Accuracy of Prenatal Echocardiographic Diagnosis and Prognosis of Fetuses With Conotruncal Anomalies
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OBJECTIVES The purpose of the study was to determine the accuracy of the prenatal echocardiographic diagnosis and prognosis of fetuses with conotruncal anomalies.

BACKGROUND The accuracy of prenatal echocardiographic diagnoses of cardiac lesions has been reported, but no previous reports specifically address fetal conotruncal anomalies.

METHODS Medical records of 61 fetuses, in which a fetal diagnosis of a conotruncal anomaly was made, were reviewed. Disease entities included were tetralogy of Fallot (TOF), double outlet right ventricle (DORV), transposition of the great arteries (TGA), and truncus arteriosus (TA).

RESULTS Fetal diagnosis was established at a median of 24.5 weeks' gestation. Termination of pregnancy was chosen in 31% (19/61) of cases. Postnatal assessment of the diagnosis was not obtained in 12 cases. Excluding two sets of conjoined twins, accurate prenatal diagnosis including definition of the great artery orientation was achieved in 36 of 47 cases (77%). Seven of 17 fetuses with DORV anatomy, of which 6 were thought to have a subpulmonary ventricular septal defect (VSD), had incorrect prenatal assessment of the great artery relationships. One fetus thought to show features of TA had aortic atresia with VSD and normal-sized left ventricle. Of the 42 pregnancies that continued, 15 had major extracardiac malformations and/or chromosomal abnormalities of which one died in utero with trisomy-13 and TA. A further nine died within the neonatal period. Among the 27 fetuses without a documented chromosomal or major extracardiac anomaly, 13 (48%) died. Overall, the survival rate beyond 28 days of life was 52% (22/42). In contrast, 75% (6/8) of fetuses with TOF, excluding the absent pulmonary valve syndrome, survived.

CONCLUSIONS Conotruncal anomalies can be diagnosed by prenatal echocardiography with a high degree of accuracy. Defining the exact spatial relationship of the great arteries is problematic in some fetuses. The overall prognosis for fetuses with a conotruncal anomaly is poor, with the exception of uncomplicated TOF. (J Am Coll Cardiol 1999;33:1696–701) © 1999 by the American College of Cardiology

Conotruncal anomalies are characterized by a defect in the conotruncal septum and encompass various lesions such as ventricular septal defect (VSD) with overriding aorta, tetralogy of Fallot (TOF), absent pulmonary valve syndrome (APVS), double outlet right ventricle (DORV), transposition of the great arteries (TGA), malposition of the great arteries (MGA) as well as truncus arteriosus (TA). Accurate echocardiographic diagnosis in utero permits counseling of the parents with regard to prognosis and treatment options.

It is of paramount importance when termination of pregnancy is being considered for the more severe cases.

Whereas postnatal transthoracic and transesophageal echocardiography permits accurate diagnosis and prognostication of conotruncal anomalies in the majority of cases, the accuracy of fetal echocardiography for these objectives has not been established. Therefore, the aim of this study was to define the accuracy of fetal echocardiography for the prenatal diagnosis of conotruncal anomalies and to examine the prognosis of those fetuses identified.

PATIENTS AND METHODS
We searched our fetal database for conotruncal anomalies diagnosed in our laboratory between January 1985 through September 1997 and included the following lesions in our study: tetralogy of Fallot, absent pulmonary valve syndrome,
double outlet right ventricle, transposition and malposition of the great arteries as well as truncus arteriosus. We reviewed the maternal and postnatal medical records pertaining to these fetuses to compare the echocardiographic identification of fetal conotruncal anomalies with those obtained at postnatal examination by echocardiography, cardiac catheterization, surgery, or autopsy. In addition, we assessed the bearing of associated extracardiac anomalies with regard to fetal outcome.

All echocardiographic studies were performed with Acuson (Sunnyvale, California) ultrasound equipment. Definition of fetal conotruncal anomalies was attempted from multiple scan planes including four-chamber, long- and short-axis as well as aortic arch and ductal arch views. Doppler color flow mapping and pulsed Doppler interrogation were used to facilitate identification of great vessel relationship, location and severity of ventricular outflow obstruction.

**Study variables.** We calculated the incidence of the conotruncal anomalies for our referral population and compared our data with those from the literature. We assessed the agreement between fetal echocardiographic definition of the great artery relationship to the underlying ventricular mass, the great artery orientation, the location of associated ventricular septal defects as well as the presence or absence of ventricular outflow tract obstructions with the other diagnostic modalities.

**Data analysis.** The Fisher exact test was performed to examine any significant differences in the mortality between the fetuses with major extracardiac anomalies and those without. Statistical significance was defined at \( p < 0.05 \).

**RESULTS**

A total of 2,470 fetal echocardiograms were obtained during the study period from which 61 fetuses (61/2,470 = incidence of 2.5% for referral population) with a prenatal diagnosis of conotruncal anomaly were enrolled. The conotruncal anomalies diagnosed prenatally were TOF (n = 18), DORV (n = 22), TGA (n = 15), and TA (n = 6) fetuses. Initial fetal echocardiograms were obtained between 19 and 38 weeks of gestation (median 24.5 weeks). Maternal age at first examination ranged between 17 and 41 years (median 30 years). The median number of echocardiographic studies performed was one, ranging from one to four examinations. Reasons for initial referral included detection of extracardiac anomalies by a routine obstetrical ultrasound examination (n = 30), suspicious obstetrical scan for congenital heart disease without extracardiac anomaly (n = 17), family history of congenital heart disease (n = 5), fetal arrhythmia (n = 4), fetal hydrops (n = 4) and a chromosomal abnormality detected by amniocentesis (n = 1). Of the 30 fetuses with extracardiac anomalies and conotruncal anomalies, the cardiac lesion was suspected in only 11 fetuses.

**Diagnostic accuracy.** The fate of all 61 fetuses thought to have a conotruncal anomaly on prenatal assessment is depicted in Figure 1 along with associated extracardiac lesions. The presence of a conotruncal anomaly was confirmed by echocardiography, cardiac catheterization, surgery, or autopsy in 47 of the 61 fetuses in whom these lesions were prenatally diagnosed. In 12 cases there was no opportunity to examine the fetus postnatally (Fig. 1). These included nine terminations of pregnancy, one intrauterine fetal death and two neonatal deaths soon after birth. One fetus was reported as having aortic stenosis and pulmonary stenosis at autopsy following termination at 22 weeks for severe hydrops. The remaining fetus had aortic atresia, large VSD and normal-sized left ventricle. This fetus had a prenatal diagnosis of truncus arteriosus.

A complete prenatal diagnosis including identification of the great artery relationship to the underlying ventricular mass, the great artery orientation as well as the location of associated ventricular septal defects was made in 36 of the 47 fetuses diagnosed with a conotruncal anomaly (77%). In 9 of the remaining 11 fetuses, the exact great artery orientation was incorrectly defined. In six of these patients with prenatally suspected double outlet right ventricle (DORV) and subpulmonary ventricular septal defect (VSD), malposition of the great arteries (MGA) was assumed from the fetal scan (Fig. 2A). However, postnatally three had normally oriented great arteries and a ventricular septal defect with overriding aorta, one had tetralogy of Fallot (TOF), one had transposition of the great arteries (TGA) with VSD and one had double outlet right ventricle with subaortic VSD. In one case, fetal transposition of the great arteries was suspected; however, postnatal examination at the referring institution following termination at 23 weeks' gestation was reported as truncus arteriosus (TA). Finally, one fetus with trisomy-18 was thought to have TGA, and a VSD was in fact a DORV with a subpulmonary VSD (Fig. 2B).

In contrast, the prenatal diagnosis of TOF or DORV with subaortic VSD agreed in most cases with the postnatal findings (Fig. 2C). Of 13 fetuses with a prenatal diagnosis of TOF and 7 with DORV, subaortic VSD and normally oriented great arteries, the prenatal definition of great artery orientation was confirmed postnatally in all but three cases. Five fetuses had a prenatal diagnosis of absent pulmonary
valve syndrome (APVS). Two pregnancies were terminated. In one 22-week fetus, examination at autopsy was recorded as showing aortic and pulmonary stenosis. Unfortunately, the pathology specimen was not available for further evaluation at our institution. The remaining three pregnancies continued; however, all died in the neonatal period, one of whom developed fetal hydrops before delivery. Truncus arteriosus was diagnosed on four occasions (Fig. 2D). Two pregnancies were aborted due to trisomy-13 in one and bilateral anophthalmos in the other. One case delivered at 39 weeks, having been referred at the 28th week of gestation. The neonatal echocardiogram showed aortic atresia with normal-sized left ventricle and a large VSD. One infant with TA survives following surgical repair.

The presence or absence of ventricular outflow tract obstructions was accurately defined in 32 of the 36 fetuses (89%) with conotruncal anomalies where postnatal analysis was possible. Two fetuses, one with the prenatal diagnosis of normal pulmonary artery and another one with pulmonary stenosis, were found postnata lly to have pulmonary stenosis and pulmonary atresia, respectively.

Nineteen of the 61 fetuses in whom the diagnosis of a conotruncal anomaly had been made were terminated electively (Fig. 1). Postmortem examination was conducted in

Figure 1. Flow diagram to depict the fate of 61 fetal diagnoses of a conotruncal anomaly. Diagnoses described are those made in the postnatal period or at autopsy. AoA = aortic atresia; APVS = absent pulmonary valve syndrome; AS = aortic stenosis; AVSD = atrioventricular septal defect; cTGA = congenitally corrected transposition of the great arteries; DORV = double outlet right ventricle; LAIs = left atrial isomerism; MGA = malposed great arteries; PS = pulmonary stenosis; Sub Ao = subaortic; TA = truncus arteriosus; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VSD = ventricular septal defect. *One patient died at two months of age. #Patient died at one month of age. ##Patient died at seven months of age.
10 cases and confirmed the presence of a conotruncal anomaly in all but one case in which the definitive diagnosis changed from APVS to severe pulmonary stenosis and aortic stenosis.

Prognosis of fetuses with conotruncal anomalies. Following the termination of 19 fetuses, 42/61 were available for determination of prognosis of fetal conotruncal anomalies. Twenty of these 42 fetuses (48%) died either prenatally \( (n = 4) \) or within the neonatal period \( (n = 16) \). The remaining 22 fetuses were born and survived, although three subsequently died, two in the second month of life and another at seven months of age. Although the statistical significance level was not reached, there was a strong trend toward a poorer prognosis of the fetuses with conotruncal anomalies and additional major extracardiac malformations.

Of the 42/61 pregnancies that continued, 14 had a chromosomal abnormality, a major extracardiac lesion or both (Fig. 3). These included trisomy-13 \( (n = 3) \), trisomy-2 mosaic \( (n = 1) \), and 13p+ \( (n = 1) \) abnormality including diaphragmatic hernia \( (n = 5) \), holoprosencephaly \( (n = 1) \), renal agenesis \( (n = 1) \), tracheoesophageal fistula \( (n = 1) \), imperforate anus \( (n = 1) \), and conjoined twin \( (n = 1) \). Nine died in the neonatal period and the remaining five survived more than 28 days following corrective surgical intervention. Twenty-seven fetuses had no documented chromosomal or major extracardiac anomaly, of whom 13 (48%) subsequently died.

Concentrating on the 39 of the 42 pregnancies that continued, in whom the correct cardiac diagnosis was available, 15 had a major extracardiac anomaly, excluding the case of a conjoined twin. Of these cases, only six (40%) survived. In contrast, of the 24 fetuses without an associated extracardiac anomaly, 67% survived. Although the numbers are too small to be of statistical value, of eight fetuses with isolated TOF (excluding those with APVS), 6 (75%) survived beyond the neonatal period. Two died: one with trisomy-13, and the other had congenital diaphragmatic hernia.

**DISCUSSION**

Diagnostic accuracy. This study shows that conotruncal anomalies can be diagnosed in fetal life by echocardiography with a high degree of accuracy. Difficulties in defining the spatial relationship of the great arteries are a limiting factor in diagnosing conotruncal anomalies in some instances. Despite this, the accuracy of prenatal diagnosis of conotruncal anomalies including the great vessel orientation was 80% in this study. This is comparable with reports that described the reliability of prenatal diagnosis of unselected cardiac anomalies \((1,2)\) although the researchers did not mention the accuracy of prenatal definition of great artery orientation, especially in DORV disease entity, which was the main source of errors in our cohort.

It is difficult to diagnose accurately the relationship of the great arteries in some fetuses. Because of varying fetal lie
and an active fetus, it can be especially difficult to establish the orientation of the great arteries. However, after birth the anteroposterior, right-left and superioinferior relationships are much simpler to establish and remain constant. In some cases, parallel appearance of the great vessels might lead to the incorrect diagnosis of MGA. Also, tortuous vessels may not lie in a single plane, and cannot always be followed throughout their entirety (3,4).

It is notable that all the fetuses with conotruncal anomalies in this series had a ventricular septal defect and that we encountered only two fetuses with isolated D-transposition of the great arteries, which is the most common conotruncal anomaly in postnatal life (5). One of the reasons seems to be the fact that a large ventricular septal defect is readily detectable in the standard four-chamber view on initial obstetric exam, whereas isolated D-transposition of the great arteries is highly likely to be missed.

Errors. On analysis of our errors we conclude that several factors were involved. Only 3 of the 11 fetuses in question were scanned below 22 weeks of gestation and all underwent termination. Therefore, fine-tuning of their complex anatomy by subsequent scans was not possible. The remaining eight fetuses were first seen for detailed fetal echocardiography at a median of 30.5 weeks' (range 26 to 38 weeks) gestation. Only two had more than one detailed scan at our institution. Therefore, fetal lie, at this more mature age, may have contributed in those where spatial relationships of the great vessels were not correctly identified particularly in the DORV group. Moreover, image quality is not as good as those scanned at an earlier gestation. The study indicates that, when a single great vessel is identified, a diligent search is necessary to exclude an atretic aorta when TA is suspected. Likewise, in suspected pulmonary atresia and VSD, careful exclusion of TA should be made.

Prognosis. This study also indicates that the prognosis of the fetuses with conotruncal anomalies is poor. As a whole, 64% (39/61) of the fetuses with a prenatal diagnosis of a conotruncal anomaly died, including elective terminations. However, of those whose pregnancy continued, 52% (22/42) survived to 28 days, but this dropped to 41% (17/41) by one year of age. This mortality is comparable with a recent report in which the mortality of the fetuses with conotruncal anomalies ranged from 50% to 65% (2).

The prognosis of the fetuses with chromosomal abnormalities or extracardiac anomalies was worse than that of the fetuses without. The final mortality before 28 days of life, excluding elective terminations, in a fetus with a “suspected” conotruncal anomaly and either a chromosomal or major extracardiac anomaly, was 59% (10/17) compared with 40% (10/25) of those fetuses without these anomalies (6–9). It is possible that the more severe cases were enrolled in this study in part due to this institution’s fetal surgical service and its referral patterns. Of the fetuses who did not have major extracardiac anomalies and died, three had heterotaxy and five had absent pulmonary valve syndrome (5,10–12). There were only two fetuses with simple TGA, of which one subsequently died in utero, though this cardiac lesion would usually have a good prognosis (5). The fact that more than 50% of the fetuses were referred because of an extracardiac anomaly may indicate that the population is skewed because usually only 20% are referred for fetal echocardiography because of a recognized extracardiac anomaly (13). Tetralogy of Fallot excluding those with absent pulmonary valve, however, had a better prognosis. In
This study demonstrates that conotruncal anomalies can be diagnosed by prenatal echocardiography with a high degree of accuracy. Difficulties in defining the spatial relationship of the great arteries can occur. This seems to be particularly so in cases of DORV. Fetal lie, image quality and late gestational age at referral may have contributed to some of these errors. The clinical outcome of the fetuses with conotruncal anomalies is poor, even without major extracardiac anomalies, except for the fetuses with tetralogy of Fallot.

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