·临床研究·

双胎绒毛膜性、出生胎龄、出生体质量不一致程度与新生儿结局分析

李　姝[1]，余慕雪[1]，冯嘉丽[1]，李晓瑜[1]，张婉婷[2]
（1. 中山大学附属第一医院儿科，广东 广州 510080；2. 中山大学中山医学院，广东 广州 510080）

摘　要：【目的】探讨双胎妊娠的单绒毛膜双羊膜囊（MCDA）和双绒毛膜双羊膜囊（DCDA）不同绒毛膜性、出生胎龄和出生体质量不一致程度与活产双胎新生儿结局的关系。【方法】回顾性分析 2015 年 1 月至 2020 年 12 月在中山大学附属第一医院住院分娩的 MCDA 和 DCDA 活产双胎新生儿临床资料，共纳入 1 504 例。MCDA 组和 DCDA 组分别为 386 例和 1 118 例。采用 t 检验、秩和检验、χ^2 检验/Fish 确切概率法比较两组新生儿结局；logistic 回归分析绒毛膜性、出生胎龄、出生体质量不一致程度和性别对双胎新生儿结局的影响。出生体质量不一致程度≥25% 双胎新生儿 168 例，MCDA 组和 DCDA 组分别为 96 例和 72 例，logistic 回归分析绒毛膜性、出生胎龄、双胎出生体质量低或高（小胎儿或大胎儿）和性别对新生儿结局的影响。【结果】在 1 504 例活产双胎新生儿中 MCDA 组出生胎龄低于 DCDA 组（$P = 0.000$）、MCDA 组出生体质量不一致程度高于 DCDA 组（$P = 0.001$）；MCDA 组出生窒息、呼吸窘迫综合征（RDS）、支气管肺发育不良（BPD）和败血症的发生率高于 DCDA 组（$P = 0.000$，$P = 0.000$，$P = 0.000$，$P = 0.000$）；出生胎龄低分别是双胎新生儿出生窒息、RDS、BPD、败血症、坏死性小肠结肠炎（NEC）≥Ⅱ期、急性肾损伤（AKI）、视网膜病变（ROP）发生以及死亡的独立危险因素（$P = 0.000$，$P = 0.000$，$P = 0.000$，$P = 0.000$，$P = 0.011$，$P = 0.000$，$P = 0.000$，$P = 0.000$），出生体质量不一致程度高分别是双胎新生儿出生窒息、RDS、BPD、败血症和 ROP 发生的独立危险因素（$P = 0.045$，$P = 0.000$，$P = 0.000$，$P = 0.004$，$P = 0.017$）；绒毛膜性不是双胎新生儿各种疾病发生和死亡的独立危险因素（P 值均 > 0.05）。在 168 例出生体质量不一致程度≥25% 双胎新生儿中，出生胎龄低分别是其出生窒息、RDS、BPD、败血症和 ROP 发生的独立危险因素（$P = 0.000$，$P = 0.000$，$P = 0.000$，$P = 0.000$，$P = 0.000$），双胎的小胎儿分别是出生窒息和 BPD 发生的独立危险因素（$P = 0.013$，$P = 0.001$）；绒毛膜性不是新生儿疾病发生的独立危险因素（P 值均 > 0.05）。【结论】绒毛膜性不是双胎新生儿不良结局发生的独立危险因素，出生胎龄低和出生体质量不一致程度高是双胎新生儿不良结局的独立危险因素；出生体质量不一致程度≥25% 双胎的小胎儿新生儿结局更差。

关键词：双胎；绒毛膜性；出生胎龄；出生体质量不一致；新生儿结局
中图分类号：R722.6　　**文献标志码：**A　　**文章编号：**1672-3554（2023）06-1030-08
DOI：10.13471/j.cnki.j.sun.yat-sen.univ（med.sci）.2023.0618

Effect of Chorionicity, Gestational Age at Birth and Birth Weight Discordance on Neonatal Outcomes in Twin Pregnancies

LI Shu[1], YU Mu-xue[1], FENG Jia-li[1], LI Xiao-yu[1], ZHANG Wan-ting[2]
（1. Department of Pediatrics, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, China;
2. Zhongshan School of Medicine, Sun Yat-sen University, Guangzhou 510080, China）
Correspondence to: YU Mu-xue; E-mail: yumuxue@mail.sysu.edu.cn

Abstract:【Objective】To investigate the effect of chorionicity, gestational age at birth and birth weight discordance

收稿日期：2023-03-20
基金项目：广东省大学生创新创业训练计划项目（S201910558049）
作者简介：李姝，第一作者，研究方向：新生儿疾病，E-mail：lish387@mail.sysu.edu.cn；余慕雪，通信作者，主任医师，研究方向：新生儿疾病，E-mail：yumuxue@mail.sysu.edu.cn

on neonatal outcomes in twin pregnancies.【Methods】We conducted a population-based retrospective study of monochorionic diamniotic (MCDA) twin pregnancies and dichorionic diamniotic (DCDA) twin pregnancies who were admitted in the First Affiliated Hospital, Sun Yat-sen University from January 2015 to December 2020. A total of 1504 live-born twins were included, with 386 cases in MCDA group and 1118 cases in DCDA groups, respectively. The comparison of neonatal outcomes between MCDA and DCDA twins was performed using *t*-test, Wilcoxon rank sum test, Chi-square test or Fisher's exact test. Logistic regression was performed to evaluate the effects of chorionicity, gestational age at birth, birth weight discordance and sex on neonatal outcomes. There were 168 live-born twins affected by inter-twin birth weight discordance≥25%, with 96 cases in MCDA group and 72 cases in DCDA groups, respectively. Logistic regression was performed to evaluate the effects of chorionicity, gestational age at birth, birth weight light or heavy (small twin or large twin) of the twin and sex on neonatal outcomes.【Results】Among the 1 504 newborns, gestational age at birth was lower in MCDA group compared with DCDA group (P = 0.000), and the degree of birth weight discordance was higher in MCDA group than that of the DCDA group (P = 0.001). Birth asphyxia, respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), and sepsis were more frequency in MCDA group compared with DCDA group (P = 0.000, P = 0.000, P = 0.000, P = 0.000). Low gestational age at birth was an independent risk factor for birth asphyxia, RDS, BPD, sepsis, necrotizing enterocolitis (NEC)≥stage Ⅱ, acute kidney injury (AKI), retinopathy of prematurity (ROP), and neonatal death respectively (P = 0.000, P = 0.000, P = 0.000, P = 0.000, P = 0.011, P = 0.000, P = 0.000, P = 0.000). High degree of birth weight discordance was an independent risk factor for birth asphyxia, RDS, BPD, sepsis and ROP respectively (P = 0.045, P = 0.000, P = 0.000, P = 0.004, P = 0.017). Chorionicity was not an independent risk factor for neonatal morbidity and death (P > 0.05). Among the 168 twins with birth weight discordance ≥25%, low gestational age at birth was an independent risk factor for birth asphyxia, RDS, BPD, sepsis and ROP, respectively (P = 0.000, P = 0.000, P = 0.000, P = 0.000, P = 0.000); small twin was an independent risk factor for birth asphyxia and BPD, respectively (P = 0.013, P = 0.001); chorionicity was not an independent risk factor for neonatal morbidity (P > 0.05).【Conclusion】Chorionicity was not an independent risk factor for adverse neonatal outcome in twin births. Low gestational age at birth and high degree of birth weight discordance were independent risk factor for adverse neonatal outcome in twin births. Small twins had increased risk of adverse neonatal outcome in twins with birth weight discordance ≥25%.

Key words: twin; chorionicitiy; gestational age at birth; birth weight discordance; neonatal outcomes

[J SUN Yat-sen Univ(Med Sci),2023,44(6):1030-1037]

辅助生殖技术和促排卵药物的应用，双胎妊娠的发生率增加，其早产发生风险明显高于单胎妊娠[1]。单绒毛膜双羊膜囊(monochorionic diamniotic，MCDA)和双绒毛膜双羊膜囊(dichorionic diamniotic，DCDA)不同绒毛膜性双胎妊娠都可以发生选择性胎儿生长受限或双胎发育不均衡，新生儿表现为出生体质量不均衡[2-3]。MCDA双胎共享一个胎盘，会发生胎盘分配不均衡、胎盘血管相吻合使双胎竞争同一循环池，会导致双胎出生体质量不一致发生；DCDA双胎各自一个胎盘，其中一个胎盘有病理改变可致出生体质量不一致发生；MCDA和DCDA双胎妊娠的胎儿畸形、胎儿挤压、脐带帆状附着以及孕妇高血压等也是出生体质量不一致的因素[3-5]。MCDA双胎妊娠存在胎盘血管吻合支，如发生动脉-静脉吻合支从动脉向静脉单向分流，双胎儿则分别成为供血胎儿和受血胎儿[6]，为双胎输血综合征(twin-to-twin transfusion syndrome，TTTS)的发病基础。TTTS是MCDA双胎妊娠的特有并发症，一直被认为是MCDA双胎妊娠新生儿不良结局的重要因素[7]，然而MCDA双胎妊娠仅8%~10%发生TTTS[6]。本研究拟分析除外TTTS的MCDA和DCDA不同绒毛膜性活产双胎的新生儿结局，并分析双胎出生胎龄和出生体质量不一致程度对新生儿结局的影响，为新生儿科医生对活产双胎的预后评估和咨询提供依据。

1　材料与方法

1.1　研究对象

本研究经中山大学附属第一医院医学伦理委员会批准，纳入2015年1月至2020年12月在中山

大学附属第一医院分娩的活产双胎进行回顾性分析,双胎妊娠绒毛膜性MCDA和DCDA诊断明确,活产双胎出生后均在我院观察治疗。排除标准为妊娠合并TTTS、减胎、一胎胎死宫内;双胎之一严重出生缺陷。

1.2 方 法

收集围产期基本信息,包括双胎妊娠孕妇年龄、受孕方式、分娩方式、妊娠期主要并发症,如妊娠期糖尿病、妊娠期高血压疾病、胎盘早剥、胎膜早破等;活产双胎新生儿资料,包括出生胎龄、出生体质量、性别等,新生儿期结局包括出生窒息、呼吸窘迫综合征(respiratory distress syndrome,RDS)、支气管肺发育不良(bronchopulmonary dysplasia,BPD)、败血症、坏死性小肠结肠炎(necrotizing enterocolitis,NEC)、急性肾损伤(acute kidney injury,AKI)、脑室内出血(intraventricular hemorrhage,IVH)、视网膜病变(retinopathy of prematurity,ROP)等以及新生儿死亡等。

孕妇妊娠期并发症诊断参照《实用妇产科学》第4版[8];新生儿期疾病诊断参照《实用新生儿学》第5版[9];MCDA和DCDA双胎绒毛膜性的判断参照我国双胎妊娠临床处理指南[10];TTTS诊断参照Quintero标准[10];严重出生缺陷参照《出生缺陷监测手册》的诊断标准[11]。根据双胎的出生体质量低或高(小胎儿或大胎儿)计算双胎出生体质量不一致程度:双胎出生体质量不一致程度=[(双胎的大胎儿出生体质量-双胎的小胎儿出生体质量)/双胎的大胎儿出生体质量]×100%。

1.3 统计学方法

采用SPSS 20.0统计软件进行统计学分析。正态分布的计量资料采用均数±标准差($\bar{x} \pm s$)表示,两组间比较采用t检验;非正态分布的计量资料采用M(P_{25}~P_{75})表示,两组间比较采用秩和检验;计数资料采用例数和百分率表示,两组间比较采用χ^2检验/确切概率法;新生儿不良结局的危险因素采用多因素logistic回归分析。所有检验采用双侧检验,$P<0.05$表示差异有统计学意义。

2 结 果

2.1 双胎妊娠围产期的基本资料

符合纳入标准双胎妊娠752例,其中MCDA双胎妊娠193例,分娩活产双胎新生儿386例;DCDA双胎妊娠559例,分娩活产双胎新生儿1 118例。MCDA和DCDA组双胎妊娠围产期的基本资料见表1。MCDA组孕妇年龄低于DCDA组($P=0.002$);MCDA组辅助生殖技术受孕率低于DCDA组($P=0.000$);两组妊娠期糖尿病、妊娠期高血压疾病、胎盘早剥和胎膜早破的发生率及剖宫产率差异均无统计学意义($P>0.05$);MCDA组双胎分娩胎龄低于DCDA组($P=0.000$);双胎的大胎儿和小胎儿的出生体质量MCDA组均分别低于DCDA组($P=0.000$,$P=0.000$);MCDA组双胎出生体质量不一致程度高于DCDA组($P=0.001$),MCDA组双胎出生体质量不一致程度≥25%的构成比高于DCDA组($P=0.000$)。

2.2 双胎的新生儿结局

活产双胎新生儿1 504例中MCDA组双胎新生儿386例、DCDA组双胎新生儿1 118例,其一般资料和新生儿结局见表2。MCDA组和DCDA组的双胎新生儿的性别构成比差异无统计学意义($P>0.05$)。MCDA组新生儿的出生胎龄和出生体质量均低于DCDA组($P=0.000$,$P=0.000$)。MCDA组新生儿出生窒息、RDS、BPD和败血症的发生率均高于DCDA组($P=0.000$,$P=0.000$,$P=0.000$,$P=0.000$);MCDA组和DCDA组NEC≥Ⅱ期、AKI、IVH≥Ⅲ级和ROP的发生率以及死亡率差异均无统计学意义(P值均>0.05)。

2.3 双胎新生儿结局的影响因素

分别以双胎新生儿疾病和死亡是否发生为因变量,不同绒毛膜性(MCDA或DCDA)、出生胎龄、双胎出生体质量不一致程度以及性别为协变量进行logistic回归分析(IVH≥Ⅲ级因例数少而不适用logistic回归分析;附表)。显示绒毛膜性不是双胎新生儿各种疾病发生和死亡的独立危险因素(P值均>0.05);出生胎龄低分别是双胎新生儿出生窒息、RDS、BPD、败血症、NEC≥Ⅱ期、AKI、ROP发生和死亡的独立危险因素[OR 95%CI=0.614(0.554,0.680),$P=0.000$;OR 95%CI=0.323(0.278,0.375),$P=0.000$;OR 95%CI=0.429(0.354,0.520),$P=0.000$;OR 95%CI=0.601(0.528,0.684),$P=0.000$;OR 95%CI=0.729(0.572,0.929),$P=0.011$;OR 95%CI=0.469(0.353,0.623),$P=0.000$;OR 95%CI=0.547(0.457,0.654),$P=0.000$;OR 95%CI=0.418(0.291,0.601),$P=0.000$],出生体质量不一致程度高分别

表1　双胎妊娠围产期的基本资料

Table1　Basic information of twin pregnancies　[$(\bar{x} \pm s)$, $n(\%)$, or $M(P_{25}\sim P_{75})$]

Basic information	MCDA group(n = 193)	DCDA group(n = 559)	$t/\chi^2/Z$	P
Age/years[1)]	31.5±5.1	32.7±4.3	−3.172	0.002
Mode of fertilization [2)]			195.203	0.000
ART	48 (24.87)	448 (80.14)		
Non-ART	145 (75.13)	111 (19.86)		
Gestational diabetes [2)]	41 (21.24)	142 (25.40)	1.348	0.246
Pregnancy-induced hypertension [2)]	27 (13.99)	60 (10.73)	1.487	0.223
Placental abruption [2)]	1 (0.52)	3 (0.54)	–	1.000
Premature rupture of membranes [2)]	11 (5.70)	57 (10.20)	3.528	0.060
Mode of delivery [3)]			–	0.537
Vaginal delivery	2 (1.04)	12 (2.15)		
Cesarean delivery	191 (98.96)	547 (97.85)		
Gestational age at delivery/weeks[4)]	35.43 (34.14~36.29)	36.71 (35.86~37.00)	−9.169	0.000
Birth weight of small twins/g[4)]	2 020.0 (1 650.0~2 320.0)	2 300.0 (2 040.0~2 500.0)	−7.509	0.000
Birth weight of large twins/g[4)]	2 300.0 (2 035.0~2 550.0)	2 560.0 (2 330.0~2 750.0)	−8.165	0.000
Birth weight discordant/%[4)]	10.74 (4.88~24.90)	9.27 (4.18~15.73)	−3.226	0.001
Birth weight discordant ≥25% [2)]	48 (24.87)	36 (6.44)	49.113	0.000

1) t test, test statistics is t; 2) χ^2 test, test statistics is χ^2; 3) Fisher's exact test; 4) Wilcoxon rank sum test, test statistics is Z; MCDA: monochorionic diamniotic; DCDA: dichorionic diamniotic; ART: assisted reproductive technology.

表2　双胎新生儿的一般资料和新生儿结局比较

Table 2　General information and neonatal outcomes of twins　[$n(\%)$, $M(P_{25}\sim P_{75})$]

General information and neonatal outcomes	MCDA group(n = 386)	DCDA group(n = 1 118)	χ^2/Z	P
Sex [1)]			1.482	0.223
Male	194 (50.26)	602 (53.85)		
Female	192 (49.74)	516 (46.15)		
Gestational age at birth/weeks [2)]	35.43 (34.14~36.29)	36.71 (35.86~37.00)	−12.971	0.000
Birth weight/g [2)]	2 180.0(1 827.5~2 440.0)	2 430.0(2 163.8~2 650.0)	−10.370	0.000
Asphyxia at birth [2)]	36 (9.33)	46 (4.11)	15.120	0.000
RDS [2)]	96 (24.87)	116 (10.38)	49.785	0.000
BPD [2)]	25 (6.48)	16 (1.43)	27.547	0.000
Sepsis [2)]	23 (5.96)	15 (1.34)	24.834	0.000
NEC ≥ stage Ⅱ [3)]	3 (0.78)	4 (0.36)	–	0.382
AKI [3)]	3 (0.78)	6 (0.54)	–	0.702
IVH ≥ grade Ⅲ [3)]	2 (0.52)	4 (0.36)	–	0.650
ROP [3)]	7 (1.81)	9 (0.81)	–	0.144
Death [3)]	4 (1.04)	5 (0.45)	–	0.246

1) χ^2 test; 2) Wilcoxon rank sum test, test statistics is Z; 3) Fisher's exact test; MCDA: monochorionic diamniotic; DCDA: dichorionic diamniotic; RDS: respiratory distress syndrome; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; AKI: acute kidney injury; IVH: intraventricular hemorrhage; ROP: retinopathy of prematurity.

是双胎新生儿出生窒息、RDS、BPD、败血症和ROP发生的独立危险因素[OR 95%CI = 1.020(1.000, 1.040), P = 0.045; OR 95%CI = 1.041(1.022, 1.060), P = 0.000; OR 95%CI = 1.056 (1.025, 1.088), P = 0.000; OR 95%CI = 1.037 (1.011, 1.063), P = 0.004; OR 95%CI = 1.049 (1.009, 1.092), P = 0.017]。

附表
Appendix table

2.4 出生体质量不一致程度≥25%的双胎新生儿结局分析

对168例出生体质量不一致程度≥25%双胎新生儿进行亚组研究分析,MCDA组和DCDA组分别有96例和72例双胎新生儿,其一般资料和新生儿结局见表3。MCDA组和DCDA组出生体质量不一致≥25%的双胎新生儿的性别构成比差异无统计学意义(P > 0.05)。MCDA组出生胎龄和出生体质量均低于DCDA组(P = 0.000, P = 0.000)。MCDA组RDS、BPD和败血症的发生率高于DCDA组(P = 0.000, P = 0.001, P = 0.007);MCDA组和DCDA组双胎新生儿出生窒息、NEC≥Ⅱ期、AKI、IVH≥Ⅲ级和ROP的发生率以及死亡率差异均无统计学意义(P值均 > 0.05)。

表3 出生体质量不一致≥25%双胎新生儿一般资料和新生儿结局比较

Table 3 General information and neonatal outcomes of birth weight discordant ≥25% twins

[n(%), $M(P_{25}$~$P_{75})$]

General information and neonatal outcomes	MCDA group(n = 96)	DCDA group(n = 72)	χ^2/Z	P
Sex [1)]			0.008	0.929
Male	46 (47.92)	35 (48.61)		
Female	50 (52.08)	37 (51.39)		
Gestational age at birth/weeks [2)]	33.15 (31.17~34.86)	35.29 (34.33~36.57)	−6.394	0.000
Birth weight/g [2)]	1 565 (1 155~1 950)	2 000 (1 713~2 500)	−5.361	0.000
Asphyxia at birth [1)]	20 (20.83)	9 (12.5)	2.000	0.157
RDS [1)]	62 (64.58)	15 (20.83)	31.720	0.000
BPD [1)]	21 (21.88)	3 (4.17)	10.536	0.001
Sepsis [1)]	17 (17.71)	3 (4.17)	7.194	0.007
NEC ≥ stage Ⅱ [3)]	2 (2.08)	0 (0)	–	0.507
AKI [3)]	2 (2.08)	1 (1.39)	–	1.000
IVH ≥ grade Ⅲ [3)]	2 (2.08)	1 (1.39)	–	1.000
ROP [3)]	6 (6.25)	3 (4.17)	–	0.734
Death [3)]	4 (4.17)	0 (0)	–	0.136

1) χ^2 test; 2) Wilcoxon rank sum test, test statistics is Z; 3) Fisher's exact test; MCDA: monochorionic diamniotic; DCDA: dichorionic diamniotic; RDS: respiratory distress syndrome; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; AKI: acute kidney injury; IVH: intraventricular hemorrhage; ROP: retinopathy of prematurity.

分别以出生体质量不一致程度≥25%双胎新生儿疾病是否发生为因变量,不同绒毛膜性(MCDA或DCDA)、出生胎龄、双胎出生体质量低或高(小胎儿或大胎儿)以及性别为协变量进行logistic回归分析(NEC≥Ⅱ期、AKI、IVH≥Ⅲ级和死亡因例数少而不适用logistic回归分析;表4)。显示绒毛膜性不是出生体质量不一致程度≥25%双胎新生儿疾病发生的独立危险因素(P值均 > 0.05);出生胎龄低分别是出生体质量不一致程度≥25%双胎新生儿出生窒息、RDS、BPD、败血症和ROP发生的独立危险因素[OR 95%CI = 0.516(0.390, 0.684), P = 0.000; OR 95%CI = 0.265(0.173, 0.406), P = 0.000; OR 95%CI = 0.289(0.174, 0.482), P = 0.000; OR 95%CI = 0.586 (0.443, 0.774), P = 0.000; OR

95%CI = 0.348(0.193,0.628),*P* = 0.000]；出生体质量不一致程度≥25%双胎的小胎儿分别是出生体质量不一致程度≥25%双胎新生儿出生窒息和BPD发生的独立危险因素[OR 95%CI = 3.565(1.313,9.682)，*P* = 0.013；OR 95%CI = 13.446(2.724,66.370),*P* = 0.001]。

表4　出生体质量不一致≥25%双胎新生儿的危险因素分析

Table 4　Analysis of risk factors for neonatal outcomes of birth weight discordant ≥25% twins

Neonatal outcomes	Variables	*P*	OR	OR 95% CI	
				lower	upper
Asphyxia at birth	MCDA twin (*vs*. DCDA twin)	0.246	0.505	0.159	1.602
	Gestational age at birth/weeks	0.000	0.516	0.390	0.684
	Small twin (*vs*. large twin)	0.013	3.565	1.313	9.682
	Male (*vs*. female)	0.642	1.255	0.483	3.262
RDS	MCDA twin (*vs*. DCDA twin)	0.075	2.382	0.917	6.185
	Gestational age at birth/weeks	0.000	0.265	0.173	0.406
	Small twin (*vs*. large twin)	0.792	0.882	0.348	2.238
	Male (*vs*. female)	0.820	0.896	0.349	2.299
BPD	MCDA twin (*vs*. DCDA twin)	0.467	2.095	0.285	15.397
	Gestational age at birth/weeks	0.000	0.289	0.174	0.482
	Small twin (*vs*. large twin)	0.001	13.446	2.724	66.370
	Male (*vs*. female)	0.835	1.148	0.312	4.229
Sepsis	MCDA twin (*vs*. DCDA twin)	0.190	2.639	0.618	11.264
	Gestational age at birth/weeks	0.000	0.586	0.443	0.774
	Small twin (*vs*. large twin)	0.056	2.984	0.972	9.157
	Male (*vs*. female)	0.067	0.345	0.111	1.076
ROP	MCDA twin (*vs*. DCDA twin)	0.212	0.237	0.025	2.275
	Gestational age at birth/weeks	0.000	0.348	0.193	0.628
	Small twin (*vs*. large twin)	0.057	7.683	0.944	62.555
	Male (*vs*. female)	0.416	2.136	0.344	13.286

MCDA: monochorionic diamniotic; DCDA: dichorionic diamniotic; RDS: respiratory distress syndrome; BPD: bronchopulmonary dysplasia; ROP: retinopathy of prematurity.

3　讨　论

3.1　出生胎龄与双胎新生儿结局

双胎妊娠的死胎风险高于单胎妊娠、并随着双胎妊娠孕龄增加而增高，产科医生要权衡胎儿和新生儿并发症风险选择分娩时机[12]。我国双胎妊娠临床处理指南建议无并发症及合并症的MCDA双胎可在严密监测下至孕37周分娩、无并发症及合并症的DCDA双胎可至孕38周考虑分娩[10]。Manuck等[13]研究示出生胎龄在23.0至36.9周之间，活产新生儿疾病发生和死亡随出生胎龄增加而降低。本研究MCDA双胎妊娠分娩胎龄低于DCDA双胎妊娠，Coutinho等[14]调查显示无TTTS的MCDA双胎妊娠分娩胎龄≤34周的构成比高于DCDA双胎妊娠，但未行新生儿出生后疾病和死亡分析。出生胎龄反映了新生儿各器官系统发育的成熟度，是新生儿疾病发生和死亡的主要决定因素，本研究校正了绒毛膜性、双胎出生体质量不一致程度及性别的影响，显示出生胎龄是新生儿出生窒息、RDS、BPD、败血症、NEC≥Ⅱ期、AKI、ROP发

生和死亡的独立危险因素,绒毛膜性并不是独立危险因素。Rizzini等[15]研究同样显示活产双胎出生胎龄是新生儿疾病发生的重要因素,而跟绒毛膜性无关,该研究纳入双胎妊娠同样排除了合并TTTS和严重出生缺陷,但是仅纳入出生胎龄≥36周的双胎新生儿,其新生儿各种疾病发生率不高,因而未单独疾病发生分析,发生任何一个疾病(如RDS、败血症)即表示有新生儿疾病发生。本研究纳入本中心近年分娩活产双胎,资料更为全面,样本量较大且为单中心的临床资料,因而围产期处理干预稳定、偏差小。Leduc等[16]研究校正了出生胎龄,同样排除TTTS和出生缺陷的影响,但未校正双胎出生体质量不一致程度,显示MCDA双胎新生儿IVH≥Ⅲ级发生率高于DCDA双胎、而出生后气管插管率跟DCDA双胎无差异,但无呼吸系统发病情况报告。然而,Park等[17]研究中DCDA双活胎平均出生胎龄为34^{+3}周,低于本研究和Leduc等[16]报告DCDA双活胎的出生胎龄,该研究则显示无TTTS的MCDA和DCDA双胎新生儿出生胎龄和出生窒息发生无差异。

3.2 双胎出生体质量不一致程度与新生儿结局

目前双胎出生体质量不一致程度截点尚无明确标准。双胎出生体质量不一致程度以15%~30%及以上为截点均有研究报道。尽管纳排双胎标准有不同,大部分研究显示出生体质量不一致程度截点以上的双胎的新生儿疾病或死亡发生率高于出生体质量一致程度在截点以下的双胎[18-20]。Tan等[21]认为出生体质量不一致的双胎容易发生早产,出生胎龄低则是出生体质量不一致双胎新生儿不良结局的影响因素。本研究将出生胎龄进行校正后提示出生体质量不一致程度高的双胎新生儿结局仍差,出生体质量不一致程度高是双胎新生儿出生窒息、RDS、BPD、败血症和ROP发生的独立危险因素。Fumagalli等[22]研究校正出生胎龄和性别等影响后示出生体质量不一致程度≥20%~40%以上的双胎新生儿需要更长的住院时间。鉴于TTTS作为MCDA双胎生长不一致的发生因素[3]、胎儿结构畸形或染色体异常的MCDA或DCDA双胎妊娠均可致双胎出生体质量不一致的发生且围产结局不良[5],本研究排除了TTTS和严重出生缺陷的双胎病例。因此提示了双胎出生体质量不一致高可能是一个潜在的围产病理因素,在新生儿不良结局中扮演一定角色,有关机制需进一步探究,双胎出生体质量不一致高可作为新生儿结局不良的参考预测指标,新生儿科医生要对双胎出生体质量不一致的救治采取积极措施。

3.3 双胎的小胎儿与新生儿结局

鉴于英国国家卫生与临床优化研究所指南建议双胎妊娠监测双胎体质量不一致≥25%应转诊到三级胎儿医学中心[23]及我国以双胎估测体质量相差≥25%为双胎生长不一致诊断标准[10],本研究以双胎出生体质量不一致程度≥25%为截点进行亚组分析。本研究显示出生胎龄低分别是这些双胎新生儿出生窒息、RDS、BPD、败血症和ROP发生的独立危险因素,而绒毛膜性不是这些新生儿疾病发生的独立危险因素;此外本研究显示出生体质量不一致程度≥25%双胎,小胎儿是出生窒息和BPD发生的独立危险因素。跟本研究结论类似的我国一项多中心研究,其显示双胎较单胎新生儿,尤其是双胎中的较低出生体质量者[24]更易发生出生窒息,绒毛膜性并不是双胎新生儿出生窒息风险的显著决定因素。Di等[20]排除合并TTTS、纳入出生胎龄≥34周的双胎荟萃分析示双胎出生体质量不一致程度大于以15%~30%截点的大小胎儿新生儿呼吸、神经系统及感染性疾病发生无差异。而Boghossian等[25]研究示出生体质量401~1 000 g或出生胎龄22~28周的双胎出生体质量不一致程度>30%的小胎儿较出生体质量不一致程度≤14%的小胎儿更易发生BPD;Groene等[26]对出生体质量不一致程度≥20%的双胎研究示小胎儿较大胎儿更易发生BPD,这很可能其处于宫内慢性缺氧状态,呼吸系统发生持续结构和功能变化,肺泡形成受损,肺发育异常增加了出生后肺损伤的易损性[27]。

3.4 本研究的局限性

本研究有一定的局限性,一是本研究没有进行分析双胎妊娠导致早产发生和双胎出生体质量不一致的围产因素;二是本研究没有对新生儿不良结局的严重程度进一步行分层分析,且部分新生儿结局发生事件数量少而未能纳入回归分析,影响了研究的效力;三是没有对活产双胎新生儿进行远期随访研究。

综上所述,绒毛膜性不是双胎新生儿不良结局发生的独立危险因素,出生胎龄低和出生体质量不一致程度高是双胎新生儿出生窒息、RDS、BPD、败血症和ROP等不良结局发生的独立危险因素;出生体质量不一致程度≥25%双胎的小胎儿新生儿结局更差,更易于发生出生窒息和BPD。

参考文献

[1] Practice Committee of American Society for Reproductive Medicine. Multiple gestation associated with infertility therapy: an American Society for Reproductive Medicine Practice Committee opinion[J]. Fertil Steril, 2012, 97(4): 825-834.

[2] Antonakopoulos N, Pateisky P, Liu B, et al. Selective fetal growth restriction in dichorionic twin pregnancies: diagnosis, natural history, and perinatal outcome[J]. J Clin Med, 2020, 9(5): 1404.

[3] Breathnach FM, Malone FD. Fetal growth disorders in twin gestations[J]. Semin Perinatol, 2012, 36(3): 175-181.

[4] Wang Y, Zeng H, Liu J, et al. Gestational hypertensive disease and birthweight discordance in twin pregnancies: a systematic review and meta-analysis[J]. J Matern Fetal Neonatal Med, 2021: 1-9.

[5] Miller J, Chauhan SP, Abuhamad AZ. Discordant twins: diagnosis, evaluation and management[J]. Am J Obstet Gynecol, 2012, 206(1): 10-20.

[6] Society for Maternal-Fetal Medicine, Simpson LL. Twin-twin transfusion syndrome[J]. Am J Obstet Gynecol, 2013, 208(1): 3-18.

[7] Di Mascio D, Khalil A, D'Amico A, et al. Outcome of twin-twin transfusion syndrome according to Quintero stage of disease: systematic review and meta-analysis[J]. Ultrasound Obstet Gynecol, 2020, 56(6): 811-820.

[8] 徐丛剑，华克勤. 实用妇产科学(第4版)[M]. 北京：人民卫生出版社，2018：112-456.
Xu CJ, Hua KQ. Practice of obstetrics & gynecology (4th edition) [M]. Beijing: People's Medical Publishing House, 2018: 112-456.

[9] 邵肖梅，叶鸿瑁，丘小汕. 实用新生儿学(第5版)[M]. 北京：人民卫生出版社，2019：390-1039.
Shao XM, Ye HM, Qiu XS. Practice of Neonatology (5th edition) [M]. Beijing: People's Medical Publishing House, 2019: 390-1039.

[10] 中华医学会围产医学分会胎儿医学学组，中华医学会妇产科学分会产科学组. 双胎妊娠临床处理指南(2020年更新)[J]. 中华围产医学杂志，2020，23(8)：505-516.
Fetal Medicine Subgroup, Chinese Society of Perinatal Medicine, Chinese Medical Association, SubgroupObstetrics, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Guideline for management of twin pregnancy (2020 update) [J]. Chin J Perinat Med, 2020, 23(8): 505-516.

[11] WHO, CDC, ICBDSR. Birth defects surveillance: a manual for programme managers, second edition[M]. Geneva: World Health Organization, 2020: 2-172.

[12] Cheong-See F, Schuit E, Arroyo-Manzano D, et al. Prospective risk of stillbirth and neonatal complications in twin pregnancies: systematic review and meta-analysis [J]. BMJ, 2016, 354: i4353.

[13] Manuck TA, Rice MM, Bailit JL, et al. Preterm neonatal morbidity and mortality by gestational age: a contemporary cohort[J]. Am J Obstet Gynecol, 2016, 215(1): 101-103.

[14] Coutinho NF, Domingues AP, Vide TM, et al. Monochorionic versus dichorionic twins: Are obstetric outcomes always different?[J]. J Obstet Gynaecol, 2016, 36(5): 598-601.

[15] Rizzini N, Fratelli N, Negri B, et al. Chorionicity, birth weight discordance and neonatal morbidity in uncomplicated twin pregnancies delivered from 36 weeks[J]. Eur J Obstet Gynecol Reprod Biol, 2022, 271: 214-218.

[16] Leduc L, Takser L, Rinfret D. Persistance of adverse obstetric and neonatal outcomes in monochorionic twins after exclusion of disorders unique to monochorionic placentation [J]. Am J Obstet Gynecol, 2005, 193(5): 1670-1675.

[17] Park YH, Kim YN, Im DH, et al. Neonatal outcomes between discordant monochorionic and dichorionic twins[J]. J Matern Fetal Neonatal Med, 2021, 34(13): 2080-2088.

[18] Breathnach FM, Mcauliffe FM, Geary M, et al. Definition of intertwin birth weight discordance[J]. Obstet Gynecol, 2011, 118(1): 94-103.

[19] Jahanfar S, Lim K, Ovideo-Joekes E. Birth weight discordance and adverse perinatal outcomes [J]. J Perin Med, 2017, 45(5): 603-611.

[20] Di Mascio D, Acharya G, Khalil A, et al. Birthweight discordance and neonatal morbidity in twin pregnancies: A systematic review and meta-analysis [J]. Acta Obstet Gynecol Scand, 2019, 98(10): 1245-1257.

[21] Tan H, Wen SW, Fung Kee Fung K, et al. The distribution of intra-twin birth weight discordance and its association with total twin birth weight, gestational age, and neonatal mortality [J]. Eur J Obstet Gynecol Reprod Biol, 2005, 121(1): 27-33.

[22] Fumagalli M, Schiavolin P, Bassi L, et al. The impact of twin birth on early neonatal outcomes[J]. Am J Perinatol, 2016, 33(1): 63-70.

[23] Twin and Triplet Pregnancy[M]. London: National Institute for Health and Care Excellence (NICE), 2019: 46-50.

[24] Cui H, Wang Z, Yu J, et al. Birthweight is an independent predictor of birth asphyxia in twins: a retrospective cross-sectional cohort study of 5337 Chinese twins[J]. Eur J Obstet Gynecol Reprod Biol, 2021, 257: 106-113.

[25] Boghossian NS, Saha S, Bell EF, et al. Birth weight discordance in very low birth weight twins: mortality, morbidity, and neurodevelopment[J]. J Perinatol, 2019, 39(9): 1229-1240.

[26] Groene SG, Spekman JA, Te PA, et al. Respiratory distress syndrome and bronchopulmonary dysplasia after fetal growth restriction: lessons from a natural experiment in identical twins[J]. EClinicalMedicine, 2021, 32: 100725.

[27] Sehgal A, Gwini SM, Menahem S, et al. Preterm growth restriction and bronchopulmonary dysplasia: the vascular hypothesis and related physiology [J]. J Physiol, 2019, 597(4): 1209-1220.

（编辑　余　菁）