

单绒毛膜双胎合并脐动脉反向灌注序列的预后影响因素

陈清华¹, 陈华娟¹, 彭 软²

(1. 惠州市第一人民医院 超声科, 广东 惠州 5160031; 2. 中山大学附属第一医院 超声科, 广东 广州 510080)

摘要:【目的】评估不同超声特征和治疗方式对双胎脐动脉反向灌注序列(TRAP)泵血胎预后的影响。【方法】回顾性分析2010年1月4日至2015年8月30日在我院行产前超声检查诊断为双胎脐动脉反向灌注序列的单绒毛膜双胎病例共55例,记录产前超声检查结果及以下指标:脐动脉返流胎/泵血胎估重比、泵血胎胎儿水肿、泵血胎心脏扩大、泵血胎羊水过多、无心胎羊水过少及TRAP治疗方式。应用Logistic回归分析各超声指标及不同治疗方式与泵血胎死亡的相关性。【结果】研究期间我院产前超声诊断双胎脐动脉反向灌注序列共55例,失访3例,有妊娠结局随访结果共52例。21例行选择性减胎术,13例终止妊娠;18例行期待治疗、定期超声监测。剔除选择终止妊娠病例,分为定期超声监测组(18例)和选择性减胎组(21例),其泵血胎存活率分别是66.7%、71.4%, $P=0.748$,且两组各超声特征和预后指标差异均无统计学意义。除外选择终止妊娠病例,对39例选择定期超声监测和选择性减胎术病例应用Logistic回归分析显示泵血胎心脏扩大($OR=21.73$, 95%CI: 1.15 ~ 203.89, $P < 0.001$)是泵血胎(宫内或新生儿)死亡的独立风险因素。【结论】泵血胎各预后指标在定期监测组和选择性减胎组差异无统计学意义。泵血胎心脏扩大是泵血胎(宫内或新生儿)死亡的独立风险因素。

关键词:单绒毛膜双胎;期待治疗;选择性减胎;预后;双胎脐动脉反向灌注序列

中图分类号:R71 **文献标志码:**A **文章编号:**1672-3554(2017)03-0386-04

Prognosis for Monochorionic Twins with Twin Reversed Arterial Perfusion Sequence

CHEN Qing-Hua¹, CHEN Hua-Juan¹, PENG Ruan²

(1. Department of Ultrasound; The First People's Hospital of Huizhou, Guangdong Huizhou 516003, China; 2. Department of Ultrasound; The First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, China)

Corresponding to: PENG Ruan; E-mail: pengruan1123@163.com

Abstract:【Objective】The purpose of this study was to evaluate the association of ultrasound findings and different treatments with the prognosis of the pump twin in twin reversed arterial perfusion sequence (TRAP). 【Methods】The 55 cases that were diagnosed as TRAP during the period from January 4th 2010 and August 31st 2015 were included. Ultrasound appearances of monochorionic twins were documented in detail when the twins were diagnosed with TRAP initially. At the initial evaluation, presence or absence of the following abnormalities were documented, including the ratio of the acardiac twin to the weight of the pump twin, hydrops fetalis in the pump twin, cardiomegaly in the pump twin, polyhydramnios in the pump twin, oligohydramnios in the acardiac twin and different treatments. The relationship between these ultrasound characteristics and different treatments with mortality of pump twin were analyzed with logistic regression. 【Results】A total of 55 cases with TRAP were diagnosed in our institution and three cases were lost to follow up. Selective reduction was performed in 21 cases, termination of pregnancies in 13 and expectant management in 18. Excluding the cases that underwent termination of pregnancy, the remaining 39 cases were divided into two groups according treatment, expectant management group ($n=18$) and selective reduction group ($n=21$). Overall survival rate of the pump twin in these two groups was 66.7% and 71.4%, respectively, $P = 0.748$. The markers of perinatal outcome were not significantly different between expectant management group and selective reduction group. Logistic regression demonstrated that cardiomegaly in the pump twin ($OR=21.73$, 95%CI: 1.15 ~ 203.89, $P < 0.001$) were significant correlated with mortality of the pump twin. 【Conclusion】The prognosis

收稿日期:2017-02-24

基金项目:国家自然科学基金青年科学基金(81501491)

作者简介:陈清华,副主任医师,研究方向:产前超声诊断;彭软,通信作者,研究方向:复杂性单绒毛膜双胎产前诊断, E-mail: pengruan1123@163.com。

markers were not significantly different between conservative management and selective reduction group. Cardiomegaly in the pump twin should be considered as risk predictors for mortality of the pump twin in TRAP.

Key words: monochorionic twins; expectant management; selective reduction; prognosis; TRAP

[J SUN Yat-sen Univ (Med Sci), 2017, 38(3):386-389]

双胎脐动脉反向灌注序列(twin reversed arterial perfusion sequence, TRAP)是指一胎无心畸形并多器官发育不全(无心胎),其无自己的胎盘份额,由另一胎(泵血胎)通过动脉-动脉吻合支向其供血,射频消融减胎可有效预防泵血胎发生高输出量型心力衰竭和宫内死亡^[1]。泵血胎心脏扩大、羊水过多、胎儿水肿可能都是其预后不良的超声指征^[2],但何者是最有效的超声指标目前尚不得而知。本研究对不同超声指标和治疗方式与TRAP泵血胎预后的预测价值进行分析阐述,旨在为TRAP的预后及临床处理提供更详实的数据资料和循证学依据。

1 材料与方法

1.1 研究对象

纳入2010年1月至2014年12月早孕期超声检查提示单绒毛膜双胎,且校正孕周后在本院行产前超声检查,产前系统超声检查提示单绒毛膜双胎。TRAP超声诊断标准:表现为类肿瘤样结构,扫查“瘤”内可见软组织和脊柱、骨结构,无头颅、无心脏,部分可见下肢结构,由于脐动脉返流胎多有严重水肿,“瘤”内可见散在圆形液性暗区,在“瘤体”的边缘可见脐带回声进入“瘤”内,无胎心搏动,但仍有胎动及生长,彩超显示脐带和“瘤”内有脐动脉血流信号和频谱,与泵血胎的心率一致。

治疗前孕妇及家属均签署手术知情同意书。本研究项目已通过本机构伦理委员会审查。

1.2 仪器及检查方法

采用 Voluson 730 Expert、GE logic7、Voluson E8(GE)彩色多普勒超声诊断仪,经腹扫查,探头频率3.5~5.0 MHz。常规系统扫查泵血胎全身结构及附属结构,测量生物学指标,判断孕周、估计体重(estimated fetal weight, EFW);测量最大羊水深度,胎盘厚度;检测胎儿脐动脉及大脑中动脉血流频谱;测量心胸面积比。观察返流胎脐动脉的起源位置;测量返流胎前后径、横径和长径及返

流胎羊膜腔最大羊水池深度。

1.3 产前检查及处理

建议泵血胎和返流胎行染色体G显带核型分析和染色体微阵列(chromosomal microarray analysis, CMA)检测。CMA检测前向孕妇及家属交代CMA技术的作用和局限性,其中包括对于少数新发的染色体畸变,数据库或者文献资料中未见报道的,造成该畸变致病性无法确定,可能需要结合父母或者父母的家系进行检测综合分析等。

依据孕妇及家属意愿选择继续妊娠、选择性减胎或终止妊娠。选择性减胎术式的选择依据双胎位置、胎盘位置、脐带长短、返流胎羊水量等因素选择,向家属告知不同术式的风险及并发症,然后选择合适的减胎方式,记录拟减胎及保留胎羊水量情况。

1.4 统计学分析

应用SPSS16.0统计分析软件进行处理。连续性变量表述方式采用中位数(最小值~最大值),统计分析采用非参数秩和检验;计数资料表述方式采用例数(百分比,%),统计分析采用 χ^2 检验或Fisher确切概率法。泵血胎的体重估算方法:(前后径×横径×长径×3.14)/2,认为泵血胎密度为1 mg/mL,即1 mL等于1 mg。应用Logistic回归分析脐动脉返流胎/泵血胎估重比、泵血胎胎儿水肿、泵血胎心脏扩大、泵血胎羊水过多、无心胎羊水过少及TRAP治疗方式等指标与发生胎儿死亡的相关性,采用逐步进入法统计可进入回归方程的指标(进入回归方程的显著性差异水平设定为<0.05)。产前超声指标与泵血胎死亡的相关性用优势比(odds ratio, OR)表示。

2 结果

2.1 基本临床资料

依据双胎脐动脉反向灌注序列诊断标准共55例入组,其中52例(94.5%, 52/55)为自然受孕,3例(5.8%, 3/52)为IVF-ET后妊娠。失访3例,52例有随访结果,泵血胎性别不详12例,女:男=

24:16。21例行选择性减胎术,其中1例为双极脐带电凝减胎,20例为射频消融减胎;13例选择终止妊娠;18例行期待治疗、定期超声监测。

本组52例有追踪结果的病例中,16例未行染色体核型和CMA检测。22例仅行染色体核型检查,其中20例染色体核型检查正常,1例正常胎为“46,XX”而脐动脉反流胎结果提示“47,XX,+9”;1例正常胎“46,XX[21]/46XY[7]”,异常胎未查。14例行染色体核型和CMA检测,12例染色体核型正常且CMA检测未检出拷贝数变异,1例正常胎和异常胎结果均提示新生的22q11.21致病性的拷贝数变异,但片段大小不同。1例正常胎染色体核型正常,CMA结果提示良性拷贝数变异(copy number variations, CNV),异常胎未行染色体和CMA检测。

2.2 产前超声特征

产前超声诊断双胎脐动脉反向灌注序列的孕周中位数是19⁺³周(12⁺¹~30⁺³周)。4例(7.7%,4/52)产前超声诊断时脐动脉返流胎内未见明显血供,18例(34.6%,18/52)返流胎的脐动脉自泵血胎的脐带胎盘附着处发出,22例(42.3%,22/52)返流胎的脐动脉自胎盘表面的脐血管分支发出,4例(7.7%,4/52)返流胎的脐动脉自泵血胎脐带的游离段发出,4例(7.7%,4/52)无法显示返流胎的脐动脉起源。10例(19.2%,10/52)合并泵血胎羊水过多,4例(7.7%,4/52)合并脐动脉返流胎羊水过少,7例(13.5%,7/52)同时合并另一胎(泵血胎)心脏扩大,1例(1.9%,1/52)同时合并泵血胎胎儿水

肿,6例(11.5%,6/52)泵血胎定期超声监测或减胎后发生宫内死亡。

2.3 不同治疗方式组超声特征和泵血胎预后的比较

52例有妊娠随访结果的病例中,按照治疗方式将双胎脐动脉反向灌注序列组分为期待治疗(定期超声监测)组(18例)和选择性减胎组(21例),其泵血胎存活率分别是66.7%(12/18)和71.4%(15/21), $P = 0.748$,且各超声特征和预后指标差异均无统计学意义,详见表1。

按照脐动脉返流胎/泵血胎估重比是否大于50%,分为脐动脉返流胎/泵血胎估重比 $\geq 50\%$ 组和脐动脉返流胎/泵血胎估重比 $< 50\%$ 组,其泵血胎存活率分别是60.0%(15/25)和85.7%(12/14),其差异具有统计学意义($P = 0.040$)。

2.4 泵血胎的预后影响因素分析

除外选择终止妊娠病例,对39例选择定期超声监测和选择性减胎术病例,应用Logistic回归分析分析脐动脉返流胎/泵血胎估重比 $\geq 50\%$ 、泵血胎胎儿水肿、泵血胎心脏扩大、泵血胎羊水过多、无心胎羊水过少及不同治疗方式与泵血胎死亡的关系。Logistic回归分析结果显示泵血胎心脏扩大(OR = 21.73, 95%CI: 1.15 ~ 203.89, $P < 0.001$)是其(宫内或新生儿)死亡的独立风险因素。

3 讨论

近几年热消融被广泛应用于肿瘤治疗,新近

表1 双胎脐动脉反向灌注序列的超声特征和预后指标的比较

Table 1 Comparisons of the characteristics and prognosis of the twin reversed arterial perfusion sequence in the expectant management group and selective reduction group

Markers	Expectant management Group (n = 18)	Selective reduction Group (n = 21)	P
Median gestational at diagnosis/weeks	19 ⁺³ (12 ⁺¹ -29 ⁺¹)	20(13 ⁺⁵ -30 ⁺³)	0.822
Polyhydraminos in the pump twin/%	11.1(2/18)	33.3(7/21)	0.101
Survival rate of the pump twin/%	66.7(12/18)	71.4(15/21)	0.748
Cardiomegaly in the pump twin/%	5.6(1/18)	4.8(1/21)	0.768
Hydrops fetalis in the pump twin/%	0	0	-
Oligohydraminos in the TRAP twin/%	5.6(1/18)	9.5(2/21)	0.911
The ratio of the acardiac twin to the weight of the pump twin $\geq 50\%$	50.0(9/18)	76.1(16/21)	0.089
Complication rate/%	0(0/18)	9.5(2/21)	0.490 ¹⁾

Fisher exact test

被应用于单绒毛膜双胎的选择性减胎^[1,3],且临床效果较好。文献报道双胎脐动脉反向灌注序列,若未进行干预泵血胎的存活率约是50%,而行选择性减胎术后泵血胎存活率约是85%~90%^[4-5]。但是选择性减胎术需有一定指征。Moore等^[6]首先提出脐动脉返流胎和泵血胎体重比值设定为50%,采用50%作为诊断阈值时其预测泵血胎早产和死亡的敏感度分别是86%和64%,但是其特异度相对较低,分别是67%和42%。当脐动脉返流胎与供血胎体重比值>70%时,发生充血性心力衰竭的风险是30%^[6]。本研究显示脐动脉返流胎/泵血胎估重比 $\geq 50\%$ 组和 $< 50\%$ 组,其泵血胎存活率差异有统计学意义。产前临床工作中仅能粗略估计脐动脉返流胎重量,对其准确评估具有一定难度。

本研究结果显示不同治疗方式泵血胎各预后指标差异无统计学意义。目前本机构选择性减胎术多在孕18周后进行,但是新近研究表明,泵血胎1/3在孕16周前发生宫内死亡或是脐动脉返流胎内血供停止,此时,发生流产、泵血胎宫内死亡或泵血胎出现后遗症的风险较高^[7-8]。双胎脐动脉反向灌注序列与其它复杂性单绒毛膜囊双胎,如双胎输血综合征、选择性宫内生长受限及双胎贫血-红细胞增多序列等不同在于,双胎脐动脉反向灌注序列可在早孕期诊断。Pagani等^[9]回顾性分析十年之内的双胎脐动脉反向灌注序列,发现早孕期或中孕早期诊断并干预与中孕期干预病例其胎儿丢失率和总体存活率差异无统计学意义,但是前者心衰、早期胎膜早破发生率较后者低且分娩孕周和新生儿出生体重较后者高。因此,产前行选择性减胎术是否可提高泵血胎存活率及选择性减胎术时机尚需前瞻性大样本研究证实。

本研究的独特之处在于对脐动脉返流胎的血供情况进行观察,因选择性减胎术的主要目的在于对脐动脉返流胎的供血血管进行凝固或消融,使其内血流断流,进而阻止其停止生长,防止泵血胎发生心力衰竭,亦防止无心胎内含氧量较低的血液进入泵血胎。若脐动脉返流胎已无血供,则可无需行选择性减胎术。此外,本研究中应用多因素分析方法,分析结果显示泵血胎心脏扩大是其预后不良的独立风险因素。因此,在临床工作中若产前超声监测发现泵血胎心胸面积比超

过正常范围时,则应向孕妇告知泵血胎可能预后不良,或是改为行选择性减胎术。

综上所述,泵血胎各预后指标在定期监测组和选择性减胎组差异无统计学意义。泵血胎心脏扩大是泵血胎(宫内或新生儿)死亡的独立风险因素。

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(编辑 王晓鹰)