

辅助生殖技术助孕与自然受孕双绒毛膜双胎妊娠结局比较

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摘要 目的 探讨辅助生殖技术(ART)助孕与自然受孕双绒毛膜双羊膜囊(DCDA)双胎的妊娠结局差异,为ART助孕DCDA双胎围产期管理提供依据。**方法** 回顾性分析549例DCDA双胎孕产妇的临床资料,根据受孕方式分为ART助孕组(423例)和自然受孕组(126例),比较两组孕产妇的一般资料、妊娠并发症及新生儿结局。**结果** 在一般资料方面,ART助孕组的年龄、流产次数、初产妇比例、高龄产妇比例和产后24 h出血量高于自然受孕组,产次和瘢痕子宫比例低于自然受孕组($P < 0.05$)。在妊娠并发症方面,ART助孕组的妊娠期高血压疾病、胎盘粘连、产后出血的发生率以及子宫动脉上行支结扎术的应用率更高($P < 0.05$)。两组新生儿相关指标差异均无统计学意义。校正年龄、流产次数和分娩次数等混杂因素后,ART仍可增加妊娠期高血压疾病、胎盘粘连、产后出血的发生风险($P < 0.05$),但不会增加新生儿不良结局的风险。进一步的孕周亚组分析显示,在晚期早产亚组中,ART相关的妊娠并发症风险依然增高($P < 0.05$);在晚期早产及足月亚组中,两组新生儿结局的无差异。**结论** ART助孕DCDA双胎孕产妇妊娠期高血压疾病、胎盘粘连、产后出血的发生风险增加,临床应加强孕期血压及产后出血量的监测,针对性防控并发症,改善妊娠结局。

关键词 辅助生殖技术;自然妊娠;双胎妊娠;妊娠结局;胎盘粘连;产后出血;妊娠期高血压

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近年来,我国与生育相关的人口结构面临显著变化。在生育率持续走低的同时,不孕不育发生率由2007年的12%上升至2020年的18%,目前仍呈上升态势^[1]。加之生育政策的全面调整优化(如“二孩”“三孩”政策相继实施)以及女性生育年龄普遍推迟(高龄产妇比例逐年攀升),共同促使通过辅助生殖技术(assisted reproductive technology, ART)助孕的孕产妇数量逐年增加^[2]。临床实践常倾向于移植多枚胚胎,这一做法提高了双胎妊娠比例。而双胎妊娠本身即属高危妊娠范畴,其母体并发症及围产儿不良结局的发生风险显著高于单胎妊娠。

ART助孕是否进一步增加双胎孕产妇不良围产结局风险,目前学术界尚未达成共识。该研究通过系统收集ART助孕与自然受孕双绒毛膜双羊膜囊(dichorionic diamniotic, DCDA)双胎孕产妇及其新生儿的临床资料,旨在比较两组母婴围产结局的

差异。研究结果可为临床提供更精准的ART咨询依据,并为提升母婴健康水平提供理论支持。

1 材料与方法

1.1 病例资料 选取2022年5月—2025年5月在安徽医科大学第一附属医院产科分娩的549例DCDA双胎孕产妇为研究对象。根据受孕方式将其分为ART助孕组(423例)和自然受孕组(126例)。

纳入标准:①完成产检和活产分娩的DCDA双胎孕产妇;②分娩孕周 ≥ 28 周;③自然受孕或ART助孕妊娠,ART方式包括体外受精-胚胎移植、胞质内单精子注射、胚胎植入前遗传学诊断3种受孕方式;④临床相关资料完整。**排除标准:**①使用供卵、供精;②由3胎及以上的多胎妊娠减胎至双胎妊娠;③妊娠前合并严重的内外科疾病;④双胎之一为死胎;⑤临床相关资料不完整。本研究经医院医学伦理委员会审批通过(PJ 2025-07-96),符合豁免知情同意的相关规定,已豁免患者知情同意。

1.2 研究方法 采用回顾性研究设计,比较ART助孕组与自然受孕组孕产妇妊娠期间的妊娠并发症发生情况及母婴妊娠结局。通过电子病历系统、电话回访等方式获取研究对象的围产期资料。主

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要包括以下几个方面。① 基本资料:年龄、高龄产妇(≥ 35 岁)、身高、体质量、孕前体质量指数(body mass index, BMI)、孕期体质量增长、分娩孕周、孕产次、分娩方式、瘢痕子宫和产后出血量,同时根据分娩孕周,将研究对象进一步划分为早期早产($28^{+0} \sim 33^{+6}$ 周)、晚期早产($34^{+0} \sim 36^{+6}$ 周)及足月(≥ 37 周)3组。② 妊娠期并发症:妊娠期高血压(hypertensive disorders of pregnancy, HDP)、妊娠期糖尿病(gestational diabetes mellitus, GDM)、妊娠期肝内胆汁淤积症(intrahepatic cholestasis of pregnancy, ICP)、前置胎盘、胎儿生长受限、双胎生长不一致、胎膜早破(premature rupture of membranes, PROM)、胎盘粘连、产后出血以及产后出血的手术止血方法(子宫球囊放置术、子宫捆绑术、双侧子宫动脉上行支结扎术)。③ 新生儿结局:新生儿出生一般信息,包括体质量、身长、头围;新生儿并发症及结局,早产、低出生体质量儿、新生儿窒息、呼吸窘迫综合征(neonatal respiratory distress syndrome, NRDS)、湿肺、肺炎、高胆红素血症、新生儿畸形以及是否转入新生儿科。④ 根据分娩孕周进行亚组分析。考虑到亚组样本量差异,其结果主要用于描述性参考和趋势观察,主体结论仍基于整体人群及校正主要混杂因素的多因素 Logistic 回归分析。

1.3 统计学处理 采用 SPSS 23.0 软件对数据进行统计分析。正态分布的定量资料用 $\bar{x} \pm s$ 表示,组间比较采用 t 检验;非正态分布的定量资料用

$M(P_{25}, P_{75})$ 表示,组间比较采用 Mann-Whitney U 检验;定性资料用 $n(\%)$ 表示,组间比较采用 χ^2 检验。采用多因素 Logistic 回归模型,对孕妇年龄、流产次数、孕产次等潜在的混杂因素进行调整后,分析 ART 本身与妊娠期并发症及妊娠结局之间是否存在独立的关联关系。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组孕产妇病例资料比较 ART 助孕组的年龄高于自然受孕组($P < 0.001$);流产次数高于自然受孕组($P = 0.007$);产次少于自然受孕组($P < 0.001$);24 h 出血量多于自然受孕组($P = 0.003$);初产妇比例高于自然受孕组($P < 0.001$);高龄孕产妇比例高于自然受孕组($P < 0.001$);瘢痕子宫比例低于自然受孕组($P = 0.046$)。两组在孕期体质量增长、孕前 BMI、分娩孕周、剖宫产率和孕次差异无统计学意义。见表 1。

2.2 两组孕产妇妊娠并发症比较 ART 助孕组的 HDP 发生率高于自然受孕组($P = 0.014$);胎盘粘连发生率高于自然受孕组($P = 0.006$);产后出血发生率高于自然受孕组($P = 0.001$);产后出血的手术止血方法中双侧子宫动脉上行支结扎术($P = 0.001$)应用率高于自然受孕组。两组在 GDM、ICP、前置胎盘、胎儿生长受限、胎膜早破等方面差异均无统计学意义。见表 2。

2.3 两组受孕方式新生儿结局比较 两组新生儿

表 1 两组孕产妇基本资料比较 [$M(P_{25}, P_{75}), n(\%)$]

Tab. 1 Comparison of baseline characteristics between the two groups [$M(P_{25}, P_{75}), n(\%)$]

Item	Spontaneous conception group ($n=126$)	ART group ($n=423$)	Z/χ^2 value	P value
Maternal age (years)	29.0 (27.0, 32.0)	32.0 (30.0, 35.0)	-7.075	<0.001
Pre-pregnancy BMI (kg/m^2)	22.0 (20.2, 24.2)	22.0 (20.2, 24.7)	-0.369	0.712
Weight gain (kg)	15.0 (13.0, 20.0)	15.0 (12.0, 20.0)	-0.703	0.482
Gestational weeks	36.6 (35.3, 37.3)	36.4 (35.1, 37.1)	-1.379	0.168
Gestational weeks groups				
≥ 37	51 (40.5)	152 (35.9)	0.860	0.354
$34^{+0} \sim 36^{+6}$	61 (48.4)	202 (47.8)	0.017	0.897
$28^{+0} \sim 33^{+6}$	14 (11.1)	69 (16.3)	2.046	0.153
Primipara	88 (69.8)	360 (85.1)	15.069	<0.001
Advanced maternal age	8 (6.3)	119 (28.1)	25.907	<0.001
Gravidity	1.5 (1.0, 3.0)	2.0 (1.0, 3.0)	-1.097	0.273
Abortions	0 (0, 1.0)	1.0 (0, 1.0)	-2.706	0.007
Parity	1.0 (1.0, 2.0)	1.0 (1.0, 1.0)	-3.866	<0.001
Scarred uterus	14 (11.1)	25 (5.9)	3.979	0.046
Cesarean delivery	115 (91.3)	394 (93.1)	0.505	0.477
24 hour blood loss (mL)	577.5 (500.0, 710.0)	640.0 (535.0, 795.0)	-2.977	0.003

在一般资料、相关并发症及结局等方面比较,差异无统计学意义。见表3、表4。

2.4 多因素 Logistic 回归分析 采用多因素 Logistic 回归分析对年龄、产次、流产次数等混杂因素进行校正,结果显示 ART 仍会增加 HDP、胎盘粘连、产后出血的发生风险($P < 0.05$),见表5;但 ART 不会增加新生儿相关并发症以及不良妊娠结局的风险($P > 0.05$),见表6。

2.5 不同孕周亚组妊娠并发症比较 在晚期早产组($n=263$)中,ART 组妊娠期高血压疾病[60(29.7%) vs 6(9.8%), $P=0.002$]、胎盘粘连[27(13.4%) vs 2(3.3%), $P=0.027$]的发生率及子宫动脉上行支结扎术应用率[23(8.7%) vs 0(0.0%), $P=0.006$]仍显著高于自然受孕组。此外,ART 组产后出血发生率也呈现增高趋势[27(11.4%) vs 2(3.3%), $P=0.058$]。与整体人群的分析结论一致,

表2 两组孕产妇妊娠合并症比较 [n(%)]

Tab. 2 Comparison of pregnancy complications between the two groups [n(%)]

Item	Spontaneous conception group (n=126)	ART group (n=423)	χ^2 value	P value
HDP	15 (11.9)	92 (21.7)	5.996	0.014
GDM	33 (26.2)	117 (27.7)	0.106	0.745
ICP	7 (5.6)	22 (5.2)	0.024	0.876
Placenta previa	1 (0.8)	14 (3.3)	1.463*	0.227
Fetal growth restriction	2 (1.6)	8 (1.9)	0.050*	0.823
Discordant fetal growth	8 (6.3)	13 (3.1)	2.832	0.092
PROM	14 (11.1)	61 (14.4)	0.902	0.342
Placenta adhesion	6 (4.8)	58 (13.7)	7.551	0.006
Placental abruption	0 (0)	2 (0.4)	-	>0.999
Postpartum hemorrhage	3 (2.4)	53 (12.5)	10.916	0.001
Intrauterine balloon tamponade	2 (1.6)	25 (5.9)	3.880	0.050
B-Lynch suture	8 (6.3)	45 (10.6)	2.048	0.152
Ascending uterine artery ligation	1 (0.8)	39 (9.2)	10.204	0.001

-: analyzed by Fisher's exact test; *: chi-square value with continuity correction.

表3 两组新生儿一般资料比较 [M(P₂₅, P₇₅)]

Tab. 3 Comparison of baseline characteristics of neonates between the two groups [M(P₂₅, P₇₅)]

Item	Spontaneous conception group (n=126)	ART group (n=423)	Z value	P value
Larger fetus weight (kg)	2.50 (2.25, 2.75)	2.51 (2.21, 2.75)	-0.161	0.872
Smaller fetus weight (kg)	2.39 (2.10, 2.68)	2.47 (2.15, 2.71)	-1.231	0.218
Larger fetus length (cm)	47.00 (45.00, 48.00)	47.00 (45.00, 48.00)	-1.000	0.318
Smaller fetus length (cm)	46.00 (44.75, 48.00)	47.00 (45.00, 48.00)	-0.509	0.611
Larger fetus head circumference (cm)	33.00 (32.00, 34.00)	33.00 (32.00, 34.00)	-0.621	0.535
Smaller fetus head circumference (cm)	33.00 (32.00, 34.00)	33.00 (32.00, 34.00)	-1.329	0.184

表4 两组新生儿并发症及结局情况比较 [n(%)]

Tab. 4 Comparison of complications and outcomes of neonates between the two groups [n(%)]

Item	Spontaneous conception group (n=252)	ART group (n=846)	Z/ χ^2 value	P value
Preterm infant	152 (60.3)	542 (64.1)	0.587	0.444
Low birth weight infant	112 (44.4)	379 (44.8)	0.010	0.921
Neonatal asphyxia	20 (7.9)	59 (7.0)	0.269	0.604
NRDS	12 (4.8)	47 (5.6)	0.241	0.624
Pathological jaundice	11 (4.4)	59 (7.0)	2.214	0.137
Neonatal pneumonia	5 (2.0)	11 (1.3)	0.632	0.426
Neonatal transient tachypnea	8 (3.2)	42 (5.0)	1.431	0.232
Transfer to neonatal department	91 (36.1)	331 (39.1)	0.746	0.388
Fetal malformation	4 (1.6)	4 (0.5)	1.971	0.160

表5 ART与妊娠并发症关联性的多因素Logistics回归分析

Tab. 5 Multivariate Logistic regression analysis of the association between ART and pregnancy complications

Item	β	Wald	Unadjusted			Adjusted		
			OR	95% CI	P value	OR	95% CI	P value
HDP	0.721	5.806	2.057	1.144 – 3.698	0.016	1.920	1.028 – 3.585	0.041
Placenta adhesion	1.156	6.857	3.178	1.338 – 7.551	0.009	3.256	1.310 – 8.088	0.011
Postpartum hemorrhage	1.770	8.633	5.873	1.803 – 19.131	0.003	4.946	1.467 – 16.671	0.010

表6 ART与新生儿并发症及结局关联性的多因素Logistics回归分析

Tab. 6 Multivariate Logistic regression analysis of the association between ART and neonatal complications and outcomes

Item	β	Wald	Unadjusted			Adjusted		
			OR	95% CI	P value	OR	95% CI	P value
Preterm infant	0.160	1.172	1.173	0.879 – 1.566	0.279	1.251	0.911 – 1.719	0.167
Low birth weight infant	0.014	0.010	1.014	0.764 – 1.346	0.996	0.999	0.734 – 1.361	0.996
Neonatal asphyxia	-0.140	0.269	0.870	0.513 – 1.474	0.604	0.837	0.471 – 1.489	0.545
NRDS	0.163	0.240	1.176	0.614 – 2.254	0.624	0.922	0.460 – 1.848	0.819
Pathological jaundice	0.496	2.174	1.642	0.849 – 3.177	0.140	1.480	0.732 – 2.989	0.275
Neonatal pneumonia	0.466	1.407	1.593	0.738 – 3.439	0.235	0.586	0.179 – 1.924	0.379
Neonatal transient tachypnea	-0.430	0.623	0.651	0.224 – 1.891	0.430	1.570	0.688 – 3.584	0.284
Transfer to neonatal department	0.128	0.745	1.137	0.849 – 1.522	0.388	1.260	0.916 – 1.732	0.155
Fetal malformation	-1.222	2.957	0.295	0.073 – 1.186	0.085	0.239	0.048 – 1.193	0.081

表明ART与特定并发症的关联具有稳健性。

2.6 不同孕周亚组新生儿并发症及结局比较 不同孕周亚组的新生儿并发症及结局比较分析显示,在晚期早产及足月亚组中,ART与自然受孕双胎的新生儿并发症及结局发生率差异均无统计学意义,进一步支持了ART未增加DCDA双胎新生儿不良结局风险的总体结论。在早期早产亚组中,因自然受孕组样本量极其有限($n=28$),统计效能不足,观察到的组间差异可能由偶然因素导致,结果的稳定性和解释力有限。

3 讨论

自首例试管婴儿诞生以来,ART已成为解决不孕问题的重要方法。ART的临床应用显著提高了双胎妊娠发生率,全球每年约有160万对双胎胎儿诞生^[3]。ART是否会进一步增加双胎妊娠的风险,目前仍存在争议。部分研究^[4]认为ART可能增加围产期相关风险,也有观点^[5]指出差异源于混杂因素而非ART本身。因此,本研究通过回顾性分析近3年内于安徽医科大学第一附属医院产科住院分娩的DCDA双胎孕产妇临床资料,系统比较ART助孕组与自然受孕组的妊娠并发症及围产结局差异,为临床优化ART双胎围产期管理提供参考。

本研究显示,ART助孕组孕产妇平均年龄、流

产次数、初产妇比例高于自然受孕组,而其产次以及瘢痕子宫比例则低于自然受孕组。该差异与ART患者多伴有高龄、不孕病史等临床特征一致,也与已有文献^[6]报道相符。高龄和多次流产史是不孕症发生的常见因素,亦是ART助孕的主要指征。而该群体生育困难导致产次较低,剖宫产手术史相应减少,因此瘢痕子宫比例相应减少。

本研究显示,ART助孕组孕产妇HDP的发生率高于自然受孕组,与多项已有研究^[7-8]结论一致。这可能是因为ART卵巢刺激导致的高雌激素状态引起血管内皮功能紊乱^[9],同时胚胎操作可能影响胎盘滋养细胞的功能与侵袭能力,造成胎盘浅着床和灌注不足,进而通过抗血管生成因子释放激活相关系统引发血压升高^[10]。ART助孕组胎盘粘连的发生率高于自然受孕组,该结果与之前的报道^[11]相符。该现象是多因素共同作用的结果。首先,ART可能干扰子宫内膜的正常蜕膜化过程,导致蜕膜层变薄或功能缺陷^[12];同时,体外培养环境及外源性激素刺激可能引起滋养层细胞侵袭性异常增强,使其更易突破蜕膜-肌层界面^[13];加之ART人群常伴高龄、既往宫腔操作史等高危因素,进一步加剧子宫内膜损伤风险,最终促进胎盘粘连发生。在妊娠结局方面,ART助孕组产后出血发生率较高,与既往研究结果^[14]一致。可能因为ART相关操作损伤

子宫内膜基底层,干扰蜕膜化过程,增加胎盘附着异常风险,且常合并妊娠期高血压疾病影响凝血功能,加之高龄、剖宫产率高等特点,均增加出血风险。因此,ART双胎孕产妇需积极采取产后出血预防措施,产后密切监测生命体征及出血量。

本研究结果中,与自然受孕相比,ART不会增加DCDA双胎新生儿不良结局的发生风险,这与多项研究结果^[15-16]一致。可能得益于ART妊娠接受更频繁缜密的产前检查,有助于早期处理潜在并发症,也印证了当前ART助孕的安全性。

亚组分析表明,晚期早产组中ART组HDP、胎盘粘连等并发症的发生风险依然增高,与整体分析结论一致,支持了ART是独立于孕周的母体风险因素。早期早产亚组因自然受孕组样本量过小,统计效能不足。本研究已通过组间均衡性比较证实两组孕周分布无差异,因此未将孕周纳入多因素Logistic回归模型以避免多重共线性,保证核心变量(ART)效应估计稳定。未来需开展大规模前瞻性研究,分层分析不同孕周区间ART的独立风险。

本研究优势在于纳入对象接受同质化管理,排除绒毛膜性影响,且通过多因素Logistic回归排除混杂因素干扰,数据真实性可靠。本研究不足为未区分不同ART技术,且单中心研究易产生选择性偏倚,后续需扩大样本量开展多中心研究,进一步明确ART与双胎围产结局的关系。

综上所述,本研究说明ART助孕增加DCDA双胎孕产妇HDP、胎盘粘连及产后出血的发生风险。临床应将ART双胎孕产妇作为高危人群进行管理,加强孕期监测、积极防治妊娠期高血压等并发症,尤其重视产后出血的一级预防和应急准备。建议严格掌握胚胎移植指征,推行个体化移植策略。未来仍需开展多中心前瞻性研究进一步明确ART对母胎结局的远期影响,为优化助孕策略及围产期管理提供更强证据支持。

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Pregnancy outcomes in dichorionic twins: comparing assisted reproductive technology and spontaneous conception

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Abstract Objective To investigate the differences in pregnancy outcomes between dichorionic diamniotic (DCDA) twin pregnancies conceived *via* assisted reproductive technology (ART) and those from spontaneous conception, in order to provide evidence for the perinatal management of ART-conceived DCDA twins. **Methods** A retrospective analysis was conducted on the clinical data of 549 DCDA twin parturients. Based on the mode of conception, they were divided into ART group (423 cases) and spontaneous conception group (126 cases). The baseline characteristics, pregnancy complications and neonatal outcomes were compared between the two groups. **Results** Regarding baseline characteristics, the ART group had higher maternal age, number of previous abortions, proportions of primiparas, proportions of advanced maternal age and greater 24-hour postpartum blood loss, but lower parity and proportion of scarred uterus compared to the spontaneous conception group ($P < 0.05$). For pregnancy complications, the ART group exhibited higher incidences of hypertensive disorders of pregnancy, placental adhesion, postpartum hemorrhage and a higher application rate of uterine artery ascending branch ligation ($P < 0.05$). There were no statistically significant differences in neonatal-related indicators between the two groups. After adjusting for confounding factors such as age, number of abortions and parities, ART remained an independent risk factor for hypertensive disorders of pregnancy, placental adhesion and postpartum hemorrhage ($P < 0.05$), while it did not increase the risk of adverse neonatal outcomes. Further subgroup analysis by gestational age showed that in the late preterm subgroup, the risk of ART-related pregnancy complications remained elevated ($P < 0.05$). Additionally, neonatal outcomes showed no significant difference between the two groups in both the late preterm and term subgroups. **Conclusion** ART increases the risk of hypertensive disorders of pregnancy, placental adhesion and postpartum hemorrhage in DCDA twin parturients. Clinically, enhanced monitoring of blood pressure during pregnancy and blood loss during delivery and postpartum, along with targeted prevention and management of these complications, are crucial for improving pregnancy outcomes.

Key words assisted reproductive technology; spontaneous pregnancy; twin pregnancy; pregnancy outcome; placental adhesion; postpartum hemorrhage; hypertensive disorders of pregnancy

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