Congenital heart defects: from a prenatal perspective

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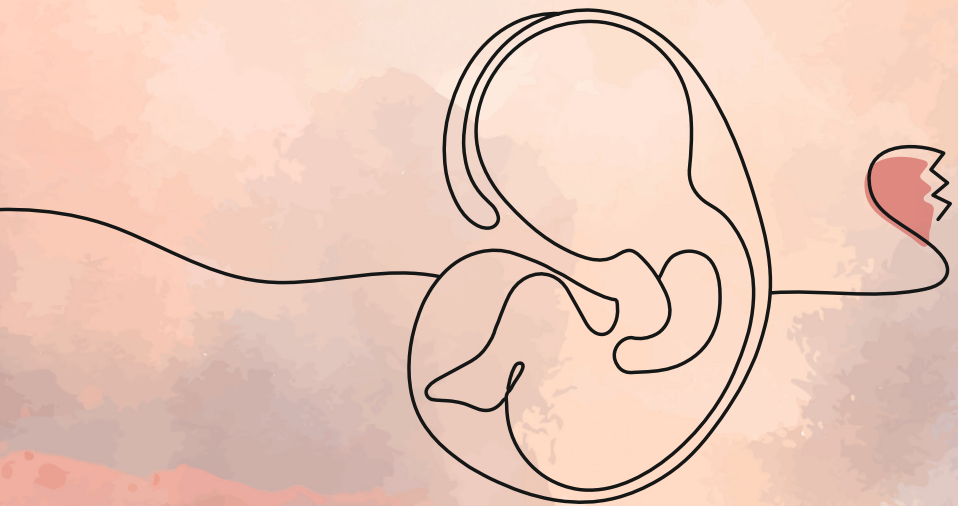

CHAPTER 2

Why are congenital heart defects being missed?

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ABSTRACT

Objectives

Congenital heart defects (CHD) are still frequently missed in prenatal screening programs, which can result in severe morbidity or even death. The aim of this study was to evaluate the quality of fetal heart images, obtained during the second-trimester standard anomaly scan (SAS) in cases of CHD, to explore factors associated with a missed prenatal diagnosis.

Methods

All cases born with an isolated severe CHD from 2015 to 2016 were extracted from the PRECOR registry. Severe CHD was defined as the need for surgical repair in the first year of life. Each cardiac view (four-chamber view (4CV), three-vessel (3V) view and left and right ventricular outflow tract (LVOT, RVOT) views) obtained during the SAS was scored for technical correctness on a scale of 0 to 5 by two fetal echocardiography experts, blinded to the diagnosis of CHD and whether it was detected prenatally.

Results

A total of 114 isolated CHD cases were analyzed, of which 58 (50.9%) were missed and 56 (49.1%) were detected on the SAS. The defects comprised transposition of the great arteries (17%), aortic coarctation (16%), tetralogy of Fallot (10%), atrioventricular septal defect (6%), aortic valve stenosis (5%), ventricular septal defect (18%) and other defects (28%). No differences were found in fetal position, obstetric history, maternal age or body mass index (BMI) or gestational age at examination between missed and detected cases. Compared with the detected group, the missed group had significantly lower cardiac examination quality scores (adequate score (≥ 12) in 36% *vs* 68%; $P = 0.002$), rate of proper use of magnification (58% *vs* 84%; $P = 0.01$) and quality scores for each individual cardiac plane (4CV (2.7 *vs* 3.9; $P < 0.001$), 3V view (3.0 *vs* 3.8; $P = 0.02$), LVOT view (1.9 *vs* 3.3; $P < 0.001$) and RVOT view (1.9 *vs* 3.3; $P < 0.001$)). In 49% of missed cases, the lack of detection was due to poor adaptational skills resulting in inadequate images; in 31%, the images showed an abnormality (mainly septal defects and aortic arch anomalies), which had not been recognized at time of the scan; whereas in 20%, the cardiac planes had been properly obtained, but showed normal anatomy.

Conclusions

A lack of adaptational skills, as opposed to circumstantial differences, appears to play an important role in prenatally undetected CHDs. Despite adequate quality of the images, the CHD was not recognized in 31% of cases. A high volume of SAS performed by each sonographer, in particular when performed in a large screening center, contributes to prenatal detection. In 20% of the undetected cases, the CHD was not visible, even though the quality of the images was good.

INTRODUCTION

Congenital heart defects (CHD) are the most common birth defect, with a prevalence of approximately 5-8 per thousand live births. Ultrasound in pregnancy enables prenatal diagnosis of CHD, which allows for delivery in a facility with appropriate postnatal care. Prenatal identification of CHD has been shown to decrease mortality and perioperative morbidity and may improve neurodevelopmental outcome.[1-5]

Prenatal detection of CHD, however, still fails in approximately half of the cases.[6] Screening programs in most developed countries have reported a detection rate (DR) of only 30-60%, which varies according to type of cardiac defect.[7-19] Although prenatal DRs have increased gradually over the past few years, the identification of modifiable factors, if targeted appropriately, could potentially increase the sensitivity of current screening programs to achieve a DR of 80-90%, as reported in single centers-studies.[20-22]

The most commonly missed severe CHDs are conotruncal lesions, such as transposition of the great arteries, tetralogy of Fallot, double outlet right ventricle and truncus arteriosus, as the four-chamber view may be falsely reassuring in the majority of these cases. The outflow tract views, which are necessary to detect these lesions, are more challenging to capture in a routine screening setting.[13] Cases with an isolated heart defect that present with a normal four-chamber view therefore appear to be the most likely to be missed, especially in the absence of known risk factors or additional structural anomalies.[23-28] It has also been speculated that human factors, such as experience, might be associated with failure to detect fetal CHD, as large differences in DRs can be found between healthcare facilities and geographical areas within the same country.[24, 25]

Therefore, this study aimed to identify factors that contribute to the failure to detect CHD, by auditing *original* images obtained during the second-trimester standard anomaly scans (SAS) of fetuses with undetected and detected CHD, in order to potentially improve antenatal DRs.

METHODS

Selection of cases

Screening for congenital anomalies is performed in The Netherlands based on a strict national SAS protocol, similar to the ISUOG protocol.[29] Every sonographer who performs SAS examinations is required to pass a national standardized examination and is monitored every two years, by evaluation of three randomly selected SAS, in order to assess their competence. If a sonographers does not pass this assessment, their qualification is withdrawn, and they are no longer able to perform SAS. This national screening program has resulted in one of the highest DRs for CHD worldwide[6, 30], which is reflected in the 82% detection rate for transposition of the great arteries.[31]

The Amsterdam University Medical Centers, location AMC and VUMC, and Leiden University Medical Center collaborate in the care for children with CHD in the Amsterdam-Leiden regions. All subjects with either a prenatal diagnosis of CHD or a postnatal diagnosis of *severe* CHD in these regions have been registered in the PRECOR database since 2002. Severe CHD is defined as the need for surgery or therapeutic cardiac catheterization within the first year of life. Data collection for this registry has been described previously.[23] This registry was used to identify all cases of *severe* isolated CHD, delivered in the period 2015-2016. We decided to include only recent cases, as the three-vessel view was introduced as a mandatory plane in 2012 and to ensure retrieval of the original ultrasound images in the majority of cases. Cases that did not undergo SAS in the second trimester, were excluded.

The mothers of CHD subjects were sent a letter with information regarding the study and an informed consent form to return if they were willing to participate. Mothers of CHD subjects that were not alive at the time of recruitment were excluded from the study, as requested by the ethical review board of our institution, but we ascertained the type of lesion in these cases from the PRECOR database. Following receipt of informed consent, mothers were contacted once to retrieve the location at which the SAS had been performed. Included subjects were allocated to either the group with or without a prenatal diagnosis of CHD.

Data collection

We collected the original ultrasound images from the SAS and pregnancy data. If data were missing, midwives were contacted for additional information. From 2007 onwards, the national prenatal screening database PERIDOS has registered all pregnant women who undergo SAS in The Netherlands. This database was used to retrieve information regarding the volume of SAS performed per year at each prenatal screening center,

and by each sonographer, as well as the sonographer's years of experience at the time of the SAS.

We developed a standard form to assess the quality of the ultrasound examination, as an indicator of the sonographer's technical skills, and additional parameters of interest. In order to assess objectively the quality of the cardiac examination, each of the four standard cardiac planes received a score between 0 and 5, resulting in a maximum total score of 20 for the entire cardiac examination. The score was based on the number of quality criteria met for that specific plane (Table 1). For example, if 3/5 criteria were met, the plane received a score of 3 (adequate quality). If the sonographer obtained multiple images of the same cardiac plane, these were assessed together. In case clips were recorded, they were assessed in the same manner. A cardiac examination with a total score of ≥ 12 (average score of ≥ 3 for each plane) was considered adequate, whereas a total score < 12 was considered inadequate. Examples of cardiac images with their respective scores, are depicted in Figure 1. A fetal medicine consultant [M.C.H.], specialized in fetal cardiology, and a senior cardiac sonographer [A.K.K.T.] scored the images together and were blinded to patient characteristics, diagnosis and whether the CHD had been detected prenatally. To quantify the reliability of this scoring system, 27 cases were scored twice to calculate the intraclass correlation coefficient (ICC)[32]. The time interval between the first and repeat assessments was more than 6 months in order to avoid recall bias.

Table 1. Criteria for quality assessment of cardiac planes obtained during second-trimester standard anomaly scan.

Four-chamber view (4CV)	**Left ventricular outflow tract (LVOT)**
• Complete depiction of both atrial chambers • Complete depiction of both ventricles • Cardiac crux visible • Clear visualisation of both AV valves • Clear visualisation of the ventricular septum	• Plane approximately at level of LVOT • Chosen plane at the maximum size of the vessel • Visibility of the aortic valve • Perimembranous septum visible in the plane • Complete long-axis from LV apex to ascending aorta visible
Right ventricular outflow tract (RVOT)	**Three-vessel view (3VV)**
• Plane approximately at level of RVOT • Depicted at maximum size of the vessel • Visibility of the pulmonary valve • Upper part of RV visible • Pulmonary artery visible from RV to arterial duct	• True transverse plane through the chest • Pulmonary artery (PA) visible from right ventricle to arterial duct • Valve (PA) visible • Clear depiction of the aorta • Clear depiction of right superior caval vein

AV, atrioventricular; LV, left ventricle; LVOT, left ventricular outflow tract; RV, right ventricle; RVOT, right ventricular outflow tract

The collected baseline characteristics comprised gestational age at screening, maternal age, body mass index, obstetric and medical history, multiple pregnancy, fetal gender, CHD diagnosis and the sonographer's and screenings center's experience and volume. We evaluated fetal position, resolution of the ultrasound images (amount of detail in the image that could be obtained), use of magnification, visibility of the heart defect and quality of each of the four cardiac planes: four-chamber view (4CV), three-vessel view (3VV) and the left and right outflow tracts (LVOT, RVOT).

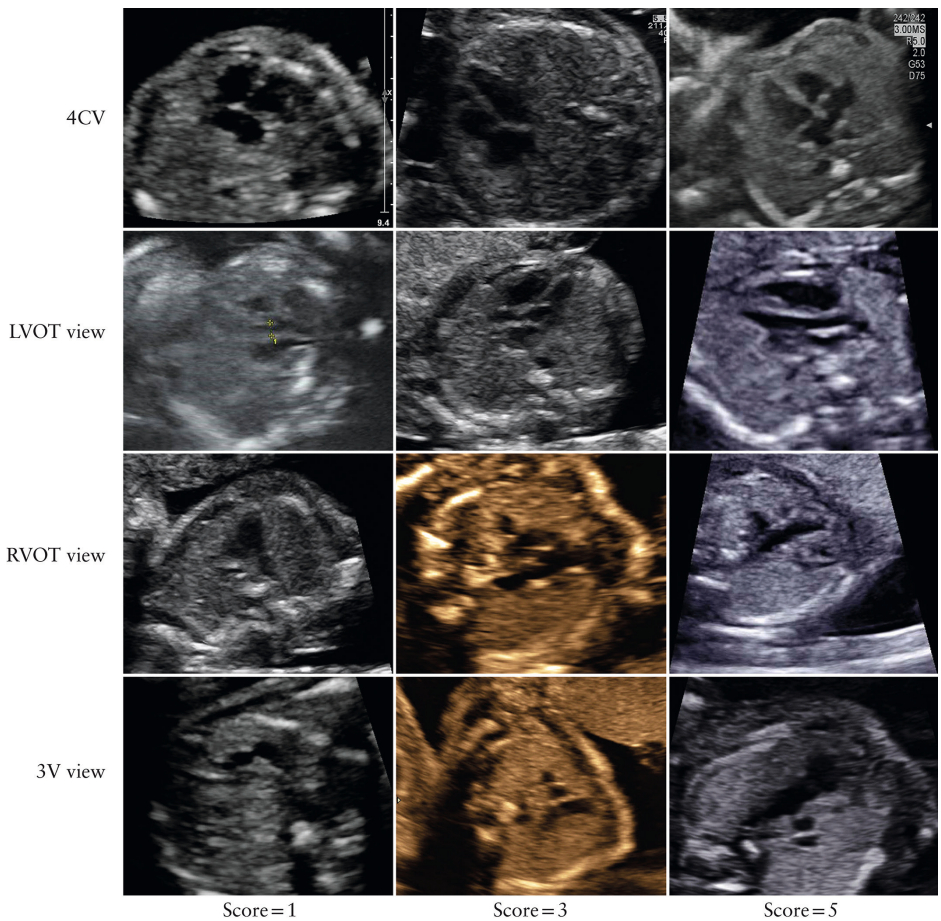

Figure 1. Visual scoring system. Examples of ultrasound images of the fetal heart in four-chamber (4CV), left ventricular outflow tract (LVOT), right ventricular outflow tract (RVOT) and three-vessel (3V) views, that obtained quality score of 1, 3 or 5, in cases with severe congenital heart disease at birth.

Fetal position was classified based on the position of the spine on an analog clock. A position of the spine from 10 to 2 o'clock (clockwise) was considered to be unfavorable, whereas the rest was scored as favorable. Sonographer and screening center volume, as well as the experience of the sonographer in years, was assessed for the year in which the SAS had been performed. Image resolution was scored on a five-point Likert scale, in which 1 represented poor resolution (lots of noise, multiple speckles, grey amniotic fluid) and 5 represented good resolution (clear black amniotic fluid, lots of detail visible in the image).

In order to gain insight into the completeness and quality of the SAS in normal cases, we retrieved the results from routine quality monitoring assessments in the Leiden region (in 2015). In these assessments, the four standard cardiac planes were scored as either 0 (inadequate), 1 (adequate) or a (absent). Normal cases could not be recruited in the same way in which CHD cases were as, in The Netherlands, only the physician who treated the patient is allowed to approach them. First, we collected the results from three normal scans obtained by sonographers in the Leiden region who missed a heart defect in the current cohort. Second, results from three normal scans performed by a random sample of 40 sonographers in the Leiden region were evaluated. We then assessed whether cardiac examination quality differed significantly between these two groups. As the evaluation in the national monitoring system had been performed in less detail, direct comparison of scores between the normal and CHD cases was not possible.

Statistical analysis

All variables of interest, that may possibly influence the ability to detect CHD prenatally, were compared between the undetected and detected group. Univariate and multivariate regression analyses were performed to assess whether the quality of the ultrasound examination was influenced by the sonographer's or screening center's experience.

To identify potential causes for a missed prenatal diagnosis, we considered the adequacy of the cardiac examination (total score < or ≥ 12) alongside the visibility of the heart defect, as assessed by the expert examiners [M.C.H. and A.K.K.T.], in all undetected cases. These were used to define three types of causes for a missed prenatal diagnosis. The first involved the sonographer being unable to obtain technically correct cardiac planes in cases with abnormal anatomy. These cases were missed due to *a lack of adaptational skills* and comprised all undetected cases in which the total quality score was < 12 and the heart defect was not clearly visible, according to our

experts examiners, because of suboptimal planes. The second cause was when the heart defect was *not recognized*, despite being clearly visible on the retrieved images, irrespective of the quality of the planes. Undetected heart defects that were not visible despite good quality of the images (total score ≥ 12) were classified as *inevitable (3)*. These three causes of a missed diagnosis in undetected cases were assessed according to the type of CHD.

Categorical variables were compared using a χ^2-test and continuous variables were compared using the independent t-test. ICC estimates and their 95% CI were calculated based on a mean-rating (k = 2), consistency-agreement, two-way mixed-effects model. IBM SPSS Statistics 23.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. A P-value < 0.05 was considered statistically significant.

RESULTS

A total of 198 cases of severe CHD without an additional anomaly, born in 2015-2016, were extracted from the PRECOR registry. All mothers were approached to participate in the study, except for 12 cases (6.1%), in which the infant was not alive at time of recruitment. These 12 cases comprised univentricular heart defects (67%; all of which were detected prenatally) and other defects (33%; of which 80% were detected and 20% were undetected). We did not receive a response from 51 subjects (25.8%) and 10 (5.1%) chose not to participate in the study. Eleven subjects (5.6%) did not undergo SAS in the second trimester, because they had indications, mainly increased nuchal translucency, for an advanced diagnostic scan, including fetal echocardiography. This resulted in a total of 114 cases eligible for inclusion, of which 58 (50.9%) were undetected and 56 (49.1%) were detected prenatally (Figure 2).

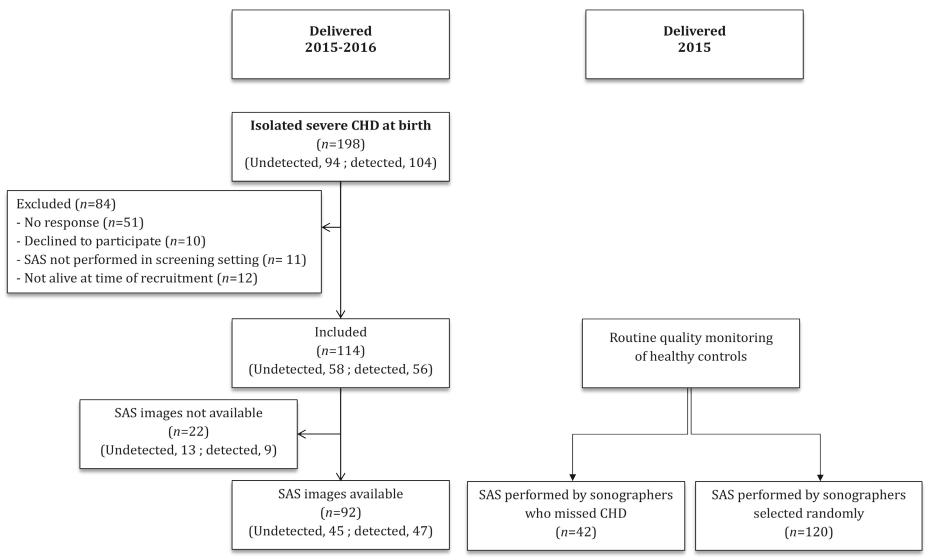

Figure 2. Flowchart summarizing inclusion of fetuses with severe congenital heart disease (CHD) at birth and normal controls. SAS, standard anomaly scan.

At baseline, significantly more women had a history of abdominal surgery in the undetected group (33.3%) compared to the detected group (9.5%) (p=0.01). This difference, however, could not be accounted for in subsequent analysis, as this information was missing in 39% of cases. The two groups did not differ significantly in any of the other parameters assessed at baseline (Table 2).

Table 2. Baseline characteristics

	Undetected (n=58)		Detected (n=56)		P	(95% CI)
Characteristic						
Gestational age at screening (weeks)	20.0	(±0.72)	20.0	(±0.95)	0.96	(-0.31 ; 0.32)
Ultrasound scan repeated	5	12.5%	6	15.0%	0.75	
Maternal age (years)#	31.6	(±4.33)	31.6	(±4.62)	0.98	(-1.68 ; 1.64)
Maternal obesity †	22	(53.7%)	17	(34.0%)	0.06	
Multigravid	31	(62.0%)	38	(69.1%)	0.45	
History of abdominal surgeries	9	33.3%	4	9.5%	**0.01***	
Pregnancy complication	12	40.0%	6	21.4%	0.13	
Multiple pregnancy	3	6.5%	6	10.7%	0.46	
Fetal sex male	38	65.5%	27	48.2%	0.06	
Experience						
Sonographer (yr) §	5.6	(2.67)	5.6	(2.98)	0.92	(-1.09 ; 1.21)
Sonographer (SAS/yr) §	343.4	(247.00)	410.0	(289.50)	0.22	(-173.12 ; 39.88)
Screening center (SAS/yr) §	1289.3	(1041.80)	1157.5	(1076.21)	0.54	(-290.92 ; 554.53)

Data is given as n (%) or mean (± SD).
* A p-value < 0.05 was considered statistically significant.

mean is given as this did not differ significantly from median (interval not skewed).
† Obesity is defined as a body mass index (BMI) > 25 kg/m2.
§ Calculated using data from end of year in which case underwent prenatal screening.

Ultrasound images could be retrieved from the initial screening center in 92/114 (80.7%) CHD cases. Sonographer use of magnification was significantly poorer amongst sonographers in the undetected group (p=0.01). The proportion of cases with unfavorable fetal position did not differ significantly between the groups, which demonstrates that the majority of sonographers waited until the fetus was in a favorable position to assess the heart. The quality of the cardiac examination, overall and for each of the cardiac planes separately, was significantly lower in undetected CHD cases. In the undetected group, the cardiac examination was more frequently incomplete i.e. ≥1 cardiac planes not obtained or saved (46.7% vs 22.2%; p=0.02). The expert assessors classified the defect as being clearly visible in 83.7% of detected cases, compared to only 31.1% of undetected cases (p<0.001), due mainly to technically incorrect cardiac planes (Table 3). The cardiac examination received an inadequate score in a higher proportion of missed CHD cases (64.4%) than in normal controls evaluated by the same

sonographers (14.7%), although different scoring systems were used. With regards to the completeness and quality of the cardiac examinations in normal cases, those performed by sonographers who missed a defect did not differ significantly from those performed by randomly selected sonographers (Table 4). The ICC for quality scoring of the overall cardiac examination (0.88, 95% CI 0.75 – 0.95) and for each of the cardiac planes separately (varying from 0.77 to 0.89) demonstrated good to excellent intrarater agreement.

Table 3. Analysis of the standard anomaly scan

	Undetected CHD (n=45)		Detected CHD (n=47)		p	95% CI of difference
Characteristic						
Unfavorable fetal position[a]	4	8.9%	3	6.7%	1.00	
Amniotic fluid volume†	3.0	(±0.16)	3.0	(±0.00)	0.32	(-0.08 ; 0.03)
Use of magnification						
Poor	2	5.0%	3	6.8%		
Average	15	37.5%	4	9.1%	**0.01***	
Good	23	57.5%	37	84.1%		
Image resolution						
Poor	4	9.1%	0	0.0%		
Below average	8	18.2%	9	21.4%		
Average	21	47.7%	17	40.5%	0.18	
Above average	9	20.5%	10	23.8%		
Good	2	4.5%	6	14.3%		
Quality assessment						
Quality score [0-20] ‡	9.4	(±5.24)	14.2	(±5.51)	**<0.001***	(-7.05 ; -2.52)
Four-chamber view [0-5]	2.7	(±1.47)	3.9	(±1.26)	**<0.001***	(-1.78 ; -0.62)
Three vessel view [0-5]	3.0	(±1.58)	3.8	(±1.57)	**0.02***	(-1.46 ; -0.14)
Left ventricular outflow tract [0-5]	1.9	(±1.57)	3.3	(±1.75)	**<0.001***	(-2.02 ; -0.62)
Right ventricular outflow tract [0-5]	1.9	(±1.95)	3.3	(±1.87)	**<0.001***	(-2.27 ; -0.67)
Inadequate cardiac scan §	29	(64.4%)	14	(31.8%)	**0.002***	
Incomplete cardiac scan ¶	21	(46.7%)	10	(22.2%)	**0.02***	

Table 3. *(Continued)*

	Undetected CHD (n=45)		Detected CHD (n=47)		p	95% CI of difference
Detectable						
CHD clearly visible **	14	(31.1%)	36	(83.7%)	**<0.001***	

Data are given as n (%) or mean (±SD).
* A p-value < 0.05 was considered statistically significant.

a. Unfavorable fetal position: all positions in which the fetal spine is lying towards the probe (on the opposite site of the maternal spine), i.e. from 10 to 2 o'clock (clockwise), were classified as unfavorable.
† Scored on 5-point Likert scale as follows: 1, anhydramnios; 3, normal volume of amniotic fluid; and 5, polyhydramnios.
‡ Scored 1–5 for each plane; score = 0 if not obtained
§ Total quality score < 12
¶ ≥1 of the cardiac planes not obtained or saved
** CHD clearly visible: original images showed abnormal cardiac anatomy according to our fetal echo experts [MH, AT].

Table 4. Routine quality assessment of cardiac images from the SAS in uncomplicated pregnancies

	Performance of a sonographer					
	who missed a CHD[1] (n=42)		who was selected randomly[2] (n=120)		p	95% C.I.
Quality score						
Quality score [0-4] ‡	3.14	(±0.90)	3.20	(±0.87)	0.72	(-0.24 ; 0.27)
Four-chamber view [0-1]	0.93	(±0.26)	0.96	(±0.20)	0.45	(-0.37 ; 0.25)
Three vessel view [0-1]	0.86	(±0.35)	0.88	(±0.32)	0.66	(-0.11 ; 0.05)
Left ventricular outflow tract [0-1]	0.71	(±0.46)	0.68	(±0.47)	0.64	(-0.14 ; 0.09)
Right ventricular outflow tract [0-1]	0.64	(±0.48)	0.68	(±0.46)	0.63	(-0.13 ; 0.20)
Inadequate cardiac scan§	6	(14.3%)	25	(20.8%)	0.35	
Incomplete cardiac scan ¶	10	(23.8%)	31	(25.8%)	0.80	

Data are given as mean (± SD) or n (%).
Three scans included per sonographer.
Quality assessment data based on results of quality monitoring assessments in Leiden region in 2015.
‡ Maximum score of 1 for each plane.
§ Quality score of 0 for ≥ 2 planes.
¶ ≥ 1 plane not obtained or saved.
1. Assessment of the standard performance of sonographers, that missed a CHD in our cohort, in uncomplicated pregnancies
2. Assessment of the standard performance of sonographers, randomly selected from the same population, in uncomplicated pregnancies.

On univariate regression analysis, the volume of SAS performed per year by each sonographer and screening center had a small, but significant, influence on the quality of the cardiac scan in CHD cases. Multivariate regression analysis, however, showed that only an increase in the number of SAS performed by each sonographer significantly improved the overall score of the cardiac examination (Table 5).

Table 5. Analysis of the association between experience and quality of the cardiac examination in fetus with severe CHD (n=92)

Variable	Regression coefficient (95% CI)	SE	*P*
Univariate analysis			
Sonographer experience in years	0.07 (−0.410 to 0.548)	0.24	0.78
Volume of SAS performed in *n*/year			
Per sonographer	0.007 (0.001 to 0.013)	0.003	0.02
Per screening center	0.001 (0.000 to 0.003)	0.001	< 0.05
Multivariate analysis			
Volume of SAS performed in *n*/year			
Per sonographer	0.006 (0.000 to 0.012)	0.003	< 0.05
Per screening center	0.001 (0.000 to 0.002)	0.001	0.15

SE, standard error.

Analysis of undetected CHD cases revealed that the quality of the cardiac examination was inadequate and the defect was not clearly visible due to *lack of adaptational skills* in 22/45 cases (48.9%). In 14/45 undetected cases (31.1%), the heart defect was visible on the cardiac planes obtained and was therefore classified as *a lack of recognition*. In 9/45 cases (20.0%), the heart defect was not visible even though the quality of the images was adequate; these undetected cases were therefore classified as *inevitable*. Images of undetected cases belonging to either one of the three categories for a missed prenatal diagnosis are depicted in Figure 3.

Aortic coarctation, transposition of the great arteries and tetralogy of Fallot were diagnoses that were often not recognized. The inevitable group involved mainly CHD types that are speculated to be difficult to diagnose prenatally, such as aortic coarctation or total anomalous pulmonary venous return. This study shows that these diagnoses indeed show normal images in a considerable number of cases. Table 6 reports the cardiac diagnoses included in this study in relation to the respective proportion that was prenatally diagnosed, causes for a missed prenatal diagnosis and scores on each of the four cardiac planes.

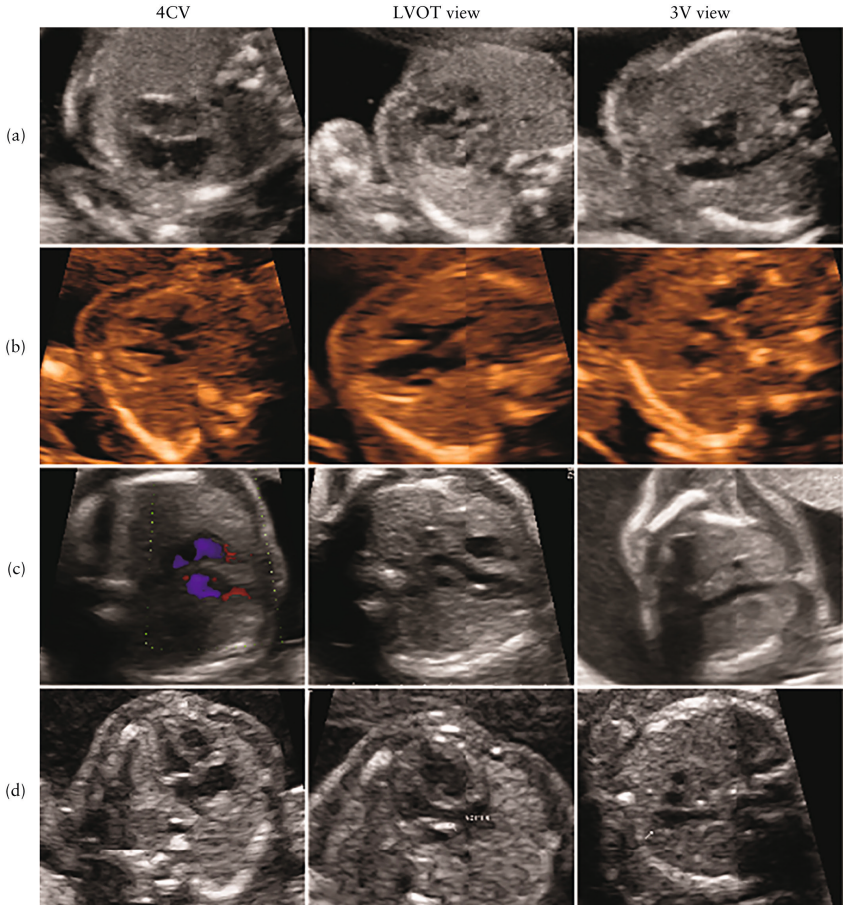

Figure 3. Ultrasound images of fetal heart in four-chamber (4CV), left ventricular outflow tract (LVOT) and three-vessel (3V) views in four cases with severe congenital heart disease at birth that was missed on prenatal ultrasound examination due to poor adaptational skills of sonographer (a), inability of sonographer to recognize defect (b,c) or defect not being visible despite adequate image quality (d).

(a) Case of atrioventricular septal defect missed prenatally due to poor adaptational skills of sonographer. In 4CV, atria are blurred, plane is not taken at proper level (too far towards diaphragm, showing atrioventricular valve annuli instead of valves). Only ventricles and septum are visible. LVOT view quality was scored 1 as aorta is barely recognizable.

(b) Case of tetralogy of Fallot that was not recognized by sonographer; although quality of planes is inadequate (total score of 6), ventricular septal defect can be identified with over-riding aorta. In 3V view, it is clearly visible that pulmonary artery is small and ascending aorta is relatively large. Right aortic arch is visible just anterior to spine.

(c) Case of transposition of great arteries that was not recognized by sonographer despite planes having adequate quality score; as only two vessels (right superior caval vein and ascending aorta arising from right ventricle) are visible in 3V view, which is typical for this diagnosis.

(d) Case of coarctation of aorta that was classified as inevitably missed, as quality of cardiac examination was adequate (total score of ≥ 12), and in particular, no discrepancies in size of ventricles or great arteries were evident on any cardiac images obtained.

Table 6. Overview of the types of CHD included in this study with the respective causes for a missed diagnosis and scores on the four cardiac plan

CHD diagnosis	Prenatal detection			US available	Causes for a missed diagnosis			4CV		3VV		LVOT		RVOT	
					Technical skills‡	§ Not recognized	Inevitable ¶	mean	score ≥3	mean	score ≥3	mean	score ≥3	mean	score ≥3
TAPVR	All	3	2.6%	3				3.3	66.7%	3.3	66.7%	1.0	33.3%	1.7	33.3%
	Undetected	3	100.0%	3	66.7%		33.3%	3.3	66.7%	3.3	66.7%	1.0	33.3%	1.7	33.3%
Ventricular septal defect*	All	21	18.4%	16				2.9	56.3%	2.6	43.8%	1.9	31.3%	1.4	25.0%
	Undetected	18	85.7%	13	76.9%		23.1%	2.8	53.8%	2.6	46.2%	1.8	30.8%	1.2	23.1%
Double aortic arch	All	4	3.5%	2				4.5	100.0%	4.0	100.0%	4.5	100.0%	4.5	100.0%
	Undetected	3	75.0%	2		50.0%	50.0%	4.5	100.0%	4.0	100.0%	4.5	100.0%	4.5	100.0%
Tetralogy of Fallot	All	4	3.5%	4				3.8	75.0%	4.0	100.0%	3.5	75.0%	3.3	75.0%
	Undetected	3	75.0%	3		66.7%	33.3%	3.7	66.7%	4.0	100.0%	3.3	66.7%	3.0	66.7%
Aortic coarctation	All	18	15.8%	13				2.5	46.2%	3.9	76.9%	2.5	53.8%	3.0	53.8%
	Undetected	12	66.7%	9	11.1%	77.8%	11.1%	2.1	33.3%	3.9	77.8%	2.0	33.3%	2.4	44.4%
Aortic stenosis	All	6	5.3%	6				3.2	66.7%	2.7	50.0%	2.2	50.0%	2.7	66.7%
	Undetected	4	66.7%	4	50.0%	50.0%		3.0	75.0%	2.8	50.0%	2.3	50.0%	2.3	50.0%
Pulmonary valve stenosis	All	3	2.6%	2				3.5	50.0%	3.5	100.0%	3.0	50.0%	3.0	50.0%
	Undetected	2	66.7%	1	100.0%			2.0	0.0%	3.0	100.0%	2.0	0.0%	2.0	0.0%
Atrioventricular septal defect	All	7	6.1%	5				3.8	60.0%	4.2	100.0%	2.4	40.0%	3.2	60.0%
	Undetected	2	28.6%	2	50.0%		50.0%	3.5	50.0%	4.0	100.0%	0.5	0.0%	3.5	50.0%
Shone's complex	All	3	2.6%	2				3.5	50.0%	4.5	100.0%	2.0	50.0%	4.5	100.0%
	Undetected	1	33.3%	0											

Table 6. *(Continued)*

CHD diagnosis	Prenatal detection			US available	Causes for a missed diagnosis			4CV		3VV		LVOT		RVOT	
					Technical skills‡	§ Not recognized	Inevitable ¶	mean	score ≥3	mean	score ≥3	mean	score ≥3	mean	score ≥3
Transposition of the great arteries	All	19	16.7%	18				3.8	82.4%	3.9	82.4%	3.8	76.5%	3.4	72.2%
	Undetected	3	15.8%	3	33.3%	66.7%		1.7	33.3%	1.7	33.3%	2.0	33.3%	0.3	0.0%
Double outlet right ventricle – ToF	All	7	6.1%	5				3.6	80.0%	4.2	100.0%	3.8	80.0%	3.4	80.0%
	Undetected	0	0.0%	0											
Interrupted aortic arch	All	2	1.8%	2				4.0	100.0%	3.5	50.0%	0.5	0.0%	1.5	50.0%
	Undetected	0	0.0%	0											
Common arterial trunk	All	2	1.8%	1				3.0	100.0%	0.0	0.0%	0.0	0.0%	0.0	0.0%
	Undetected	0	0.0%	0											
Pulmonary valve atresia - IVS	All	2	1.8%	1				4.0	100.0%	0.0	0.0%	0.0	0.0%	0.0	0.0%
	Undetected	0	0.0%	0											
Unbalanced AVSD	All	2	1.8%	2				4.0	100.0%	4.0	100.0%	2.0	50.0%	2.5	50.0%
	Undetected	0	0.0%	0											
Miscellaneous	All	11	9.6%												
	Undetected	6	54.5%												
Total	**All**	**114**	**100**	**92**	**48.9%**	**31.1%**	**20.0%**	**3.3**	**66.3%**	**3.4**	**68.9%**	**2.6**	**51.7%**	**2.6**	**54.4%**

Data are given as n or n, %. * requiring surgery in the first year of life
‡ Cardiac examination had inadequate quality score (< 12) and heart defect was not clearly visible.
§ Defect was clearly visible on images but was not recognized by sonographer, irrespective of examination quality.
¶ Defect was not visible despite adequate quality score (≥ 12).

3V, three-vessel view; 4CV, four-chamber view; AVSD, atrioventricular septal defect; CoA, coarctation of the aorta; DORV, double outlet right ventricle; LVOT, left ventricular outflow tract view; PA/IVS, pulmonary atresia with intact ventricular septum; PVS, pulmonary valve stenosis; RVOT, right ventricular outflow tract view; TAPVR, total anomalous pulmonary venous return; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

DISCUSSION

This study audited images obtained during the second-trimester SAS to identify potential causes for a missed prenatal diagnosis of CHD, by comparing ultrasound examinations between undetected and detected cases. Although sonographers practiced in a high-quality screening program, our results showed that the cardiac planes obtained during the SAS were of significantly better quality in detected compared with undetected CHD cases. Cardiac examinations appeared of better quality when performed by sonographers, who carried out a greater number of SAS per year.

Sonographers who missed a CHD diagnosis were not poorly trained, as all had passed the national quality assessment. At the initial assessment 25% of sonographers, however, did not obtain or save all cardiac planes, indicating that they either accepted technically incorrect planes or did not obtain and save all cardiac planes in a structured manner. The poorer performance in CHD cases may also be explained by slightly impaired motor skills when acquiring accurate planes in abnormal anatomy, combined with a lack of gut feeling for detection of abnormal cases. We hypothesize that the poorer performance in missed cases may be attributed to certain personality traits and lack of adaptational skills. The second reason for a missed prenatal diagnosis was failure to recognize the CHD despite being visible on the images, which involved mainly subtle signs, such as asymmetry in the 4CV and discrepancy between the size of aorta and the pulmonary trunk in aortic coarctation. Missed prenatal diagnosis was classified inevitable in 20% of undetected cases, which may be explained partly by development later in gestation.

Although further analysis revealed a small, but significant, positive association between sonographer volume (number of SAS performed per year) and quality of the cardiac planes, quality was not associated with sonographer experience in years. This indicates that a minimum number of examinations per year might be necessary to maintain skills and develop a 'gut feeling' for detection of abnormalities.[34] We speculate that sonographers performing a low volume of examinations may be more likely to question their own capability and accept technically incorrect cardiac planes, whereas those performing a high volume of examinations will rely on their technical skills to obtain the cardiac images properly, trust their 'gut feeling' that the images are abnormal due to differences in fetal anatomy and refer the case to a specialized fetal medicine unit. The screening center's size was also independently associated with superior quality of the cardiac planes. This might be explained by their increased exposure to abnormal scans, as high-volume sonographers will most likely work in large screening centers, which enables them to review difficult cases with fellow-sonographers. A French study

confirmed this by showing that meetings in which cases are discussed, contribute to increased DRs in conjunction with training.[34] The recording of videoclips during the SAS might also enhance screening results and aid the review of difficult cases. The fact that high volume was associated with better quality of the examination, but not with increased prenatal detection, may be explained by a lack of power, as 20% of the missed cases were inevitable and allocated to undetected cases by definition.

Cardiac images in undetected cases scored particularly low for the outflow tract planes, which was not the case in the detected group. Previous cohort studies have confirmed that assessment of the outflow tracts, including the 3VV or three vessels and trachea view (3VT), is valuable for prenatal detection.[31, 35, 36] The use of universal guidelines and increased effort to obtain these outflow tract views has therefore shown to increase prenatal DRs.[9, 18] Specific training programs, focused on achieving satisfactory views of the heart, were able to improve significantly DRs 60%.[28, 36-39] As DRs in our region are already above 60%[23], we hypothesize that monitoring, alongside training, is imperative to assure strict adherence to protocol and to reach higher DRs.

Our results also suggest that an increase in the annual volume of SAS performed by the sonographers, rather than their experience in years, can improve quality. Setting up large screening centers with sonographers performing a high volume of examinations might be the final step to reach DRs of the previously mentioned goal of 80%, because it will ensure sufficient exposure to abnormal cardiac images and create an environment that potentially counteracts the above described character traits. This is in line with the current opinion that centralization of care improves quality. Factors that possibly hamper proper cardiac assessment, such as maternal obesity or unfavorable fetal position, were not found to influence the prenatal detection of CHD, which is in accordance with previous reports.[24,25,40,41]

Although this topic can be studied only retrospectively, this design led to some inevitable limitations. First, it is not possible to determine if improved quality of images led directly to detection of the heart defect, rather than *vice versa*. Second, we had to obtain consent from the mothers in order to retrieve the images, which may have resulted in selection bias. The inclusion of only live cases should not affect the study's clinical value significantly, because the cases that resulted in termination of pregnancy or neonatal demise comprised mainly univentricular defects with DRs of nearly 100% in our country.[23] However, this did impede blinding of assessors to whether a heart defect was present, as we were unable to retrieve the original images from healthy fetuses. Finally, the distribution of diagnoses differed between the two groups. This, however, does not affect our primary results, as sonographers are still obliged to

acquire and save proper cardiac planes, even if they assume a structurally normal heart, as described in our national SAS protocol.[42]

In conclusion, the quality of the cardiac examination, at the time of second-trimester screening, appears to be the cornerstone in improving prenatal DRs for CHD in a low-risk population. Although it seems obvious that sonographers performing a high volume of scans are more likely to retain technical skills and remain qualified, this association has not been demonstrated previously. The volume of examinations performed by a sonographer, alongside training, was shown to be equally important in ensuring adequate examination of the fetal heart and recognition of abnormality. Future research should therefore consider performing more extensive audit studies and evaluating annual volume targets for sonographers who perform SAS, in order to maintain their competence.

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