0.865	1.08 (0.66-1.77)	0.752
	Cumulative pregnancy rate	128/211 (60.7%)	127/230 (55.2%)	1.03 (0.64-1.66)	0.289	0.97 (0.63-1.50)	0.895	—	—
	Cumulative live birth rate	109/211 (51.7%)	112/230 (48.7%)	0.89 (0.61-1.29)	0.599	1.02 (0.67-1.56)	0.936	—	—
Li Guangwei Index	Clinical pregnancy rate	47/230 (20.4%)	48/241 (19.9%)	1.03 (0.64-1.66)	0.980	1.04 (0.64-1.69)	0.865	1.08 (0.66-1.77)	0.752
	Cumulative pregnancy rate	128/211 (60.7%)	127/230 (55.2%)	1.91 (0.45-9.59)	0.289	0.97 (0.63-1.50)	0.895	—	—
	Cumulative live birth rate	109/211 (51.7%)	112/230 (48.7%)	0.89 (0.61-1.29)	0.599	1.02 (0.67-1.56)	0.936	—	—
Bennett ISI	Clinical pregnancy rate	46/224 (20.5%)	49/247 (19.8%)	1.04 (0.65-1.68)	0.941	1.03 (0.63-1.69)	0.896	1.09 (0.66-1.79)	0.744
	Cumulative pregnancy rate	127/209 (60.8%)	128/232 (55.2%)	0.97 (0.59-1.60)	0.275	0.97 (0.63-1.50)	0.890	—	—
	Cumulative live birth rate	108/209 (51.7%)	113/232 (48.7%)	0.89 (0.61-1.29)	0.598	1.02 (0.67-1.57)	0.928	—	—

OR: odds ratio. Model 1 was unadjusted. Model 2 was adjusted for age, BMI, duration of infertility, and AMH. Model 3 was further adjusted for the day of embryo transfer and the number of embryos transferred in fresh cycles, based on Model 2.

表 4 动态IR指标与妊娠结局的关联（主要结局）

Table 4 Association between dynamic IR indicators and pregnancy outcomes (primary outcomes)

Grouping variable	Outcome variable	Non-IR group (low level)	IR group (high level)	Model 1		Model 2		Model 3	
				OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
AUC ratio	Clinical pregnancy rate	39/203 (19.2%)	37/185 (20.0%)	1.05 (0.62-1.79)	0.946	1.06 (0.64-1.77)	0.812	1.05 (0.62-1.77)	0.859
	Cumulative pregnancy rate	117/207 (56.5%)	100/173 (57.8%)	1.05 (0.69-1.62)	0.883	1.00 (0.65-1.54)	0.990	—	—
	Cumulative live birth rate	106/207 (51.2%)	84/173 (48.6%)	0.90 (0.60-1.35)	0.680	0.89 (0.58-1.35)	0.588	—	—
Matsuda index	Clinical pregnancy rate	36/178 (20.2%)	40/210 (19.0%)	0.93 (0.54-1.59)	0.871	0.96 (0.56-1.64)	0.868	1.00 (0.58-1.72)	0.996
	Cumulative pregnancy rate	110/172 (64.0%)	107/208 (51.4%)	0.60 (0.39-0.92)	0.019	0.61 (0.39-0.97)	0.036	—	—
	Cumulative live birth rate	94/172 (54.7%)	96/208 (46.2%)	0.71 (0.47-1.07)	0.122	0.77 (0.49-1.21)	0.262	—	—
Gutt index	Clinical pregnancy rate	36/178 (20.2%)	40/210 (19.0%)	0.93 (0.54-1.59)	0.871	0.95 (0.56-1.61)	0.843	0.94 (0.55-1.60)	0.820
	Cumulative pregnancy rate	105/166 (63.3%)	112/214 (52.3%)	0.64 (0.41-0.99)	0.043	0.66 (0.42-1.03)	0.066	—	—
	Cumulative live birth rate	87/166 (52.4%)	103/214 (48.1%)	0.84 (0.56-1.26)	0.469	0.90 (0.58-1.40)	0.638	—	—

OR: odds ratio. Model 1 was unadjusted. Model 2 was adjusted for age, BMI, duration of infertility, and AMH. Model 3 was further adjusted for the day of embryo transfer and the number of embryos transferred in fresh cycles, based on Model 2. Bold values indicate $P < 0.05$.

生成素对卵巢间质细胞的协同刺激作用,促进雄激素分泌,导致高雄激素血症;高雄激素血症又反过来加重IR,形成恶性循环^[28-29]。研究表明IR会影响颗粒细胞功能和子宫内膜容受性^[30-32],进而干扰胚胎着床及妊娠早期的维持,这可能是导致辅助生殖结局较差的重要原因。因此,及时、准确地评估IR情况对PCOS患者IVF/ICSI-ET治疗过程中的临床决策具有重要意义。

本研究使用的IR评估指标目前主要在内分泌领域进行广泛应用。静态指标主要基于FPG和FPI,能够反映基础代谢状态下胰岛素对肝脏的抑制作用及其敏感性^[33-34]。这类指标操作简便,适合大规模人群筛查^[35]。然而,这些

指标仅反映空腹状态下的代谢情况,无法明确葡萄糖负荷状态下胰岛的动态变化^[36-38],可能导致对IR程度的低估。动态指标则能够更全面地评估胰岛素在葡萄糖负荷状态下对肝脏、骨骼肌及脂肪等组织的整体代谢调节功能^[39-40]。而本研究结果也显示出动态指标与胚胎质量及妊娠结局的相关性明显优于静态指标,尤其在评估D3优胚率、累积妊娠率时表现出更高的敏感性,提示在PCOS患者辅助生殖治疗中,基于OGTT的动态IR评估可能更有助于全面反映代谢状态并优化个体化治疗策略。

HOMA-IR作为最常用IR评估工具,已有较多研究探讨其与PCOS患者辅助生殖结局之间的关系,但结果尚不

一致。一些研究发现,使用HOMA-IR进行诊断时,合并IR的PCOS患者临床妊娠率和活产率显著低于非IR患者,但优质胚胎率、着床率和流产率无明显差异^[13-14]。也有研究指出,IR患者的早期流产风险显著升高,尤其在合并 β 细胞功能障碍时更为明显,活产率也显著下降^[15]。还有部分研究指出,基于HOMA-IR诊断的IR可能与胚胎质量下降相关,但未表现出与妊娠结局的显著联系^[41],亦有研究认为IR对卵母细胞发育及胚胎质量无明显影响^[42-43]。本研究中,采用HOMA-IR对PCOS患者进行分组后,同样未观察到IR组与非IR组在胚胎质量和妊娠结局方面存在显著差异,与部分既往研究结果相符。而在采用动态指标Matsuda指数进行分组研究时,有研究显示IR组的D3优质胚胎率和D3可用率均低于非IR组^[17],本研究中调整协变量后也观察到两组在D3胚胎可用率方面存在差异,且IR组累积妊娠率显著低于非IR组累积妊娠率。此外,Gutt指数进行分组研究后也显示出D3优胚率的差异,提示动态IR指标反映辅助生殖结局方面可能更具敏感性。

在本研究中,动态IR指标在新鲜周期妊娠率和活产率分析中未见显著差异,而在累积妊娠率分析中差异显著,这可能与PCOS患者COS期间的内分泌环境、移植胚胎质量以及IR的长期影响有关。有研究表明,高水平雌孕激素可导致子宫内膜与胚胎发育不同步,高雄激素状态进一步影响子宫内膜容受性^[44-45],从而掩盖代谢影响的短期作用。而FET能改善子宫内膜容受性^[46],规避COS带来的内膜不利因素^[47],使IR相关的代谢效应更易显现。此外,新鲜周期移植通常选择优质胚胎,单次移植效果可能掩盖胚胎质量差异,而累积妊娠率综合反映促排周期内胚胎的质量与数量,且IR对卵巢功能和子宫环境的长期影响逐渐累积,因此更易揭示IR对整体辅助生殖结局的影响。

但本研究也存在一定的局限性。首先,本研究为单中心回顾性设计,部分FET周期移植胚胎数量和移植日型记录不全,难以在统计模型中同时精确调整每次移植信息;由于目前尚无统一标准用于界定PCOS患者的IR状态,本研究以各评估指标的中位数作为分组依据,存在丢失连续变量信息的局限性,可能对结果的稳定性产生一定影响;在胚胎质量分析中,本研究采用了基于组内全部患者总体胚胎数的比例计算方法,生育结局以患者数为分母,无法完全反映每位患者胚胎质量的个体差异,也可能低估胚胎间变异对结局的影响。未来研究可依托多中心、大样本的前瞻性队列,进一步验证以Matsuda指数、Gutt指数等动态IR指标在辅助生殖结局评估中的稳定性及预测能力,并探索更为全面、个体化的胚胎质量评

估方法,为临床应用的规范化提供更有力的依据。

总之,本研究发现,动态IR指标Matsuda指数和Gutt指数在评估PCOS患者辅助生殖结局方面具有潜在价值。Gutt指数定义的IR组在D3优胚率指标上表现较差,Matsuda指数定义的IR组累积妊娠率显著下降而静态IR指标未表现出与辅助生殖结局的明确关联。这提示动态IR指标可能更敏感地反映PCOS患者的代谢状态,其在辅助生殖结局评估中的应用前景值得进一步探讨与验证。

* * *

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参 考 文 献

- [1] LI M, CHI X, WANG Y, *et al.* Trends in insulin resistance: Insights into mechanisms and therapeutic strategy. *STTT*, 2022, 7(1): 216. doi: [10.1038/s41392-022-01073-0](https://doi.org/10.1038/s41392-022-01073-0).
- [2] PETERSEN M C, SHULMAN G I. Mechanisms of insulin action and insulin resistance. *Physiol Rev*, 2018, 98(4): 2133-2223. doi: [10.1152/physrev.00063.2017](https://doi.org/10.1152/physrev.00063.2017).
- [3] CALCATERRA V, VERDUCI E, CENA H, *et al.* Polycystic ovary syndrome in insulin-resistant adolescents with obesity: The role of nutrition therapy and food supplements as a strategy to protect fertility. *Nutrients*, 2021, 13(6): 1848. doi: [10.3390/nu13061848](https://doi.org/10.3390/nu13061848).
- [4] SIRMANS S M, PATE K A. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clin Epidemiol*, 2013, 6: 1-13. doi: [10.2147/CLEP.S37559](https://doi.org/10.2147/CLEP.S37559).
- [5] STENER-VICTORIN E, TEEDE H, NORMAN R J, *et al.* Polycystic ovary syndrome. *Nat Rev Dis Primers*, 2024, 10(1): 27. doi: [10.1038/s41572-024-00511-3](https://doi.org/10.1038/s41572-024-00511-3).
- [6] HOMBURG R. Management of infertility and prevention of ovarian hyperstimulation in women with polycystic ovary syndrome. *Best Pract Res Clin Obstet Gynaecol*, 2004, 18(5): 773-788. doi: [10.1016/j.bpobgyn.2004.05.006](https://doi.org/10.1016/j.bpobgyn.2004.05.006).
- [7] COSTELLO M, GARAD R, HART R, *et al.* A review of first line infertility treatments and supporting evidence in women with polycystic ovary syndrome. *Med Sci (Basel)*, 2019, 7(9): 95. doi: [10.3390/medsci7090095](https://doi.org/10.3390/medsci7090095).
- [8] COSTELLO M F, GARAD R M, HART R, *et al.* A review of second- and third-line infertility treatments and supporting evidence in women with

- polycystic ovary syndrome. *Med Sci (Basel)*, 2019, 7(7): 75. doi: [10.3390/medsci7070075](#).
- [9] SHA T, WANG X, CHENG W, *et al.* A meta-analysis of pregnancy-related outcomes and complications in women with polycystic ovary syndrome undergoing IVF. *Reprod Biomed Online*, 2019, 39(2): 281-293. doi: [10.1016/j.rbmo.2019.03.203](#).
- [10] TANG K, WU L, LUO Y, *et al.* *In vitro* fertilization outcomes in women with polycystic ovary syndrome: a meta-analysis. *Eur J Obstet Gynecol Reprod Biol*, 2021, 259: 146-152. doi: [10.1016/j.ejogrb.2021.02.023](#).
- [11] MATORRAS R, PIJOAN J I, LAÍN Z L, *et al.* Polycystic ovarian syndrome and miscarriage in IVF: Systematic revision of the literature and meta-analysis. *Arch Gynecol Obstet*, 2023, 308(2): 363-377. doi: [10.1007/s00404-022-06757-0](#).
- [12] LIU S, MO M, XIAO S, *et al.* Pregnancy outcomes of women with polycystic ovary syndrome for the first *in vitro* fertilization treatment: a retrospective cohort study with 7678 patients. *Front Endocrinol*, 2020, 11: 575337. doi: [10.3389/fendo.2020.575337](#).
- [13] 丁凤娟, 万彦伶, 郝翠芳. PCOS患者胰岛素抵抗与肥胖对IVF结局的影响. *生殖医学杂志*, 2019, 28(5): 462-468. doi: [10.3969/j.issn.1004-3845.2019.05.003](#).
- DING F J, WAN Y L, HAO C F. Effects of insulin resistance and obesity on IVF outcomes in patients with PCOS. *Journal of Reproductive Medicine*, 2019, 28(5): 462-468. doi: [10.3969/j.issn.1004-3845.2019.05.003](#).
- [14] 胡玥玥, 张昌军. 胰岛素抵抗指数对PCOS不孕患者IVF-ET治疗妊娠结局的预测. *中国医药导报*, 2017, 14(35): 66-70.
- HU Y Y, ZHANG C J. Predictive of insulin resistance indices for pregnancy outcomes in infertile patients with PCOS undergoing IVF-ET. *China Medical Herald*, 2017, 14(35): 66-70.
- [15] HUANG W, LIU C, DING L, *et al.* The effect of β -cell dysfunction on reproductive outcomes of PCOS undergoing IVF or ICSI embryo transfer cycles: a retrospective cohort study. *Front Endocrinol*, 2024, 15: 1327041. doi: [10.3389/fendo.2024.1327041](#).
- [16] CAKIROGLU Y, DOGER E, VURAL F, *et al.* Impact of insulin resistance and obesity on intracytoplasmic sperm injection outcomes in young women with polycystic ovary syndrome. *North Clin Istanb*, 2017, 4(3): 218-224. doi: [10.14744/nci.2017.79663](#).
- [17] HU Z, ZENG R, TANG Y, *et al.* Effect of oral glucose tolerance test-based insulin resistance on embryo quality in women with/without polycystic ovary syndrome. *Front Endocrinol*, 2024, 15: 1413068. doi: [10.3389/fendo.2024.1413068](#).
- [18] GASTALDELLI A. Measuring and estimating insulin resistance in clinical and research settings. *Obesity (Silver Spring, Md.)*, 2022, 30(8): 1549-1563. doi: [10.1002/oby.23503](#).
- [19] GONG R, LIU Y, LUO G, *et al.* Using optimal subset regression to identify factors associated with insulin resistance and construct predictive models in the US adult population. *Endocr Connect*, 2022, 11(7): e220066. doi: [10.1530/EC-22-0066](#).
- [20] SARTORELLI D S, FRANCO L J, DAMIÃO R, *et al.* Dietary glycemic load, glycemic index, and refined grains intake are associated with reduced beta-cell function in prediabetic Japanese migrants. *Arq Bras Endocrinol Metabol*, 2009, 53(4): 429-434. doi: [10.1590/s0004-27302009000400007](#).
- [21] TOSI F, BONORA E, MOGHETTI P. Insulin resistance in a large cohort of women with polycystic ovary syndrome: A comparison between euglycaemic-hyperinsulinaemic clamp and surrogate indexes. *Human Reproduction (Oxford, England)*, 2017, 32(12): 2515-2521. doi: [10.1093/humrep/dex308](#).
- [22] 中华医学会糖尿病学分会胰岛素抵抗学组(筹). 胰岛素抵抗评估方法和应用的专家指导意见. *中华糖尿病杂志*, 2018, 10(6): 377-385. doi: [10.3760/cma.j.issn.1674-5809.2018.06.001](#).
- Insulin Resistance Study Group of the Chinese Diabetes Society. Expert consensus on the assessment and clinical application of insulin resistance. *Chinese Journal of Diabetes*, 2018, 10(6): 377-385. doi: [10.3760/cma.j.issn.1674-5809.2018.06.001](#).
- [23] TEEDE H J, MISSO M L, COSTELLO M F, *et al.* Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*, 2018, 33(9): 1602-1618. doi: [10.1093/humrep/dey256](#).
- [24] 中国医师协会生殖医学专业委员会. 人类卵裂期胚胎及囊胚形态学评价中国专家共识中华生殖与避孕杂志, 2022, 42(12): 1218-1225. doi: [10.3760/cma.j.cn101441-20220619-00266](#).
- Reproductive Medicine Committee of the Chinese Medical Doctor Association. Chinese expert consensus on morphological evaluation of human cleavage-stage embryos and blastocysts. *Chinese Journal of Reproduction and Contraception*, 2022, 42(12): 1218-1225. doi: [10.3760/cma.j.cn101441-20220619-00266](#).
- [25] GARDNER D K, SCHOOLCRAFT W B. Culture and transfer of human blastocysts. *Curr Opin Obstet Gynecol*, 1999, 11(3): 307-311. doi: [10.1097/00001703-199906000-00013](#).
- [26] ESHRE Guideline Group on Good Practice in IVF Labs; De los SANTOS M J, APTER S, *et al.* Revised guidelines for good practice in IVF laboratories (2015). *Hum Reprod*, 2016, 31(4): 685-686. doi: [10.1093/humrep/dew016](#).
- [27] 孙青, 黄国宁, 孙海翔, 等. 胚胎实验室关键指标质控专家共识. *生殖医学杂志*, 2018, 27(9): 836-851. doi: [10.3969/j.issn.1004-3845.2018.09.003](#).
- SUN Q, HUANG G N, SUN H X, *et al.* Expert consensus on quality control of key performance indicators in the embryology laboratory. *Journal of Reproductive Medicine*, 2018, 27(9): 836-851. doi: [10.3969/j.issn.1004-3845.2018.09.003](#).
- [28] WANG J, WU D, GUO H, *et al.* Hyperandrogenemia and insulin resistance: The chief culprit of polycystic ovary syndrome. *Life Sci*, 2019, 236: 116940. doi: [10.1016/j.lfs.2019.116940](#).
- [29] LI L, GE H, ZHOU J, *et al.* Polycystic ovary syndrome and adverse pregnancy outcomes: Potential role of decidual function. *Drug Discov Therap*, 2024, 17(6): 378-388. doi: [10.5582/ddt.2023.01096](#).
- [30] LUO Z, WANG L, WANG Y, *et al.* Impact of insulin resistance on ovarian sensitivity and pregnancy outcomes in patients with polycystic ovary syndrome undergoing IVF. *J Clin Med*, 2023, 12(3): 818. doi: [10.3390/jcm12030818](#).
- [31] 吴亚妹, 马宁, 黄兹宝, 等. 胰岛素抵抗影响多囊卵巢综合征发病及机制的研究进展. *生殖医学杂志*, 2021, 30(9): 1247-1251. doi: [10.3969/j.issn.1004-3845.2021.09.023](#).
- WU Y M, MA N, HUANG Z B, *et al.* Research progress on the role and mechanisms of insulin resistance in the pathogenesis of polycystic ovary syndrome. *Journal of Reproductive Medicine*, 2021, 30(9): 1247-1251. doi: [10.3969/j.issn.1004-3845.2021.09.023](#).
- [32] 刘音, 鲁娣, 宋殿荣. 胰岛素抵抗对多囊卵巢综合征生殖内分泌及代谢的影响. *国际妇产科学杂志*, 2023, 50(2): 190-195. doi: [10.12280/gjfcx.20230032](#).
- LIU Y, LU D, SONG D R. Effects of insulin resistance on reproductive endocrinology and metabolism in patients with polycystic ovary syndrome. *Int J Gynecol Obstet*, 2023, 50(2): 190-195. doi: [10.12280/gjfcx.20230032](#).
- [33] MUNIYAPPA R, LEE S, CHEN H, *et al.* Current approaches for assessing insulin sensitivity and resistance *in vivo*: Advantages, limitations, and appropriate usage. *Am J Physiol Endocrinol Metabol*, 2008, 294(1): E15-26. doi: [10.1152/ajpendo.00645.2007](#).
- [34] PARK S Y, GAUTIER J F, CHON S. Assessment of insulin secretion and insulin resistance in human. *Diabetes Metabol J*, 2021, 45(5): 641-654. doi: [10.4093/dmj.2021.0220](#).
- [35] WONGWANANURUK T, RATTANACHAIYANONT M, LEERASIRI P, *et al.* The usefulness of homeostatic measurement assessment-insulin resistance (HOMA-IR) for detection of glucose intolerance in Thai women of reproductive age with polycystic ovary syndrome. *Int J Endocrinol*, 2012, 2012: 571035. doi: [10.1155/2012/571035](#).
- [36] SINGH B, SAXENA A. Surrogate markers of insulin resistance: A review. *World J Diabet*, 2010, 1(2): 36-47. doi: [10.4239/wjd.v1.i2.36](#).
- [37] LEWANDOWSKI K C, PŁUSAJSKA J, HORZELSKI W, *et al.* Limitations of insulin resistance assessment in polycystic ovary syndrome. *Endocr Connect*, 2018, 7(3): 403-412. doi: [10.1530/EC-18-0021](#).

- [38] HUO Y, JI S, YANG H, *et al.* Differential expression of microRNA in the serum of patients with polycystic ovary syndrome with insulin resistance. *Ann Transl Med*, 2022, 10(14): 762. doi: [10.21037/atm-22-2941](https://doi.org/10.21037/atm-22-2941).
- [39] JOVANOVSKA-MISHEVSKA S, ATANASOVA-BOSHKU A, BITOSKA I, *et al.* Indexes of insulin resistance in hyperinsulinemic polycystic ovary syndrome in a macedonian cohort of women of reproductive age: a cross-sectional study. *Open Access Maced J Med Sci*, 2016, 4(4): 607-612. doi: [10.3889/oamjms.2016.107](https://doi.org/10.3889/oamjms.2016.107).
- [40] 宋文娟, 吴俊杰, 李玉涛, 等. 2型糖尿病患者肥胖与内分泌指数的关系研究. *预防医学*, 2020, 32(5): 508-511. doi: [10.19485/j.cnki.issn2096-5087.2020.05.019](https://doi.org/10.19485/j.cnki.issn2096-5087.2020.05.019).
SONG W J, WU J J, LI Y T, *et al.* Association between obesity and endocrine indices in patients with type 2 diabetes mellitus. *Preventive Medicine*, 2020, 32(5): 508-511. doi: [10.19485/j.cnki.issn2096-5087.2020.05.019](https://doi.org/10.19485/j.cnki.issn2096-5087.2020.05.019).
- [41] LI X, LUAN T, WEI Y, *et al.* The association between triglyceride glucose-body mass index and in vitro fertilization outcomes in women with polycystic ovary syndrome: a cohort study. *J Ovarian Res*, 2024, 17(1): 90. doi: [10.1186/s13048-024-01416-1](https://doi.org/10.1186/s13048-024-01416-1).
- [42] CHANG E M, HAN J E, SEOK H H, *et al.* Insulin resistance does not affect early embryo development but lowers implantation rate in *in vitro* maturation-*in vitro* fertilization-embryo transfer cycle. *Clin Endocrinol*, 2013, 79(1): 93-99. doi: [10.1111/cen.12099](https://doi.org/10.1111/cen.12099).
- [43] YANG T, YANG Y, ZHANG Q, *et al.* Homeostatic model assessment for insulin resistance is associated with late miscarriage in non-dyslipidemic women undergoing fresh IVF/ICSI embryo transfer. *Front Endocrinol*, 2022, 13: 880518. doi: [10.3389/fendo.2022.880518](https://doi.org/10.3389/fendo.2022.880518).
- [44] WEI S Y, ZHANG J L, GUAN H Q, *et al.* High androgen level during controlled ovarian stimulation cycle impairs endometrial receptivity in PCOS patients. *Sci Rep*, 2024, 14(1): 23100. doi: [10.1038/s41598-024-74295-7](https://doi.org/10.1038/s41598-024-74295-7).
- [45] SHAPIRO B S, DANESHMAND S T, GARNER F C, *et al.* Evidence of impaired endometrial receptivity after ovarian stimulation for *in vitro* fertilization: a prospective randomized trial comparing fresh and frozen-thawed embryo transfer in normal responders. *Fertil Steril*, 2011, 96(2): 344-348. doi: [10.1016/j.fertnstert.2011.05.050](https://doi.org/10.1016/j.fertnstert.2011.05.050).
- [46] BORGES E J, BRAGA D P A F, SETTI A S, *et al.* Strategies for the management of OHSS: results from freezing-all cycles. *JBRA Assisted Reproduct*, 2016, 20(1): 8-12. doi: [10.5935/1518-0557.20160003](https://doi.org/10.5935/1518-0557.20160003).
- [47] ADEVIYE ERŞAHIN A, ACET M, ERŞAHIN S S, *et al.* Frozen embryo transfer prevents the detrimental effect of high estrogen on endometrium receptivity. *J Turkish German Gynecol Assoc*, 2017, 18(1): 38-42. doi: [10.4274/jtgga.2016.0186](https://doi.org/10.4274/jtgga.2016.0186).

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