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ORIGINAL ARTICLE

Prenatal diagnosis of cardiac defects: accuracy and benefit

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ABSTRACT

Objective The prenatal diagnosis of cardiac defects can potentially reduce postnatal morbidity and mortality. We wanted to evaluate prenatal cardiac diagnosis accuracy in a population referred for echocardiography.

Methods Single centre retrospective study of echocardiography referrals between April 1999 and December 2008. We compared the prenatal and postnatal cardiac diagnoses, the modified Aristotle and Wald scores. The final diagnosis Wald score was used to evaluate benefit.

Results Six hundred fetuses were included. Diagnoses included: normal heart (312, 52%); congenital heart defect (CHD) (231, 38.5%); primary arrhythmia (39, 6.5%); or cardiomyopathy, myocarditis or cardiac tumor (18, 3%). The prenatal and postnatal Aristotle and Wald scores correlated in 81% and 86%, respectively, each with significant differences in 22 cases. Four significant CHDs were misdiagnosed, the surgical prediction was incorrect in 7 and 13 false positive diagnoses of aortic coarctation were made. In 76% (455/600) fetuses prenatal diagnosis was considered beneficial. The average CHD Aristotle score was 9.5 ± 5.0. In babies with CHDs and normal karyotype the score was either 6.5 ± 5.0, 12.9 ± 3.1 or 13.2 ± 2.9, in survivors, cases of postnatal demise and cases of pregnancy termination, respectively.

Conclusion Prenatal diagnosis was accurate and the counselling appropriate in most cases; however, a few errors were made. The diagnosis of aortic coarctation remains challenging. © 2012 John Wiley & Sons, Ltd.

INTRODUCTION

Congenital heart defects (CHDs) are the most common congenital malformations with a reported incidence of 8 to 10/1000 live births. About a third are severe and responsible for significant mortality and morbidity in the neonatal period and infancy.[1–4] The majority of CHDs can be diagnosed prenatally by fetal echocardiography. The detection rate of ultrasound screening for CHDs remains disappointing because it does not exceed 50%. After adequate selection and referral to a specialized unit, fetal echocardiography can yield a complete diagnosis in 85% to 95% of cases.[3–12] Early knowledge of cardiac pathology allows for counselling, monitoring of progression, initiation of patient-tailored (intra-uterine and postnatally) treatment and planned delivery.[10,13] Prenatal cardiac diagnosis has been shown to reduce the postnatal morbidity and mortality of some CHDs, in particular those that are ductal dependent.[14–21] Furthermore, it enables an understanding of the progression of complex lesions with

possible complications such as arrhythmias and cardiac failure.[4,19,22,23] Because the counselling, management options and determination of fetal prognosis depend on a correct and complete diagnosis, it is crucial that the fetal echocardiogram is as accurate as possible.

Evaluation of the accuracy and benefit of prenatal cardiac diagnosis is challenging, because of the different prenatal and postnatal spectra of disease (the prenatal spectrum tending to be more complex and severe), the difficulty in the description of complex CHDs, the progression of lesions during pregnancy, the complexity of the postnatal course and the influence of associated anomalies.[4,6,7,9,21,23–25] In the literature various scoring systems have been proposed to assess prenatal diagnosis. The Medical-Aristotle-Personal and eXtracardiac score,[26] based on the surgical Aristotle score of Lacour-Gayet et al.[27] scores the CHD in terms of its complexity and impairment caused. The scoring system of Wald and Kennard[28] and Wald et al.[29] classifies CHDs according to the

availability of, and necessity for, an intervention that could improve outcome and can therefore be used to evaluate the potential benefit of prenatal diagnosis using fetal echocardiography.

The aims of this study were to evaluate the accuracy of fetal echocardiography and the appropriateness of the prenatal counselling given, and the benefit of prenatal diagnosis in our institution using modifications of existing scoring systems.

METHODS

A retrospective study of all fetuses referred to our fetal medicine unit for echocardiography between April 1999 and December 2008 was performed. The echocardiography was predominantly performed by a pediatric cardiologist (SAC) and/or experienced fetal medicine specialist (CB).

Data collected included: gestational age at diagnosis of the cardiac defect; prenatal echocardiographic diagnosis (in cases of changing lesions, e.g. closure of a ventricular septal defect (VSD), the diagnosis at last echocardiogram was considered final); extra-cardiac anomalies; fetal karyotype; postnatal cardiac diagnosis (based on the postnatal echocardiogram, cardiac catheterization report, operation report, magnetic resonance imaging (MRI) report, or post mortem report); prenatal and postnatal management (termination of pregnancy (TOP), interventions: cardiac catheterization or surgery) and outcome. Data were collected from fetal echocardiography reports, the prenatal patient database (Astraia, Munchen, Germany), hospital electronic patient records, patient files and telephonic consults.

Complex CHDs were classified according to the major defect present. Prognostic features such as valvular abnormalities, ventricular hypoplasia, vessel stenosis and size and location of septal defects were noted. Heterotaxia was classified separately.

Patients were allocated a prenatal and postnatal modified Aristotle,[27] and Wald score,[29] as detailed below. Cardiomyopathies, myocarditis or cardiac tumors and primary arrhythmias were not scored. Patent arterial duct and secundum atrial septal defect were considered as normal hearts because these defects are physiological in the fetus.

Accuracy

The accuracy of the prenatal diagnosis and counselling was evaluated by comparing the prenatal and postnatal diagnoses and the prenatal and postnatal modified Aristotle and Wald scores. A difference of $\geq \pm 5$ points in the Aristotle scores was considered significant. Differences in the allocation of Wald categories B, C and F were considered significant.

Benefit

Prenatal diagnosis was considered beneficial in; Wald categories B, C and F,[29] fetuses where a TOP was performed after the detection of a significant noncardiac problem, fetuses with an arrhythmia or cardiomyopathy, myocarditis or cardiac tumor, and in fetuses with a normal heart where a justifiable positive reassurance of the parents was possible. In these cases there was either an initial suspicion of abnormality or an increased risk for a cardiac defect such as an increased nuchal translucency.[30]

Modified Aristotle score

The Aristotle score, developed by an international group of experts, allows precise scoring of cardiothoracic surgical procedures based on the cardiac diagnosis, the surgical procedure required (palliation/repair), operative complexity, repeated operations and comorbidity. The more complex lesions get the higher scores. A detailed description of the scoring system can be found in the work of Lacour-Gayet et al.[27] The score was designed for CHDs requiring surgery. We also applied it to CHDs and genetic conditions not considered for/requiring surgery. To accommodate this, the following modifications were made: a normal heart was scored 0; minor CHDs not requiring surgery or catheter intervention received a score of 1; a score of 1 was added for Trisomy 18; when more than one operation was required, the score attributed was that of the operation required with the highest score and the resternotomy score (2) was added.

For example: a VSD without comorbidity, requiring one operation for closure, scored a 6 using the Aristotle score, while a hypoplastic left heart syndrome (HLHS) associated with Turner syndrome was allocated 14.5 (Norwood operation scores the highest of the three operations expected in the Fontan pathway) +2 (several operations expected) +0.5 (Turner syndrome) = 17.

A small VSD was scored a 1, one requiring surgery a 6. An incorrect prediction of surgical need in a case with VSD results in a prenatal and postnatal score difference of 5, which was considered significant.

Wald score

This score classifies CHDs according to the availability of, and necessity for, an intervention that could improve outcome.[28,29] There are 6 categories as follows:

A. Defect that is lethal in the intrauterine/neonatal period regardless of treatment, for example left isomerism with complete heart block and hydrops.
B. Defect that is not satisfactorily reparable and can lead to serious disability, for example HLHS.
C. Defect that is not satisfactorily reparable after birth, for which in utero treatment reduces morbidity.
D. Defect that can be diagnosed prenatally but for which evidence of benefit is lacking in terms of cardiac survival following prenatal diagnosis, for example Tetralogy of Fallot.
E. Defect that is not serious enough to require intervention in childhood, so antenatal detection is not required, for example mild pulmonary stenosis, small VSD.
F. Defect that if diagnosed prior to birth would lead to altered postnatal management for which there is evidence that this improves prognosis, for example transposition of the great arteries (TGA).

Because category allocation may be subjective, we carefully followed the guidelines as given in the appendix of Wald et al.[29] We added an additional category to the original classification: **G**. Normal heart.

RESULTS

Complete follow-up was available in 600/ 605 (99.2%) fetuses referred for fetal echocardiography. The final cardiac

diagnoses were; normal heart in 312 (52%), CHD in 231 (38.5%), primary arrhythmia in 39 (6.5%) and cardiomyopathy, myocarditis or a cardiac tumor in 18 (3%). The prenatal and postnatal cardiac diagnoses are shown in Table 1.

Of the 600 fetuses, 166 (27.7%) died either prenatally or postnatally. Of the fetuses with CHD, 119 (51.5%) died. There were 128 fetal deaths (29 intrauterine deaths, 98 TOPs, 1 stillbirth). In 80/128 cases of fetal demise, (one of them with a cardiomyopathy), the diagnosis could not be verified postnatally because no postmortem examination or MRI was performed.

Aristotle and Wald scores were allocated to 541 fetuses prenatally and 464 fetuses were allocated postnatal scores. Four hundred sixty-two fetuses were allocated both prenatal and postnatal scores. Two fetuses prenatally diagnosed with cardiomyopathy, myocarditis or a cardiac tumor (thus not allocated prenatal scores) had normal hearts postnatally. These two fetuses, along with the 80 mentioned cases of fetal demise without verifiable diagnosis, were excluded from the comparative analysis because two scores were not available for comparison.

The overall Aristotle score was 3.7 ± 5.4 prenatally and 3.4 ± 5.4 postnatally. The average difference between the overall prenatal and postnatal scores was 0.23 ± 1.9 (range -10.8 to $+16.5$). In 374/462 (81%) fetuses, the Aristotle scores were identical and in 88 (19%) they differed. In 50 of these 88 (57.2%) fetuses, there was only a difference of 0.5 or 1. In 58/88 (64.8%) the prenatal score was higher than the postnatal score. The details of the 22 (4.8%) cases with a difference of $\geq \pm 5$ in the Aristotle scores are shown in Table 2.

The prenatal and postnatal Wald scores correlated in 397/462 (85.9%) fetuses. Significant differences were found in 22 cases, the details are also shown in Table 2.

Significant false positive diagnoses included HLHS in a young fetus (gestational age $13 + 5$ weeks) with trisomy 21 and hydrops, suspected aortic coarctation (13 cases) and double outlet right ventricle (DORV). The need for and type of surgery was incorrectly predicted in three cases with VSD, two cases with borderline ventricles and one with Ebstein's anomaly. The false negative diagnoses of note were transposition of the great arteries (TGA) aortic interruption, and a large malalignment VSD was actually a truncus arteriosus. A case of DORV with pulmonary stenosis turned out to have a Taussig–Bing TGA (Table 2).

Of the 27 prenatally suspected aortic arch abnormalities (ventricular disproportion (13), aortic coarctation (8), aortic interruption (4), aortic atresia with arch hypoplasia (2)), only ten were confirmed postnatally (excluding four cases of fetal demise without diagnosis verification). In six of these 27 cases, transient ventricular disproportion was found postnatally. It resolved as the pulmonary vascular resistance dropped.

The average Aristotle score in the fetuses with a final diagnosis of CHD was 9.5 ± 5.0. In surviving babies with CHDs and normal or assumed normal karyotype, it was 6.5 ± 5.0 and 12.9 ± 3.1 in those that died postnatally. The score was 13.2 ± 2.9 in fetuses with a CHD and normal karyotype where a TOP was performed.

The Wald categories at final diagnosis were as follows: A (2), B (39), C (0), D (60), E (46), F (84), G (310). We considered prenatal diagnosis to be *potentially* beneficial in 477/600 (79.5%) fetuses. These were the 123 fetuses categories B, C

Table 1 Cardiac diagnoses made prenatally and postnatally

Diagnoses	Prenatal diagnosis	Postnatal diagnosis	Postnatal diagnosis verification not possible[a]
Normal heart	300	285	27
AVSD (+HLV)	33 (9)	17 (4)	16 (4)
Ventricular septal defect	45	25	2
Transposition of great arteries (DD)	21 (5)	18 (2)	5 (3)
Double outlet right ventricle (+ HLV, +PS)	28 (11, 8)	13 (3, 6)	9 (5, 1)
Minor cardiac defects	16	17	2
Heterotaxia	19	15	3
Hypoplastic left heart syndrome	16	13	3
HRV (TA/TS, Ebstein's anomaly, critical pulmonary stenosis, pulmonary atresia with IVS)	16 (6, 3, 2, 2)	13 (5, 3, 2, 2)	2 (1, 0, 0, 0)
Tetralogy of Fallot (+Pulmonary atresia)	9 (3)	10 (4)	3 (2)
Aortic arch abnormalities (CoA, IAA)	13 (8, 4)	10 (5, 3)	3 (1, 2)
Ventricular disproportion	13	7	1
Abnormal systemic venous return	4	5	1
Double inlet left ventricle	6	4	2
Truncus arteriosus[b]	4	4	—
Aortic valve abnormalities (Critical AS, Aortic regurgitation)	3 (2, 1)	3 (2, 1)	—
Absent pulmonary valve syndrome	1	1	—
SV/ CS atrial septal defect	1	2	—
Giant right atrium	1	1	—
Scimitar syndrome	0	1	—
Arrhythmia[c]	40	39	—
Cardiomyopathy/ myocarditis/ tumor[c]	19	17	1
TOTAL	600	520	80

AS, aortic stenosis; AVSD, atrioventricular septal defect; CoA, coarctation of the aorta; CS, coronary sinus; DD, double discordance; HLV, hypoplastic left ventricle; HRHS, hypoplastic right heart syndrome; HRV, hypoplastic right ventricle; IAA, interrupted aortic arch; IVS, intact ventricular septum; PS, pulmonary stenosis; SV, sinus venosus; TA/TS, tricuspid atresia/stenosis.
[a]All fetuses in this column were not allocated a postnatal score.
[b]One false positive and one false negative.
[c]Fifty-seven of these cases were not allocated pre or postnatal Wald or Aristotle scores. Two fetuses were only allocated a postnatal score as cardiac dysfunction was not found postnatally.

and F; 49 fetuses not allocated to B, C or F where a TOP was performed after prenatal diagnosis; 17 fetuses allocated Wald category D where a significant noncardiac problem

Table 2 **Table showing the important differences between the prenatal and postnatal diagnoses and Aristotle and Wald scores**

Prenatal diagnosis	Postnatal diagnosis	Pre-Aristotle	Post-Aristotle	Differ-ence	Pre-Wald	Post-Wald	Contributing factors
Normal heart	Interrupted aortic arch	0	10.8	−10.8*	G**	F	Scan by junior ultrasonographer
Normal heart	Transposition of great arteries	0	10	−10*	G**	F	Maternal obesity, outdated ultrasound equipment in labour ward used at 36+5 weeks' gestation, afterhours echo
Malalignment VSD	Truncus arteriosus	6	13	−7*	D**	B	Maternal BMI 32.6 (several attempts were made to visualize the heart better), fetal position.
VSD (minor defect)	VSD (Swiss cheese, major defect, 3 interventions), ASD + 46, XX.ish del(22)(q11.2)	1	9	−8*	E	D	Scan by less experienced ultrasonographer
DORV + PS	TGA (Taussig–Bing type)	10	11	−1	D**	F	Maternal BMI 33.3, very poor visualization
DORV, subaortic stenosis, dysplastic tricuspid valve, hydrops	Heterotaxia, severe subaortic stenosis, polyvalvular disease, VSD, CoA, hydrops, biliary atresia	16.5	17.5	−1	F	F	Late fetal echo (33+3 weeks' gestation)
Right isomerism, dextrocardia, pulmonary atresia + VSD	Situs inversus, AV discordance, single outlet, aorta out RV, pulmonary atresia + VSD	12	11.5	0.5	F	F	—
DORV, hypoplastic LV, TGA, mitral stenosis, straddling and overriding mitral valve, CoA	Double discordance, hypoplastic RV, VSD, overriding pulmonaryartery, straddling and overriding tricuspid valve	11	13	2	F	F	—
Truncus arteriosus + 46, XY.ish del(22) (q11.2)	Pulmonary atresia + VSD + 46, XY.ish del(22)(q11.2)	14	12	2	B**	F	Early fetal echo (14+5 weeks' gestation)
Dextrocardia, atrio-ventricular discordance, single outlet, aorta out RV, pulmonary atresia, + VSD	Pulmonary atresia + VSD	13.5	11	2.5	F	F	Maternal BMI 27.3
Hypoplastic RV, VSD	Borderline RV, dysplastic tricuspid valve, large VSD (1.5 repair)	11	8	3	B**	D	
DORV with hypoplastic left ventricle + 47, XY+i(12)(p10)[9]/46, XY[1]	VSD + 47, XY+i(12)(p10)[9]/46, XY[1]	11.5	6.5	5*	B**	D	
VSD (major defect) [3]	VSD (minor defect, no surgery) [3]	6 [3]	1 [3]	5 [3]*	D [3]	E [3]	
Ebstein's anomaly (major defect surgery anticipated)	Ebstein's anomaly (minor defect, no surgery required)	7	1	6*	B**	E	
13 cases of suspected CoA [3] and ventricular disproportion [10];	VSD (major) and ASD [2], (1+ 47, XY+21);	10 (1)	7 (1)	2 (2)	F (13)**	D (2)	Late fetal echo, (gestational age > 34 weeks' gestation) [5]
- Isolated [7]	Ventricular disproportion [5],	9 (1)	6 (1)	7 (7)*		E (7)	
(1+ 47, XY+21,	(2 with abN chromosomes,	8.5 (1)	3 (1)	8 (4)*		G (4)	Maternal BMI: 26 (1); 34.5 (1)

Table 2 *Continued*

Prenatal diagnosis	Postnatal diagnosis	Pre-Aristotle	Post-Aristotle	Difference	Pre-Wald	Post-Wald	Contributing factors
1+ 46, X,r(Y)[p11.32q11.1],	1+ extra-cardiac abnormality;						
1+ extra-cardiac abnormality;	Aortic valve abnormality (1);	8 (10)	1.5 (1)				
+ Aortic valve abnormality (2),	VSD (minor), ASD and VCSS (1);	1 (5)					
+ VSD (3)							
+ VSD and VCSS (1)	Normal heart (4)		0 (4)				
Left isomerism, dextrocardia, hypoplastic left ventricle, mitral and aortic stenosis, VCSS, CoA	Situs inversus, borderline left ventricle, mitral and aortic stenosis, VCSS, CoA	17.5	6.5	11*	F	F	Maternal BMI 26
Hypoplastic left heart syndrome +hydrops + 47, XY+21	Normal heart +hydrops + 47, XY+21	19.5	3	16.5*	F**	G	Early fetal echo (13+5 weeks' gestation), maternal obesity

( ), number of cases; abN, abnormal; ASD, atrial septal defect; BMI, body mass index; CoA, coarctation of the aorta; DORV, double outlet right ventricle; RV, right ventricle; TAPVD, total anomalous pulmonary venous drainage; TGA, transposition of the great arteries; VCS(S), vena cava superior (sinistra); VSD, ventricular septal defect.
*Difference between Aristotle scores ≥ ± 5.
**Significant difference between Wald scores.

was detected but the pregnancy was continued; 57 fetuses with an arrhythmia or cardiomyopathy, myocarditis or a cardiac tumor and 231 fetuses with a normal heart where a justifiable positive reassurance of the parents was possible. Prenatal diagnosis was *actually* beneficial in 455/600 (75.8%) fetuses. If only the cardiac pathology is considered, then prenatal diagnosis was beneficial in 180/288 (62.5%).

DISCUSSION

This study gives an insight into the accuracy and benefit of prenatal diagnosis in our fetal medicine unit over almost 10 years. The prenatal and postnatal assessments correlated in the majority of cases and the counselling regarding expected postnatal course was appropriate in most cases. Prenatal diagnosis was assessed as beneficial in 76% of the fetuses seen. The mortality rate was high and the fetal outcome and the decision for TOP correlated with the severity of the CHD.

Evaluation of the accuracy and benefit of prenatal diagnosis is challenging. CHDs may be complex, progression/regression may occur during pregnancy, the postnatal course may be complex and associated anomalies may affect outcome. Ventricular or main artery size, degree of valvular stenosis and comorbidity may have a profound impact on the prognosis and need to be considered when counselling families and planning management.[4,21,23,31] Scoring systems can assist in the evaluation of prenatal diagnosis by transforming the diagnoses into categories (Wald score),[28,29] or numerals (Aristotle score) representing CHD complexity, management, impairment and comorbidity. Probably a numerical score is more specific for this indication. Allocation of the Wald score may be subjective and the scoring of severity is not sequential.

The study population consisted of fetuses referred for specialized echocardiography making this a selected high-risk population. As a consequence, the aim of the study was to evaluate the accuracy of specialized fetal echocardiography and not to evaluate detection rates of prenatal screening for CHDs. Previous studies have reported accuracy rates between 85% and 95% in experienced hands.[4,5,8,10] In the 462 fetuses allocated both prenatal and postnatal scores the Aristotle and Wald scores correlated in 81% and 86%, and significant differences were found in 22 cases. Unfortunately, three major CHDs were missed: transposition of the great arteries, truncus arteriosus and interrupted aortic arch. One false positive diagnosis of HLHS was made. Maternal obesity, ultrasound equipment quality, experience of the sonographer and extremes of gestational age played a role in these misdiagnoses (see Table 2). Thirteen false positive diagnoses of aortic coarctation were made. The challenging nature of antenatal diagnosis of aortic coarctation, especially in late gestation, has already been recognized.[12,32–36]

An objective assessment of the benefit of prenatal diagnosis requires a population study where postnatal outcome and prenatal detection of CHD is known in all cases. This was not the setting of the present study, which focused on the outcome of a preselected population. Our evaluation of benefit may be seen as subjective considering

the categorical score used and the inclusion of assumed psychological benefit for the parents at confirmation of a normal heart. In future population studies the use of numeric scoring systems may assist in the identification of lesions of similar severity for a more objective evaluation of the benefit of prenatal diagnosis.

In conclusion, the prenatal diagnosis of cardiac lesions by echocardiography in our fetal medicine unit was accurate and the counselling appropriate in the majority of cases. Unfortunately, a few major lesions were misdiagnosed and the prenatal diagnosis of aortic coarctation remains challenging.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Prenatal cardiac diagnosis accuracy rates of 85-95% have been reported in experienced hands.
- Reports on its benefit have been conflicting. Benefit has only been shown in ductal dependant cardiac lesions. The more severe fetal spectrum has biased previous comparative studies.

WHAT DOES THIS STUDY ADD?

- Scoring systems (this study) allow for the evaluation of prenatal diagnosis using categoral and numerical comparisons of severity. They may assist in future evaluation of benefit.

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