Aortic Root Dilatation in Adults with Surgically Repaired Tetralogy of Fallot
A Multicenter Cross-Sectional Study

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Background—Although aortic root pathology has been described in patients with tetralogy of Fallot, the scope of the problem remains poorly defined. We sought to determine the prevalence and predictors of aortic root dilatation in adults with repaired tetralogy of Fallot.

Methods and Results—A multicenter cross-sectional study was conducted with standardized reassessment of echocardiographic parameters in 474 adults (≥18 years) with surgically repaired tetralogy of Fallot or pulmonary atresia with ventricular septal defect. The aortic root was measured in a parasternal long-axis view, in diastole, at the level of the sinus of Valsalva. Prevalence and predictors of an absolute diameter ≥40 mm and of an observed-to-expected ratio >1.5 were assessed. The aortic root dimension was ≥40 mm in 28.9% (95% confidence interval, 26.9%–30.9%). In multivariate analyses, the only independently associated factor was male sex (odds ratio, 4.48; 95% confidence interval, 1.55–12.89; P=0.006). The prevalence of an observed-to-expected aortic root dimension ratio >1.5 was 6.6% (95% confidence interval, 5.3%–7.9%). It was associated with pulmonary atresia and moderate or severe aortic regurgitation in univariate analyses, but no independent predictor was identified. The side of the aortic arch was not associated with aortic root dimension. The prevalence of moderate or severe aortic regurgitation was 3.5% (95% confidence interval, 2.7%–4.2%).

Conclusions—Although nearly one third of adults with repaired tetralogy of Fallot have an aortic root diameter ≥40 mm, the prevalence of a dilated aortic root, when defined by an indexed ratio of observed-to-expected values, is low. Similarly, moderate or severe aortic regurgitation is uncommon. (Circulation. 2013;127:172-179.)

Key Words: aorta • aortic regurgitation • congenital • heart defects • tetralogy of Fallot

Tetralogy of Fallot (TOF) is the most prevalent cyanotic congenital heart defect.1 At birth, the aorta overrides a ventricular septal defect, which directs flow from the right ventricle toward the aortic root. Increased and altered flow through the overriding aorta and an uneven sharing of conotruncal tissue between the aorta and pulmonary artery may contribute to aortic root dilatation. Indeed, it has been suggested that prompt surgical repair of TOF in infancy may prevent such dilatation.2 Moreover, histological studies of aortas in patients with TOF have reported striking similarities to the aortas of patients with Marfan syndrome.3 The aortic wall is characterized by fragmentation of elastic lamellae, medionecrosis, muscle disarray, and fibrosis,3 with aortopathy detected as early as infancy.3

Clinical Perspective on p 179

Despite the concern that TOF patients may harbor an aortopathy that can lead to aortic regurgitation, aortic aneurysms,
and, potentially, aortic dissection, the scope of the problem remains uncertain. Prevalence estimates of aortic root dilatation have ranged from 15% to 87% with the use of various criteria. Moderate to severe aortic regurgitation has also been reported in up to 12.5% of adults with TOF and dilated aortic roots. The incidence of aortic dissection and surgical intervention remains unknown. Moreover, features associated with aortic dilatation are not fully understood. We therefore sought to determine the prevalence and predictors of aortic root dilatation in adults with repaired TOF.

Material and Methods

Patient Population
The study population comprised adults (≥18 years of age) with surgically repaired TOF or pulmonary atresia with ventricular septal defect, identified by the participating centers from the Alliance for Adult Research in Congenital Cardiology (see the Appendix in the online-only Data Supplement). Patients were required to have had a transthoracic echocardiogram and an outpatient visit within 2 years preceding data collection, which was conducted between September 2007 and October 2008. Patients were excluded if they had coexisting complex congenital abnormalities (single ventricle physiology, Fontan operation, transposition of the great arteries), connective tissue disorder, or uninterpretable echocardiographic images, as determined by each site investigator. Patients with atrioventricular canal defects were not excluded.

Study Design
A multicenter cross-sectional study was conducted with standardized reassessment of all echocardiographic parameters. Demographic, clinical, and echocardiographic data were collected on preprinted case report forms. Deidentified data were sent to a single center for consolidation and review for internal consistency and validity. Data queries were issued to each center for missing, incomplete, or inconsistent information, illegible entries, invalid formats, and invalid codes to resolve discrepancies on a per-patient basis. The study was approved by each participating center’s institutional review board. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the article as written.

Demographic and Clinical Data
Details regarding demographic variables, anatomy, surgical and obstetric history, and medical therapy were collected. Demographic variables included date of birth, sex, height, weight, body surface area, and blood pressure. Anatomic and surgical characteristics included pulmonary atresia, sidedness of the aortic arch, number and type of previous palliative shunts, transannular patches, and conduits.

Echocardiographic Data
Echocardiographic parameters were reviewed and reassessed with a standardized protocol and uniform definitions. Left ventricular (LV) internal dimensions (diastole and systole) were determined in parasternal long-axis views. Color, continuous wave, and pulse-wave Doppler data for all valves were recorded.

Aortic valve regurgitation was quantified as (0) absent, (1) mild (regurgitant jet width/LV outflow tract diameter <30%, no flow reversal in the descending aorta, pressure half-time >400 ms), (2) moderate (regurgitant jet width/LV outflow tract diameter, 30%–59%; early flow reversal in descending aorta or pressure half-time, 251 ms–399 ms), or (3) severe (regurgitant jet width/LV outflow tract diameter >60%; holodiastolic reversal in descending aorta or pressure half-time <250 ms).

Aortic Root Dilatation
The aortic root was measured at the level of the sinus of Valsalva and proximal ascending aorta in diastole, in a parasternal long-axis view. Linear measurements were taken from leading edge to leading edge on bidimensional echocardiographic images. Aortic root size was considered as an absolute value and relative to the expected diameter for body size. In absolute terms, a sinus of Valsalva diameter of ≥40 mm was considered indicative of aortic root dilatation. Aortic root dilatation was also defined as a ratio of observed-to-expected aortic root diameter of >1.5, according to standard normograms for aortic root size in healthy adults, as adapted from Roman et al and indexed to body surface area and age.

Statistical Analysis
Normally distributed continuous variables are presented as mean±standard deviation and nonnormally distributed continuous variables as median and interquartile range (25th, 75th percentile). Normality was assessed by the Shapiro-Wilk test and normal probability plot. Categorical variables are presented as frequency (percentage). Comparisons of continuous variables between patients with and without aortic root dilatation were performed by using independent Student t tests or Wilcoxon rank sum tests, depending on their distribution. Comparisons of categorical variables in patients with and without aortic root dilatation were performed by using Fisher exact tests. Relationships between continuous variables were assessed by using Pearson or Spearman correlation coefficients, depending on their distribution. Predictors of aortic root dilatation were assessed in univariate and multivariate logistic regression models. Variables associated with probability values <0.2 in univariate analyses were included in multivariate models. Additional factors potentially associated with aortic root dilatation based on substantive knowledge were entered in multivariate logistic regression models provided that the ratio between outcome events (ie, number of patients with dilated aortic roots) and exposure variables remained >10:1. Analyses were performed separately according to the 2 definitions of aortic root dilatation (ie, sinus of Valsalva diameter ≥40 mm and ratio of observed-to-expected aortic root diameter >1.5). All probability values were 2-sided. The threshold for statistical significance was set at 0.05. Statistical analyses were performed using SAS software version 9.2 (SAS Institute, Inc; Cary, NC).

Results

Baseline Characteristics
The Figure provides an overview of the study population. From the 556 patients enrolled in the Alliance for Adult
Research in Congenital Cardiology cross-sectional study, 546
adults with TOF or pulmonary atresia/ventricular septal defect
had echocardiographic assessment of aortic regurgitation. Of
the 474 patients with aortic root diameter measurements at the
level of the sinus of Valsalva, 333 had body surface area data
available for indexing. Preoperative echocardiographic stud-
ies were sought and retained for analysis for 6 patients with
previous aortic valve repair or replacement and for 2 patients
with previous aortic root replacement. Preoperative echocar-
diograms were not available for 3 patients, who were excluded
from analysis.

Baseline characteristics according to the presence or
absence of aortic root dilatation are summarized in Tables 1
and 2. Patients with an aortic root dimension ≥40 mm at the
sinus of Valsalva (Table 1) were older and more likely to be
male, have hyperlipidemia, and receive angiotensin-converting
enzyme inhibitors. Corrective surgery was performed later
in life, and systemic-to-pulmonary shunts were present for a
longer period of time. Larger LV end-diastolic and right ven-
tricular outflow tract diameters were observed. Patients with
an observed-to-expected aortic root diameter >1.5 (Table 2)
were likewise older at the time of corrective surgery (with a
nonsignificantly longer shunt duration), and trended toward
a higher prevalence of pulmonary atresia ($P=0.05$) and moder-
ate or severe aortic regurgitation ($P=0.06$).

Prevalence of Aortic Root Dilatation and Aortic
Regurgitation

The prevalence of aortic root dilatation differed markedly
according to the definition used. If an absolute cutoff value of
≥40 mm at the sinus of Valsalva was used to define a dilated
aortic root, the prevalence was 28.9% (137 of 474 patients;
95% confidence interval [CI], 26.9%–30.9%). In contrast, an
observed-to-expected aortic root diameter ratio cutoff value
>1.5 yielded a prevalence estimate of 6.6% (22 of 333 patients;
95% CI, 5.3%–7.9%). Overall, 46 patients (prevalence, 9.7%;
95% CI, 7.0%–12.4%) had an aortic root diameter ≥45 mm,
and 11 patients (prevalence, 2.3%, 95% CI, 1.0%–3.7%) had
an aortic root diameter ≥50 mm. The diastolic diameter of the

### Table 1. Baseline Characteristics According to Aortic Root Diameter

<table>
<thead>
<tr>
<th>Aortic Root Diameter at Sinus of Valsalva</th>
<th>≥40 mm (n=137)</th>
<th>&lt;40 mm (n=337)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>42±13</td>
<td>34±11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>93 (68)</td>
<td>126 (37)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.9 (0.2)</td>
<td>1.7 (0.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aortic root diameter, mm*</td>
<td>43 (41, 46)</td>
<td>34 (31, 36)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age at repair, y*</td>
<td>7 (5, 13)</td>
<td>5 (2, 7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration of shunt, y*</td>
<td>7 (4, 11)</td>
<td>4 (3, 7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Central shunt, n (%)</td>
<td>18 (13)</td>
<td>32 (10)</td>
<td>0.25</td>
</tr>
<tr>
<td>LV end-diastolic diameter, mm</td>
<td>49±7</td>
<td>45±6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pulmonary atresia, n (%)</td>
<td>14 (10)</td>
<td>24 (7)</td>
<td>0.27</td>
</tr>
<tr>
<td>Aortic regurgitation ≥ moderate, n (%)</td>
<td>9 (7)</td>
<td>10 (3)</td>
<td>0.12</td>
</tr>
<tr>
<td>Previous pregnancy, n (% of women)</td>
<td>24 (62)</td>
<td>93 (50)</td>
<td>0.22</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>23 (17)</td>
<td>38 (12)</td>
<td>0.13</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>5 (4)</td>
<td>12 (4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>27 (20)</td>
<td>26 (8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking history, n (%)</td>
<td>26 (21)</td>
<td>42 (14)</td>
<td>0.08</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>41 (30)</td>
<td>58 (17)</td>
<td>0.003</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor, n (%)</td>
<td>36 (27)</td>
<td>33 (10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>β-Blocker, n (%)</td>
<td>46 (34)</td>
<td>85 (26)</td>
<td>0.09</td>
</tr>
<tr>
<td>Right aortic arch, n (%)</td>
<td>58 (56)</td>
<td>159 (61)</td>
<td>0.35</td>
</tr>
<tr>
<td>RVOT diameter, mm</td>
<td>36±10</td>
<td>32±9</td>
<td>0.003</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; ACE, angiotensin-converting enzyme; and RVOT, right ventricular outflow tract.

*Continuous nonnormally distributed variables are summarized by median and interquartile range (25th, 75th percentile).
ascending aorta was available in 252 patients, 47 of whom had an ascending aorta ≥40 mm, yielding a prevalence estimate of 18.7%; 95% CI, 13.8%–23.5%.

Aortic regurgitation data were complete in nearly all patients (n=546, >99%). The prevalence of moderate or severe aortic regurgitation was 3.5% (n=19; 95% CI, 2.7%–4.2%).

Factors Associated with Aortic Root Dilatation

A weak but highly significant correlation (Spearman rho=0.28; P<0.0001; n=337) was observed between the sinus of Valsalva diameter and body surface area. No correlation between aortic root diameter and systolic blood pressure was identified (Spearman rho=0.05; P=0.51; n=188). Factors associated with aortic root dilatation according to both definitions are listed in Table 3. Corresponding multivariate analyses are summarized in Table 4. The only factor independently associated with an aortic root diameter ≥40 mm was male sex (odds ratio, 4.48; 95% CI, 1.55–12.89; P=0.006). Selection of covariates for the model was performed as described above. Pulmonary atresia was entered in the model despite its probability value of 0.27 based on substantive previous knowledge.5 No significant multivariate association was identified for aortic dilatation defined by an observed-to-expected aortic diameter ratio >1.5.

Discussion

Surgeries for TOF have increasingly included intervention on the ascending aorta,17 because a potential, but unquantified, risk for aortic dissection was recognized in some patients with an enlarged aorta.9,10 To our knowledge, this Alliance for Adult Research in Congenital Cardiology study is the largest to assess the prevalence and predictors of aortic root dilatation in patients with TOF. When an absolute threshold of 40 mm was used to define a dilated aortic root, a prevalence of 28.9% was observed. This finding is of clinical importance, because management guidelines and surgical indications are based on absolute aortic root diameters.18 For example, the American College of Cardiology/American Heart Association thoracic aorta guidelines suggest that patients with aortic root diameters between 35 and 44 mm undergo annual aorta-imaging studies.18 Guidelines also recommend yearly imaging studies in patients with bicuspid aortic valves and a sinus of Valsalva or ascending aorta diameter >40 mm.19 Moreover, studies that have used absolute cutoff values to define aortic dilatation reported lower risks of dissection or rupture for aneurysms <40 mm, although 40% of patients who presented with dissections had aortic diameters <50 mm.20–22

Proposed techniques for measuring the aortic root vary according to the imaging modality. We reported leading edge to leading edge measurements for consistency with previous studies and to allow comparisons of aortic root diameters with expected values derived from normograms based on these measurements.16 National guidelines suggest measuring the aortic diameter at reproducible anatomic landmarks, perpendicular to the axis of blood flow.18 External diameters are recommended for computed tomography and magnetic resonance imaging, and internal diameters for echocardiography.18
Because the aortic root can be asymmetrical, the widest diameter, typically at the midsinus level, should be measured. An alternative method to measuring the aortic root by magnetic resonance imaging relies on a short-axis view at the sinus level obtained from 2 orthogonal long-axis views of the LV outflow tract. Root dimensions may be measured from cusp to cusp or from cusp to commissure, producing 3 diameters that are subsequently averaged.

The optimal definition for aortic root dilatation remains controversial. Normal aortic size is determined by age, sex, body size, location of the measurement, and robustness of the imaging modality. Consequently, normograms and z scores that adjust for age and body size are thought to more accurately identify aortic root dilatation. In the current study, body surface area correlated with aortic root diameter in the patients with TOF population, but the correlation was weaker than reported in the general population. Body surface area was not independently associated with an aortic root ≥ 40 mm.

z scores may underestimate aortic dilatation, particularly in larger patients. In addition to the absolute cutoff value ≥ 40 mm, we, therefore, also considered an alternative previously proposed definition of aortic root dilatation based on an observed-to-expected aortic root diameter ratio >1.5.5

With such a definition, the prevalence of aortic root dilatation was found to be 6.6%, considerably lower than the 14.8% rate reported by Niwa et al with the use of the same criterion. This discrepancy may reflect, in part, methodological differences such as the larger sample size and systematic reassessment of echocardiographic parameters in the current study. Differences in study populations cannot be excluded because the baseline characteristics for the 216 patients in Niwa et al’s study were not reported. On the whole, patients with a dilated aortic root in our study were older than in previous observational studies such that aortic root size may be influenced to a greater extent by acquired risk factors such as hypertension, hyperlipidemia, and atherosclerosis, which were associated with aortic root dilatation in univariate analysis.

Our main results, as corroborated by other groups, show that the prevalence of aortic root dilatation is low, when defined by an observed-to-expected aortic root diameter ratio >1.5. To place these results in perspective, the prevalence of ascending aortic dilatation >40 mm by echocardiography in adults with a bicuspid aortic valve was 15% at baseline and increased to 39% after a follow-up of 15 years, which is comparable with the prevalence that we observed in patients with TOF. In contrast, the prevalence of aortic root dilatation using similar criteria in adults with Marfan syndrome has been reported to be 60% to 80%.

Predictors of Aortic Root Dilatation
Factors associated with an aortic dimension ≥40 mm at the sinus of Valsalva reported by previous studies include a right aortic arch, longer time from palliation to corrective surgery, and an increased LV end-diastolic diameter. We found no correlation between aortic root diameter and systolic blood pressure.

Table 3. Factors Associated With a Dilated Aortic Root in Univariate Analyses

<table>
<thead>
<tr>
<th>Factor</th>
<th>Sinus of Valsalva ≥40 mm OR (95% CI)</th>
<th>P</th>
<th>Observe-to-Expected &gt;1.5 OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per year</td>
<td>1.06 (1.04–1.07)</td>
<td>&lt;0.0001</td>
<td>1.01 (0.97–1.04)</td>
<td>0.65</td>
</tr>
<tr>
<td>Male sex</td>
<td>3.54 (2.32–5.39)</td>
<td>&lt;0.0001</td>
<td>1.70 (0.71–4.09)</td>
<td>0.24</td>
</tr>
<tr>
<td>Body surface area, per m²</td>
<td>15.2 (4.88–47.27)</td>
<td>&lt;0.0001</td>
<td>...*</td>
<td>...*</td>
</tr>
<tr>
<td>Age at repair, per year</td>
<td>1.06 (1.04–1.09)</td>
<td>&lt;0.0001</td>
<td>1.02 (0.98–1.05)</td>
<td>0.41</td>
</tr>
<tr>
<td>Duration of shunt, per year</td>
<td>1.08 (1.04–1.13)</td>
<td>&lt;0.0001</td>
<td>1.01 (0.95–1.07)</td>
<td>0.82</td>
</tr>
<tr>
<td>Central shunt</td>
<td>1.44 (0.78–2.67)</td>
<td>0.24</td>
<td>0.76 (0.17–3.41)</td>
<td>0.72</td>
</tr>
<tr>
<td>LV end-diastolic diameter, per mm</td>
<td>1.11 (1.07–1.15)</td>
<td>&lt;0.0001</td>
<td>1.02 (0.95–1.09)</td>
<td>0.68</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>1.47 (0.74–2.94)</td>
<td>0.27</td>
<td>3.04 (1.04–8.88)</td>
<td>0.04</td>
</tr>
<tr>
<td>Aortic regurgitation ≥ moderate</td>
<td>2.29 (0.91–5.78)</td>
<td>0.08</td>
<td>4.25 (1.09–16.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Previous pregnancy</td>
<td>0.52 (0.32–0.87)</td>
<td>0.01</td>
<td>0.91 (0.33–2.56)</td>
<td>0.86</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.57 (0.90–2.76)</td>
<td>0.12</td>
<td>1.67 (0.53–5.20)</td>
<td>0.38</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.01 (0.35–2.91)</td>
<td>0.99</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>2.88 (1.61–5.16)</td>
<td>0.0004</td>
<td>0.33 (0.04–2.54)</td>
<td>0.29</td>
</tr>
<tr>
<td>Smoking history</td>
<td>1.66 (0.96–2.86)</td>
<td>0.07</td>
<td>1.03 (0.29–3.69)</td>
<td>0.97</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>2.04 (1.29–3.24)</td>
<td>0.003</td>
<td>0.88 (0.29–2.68)</td>
<td>0.81</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>3.22 (1.91–5.44)</td>
<td>&lt;0.0001</td>
<td>0.84 (0.24–2.94)</td>
<td>0.78</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>1.49 (0.97–2.30)</td>
<td>0.07</td>
<td>0.76 (0.27–2.13)</td>
<td>0.61</td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>0.80 (0.51–1.27)</td>
<td>0.34</td>
<td>0.81 (0.29–2.24)</td>
<td>0.68</td>
</tr>
<tr>
<td>RVOT diameter, per mm</td>
<td>1.04 (1.01–1.06)</td>
<td>0.003</td>
<td>1.02 (0.97–1.07)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

OR indicates odds ratio; CI, confidence interval; LV, left ventricular; ACE, angiotensin-converting enzyme; RVOT, right ventricular outflow tract; and N/A, not applicable because of the absence of patients with diabetes mellitus and an observed-to-expected aortic root dimension ratio >1.5.

*Adjustment for body surface area is included in the definition of aortic root dilatation.
pressure, although antihypertensive pharmacological agents may have mitigated such an association (Table 1). In our multivariate analysis, male sex was the only factor independently associated with aortic root size. The association between aortic arch sidedness and aortic root dilatation was not statistically significant in univariate analysis. In patients with and without an aortic root dimension ≥40 mm, the prevalence of a right aortic arch was 55.8% and 61.2%, respectively (P=0.35). These prevalence rates are comparable to reported estimates by Niwa et al.5 However, the observed overall prevalence of a right-sided aortic arch was higher than previously reported in TOF in general (≈25%).28

Pulmonary atresia and moderate or severe aortic regurgitation were associated with an observed-to-expected sinus of Valsalva diameter >1.5 by univariate analysis. Although analyses were limited by the lower than expected prevalence of aortic root dilatation using this criterion (ie, 6.6%), these associations tended toward significance in the multivariate model (odds ratio for pulmonary atresia 2.17, 0.69–6.88, P=0.19; odds ratio for moderate or severe aortic regurgitation 0.95, 0.17–5.45, P=0.96) However, the observed overall prevalence of a right-sided aortic arch was higher than previously reported in TOF in general (≈25%).28

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It may be hypothesized that, in patients with pulmonary atresia, excessive flow through the aorta before repair may favor aortic growth and dilatation. However, Tan et al4 observed no correlation between grade 2 or 3 histological changes in the aortic wall and pulmonary atresia, male sex, right aortic arch, or previous palliative surgery. Another potential explanation for aortic root dilatation in patients with pulmonary atresia includes the disproportionate sharing of conotruncal tissue between aorta and pulmonary artery.29 Measures reflecting the distribution of conotruncal tissue may include the pre-repair oxygen saturation and pulmonary annulus diameter. It may also be of interest to explore a potential association between aortic root and pulmonary artery dilatation, as a marker of the potential for both great arteries to enlarge.

Age at repair was not an independent predictor of aortic root dilatation in multivariate analysis. It has been suggested that earlier repair may prevent aortic root dilatation in TOF patients.2 In our cohort, the median age at repair was between 5 and 9 years in all subgroups (Tables 1 and 2). We cannot exclude the possibility that repair within the first year of life may have an impact on subsequent aortic root dilatation.

Finally, the overall prevalence of moderate or severe aortic regurgitation observed in our study was also low (ie, 3.5%). However, 13.6% of patients with a dilated aortic root, as defined by the indexed ratio, had at least moderate aortic regurgitation, a value similar to the 13% rate reported by Niwa et al.5 The lack of association between previous pregnancies and aortic root dilatation is worthy of mention, considering the importance of this issue in women with TOF.

Aortic Dissection

Although acute aortic events cannot be ignored, only 3 cases of aortic dissection have been reported in patients with TOF thus far, rendering it an exceedingly rare complication.9–11 All cases occurred in young men with severely dilated ascending aortas (93, 70.5, and 70 mm). Two had undergone TOF repair later in life (6 and 21 years of age) and experienced major gaps in care.9,10 One occurred in a young man with a 22q11 deletion.11 In our multicenter study, we identified 6 patients with previous aortic valve repair or replacement and 2 patients with previous aortic root replacement, none of whom had undergone surgery for aortic dissection.
Limitations

Data collection was retrospective in nature. Although echocardiographic data were reassessed with a standardized protocol to limit interobserver variability, such variability was not quantified. In general, interobserver variability for aortic root diameter measurements has consistently been shown to be small and clinically insignificant. Analyses were limited to the sinuses of Valsalva diameter because of the completeness of the dataset. In contrast, 61% of patients had measurements at the sinotubular junction, and 55% of patients had measurements at the level of the ascending aorta. Although the cross-sectional design was selected to provide an estimate of aortic root dilatation in a large cohort of adult survivors with repaired TOF, it does not provide longitudinal information on aortic root size and does not capture patients with fatal aortic events <18 years of age, if any. In addition, 22q11 mutation status was not assessed in this cohort. Finally, cause-and-effect associations cannot be inferred from cross-sectional studies.

Conclusions

Aortopathy in TOF, with aortic dilatation and moderate or severe aortic regurgitation, appears to be a less common issue than previous estimates derived from smaller studies would suggest. In this multicenter cross-sectional study of 474 adults with surgically repaired TOF, the aortic root diameter was ≥40 mm at the sinuses of Valsalva in 28.9%. However, the overall prevalence of aortic root dilatation, as defined by an indexed observed-to-expected ratio, was only 6.6%, and moderate or severe aortic regurgitation was present in 3.5% of patients. Aortic arch sidedness was not associated with aortic root dilatation, and no independent predictor was identified. The paucity of documented adverse events and the results of this study should provide some reassurance to patients and physicians regarding aortic root outcomes in TOF.

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Disclosures

None.

References

CLINICAL PERSPECTIVE

The number of adults with repaired tetralogy of Fallot is increasing. Aortic root dilatation has been observed on longitudinal follow-up of patients with tetralogy of Fallot. Histological studies of aortas in patients with tetralogy of Fallot have reported striking similarities to the aortas of patients with Marfan syndrome. Despite the concern that patients with tetralogy of Fallot may harbor an aortopathy that can lead to aortic regurgitation, aortic aneurysms, and, potentially, aortic dissection, the scope of the problem remains uncertain. This multicenter study is the largest to assess the prevalence and predictors of aortic root dilatation in patients with tetralogy of Fallot. When an absolute threshold of 40 mm was used to define a dilated aortic root, a prevalence of 28.9% was observed. In multivariate analyses, the only independently associated factor was male sex. In contrast, an observed-to-expected aortic root diameter ratio cutoff value >1.5 yielded a prevalence estimate of 6.6%. No independent predictor was identified. Our results demonstrate that predictors of aortic root dilatation depend on the definition used to describe aortic root dilatation. Specifically, duration of systemic-to-pulmonary shunt, pulmonary atresia, right aortic arch, aortic regurgitation, and ventricular dimensions are not associated with aortic root dilatation. Aortopathy in tetralogy of Fallot, with aortic dilatation and moderate or severe aortic regurgitation, appears to be a less common issue than previous estimates derived from smaller studies would suggest. The paucity of documented adverse events and the results of this study should provide some reassurance regarding aortic root outcomes in tetralogy of Fallot.
Aortic Root Dilatation in Adults with Surgically Repaired Tetralogy of Fallot: A Multicenter Cross-Sectional Study
from the Alliance for Adult Research in Congenital Cardiology (AARCC)

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SUPPLEMENTAL MATERIAL

APPENDIX

1. List of participating centers to the Alliance for Adult Research in Congenital Cardiology (AARCC):

Oregon Health and Science University, Portland, OR; University of California, Los Angeles, CA; University of Washington, Seattle, WA; Montreal Heart Institute, Université de Montréal, Quebec; Boston Adult Congenital Heart Service, Children’s Hospital Boston and Brigham and Women’s Hospital, MA; Ohio State University, Columbus, OH; University of Colorado, Denver, Colorado; Medical College of Wisconsin, Milwaukee, WI; Columbia University, New York, NY; Hershey Medical Center, Pennsylvania State University, Hershey, PA; and University of Pennsylvania, Philadelphia, PA.