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Outcome and requirement for surgical repair following prenatal diagnosis of ventricular septal defect

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KEYWORDS: chromosomal defects; extracardiac abnormalities; fetal heart; ventricular septal defect

ABSTRACT

Objective *To document outcome following prenatal diagnosis of ventricular septal defects (VSDs), particularly associated anomalies and the requirement for surgical closure of the defect.*

Methods *All cases of prenatal diagnosis of a VSD made by fetal cardiologists at a tertiary fetal medicine referral center in the period January 2002 to December 2011 were extracted from our database. Data regarding fetal cardiac diagnosis, extracardiac anomalies, nuchal translucency thickness and karyotype were noted.*

Results *A total of 171 cases fulfilled our selection criteria. Of these, 69% were diagnosed with a perimembranous VSD and 31% with a muscular defect. The median gestational age at diagnosis was 21 + 6 (range, 12 + 0 to 37 + 3) weeks. Owing to severe extracardiac or genetic conditions, pregnancy resulted in intrauterine death or termination in 49% cases, and postnatal death occurred in 9% of cases. Seventy-two babies were liveborn, and were regarded as potential surgical candidates if hemodynamics suggested that surgery was indicated. Surgical closure of the VSD proved necessary in 50% of the patients with a perimembranous VSD and 13% of those with a muscular VSD. All patients operated on survived surgical repair. No karyotypic abnormalities were identified in fetuses with VSDs that had normal first-trimester screening and no other sonographic abnormalities.*

Conclusions *A high proportion of VSDs diagnosed during fetal life (29%) require postnatal surgical intervention. The assessment of hemodynamic significance from fetal echocardiography is imperfect. The presence of extracardiac abnormalities or abnormal results on first-trimester screening has a major impact on the incidence of karyotypic abnormalities in affected fetuses. This should inform discussions with parents about invasive testing.* *Copyright © 2013 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Ventricular septal defects (VSDs) can be diagnosed during fetal life, and a high association with extracardiac and chromosomal abnormalities has been reported[1]. However, the diagnosis of VSDs during fetal life presents a number of challenges. The right and left ventricular pressures are equal so there is no major left to right shunt, and the flow pattern across defects is typically low velocity and bidirectional. The membranous portion of the ventricular septum is thin and prone to image 'drop out', so there is the potential for both false-positive and false-negative diagnoses. Furthermore, a confident diagnosis of some types of VSD, for example doubly committed subarterial defects, is quite difficult during fetal life because the required sonographic views may not be readily obtainable. The prenatal diagnosis of fetal heart defects will depend on the sonographer's expertise in cardiac evaluation[2]. The ability to diagnose an isolated VSD is influenced by the quality of the image obtained, the size of the defect, use of color-flow Doppler and the gestational age at the time of the scan. During screening examinations of the fetal heart, detection of a VSD often depends on its visualization on cross-sectional images, which can lead to a bias towards medium- or large-sized defects. In addition, detailed echocardiography is often part of the assessment of fetuses with extracardiac malformations, these fetuses having a high rate of associated chromosomal and other defects[3–7]. Set against this, in recent years, highly sensitive color-flow Doppler ultrasound has been used increasingly to study the fetal heart, and smaller VSDs, particularly muscular ones, may be diagnosed on color-flow Doppler even when they are not visible on gray-scale cross-sectional images alone[8].

VSDs are normally categorized according to their position when visualized from the right ventricular aspect, the categories being perimembranous, doubly committed subarterial and muscular. Perimembranous defects are in the membranous portion of the ventricular septum, adjacent to the tricuspid valve, but may have

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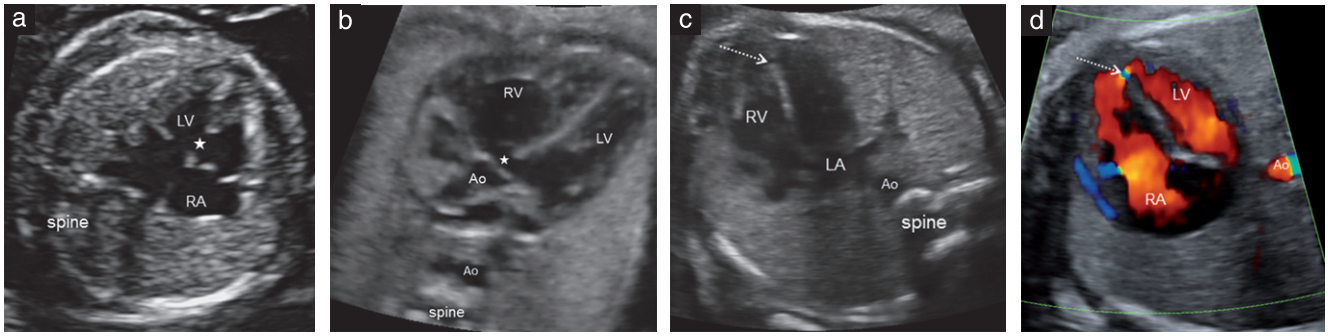

Figure 1 (a) Apical four-chamber view of the fetal heart at 20 weeks' gestation, showing a large perimembranous inlet ventricular septal defect (VSD). Loss of continuity of ventricular septum is indicated (⋆). (b) Apical four-chamber view of the fetal heart at 20 weeks, showing a large perimembranous outlet VSD and mild aortic override. Loss of continuity of ventricular septum to anterior wall of aorta is indicated (⋆). (c) Apical four-chamber view of the fetal heart at 24 weeks, showing a small apical muscular VSD (arrow) that closed spontaneously during infancy. (d) Color Doppler view of the fetal heart, showing left-to-right flow across the septum (blue color; arrow) but color/pulsed Doppler confirmed a bidirectional flow pattern. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

extension into the ventricular inlet or outlet. In doubly committed subarterial defects there is a superior position with fibrous continuity between the aortic and pulmonary valves. Muscular defects have entirely muscular boundaries and can be subdivided into outlet, inlet and trabecular defects (Figure 1)[9].

Following prenatal diagnosis of a VSD, several facets are germane to parental counseling with respect to the prognosis. The first is the potential for the VSD to be associated with chromosomal abnormalities and other fetal anomalies that may impact heavily on the prognosis. We present here data on the incidence of karyotypic abnormalities, according to the presence or absence of other sonographic or screening markers. Secondly, parents are concerned about the potential need for cardiac surgery if the defect proves hemodynamically significant postnatally. We present data on the outcome following surgery in a prenatally diagnosed cohort, and the accuracy of fetal cardiology for the prediction of the need for repair.

The aims of our study were to document outcome following prenatal diagnosis of a VSD, particularly associated anomalies and requirement for surgical repair.

PATIENTS AND METHODS

A retrospective audit of all cases of prenatal diagnosis of a VSD made by three fetal cardiologists at a tertiary referral center between January 2002 and December 2011 was performed. Additional data regarding fetal ultrasound examination, nuchal translucency thickness, karyotype and extracardiac anomalies were collected from our database (ViewPoint 5.6; GE Medical Systems, Solingen, Germany).

Only cases with the usual atrial arrangement and concordant atrioventricular and ventriculoarterial connections, with an interventricular communication (or VSD) were included ($n = 187$). Fetuses with major additional cardiac abnormalities, for example transposition of the great arteries, were excluded from the analysis. However, fetuses with subtle additional cardiac variants, such as an aberrant right subclavian artery, right aortic arch, persistent left superior vena cava and polyvalvular dysplasia were not excluded, as these findings would not influence the postnatal cardiac management of the VSD. The variants listed above have been regarded as potential markers for underlying genetic abnormality, and the data were analyzed to take account of this potential association.

For the purposes of this study, VSDs were divided into two major groups. Those in the membranous portion of the ventricular septum were classified as 'perimembranous' and were further subdivided on the basis of inlet or outlet extension. Muscular defects were those with entirely muscular boundaries, and the position – whether inlet, outlet or midtrabecular – was noted. We were not confident that doubly committed subarterial defects could be identified consistently during fetal life, so these were not categorized separately. In addition, the size of the VSD was documented by the attending fetal cardiologist, with a description of the defect as small, medium or large. The working definitions of size in our department were that small defects could only be seen on color-flow Doppler and/or measured < 2 mm in diameter. Medium defects could be seen on two-dimensional (2D) and color-flow Doppler and were > 2 mm in diameter. Large defects were visible on 2D alone and were similar in size to the aortic valve.

Conventional fetal echocardiography, which utilized 2D, pulsed-wave and color-flow Doppler, was performed to assess anatomy and make a diagnosis in all cases. All patients were examined transabdominally, using an Acuson Aspen Advanced (Acuson, Mountain View, CA, USA) with a 4–7-MHz sector probe or the Voluson E8 (GE Medical Systems) with a 4–8-MHz sector probe.

Prenatal and postnatal morphological cardiac diagnoses were recorded. Information about prenatal or postnatal outcome, including cardiac surgery and additional extracardiac anomalies, was obtained from the tertiary hospital in which postnatal cardiac assessment was performed, or by direct communication with the general practitioner or parents.

Statistical analysis

The incidence of aneuploidy and requirement for surgical closure between the different types of VSD were analyzed using chi-square analysis; $P < 0.05$ was regarded as statistically significant.

RESULTS

One hundred and eighty-seven fetuses with the diagnosis of a VSD were identified between 12 + 0 and 37 + 3 weeks' gestation (median, 21 + 6 weeks). Indications for referral included: suspected cardiac anomaly in 83 (44.4%), known extracardiac abnormality in 56 (29.9%), increased nuchal translucency in 20 (10.7%) and other abnormal markers at first-trimester screening in eight (4.3%). The remaining 20 cases (10.7%) were seen for maternal risk factors, such as a family history of congenital heart disease or because of a monochorionic twin pregnancy.

In 16 out of 187 fetuses (8.6%), there was incomplete postnatal information, in five of which trisomy 18 was confirmed or highly suspected. Hence, 171 cases with complete cardiac postnatal outcome were analyzed further in our study. Of these 171 cases, 118 (69.0%) were diagnosed with a perimembranous VSD and 53 (31.0%) with a muscular defect.

Twenty-nine (17.0%) of the 171 cases had additional subtle cardiac variants. Seven had an aberrant right subclavian artery, six a persistent left superior vena cava, in 10 cases there was polyvalvular dysplasia and a further six had a right aortic arch.

Owing to severe extracardiac or genetic conditions, the pregnancy resulted in intrauterine death or termination in 83 (48.5%) cases, and there were 16 (9.4%) neonatal or infant deaths.

A total of 88 fetuses were liveborn. In sixteen cases, severe chromosomal or extracardiac anomalies, for example trisomy 18, were present so, after discussion with parents, surgery was not undertaken. Thus, 72 babies were liveborn and were regarded as potential surgical candidates if hemodynamics suggested that surgery was indicated. The postnatal cardiac diagnosis differed from the prenatal diagnosis in three of 72 cases (4.2%), comprising two atrioventricular septal defects (AVSDs) that were prenatally diagnosed as inlet VSDs, and one case of tetralogy of Fallot that was prenatally diagnosed as an outlet VSD. In 11/72 cases (15.3%), the defect was present at the time of the last prenatal echocardiogram but was not present at the time of initial postnatal echocardiography, indicating that these defects closed late in gestation or early in the postnatal period (Figure 2). In 13 cases, the VSD was confirmed postnatally but closed

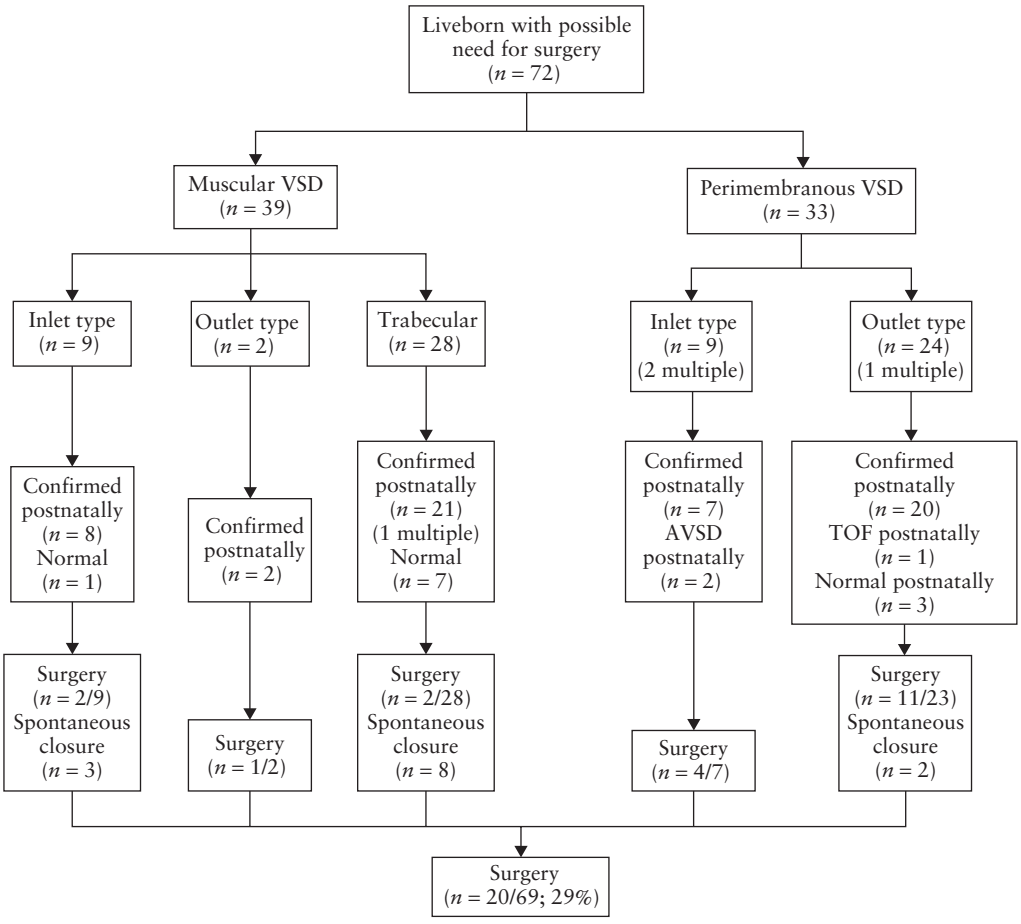

Figure 2 Flow-chart showing categories of ventricular septal defect (VSD) and need for closure according to type of defect in 72 liveborn babies who were regarded as potential candidates for surgery. AVSD, atrioventricular septal defect; TOF, tetralogy of Fallot.

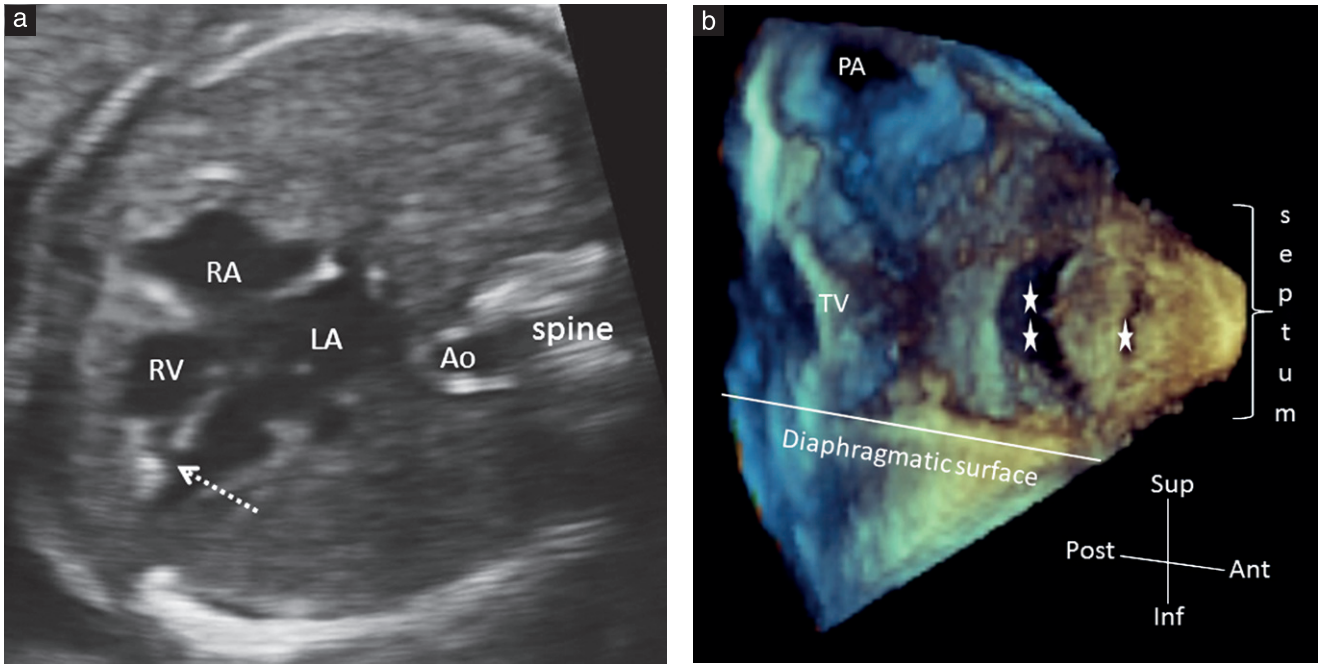

Figure 3 Prenatal (a) and postnatal (b) echocardiograms in a case thought to have a small ventricular septal defect (VSD) prenatally, which had to be closed during infancy due to a large left-to-right shunt. (a) Prenatal two-dimensional echocardiogram at 20 weeks' gestation showing a single small trabecular muscular VSD (arrow). (b) Postnatal three-dimensional transthoracic echocardiogram of the defect rendered in an 'anatomic' orientation to demonstrate the interventricular communication. This view from the right ventricle demonstrates a large (★★) muscular VSD and an additional (★) more apical muscular VSD. In the four-chamber view, the minor axis of such 'slit-like' defects is visualized, which underestimates the true extent of the defect. Ant, anterior; Ao, aorta; Inf, inferior; LA, left atrium; PA, pulmonary artery; Post, posterior; RA, right atrium; RV, right ventricle; Sup, superior; TV, tricuspid valve.

spontaneously during postnatal follow-up. Therefore, 31 (43.1%) patients had a muscular and 27 (37.5%) had a perimembranous VSD diagnosed postnatally. Surgical closure of the VSD proved necessary in 20 (29.0%) of 69 cases. The need for closure differed according to the type of VSD: 50.0% (15/30) of the patients with a perimembranous VSD required surgery compared with 12.8% (5/39) of those with a muscular VSD (Figure 2) ($P = 0.0007$). The majority of patients were operated on in the first 2 years following birth owing to either heart failure or aortic valve regurgitation due to prolapse of a coronary leaflet into the defect. All patients operated on survived surgical repair. The requirement for surgical repair of VSDs that were considered to be small, medium or large prenatally was 13.9% (5/36), 42% (11/26) and 57.1% (4/7), respectively. All cases in which the defects that were judged to be small prenatally and that required postnatal closure turned out to have multiple VSDs. An example is shown in Figure 3.

The risk of karyotypic abnormality in relation to the type of VSD, associated extracardiac anomalies and other markers such as increased nuchal translucency, is summarized in Figure 4. No karyotypic abnormality was identified in fetuses with VSDs that had normal nuchal translucency and no other sonographic abnormality. Conversely, fetuses with VSDs (muscular or perimembranous) had a much higher incidence of chromosomal abnormalities if other sonographic markers or abnormal screening tests were present. Our subdivision of fetuses with associated intracardiac variations was deliberate, to assess whether this impacted on the incidence of karyotypic abnormalities. One of six such fetuses with an additional aberrant right subclavian artery had a karyotypic abnormality even in the absence of other markers or anomalies (Figure 4). Nuchal translucency was increased in 27 (19.0%) of the 142 fetuses in which this measurement was known.

There was a higher rate of aneuploidy in the group with a perimembranous VSD (69/118 (58.5%)) than in the group with a muscular defect (10/53 (18.9%)) ($P = 0.006$).

DISCUSSION

This study confirms that a relatively large proportion of fetuses in which a VSD is diagnosed will need to undergo surgery. Of the liveborn fetuses in our series (excluding three misdiagnoses), 29.0% (20/69) required surgery. The opinion of the fetal cardiologist with respect to the size of the defect did impact on the necessity for surgical closure. Around half of fetuses with medium or large defects required repair, but 13.9% (5/36) of VSDs that were thought to be small during fetal life also had to undergo postnatal repair. The reasons why a 'small' VSD might require surgical repair can relate to the morphology of the defect. Many defects are not circular in shape and may be more slit-like. The effect of this is that when they are 'cut' in a single sonographic plane the defect may appear small, but this may not represent the full extent of the defect. An example of this is seen in Figure 3, which shows that the four-chamber projection may cut the minor axis of the

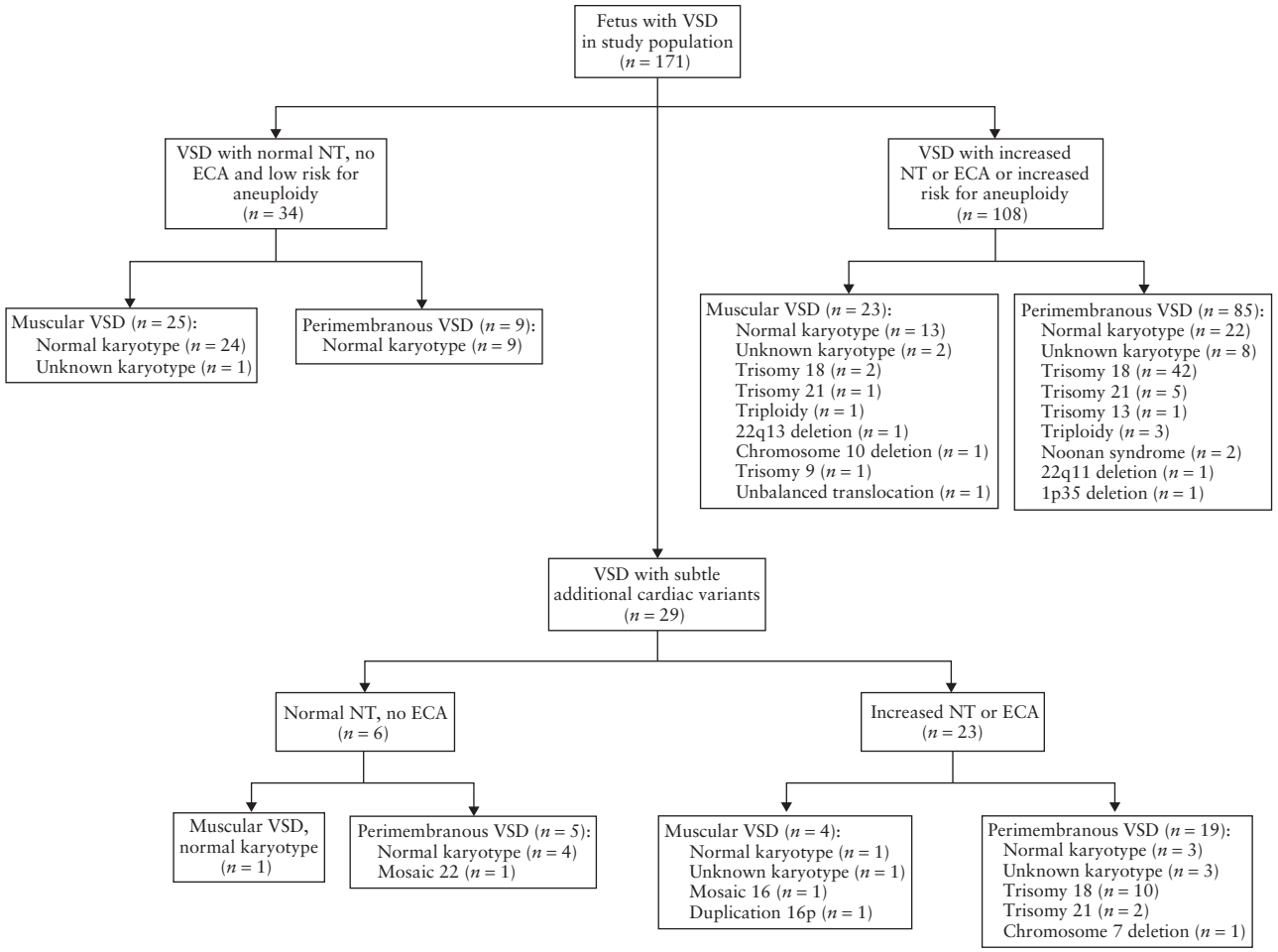

Figure 4 Flow-chart showing risk of karyotypic abnormality in relation to type of ventricular septal defect (VSD), associated extracardiac anomalies (ECA) and other markers in 171 fetuses with a VSD. NT, nuchal translucency.

VSD so that the potential hemodynamic effect is underestimated during fetal life. Advances in three-dimensional echocardiography may assist in assessing this during fetal life[10,11].

The postnatal diagnosis differed from the prenatal diagnosis in three cases. Two fetuses with a prenatal diagnosis of an inlet VSD were found to have AVSDs postnatally and one case prenatally diagnosed as an outlet VSD was diagnosed with tetralogy of Fallot after birth. The ventricular component of an AVSD occupies part of the inlet septum, and in each of these cases of AVSD the atrial component of the AVSD was small. The case in which tetralogy of Fallot was diagnosed postnatally had well developed pulmonary arteries, without right ventricular outflow tract obstruction and only a mild degree of aortic override.

The incidence of prenatal or postnatal spontaneous closure of all VSDs recognized during fetal life was 24 of 72 liveborn cases (33.3%), which is consistent with the results of previous work[5]. We cannot determine from our data whether closure occurred during fetal life or early postnatally, but these defects were confidently diagnosed on 2D ultrasound and confirmed on color Doppler with bidirectional flow before birth, and were not present on the initial postnatal echocardiogram. A major additional consideration following prenatal detection of a VSD is the possibility that there may be an underlying karyotypic abnormality[3–7]. The data we report confirm that the incidence of such abnormalities is heavily influenced by the presence of sonographic abnormalities or positive screening test results. For fetuses with normal nuchal translucency and no other anomalies, we did not identify any karyotypic abnormality among 33 fetuses that were karyotyped. Conversely, 63 of 108 fetuses (58.3%) with VSDs and other sonographic abnormalities had an underlying karyotypic abnormality or syndromic diagnosis (Figure 4). In one of six cases, the finding of an additional cardiac variant was associated with a karyotypic abnormality, even in the absence of other markers. These data suggest that for fetuses with 'isolated' VSDs (i.e. without other sonographic abnormalities or markers) the incidence of karyotypic abnormality is likely to be low, whereas there is a far higher incidence when such anomalies co-exist. This has significant implications for parental decision-making with respect to invasive testing.

In conclusion, a relatively high proportion of VSDs diagnosed during fetal life (29.0%) require postnatal surgical intervention. An excellent outcome can be anticipated for infants that do undergo surgery. The judgment of hemodynamic significance from fetal echocardiography

is imperfect, as 13.9% of 'small' VSDs had to be closed postnatally. The presence of extracardiac sonographic abnormalities or abnormal findings on first-trimester screening has a major impact on the incidence of karyotypic abnormalities in affected fetuses. This should inform discussions with parents about invasive testing.

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