Prenatal Screening for Major Congenital Heart Disease
Superiority of Outflow Tracts Over the 4-Chamber View

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Objective. The purpose of this study was to determine the relative importance of the 4-chamber view (4CV) compared with the outflow tract views (OFTVs) in prenatal screening for major congenital heart disease (CHD). Methods. We prospectively evaluated 200 consecutive infants undergoing cardiac surgery at our institution for major CHD. By reviewing the infants’ medical records and conducting bedside interviews with their parents or guardians, we evaluated detection rates both prenatally and postnatally (before and after discharge to home), and we noted any prenatally identifiable risk factors for CHD. For each infant, we determined whether the 4CV or OFTVs would be expected to have been normal or abnormal on routine midgestation screening fetal sonography. Results. A prenatal diagnosis of CHD was made in 65 infants (33%): 30 of 124 low-risk pregnancies (24%) and 35 of 76 high-risk pregnancies (46%). An abnormal screening midgestation 4CV would have been expected in up to 63% of the infants, whereas abnormal midgestation OFTVs would have been expected in up to 91% of the infants. Thus, the potential sensitivity for detecting major CHD was higher with the OFTVs than with the 4CV (91% versus 63%; \(P < .001\)). Moreover, the OFTVs were more sensitive than the 4CV for detecting ducal-dependent forms of CHD. Diagnosis after discharge to home occurred in 39 of 135 postnatal diagnoses (29%), including many cases of isolated outflow tract abnormalities requiring early invasive intervention. Conclusions. Cases of major neonatal CHD with OFTV abnormalities predominate over cases with 4CV abnormalities, particularly among those forms of CHD requiring early invasive intervention. Key words: congenital heart disease; fetal heart; 4-chamber view; outflow tracts; prenatal screening.

Abbreviations
AS, aortic stenosis; AVC, atrioventricular canal; CHD, congenital heart disease; CoA, coarctation of the aorta; DORV, double-outlet right ventricle; 4CV, 4-chamber view; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; OFTV, outflow tract view; PA, pulmonary atresia; PS, pulmonary stenosis; TA, tricuspid atresia; TGA, D-transposition of the great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect

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prenatal detection of severe forms of CHD,\textsuperscript{18,19} more recently has failed to detect a large percentage of CHD,\textsuperscript{20} including major defects that would be expected to have an abnormal 4CV.\textsuperscript{2} Weaknesses in the acquisition, interpretation, and scope of the 4CV have been well described.\textsuperscript{21} On the other hand, the outflow tract views (OFTVs), when added to the 4CV, improve the sensitivity for major forms of CHD.\textsuperscript{20,22–26} Nevertheless, in part because the 4CV appears easier to obtain than the OFTVs,\textsuperscript{2,17} the 4CV has remained the central focus of current approaches to prenatal screening for CHD.\textsuperscript{22} Current formal guidelines emphasize the importance of the 4CV, recommending an attempt to include the OFTVs “when technically feasible.”\textsuperscript{27–29}

Although current approaches to prenatal screening for CHD remain flawed, it remains unclear which direction to take to improve detection rates: expansion of 4CV training or greater emphasis on the OFTVs. Although the OFTVs appear more challenging than the 4CV to acquire and interpret, effective evaluation of both the 4CV and OFTVs may be achieved with adequate training.\textsuperscript{20,22,23,30–33}

Our impression has been that prenatal screening of the OFTVs may carry even greater clinical importance than 4CV screening. This study sought to compare the potential sensitivity of the 4CV and OFTVs in prenatally detecting major forms of CHD, particularly those forms of CHD dependent on the ductus arteriosus/foramen ovale and, as a result, likely to require neonatal intervention.

**Materials and Methods**

We prospectively enrolled 200 infants younger than 1 year admitted consecutively to our institution for cardiac surgery. Approval for this study was obtained from the Institutional Review Board at Childrens Hospital Los Angeles, and informed consent was obtained from the parent or guardian of each subject. Inclusion criteria included age younger than 1 year at the time of cardiac surgery and admission to the Childrens Hospital Los Angeles cardiothoracic intensive care unit, with performance of cardiac surgery for previously unoperated CHD during the study period. Evaluations included review of patients’ medical records and bedside interviews with patients’ mothers or primary caregivers. Data collected included the detailed cardiac diagnosis from postnatal transthoracic echocardiography, gestational age at the time of the latest fetal sonography (if any), timing of initial cardiac diagnosis (prenatal, early neonatal, or after discharge to home), and identifiable risk factors for CHD,\textsuperscript{34} in this study limited to chronic maternal disease (ie, diabetes and systemic lupus erythematosus), maternal/family history of CHD, fetal exposure to known teratogens, abnormal extracardiac findings on screening sonography, and chromosomal abnormalities.

Definitions and classifications of pregnancies and specific forms of CHD were determined before enrolling patients. Pregnancies were defined as high or low risk on the basis of the presence or absence of an identifiable risk factor for CHD. Major CHD was defined as CHD requiring cardiac surgery during the first year of life. Specific diagnoses of CHD were classified in terms of whether ideally performed midgestation screening fetal sonography\textsuperscript{27–29,34} would retrospectively have shown an abnormal 4CV, OFTVs (aortic/pulmonary valves with crossing great arteries), or both (Table 1). This classification scheme was based on extensive clinical experience with prenatal screening and fetal echocardiography, previously described postnatal characteristics of the apical 4CV and OFTVs,\textsuperscript{35} and similar classification schemes proposed previously by others.\textsuperscript{2,15,17,18,20,22,36} Because some forms of CHD, such as coarctation of the aorta (CoA), may legitimately have variable 4CV and OFTV appearances at 18 to 22 weeks’ gestation, an additional category of “possibly abnormal” was included in the classification scheme. The classification of expected appearances of the 4CV and OFTVs into 3 categories (definitely normal, possibly abnormal, and definitely abnormal) enabled data to be analyzed under 2 scenarios: an optimistic “best case” scenario, in which possibly abnormal expected findings were classified as abnormal (detectable), and a conservative “worst case” scenario, in which possibly abnormal expected findings were classified as normal (undetectable) (Table 2). \(\chi^2\) statistics were used to compare nonparametric variables and proportions. All analyses were
conducted with SPSS 14.0 statistical software (SPSS Inc, Chicago, Illinois). Statistical significance was determined as $P < .05$.

Results

Between September 2005 and February 2007, we prospectively enrolled 200 consecutive patients in this study. No patient’s parents or guardians declined to participate. Seventy-six of 200 pregnancies (38%) had identifiable risk factors for CHD (excluding fetal cardiac abnormalities detectable on screening sonography); most cases of CHD occurred in low-risk pregnancies. Fetal sonography was performed at or beyond 18 weeks’ gestation in 98% of the patients. A prenatal diagnosis of CHD was made in 33% of the infants: 30 of 124 low-risk pregnancies (24%) and 35 of 76 high-risk pregnancies (46%).

Specific Defects: Distribution, Timing of Diagnosis, and Identifiable Risk Factors

The 4 most common diagnoses together constituted more than half of the cases: tetralogy of Fallot (TOF; 17%), CoA (13%), D-transposition of the great arteries (TGA; 12%), and hypoplastic left heart syndrome (HLHS; 10%; Figure 1). Large ventricular septal defects (VSDs) and a balanced atrioventricular canal (AVC), the 2 next most common diagnoses, each accounted for 8% of the cases.

A prenatal diagnosis was made in 33% of cases. Among the 5 most common diagnoses, the rates of prenatal diagnosis were 60% for HLHS, 44% for a balanced AVC, 32% for TOF, 19% for CoA, and 17% for TGA. Among those cases not prenatally diagnosed, a postnatal diagnosis was made after discharge to home in 29% of cases.

An identifiable risk factor for CHD was present in 38% of pregnancies. A chromosomal abnormality was present in 10 patients (5%). An identifiable risk factor of some type was present in 50% or more of the cases of an interrupted aortic arch (IAA), pulmonary stenosis (PS), TOF, truncus arteriosus, and a balanced AVC but in no cases of aortic stenosis (AS), Ebstein anomaly, or tricuspid atresia (TA). Risk factors were present in less than one-fourth of cases of CoA, just less than one-third of cases of HLHS, and just more than one-third of cases of TGA.

Expected Cardiac Findings on Screening Fetal Sonography: Distribution, Timing of Diagnosis, and Identifiable Risk Factors

Congenital heart disease that would be expected to have abnormal screening OFTVs was more common than CHD that would be expected to have an abnormal screening 4CV in both the best case scenario (91% versus 63%; $P < .001$) and worst case scenario (63% versus 31%; $P < .001$; Figure 2). The least common detectable category in both the best and worst case scenarios was an abnormal 4CV associated with normal OFTVs. In contrast, CHD expected to have had an abnormal 4CV tended to have a slightly higher rate of prenatal detection compared with CHD expected to have had abnormal OFTVs (best case scenario, 36% versus 32%; $P = .55$; worst case scenario, 53% versus 34%; $P = .01$).

Among the 76 pregnancies with identifiable risk factors, the proportion of an expected abnormal 4CV was lower than the proportion of expected abnormal OFTVs (best case scenario, 53% versus 87%; $P < .001$; worst case scenario, 29% versus 64%; $P < .001$). However, pregnancies

Table 1. Expected Cardiac Findings on Screening Fetal Sonography

<table>
<thead>
<tr>
<th>Defect</th>
<th>4CV</th>
<th>OFTV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAPVR</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Muscular VSD (large)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Membranous VSD (large)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Malalignment VSD (large)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Balanced AVC</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Unbalanced AVC</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mitral atresia</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>TA</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Ebstein anomaly/TVD</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Severe AS</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Aortic atresia</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Severe PS</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>PA/IVS</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>TOF</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>TOF/APV</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>DORV</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>TGA</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>L-TGA</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Single ventricle</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Aortic arch obstruction</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Classification: 1, normal; 2, possibly abnormal; and 3, abnormal. APV indicates absent pulmonary valve; IVS, intact ventricular septum; L-TGA, congenitally corrected TGA; TAPVR, total anomalous pulmonary venous return; and TVD, tricuspid valve dysplasia; other abbreviations are as in text.
with an expected abnormal 4CV in the presence of normal OFTVs represented the category with the highest incidence of identifiable risk factors.

**Cases That Theoretically Would Have Been Missed With 4-Chamber Versus Outflow Tract Screening**

In the best case scenario, screening with the 4CV would have missed 74 of 200 cases (37%), at least 80% of which were potentially ductal dependent after delivery (TOF; TGA, and double-outlet right ventricle [DORV]). In contrast, screening with the OFTVs would have missed 18 of 200 cases (9%; \( P < .001 \) compared with 37% by 4CV), distributed between large VSDs and balanced AVC defects with no potentially ductal-dependent cases of CHD.

Similarly, in the worst case scenario, the 4CV compared poorly with the OFTVs in terms of the percentage of defects that theoretically would have been missed at midgestation (69% versus 38%; \( P < .001 \)).

**Isolated and Combined Sensitivities of the 4CV and OFTVs**

Compared with abnormalities of the 4CV, abnormalities of the OFTVs were far more common, making the potential sensitivity of the OFTVs greater than that of the 4CV (Table 3). In actuality, however, OFTV abnormalities tended to be less frequently detected prenataily than 4CV abnormalities. As expected, the combined sensitivity of the 4CV and OFTVs was greater than the sensitivity of the 4CV or OFTVs alone, potentially detecting between 77% (worst case scenario) and 100% (best case scenario) of cases of major CHD.

**Discussion**

The primary findings of this study show that the OFTVs may be more important than the 4CV for the prenatal detection of major CHD. Most cases of major CHD (including defects dependent on the ductus arteriosus and foramen ovale) may be detectable at midgestation with OFTV screening. The 4CV, in comparison, appears able to detect a smaller percentage of cases of major CHD and fails to detect many of those defects most likely to benefit from prenatal diagnosis. As expected, the greatest sensitivity for CHD comes with a combination of 4CV and OFTV screening. These findings emphasize the need for a paradigm shift in prenatal screening for CHD, away from a focus on the 4CV as an end in itself and toward the 4CV as a starting point in conjunction with obligatory OFTV screening.

**Classification Scheme for Expected Midgestation 4CV/OFTV Findings**

We classified each case of CHD in terms of expected findings (4CV and OFTVs) on routine midgestation screening sonography. For several reasons, we think that our classification scheme
is superior to others previously described. In contrast to previously proposed binary (dichotomous) classification schemes, our scheme categorized each view as normal, possibly abnormal, or abnormal, recognizing that many defects (such as CoA) may legitimately have variable findings on midgestation screening sonography. Furthermore, consistent with postnatal experience sweeping the image plane from the apical 4CV to the outflow tracts, we distinguished VSDs in the inlet and muscular regions (potentially detectable on the 4CV) from those in the membranous and malalignment regions (potentially detectable on the OFTVs); others have classified all VSDs as abnormalities of either the 4CV or OFTVs. Finally, on the basis of our clinical experience and published postnatal descriptions, we disagree with those who have classified TOF, DORV, and PS as 4CV abnormalities, leading to inflated estimates of the power of the 4CV to detect major forms of CHD. We suggest that abnormalities of the outflow tracts should be categorized as such, despite their potential association in some cases with variable degrees of ventricular disproportion or left axis deviation of the 4CV.

**Infants With CHD: Predominance of Outflow Tract Abnormalities**

Our findings that OFTV abnormalities predominate over 4CV abnormalities have been confirmed by other investigators of all age groups of infants with major forms of CHD. The 6 most common diagnoses in our cohort (TOF, CoA, TGA, HLHS, AVC, and VSDs) have previously been described, with a remarkably similar distribution, among infants requiring invasive intervention during the first 6 months of life and among all fetuses expected to require surgery at some point for CHD. Midgestation screening of these defects would be expected to reveal isolated abnormalities of the OFTVs (TOF and TGA), abnormalities of both the 4CV and OFTVs (HLHS), possible abnormalities of both the 4CV and OFTVs (CoA), abnormalities of either the 4CV or OFTVs (VSDs), or isolated abnormalities.

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**Figure 1.** Specific defects: distribution, timing of diagnosis, and identifiable risk factors. AA indicates aortic atresia; BAVC, balanced AVC; and SV, single ventricle; other abbreviations are as in text and Table 1.
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Figure 2. Expected cardiac findings on screening fetal sonography: distribution, timing of diagnosis, and identifiable risk factors. 

of the 4CV (AVC). In a large study by Hoffman and Kaplan, these same 6 diagnoses, along with aortic and pulmonary valve stenosis (OFTV abnormalities), similarly represented the most common forms of CHD likely to occur in ill neonates or during early infancy.

**Neonatal Intervention for CHD: Predominance of Outflow Tract Abnormalities**

Congenital heart disease typically requires early neonatal intervention because of either (1) closure of the ductus arteriosus in lesions dependent on the ductus for systemic blood flow (severe AS, CoA, IAA, or HLHS), pulmonary blood flow (severe PS, pulmonary atresia [PA], TOF; or DORV), or oxygenation (TGA) or (2) inadequacy of the foramen ovale for oxygenation (TGA) or cardiac output (HLHS). With a delay in diagnosis and treatment, affected neonates may have substantial physiologic impairment and, as a result, avoidable morbidity and mortality.

We and others have found that defects with OFTV abnormalities predominate over 4CV abnormalities among infants requiring early invasive intervention for CHD. Two independent groups found TGA (isolated OFTV abnormality) in 25% of infants who required surgery for CHD during the first 2 months of life. Brown and colleagues found aortic arch obstruction (non-HLHS), TGA, and PA together to represent 73% of infants who required invasive intervention during the first month of life; all of these defects would be expected to have normal 4CVs and abnormal/possibly abnormal OFTVs at midgestation.

Other investigators have studied neonates with CHD who required invasive intervention during the first month of life. During the first 2 weeks of life, TGA and various forms of aortic arch obstruction (including HLHS) together account for almost two-thirds of infants who require invasive intervention. Among those neonates found by Schultz and colleagues to have substantial physiologic impairment during the first 12 hours after delivery (HLHS with a restrictive foramen ovale, TGA, IAA, and PA with an intact ventricular septum), all would have had abnormal OFTVs, but only HLHS and PA with an intact ventricular septum would likely have had abnormal 4CVs. Furthermore, among those who decompensated during the first 12 hours after delivery, 91% had aortic arch obstructions, 6% had TGA, and the remaining 3% had truncus arteriosus; all such neonates would have had abnormal or possibly abnormal OFTVs, whereas only the 58% with HLHS would have been expected to have had abnormal 4CVs.

Although the most common 4CV abnormality that requires early intervention (HLHS) invariably coexists with detectable OFTV abnormalities, other OFTV abnormalities that require early intervention (TGA, TOF; DORV, PA with an intact ventricular septum, truncus arteriosus, severe AS, severe PS, IAA, and CoA) typically coexist with either a normal 4CV (TGA, TOF; DORV, and truncus arteriosus) or a possibly normal 4CV (PA with an intact ventricular septum, severe PS, severe AS, IAA, and CoA). Malalignment VSDs, expected to be seen on the OFTVs but not the 4CV, commonly occur in the presence of AS and

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### Table 3. Isolated and Combined Sensitivities of the 4CV and OFTVs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Abnormal 4CV</th>
<th>Abnormal OFTVs</th>
<th>Abnormal 4CV/OFTVs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Best case scenario (possibly abnormal view classified as abnormal/detectable)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential sensitivity, n (%)</td>
<td>126/200 (63)</td>
<td>182/200 (91)</td>
<td>200/200 (100)</td>
</tr>
<tr>
<td>Actual sensitivity, n (%)</td>
<td>45/200 (23)</td>
<td>59/200 (30)</td>
<td>65/200 (33)</td>
</tr>
<tr>
<td>Actual detection rate, n (%)</td>
<td>45/126 (36)</td>
<td>59/182 (32)</td>
<td>65/200 (33)</td>
</tr>
<tr>
<td><strong>Worst case scenario (possibly abnormal view classified as normal/undetectable)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential sensitivity, n (%)</td>
<td>62/200 (31)</td>
<td>125/200 (63)</td>
<td>153/200 (77)</td>
</tr>
<tr>
<td>Actual sensitivity, n (%)</td>
<td>33/200 (17)</td>
<td>42/200 (21)</td>
<td>58/200 (29)</td>
</tr>
<tr>
<td>Actual detection rate, n (%)</td>
<td>33/62 (53)</td>
<td>42/125 (34)</td>
<td>58/153 (38)</td>
</tr>
</tbody>
</table>

*p* Comparing 4CV with OFTVs.

* Comparing OFT with 4CV/OFTVs (combined evaluation of 4CV and OFTVs).
aortic arch obstruction, defects likely to be ductal dependent and to require early intervention. Moreover, the more common abnormalities of the 4CV (AVC and muscular VSDs), although less likely to be associated with OFTV abnormalities, are also less likely to require early intervention. The less common 4CV abnormalities (TA and Ebstein anomaly) typically occur in conjunction with detectable OFTV abnormalities. In short, compared with 4CV screening, OFTV screening would be expected to miss far fewer cases of major CHD requiring early intervention.

Current Rates of Prenatal Detection of OFTV and 4CV Abnormalities

We and others have found that prenatal detection rates for major CHD disease remain poor regardless of how major CHD is defined: requiring invasive intervention during the first 30 days (20%–44%),4,6 requiring invasive intervention within the first 60 days (27%),31 likely requiring surgery at some point in time (57%),38 or requiring invasive intervention in the first 6 months of life or developing symptoms during the first month (36%).17 Although current approaches to prenatal screening for CHD remain flawed, they remain particularly ineffective for detecting abnormalities of the OFTVs. We and others have found that abnormalities of the 4CV tend to be detected more commonly than abnormalities of the OFTVs.2,4,6,17,20,31,38 Among infants with CHD requiring invasive intervention during the first 6 months, Jaeggi and colleagues2 found a 35% detection rate for 4CV abnormalities compared with a 7% detection rate for OFTV abnormalities. As a prototype example, prenatal detection rates for TGA range from 6% to 25%.6,31,39

In our experience, patients with identifiable risk factors had a higher rate of prenatal diagnosis than those without identifiable risk factors (46% versus 24%). Fetuses identified as at risk for CHD are more likely to undergo a comprehensive fetal cardiac evaluation than those not identified as at risk. Nevertheless, less than half of the patients with identifiable risk factors had CHD detected prenatally. Anecdotally, in our experience, many identifiable risk factors were not prenatally identified, and some fetuses identified as at risk for CHD were not referred for formal fetal echocardiography.

Delayed Postnatal Detection of Major Forms of CHD

At the same time that prenatal detection of major CHD can prevent substantial physiologic impairment during the first 12 to 24 hours after delivery,4 early detection can further minimize morbidity and mortality by preventing inadvertent discharge to home of infants with major CHD who have not yet decompensated from their condition. In our study cohort, 29% of postnatal diagnoses occurred after discharge to home, consistent with the 20% to 55% delayed postnatal diagnosis rates found by other investigators of neonates with major CHD.4,6,7,39 Moreover, neonatal deaths related to undiagnosed CHD account for 10% of infant mortality secondary to CHD and 25% of infants with CHD who die during the first week of life.5

In our experience, defects with an abnormal 4CV and normal OFTVs (predominantly AVC and muscular VSDs) represent the most common category of detectable abnormalities to be missed postnatally, consistent with the findings of Wren and colleagues,7 who found the highest percentage of postnatal diagnoses after discharge to home in infants with AVC. These defects, however, generally do not require early invasive intervention. On the other hand, we also found that 48% of postnatal diagnoses of CoA occurred after discharge to home, and others have found that up to 75% of postnatal diagnoses occurring after discharge to home involved some form of aortic arch obstruction (HLHS, IAA, CoA, or AS).39 In the series by Wren and colleagues2 of infants dying of undiagnosed CHD, all had either substantial outflow tract obstruction (HLHS, CoA, TOF, PS, AS, IAA, or PA) or inadequate mixing (HLHS or TGA). Although some cases of isolated CoA may be missed even with OFTV screening, the difficulty with postnatal detection of ductal-dependent forms of CHD amplifies the importance of prenatal screening of the OFTVs.

Major CHD and Associated Risk Factors

The etiologic association between major CHD and chronic maternal disease,40 fetal exposure to known teratogens,40 and transmissible genetic syndromes41 has been well described. We found an overall rate of identifiable extracardiac risk factors of 38% in our cases, with a chromosomal
abnormality in 10 patients (5%). No major difference in the prevalence of identifiable risk factors was found between 4CV and OFTV abnormalities. Although the prenatal diagnosis of CHD may be prompted by the identification of maternal or familial risk factors, the prenatal recognition of CHD may itself lead to the detection of fetal extracardiac structural or chromosomal abnormalities that may otherwise have gone overlooked. The presence of risk factors in fetuses with isolated 4CV abnormalities (such as trisomy 21 in association with AVC) contributes to the importance of continuing to improve the screening evaluation for 4CV abnormalities.

**Feasibility: 4-Chamber Versus Outflow Tract Screening**

Beyond its perceived ability to detect most cases of major CHD, the 4CV has remained the focus of prenatal screening because 4CV abnormalities have been easier to detect than OFTV abnormalities. However, despite the current challenges and weaknesses of prenatal screening for CHD, those who perform prenatal screening can be trained effectively to evaluate both the 4CV and OFTVs. Although such training will require time, planning, oversight, and additional resources, we agree with others that the training involved to improve prenatal evaluation of the 4CV and, more importantly, OFTVs, would be less costly than universal fetal echocardiography, as recently proposed by Acherman and colleagues.42

**Limitations**

Several limitations of this study merit acknowledgment. First, we assumed that prenatal detection of CHD necessarily leads to accurate prenatal diagnosis of CHD. We think this assumption was valid, given that fetal echocardiography has been shown to be highly accurate in the diagnosis of major forms of CHD, including outflow tract abnormalities.44 Second, in our population of infants with major CHD, the incidence and distribution of identifiable risk factors, as well as the ratio of 4CV to OFTV abnormalities, may differ from that seen prenatally. The prenatal diagnosis of CHD, particularly when associated with chromosomal abnormalities, may lead to termination of pregnancy, and one of the most common isolated 4CV abnormalities (AVC) carries a relatively high association with aneuploidy.41 Third, this retrospective study of 200 infants undergoing heart surgery may have missed cases of severe CHD that failed to undergo surgery. A review of the literature contained herein, however, suggests that our series of 200 patients resembled other series of major forms of CHD, and OFTV abnormalities predominated even among the most severe forms of neonatal CHD that may not have undergone surgery. Fourth, we have found that even routine and effective screening of the 4CV and OFTVs may fail to detect a substantial percentage (up to 23%) of cases of major CHD, including CoA and total anomalous pulmonary venous return. Further work is needed to improve the prenatal detection of these important groups of CHD.

Finally, our method of classifying CHD according to expected findings at midgestation, although similar to previously described classification schemes and based on extensive experience with fetal and neonatal cardiac imaging, has not been prospectively tested or reproduced by others. Moreover, whereas some cases of outflow tract abnormalities have been associated with some degree of left axis deviation of the 4CV, we and others classified these defects as having a normal 4CV. As a result, we may have underestimated the sensitivity of the 4CV to detect some forms of CHD. However, had we classified these defects as having a possibly abnormal 4CV, we would still have found the OFTVs (in the most conservative scenario, wherein potentially abnormal views were classified as normal or undetectable) to have double the sensitivity of the 4CV for prenatally detecting major forms of CHD. We suggest that screening for major forms of CHD involving the outflow tracts should include evaluation of the outflow tracts, rather than relying on what we consider to be an indirect, unreliable, and frequently subtle finding on the 4CV.

**Conclusions**

The 4CV has long represented the essence of prenatal screening for CHD. Increasingly, however, major weaknesses with the 4CV have been described, and the OFTVs have been recommended, when technically feasible, in the
midgestation screening evaluation of low-risk pregnancies. Our findings go further, however, and suggest that the OFTVs, compared with the 4CV, may carry twice the sensitivity for the prenatal detection of major CHD, particularly those lesions most likely to benefit from prenatal detection. Although 4CV screening appears easier and currently more successful and prevalent than OFTV evaluation, both approaches may be performed jointly and effectively with adequate training. We suggest that the crux of prenatal screening for major CHD lies in the OFTVs, not in the 4CV. As a result, we recommend consideration of a paradigm shift in prenatal screening for CHD, away from the 4CV as an end in itself and toward a more consistent and thorough evaluation of the entire heart, starting with the 4CV but emphasizing the importance of obligatory OFTV screening.

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