Echocardiographic Predictors of Aortopulmonary Collaterals in Infants With Tetralogy of Fallot and Pulmonary Atresia

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**OBJECTIVES**

This study was designed to identify echocardiographic predictors of aortopulmonary collaterals (APCs) in infants with tetralogy of Fallot and pulmonary atresia (TOF/PA) and to prospectively validate these predictors.

**BACKGROUND**

In patients with TOF/PA, routine preoperative diagnostic cardiac catheterization is usually performed to determine the presence and distribution of APCs and the anatomy of the branch pulmonary arteries.

**METHODS**

The clinical and diagnostic imaging data of infants with TOF/PA treated between 1990 and 2000 were reviewed. Patients were classified into two groups based on cineangiographic findings: 1) no APCs (n = 34), and 2) ≥1 APCs (n = 59). Echocardiographic variables were examined for their ability to identify patients having ≥1 APCs.

**RESULTS**

Median branch pulmonary artery diameter Z scores were significantly larger in patients without APCs compared with those having ≥1 APCs: −0.56 versus −3.24 for the left pulmonary artery and −0.76 versus −3.46 for the right pulmonary artery (p < 0.001). The presence of a branch pulmonary artery diameter Z score ≤ −2.5 was 88% sensitive and 100% specific for the presence of ≥1 APCs. Detection of APCs by color Doppler was 93% sensitive and 91% specific. A combination of branch pulmonary artery diameter Z score ≤ −2.5 or patent ductus arteriosus diameter ≤ 2 mm was 97% sensitive and 100% specific for the presence of ≥1 APCs. The diagnostic accuracy of these echocardiographic variables was subsequently validated in a prospective study of 11 infants.

**CONCLUSIONS**

Echocardiography is a sensitive and specific test for the detection of ≥1 APCs in infants with TOF/PA. These data can be used to select patients who can undergo complete repair of TOF/PA without further preoperative diagnostic imaging. (J Am Coll Cardiol 2003;41: 852–7) © 2003 by the American College of Cardiology Foundation

In infants with tetralogy of Fallot and pulmonary atresia (TOF/PA), the central pulmonary arteries may be hypoplastic, discontinuous, or absent, and the pulmonary vascular bed may be supplied with blood flow from a patent ductus arteriosus (PDA), from aortopulmonary collaterals (APCs), or from a combination of both (1–3). Surgical management of these infants has evolved over the past 15 years with a tendency towards primary complete repair that includes closure of the ventricular septal defect, right ventricle-to-pulmonary artery patch or conduit, and, when present, recruitment of as many APCs as possible (4). Preoperative knowledge of all sources of pulmonary blood supply and the anatomy of the central pulmonary arteries is therefore essential for surgical planning. Cardiac catheterization has been the standard method for the diagnosis of APCs in infants with TOF/PA (5,6). However, in newborns and young infants with cyanotic congenital heart disease, cardiac catheterization has significant disadvantages, including risks of morbidity, mortality, and subsequent occlusion of blood vessels used for vascular access (7–9). Because of these drawbacks and the likely need for additional postoperative transcatheter diagnostic and interventional procedures such as pulmonary artery dilations, noninvasive preoperative triage of infants with TOF/PA into those with and without APCs is desirable.

Previous reports have shown that two-dimensional and color Doppler echocardiography can accurately delineate the anatomy of the central pulmonary arteries in infants with TOF/PA (10,11). However, the sensitivity, specificity, and predictive values of echocardiography at distinguishing between infants with and without APCs have not been investigated. The present study, therefore, was undertaken to examine the following hypotheses: 1) the extent of APCs is inversely related to the diameters of the central pulmonary arteries, and 2) transthoracic echocardiography can serve as a diagnostic test for the detection of APCs in infants with TOF/PA.

**METHODS**

**Study design and patients.** The study included two components. First, echocardiographic variables predictive of ≥1 APCs were identified in a cross-sectional study of 93 infants with TOF/PA managed between January 1, 1990, and August 1, 2000. Patients were identified using the computerized database of the Cardiovascular Program at Children's Hospital Boston. Patients were included if they met the...
following criteria: 1) age at diagnosis <1 year, 2) cineangiogram available for review, 3) preoperative echocardiogram available for review, and 4) no surgical procedure preceding the initial echocardiogram. In the second phase of the study, the echocardiographic variables identified to be predictive of APCs in the cross-sectional study were validated by prospectively applying them to infants with TOF/PA treated between August 2000 and July 2002. The Committee on Clinical Investigation at Children’s Hospital gave permission to conduct a medical record and database review.

**Echocardiography.** Echocardiograms were performed using several commercially available cardiac ultrasound scanners. The examination protocol included two-dimensional and Doppler imaging from the subxiphoid, apical, parasternal, and suprasternal views, with particular attention to the morphology of the right ventricular outflow tract, main and branch pulmonary arteries, PDA, and evidence of APCs by color Doppler flow mapping. Studies were recorded on 1.27 cm (0.5 in.) super-VHS videocassette tapes. Most echocardiograms were performed under either oral chloral hydrate or intravenous sedation. All preoperative echocardiograms were reviewed offline by an investigator who was unaware of the findings at catheterization, surgery, or postmortem examination. Measurements were performed using electronic calipers on a cardiac ultrasound scanner. To assess interobserver variability, a subset of 14 echocardiograms was randomly selected for review by a second observer who was unaware of the findings of the first investigator.

The diameters of the left pulmonary artery (LPA) and right pulmonary artery (RPA) were measured from two-dimensional images in the parasternal short-axis view as shown in Figure 1. This view was also used to document LPA-to-RPA direct continuity and to determine the presence or absence of a main pulmonary artery. The PDA was imaged from a high parasternal or a suprasternal notch window and its smallest caliber, usually at the pulmonary end, was measured from color Doppler flow images. A PDA was defined as a vessel connecting the undersurface of the aortic isthmus with the pulmonary artery bifurcation. In patients with a right aortic arch, a left-sided PDA may arise from the proximal left subclavian artery ending at the pulmonary artery bifurcation. An APC was defined as a vessel that connects the descending aorta or one of the brachiocephalic arteries with a pulmonary termination ei-
ther at the distal branch pulmonary arteries or within the lung parenchyma. All transthoracic and subcostal views were used to detect APCs by color Doppler flow mapping.

The following variables were recorded: demographics; weight; height; body surface area (BSA); the smallest diameters of the LPA, RPA, and PDA; presence or absence of a main pulmonary artery; presence or absence of APCs by color Doppler; and whether the proximal branch pulmonary arteries were in direct continuity. The diameters of the branch pulmonary arteries were adjusted to BSA and were expressed as Z scores. The lowest Z score of the group was assigned to patients with an absent branch pulmonary artery. Normal control values were obtained from 138 subjects without known heart disease whose age ranged from birth to 18 years and whose BSA ranged from 0.18 to 2.1 m².

Catheterization. An experienced pediatric interventional cardiologist, blinded to the echocardiographic findings, reviewed the cineangiograms. Cardiac catheterization findings were used as the reference standard to classify patients into one of the following groups: 1) no APCs, and 2) ≥1 APCs.

Statistical analysis. Continuous variables are presented as median values and range. Demographic and echocardiographic variables were compared for patients in the two outcome groups using the Wilcoxon rank-sum test for continuous variables and Fisher exact test for categorical variables. Sensitivity, specificity, and positive and negative predictive values with 95% confidence limits were calculated to assess the ability of echocardiography to identify patients having ≥1 APCs. Interobserver reliability of LPA and RPA measurements was analyzed using a paired t test. A receiver-operator characteristic (ROC) curve was used to identify which pulmonary artery Z score provided the best combination of sensitivity and specificity for predicting the presence of APCs, and also to quantify the predictive power of additional echocardiographic variables. A commercially available statistical package was used for data analysis (STATA version 6.0, College Station, Texas).

RESULTS

Cross-sectional study. Of the 93 patients who fulfilled inclusion criteria, 34 (37%) were classified as having no APCs and 59 (63%) were classified as having ≥1 APCs. Their demographic characteristics and the reference standards used to classify them are summarized in Table 1.

Echocardiographic variables. Figure 2 shows the Z scores of the smallest diameters of the branch pulmonary arteries in patients with no APCs compared with those having ≥1 APCs. The median LPA diameter Z score was significantly larger in patients without APCs compared with those having ≥1 APCs.

| Table 1. Demographic Characteristics and Reference Standards in 93 Infants With TOF/PA |
|-----------------------------------------------|-------------------|---------------------|
| No APCs (n = 34) | ≥1 APCs (n = 59) | p Value |
| Median age at echo (days) (range) | 1 (0.5–129) | 57 (0.5–323) | < 0.001 |
| Median weight (kg) (range) | 3.0 (1.0–5.0) | 4.2 (1.3–8.0) | < 0.001 |
| Median BSA (m²) (range) | 0.21 (0.10–0.29) | 0.25 (0.13–0.40) | < 0.001 |
| Male gender (%) | 59% | 49% | 0.40 |
| Reference standard | | | |
| Preoperative catheterization | 19 (56%) | 51 (86%) | 0.002 |
| Postoperative catheterization | 15 (44%) | 8 (14%) | |

APCs = aortopulmonary collaterals; BSA = body surface area; TOF/PA = tetralogy of Fallot/pulmonary atresia.

Figure 2. Comparison of branch pulmonary artery diameter Z score between patients with ≥1 aortopulmonary collaterals (APCs) and those without APCs. Circles represent individual data points. The median values and the corresponding 10th to 90th percentiles are shown for each group. LPA = left pulmonary artery; RPA = right pulmonary artery.
having ≥1 APCs (−0.56 [−2.30 to 1.07] vs. −3.24 [−4.74 to 3.64], p < 0.001), as was the median RPA diameter Z score (−0.76 [−2.37 to 0.54] vs. −3.46 [−5.53 to 0.62], p < 0.001). Confluent branch pulmonary arteries were demonstrated by echocardiography in all patients having no APCs. One or both branch pulmonary arteries were not visualized in 21 (36%) of the 59 patients with ≥1 APCs. Branch pulmonary artery diameter Z score 2.5 had ≥1 APCs. Branch pulmonary artery diameter Z score ≤−2.5, PDA diameter ≤2 mm, and evidence for APCs by color Doppler flow mapping were all highly sensitive and specific at identifying patients having ≥1 APCs (area under the ROC curve ≥0.92). A combination of individual variables yielded a better predictive profile than each variable separately. The area under the ROC curve was highest (0.98) for the combination of branch pulmonary artery diameter Z score ≤−2.5 or a PDA diameter ≤2 mm. The same prediction model was found also to be sensitive and specific in the subgroup of patients with confluent branch pulmonary arteries, with an area under the ROC curve of 0.89 for branch pulmonary artery diameter Z score ≤−2.5, 0.92 for evidence for APCs by color Doppler, and 0.94 for a PDA diameter ≤2 mm.

**Prospective validation study.** Of the 11 infants with TOF/PA who were managed between August 2000 and July 2002 and who had either a catheterization or magnetic resonance angiography, 5 (45%) had no APCs based on reference standards. These five patients were correctly identified by LPA and RPA diameter Z scores >−2.5; all had a PDA ≥2 mm, and four had no evidence of APCs by color Doppler. Of the six (55%) patients with ≥1 APCs by reference standards, all had APCs by color Doppler, all had a PDA ≤2 mm, and five met the criteria of one or both branch pulmonary artery diameter Z scores ≤−2.5. Using the combination of branch pulmonary artery diameter Z score ≤−2.5 or PDA ≤2 mm to predict a patient having ≥1 APCs, all 11 patients were correctly classified.

**DISCUSSION**

The results of this study demonstrate that in unoperated infants with TOF/PA, transthoracic echocardiography can

Figure 3. Receiver-operator characteristic curve of branch pulmonary artery diameter Z score. Left or right pulmonary artery diameter Z score ≤−2.5 had the maximum sensitivity and specificity for identifying patients having ≥1 aortopulmonary collaterals.
Table 2. Diagnostic Test Characteristics of Echocardiographic Variables (95% Confidence Intervals)

<table>
<thead>
<tr>
<th>Predictor of ≥1 APCs</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Area Under ROC Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5</td>
<td>88 (77, 95)</td>
<td>100 (90, 100)</td>
<td>100 (93, 100)</td>
<td>83 (68, 93)</td>
<td>0.94</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2</td>
<td>95 (86, 99)</td>
<td>82 (65, 93)</td>
<td>90 (80, 96)</td>
<td>90 (74, 98)</td>
<td>0.89</td>
</tr>
<tr>
<td>APCs by color Doppler</td>
<td>93 (83, 98)</td>
<td>91 (76, 98)</td>
<td>95 (85, 99)</td>
<td>89 (73, 97)</td>
<td>0.92</td>
</tr>
<tr>
<td>PDA diameter ≤ 2 mm</td>
<td>93 (83, 98)</td>
<td>100 (89, 100)</td>
<td>100 (93, 100)</td>
<td>89 (74, 97)</td>
<td>0.97</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5 or PDA diameter ≤ 2 mm</td>
<td>97 (88, 100)</td>
<td>100 (89, 100)</td>
<td>100 (94, 100)</td>
<td>94 (80, 99)</td>
<td>0.98</td>
</tr>
<tr>
<td>PDA diameter ≤ 2 mm or APCs by color Doppler</td>
<td>97 (88, 100)</td>
<td>91 (75, 98)</td>
<td>95 (86, 99)</td>
<td>94 (79, 99)</td>
<td>0.94</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5 or APCs by color Doppler</td>
<td>97 (88, 100)</td>
<td>91 (76, 98)</td>
<td>95 (86, 99)</td>
<td>94 (80, 99)</td>
<td>0.93</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5 or APCs by color Doppler or PDA diameter ≤ 2 mm</td>
<td>98 (91, 100)</td>
<td>91 (75, 98)</td>
<td>95 (86, 99)</td>
<td>97 (83, 100)</td>
<td>0.95</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5 and PDA diameter ≤ 2 mm</td>
<td>86 (75, 94)</td>
<td>100 (89, 100)</td>
<td>100 (93, 100)</td>
<td>80 (64, 91)</td>
<td>0.93</td>
</tr>
<tr>
<td>PDA diameter ≤ 2 mm and APCs by color Doppler</td>
<td>89 (78, 96)</td>
<td>100 (89, 100)</td>
<td>100 (93, 100)</td>
<td>84 (69, 94)</td>
<td>0.95</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5 and APCs by color Doppler</td>
<td>84 (73, 93)</td>
<td>100 (90, 100)</td>
<td>100 (93, 100)</td>
<td>79 (64, 90)</td>
<td>0.92</td>
</tr>
<tr>
<td>Branch pulmonary artery diameter Z ≤ −2.5 and APCs by color Doppler or PDA diameter ≤ 2 mm</td>
<td>84 (72, 92)</td>
<td>100 (89, 100)</td>
<td>100 (93, 100)</td>
<td>78 (62, 89)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

APCs = aortopulmonary collaterals; NPV = negative predictive value; PDA = patent ductus arteriosus; PPV = positive predictive value; ROC = receiver-operator characteristic.

be used to differentiate between patients with and without APCs. Specifically, branch pulmonary artery diameter Z score ≤ −2.5, PDA diameter ≤ 2 mm, and evidence of APCs by color Doppler flow mapping were each sensitive and specific tests with an area under the ROC curve ranging from 0.92 to 0.97. The test performance of transthoracic echocardiography further improved when a branch pulmonary artery diameter Z score ≤ −2.5 or PDA diameter ≤ 2 mm were combined, yielding 97% sensitivity and 100% specificity.

The concept that branch pulmonary artery diameter is inversely related to the extent of APCs in TOF/PA has been previously demonstrated in an autopsy study (12). Acherman et al. (11) demonstrated that patients having a PDA had larger branch pulmonary arteries than patients having no PDA and that the main sources of pulmonary blood flow in this disease can be determined by echocardiography. In a study based on cineangiography, Hadjo et al. (13) found a significantly higher McGoon ratio (ratio of the combined diameters of the branch pulmonary artery divided by the diameter of the descending aorta at the level of the diaphragm) in patients having pulmonary blood supply solely through a PDA compared with patients having ≥1 APCs. The usefulness of color Doppler echocardiography in the assessment of APCs in infants with TOF/PA has been previously demonstrated (10,11). Smyllie et al. (10) reported that the use of color Doppler flow mapping resulted in improved sensitivity of the definition of pulmonary blood supply compared to two-dimensional echocardiography alone. However, they also found that color Doppler flow mapping falsely suggested the presence of APCs in 16% of patients who were found by cineangiography to have no APCs. The results of the present study are in agreement with those of Smyllie et al., with 9% of patients without APCs by reference standards having being misidentified (false positive). These observations likely reflect the highly sensitive nature of color Doppler flow mapping. It is possible that flow signals from bronchial and intercostal arteries may have been confused with APCs.

**Clinical implications.** The continued trend towards primary complete repair of TOF/PA in infancy has reinforced the importance of accurate delineation of all sources of pulmonary blood supply prior to surgery (4). Cardiac catheterization with X-ray angiography has been routinely performed before surgical repair (4–6). The results of this study indicate that transthoracic echocardiography can reliably identify infants with TOF/PA who are unlikely to have APCs and have confluent central pulmonary arteries. Previous experience indicates that these patients can undergo surgical repair without a preoperative cardiac catheterization (14). For patients identified by transthoracic echocardiography as being at risk for APCs and/or branch pulmonary artery discontinuity, magnetic resonance angiography provides a safe and accurate noninvasive alternative to catheterization (15,16). In our opinion, use of cardiac catheterization can be limited to the minority of patients with excessive APCs and pulmonary overcirculation in whom preoperative coil occlusion of the collaterals is deemed necessary.

The diagnostic approach described here for infants with TOF/PA has several advantages that are worth noting. The majority of these patients undergo cardiac catheterization later in life, including interventional procedures such as balloon dilation or stent placement for relief of pulmonary artery stenosis (17,18). Avoiding a preoperative catheterization has several potential advantages including reduced risks of morbidity and mortality, avoiding ionizing radiation exposure, preserving vascular access for future interventional catheterization procedures, and lower cost (7–9,19).
Study limitations. The confounding effect of prostaglandin E on PDA and branch pulmonary artery diameters could not be reliably assessed. For example, in a number of patients who underwent an echocardiogram during the first 1 to 2 days of life, prostaglandin E was started during the examination once the presence of pulmonary atresia was established. We also recognize the often long and tortuous nature of the ductus arteriosus in TOF/PA. We therefore chose to measure its caliber at the pulmonary end because measurements in this location are likely more reproducible. However, other variables such as length also influence the amount of pulmonary blood flow through the ductus arteriosus.

Conclusions. Echocardiography is a sensitive and specific diagnostic test for the presence of APCs in infants with TOF/PA. The presence of a branch pulmonary artery diameter Z score ≤ −2.5 or a PDA diameter ≤ 2 mm is the most sensitive and specific test for the presence of ≥1 APCs. Infants with TOF/PA who have confluent branch pulmonary arteries with a minimal diameter Z score > −2.5 and a minimal PDA diameter > 2 mm by echocardiography are unlikely to have APCs and can undergo surgical repair without a preoperative cardiac catheterization.

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REFERENCES
