

EDITORIAL COMMENT

## Bicuspid Aortic Valve and Aortopathy: See the First, Then Look at the Second\*

Rosario V. Freeman, MD, MS, Catherine M. Otto, MD

Seattle, Washington

Bicuspid aortic valve (BAV) disease is the most common congenital cardiac anomaly, with a prevalence in the general population between 0.5% and 2% (1). There is significant cardiac morbidity associated with BAV disease, predominantly due to progressive valve dysfunction (stenosis or regurgitation) that requires surgical intervention for symptom relief or prevention of left ventricular dysfunction, or less commonly, for complications of endocarditis (2,3). We now understand that BAV disease is more than simply having 2, instead of 3, aortic valve leaflets. BAV disease encompasses a spectrum of phenotypic manifestations that not only includes valve dysfunction, but also abnormalities of the ascending aorta. Less common cardiovascular abnormalities may also occur, such as aortic coarctation, atrial septal defects, and ventricular septal defects.

[See page 150](#)

Long-term cardiovascular outcomes in adults with a BAV were defined in 2 recent clinical studies. In a series of 642 asymptomatic adults with a BAV, most (63%) had normal or mildly abnormal valve function at baseline. Over an average 9 years of follow-up, about 25% required surgery for symptomatic valve disease, left ventricular dysfunction, ascending aortic dilation, or endocarditis. Independent predictors of adverse cardiovascular events were age >30 years and at least moderate aortic valve dysfunction at

baseline (3). Similarly, in another series of 212 asymptomatic adults with a BAV and at most mild valve dysfunction, primary cardiac outcomes were frequent over follow-up, occurring in 42% of participants. In this study, independent predictors for primary outcomes were older age (>50 years), presence of valve degeneration at baseline, and a baseline aortic dimension of >40 mm (2). Importantly, these studies demonstrated that although the cardiac morbidity associated with a BAV is significant, overall life expectancy is not shortened relative to general population estimates. In the Olmstead County study, survival was 97% and 90% at 10 and 20 years, respectively, from diagnosis (2). Similarly, in the Toronto cohort, 10-year survival was 97% (3).

BAV disease is not confined to the valve leaflets; the aorta also is abnormal. Compared with normal adults with a trileaflet aortic valve, BAV patients have larger dimensions of the aortic sinuses and ascending aorta, abnormal aortic elasticity, and are at risk for progressive aortic dilation and dissection (4). In the past, aortic dilation was thought to be primarily a hemodynamic consequence of the eccentric ejection jet created by the bicuspid valve. However, histopathologic studies now support an underlying connective tissue disease process with elastin fragmentation, irregularities in smooth muscle integrity, and increased collagen deposition (5). Dilation is often progressive, with an average annual change in diameter ranging from 0.2 to 1.2 cm/year (6). Risk factors for more rapid progression of aortic dilation include hypertension, male sex, concurrent valve disease, and older age. In the study by Tzemos et al. (3), 280 patients (45%) developed dilation of the aortic sinus, ascending aorta, or both at follow-up. In a subsequent publication from the Olmstead County cohort, which included 416 pa-

\*Editorials published in the *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

From the Division of Cardiology, Department of Medicine, University of Washington, Seattle, Washington. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

tients, although 53% of patients eventually required aortic valve replacement, a significant portion of patients (25%) also ultimately required surgical intervention for aortopathy (6). Because not all patients are at risk for progressive aortic dilation, the clinical challenge is in identifying which patients are at highest risk for aortic complications and might therefore require more frequent imaging evaluation.

In this issue of *JACC*, a study by Kang et al. (7) focuses on the potential value of computed tomographic angiography (CTA) to more precisely define BAV phenotypes and to characterize the associated aortopathy. Typically, bicuspid valve cusps are asymmetric with fusion along a commissural line, which creates 2 cusps of unequal size. Similar to other series, this study found that fusion of the right and left coronary cusps (anterior-posterior [AP] leaflet type) was the most common pattern, occurring in 56% of patients, with fusion of the right and noncoronary cusps (right-left [RL] leaflet type) seen in the remaining 44% of patients. Although the study suggests that the RL phenotype is associated with valve stenosis and the AP phenotype with regurgitation, this should be considered a hypothesis, not a conclusion. All the subjects in this study were referred for preoperative CTA; thus, all had significant valve dysfunction and/or aortic dilation and should not be considered representative of an unselected group of BAV patients. Kang et al. (7) also found that leaflet phenotype was associated with different patterns of aortic dilation. Normal aortic shape and dimensions were seen more often in BAV patients with an AP leaflet phenotype, whereas those with a RL leaflet phenotype more often had aortic dilation extending to the arch. These findings parallel a study from our group that demonstrated larger and stiffer aortic sinuses with the AP phenotype and larger aortic arch dimensions with the RL leaflet phenotype (8,9). These differences in aortic anatomy and valve function associated with different valve phenotypes support the possibility that BAV disease is not a uniform disease process.

Despite the insights into the disease process provided by this study, which was performed with computed tomography, from a practical point of view, echocardiography remains the key imaging approach in adults with BAV disease. CTA is only an adjunct in selected patients. BAV disease is usually asymptomatic, often incidentally diagnosed on echocardiography obtained for other indications or suspected on physical examination with auscul-

tation of a murmur or a mid-systolic "click." Transthoracic echocardiography has a high sensitivity and specificity for the diagnosis of a BAV. Characteristic findings include an eccentric diastolic leaflet closure plane and systolic doming of the leaflets in long-axis views. The number of valve leaflets, the type of leaflet fusion, and the presence or absence of a raphe can be reliably determined in short-axis views. Doppler echocardiography allows accurate measurement of the severity of valve stenosis and regurgitation. If transthoracic image quality is not adequate, transesophageal echocardiography often provides improved visualization of aortic leaflet morphology. Three-dimensional imaging of the aortic valve may further improve the accuracy of echocardiography for diagnosis of BAV disease.

Echocardiography allows evaluation of the aortic sinuses and, by moving the transducer up 1 intercostal space, the proximal ascending aorta. Because of the low cost, lack of ionizing radiation, and wide availability, echocardiography is often used to evaluate and follow the aortopathy associated with BAV disease. However, for a more comprehensive evaluation of aortic anatomy, CTA or magnetic resonance angiography (MRA) both provide comprehensive tomographic evaluation of the entire aorta, and are particularly helpful when visualization of the ascending aorta by echocardiography is limited. Our approach in patients newly diagnosed with BAV is to obtain an index tomographic (CTA or MRA) imaging study of the aorta to determine the pattern and severity of aortic dilation. If there is no significant dilation or if echocardiography adequately visualizes the aorta, then serial routine CTA or MRA imaging is not indicated. In patients who have disease progression necessitating aortic valve replacement, aortic surgery, or both, pre-surgical CTA or MRA imaging provides a better understanding of the extent of aortic involvement to aid in surgical planning and graft choice.

A majority of patients with BAV disease will have disease progression requiring surgery over the course of their lifetime, most often for valve stenosis or regurgitation, with established clinical guidelines providing recommendations on optimal timing of intervention (10). Clinical recommendations for surgical intervention for the aortopathy associated with BAV disease are less well defined, but most centers recommend intervention at an aortic diameter greater than ~50 to 55 mm, independent of valve disease. Aortic graft replacement may also be considered at a smaller aortic diameter (45 to 50 mm) in patients who are otherwise undergoing

aortic valve surgery or if there is evidence of rapid disease progression (interval increase in aortic diameter  $>5$  mm over 6 months.)

Although adults with BAV disease can have excellent clinical outcomes with appropriate disease monitoring and with correctly timed intervention to prevent adverse events, our current approach is largely pragmatic with little understanding of the underlying disease process. Several studies, such as the one by Kang et al. (7), suggest that there is more than 1 BAV phenotype with different clinical associations. Do these different phenotypes also have

different genetics and different clinical outcomes? Until we can identify which patients with BAV disease are at risk for aortic dissection and would benefit from prophylactic aortic intervention, we will need to continue serial imaging of all BAV patients to detect the few who have progressed to surgical disease.

---

**Reprint requests and correspondence:** Dr. Catherine M. Otto, Division of Cardiology, Box 356422, University of Washington School of Medicine, Seattle, Washington 98195. *E-mail:* [cmotto@u.washington.edu](mailto:cmotto@u.washington.edu).

---

## REFERENCES

1. Siu SC, Silversides CK. Bicuspid aortic valve disease. *J Am Coll Cardiol* 2010;55:2789-800.
2. Michelena HI, Desjardins VA, Avierinos JF, et al. Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. *Circulation* 2008;117:2776-84.
3. Tzemos N, Therrien J, Yip J, et al. Outcomes in adults with bicuspid aortic valves. *JAMA* 2008;300:1317-25.
4. Michelena HI, Khanna AD, Mahoney D, et al. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA* 2011;306:1104-12.
5. Braverman AC, Guven H, Beardslee MA, Makan M, Kates AM, Moon MR. The bicuspid aortic valve. *Curr Probl Cardiol* 2005;30:470-522.
6. La Canna G, Ficarra E, Tsagalau E, et al. Progression rate of ascending aortic dilation in patients with normally functioning bicuspid and tricuspid aortic valves. *Am J Cardiol* 2006;98:249-53.
7. Kang J-W, Song HG, Yang DH. Association between bicuspid aortic valve phenotype and patterns of valvular dysfunction and bicuspid aortopathy: comprehensive evaluation using MDCT and echocardiography. *J Am Coll Cardiol Img* 2013;6:150-61.
8. Schaefer BM, Lewin MB, Stout KK, Gill E, Prucitt A, Byers PH, Otto CM. The bicuspid aortic valve: an integrated phenotypic classification of leaflet morphology and aortic root shape. *Heart* 2008;94:1634-8.
9. Schaefer BM, Lewin MB, Stout KK, Byers PH, Otto CM. Usefulness of bicuspid aortic valve phenotype to predict elastic properties of the ascending aorta. *Am J Cardiol* 2007;99:686-90.
10. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *J Am Coll Cardiol* 2006;48:e1-148.

---

**Key Words:** aortopathy ■  
bicuspid aortic valve ■  
computed tomographic  
angiography ■ echocardiography.