Science of BAV Aortopathy

• No uniform definition
• Patterns of dilatation are diverse
• Marked heterogeneity
  – Molecular defects, clinical phenotypes
• Genetic basis questioned
• No unified surgical strategy
• Guidelines thresholds keep changing
• Controversy - Pattern of dilation/cusp fusion predict disease progression and rupture risk?
• No biomarkers yet identified
• No RCTs – surgical or pharmacological approaches
Risk of Aneurysm Formation and Aortic Dissection After Definite Bicuspid Aortic Valve Diagnosis

Michelena, H. I. et al. JAMA 2011;306:1104-1112
52% believed genetics, 2% believed valve hemodynamics

61% believed in resection at 45mm at time of AVR

33% performed resection at >40mm at time of AVR

55% believed in resection if >50mm without AVR
Long-Term Risk for Aortic Complications After Aortic Valve Replacement in Patients With Bicuspid Aortic Valve Versus Marfan Syndrome

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BACKGROUND Bicuspid aortic valves are associated with valve dysfunction, ascending aortic aneurysm and dissection. Management of the ascending aorta at the time of aortic valve replacement (AVR) in these patients is controversial and has been extrapolated from experience with Marfan syndrome, despite the absence of comparative long-term outcome data.

OBJECTIVES This study sought to assess whether the natural history of thoracic aortopathy after AVR in patients with bicuspid aortic valve disease is substantially different from that seen in patients with Marfan syndrome.

METHODS In this retrospective comparison, outcomes of 13,205 adults (2,079 with bicuspid aortic valves, 73 with Marfan syndrome, and 11,053 control patients with acquired aortic valve disease) who underwent primary AVR without replacement of the ascending aorta in New York State between 1995 and 2010 were compared. The median follow-up time was 6.6 years.

RESULTS The long-term incidence of thoracic aortic dissection was significantly higher in patients with Marfan syndrome (5.5 ± 2.7%) compared with those with bicuspid valves (0.55 ± 0.21%) and control group patients (0.41 ± 0.08%, p < 0.001). Thoracic aortic aneurysms were significantly more likely to be diagnosed in late follow-up in patients with Marfan syndrome (10.8 ± 4.4%) compared with those with bicuspid valves (4.8 ± 0.8%) and control group patients (1.4 ± 0.2%) (p < 0.001). Patients with Marfan syndrome were significantly more likely to undergo thoracic aortic surgery in late follow-up (10.4 ± 4.3%) compared with those with bicuspid valves (2.5 ± 0.6%) and control group patients (0.50 ± 0.09%) (p < 0.001).

CONCLUSIONS The much higher long-term rates of aortic complications after AVR observed in patients with Marfan syndrome compared with those with bicuspid aortic valves confirm that operative management of patients with bicuspid aortic valves should not be extrapolated from Marfan syndrome and support discrete treatment algorithms for these different clinical entities. (J Am Coll Cardiol 2015;65:2363–9) © 2015 by the American College of Cardiology Foundation.
Bicuspid aortic valve syndrome: heterogeneous but predictable?

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This editorial refers to ‘Aortic elasticity and size in bicuspid aortic valve syndrome’ by S. Nistri et al.,† on page 472

Bicuspid aortic valve (BAV) has long been associated with a spectrum of vascular complications such as ascending aortic dilatation, aortic aneurysms, and catastrophic aortic root dissection. The mechanism responsible for the associated vascular complications in this seemingly benign and common congenital lesion of aortic valve morphology remains controversial. Some argue that flow dynamics from the mis-shaped outflow valve result in aberrant post-valvular haemodynamics that trigger progressive aortic dilatation. In many patients with advanced valve disease, this mechanism probably contributes to the development of dilatation of the aortic root; however, in others it is likely that the aortic wall is pre-disposed to dilatation due to genetic or environmental factors. The implications of this heterogeneity are numerous. The candidate genes and molecular markers that mediate the valve and aortic complications remain elusive. It is tempting to speculate that BAVS is a final common pathway for a wide variety of altered molecular events and genetic defects. Perhaps similar to left ventricular dilatation in the failing heart, BAV and associated aortic dilatation result from different aetiologies but manifest similarly on a clinical basis. Because the lesion may have diverse molecular triggers, it may be difficult to characterize the inciting events that result in a BAV and its associated aortopathy. Currently, extracellular matrix dysregulation and cell death pathways show promise as important molecular mechanisms of the aortopathy, while candidate genes such as NOTCH may reflect important genetic influence. An improved understanding of the cellular and molecular mechanisms that underpin the aortopathy of BAV will undoubtedly lead to improved prevention and treatment of the condition.
Valvular Heart Disease

Bicuspid Aortic Cusp Fusion Morphology Alters Aortic Three-Dimensional Outflow Patterns, Wall Shear Stress, and Expression of Aortopathy

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Background—Aortic 3-dimensional blood flow was analyzed to investigate altered ascending aorta (AAo) hemodynamics in bicuspid aortic valve (BAV) patients and its association with differences in cusp fusion patterns (right-left, RL versus right-noncoronary, RN) and expression of aortopathy.

Methods and Results—Four-dimensional flow MRI measured in vivo 3-dimensional blood flow in the aorta of 75 subjects: BAV patients with aortic dilatation stratified by leaflet fusion pattern (n=15 RL-BAV, mid AAo diameter=39.9±4.4 mm; n=15 RN-BAV, 39.6±7.2 mm); aorta size controls with tricuspid aortic valves (n=30, 41.0±4.4 mm); healthy volunteers (n=15, 24.9±3.0 mm). Aortopathy type (0–3), systolic flow angle, flow displacement, and regional wall shear stress were determined for all subjects. Eccentric outflow jet patterns in BAV patients resulted in elevated regional wall shear stress (P<0.0125) at the right-anterior walls for RL-BAV and right-posterior walls for RN-BAV in comparison with aorta size controls. Dilatation of the aortic root only (type 1) or involving the entire AAo and arch (type 3) was found in the majority of RN-BAV patients (87%) but was mostly absent for RL-BAV patients (87% type 2). Differences in aortopathy type between RL-BAV and RN-BAV patients were associated with altered flow displacement in the proximal and mid AAo for type 1 (42%–81% decrease versus type 2) and distal AAo for type 3 (33%–39% increase versus type 2).

Conclusions—The presence and type of BAV fusion was associated with changes in regional wall shear stress distribution, systolic flow eccentricity, and expression of BAV aortopathy. Hemodynamic markers suggest a physiological mechanism by which the valve morphology phenotype can influence phenotypes of BAV aortopathy. (Circulation. 2014;129:673-682.)

Key words: aortic diseases ■ bicuspid aortic valve ■ hemodynamics ■ magnetic resonance imaging