An Echocardiographic Model Predicting Severity of Aortic Regurgitation in Congenital Heart Disease

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Background—Multiple echocardiographic parameters have been identified to predict the severity of aortic regurgitation (AR) with variable reliability. This study was performed to identify which echocardiographic parameters best predict the severity of AR in a cohort of patients with congenital heart disease, using cardiovascular MRI quantification as a reference standard.

Methods and Results—The study involved 2 phases. In phase 1, predictive models were developed on the basis of multivariable analysis of various morphometric and Doppler variables obtained from 174 echocardiograms that best predicted the severity of AR as defined by paired cardiovascular MRI examinations. A nonlinear estimate of regurgitation fraction, using the variables parasternal vena contracta-derived area divided by body surface area and abdominal aorta Doppler retrograde velocity-time integral divided by antegrade velocity-time integral, was identified through multivariable analysis as the best predictive model for AR fraction. In phase 2, the predictive models were prospectively tested on 43 echocardiographic examinations for which a paired cardiovascular MRI was performed. The agreement between the observed and predicted AR fraction was assessed using Bland-Altman analysis. For the 30 studies of the validation data set that had adequate quality images of both the parasternal vena contracta width and the abdominal aorta flow profile, the predicted AR values had a mean bias±SD of 0.4±7.3% (P=0.80).

Conclusions—A model using the 2 variables parasternal vena contracta-derived area divided by body surface area and abdominal aorta Doppler retrograde velocity-time integral divided by antegrade velocity-time integral can predict AR severity in patients with a wide variety of congenital heart disease. (Circ Cardiovasc Imaging. 2010;3:542-549.)

Key Words: valvular heart disease ■ aortic regurgitation ■ pediatrics ■ echocardiography ■ magnetic resonance imaging ■ pediatrics and congenital heart disease

Quantification of the severity of aortic regurgitation (AR) has been a goal for pediatric cardiologists since the earliest cardiac imaging techniques were available. The importance of accurately defining AR severity has become paramount with the increasing population of older patients with congenital heart disease (CHD) and worsening AR and in patients with palliated CHD who manifest altered hemodynamic and physiological states. Problems with defining AR severity in CHD include technical limitations inherent to current imaging modalities that limit accurate quantification of the volume of regurgitation, a lack of reference values standardized to body size with which to categorize the severity of regurgitation, and altered cardiac anatomy and physiology that preclude the use of several common methods of quantification developed in adult patients.1

Clinical Perspective on p 549

Cardiovascular MRI (CMR) has been shown to be a highly accurate and reproducible test for the quantitative evaluation of AR in CHD.2 Nevertheless, echocardiography is more commonly used because of its widespread availability and low cost. Although various qualitative and quantitative methods of assessing AR severity by echocardiography are available,3 it remains unclear which of these methods is most accurate. We sought to identify the most accurate and practical method of quantifying AR severity by echocardiography in a group of patients with CHD, using CMR as a reference standard.

Methods

Study Design

The study was performed in 2 phases. In phase 1, prediction models were developed on the basis of multiple echocardiographic variables from patients with AR. In phase 2, the prediction models were applied prospectively to paired echocardiographic and CMR studies to evaluate their diagnostic accuracy in an independent study sample.

Phase 1

The Cardiovascular Computer Database at the Children’s Hospital Boston (Boston, Mass), which contains information on all noninvasive imaging procedures and clinical patient information, was que-
ried for all patients who had a reported AR fraction by CMR between January 2000 and August 2006. Patients were included if they had both a reported AR fraction by CMR and a transthoracic or transesophageal echocardiogram within 90 days of the CMR. Patients who had previously undergone a Ross procedure or Stansel anastomosis were included in the study. Patients were excluded from the study if they had an interim surgical or interventional catheterization procedure between the 2 imaging studies, there was a change in patient clinical status between the 2 studies, there was a persistent arrhythmia during the CMR or echocardiogram that prevented optimal measurements of variables, or the echocardiogram did not contain information pertinent to the study protocol. No patient with a pacemaker was included in the study because the presence of a pacemaker is a relative contraindication to CMR at our institution. Demographic data were obtained from medical records and included sex, age, weight, and height at the time of both imaging studies; diagnosis; and preceding surgical or catheter interventions. This study was approved by the Department of Cardiology Scientific Review Committee and the Children’s Hospital Boston Committee on Clinical Investigation.

**CMR**

The CMR protocol used in this study has been previously described in detail. Briefly, studies were performed with a commercially available 1.5-T scanner. An 8-channel torso or cardiac phased-array radiofrequency coil was used in patients weighing >10 kg, or a head coil was used in those weighing ≤10 kg. For patients who were unable to cooperate, general anesthesia was used according to a previously published anesthetic and monitoring protocol. Biventricular volumes and function were assessed using a breath-hold ECG-triggered steady-state free precession cine sequence in 2- and 4-chamber planes followed by 12 contiguous short-axis slabs perpendicular to the long axis of the left ventricle (LV) extending from the plane of the atroventricular valve to the apex (slice thickness, 6 to 8 mm; interslice space, 0 to 2 mm). LV and right ventricular end-diastolic (maximal), end-systolic (minimal), and stroke volumes were measured using commercially available software as previously described. Body surface area (BSA) was calculated using the Haycock formula.

Flow measurements were performed in the main pulmonary artery and proximal ascending aorta using a retrospectively gated velocity-encoded cine MRI pulse sequence during free breathing. Quantification of flow volume and calculation of AR was performed using commercially available software. The underlying principles and analysis techniques for velocity-encoded cine MRI have been described previously.

AR fractions defined as retrograde flow volume divided by antegrade flow volume through the aortic valve were derived from 1 or more of the following data sets in each examination, depending on patient anatomy and physiological status: (1) through-plane phase velocity flow measurements in the proximal ascending aorta, (2) through-plane phase velocity flow measurements in the aorta and pulmonary artery, and (3) stroke volume differential between the right ventricle and LV. Mild regurgitation was defined as <20%, moderate as 20% to 40%, and severe as >40%.

**Echocardiography**

Echocardiograms were performed using several commercially available scanners with transducer frequencies appropriate for body size and acoustic windows. Studies were either digitized from archived 1.27-cm super-VHS videocassette tape or reviewed as digitally archived images from digital workstations. Measurements were performed by a single observer (R.S.B.) who was blinded to the CMR data.

The following anatomic, morphometric, and Doppler variables were retrospectively obtained both directly from echocardiogram images and indirectly from reports: (1) aortic valve morphology (bicommissural versus tricommissural versus prosthetic); (2) character of the regurgitation jet (central versus mural versus commissural and free versus adherent); (3) regurgitant jet deceleration rate and pressure halftime; (4) regurgitant jet vena contracta width from apical, parasternal (PVC), and transesophageal long-axis echocardiographic views (Figure 1); (5) subjective image quality from which vena contracta measurements and abdominal aorta Doppler antegrade and retrograde VTI measurements. A, Mild AR, B, Moderate AR, C, Severe AR. PVC-derived area = π(PVC width/2)².

Flow quantification of AR by echocardiogram as described in the next paragraph. Note that AR refers to both native and neoaortic regurgitation. If a patient had 2 semilunar valves connected to the aorta, only the feasible measurements were performed. The rationale for the use of z scores to evaluate allometric data in patients has been described previously.

Flow quantification of AR by echocardiography was defined as retrograde aortic flow volume divided by antegrade aortic flow volume. If possible, the maximum number of the following flow quantification techniques possible were performed on each study: (1) mitral versus aortic flow, (2) pulmonary artery versus aortic flow, (3) mitral flow versus LV stroke volume, (4) pulmonary artery flow versus LV stroke volume, and (5) the same flow quantification methods with and without angle correction of aortic flow. Flow across a valve was calculated as VTI (cm) × cross-sectional area of the valve annulus (cm²). The VTI was measured by pulsed-wave Doppler during the diastolic phase for the mitral valve and the systolic phase for the aortic and pulmonary valves. LV stroke volume was defined as diastolic volume—systolic volume. Of note, some echocardiographic flow quantification methods were excluded.

**Figure 1.** Examples of PVC width measurements and abdominal aorta Doppler antegrade and retrograde VTI measurements. A, Mild AR, B, Moderate AR, C, Severe AR. PVC-derived area = π(PVC width/2)².
from individual studies based on the presence of the following confounding factors: more-than-trivial tricuspid, mitral, or pulmonary regurgitation; a prosthetic pulmonary valve; single-ventricle physiology; or the presence of a hemodynamically significant left-to-right or right-to-left shunt. For example, if there was moderate mitral regurgitation, the AR fraction was not calculated through the mitral-versus-aortic flow method.

The variables apical vena contracta width and PVC width (both linear dimensions) were transformed into estimates of area (using the equation \( \pi r^2 \) or \( \pi (PVC \text{ width}/2)^2 \)) so that multiple regurgitation jets in a single patient could be added together and treated as a single variable (PVC-derived area).

Measurements of effective regurgitant orifice area were not performed using the proximal isovelocity surface area method because appropriate images were not routinely obtained, and the study was retrospective in nature.

**Phase 2**

A new group of patients with a measured AR fraction by CMR and a paired echocardiogram (n=43) was prospectively studied from September 2006 through October 2007. The same inclusion and exclusion criteria used in phase 1 of the study were applied to phase 2 study patients, and the same demographic data were obtained. Echocardiographic and CMR analyses were performed using the same protocol as in phase 1. Only the echocardiographic variables pertinent to the prediction models were obtained and recorded from these prospective studies. To assess interobserver variability, measurements of the echocardiographic parameters were performed by 2 observers (R.S.B., R.M.) who were blinded to the CMR data and to each other’s measurements.

**Statistical Analysis**

The first data set was used for model generation (studies conducted between January 2000 and August 2006) and the second for model validation (September 2006 to October 2007). Using the model-generation data, the bivariate relationship between AR fraction and each of the echocardiographic measurements was estimated using Wilcoxon rank-sum tests for categorical measurements and Spearman correlation coefficients for continuous measurements.

When generating the prediction model for AR fraction, we bounded predicted values of AR fraction between 0 and a specified upper limit (\( \lambda = 1 \)) using the following generalized linear model:

\[
\log \left( \frac{Y_i/n_i}{1 - Y_i/n_i} \right) = \beta_0 + \beta_1 x_{i1} + \cdots + \beta_k x_{ik} + e_i
\]

where for the ith patient (\( i = 1, \ldots, n \)), \( Y_i \) = (AR fraction); \( N_i \) is any power of 10 that ensures that \( Y_i \) is a random integer, \( k \) is the number of covariates in the model, \( x_{ij} \) is the value of the jth covariate, and \( e_i \) is a random error term. This model was fit using generalized estimating equations assuming that \( Y_i \) followed a binomial distribution and that \( \lambda = 0.6 \). Estimation was invariant to the magnitude of \( N_i \) and robust estimates were used to adjust for within-subject repeated measures.

Variables with a \( P \leq 0.05 \) were included in the final multivariable model, and goodness of fit was assessed with \( R^2 \). Predicted values of regurgitation fraction were obtained by solving Equation 1 for \( Y \) and substituting the estimated coefficients, as in Equation 2:

\[
\text{Predicted AR fraction} = \frac{\lambda}{1 + e^{-(\beta_0 + \beta_1 x_{i1} + \cdots + \beta_k x_{ik})}}
\]

Multiple imputation techniques were used to assess the effect of missing data on the coefficient estimates of the final prediction model. Observations of the predictor variables were log-transformed before imputation in order to better approximate multivariate normality. Because the natural log of zero is undefined, observations where at least 1 covariate value was 0 were excluded from the imputation. Ten imputations were performed, and the imputed parameter estimates and SEs are reported.

In phase 2, the coefficients of the prediction model generated in phase 1 were applied to the echocardiographic data of a single reader in the validation data set, and predicted values of AR fraction were calculated. Comparisons of the predicted AR fraction to the CMR values of regurgitation fraction were made with Bland-Altman analysis, including reporting of mean bias±SD, and the 95% prediction limits were calculated. The 1-sample t test was used to test for significant bias. Interobserver agreement between the repeated measurements of the echocardiographic variables in the validation data set also was assessed using Bland-Altman analysis. Intraclass correlation coefficients were calculated. In all analyses, statistical significance was achieved with a 2-sided \( P < 0.05 \). Statistical analyses were performed using SAS version 9.2 for Windows.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

**Results**

**Phase 1**

In this phase, 135 patients were identified with a total of 174 paired echocardiogram and CMR encounters. Patient and study characteristics are shown in Table 1. The average time interval between echocardiogram and paired CMR was 10 ± 32 days (minimum to maximum, 0 to 90 days). The severity of AR varied among patient categories (mild, 46%; moderate, 38%; severe, 16%), and the patient population represented a large number of CHD diagnoses (Table 1). Note that among the 34 patients aged <10 years, there was only 1 who weighed <10 kg.

**Bivariate Analysis**

There was a statistically significant correlation between a large number of parameters and the degree of AR defined by CMR (Tables 2 and 3).

**Prediction Models**

Single-variable and multivariable models predicting AR fraction were developed with the model-generation data set. In single-variable analyses, we identified that AR fraction significantly increases with PVC-derived area up to 0.05 cm\(^2\)/m\(^2\) (\( P < 0.0001 \)); after that point, the relationship levels off, with significant, but less-rapid increases in the AR fraction with PVC-derived area (\( P < 0.0001 \)) (Figure 2). The cut point of 0.05 was the value that maximized \( R^2 \). Additionally, higher values of abdominal aorta Doppler retrograde VTI divided by antegrade VTI (VTI ratio) were predictive of AR fraction (\( P < 0.0001 \)) (Figure 3). Both variables remained independent predictors of AR fraction in multivariable modeling (Table 4). Figure 4 shows predicted values of AR fraction as a function of PVC-derived area divided by BSA for several values of the VTI ratio.

The effect of missing data on the final prediction model was assessed using multiple imputation techniques. Of the 174 studies in the model-generation data set, 160 (92%) had measurements of PVC-derived area, abdominal aorta Doppler VTI ratio, or both. After excluding 12 patients with at least 1 covariate value equal to 0, 148 (85%) studies were available for multiple imputation. The estimated coefficients following multiple imputation were similar to those of the complete case analysis (Table 4).

Indices of LV size (end-diastolic dimension and end-diastolic volume) were not found to be independent predictors of the severity of AR. Because >10% of the patients had abnormal ventricular geometry with either single-ventricle
Table 1. Demographic and Clinical Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>135</td>
</tr>
<tr>
<td>Male sex</td>
<td>95 (70)</td>
</tr>
<tr>
<td>Age at echocardiogram, y</td>
<td>19.8 ± 12.1 (0.23–66)</td>
</tr>
<tr>
<td>No. of patients aged &lt;18 y</td>
<td>96</td>
</tr>
<tr>
<td>No. of patients aged &lt;10 y</td>
<td>34</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.56 ± 0.46 (0.32–2.54)</td>
</tr>
<tr>
<td>No. of patients with BSA &lt;1.4 m²</td>
<td>51</td>
</tr>
<tr>
<td>No. of studies per patient</td>
<td>1.3 ± 0.8</td>
</tr>
<tr>
<td>Patients with &gt;1 study</td>
<td>22 (16)</td>
</tr>
</tbody>
</table>

Diagnosis*:
- Bicommissural or unicommissural aortic valve 54 (40)
- Repaired tetralogy of Fallot or truncus arteriosus 25 (19)
- Coarctation of the aorta 20 (15)
- Repaired ventricular septal defect 11 (8)
- Palliated single ventricle 9 (7)
- Subaortic stenosis 7 (5)
- Repaired transposition of the great arteries 7 (5)
- Other† 36 (27)

Primary intervention*:
- No intervention 33 (24)
- Surgical or catheterization arch repair 26 (19)
- Tetralogy of Fallot repair 16 (12)
- Surgical or catheterization aortic valvuloplasty 28 (21)
- Arterial switch operation 9 (7)
- Single-ventricle palliation 9 (7)
- Truncus arteriosus repair 9 (7)
- Ventricular septal defect closure 10 (7)
- Ross procedure 6 (4)
- Other‡ 9 (7)

Table 2. Bivariate Analysis Comparing Continuous Variables With AR Fraction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median AR Fraction (Q1, Q3)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve morphology</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tricusssural</td>
<td>85</td>
<td>0.14 (0.06, 0.31)</td>
</tr>
<tr>
<td>Bi- or unicommissural</td>
<td>84</td>
<td>0.30 (0.19, 0.39)</td>
</tr>
<tr>
<td>Jet origin</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Central</td>
<td>78</td>
<td>0.15 (0.07, 0.30)</td>
</tr>
<tr>
<td>Mural or commissural</td>
<td>78</td>
<td>0.32 (0.21, 0.42)</td>
</tr>
<tr>
<td>Jet direction</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Free</td>
<td>58</td>
<td>0.11 (0.06, 0.19)</td>
</tr>
<tr>
<td>Adherent</td>
<td>98</td>
<td>0.30 (0.24, 0.42)</td>
</tr>
<tr>
<td>No. parasternal regurgitation jets</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>0–1</td>
<td>108</td>
<td>0.19 (0.09, 0.33)</td>
</tr>
<tr>
<td>2–3</td>
<td>34</td>
<td>0.35 (0.27, 0.45)</td>
</tr>
</tbody>
</table>

Q1 indicates 25th percentile; Q3, 75th percentile.

in the multivariable model, aortic or subaortic stenosis was not found to be an independent predictor of AR fraction. In the final prediction models, the coefficients for PVC-derived area were similar in both groups of patients.

Phase 2

The prediction model was prospectively tested with data on 43 studies performed since the time of the initial analysis. The method by which AR fraction was calculated is shown in Figure 5.

For the 30 studies of the validation data set that had adequate quality images of both PVC width and abdominal aorta flow profile, the model had an $R^2=0.72$, and the predicted values had

Table 3. Bivariate Analysis Comparing Continuous Variables With AR Fraction

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Median AR Fraction (Q1, Q3)</th>
<th>Correlation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVC-derived area ÷ BSA</td>
<td>142</td>
<td>0.09 (0.04, 0.20)</td>
<td>0.73</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Jet cross-section ÷ BSA</td>
<td>126</td>
<td>0.31 (0.14, 0.52)</td>
<td>0.68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV stroke volume ÷ BSA</td>
<td>104</td>
<td>70.3 (55.2, 84.5)</td>
<td>0.45</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stroke volume by flow index, L/min per m²</td>
<td>126</td>
<td>5.0 (3.7, 7.6)</td>
<td>0.59</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Abdominal aorta VTI ratio</td>
<td>119</td>
<td>0.19 (0.08, 0.41)</td>
<td>0.67</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thoracic descending aorta VTI ratio</td>
<td>55</td>
<td>0.40 (0.21, 0.55)</td>
<td>0.73</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV end-diastolic dimension z score</td>
<td>99</td>
<td>2.5 (1.3, 4.4)</td>
<td>0.50</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV end-diastolic volume z score</td>
<td>102</td>
<td>3.4 (1.7, 5.6)</td>
<td>0.55</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AR % (aortic vs pulmonary artery flow)</td>
<td>18</td>
<td>0.40 (0.06, 0.59)</td>
<td>0.80</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Jet pressure halftime</td>
<td>27</td>
<td>413 (357, 469)</td>
<td>-0.43</td>
<td>0.03</td>
</tr>
<tr>
<td>Jet deceleration slope</td>
<td>27</td>
<td>302 (228, 352)</td>
<td>0.41</td>
<td>0.04</td>
</tr>
<tr>
<td>Aortic root z score</td>
<td>117</td>
<td>2.8 (1.6, 5.2)</td>
<td>0.01</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Q1 indicates 25th percentile; Q3, 75th percentile.
*Median value of data point.

physiology or nonsystemic LV, the analyses were repeated after excluding these groups. The results were unchanged.

Additionally, the presence of aortic or subaortic stenosis did not appear to confound our interpretation of the data. To test this hypothesis, cases were divided into 2 subgroups (81 patients with aortic or subaortic stenosis and 91 patients without aortic or subaortic stenosis), and bivariate and multivariable analyses were performed on both groups. The subgroup with aortic or subaortic stenosis was found to have a higher mean AR fraction; and aortic flow measurements by the 5/6 area × length technique tended to be higher. However,
a mean bias±SD of 0.4±7.3% (P=0.80). The Bland-Altman plot is shown in Figure 6. Bland-Altman plots of interobserver variability for both abdominal aorta VTI ratio and PVC-derived area are shown in Figures 7 and 8.

**Discussion**

AR affects a significant proportion of patients with pre- and postoperative CHD. For example, in a cohort of 164 patients with unoperated bicuspid aortic valves who had not had a previous episode of endocarditis, the overall prevalence of more-than-trivial AR reached 32% in follow-up. Another study of long-term follow-up of patients with postoperative tetralogy of Fallot reported a prevalence of 20% of patients with AR. Accurate information about the severity of AR is imperative in clinical decision-making.

The assessment of AR severity by echocardiography, especially when distinguishing between moderate and severe, can be difficult. Qualitative assessment of AR severity by echocardiography has been shown to be unreliable when compared with CMR measurements of AR fraction. In addition, certain methods for the evaluation of AR severity by echocardiography cannot be applied to patients with some forms of CHD. For example, one cannot evaluate the degree of LV dilatation in a patient with hypoplastic left heart syndrome after single-ventricle palliation.

![Figure 2](image1.png)

**Figure 2.** Observed and predicted AR fraction based on PVC-derived area divided by BSA (143 studies; 113 patients; $R^2=0.53$).

![Figure 3](image2.png)

**Figure 3.** Observed and predicted AR fraction based on abdominal aorta Doppler VTI ratio (119 studies; 96 patients; $R^2=0.40$).

![Figure 4](image3.png)

**Figure 4.** Predicted values of AR fraction from multivariable modeling where both PVC-derived area divided by BSA and abdominal aorta Doppler VTI ratio remained independent predictors of AR fraction (101 studies; 82 patients; $R^2=0.63$).

Previous studies in predominantly adult patients have identified multiple parameters as useful in the evaluation of AR severity, culminating in a comprehensive review article published by the American Society of Echocardiography. Although this study underscored the advantages and disadvantages of different methods of defining AR severity, no single method was deemed adequate when used in isolation. Furthermore, determination of which methods may be applicable to patients with CHD remained unclear.

Previous research protocols comparing AR severity by echocardiography and CMR have used the following aim: to define what percentage of AR by CMR constitutes mild, moderate, and severe, using the echocardiographic appearance as a gold standard. The present research study uses an alternative methodology, using CMR as a highly reproducible test to determine which echocardiographic variables best predict AR severity.

The results of this study showing that PVC-derived area divided by BSA and abdominal aorta Doppler VTI ratio are the best independent predictors of AR severity are congruent with previous

<table>
<thead>
<tr>
<th>Variable</th>
<th>Complete Cases (n=101)</th>
<th>Multiple Imputation (n=148)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If PVC-derived area ÷ BSA ≤ 0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-2.62 ± 0.25</td>
<td>-2.48 ± 0.15</td>
</tr>
<tr>
<td>PVC-derived area ÷ BSA</td>
<td>31.42 ± 6.38</td>
<td>33.18 ± 3.77</td>
</tr>
<tr>
<td>VTI ratio</td>
<td>2.33 ± 0.36</td>
<td>1.83 ± 0.26</td>
</tr>
<tr>
<td>If PVC derived area ÷ BSA &gt; 0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-1.18 ± 0.18</td>
<td>-0.94 ± 0.07</td>
</tr>
<tr>
<td>PVC derived area ÷ BSA</td>
<td>2.66 ± 0.69</td>
<td>2.41 ± 0.28</td>
</tr>
<tr>
<td>VTI ratio</td>
<td>2.33 ± 0.36</td>
<td>1.83 ± 0.26</td>
</tr>
</tbody>
</table>

Table 4. Estimated Coefficients of the Multivariable Model Predicting CMR AR Fraction

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Method of calculating AR fraction

\[
PVC\text{ derived area} + BSA = \pi \left( \frac{PVC\text{ width #1}}{2} \right)^2 + \pi \left( \frac{PVC\text{ width #2}}{2} \right)^2 + \pi \left( \frac{PVC\text{ width #3}}{2} \right)^2 + BSA
\]

\[VTI\text{ ratio} = \frac{\text{Abdominal aorta retrograde VTI}}{\text{Abdominal aorta antegrade VTI}}\]

If \( PVC\text{ derived area} + BSA \leq 0.05 \), then
\[
y = -2.62 + (31.42 \times PVC\text{ derived area} + BSA) + (2.33 \times VTI\text{ ratio})
\]

If \( PVC\text{ derived area} + BSA > 0.05 \), then
\[
y = -1.18 + (2.66 \times PVC\text{ derived area} + BSA) + (2.33 \times VTI\text{ ratio})
\]

\[
\text{Predicted AR fraction} = \frac{0.6}{1 + e^{-y}}
\]

The model can be applied to most patients with CHD and is useful in a number of scenarios in which confounding factors would prohibit the use of other methods. Both parameters (PVC derived area divided by BSA and abdominal aorta VTI ratio) can be used in multiple different disease processes, including atrioventricular valve regurgitation, intracardiac shunts, and single-ventricle physiology.
Study Limitations

Given the retrospective nature of this study, the number of testable variables was limited to those that are examined routinely. For example, the variables of aortic flow versus pulmonary artery flow and thoracic descending aorta VTI ratio both had a relatively high correlation with the CMR-derived AR fraction (Table 3); however, the appropriate images were not routinely obtained in enough patients for these variables to reach statistical significance as independent predictors. With respect to aortic flow versus pulmonary artery flow, this type of parameter would have limited utility in the setting of repaired or palliated CHD because many patients lack a nonstenotic native pulmonary valve and normal circulatory physiology. Although thoracic descending aorta VTI ratio may be a slightly better predictor of AR fraction than abdominal aorta VTI ratio (Table 3), this hypothesis was not testable, and the difference in correlation coefficients would not suggest a major improvement in the prediction model. In addition, the prediction model is not relevant in the setting of aortopulmonary shunt, aortovenous fistula, or other aortic runoff lesions, which confound the presence of aortic diastolic retrograde flow.

This and previous studies have recognized a correlation between LV end-diastolic volume or dimension and the severity of AR, and according to the 2008 American College of Cardiology/American Heart Association Task Force on Practice Guidelines, LV size is one major parameter used to decide on aortic valve replacement in patients with AR. However, neither LV end-diastolic volume nor dimension by echocardiography revealed themselves as independent predictors of AR fraction in any of our predictive models and may be related to factors unique to this patient population. For example, our population represented a wide range of cardiac anatomy and physiology, and >10% of the population comprised patients with single-ventricle physiology, multiple left-sided obstructive lesions, or systemic right ventricles. However, when eliminating patients with single-ventricle physiology and those with systemic left ventricles, variables reflecting LV size did not become new independent predictors of AR fraction.

Interobserver variability was relatively low for abdominal aorta VTI ratio measurements (Figure 7). Interobserver variability also was low for smaller PVC measurements; however, for larger values, the interobserver variability increased (Figure 8). The potential for relatively large variations in predicted AR fraction may limit the clinical utility of the model in individual patients, but this has not been clinically tested. The relatively high interobserver variability at higher AR fractions highlights the limitation of measuring a linear regurgitation jet dimension from 1 angle of interrogation in patients with severe AR characterized by complex regurgitation morphology. There may be additional variables or a combination of variables that are difficult to identify and reliably measure by standard echocardiography. For example, because the AR jet is a 3D structure with variable size and orientation throughout the cardiac cycle, echocardiographic sweeps through the jet may give more information about the size of the vena contracta than would still images. With an improvement in temporal and spatial resolution as well as postprocessing techniques by 3D echocardiography, it may become possible to establish more-accurate quantitative methods of evaluating the true cross-sectional area of the vena contracta or the true volume of antegrade and retrograde flow through the aortic valve. Finally, it is important to recognize that although CMR is the best available clinical test for AR quantification, its accuracy can be affected by background phase offset errors and other technical limitations.

Conclusions

Our model using 2 variables, PVC-derived area divided by BSA and abdominal aorta Doppler VTI ratio, can effectively
predict the severity of AR in patients with congenital heart disease.

**Disclosures**

None.

**References**


**Clinical Perspective**

Echocardiographers have had difficulty accurately predicting the severity of aortic regurgitation (AR), and consequently, >20 different echocardiographic measures have been suggested to quantify AR. This study defined 2 independent predictors of AR severity by 2D echocardiography in a population of patients with congenital heart disease, using cardiovascular MRI as a reference standard. The 2 parameters, parasternal vena contracta-derived area divided by body surface area (based on the parasternal vena contracta width), and abdominal aorta Doppler retrograde velocity-time integral divided by antegrade velocity-time integral are relatively easy to obtain and can be measured in nearly any patient with congenital heart disease. Furthermore, these metrics adjust for changes in body size and are more relevant to the pediatric population. Using these 2 parameters, we defined a prediction model that estimates the percentage of AR. In a prospective subset of patients, the predicted AR values had a mean bias±SD of 0.4±7.3% (P=0.80). The interobserver variability in measurements of parasternal vena contracta width increased substantially at higher AR fractions, potentially limiting the ability of the model to predict percentage of AR at higher degrees.
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Rebecca S. Beroukhim, Dionne A. Graham, Renee Margossian, David W. Brown, Tal Geva and Steven D. Colan

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