

静脉导管缺失的产前超声诊断及妊娠结局分析

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【摘要】 目的 研究静脉导管缺失(absent ductus venosus, ADV)胎儿的产前超声图像特征及其与妊娠结局的关系。**方法** 回顾性分析2017年1月—2020年2月期间在复旦大学附属妇产科医院超声科行高危超声检查诊断为静脉导管缺失的21例胎儿的超声图像和妊娠结局。根据Achiron等的新分类方法,按脐静脉-门静脉系统中分流部位进行产前超声分型:I型为脐静脉-体静脉分流(umbilical-systemic shunts, USS);II型为“静脉导管”-体静脉分流(ductus venosus-systemic shunts, DVSS);III型为门静脉-体静脉分流(portal-systemic shunts, PSS);III型分为III a型肝内门-体静脉分流(intrahepatic portal-systemic shunts, IHPSS)和III b型肝外门-体静脉分流(extrahepatic portal-systemic shunts, EHPSS)。通过查阅病史、收集影像学报告和电话随访妊娠结局至产后42天(活产、产后超声、肝功能检查或常规体检结果)的资料。**结果** 21例ADV胎儿分为3种类型:I型(USS)10例(47.6%),II型(DVSS)7例(33.3%),III a型(IHPSS)4例(19.0%)。USS型病例中有6例(60%)合并心脏增大;IHPSS型病例中2例(50%)肝内门静脉-肝静脉瘘胎儿心脏增大;而DVSS型病例未合并心脏增大($P=0.012$)。合并心内外畸形共16例(76.2%),在上述3种类型中分别为9例(90%)、4例(57.1%)和3例(75%)($P=0.288$)。合并胎儿生长受限共3例,在上述3种类型中所占比例分别为10%、28.6%和0($P=0.309$)。妊娠结局:5例失访;9例引产,均合并严重胎儿畸形;7例活产,USS型、DVSS型和IHPSS型活产数分别为1例(10%)、4例(57.1%)和2例(50%)($P=0.077$)。**结论** 本研究中ADV胎儿3种类型具有显著的超声特征。USS型胎儿合并心脏增大及心内外畸形率高,妊娠结局差;ADV胎儿的妊娠结局与分型及是否合并心脏增大和畸形有关。

【关键词】 静脉导管缺失(ADV); 胎儿; 产前诊断; 彩色多普勒超声; 妊娠结局

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Prenatal ultrasonographic diagnosis and pregnancy outcomes of absent ductus venosus

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【Abstract】 Objective To study the prenatal ultrasonographic findings of absent ductus venosus (ADV) and its relationship with pregnancy outcomes. **Methods** Sonograms and clinical data of 21 ADV cases who visited ultrasound diagnosis department of Obstetrics and Gynecology, Fudan University from Jan 2017 to Feb 2020 were retrospectively reviewed. The cases of ADV were analyzed according to the new classification of Achiron, et al's: Type I was umbilical-systemic shunt (USS); Type II was ductus venosus-systemic shunt (DVSS); Type III was divided into Type III a, intrahepatic portal-systemic shunt (IHPSS) and Type III b, extrahepatic portal systemic shunt (EHPSS). Fetomaternal clinical characteristics and outcomes (postnatal follow-ups to 42 days) were investigated by means of medical files, imaging documentation and telephone interviews (live birth, postpartum ultrasound, liver function, or routine physical examination results) with the mothers. **Results** A total of 21 cases were identified in 3

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types: 10 (47.6%) with Type I, 7 (33.3%) with Type II and 4 (19.0%) with Type III a. There were 6 cases (60%) combined with cardiomegaly in type I, 2 cases (50%) combined with cardiomegaly in Type III a, and there was no case combined with cardiomegaly in Type II ($P=0.012$). A total of 16 cases (76.2%) were combined with intracardiac and extracardiac malformations, i.e., 9 cases (90%), 4 cases (57.1%) and 3 cases (75%) in the three types, respectively ($P=0.288$). There were 3 cases with fetal growth restriction, accounting for 10%, 28.6% and 0 in the three types, respectively ($P=0.309$). Pregnancy outcomes: 5 cases were lost to follow-up; 9 cases with severe malformations were terminated of pregnancy; the remaining 7 cases were born lively, 1 case (10%), 4 cases (57.1%) and 2 cases (50%) in the three types, respectively ($P=0.077$). **Conclusion** In this study, there were significant ultrasonographic findings in three types of ADV. The incidences of cardiomegaly and intracardiac and extracardiac malformations were higher in USS type cases with poor outcomes. Postnatal outcome was associated with the types of ADV, the presence and severity of cardiomegaly, and associated malformations.

【Key words】 absent ductus venosus (ADV); fetus; prenatal diagnosis; color doppler flow imaging; pregnancy outcome

静脉导管(ductus venosus, DV)是胎儿期特有的三大重要血液循环通道之一,由脐静脉入肝后与门静脉窦汇合后发出,并连接隔下前庭(即DV及三条肝静脉汇入下腔静脉处),为一入口窄、出口宽的漏斗形管道^[1]。DV可来自胎盘的富含氧和营养物质的血液经过隔下前庭导入右心房,直接经卵圆孔进入左心系统,供应胎儿头颈部及上肢^[2]。若在门静脉窦和隔下前庭之间未见静脉导管,则将其定义为静脉导管缺失(absent ductus venosus, ADV)^[3-4]。ADV是一种少见的胎儿静脉系统异常,与许多胎儿疾病有关。但由于其发生率低,既往文献报道病例数较少^[5-6]。ADV常伴发胎儿水肿,心内外畸形以及染色体异常等,且不同类型ADV妊娠结局差异较大^[7-9]。既往产前超声将静脉导管缺失诊断分为肝外型 and 肝内型^[7,10], Achiron 等于 2016 年提出“脐-门-体静脉分流”的宫内分类方法^[11],此后按照此新分类方法的研究逐渐增多^[12-15]。

本研究旨在分析并总结我院 21 例产前超声诊断为 ADV 的胎儿超声图像表现及妊娠结局,为进一步认识并准确诊断该疾病以及产前咨询和临床处理提供依据。

资 料 和 方 法

研究对象 2017 年 1 月—2020 年 2 月在复旦大学附属妇产科医院超声科行高危超声检查诊断为

胎儿 ADV 的 21 例孕妇,其中单胎 19 例,双胎 2 例,均为单绒毛膜双羊膜囊双胎(monochorionic-diamniotic twin, MCDA),且均为双胎之一出现 ADV。孕妇年龄 22~37 岁,平均(29.00 ± 5.22)岁;确诊孕周 13.3~37.0 周,平均确诊孕周(24.88 ± 6.03)周,孕周由妊娠末次月经或妊娠早期超声检查确定。

仪器和方法 采用 GE Voluson E8 和 E10 型彩色多普勒超声诊断仪,探头频率为 3.5~8 MHz。回顾性分析 21 例 ADV 胎儿的产前超声的图像特征和临床资料。所有病例均因常规早孕期颈项透明层(nuchal translucency, NT)检查、中孕期大畸形筛查或中、晚孕期常规超声检查发现脐静脉、肝内静脉或其他系统异常,为进一步诊断而进行的高危超声检查。高危超声由 2 名经验丰富的高年资医师诊断。具体检查内容包括胎儿各生长径线、胎儿各系统结构以及胎盘、羊水和脐带等。当二维及彩色多普勒超声在门静脉窦和静脉前庭之间未探及静脉导管时,诊断为胎儿 ADV;并仔细检查脐静脉的走行以及其与周围静脉、心脏的关系。

根据 Achiron 等^[11]在 2016 年提出的分类方法,按脐静脉-门静脉系统中分流部位进行产前超声分型。I 型:脐静脉-体静脉分流(umbilical-systemic shunts, USS),超声表现为脐静脉未与左门静脉形成正常肝内连接后发出 DV,而是脐静脉直接连接体静脉系统,即异常分流起源于脐静脉、引流入体

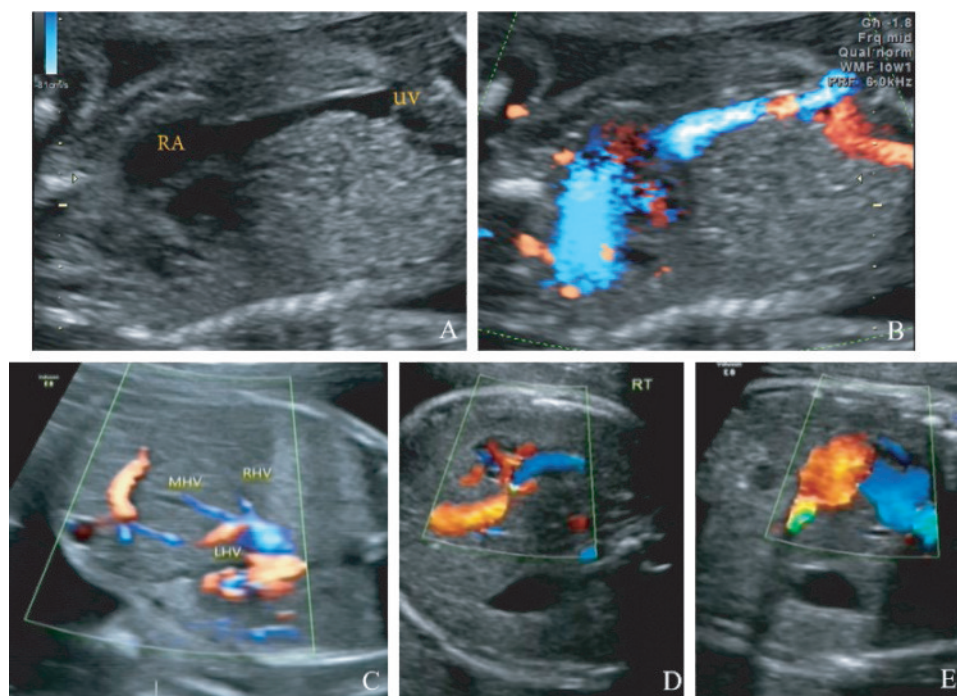
静脉系统;Ⅱ型:“静脉导管”-体静脉分流(ductus venosus-systemic shunts, DVSS),超声表现为脐静脉与左门静脉形成正常肝内连接,发出“DV”后引流入非隔下前庭部位的下腔静脉或肝静脉,即异常分流的起源是正常部位(脐静脉与门静脉窦汇合后)、引流入部位异常;Ⅲ型:门静脉-体静脉分流(portal-systemic shunts, PSS)。Ⅲ型可分Ⅲa型肝内门-体静脉分流(intrahepatic portal-systemic shunts, IHPSS)和Ⅲb型肝外门-体静脉分流(extrahepatic portal-systemic shunts, EHPSS),其中IHPSS超声表现为异常分流起源于肝内门静脉分支,引流入肝静脉或下腔静脉,可为一支或数支分流的异常连接,亦可表现为门静脉-肝静脉瘘。收集和查阅病史、影像学报告和电话随访妊娠结局至产后42天(是否活产、产后超声、肝功能检查或常规体检结果)的资料进行研究。本研究为横断面回顾性研究,高危超声检查前每位孕妇均签署知情同意书。

统计学分析 使用IBM SPSS 26.0进行统计分析。组间差异定量数据采用ANOVA检验,定性数据

采用Fisher精确检验; $P<0.05$ 为差异有统计学意义。

结 果

超声分型 共纳入21例ADV胎儿(表1),参考以往文献报道的分类方法^[11],根据分流部位进行分类:I型USS 10例(47.6%);Ⅱ型DVSS 7例(33.3%);Ⅲa型IHPSS 4例(19.0%)。其中I型中有4例为脐静脉(umbilical vein, UV)直接回流右心房(right atrium, RA)(图1A、1B),4例脐静脉直接连接下腔静脉(inferior vena cava, IVC),1例脐静脉连接髂静脉,1例脐静脉连接奇静脉;Ⅱ型中6例为脐静脉入肝与门静脉窦汇合后发出分支连接肝静脉(图1C),1例为脐静脉入肝与门静脉窦汇合后发出分支连接隔下前庭下方的下腔静脉;Ⅲ型中1例右门静脉分支连接下腔静脉,1例肝内门静脉分支连接肝静脉,另外2例表现为肝内血管团即门静脉-肝静脉瘘(图1D、1E),周边连接门静脉及肝静脉分支。



A&B: Umbilical-systemic shunt (USS), 2D and Color Doppler image in the sagittal plane showing direct connection between umbilical vein (UV) and right atrium (RA) (Case 4). C: Ductus venosus-systemic shunt (DVSS), Color Doppler image in the transverse plane showing connection between intrahepatic umbilical vein (UV) and the left hepatic vein (LHV) (Case 12). D&E: Intrahepatic portal-systemic shunt (IHPSS), Color Doppler images in the transverse plane showing the vascular mass in the right lobe of the liver, which is a portal vein-hepatic vein fistula. The lower edge is connected to the right portal vein, and the upper margin is connected to the right and middle hepatic veins (Case 21).

图1 静脉导管缺失的三种类型的超声图像

Fig 1 Color Doppler ultrasound images of three types in ADV

一般情况 I~III型病例诊断时孕妇年龄分别为(29.10±4.98)岁、(26.86±3.58)岁和(32.50±6.45)岁($P=0.204$),各组间差异无统计学意义;诊断孕周分别为(22.39±5.60)周、(25.19±5.20)周和(30.55±5.48)周($P=0.064$),各组间差异也无统计学意义。

超声合并异常 USS型病例中有6例合并心脏增大,占该类型的60%;IHPSS型病例中2例(50%)肝内门静脉-肝静脉瘘胎儿心脏增大;而DVSS型的7例胎儿未合并心脏增大。USS型合并心脏增大的比例明显高于其他两组($P=0.012$)。合并心内外畸形共16例(76.2%),在3种类型中分别为9例(90%)、4例(57.1%)和3例(75%)($P=0.288$),但IHPSS中3例为轻微异常;其中合并心脏畸形在3种分型中所占比例分别为40%、42.9%和25%;合

并心外异常(包括心外畸形、生长径线异常、频谱多普勒异常及胎儿羊水异常等)15例,在3种类型中所占比例分别为80%、57.1%和75%。合并FGR共3例,在3种类型中所占比例分别为10%、28.6%和0($P=0.309$)。详见表1、2。

妊娠结局 21例患儿中,5例失访,9例引产且均合并严重胎儿畸形,7例活产分为USS型、DVSS型和IHPSS型,其活产数分别为1例(10%)、4例(57.1%)和2例(50%)($P=0.077$)。1例USS型因MCDA中另外1例胎儿无结构异常而选择剖宫产,但该ADV胎儿合并畸形出生后数天死亡;4例新生儿产后1个月随访正常,1例胎儿生长受限(fetal growth restriction,FGR)产后1个月随访正常,另外1例珍贵儿合并胎儿心内外畸形和FGR,超声随访异常静脉导管产后1周闭合,心脏畸形择期手术(表1、2)。

表1 所有ADV病例的超声表现及妊娠结局

Tab 1 List of all cases with ADV: sonographic findings and pregnancy outcome

Case	Age (y)	GA	Shunt origin and drainage	Cardiomegaly	Cardiac anomalies	Other associated sonographic findings	FGR	Twin	Outcomes
Type I : Umbilical-systemic shunt									
1	31	32 wk	UV-RA	Yes	/	Hydrops, ascites, polyhydramnios, thickened PL	/	/	TOP
2	25	22 wk	UV-RA	Yes	Cardiac axis to the left, heart asymmetry (right side is bigger than left side), cardiac hypertrophy, TR, VSD	HC, AC<-2SD	Yes	/	Lost
3	28	13 wk 3 d	UV-RA	/	Heart asymmetry (left side is bigger than right side)	Occipital meningoencephalocele, focal calcifications, absence of right radius and abnormal right hand, SUV	/	/	TOP
4	37	22 wk 2 d	UV-RA	Yes	/	Cleft lip and palate	/	/	TOP
5	37	15 wk 6 d	UV-IVC	Yes	/	Omphalocele, SUV, short torso, spina bifida occulta	/	MCDA	LB (NND)
6	22	26 wk 2 d	UV-IVC	/	HLHS	/	/	/	TOP
7	27	23 wk 6 d	UV-IVC	Yes	/	/	/	/	Lost
8	28	28 wk 4 d	UV-IVC	Yes	/	ARAS, pericardial effusion, dilated intracranial veins	/	MCDA	TOP
9	25	20 wk 2 d	UV-iliac vein	/	/	Cystic hygroma, bilateral pleural effusion	/	/	TOP
10	31	20 wk 4 d	UV-azygos	/	Large VSD	Interruption of IVC	/	/	TOP
Type II : Ductus venosus-systemic shunts									
11	30	21 wk 1 d	DV-LHV	/	/	/	/	/	LB

(续表 1)

Case	Age (y)	GA	Shunt origin and drainage	Cardiomegaly	Cardiac anomalies	Other associated sonographic findings	FGR	Twin	Outcomes
12	28	27 wk	DV-LHV	/	Cardiac axis to the right, PLSV, dilated CS	Small AC and short FL, esophageal atresia, absent of GB, abdominal cyst, SUA, short NB, polyhydramnios, velamentous placenta	Yes	/	TOP
13	22	35 wk 1 d	DV-LHV	/	/	Large AC, hydrops, pleural effusion, ascites, hepatomegaly, dilated hepatic veins, abnormal UA, polyhydramnios	/	/	Lost
14	27	21 wk 3 d	DV-MHV	/	VSD, single atrium	Left subdiaphragmatic calcifications, velamentous placenta	/	/	Lost
15	22	27 wk 4 d	DV-IVC	/	/	/	/	/	LB
16	29	20 wk 4 d	DV-LHV	/	Cardiac axis to the right, VSD/overriding aorta, PLSV, dilated CS	FGR, caudal degeneration, velamentous placenta	Yes	/	LB
17	30	24 wk	DV-LHV	/	/	/	/	/	LB
Type III a: Intrahepatic portal-systemic shunts									
18	23	23 wk 6 d	RPV-IVC	/	/	Short long bones	/	/	TOP
19	37	31 wk	LPV-LHV	/	/	PRUA	/	/	LB
20	34	37 wk	Fistula of PV-HV	Yes	/	/	/	/	LB
21	36	30 wk 6 d	Fistula of PV-HV	Yes	Cardiac axis to the left, increased velocity of PA and AO, MR, TR	Abnormal MCA, polyhydramnios	/	/	Lost

CS: Coronary sinus; FGR: Fetal growth restriction; GA: Gestational age at diagnosis; HC: Head circumference; HLHS: Hypoplastic left heart syndrome; IVC: Inferior vena cava; LPV: Left portal vein; LHV: Left Hepatic vein; LB: Live birth; MCA: Middle cerebral artery; MHV: Middle hepatic vein; MCDA: Monochorionic-diamniotic twin; MR: Mitral regurgitation; NB: Nasal bone; NND: Neonatal death; PA: Pulmonary artery; PRUV: Persistent right umbilical vein; RA: Right atria; SUA: Single umbilical artery; TOP: Termination of pregnancy; TR: Tricuspid regurgitation; UA: Umbilical artery; UV: Umbilical vein; VSD: Ventricular septal defect.

表 2 各类型 ADV 病例超声表现和妊娠结局汇总

Tab 2 The summary of sonographic findings and outcomes in ADV cases

Pregnancy outcome	Total (n=21)	USS (n=10)	DVSS (n=7)	IHPSS (n=4)	F/ χ^2 value	P value
Age (y)	29.00 ± 5.01	29.10 ± 4.98	26.86 ± 3.58	32.50 ± 6.45	1.738	0.204
GA at diagnosis (wk)	24.88 ± 6.03	22.39 ± 5.60	25.19 ± 5.20	30.55 ± 5.48	3.218	0.064
Cardiomegaly	8	6	0	2	8.905	0.012
Associated anomalies	16	9	4	3	2.492	0.288
FGR	3	1	2	0	2.347	0.309
Live birth	7	1 (NND)	4	2	5.126	0.077

USS: Umbilical-systemic shunt; DVSS: Ductus venosus-systemic shunt; IHPSS: Intrahepatic portal-systemic shunts; FGR: Fetal growth restriction.

讨 论

在本研究纳入的ADV病例中,USS型所占比例最高,合并胎儿心脏增大的比例明显高于其他型($P<0.05$);其合并心脏畸形以及心外异常的发生率与其他组相比有增高的趋势,但差异无统计学意义。与之相应的是,该型病例活产率低于其他两组,这与以往结论一致^[3,11,14,16],但差异无统计学意义,推测可能与样本量较小有关。各组孕妇年龄差异无统计学意义,提示孕妇年龄与分型无关;而各组病例诊断孕周差异虽无统计学意义,但可以看出USS类诊断孕周较早,可能与本研究中病例大部分为院外建卡病例转诊来我院会诊有关。由于USS这一类静脉导管缺失病例的超声表现典型且常合并严重的结构畸形而易于被发现,导致这一类型比例在本研究中最高,诊断孕周较早。

静脉导管在调节脐静脉血流和保护胎儿免受高输出性心力衰竭的影响方面起着重要作用^[17],一方面它将一定比例的脐静脉分流入体静脉直接回流到心脏,一部分汇入门静脉营养肝脏;另一方面由于其特定的解剖位置,可以将高含氧的静脉血直接经卵圆孔射入到左心室,从而优先供应头颈部和上肢。当出现USS时其对应的两方面生理功能相应缺失,造成心脏过载,往往合并心脏增大、胎儿水肿、胸腔积液、腹腔积液和心包积液等心衰的表现,同时由于肝脏缺少来自于脐静脉的营养甚至合并肝内门静脉发育不良,本研究中75%的心脏增大来自于USS,远高于其他类型ADV胎儿的心脏增大发生率,同时其合并胎儿畸形发生率较高,其预后差,活产率低。而DVSS中,虽然有一根类似静脉导管的血管可以从脐静脉分支直接连接体静脉(本研究中为肝静脉或下腔静脉),起到了分流的作用,但是这部分脐静脉血没有直接射入左心系统,供应头颈部和上肢的血含氧量降低,因此该类型中的“静脉导管”并不是严格意义上的静脉导管^[11,18];在DVSS类型中合并畸形和终止妊娠的发生率低于USS型。而IHPSS中,DV的缺失导致全部脐静脉进入肝脏,易导致肝脏高灌注及门静脉高压,然后通过门静脉和肝静脉的异常连接分流入体静脉系统,若不发生门-肝静脉瘘,其分流量通常较小,同时该类型合并胎儿严重畸形率低,一般预后较好;

在本研究中该类型所占比例较少,而既往研究表明此类型应最为常见^[15,19],可能与肝内静脉系统不属于产前系统超声筛查的常规内容而检查不足^[16],且合并严重畸形少见,导致此类型不易被发现有关。

从研究结果来看,USS型和DVSS型均有合并FGR胎儿,USS发生FGR可能与高含氧和营养的脐静脉血流未进入肝脏有关,但可能是样本量较小的缘故,各组间FGR比例差异未见统计学意义。最终活产且预后较好者均未合并心内外畸形,产前超声检查时,除了做出准确的分型外,胎儿结构的系统筛查对于预后具有重要的参考价值。既往关于MCDA胎儿发生ADV的病例报道较少^[20],在本研究中有2例MCDA双胎之一存在ADV,且预后不佳。

本研究作为回顾性研究,尚存在不足之处:(1)收集的病例均为高危人群,无法通过各类型占比推断一般人群各类型所占比例;(2)ADV胎儿除了合并心、内外畸形外,文献报道常合并染色体异常^[17],由于仅有8例进行了染色体检查故而未纳入此指标,缺少关于染色体部分的研究结果;(3)对于胎儿肝内门静脉系统和肝外门静脉系统也缺少详尽的描述,而肝内门静脉是否完整对于胎儿预后较大的影响^[12];(4)随访病例中失访比例较大(5/21),随访结果不够详尽。

尽管如此,在此基础上探讨该少见疾病对于产前诊断和临床咨询仍具有重要的意义,有利于增强对该病的认识。由于DV最重要的作用在于将部分高含氧的脐静脉血绕过肝脏,直接进入右心房经卵圆孔并送达左心供应头颈部和上肢^[2],而胎儿期是脑部发育重要的时期,DV的缺失必然导致供应脑部的氧和营养物质明显减少,对胎儿期、新生儿期、婴儿期、儿童期甚至成人期的神经发育是否有影响值得更详尽、完善的前瞻性研究进一步探索。

综上所述,在ADV胎儿中根据脐静脉-门静脉系统中分流部位所划分的3种类型具有显著的超声特征,USS型病例合并心脏增大及心内外畸形率高,妊娠结局差;ADV胎儿的妊娠结局与分型及是否合并心脏增大和心内外畸形有关。

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