

·临床研究·

四腔心与三血管气管切面联合 HD-flow 筛查 早孕期胎儿心血管畸形的应用价值

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摘要:【目的】评估在未经选择人群中应用四腔心切面(Four-chamber view, 4CV)与三血管气管切面(3VTV)联合高分辨率血流显像技术(HD-flow)筛查早孕期(11~13⁺周)胎儿心血管畸形的诊断价值。【方法】2018年5月至2019年12月期间,在我院进行早孕期(11~13⁺周)超声检查的胎儿1145例,应用HD-flow对胎儿4CV、3VTV进行观察分析,记录检查结果和妊娠结局,通过对引产后尸解或出生后超声心动图诊断结果,比较以上两个切面及联合切面筛查早孕期胎儿心血管畸形的敏感性、特异性、阳性预测值及阴性预测值。【结果】本研究共纳入948例胎儿,共发现心血管畸形19例;早孕期超声诊断与随访结果符合12例(12/19),其中7例为复杂性先天性心脏病(CHD),共22个结构异常;早孕期超声诊断与随访结果不完全一致1例(1/19),为复杂性CHD;早孕期超声未发现房/室间隔异常6例(6/19)。19例中早孕期超声4CV显示异常6例,3VTV显示异常11例,4CV或3VTV(联合切面)显示异常13例。4CV、3VTV及联合切面对于早孕期胎儿心血管畸形的诊断敏感性分别为:31.5%、57.9%、68.4%,4CV+3VTV联合切面敏感性高于4CV,差异有统计学意义($P=0.016$);其特异性及阳性预测值均为100%($P>0.05$),阴性预测值分别为98.6%、99.1%、99.4%($P>0.05$)。【结论】在早孕期超声检查时联合4CV与3VTV叠加HD-flow较单一4CV切面能提高对胎儿心血管畸形的检出率,尤其有助于检出预后不良的重大心血管畸形。

关键词:心血管畸形;早孕期超声;产前诊断;四腔心切面;三血管气管切面

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Applying Four-Chamber View and Three-Vessel Trachea View Combined With HD-Flow to Screening Fetal Cardiovascular Malformations in First-Trimester Pregnancy

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Abstract:【Objective】To evaluate the value of four-chamber view (4CV) and three-vessel trachea view (3VTV) combined with HD-flow in screening for fetal cardiovascular malformations (CVMs) in unselected population during early pregnancy (11~13⁺ weeks).【Methods】From May 2018 to December 2019, 1145 fetuses were ultrasonically scanned routinely at 11~13⁺ weeks at our hospital. The 4CV and 3VTV of fetal hearts were assessed by Power Doppler with flow direction (high definition flow, HD-flow), and the sonographic findings and follow-up outcomes were documented. Suspected CVMs were confirmed by the postpartum echocardiography or autopsy results. The sensitivities, specificities, PPVs and NPVs of diagnostic tests were compared among the two views and combined views.【Results】There were 948 fetuses included in this study, with 19 cases of CVMs. The sonographic findings of 12 cases (12/19) with 22 CVMs were consistent entirely with the follow-up outcomes, including 7 cases of complex CVMs. In 1 case (1/19) with complex CVM, the diagno-

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sis was not entirely consistent to the autopsy result. The 6 cases (6/19) of abnormal atrioventricular septum were not detected in early pregnancy. In the 19 cases of CVMs, abnormalities were found by displaying 4CV in 8 cases, by displaying 3VTV in 11 cases, and by displaying 4CV combined with 3VTV in 13 cases. The sensitivity of 4CV, 3VTV, 4CV+3VTV was 31.5%, 57.9%, 68.4%, with significant difference between 4CV and 4CV+3VTV ($P=0.016$). The specificity and PPVs were all 100% ($P>0.05$). The NPVs of them were 98.6%, 99.1% and 99.4%, with no statistical difference ($P>0.05$).【Conclusions】 Displaying the 4CV combined with 3VTV of fetal heart in the first-trimester ultrasound examination resulted in higher detect ratio of fetal cardiovascular malformations rather than scanning only with the 4CV, especially for those serious CVMs with poor prognosis, which is important for clinical management appropriately.

Key words: cardiovascular malformation; the first trimester ultrasound; prenatal diagnosis; four chamber view; three-vessel trachea view

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先天性心脏病 (congenital heart disease, CHD) 是导致新生儿死亡的主要原因, 其发病率约为 0.8% ~ 1.0%^[1]。产前超声筛查胎儿心血管结构是 CHD 二级防治的重要手段, 目前一般在胎儿中孕期 18 周以上进行^[2], 而随着对 11-13⁺6 周胎儿进行结构与染色体异常筛查的应用日益广泛, 早孕期胎儿心脏结构筛查在国内外备受重视^[2-3]。国内学者李胜利等^[3]在 2014 年就已提出早孕期胎儿心脏四腔心切面 (four-chamber view, 4CV) 和三血管气管切面 (three-vessel trachea view, 3VTV) 的扫查技术规范, 但临床上至今依然以观察四腔心切面为主。倘若早孕期超声能增加扫查 3VTV, 可及早发现更多严重心血管畸形^[4-5]。目前国内尚无报道应用高分辨率血流显像技术 (high definition flow imaging, HD-flow) 显示 4CV 与 3VTV 对早孕期胎儿心血管畸形的诊断性试验。因此本研究将通过分析我院未经选择人群的早孕期胎儿心脏超声影像, 评估 4CV 与 3VTV 联合 HD-flow 在早孕期筛查胎儿心血管畸形中的诊断价值。

1 材料与方法

1.1 一般资料

本研究为前瞻性研究, 研究对象为未经选择人群, 即 2018 年 5 月至 2019 年 12 月期间所有在本院超声科进行常规早孕期 (11~13⁺6 周) 超声检查的胎儿。排除标准为失访或因早孕期终止妊娠未进行胎儿尸体解剖的胎儿。本研究获得了我院伦理委员会的批准 (伦理编号: 2018SYSUSH-009), 并在检查前告知孕妇本项检查的局限性和安全性。所有研究对象均签署知情同意书。

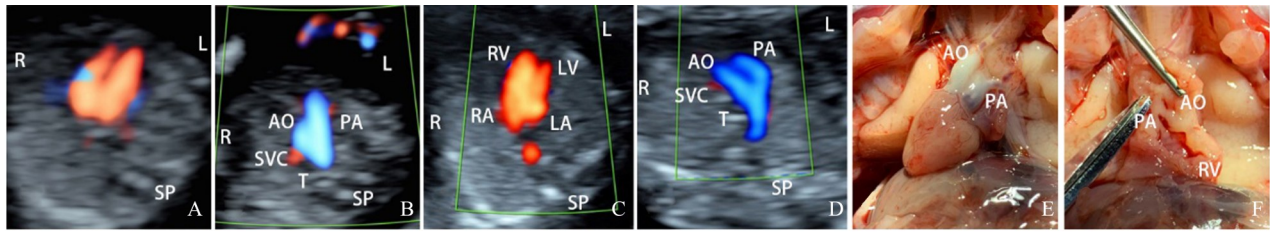
1.2 仪器和检查方法

1.2.1 仪器 GE Voluson E10、E8 (GE Healthcare, Tiefenbach, Zipf, Austria) 彩色多普勒超声诊断仪, 经腹超声探头, 探头频率为 2 ~ 8 MHz。超声仪器内配置 HD-flow 技术软件。

1.2.2 检查方法 超声检查遵循 ALARA (as low as reasonably achievable) 原则^[6]。检查时先进行早孕期超声规范化筛查, 选择胎儿心脏检查条件 (超声生物安全指数: 软组织热指数 Tis 0.5, 骨热指数 Tib 0.5, 机械指数 MI 1.0) 观察胎儿心血管结构。此时期的心脏各结构的观察分析、评估测量检查均需按照胎儿颈项透明层 (NT) 测量标准放大图像, 获得胎儿标准腹围切面后, 探头向胎儿头侧平移到相当于心脏水平即获得 4CV, 联合 HD flow 血流技术 (脉冲重复频率 0.9 kHz ~ 1.3 kHz), 显示两股自心房至心室的血流束 (图 1A), 观察二、三尖瓣口血流情况; 在 4CV 的基础上探头继续略向胎儿头侧偏移, 即获得 3VTV, 同样联合 HD flow 血流技术 (脉冲重复频率 0.9 kHz ~ 1.3 kHz), 显示满意时主动脉弓与动脉导管弓呈“V”征 (图 1B), 二者血流方向应一致。存储动态与静态图像于仪器硬盘中。所有早孕期 4CV 或 3VTV 异常的病例均由另一名专业超声医师进行第二次评估。

1.3 早孕期胎儿心血管畸形的超声诊断标准

观察胎儿心脏超声联合 HD flow 图像特征, 若 4CV 或 3VTV 显示异常, 则为可疑心血管畸形。4CV 异常包括心脏位置异常、左右心比例失常、房室数目异常、房室间隔缺损、房室瓣异常。3VTV 异常包括大动脉数目减少、大动脉血流束比例失调、主动脉弓位置异常、血流方向的异常^[7]。



A: The Four-chamber view with HD flow in a 12-weeks normal fetus; B: The three-vessels and trachea view in a 12-weeks normal fetus demonstrating the ductal arch and aortic arch (V sign); c-f: the case 3, a fetus with complex CHD in 13-week gestational age, C: On the Four-chamber view, the right ventricle (RV) is larger than the left (LV). D: On the Three-vessels and trachea view, HD flow image demonstrating the parallel course of ductal arch and aortic arch; E-F: The images of pathologic anatomy show the pulmonary artery and aorta arise from the same ventricle (RV). R: Right; L: Left; LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle; T: trachea; SP: Spine; SVC: superior vena cav; AO: ascending aorta; PA: pulmonary artery.

图1 早孕期胎儿正常及异常图像

Fig. 1 Normal and abnormal images of fetus in early pregnancy

1.4 病例追踪和证实(诊断金标准)

参照国际文献报道^[8-9], 出生后超声心动图检查或引产后尸体解剖是胎儿先天性心脏病的诊断金标准。所有早孕期产前超声诊断为CHD的胎儿, 结合产前诊断检查结果并经过详细的产前遗传咨询, 根据胎儿医学伦理学原则和胎儿父母的意愿, 选择终止妊娠或继续妊娠。继续妊娠者每隔1~2个月超声复查直至分娩, 出生后在3个月内复查超声心动图。根据实际情况, 对终止妊娠的胎儿进行病理解剖并记录结果, 对继续妊娠者在出生后追踪其手术治疗结局。

1.5 统计学方法

应用SPSS 23.0统计分析软件进行分析, 定量资料以均数±标准差($\bar{x} \pm s$)表示, 分类变量值以百分比(%)表示。采用诊断性试验四格表分别计算4CV与3VTV联合HD-flow以及两种切面联合筛查

早孕期胎儿心血管畸形检查技术的敏感性、特异性、阳性预测值及阴性预测值, 并应用卡方检验比较三种筛查方法的诊断效能, $P < 0.05$ 组间差异有统计学意义。

2 结果

2.1 研究对象一般资料

在研究期间来我院进行早孕期超声筛查胎儿共1145例, 其中单胎1129例, 双胞胎8例。按照病人的纳入与排除筛选标准(图2), 本研究共纳入948例胎儿。所纳入研究对象年龄为 29.0 ± 4.4 (岁), 身体质量指数(body mass index, BMI)为 (21.3 ± 2.9) kg/m², 胎儿头臀长(CRL)为 (64.9 ± 8.4) mm, 胎儿颈项透明层(nuchal translucency, NT)为 (1.6 ± 0.6) mm。

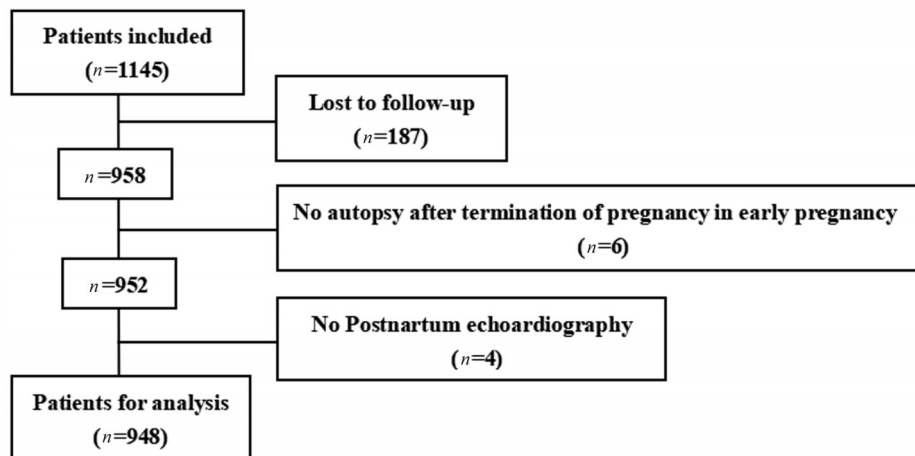


图2 患者纳入情况

Fig. 2 The results of patient enrollments

表1 19例CHD胎儿的临床情况和结局

Table 1 Clinical situation and outcome of 19 CHD fetuses

Case	CRL/mm	NT/mm	4CV	3VTV	4CV+ 3VTV	Ultrasound findings in first trimester	Final Diagnosis of CHD	Extra-cardiac abnormalities
1	72	4.1	N	A	A	disproportion of AoA and DA in 3VTV	¹⁾ TOF; VSD+PS+RAA+ AL- SA	absent nasal bone
2	65	2.4	N	A	A	disproportion of AoA and DA in 3VTV	¹⁾ TOF; VSD+OA+PS+ RLSA	
3	80	1.9	A	A	A	RHS: AVSD+DORV+ RAA	¹⁾ RHS: AVSD+DORV+RAA+ DSVC +TAPVC	Right pulmonary isomerism; Asple- nia; dextrogastria; Midline liver; in- testinal malrotation
4	64	1.0	A	A	A	RHS: AVSD+TA+ TAPVC	¹⁾ RHS: RAA+PA+ TAPVC+ DSVC	Right pulmonary isomerism; Asple- nia; dextrogastria; Midline liver and gallbladder; intestinal malrotation
5	54	1.2	N	A	A	the abnormal AoA in 3VTV	¹⁾ TGA	
6	63	2.6	N	A	A	the abnormal AoA in 3VTV	²⁾ TGA	
7	55	1.0	N	A	A	disproportion of AoA and DA in 3VTV	¹⁾ cTGA+VSD	
8	58	1.1	A	N	A	VSD	¹⁾ VSD	cervix lymphatic hygroma; multiple vertebral deformities
9	59	1.2	N	N	N	N	³⁾ VSD	
10	79	2.1	N	N	N	N	³⁾ ASD	
11	63	7.3	A	A	A	AVSD+ AAI	¹⁾ AVSD+IAA+ARSA	sternal defects
12	52	3.4	N	A	A	disproportion of AoA and DA in 3VTV	¹⁾ cTGA+VSD	absent nasal bone; strephenopodia
13	58	2.1	N	N	N	N	¹⁾ VSD	overriding fingers; spina bifida; syn- dactylism; Rocker-Bottom foot; mi- crophthalmia; micrognathia;
14	67	2.4	A	N	A	VSD	¹⁾ VSD	omphalocele; strephenopodia
15	63	1.5	N	N	N	N	³⁾ VSD	
16	66	1.6	N	N	N	N	³⁾ VSD	
17	59	1.7	N	N	N	N	³⁾ VSD	
18	84	4.3	A	A	A	single ventricle or AVSD+PS	¹⁾ single ventricle or HLHS+ IAA	cervix lymphatic hygroma
19	59	4.9	N	A	A	RAA	¹⁾ RAA+ALSA	absent nasal bone

1): autopsy; 2): postnatal surgery; 3): postnartum echocardiography; CRL: crown-rump length; NT: nuchal translucency; 4CV: four-chamber view; 3VTV: three-vessel trachea view; N: normal; A: abnormal; TOF: tetralogy of Fallot; VSD: ventricular septal defect; ASD: atrial septal defect; PS: pulmonic stenosis; RAA: right aortic arch; ALSA: aberrant left subclavian artery; OA: overriding aorta; ARSA: aberrant right subclavian artery; RHS: right heterotaxy syndrome; AVSD: atrio-ventricular septal defect; DORV: double outlet right ventricle; DSVC: double superior vena cava; TAPVC: total anomalous pulmonary venous drainage; TA: truncus arteriosus; PA: pulmonary atresia; TGA: transposition of the great arteries; cTGA: corrected transposition of the great arteries; IAA: interrupted aortic arch; HLHS: hypoplastic left heart syndrome; AOA: aortic arch; DA: ductus arteriosus.

2.2 病例结果与追踪随访情况

根据追踪随访结果,948例胎儿中发现心血管畸形19例,其中13例终止妊娠后进行了病理解剖,5例出生后进行超声心动图检查,1例出生后手术,其临床情况和结局,详见表1。早孕期超声诊断与随访结果基本符合12例(12/19),其中7例为复杂性CHD(病例1-4、7、11、12,图1C-F)。早孕期超声诊断与随访结果不完全一致1例(1/19,病例18),为复杂性CHD。早孕期超声未发现房/室间隔异常6例(6/19,病例9、10、13、15-17),包括室间隔缺损5例和房间隔缺损1例。在19例早孕期发现心血管异常胎儿中合并心外畸形10例(10/19),均终止妊娠。

2.3 各切面筛查胎儿心血管结构异常与追踪随访结果比较

在948例胎儿中,早孕期超声4CV显示异常6例,3VTV显示异常11例,4CV或3VTV(联合切面)显示异常13例。4CV、3VTV及联合切面对于早孕期胎儿心血管畸形的诊断敏感性分别为:31.5%、57.9%、68.4%,其特异性及阳性预测值均为100%($P>0.05$),阴性预测值分别为98.6%、99.1%、99.4%($P>0.05$)。采用McNemar精确检验发现,联合切面与单独4CV切面敏感性比较,差异有统计学意义($\chi^2=5.14, P=0.016$),4CV+3VTV联合切面诊断敏感性明显高于4CV;3VTV与4CV敏感性比较,差异无统计学意义($\chi^2=1.78, P=0.18$);联合切面与3VTV切面敏感性比较,差异无统计学意义($\chi^2=0.50, P=0.50$)。

3 讨论

鉴于CHD的高发病率及其围生期管理的重要性,产前超声筛查CHD的各种技术提升都具有极其重要的临床意义。4CV是筛查先天性心脏畸形最重要且最常用的切面,当4CV联合流出道切面时,产前超声筛查CHD的敏感性从30%提高到69%~83%^[10]。如果早孕期超声单独应用4CV进行胎儿心脏筛查,有可能漏掉严重的CHD,尤其是圆锥动脉干畸形,因为早孕期胎儿心脏体积小、跳动快,四腔心及流出道切面交叠在一起,对左右流出道的解剖学分析往往是不可靠的。

据报道,在11~13⁺6周的胎儿心血管结构筛查中,通过彩色多普勒或HD-Flow的应用,显示3VTV是可行的^[11]。国外目前对于早孕期胎儿推行在低危人群中进行简化的早孕期超声心动图检查^[8,11],即4CV+3VTV联合彩色多普勒或HD-flow

筛查,对于高危人群进行更详细的标准化早孕期超声心动图检查^[2],使用与中期妊娠检查相同的原则进行。国内在2012年,已有学者王银等^[4]提出联合4CV+3VTV筛查早孕期胎儿严重心脏畸形,但因为早孕期四腔心彩色血流混叠与房室间隔缺损导致的过隔血流信号分辨困难,存在这一局限性。因此这些早孕期胎儿心内结构畸形的诊断对仪器的分辨力提出了更高要求。本研究通过应用HD-flow技术显示4CV与3VTV对早孕期胎儿心血管结构进行筛查,可直接反映大部分胎儿心血管结构异常。De Robertis等认为早孕期两个切面联合HD-flow可以使CHD的检出率提高到75.8%^[11]。在国内王银等^[5]的研究中,早孕期利用4CV和3VTV诊断心脏畸形的检出率为77.78%,漏诊率为22.22%。我们的研究结果显示,在早孕期仅观察单一4CV,敏感性仅为31.5%,联合3VTV后可将敏感性提高到68.4%,略低于国内外报道的数据。分析原因是在王银等^[5]的研究中,所有心血管畸形病例中没有一例为单纯性室间隔缺损,而室缺在产前的检出率一直都比较低^[12],本研究中早孕期超声诊断室缺的检出率为28.6%(2/7)。早孕期胎儿心脏筛查时增加3VTV的显示,虽然较难以明确具体的心血管畸形类型(表1,病例1、2、5、6、12),但提示胎儿可能存在心血管畸形,尤其是圆锥动脉干畸形,不仅有利于提前进行超声结构筛查,还能够提供足够的时间给孕妇做出知情决定权并进行额外的产前诊断检查。因胎儿重大畸形或致死性畸形而尽早终止妊娠后可减少对孕妇的身心伤害^[13]。

我们的研究结果表明,在未经选择人群中,在11~13⁺6周可以筛查出大多数胎儿重大心血管畸形,但对于早孕期胎儿的轻度心血管异常诊断比较困难,比如小的室间隔缺损,本研究中6例房/室间隔异常在早孕期未被发现。其实,单纯性室间隔缺损在中孕期筛查中也容易被漏诊^[12],因为胎儿左、右心室压差较小未形成明显过隔血流造成超声难以显示病灶。另外,部分心脏缺陷是随孕周的增加而进展变化的,例如本研究病例中的房间隔发育异常(表1,病例10),产前超声难以发现。

本研究的不足之处:一、心血管异常病例数量少,尚需进行更大规模的前瞻性研究来分析4CV和3VTV在早孕期对CHD的诊断准确性^[14]。二、虽然常规的尸体解剖仍然是金标准,但由于缺乏经验丰富的合格胎儿病理学家及在自溶或胎儿较小的情况下,尸检质量也是较低的^[9],这使得早孕期发

现的胎儿心脏畸形终止妊娠后难以得到准确的病理诊断,比如病例18,无法准确诊断为单心室还是左心发育不良。

综上所述,在早孕期超声检查时4CV与3VTV

联合HD-flow较单一4CV能提高对胎儿心血管畸形的检出率,虽然较难以明确具体的大血管畸形类型,但是有助于检出预后不良的重大心血管畸形,为临床及时处理提供有效信息。

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