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Research paper

The role of first-trimester single arterial vessel sign instead of a V-sign at the level of the three-vessel and tracheal view in screening for congenital heart diseases

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Abstract

Introduction: Despite efforts from dedicated societies, prenatal detection rates (DRs) of congenital heart diseases (CHDs) remain unsatisfactory. Early cardiac scan is believed to play an important role in selecting fetuses for further assessment and to improve the DRs. The aims of the study were to compare first-trimester cardiac parameters and follow-up fetal, postnatal echocardiography and autopsy findings in fetuses presenting the single arterial vessel with fetuses presenting the "V-sign" at the level of the 3 vessels and trachea view in colour mapping (3VTVc), and to measure screening performance of the single arterial vessel in 3VTV for D-TGA and D-TGA+VSD, all CHDs, and ductal-dependent (DD) CHDs.

Material and methods: This study was a prospective observational analysis that covered 2338 pregnancy referrals. Study protocol included an early fetal echocardiography approach to the 4-chamber view in colour mapping and 3VTVc.

Results: Among single arterial vessel fetuses 2 normal hearts, 66 CHDs, including 42 DD lesions, were identified; and among "V-sign" fetuses, 1913 normal hearts, 42 CHDs, including 2 DD lesions. The single arterial vessel sign was highly sensitive (93.3%) and specific (97.3%) for D-TGA/D-TGA+VSD at the time of the early cardiac scan. Moreover, the single arterial vessel in 3VTV was highly sensitive (95.8%) and specific (98.8%) for other ductal-dependent CHDs.

Conclusions: Differentiation between the single arterial vessel sign in 3VTV and the "V-sign" is replicable and safe due to the short exposure time for colour mapping needed to obtain satisfactory images. This would help establish their use as another strong prenatal predictor of important congenital heart disease, D-TGA, and other DD-lesions.

Key words: congenital heart disease, first trimester, fetal echocardiography, transposition of great arteries

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Introduction

It is crucial to search for better screening strategies to more effectively detect congenital heart diseases (CHDs) in prenatal life, especially those that are ductal dependent. Despite many efforts from dedicated societies, prenatal detection rates (PDRs) of CHDs remain unsatisfactory, at an average level below 50% among multiple registries [1–3].

Starting from 1991, a number of authors raised the role in screening for CHDs of mid-gestational upper mediastinum fetal ultrasound projections including the following: 3-vessel (3VV), 3-vessel and trachea (3VTV), transverse aortic arch views, and a transverse section through the innominate vein [4–10]. Their major role is focused on the assessment of the number of arterial and venous vessels, their arrange-

ment, proportion in size, flow directions, the relationship of these vessels with the trachea, and the size of the thymus. The characteristics of these views in major CHDs was widely described in the literature [9, 10]. In the normal heart 3VTV presents a V-sign formed by the confluence of transverse sections through the aortic and ductal arches together with the transverse sections through the trachea and superior caval vein on its right and the thymus in the front. Due to the small size of the fetal heart in the first trimester (FT), the whole sequence of upper mediastinum views and their detailed assessment in B-mode is difficult to reproduce. This is why most authors who share their interest in the first trimester screening for CHDs despite 4-chamber view focus on 3VTV in colour mapping, which is highly reproducible [11]. Several groups of authors stated that a reduced number of arterial vessels in 3VTV in connection with 4CV findings at the time of a first-trimester scan may indicate suspicion of major ductal-dependent (DD) CHDs, like d-transposition of the great arteries (D-TGA), but also hypoplastic left heart syndrome (HLHS), or tetralogy of Fallot (TOF) [12-16]. Until now, the power of the single arterial vessel in 3VTV to detect CHDs at the time of first-trimester screening was not measured in low- or high-risk populations.

We decided to conduct this study to assess the following: 1) to compare FT parameters and follow-up fetal, postnatal echocardiography and autopsy findings in fetuses presenting the single arterial vessel in 3VTV with fetuses presenting the "V-sign" at the level 3VTV in colour mapping (3VTVc) in correlation with 4CV findings; 2) to measure screening performance of the single arterial vessel in 3VTV and of indirect FT markers for CHDs.

Material and methods

This study was a prospective observational analysis. Patient enrolment was based on cooperation between 2 screening centres and one tertiary centre in an area of south Poland. The study population sample was collected between January 2016 and April 2019 and covered 2338 singleton pregnancy referrals for early cardiac scan after FT screening. The indications for early screening were as follows: maternal age above 35 years (287), family history factors (153), assisted reproduction techniques (384), maternal serum signs of infection (136), and/or sonographic signs suspicious for CHD, such as increased NT (431), increased FT risk for major trisomies (548), the presence of TR (234), or reversed a-wave in DV velocimetry (165). Exclusion criteria were as follows: multiple gestations, multiple anomalies, aneuploidy, and loss from follow-up. The maternal body mass index was calculated in kilograms per square metre on the day of the tertiary centre scan. All tertiary centre scans were performed within 7 days after FT screening. The scan protocol covered an early cardiac and extracardiac ultrasound scan, according to the steps described by Springhall et al. [17]. The scan was accompanied by the reassessment of primary (NT, fetal heart rate [FHR]) and secondary markers of aneuploidy (nasal bone, tricuspid flow, and ductus venosus velocimetry), according to recommendations from the Fetal Medicine Foundation [18]. For the purpose of an early cardiac scan in all cases, examiners insonated the fetal chest in a manner that the fetal spine was observed at a 6 or 12 o'clock position to avoid less optimal colour mapping views or oblique sections. Then, colour flow mapping was triggered for the shortest time possible. The perfect insonation angle to the interventricular septum of approximately 45° was certainly an easy approach to the levels of the 4-chamber view in colour mapping (4CVc) and 3VTVc, allowing for a smooth shift between these levels. This was consistent with our previous study protocol [19]. Experienced physicians examined subjects with Samsung WS80, Samsung HERA W10 (Samsung Electronics, Seoul, Korea), and Voluson E8 (GE Healthcare, Zipf, Austria) ultrasound scanners (M.W. and A.N.). The risk of major trisomies was not recalculated after first-line FT screening. The factory presets of the machines were adapted to obtain images of high diagnostic value and to ensure acceptable safety limits for an early cardiac scan: the mechanical index for B-mode imaging and the soft tissue thermal index in the colour flow mode were set not to exceed a value of 1. All scans were performed with a transabdominal 3–10 MHz or 4–8 MHz transducer. In suboptimal scanning conditions, a transvaginal 3-10 MHz or 5–9 MHz transducer was applied. The abovementioned standardized settings allowed for precise early cardiac imaging and restriction of the scan duration to meet the ALARA (as low as reasonably achievable) principle [20, 21]. All tertiary centre FT findings were recorded and documented. Next, all data concerning the second trimester, third trimester, up to 2 months postnatal or autopsy findings of enrolled patients were collected and included in a database. All referred subjects provided signed consent to participate in the study, and the local Ethics Committee approved the protocol. Enrolled subjects were grouped according to the FT tertiary centre picture of the 3VTVc into a "V-sign" subgroup and a single arterial vessel in the 3VTV subgroup. Ductal dependent anomalies in the study group were classically defined as cardiac lesions requiring postnatal maintenance of arterial duct patency due to the significant obstruction of flow to systemic or pulmonary circulation in simple or complex CHDs, or in parallel circulation circuits like those observed in D-TGA. Subjects' characteristics were examined using descriptive statistics. Subsequently, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated separately for each diagnostic algorithm. All calculations were performed using SPSS version 17 data analysis software (IBM Corporation, Armonk, NY). Findings with $p < 0.05$ were considered significant.

Results

Group characteristics

All scans were performed through a transabdominal approach, and 38 patients (1.87%) required an additional transvaginal evaluation to demonstrate early fetal cardiac views mapped with a colour Doppler.

Based on 2338 referrals, 2023 subjects were included in the study population, because 105 declined to participate, aneuploidy was revealed in 52, 20 presented multiple gestation,

Table 1. Descriptive statistics of the study population

Group			CRL [mm] (weeks + days)	FHR [bpm]	NT [mm]	DV PI	MA [years]
Single arterial vessel in 3VTV	of cases		68	68	68	68	68
	Mean		66.3 (12w6d)	158.0	2.1	1.04	31.0
	Median		66.0 (12w6d)	160.0	2.1	1.00	31.0
	SD		5.7	5.9	0.5	0.1	3.4
	Minimum		58 (12w2d)	140	1.1	0.62	22
	Maximum		79 (13w5d)	170	3.6	1.64	40
	Percentile	5	58.0 (12w2d)	143.3	1.5	0.81	25.4
		95	77.0 (13w4d)	168.0	3.1	1.33	38.0
V-sign in 3VTV	of cases		1955	1955	1955	1955	1955
	Mean		64.0 (12w5d)	159.6	1.9	1.01	34.9
	Median		63.9 (12w5d)	160.0	1.7	0.99	36.0
	SD		8.7	7.7	0.8	0.1	4.6
	Minimum		45 (11w2d)	114	0.8	0.51	17
	Maximum		84 (14w1d)	196	12.7	1.45	48
	Percentile	5	50.1 (11w5d)	148.0	1.2	0.63	26.0
		95	79.4 (13w6d)	172.0	2.8	1.36	41.0
p			0.017	0.120	0.000	0.000	0.000

CRL – crown rump length expressed in millimetres and gestational age (weeks and days according to FMF tables), FHR – fetal heart rate expressed, NT – nuchal translucency , DV PI – pulsatility index values in ductus venosus, MA – maternal age.

and 128 were lost to follow up. The median maternal body mass index was 22.5 kg/m^2 (range 17.1–35.7) in the single arterial vessel in the 3VTV subgroup and 22.8 kg/m^2 (range 17.3–35.8) in the "V-sign" subgroup; the difference was not statistically significant (p = 0.07). The study group characteristics, according to maternal age, gestational age, which was expressed by crown rump length (CRL) and gestational weeks according to FMF tables, FHR, NT, and DV PI, are presented in Table 1.

Single arterial vessel sign in 3VTV and "V-sign" subgroups were statistically significantly different in terms of gestational age (p = 0.017), NT thickness (0.000), and DV PI (p = 0.000), but these differences have no clinical impact due to small discrepancies in values between the groups (Table 1). Statistically significant differences were observed in terms of maternal age (p = 0.000), showing that fetuses presenting the single arterial vessel in 3VTV had younger mothers.

Among subjects presenting the single arterial vessel in 3VTV, analyses of tricuspid flow demonstrated 20 cases of TR (29.6%), and 50 cases of TR (2.6%) were observed in the "V-sign" group, which was a statistically significant difference (p = 0.000). A reversed a-wave pattern in DV velocimetry in the single arterial vessel in 3VTV subjects was discovered in 16 cases (23.5%) vs. in 35 cases in "V-sign" fetuses (1.8%), which was also a statistically significant difference (p = 0.000).

Congenital heart disease final diagnoses and follow-up

Among single arterial vessel sign in 3VTV fetuses, 2 normal fetal hearts and 66 CHDs were identified, including 42 ductal dependent lesions. The following anomalies were also found in this group: HLHS (16), aortic arch obstruction ± ventricular septal defect (10), double outlet right ventricle (DORV) (7), D-TGA (8), D-TGA + ventricular septal defect (6), double inlet left ventricle (DILV) (4), common arterial trunk (CAT) (2), pulmonary atresia with intact interventricular septum (PAIVS) (2), l-transposition of the great arteries (L-TGA) (2), tricuspid atresia (TA) (2), tetralogy of Fallot with absent pulmonary valve syndrome (ToF-APVS) (1), tetralogy of Fallot with pulmonary atresia (ToF-PA) (1), and 2 false-positive cases.

Among "V-sign" fetuses, 1913 normal fetal hearts and 42 CHDs were identified, including 2 ductal dependent lesions. The following anomalies were identified in this group: ventricular septal defect (VSD) (18), atrioventricular septal defect (AVSD) (3), ToF (2), pulmonary stenosis (PS) (2), aortic coarctation (CoA) (3), aortic stenosis (AS) (3), DORV (1), partial anomalous pulmonary venous return (PAPVR) (2), right aortic arch (RAA) (2), premature ductal constriction (2), aorto-pulmonary window (APW) (1), aortic tunnel (1), cor triatriatum (1), and total anomalous pulmonary venous return (TAPVR) (1).

A summary of the diagnosis time, postnatal findings, and follow-up among CHDs identified in the study group is shown in Table 2.

Video analysis of early cardiac images

For all patients the recorded clips were reviewed and representative images at the levels of the 4-chamber view, 3-vessel view, and 3-vessel and tracheal view were stored. Exemplar still images of representative cardiac views of analysed fetuses are shown in Figures 1–4.

Table 2. Follow-up summary of congenital heart diseases among study subgroups with diagnosis and follow-up times

Arm of the study	Type of CHD	of cases	1st trimester findings (11-14 weeks)	2nd trimester findings (18-21 weeks)	3rd trimester additional findings (28-32 weeks)	Fetal demise – of cases	Number of live births	Postnatal additional important findings (1st day after delivery)	Neonatal death before treatment	Postnatal management up to 2 months	Late death after surgical treatment
Single arterial vessel in 3VTV	Aortic arch obstruction	10	Abnormal 4CVc –smaller inflow to the LV than to RV in 10, deviation of cardiac axis in 3; abnormal 3VTVc-missing/ hardly visible aortic arm in 10	Diagnosed as CoA in 10 with additional VSD in 4	Severe fetal growth restriction	1	9	Bicuspid aortic valve in 4	0	Surgical treatments: 9 (end-to-end anastomosis: 7; left subclavian flap repair: 2)	0
	D-TGA	14	Normal 4CVc in 14; abnormal 3VTVc convex course to the right of the single arterial arm in 3	Diagnosed as D-TGA in 6; as D-TGA+VSD in 6; as D-TGA + interatrial restriction in 2	None	0	14	None	2	Surgical treatment:12 BAS: 4; arterial switch: 12	0
	PAIVS	2	Abnormal 4CVc –smaller inflow to the RV than to LV in 2; abnormal 3VTVc-missing/ hardly visible pulmonary arm in 2	Diagnosed as PAIVS in 2	None	1	1	None	0	Surgical treatment: 1	1
	Common Arterial Trunk	2	Abnormal 4CVc in 1- deviation of the cardiac axis, normal 4CV in 1; abnormal 3VTV- single arterial arm: 1 in horizontal, 1 in oblique position	Diagnosed as common arterial trunk in 2 including 22q11 microdeletion in 1 (termination of pregnancy)	None	1 (TOP)	1	Qualified as type A1 according to Van Praagh classification	1	–	–
	DORV with sub-pulmonary VSD	3	Normal 4CVc in 3; abnormal 3VTVc convex course to the right of the single arterial arm in 3	Diagnosed as DORV with sub-pulmonary VSD in 3	None	0	3	None	0	Surgical treatment: 3, including systemic shunt in 2; and single ventricular palliation in 1;	0
	DORV with subaortic VSD and PS	4	Normal 4CVc in 4; abnormal 3VTVc-missing/ hardly visible pulmonary arm in 4	Diagnosed as DORV with subaortic VSD and PS in 4	2nd trimester diagnoses in 4	0	4	None	0	All planned for surgical treatment at the age of 5 months	0
	ToF	6	Normal 4CVc in 4; abnormal 4CVc– deviation of the cardiac axis; abnormal 3VTVc-missing/ hardly visible pulmonary arm in 6	Diagnosed as ToF in 6	2nd trimester diagnoses in 6, absent pulmonary valve in 1; additional pulmonary atresia in 1	0	6	None	0	All planned for surgical treatment later in life	0
	L-TGA	2	Abnormal 4CVc –smaller inflow to the posterior ventricle, and suspicion of AV discordance in 2; abnormal 3VTVc short convex course to the right of the single arterial arm in 2	Diagnosed as L-TGA+VSD+PS in 1; as L-TGA+ congenital heart block in 1	None	0	2	None	0	Pacemaker placement in 1; BV in 1	0

Table 2. Cont.

Arm of the study	Type of CHD	of cases	1st trimester findings (11-14 weeks)	2nd trimester findings (18-21 weeks)	3rd trimester additional findings (28-32 weeks)	Fetal demise – of cases	Number of live births	Postnatal additional important findings (1st day after delivery)	Neonatal death before treatment	Postnatal management up to 2 months	Late death after surgical treatment
	TA	2	Abnormal 4CVc– absent inflow to the anterior ventricle in 2; abnormal 3VTVc-missing/ hardly visible pulmonary arm in 2	Diagnosed as TA+PS in 2; termination of pregnancy in 1	None	2 (TOP in 1)	0	–	–	–	–
	DILV	4	Abnormal 4CVc–suspicion of large VSD in 4; abnormal 3VTVc convex course to the right of the single arterial arm in 4	Diagnosed as DILV{S,L,L} in 2, ILV{S,L,L} + pulmonary stenosis in 1, and DILV{S,D,D} in 1	None	0	4	None	0	Surgical treatment: 4; single ventricular palliation in: 4	0
	HLHS	16	Abnormal 4CVc: hyperechoic walls of a hypoplastic posterior ventricle in 10; dilated posterior ventricle with hyperechoic walls in 2; inflow only to the anterior ventricle in 16; abnormal 3VTVc in 16- missing aortic arm in 10	Diagnosed as HLHS-mitral stenosis-aortic atresia in 10; as HLHS based on critical aortic stenosis in 2 including 1 with interatrial restriction; as HLHS-mitral atresia-aortic atresia in 4 including interatrial restriction in 1 termination of pregnancy in 5	None	0	11	None	2	Surgical treatment: 9; 1st stage of single ventricular palliation: 9	1
	False aortic arch obstruction	2	Normal 4CVc in 2; abnormal 3VTVc-missing/ hardly visible aortic arm in 2	Qualified as CoA in 2 due to isthmic/ductal ratio < 0.7 in 2; aortic isthmus diameter < –2 Z-score in 2	3rd trimester signs of CoA in 2	0	2	Normal	0	None	0
"V-sign"	VSD	18	Normal 4CVc and normal 3VTVc	Normal	2nd trimester diagnoses in 6; 3rd trimester diagnoses in 10; prenatally missed: 2	0	18	New postnatal diagnoses in 2; regressed in 5	0	Planned for surgical treatment later in life: 2	0
	AVSD	3	Normal 4CVc in 1; abnormal 4CVc in 2: initially common inflow to the ventricles, which separates closer to the apex; normal 3VTVc	Diagnosed as balanced AVSD in 3	1st trimester diagnoses in 2; 2nd trimester diagnoses in 1 incl. 1 unbalanced in the setting of right atrial isomerism- underwent termination of pregnancy	1 (TOP)	2	None	0	Planned for surgical treatment later in life: 2	0
	PAPVR	2	Normal 4CVc and normal 3VTVc	Diagnosed as cardiac PAPVR in 1; normal in 1	2nd trimester diagnosis in 1; prenatally missed: 1	0	2	1 postnatal diagnosis	0	No treatment: 2	0

Table 2. Cont.

Arm of the study	Type of CHD	of cases	1st trimester findings (11-14 weeks)	2nd trimester findings (18-21 weeks)	3rd trimester additional findings (28-32 weeks)	Fetal demise – of cases	Number of live births	Postnatal additional important findings (1st day after delivery)	Neonatal death before treatment	Postnatal management up to 2 months	Late death after surgical treatment
	Aorto-pulmonary window	1	Normal 4CVc and normal 3VTVc	Diagnosed as aorto-pulmonary window + CoA in 1	None	0	1	None	0	Surgical treatment: 1	0
	PS	2	Normal 4CVc and normal 3VTVc	Diagnosed as PS in 2	None	0	2	None	0	BV: 1	0
	AS	3	Normal 4CVc and normal 3VTVc	Diagnosed as AS in 3	2nd trimester diagnosis in 2, 3rd trimester diagnosis in 1 (critical)	0	3	None	0	BV: 2, surgical treatment:1; surgical aortoplasty:1	0
	Aortic arch obstruction	3	Normal 4CVc and normal 3VTVc	Diagnosed as CoA in 2; normal in 1	None	0	3	CoA in 3, including 1 critical (from a case diagnosed in 2nd trimester)	0	Surgical treatment in 3: nd-to-end anastomosis in 3	0
	ToF	2	Normal 4CVc and normal 3VTVc	Diagnosed as ToF in 2	2nd trimester diagnosis in 1, 3rd trimester diagnosis in 1	0	2	None	0	All planned for surgical treatment later in life: 2	0
	RAA	3	Normal 4CVc in 3 and abnormal 3VTVc in 3: U-sign in 2, deviated apex of the V-sign to the right	Diagnosed as RAA with left arterial duct in 2, and with right arterial duct in 1	2 with left arterial duct, 1 with right arterial duct	0	3	None	0	No treatment	0
	DORV with subaortic VSD and no RVOT obstruction	1	Normal 4CVc and normal 3VTVc	Diagnosed as DORV with subaortic VSD and no obstruction of the right ventricular outflow tract	2nd trimester diagnosis	0	1	None	0	Systemic shunt in 1; planned for surgical treatment later in life in 1	0
	Aortic tunnel	1	Normal 4CVc and normal 3VTVc	Diagnosed as mild aortic stenosis in 1	Diagnosed as aortic tunnel in 1	0	1	None	0	Surgical treatment	0
	Cor triatriatum	1	Normal 4CVc and normal 3VTVc	Normal	Normal	0	1	Cor triatriatum in 1	0	No treatment	0
	Premature ductal constriction	2	Normal 4CVc and normal 3VTVc	Normal	Diagnosed as premature ductal constriction in 2; spontaneous regression in 2	0	2	None	0	No treatment	0

4CVc – 4-chamber view in colour mapping, 3VTVc – 3-vessel and trachea view in colour mapping, CHD – congenital heart disease, D-TGA – d-transposition of the great arteries, PAIVS – pulmonary atresia with intact interventricular septum, DORV – double outlet right ventricle, RVOT – right ventricular outflow tract, ToF – tetralogy of Fallot, L-TGA – l-transposition of the great arteries, TA – tricuspid atresia, HLHS – hypoplastic left heart syndrome, VSD – ventricular septal defect, AVSD – atrioventricular septal defect, PS – pulmonary stenosis, AS – aortic stenosis, RAA – right aortic arch, 22q11 – microdeletion 22q11, BAS – balloon atrio-septostomy, BV – balloon valvuloplasty, TOP – termination of pregnancy.

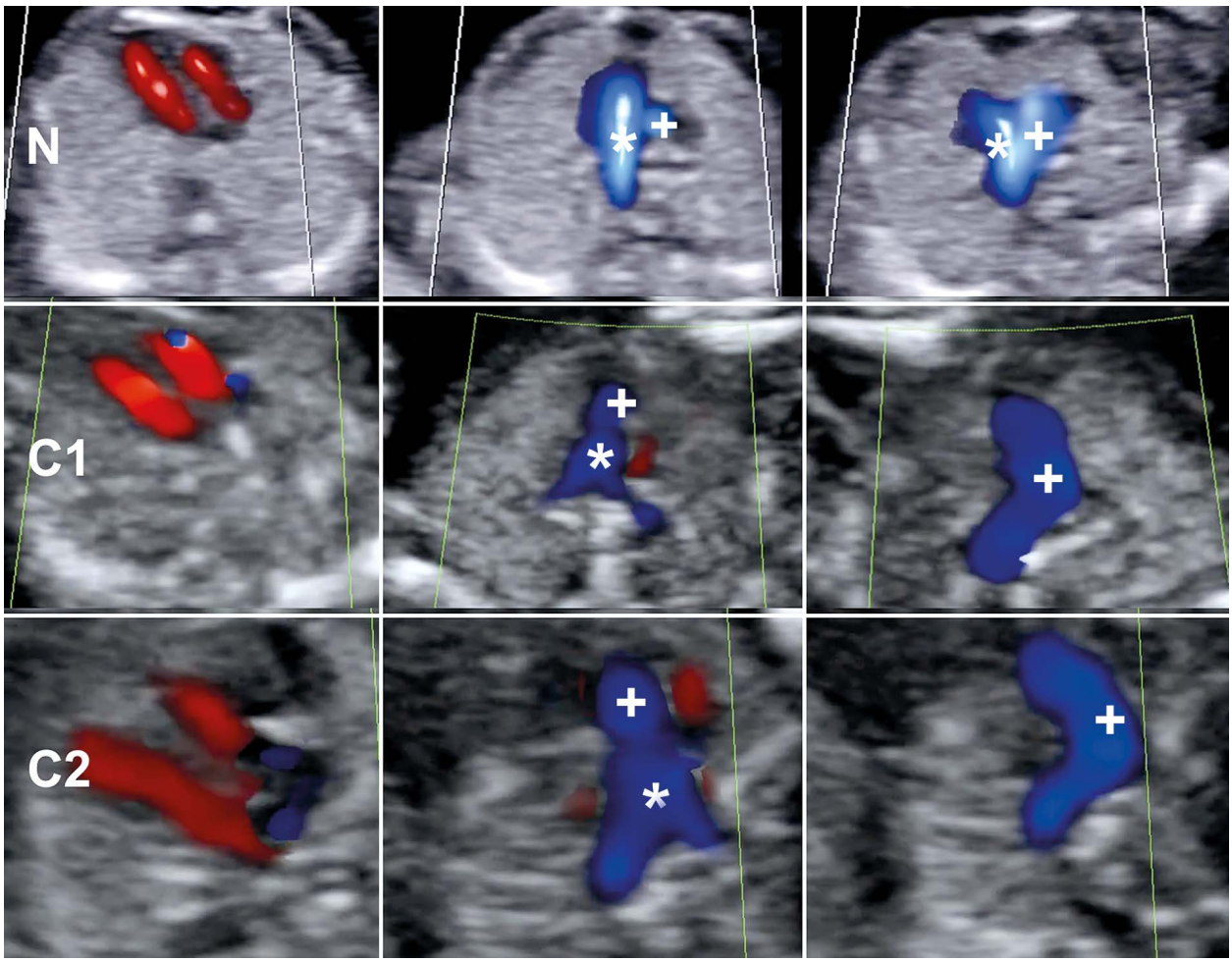

Figure 1. First-trimester transverse fetal cardiac views in the normal fetal heart (top line-N), D-transposition of the great arteries at 12 weeks and 4 days (middle line -C1), and d-transposition of the great arteries at 13 weeks and 5 days (bottom line). From the left column: the 4-chamber view in colour mapping, 3-vessel view, and 3-vessel and tracheal view

**Pulmonary artery colour Doppler signal, +the aorta.*

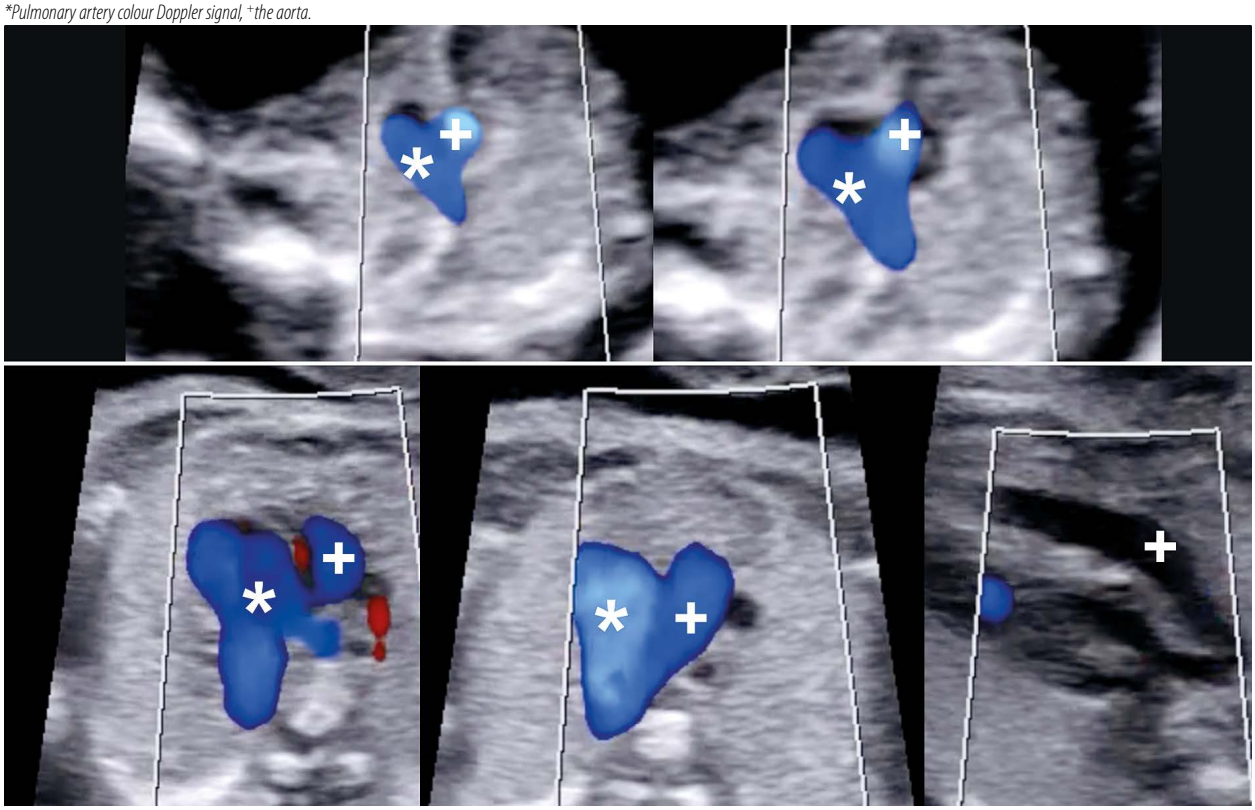

Figure 2. A case of D-transposition of the great arteries with ventricular septal defect, which presented the "V-sign" at 12 weeks and 2 days at the level of the three vessel and tracheal view (upper line). The same case also presented the "V-sign" in the second trimester at 20 weeks due to the consequence of VSD and severe rightward deviation of the infundibular septum, which allows the visualization of the "V-sign" at the level of 3VTVc

**Pulmonary artery colour Doppler signal, +the aorta.*

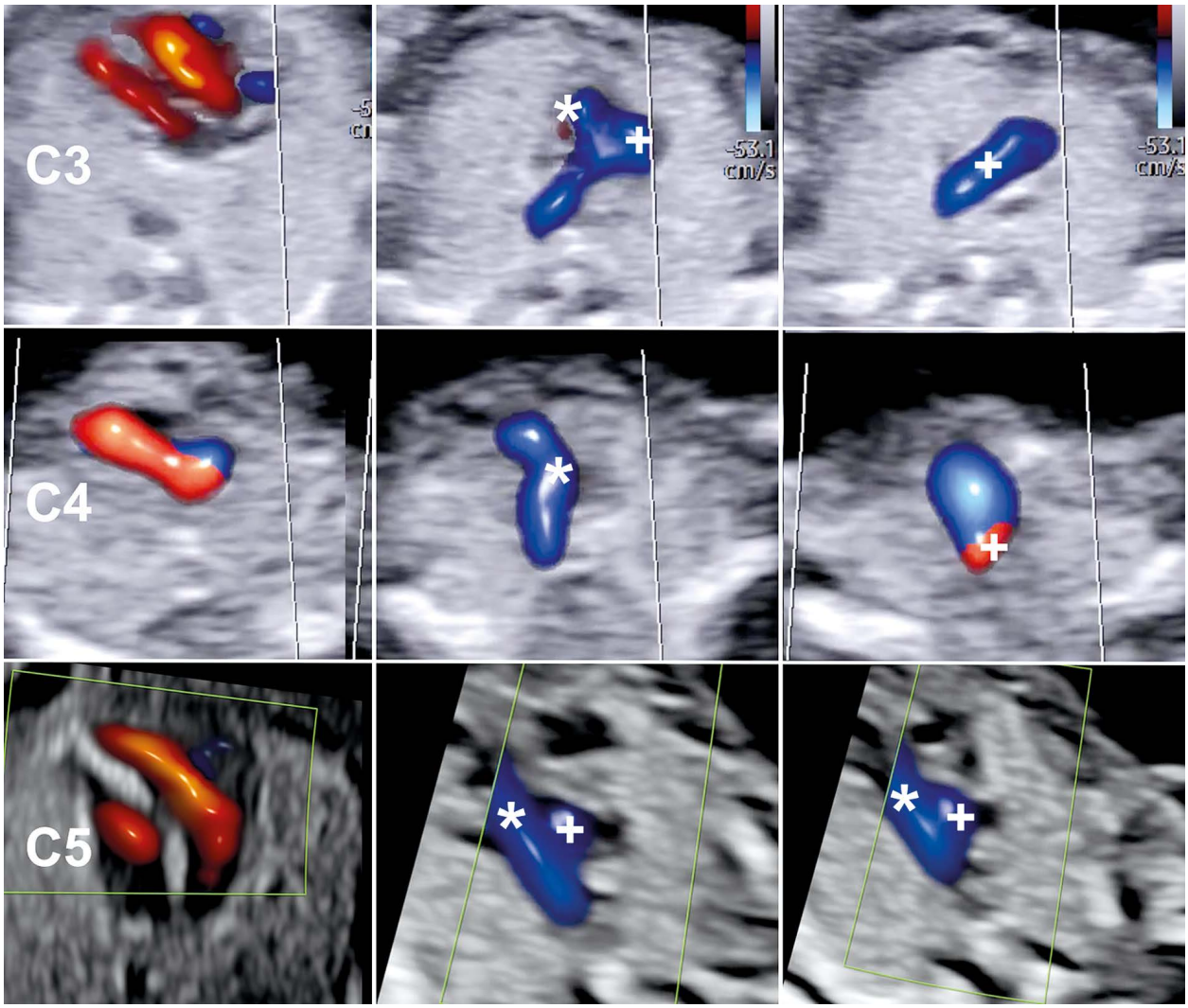

Figure 3. Examples of fetuses presenting the single arterial vessel in 3VTV diagnosed with ductal-dependent congenital heart diseases other than D-transposition of the great arteries: C3-tetralogy of Fallot with severe pulmonary stenosis, C4-hypoplastic left heart syndrome (retrograde flow in the hypoplastic aortic arch-middle right), and C5-aortic arch hypoplasia with ventricular septal defect (presents severe disproportion in size between the pulmonary artery arm and the aortic arm of the V-sign)

**Pulmonary artery colour Doppler signal, +the aorta.*

Screening performance

Screening performance for the first-trimester 3VTVc picture of the single arterial vessel in 3VTV: for D-TGA and D-TGA + VSD, for the total number of CHDs, and for DD CHDs. These findings are presented in Table 3.

In the study population, screening performance for classic FT parameters, such as NT, TR, and DV PI > 95th percentile, was calculated for CHDs in general (Table 4) and for ductal-dependent CHDs (Table 5).

Discussion

Single arterial vessel sign in 3VTV at the time of late first trimester was described as a potential indicator of D-TGA, and because of that it became related only with this specific condition by first-trimester examiners [13, 14]. Our series, as the first in the literature, demonstrates that it should be rather understood as a strong indicator of DD CHDs at this time of gestation. On the other hand, we should not forget about all the limitations of the early cardiac assessment caused by limited image resolution or difficulty in scanning high-BMI patients, which potentially produces false positive and false negative cases. However, after a detailed analysis of pros and cons, the application of 3VTVc builds a strong screening line for DD CHDs including D-TGA.

According to multiple studies, there is no question about the importance of the prenatal diagnosis of D-TGA. It is of particular significance for fetuses with an intact ventricular septum because 4–12% of neonates will develop major hemodynamic alterations that can cause death shortly after birth [22–24]. Moreover, the total cost of initial hospitalization is higher for infants without a prenatal diagnosis of D-TGA [25]. It was also observed that if D-TGA is detected prenatally, there are no differences in postnatal outcomes, independent of whether a neonate was delivered in a specialist centre or a primary hospital [26].

Due to a lack of known maternal risk factors of fetal D-TGA, it is difficult to determine a group of patients who may

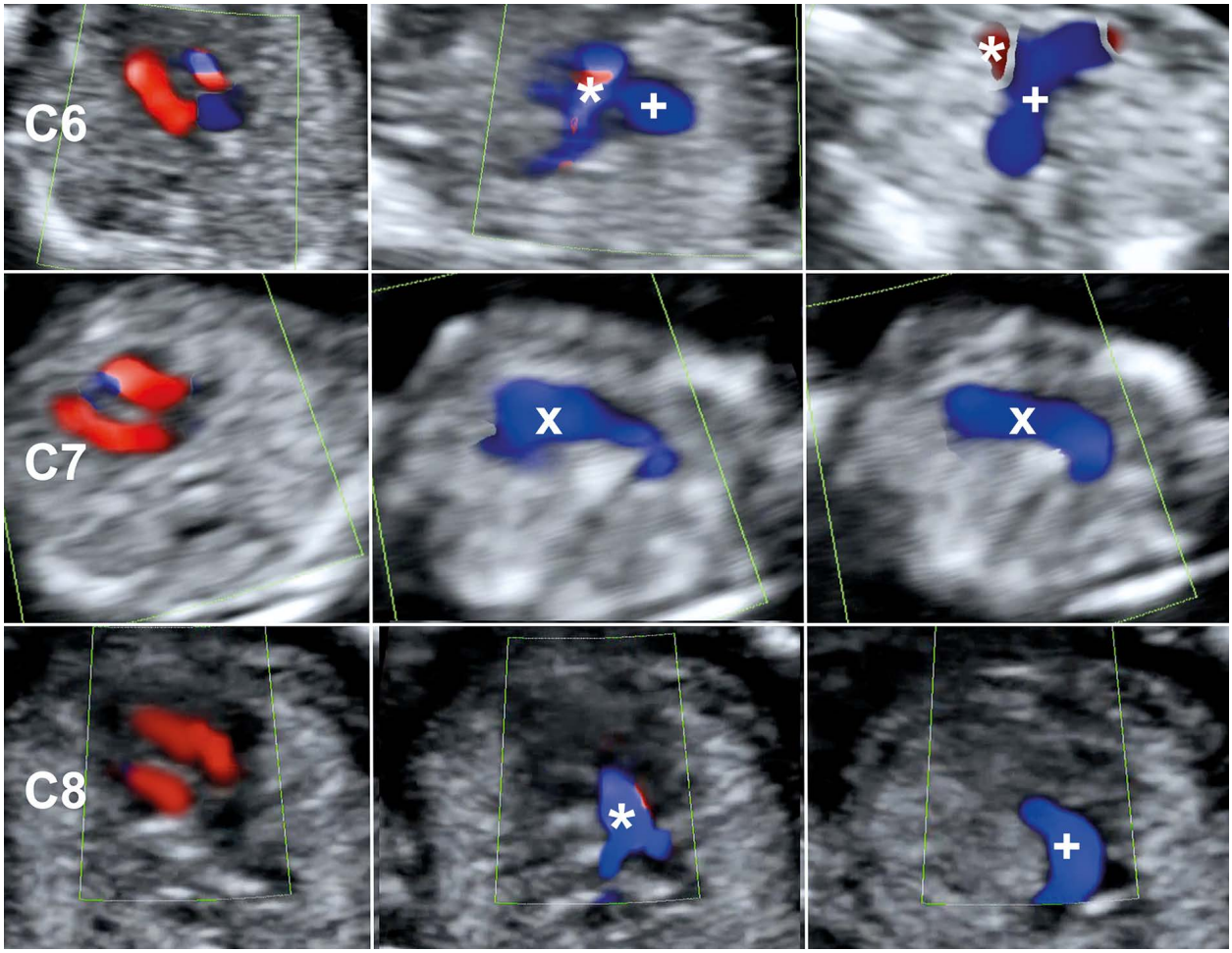

Figure 4. Examples of fetuses presenting the single arterial vessel in 3VTV diagnosed with congenital heart diseases other than D-transposition of the great arteries: C6-severe pulmonary stenosis, which evolved into pulmonary atresia with an intact interventricular septum; C7-common arterial trunk with right aortic arch; and C8-L-transposition of the great arteries (short single arterial vessel in 3VTV at the level of the three-vessel and tracheal view-lower right)

**Pulmonary artery colour Doppler signal, +the aorta, xa single great vessel – in this case -common arterial trunk.*

Table 3. Screening performance for the single arterial arm sign (single arterial vessel in 3VTV) at the level of the three-vessel and tracheal view in colour mapping in the first trimester: 1) d-transposition of the great arteries with and without ventricular septal defect (D-TGA/D-TGA+VSD), 2) for congenital heart disease (CHD), and 3) ductal-dependent congenital heart disease (DD-CHD)

Statistics	Single arterial vessel sign in 3VTV for D-TGA/D-TGA+VSD		Single arterial vessel sign in 3VTV for CHD		Single arterial vessel sign in 3VTV for DD CHD	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity (%)	93.33	68.05-99.83	36.67	29.62-44.16	95.83	85.75-99.49
Specificity (%)	97.31	96.51-97.97	99.89	99.61-99.99	98.89	98.32-99.30
+LR	34.71	25.82-46.65	337.88	83.45-1368.02	86.03	56.54-130.90
–LR	0.07	0.01-0.46	0.63	0.57-0.71	0.04	0.01-0.16
PPV	20.59	16.17-25.84	97.06	89.07-99.26	67.65	57.88-76.08
NPV	99.95	99.66-99.99	94.17	93.53-94.75	99.90	99.60-99.97
DA	97.28	96.48-97.95	94.27	93.16-95.24	98.81	98.24-99.24

+LR – positive likelihood ratio, –LR – negative likelihood ratio, PPV – positive predictive value, NPV – negative predictive value, DA – diagnostic accuracy.

be more at risk for this condition as a fetus. In recent years, increasing focus is placed on FT early cardiac screening [17, 27, 28]. Quartermain et al. analysed 31,374 patients from 91 centres between 2006 and 2012, and they showed that the DR for D-TGA with an intact interventricular septum was 27.9%, and that of VSD was 36.8% [1]. Van Velzen et al., based on an analysis of 724,089 deliveries, calculated D-TGA DRs of 50% in 2009 and 2010 and 41.7% in 2011 [29]. Another valuable report, which included 18,000 subjects from international birth defect surveillance programs, showed significant differences

Table 4. Screening performance for first-trimester nuchal translucency thickness (NT) > 95th percentile, the presence of tricuspid regurgitation (TR), and ductus venosus (DV) PI > 95th percentile for congenital heart disease (CHD) is shown

Statistics	NT > 95th percentile for CHD		TR for CHD		DV PI > 95th percentile per for CHD	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	12.64	8.18-18.36	21.43	15.70-28.11	16.48	11.41-22.69
Specificity	94.02	92.87-95.03	96.01	95.05-96.83	96.32	95.38-97.11
+LR	2.11	1.39-3.22	5.37	3.77-7.65	4.48	3.01-6.66
–LR	0.93	0.88-0.98	0.82	0.76-0.88	0.87	0.81-0.93
PPV	16.43	11.43-23.04	33.33	25.99-41.58	29.41	21.87-38.28
NPV	92.04	91.62-92.44	92.92	92.40-93.41	92.53	92.07-92.97
DA	87.08	85.59-88.48	89.66	88.29-90.92	89.52	88.14-90.79

+LR – positive likelihood ratio, –LR – negative likelihood ratio, PPV – positive predictive value, NPV – negative predictive value, DA – diagnostic accuracy.

Table 5. Screening performance for first-trimester nuchal translucency thickness (NT) > 95th percentile, the presence of tricuspid regurgitation (TR), and ductus venosus (DV) PI > 95th percentile for ductal-dependent congenital heart disease (DD-CHD) is shown.

Statistics	NT > 95th percentile for DD CHD		TR for DD CHD		DV > 95th percentile for DD CHD	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	17.39	7.82-31.42	56.52	41.11-71.07	34.78	21.35-50.25
Specificity	91.90	90.62-93.06	97.72	96.97-98.34	96.46	95.55-97.23
+LR	2.15	1.12-4.10	24.83	16.91-36.47	9.82	6.22 to 15.53
–LR	0.90	0.79-1.03	0.44	0.32-0.62	0.68	0.55-0.84
PPV	4.71	2.52-8.62	36.62	28.23-45.90	18.60	12.63-26.54
NPV	97.97	97.69-98.22	98.98	98.58-99.26	98.45	98.09-98.74
DA	90.22	88.86-91.48	96.79	95.92-97.51	95.06	94.02-95.96

+LR – positive likelihood ratio, –LR – negative likelihood ratio, PPV – positive predictive value, NPV – negative predictive value, DA – diagnostic accuracy.

among countries, and even their regions, in prenatal DRs for D-TGA [30]. A breakthrough in prenatal diagnosis was discovered in the analysis of the national Dutch registry, which showed a significant increase in the DR of D-TGA from 44.2% to 82.4% after introducing mid-gestational 3-vessel view (3VV) into the routine mid-gestational ultrasound screening [31].

It must be emphasized that it is not only of importance to diagnose D-TGA prenatally, but also to check for prognostic factors like the ones indicating to the need for urgent atrioseptostomy after delivery. Słodki et al. have recently reported on the importance of the measurement of maximum velocity of flow in pulmonary veins in this context [32].

Regarding FT screening for CHDs, most authors paid more attention to indirect parameters. This indirect approach showed unsatisfactory results. As an example, Westin et al. reported an extremely low DR at the level of 13.5% of NT ≥ 95th percentile for isolated CHD, based on a low-risk population of 16,383 patients [19]. Their findings are comparable with our results (DR of 12.64%). Another retrospective analysis, based on more than 100,000 pregnancies, showed an FT DR of 13.3% with FT indirect ultrasound markers, and a second-trimester DR of 80% with direct cardiac views [33, 34]. Our group also examined tricuspid flow and DV velocimetry in FT observational studies and found no specific patterns for particular CHDs [35, 36].

On the other hand, some authors concluded that direct early cardiac evaluation is achievable and rational, giving parents the chance to exclude approximately 60% of CHDs and to comfort them about a normal cardiac anatomy as early as possible [15, 37–42]. Early detection of various forms of CHD has been widely reported in the literature [43–45]. The only obstacle in early cardiac evaluation may be the heart size at the time of FT scan. It is also of importance that patients with a high BMI may benefit from an early cardiac evaluation performed transvaginally. This is important because obesity was determined to be a crucial factor in reducing a prenatal diagnosis of D-TGA [46].

By using direct early fetal cardiac evaluation, Volpe et al. reported 4 cases of D-TGA that were correctly diagnosed at 11–14 weeks of gestation. Unfortunately, the authors did not state which of the ultrasound findings had been the most useful in supporting the identification of D-TGA [47].

The only specific descriptions of the early diagnosis methodology for D-TGA were given by Vinals in 8 cases and by Menahem et al. in 21 cases [13, 14]. They observed the following: 1) at the level of the 3VV, the ascending aorta was located more anteriorly than the main pulmonary artery; 2) at the level of the 3VTV, 2 vessels rather than 3 were observed; and 3) the great vessel arising from the anterior ventricle (aorta) running cranially presented an atypical convexity to the right. In our study, we tested their concept in a high-risk population,

and we found that the single arterial vessel in 3VTV, which is equivalent to their observations regarding one arterial vessel at the level of the 3VTV, was highly sensitive (93.3%) and specific (97.3%) for D-TGA/D-TGA+VSD. It must be emphasized that not all D-TGA cases are detectable when using the single arterial vessel in 3VTV. Examiners should consider cases such as the one of ours shown in Figure 2, which was the consequence of VSD and severe rightward deviation of the infundibular septum, which allows the visualization of the "V-sign" at the level of 3VTVc throughout gestation instead of the single arterial vessel in 3VTV, which is characteristic for D-TGA. Surprisingly, as stated above, we found that the single arterial vessel sign in 3VTV was highly sensitive (95.8%) and specific (98.8%) for other ductal-dependent CHDs, which was not previously mentioned in the literature. Only 4.5% of ductal-dependent CHDs in our series presented the "V-sign" at the time of the FT scan. As an example, we found the single arterial vessel sign in 3VTV among the Taussig-Bing anomaly, HLHS, severe forms of aortic arch obstruction, PAIVS, ToF, and TA presenting severe right outflow tract obstruction. The first-trimester single arterial vessel in 3VTV was also present in non-ductal-dependent CHDs, such as L-TGA, or SV, which is usually connected with l- or d-transposed great arteries. It must be emphasized that the aim of the FT early cardiac scan is not to replace the second-trimester fetal echocardiography, but to select patients more effectively for detailed fetal cardiac assessment later in gestation, especially for D-TGA, which requires a better screening policy due to alarming prenatal DRs.

Conclusions

A key element of our study is the need to examine a high number of early cardiac scans performed in a high-risk population in a study group with a representative number of CHDs. Our findings and those published by other authors are very interesting because differentiation between the single arterial vessel sign in 3VTV and the "V-sign" is easily replicable and safe due to the short exposure time for colour mapping needed to obtain satisfactory images. In our opinion, if other independent groups of authors confirmed and routinely adopted the international guidelines as in latest updated ISUOG recommendations for fetal cardiac screening, this would help establish their use as another strong prenatal predictor of ductal-dependent CHDs including D-TGA [48].

Conflict of interest

The authors declare no conflict of interest.

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