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# Morphology of Bicuspid Aortic Valve in Children and Adolescents

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**OBJECTIVES** The aim of this study was to determine the relationship between aortic valve morphology and valve dysfunction.

**BACKGROUND** The morphology of the bicuspid or bicommissural aortic valve (BAV) may predict the severity of valve dysfunction. Therefore, we assessed the relationship between BAV, aortic coarctation, and the degree of valve pathology in children.

**METHODS** A retrospective review of 1,135 patients with BAV who were identified between 1986 and 1999 was performed. Patients younger than 18 years of age with BAV that was identifiable via echocardiography were included. The most recent or last study of each patient before intervention or endocarditis was reviewed. Mild stenosis was defined as a valve gradient ≥2 m/s, moderate or greater aortic stenosis as ≥3.5 m/s. Aortic regurgitation was quantified using standard criteria.

**RESULTS** Median age was 3 years (range, 1 day to 17.9 years), and 67% of the patients were male. Right-coronary and left-coronary leaflet fusion were the most common types of BAV (70%). Aortic stenosis that was moderate or greater was observed most often in patients with right-coronary and non-coronary leaflet fusion (odds ratio 2.4, 95% confidence interval 1.6 to 3.6; $p \leq 0.001$). Similarly, right-coronary and non-coronary leaflet fusion was more often associated with moderate aortic regurgitation or greater (odds ratio 2.4, 95% confidence interval 1.2 to 4.7; $p = 0.01$). The majority of patients with aortic coarctation had fusion of the right-coronary and left-coronary leaflets (89%), and aortic coarctation was associated with lesser degrees of valve stenosis or regurgitation.

**CONCLUSIONS** Analysis of BAV morphology is of clinical and prognostic relevance. Fusion of the right-coronary and non-coronary leaflets was associated with more significant valve pathology, whereas fusion of the right-coronary and left-coronary leaflets was associated overwhelmingly with aortic coarctation and less aortic valve pathology. (J Am Coll Cardiol 2004;44:1648–51) © 2004 by the American College of Cardiology Foundation

Bicuspid or bicommissural aortic valve (BAV) generally has been diagnosed in adulthood when calcification of abnormal valve leaflets becomes clinically apparent (1,2). Now, because of the wide availability of noninvasive imaging, the diagnosis of BAV is being made increasingly during childhood, even in patients with relatively normal valve function (3). Most studies documenting valve morphology have been in either small samples of patients or in adults (4–6). Sanders et al. (7) suggested a possible relationship between valve morphology and valve function in children with BAV. Therefore, we evaluated BAV morphology in a large cohort of children by two-dimensional echocardiography and assessed the association between aortic valve morphology and degree of valve pathology as well as the associations with other forms of congenital heart disease.

## METHODS

In accordance with previous published reports based on postoperative and autopsy data, we defined the BAV as having partial or complete fusion of two of the aortic valve leaflets, with or without a central raphe, resulting in partial or complete absence of a functional commissure between the fused leaflets (4). Patients with complete or partial fusion of more than two leaflets (unicommissural valve) or with truncus arteriosus were excluded. A search of the Cardiovascular Program Database at Children's Hospital (Boston, Massachusetts) was performed to identify patients age 0 to 18 years who had been diagnosed with a BAV by echocardiography between 1986 and 1999. The most recent echocardiogram, the exam prior to any surgical or catheter intervention, or the exam at least one year prior to any episode of endocarditis was reviewed for aortic valve morphology, severity of aortic stenosis, severity of aortic regurgitation, and presence of aortic coarctation or any other additional congenital cardiac malformations. Aortic stenosis was considered significant if there was a Doppler velocity of ≥2 m/s across the aortic valve; the stenosis was classified as at least moderate if the transvalvar velocity was ≥3.5 m/s. Classification of the severity of aortic regurgitation was based on composite evaluation of proximal jet width, abdominal aortic Doppler, and left ventricular end-diastolic dimension. Patients were classified as having moderate regurgitation or greater only if pan-diastolic retrograde flow

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**Abbreviations and Acronyms**
BAV = bicuspid or bicommissural aortic valve
CI = confidence interval
OR = odds ratio

was observed in the descending aorta and the left ventricular end-diastolic dimension adjusted for body surface area was >2 standard deviations above the mean. We estimated the frequency with which BAV was observed in association with other cardiac malformations by determining the total number of patients with each of the associated cardiac defects who underwent echocardiography during the same time interval.

**Statistical analysis.** Exact binomial 95% confidence intervals (CIs) were calculated for the proportions of patients with BAV among those with various types of cardiac malformations. Characteristics for patients with moderate or severe aortic valve pathology were compared with those with mild or no pathology using the Fisher exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Multivariate analyses were performed using logistic regression; odds ratios (ORs) and 95% CIs were estimated. Additional multivariate analyses evaluated the effects of age, gender, presence of coarctation, and variants of leaflet fusion on presence of aortic pathology.

## RESULTS

We identified 1,192 patients who met inclusion criteria. The aortic valve anatomy could be clearly defined by echocardiography in 1,135 (92.5%) of these patients. The median age at evaluation was 3 years (range, 1 day to 17.9 years). Of the 1,135 patients, 766 (67.4%) were males and 369 (32.5%) were females.

Bicuspid aortic valve was an isolated finding in 569 (50.1%) patients (including patients with Turner syndrome and one patient each with Trisomy 21, Noonan syndrome, and Marfan syndrome). The other 566 patients had additional congenital cardiac malformations, including most forms of simple and complex congenital heart disease. Table 1 outlines the prevalence of BAV in patients with complex congenital heart disease. The majority of BAVs were observed in patients with left-sided obstructive lesions (aortic coarctation or interruption and hypoplastic left heart syndrome) accounting for 373 of 566 (65.9%) patients with additional cardiac malformations. In patients with isolated aortic coarctation, 55% were noted to have a BAV. The incidence of BAV in patients with complex coarctation (coarctation in conjunction with additional cardiac lesions other than aortic valve disease) and hypoplastic left heart syndrome was lower than in isolated coarctation. The observed incidence in hypoplastic heart syndrome presumably represents an underestimate because of a limited ability to determine valve morphology in patients with severely hypoplastic or atretic aortic valve.

**Valve morphology.** As shown in Table 2, fusion of the right-coronary and left-coronary leaflets (absence of the intercoronary commissure) was the most common type of BAV (70.4%), both in patients with isolated BAV (58.9%) and in those with additional pathology. The vast majority of patients with coarctation (88.8%) and left heart obstructive lesions (79.4%) had right-coronary and left-coronary leaflet fusion. Fusion of the left-coronary and non-coronary leaflets (absence of the commissure between the left-coronary and non-coronary leaflets) was observed rarely (1.4%), and 9 of 16 patients with this pattern had no other structural abnormality.

**Aortic stenosis/aortic regurgitation.** The presence and severity of aortic stenosis and regurgitation were assessed in subgroup analyses of patients with isolated BAV and in those with BAV in association with aortic coarctation. Similar analyses were not performed for other lesions because of a lack of statistical power.

Moderate stenosis or greater was observed in 9.7% of patients with fusion of the right-coronary and left-coronary

**Table 1.** Bicuspid Aortic Valve and Associated Congenital Cardiac Malformations

| Associated Malformation | Number With Malformation | Number With BAV | Percent With BAV (95% Confidence Interval) |
|---|---|---|---|
| Isolated coarctation | 835 | 459 | 55 (51.5, 58.4) |
| Complex coarctation | 629 | 111 | 17.6 (14.7, 20.9) |
| HLHS or IAA | 570 | 64 | 11.2 (8.8, 14.1) |
| CAVC defect | 1,074 | 11 | 1.0 (0.5, 1.8) |
| Ebstein's anomaly | 250 | 2 | 0.8 (0.1, 2.8) |
| TAPVR | 247 | 2 | 0.8 (0.1, 2.9) |
| PAPVR | 233 | 2 | 0.9 (0.1, 3.1) |
| Tetralogy of Fallot | 1,213 | 7 | 0.6 (0.2, 1.2) |
| DORV | 773 | 5 | 0.6 (0.2, 1.5) |
| TGA | 1,567 | 1 | 0.1 (0.0, 0.4) |

In addition to those listed in Table 1, other lesions occurring in association with BAV included atrial (including sinus venosus) and ventricular septal defects, patent ductus arteriosus, supravalvar and subvalvar aortic stenosis, supravalvar and valvar mitral stenosis, pulmonary stenosis and atresia, anomalous left coronary artery from the pulmonary trunk; and anomalous origin of a branch pulmonary artery from the ascending aorta (hemitruncus).

BAV = bicuspid aortic valve; CAVC = complete atrioventricular canal defect; DORV = double-outlet right ventricle; HLHS = hypoplastic left heart syndrome; IAA = interrupted aortic arch; PAPVR = partial anomalous pulmonary venous return; TAPVR = total anomalous pulmonary venous return; TGA = transposition of the great arteries.

**Table 2.** Bicuspid Aortic Valve Morphology

| | Total Patients | Valve Morphology, N (%) | | |
|---|---|---|---|---|
| | | R-L | R-N | L-N |
| Isolated BAV | 569 | 335 (58.9) | 225 (39.5) | 9 (1.6) |
| Aortic coarctation | 295 | 262 (88.8) | 31 (10.5) | 2 (0.7) |
| Left heart defects* | 155 | 123 (79.4) | 28 (18.1) | 4 (2.6) |
| Non-left heart defects† | 116 | 79 (68.1) | 36 (31.0) | 1 (0.9) |
| All patients | 1,135 | 799 (70.4) | 320 (28.2) | 16 (1.4) |

*Includes hypoplastic left heart syndrome, Shone's syndrome, interrupted aortic arch, mitral stenosis, and left ventricular outflow tract obstruction. †Includes atrial and ventricular septal defects, atrioventricular canal defects, anomalous pulmonary venous drainage, right ventricular outflow tract obstruction, Ebstein's malformation, tetralogy of Fallot, and double-outlet right ventricle.

BAV = bicuspid aortic valve; L-N = fusion of left-coronary and noncoronary leaflets; R-L = fusion of right-coronary and left-coronary leaflets; R-N = fusion of right-coronary and non-coronary leaflets.

leaflets, in 25.9% of patients with fusion of the right-coronary and non-coronary leaflets, but in none of the patients with fusion of the left-coronary and non-coronary leaflets ($p < 0.001$). Those with moderate or severe stenosis tended to be younger (median age 1.9 vs. 4.6 years; $p = 0.02$); differences between males and females were not observed. Among patients with isolated BAV, moderate aortic stenosis or greater was more likely in patients with fusion of the right-coronary and non-coronary leaflets compared with other valve morphologies (OR 2.4, 95% CI 1.6 to 3.6; $p < 0.001$). In a multivariate model controlling for age and gender, patients with fusion of the right-coronary and non-coronary leaflets had a more than twofold higher odds of having moderate aortic stenosis or greater (OR 2.3, 95% CI 1.5 to 3.6; $p \leq 0.001$).

At least mild aortic regurgitation was observed in 33.1% of patients with BAV, but moderate aortic regurgitation or greater was uncommon in our population (4.5%). Patients who did have moderate or severe aortic regurgitation were older than those who did not (median age 9.2 vs. 4.1 years; $p < 0.001$). When compared with the other two types of BAV, patients with fusion of the right-coronary and non-coronary leaflets were more likely to have at least moderate aortic regurgitation (OR 2.4, 95% CI 1.2 to 4.7; $p = 0.01$). After adjusting for age and gender, patients with right-coronary and non-coronary leaflet fusion had two-fold higher odds of at least moderate aortic regurgitation (OR 2.0, 95% CI 1.4 to 2.8; $p = 0.0002$).

Bicuspid aortic valve in conjunction with aortic coarctation was associated with a lower prevalence of valve obstruction and regurgitation. As shown in Table 3, adjusting for valve morphology, age, and gender in a multivariate analysis, the odds of a patient with a BAV having no stenosis were four times higher and the odds of no regurgitation were nearly three times higher if the patient had concomitant coarctation.

## DISCUSSION

Bicuspid aortic valve is the most common congenital cardiac malformation and is present in 1% to 2% of the general population (8–10). Both genetic and environmental causes of the BAV have been suggested, but the pathogenesis remains unclear (11). Bicuspid aortic valve is associated with significant complications in one third of patients. Ward (12) suggested that the BAV might be responsible for more deaths and morbidity than the combined effects of all other types of congenital heart defects. Given the significant impact the BAV has on health, it is important to determine risk factors for the development of valve dysfunction. Children who present with BAV should be an ideal population for study, given the ability to accurately determine valve morphology noninvasively in the majority of patients (3).

**Table 3.** Multivariable Predictors of Better Valve Function

| | Odds Ratio | 95% Confidence Interval | p Value |
|---|---|---|---|
| Aortic stenosis | | | |
| Coarctation | 4.0 | (2.8–5.8) | <0.001 |
| R-L | 2.8 | (2.0–3.9) | <0.001 |
| L-N | 17.2 | (2.1–138) | 0.007 |
| Male | 0.74 | (0.53–1.0) | 0.08 |
| Age, per 5-yr increase | 1.0 | (0.86–1.2) | NS |
| Aortic regurgitation | | | |
| Coarctation | 2.7 | (1.8–4.1) | <0.001 |
| R-L | 2.0 | (1.4–2.8) | <0.001 |
| L-N | 2.9 | (0.65–12.5) | 0.16 |
| Male | 0.61 | (0.42–0.89) | 0.009 |
| Age, per 5-yr increase | 0.41 | (0.35–0.49) | <0.001 |

L-N = fusion of left-coronary and non-coronary leaflets; R-L = fusion of right-coronary and left-coronary leaflets.

Previously published studies have shown that BAV is a common finding in isolation, identified in 0.5% to 2% of the population and has been observed in conjunction with many other types of congenital heart lesions (2,13,14). In addition, there is a well-documented association of BAV with aortic coarctation (15). Our study found that BAV was occasionally present in almost all forms of congenital heart disease with an incidence that generally does not exceed that in the general population but was certainly seen much more frequently in patients with left-heart obstructive lesions. We found a 55% incidence of BAV in patients with isolated aortic coarctation and an 11% incidence in patients with hypoplastic left heart syndrome or interrupted aortic arch.

The majority of previously published reports have assumed that all types of BAV are similar and have not differentiated between type of leaflet fusion when assessing valve dysfunction and progression (2,6,16,17). Our study demonstrates that aortic valve morphology is an important determinant of the risk for aortic stenosis and aortic regurgitation, at least through childhood and adolescence. We found that patients with BAV with fusion of the right-coronary and non-coronary leaflets had more than twice the risk of aortic stenosis and regurgitation compared with other types of BAV. Conversely, the combination of BAV and aortic coarctation was associated with milder aortic valve disease, regardless of the pattern of leaflet fusion, compared with BAV without aortic coarctation.

**Study limitations.** This study represents the population of children with BAV referred for echocardiography. Patients with clinically insignificant BAV may not be referred for evaluation or echocardiography because of a lack of physical findings. The association of congenitally BAV with other complex structural heart disease may well represent an underestimate of the true incidence because of greater difficulties in diagnosis under these circumstances. In addition, the relationship between aortic stenosis and regurgitation and the type of BAV observed in children may be substantially different from that seen in adults with an aging, calcific valve.

**Conclusions.** Our study clearly demonstrates that BAV occurs in isolation and in association with many forms of congenital heart disease referred for echocardiographic evaluation. In addition, BAV morphology in childhood and adolescence is highly correlated with valve dysfunction. These findings are helpful in predicting which patients, at least prior to adulthood, are likely to have a benign cardiac course and which are at greater risk for progressive aortic valve disease.

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