Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Current Concepts

Bicuspid Aortopathy

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Supplementary Section

Figure S1: Bicuspid valve morphology pattern may influence aortopathy pattern

Figure S2: Long term risk of aneurysm formation, aortic dissection and need for aortic surgery

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References
Figure S1: Bicuspid Valve Morphology Pattern May Influence Aortopathy Pattern

Coregistered steady-state free precession images (panels i-iii) define anatomic landmarks and allow for determination of the direction and propagation of systolic flow jet (panels iv and v). In the right-left (RL) bicuspid aortic valve lesion shown (panel iii), the jet would be aimed towards the right-anterior aorta wall of the ascending aorta and will impact and travel along the right-anterior aorta wall in a right-handed helical direction. (Adapted with permission from Barker AJ, et al. Circulation Cardiovascular imaging 2012;5:457-66.)¹

A right and noncoronary cusp (RN) fusion (panels i to iv) would yield a jetting pattern towards the posterior wall of the aorta, opposite from the fused right and noncoronary cusp. The peak wall shear stress (WSS) for this patient occurs at the RP position (black closed arrow) instead of at the RA position for right-left (RL) bicuspid aortic valve patients (panel v). The incomplete opening of the fused cusp appears to influence the direction of the velocity jet (black open arrow) and thus the position of the peak WSS eccentricity (panel vi). A, anterior; LA, left-anterior; L, left; LP, left-posterior; P, posterior and RP, right-posterior; R, right; RA, right-anterior. (Adapted with permission from Barker AJ, et al. Circulation Cardiovascular imaging 2012;5:457-66.)
In the top panel, risk of aortic aneurysm 25 years after diagnosis in 384 patients (32 patients with baseline aneurysm excluded) and risk of aortic dissection 25 years after diagnosis in the entire study group of 416 patients. In the bottom panel, risk of aortic surgery 25 years after diagnosis in the entire study group. (Reprinted with permission from Michelena HI et al. JAMA 2011;306:1104-12). Of the 416 cohort patients, 49 patients underwent surgery of the thoracic aorta, 11 patients underwent surgery for aortic coarctation or recoarctation and 2 for ascending aortic dissection. The 25 year risk of aortic surgery after diagnosis was 25%.
Table S 1:  Selected Recently Published Studies Examining Outcomes of Aorta Surgery in Individuals with Bicuspid Aortic Valves*

<table>
<thead>
<tr>
<th>Inclusion Criteria and years of operation</th>
<th>Number of patients (n)</th>
<th>In hospital or 30 day mortality</th>
<th>Long Term Outcomes</th>
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<tbody>
<tr>
<td>Patients undergoing bicuspid aortic valve surgery (AoV) (1993 – 2003)³</td>
<td>• AoV alone (n= 1449) and with ascending aortic repair (n=361) • Propensity matching of 202 pairs of AoV alone and AoV plus ascending aorta repair patients</td>
<td>Mortality of AoV alone (1.2%) group similar to that in AoV plus ascending aorta repair group (1.1%)</td>
<td>Matched cohort: AoV plus ascending aorta group had similar 10 year survival (86%) and freedom from late aortic events (97%) compared to AoV alone group (85% and 95% respectively)</td>
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<td>Patients undergoing aorta replacement (2005 – 2009)⁴</td>
<td>• n=100 • 16% had prior aortic valve replacement • 82% underwent concomitant arch replacement</td>
<td>1%</td>
<td>No deaths or reoperation at mean follow up of 16 months</td>
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<tr>
<td>Patients undergoing repair or replacement of ascending aorta and did not required arch replacement (1988-2007)⁵</td>
<td>• n=422</td>
<td>1.7%</td>
<td>• 90% - 5 year survival • 94% - 5 year freedom from late reoperation • None of late reoperation was for arch dilatation</td>
</tr>
<tr>
<td>Patients undergoing AoV with replacement of ascending aorta (1979 – 1997)⁶</td>
<td>• n=143</td>
<td>2.1%</td>
<td>• 82% - 10 year event free survival • Late outcomes not predicted by operative techniques</td>
</tr>
<tr>
<td>Patients undergoing Tirone David valve-sparing aortic root replacement and cusps repair (1997-2011)⁷</td>
<td>• n=75</td>
<td>1.3%</td>
<td>• No late deaths at median follow up of 3 years • 90% - 3 years freedom from late reoperation</td>
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<tr>
<td>Patients undergoing aortic valve preserving surgery⁸</td>
<td>• Overview of 30 studies published 1994 - 2011 • 25 of 30 studies were of combined aortic valve repair</td>
<td>0 – 5%</td>
<td>• 82-100% - 5 year survival • 43-100% - 5 year freedom from</td>
</tr>
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</table>
Surgical techniques varied within each study and across studies, reflecting institutional expertise, patient selection, heterogeneity in patient’s aortopathy pattern, and different threshold for interventions on the aorta. Readers interested in further details regarding surgical decision making, perioperative management, and strategy (open vs. closed distal anastomosis), arch reconstructive options, and use of cerebral protection strategies are referred to the comprehensive 2010 Guidelines document.9
Table S 2: Management of Pregnant Women with Bicuspid Aortopathy*

Prior to Pregnancy

- Women with a bicuspid aortic valve should undergo imaging of the entire aorta before pregnancy.\(^{10}\)
- Prepregnancy evaluation in women with bicuspid aortic valve and aortopathy should be performed by practitioners with expertise in the management of pregnant women with heart disease.
- Women with ascending aorta and/or root dimension >45 mm should be advised against pregnancy.\(^{11,12}\)
- Women with mildly dilated ascending aorta/root (40-45 mm) likely represent an intermediate risk group for which pregnancy is relatively contraindicated and who will require close medical surveillance during pregnancy.\(^{12}\)
- Threshold for surgery prior to pregnancy is similar to that of the general population of individuals with bicuspid aortopathy without concomitant valvular dysfunction (50-55 mm)\(^ {10,12}\).
- Body surface area should be taken into account in small women. Aortic diameter to body surface area index has been proposed as an alternative threshold for pre-pregnancy surgical consideration but the suggested threshold was extrapolated from women with Turner’s syndrome.\(^ {10}\)

Antepartum and Peripartum

- Women with bicuspid aortopathy should receive their ante- and peripartum care by multidisciplinary health care team with expertise in heart disease in pregnancy.
- Women with dilated aorta should have strict blood pressure control.\(^ {10}\)
- Repeated echocardiographic imaging every 4–12 weeks during pregnancy should be performed in women with bicuspid aortopathy.\(^ {10}\)
- MRI (without gadolinium) is recommended if there is an indication for imaging of distal ascending aorta, aortic arch or descending aorta during pregnancy.\(^ {10}\)
- Transesophageal echocardiography is an alternative to MRI for imaging of aorta during pregnancy.\(^ {9}\)
- Beta adrenergic blockers, to reduce shear stress on the aorta, may be considered during pregnancy in women with dilated aorta.
- Women with bicuspid aortopathy or history of dissection should deliver in a centre where cardiothoracic surgery is available.\(^ {10}\)
- Cesarean delivery should be considered for aorta > 45 mm.\(^ {10}\)
- For women with aorta < 40 mm, Cesarean delivery is reserved for obstetric or fetal indications.\(^ {10}\)
- Regional anesthesia and assisted 2nd stage should be considered for vaginal delivery of women with aortopathy.\(^ {10}\)
- Repeat cardiac imaging should be performed around the 6th postpartum month, in order to evaluate for progression of aortopathy

* The risk of pregnancy in women with bicuspid aortic valve and dilated aorta has not been systemically examined. Recommendations from guidelines are primarily based on small series, extrapolations from studies of nonpregnant individuals, and expert opinion.⁹,¹⁰,¹²,¹³
Table S 3: Exercise Considerations In Individuals with Bicuspid Aortopathy

1. Patients with aortic aneurysm (>50% of expected dimension) or previously repaired aortic dissection should avoid strenuous lifting, pushing, or straining that would require a Valsalva maneuver\textsuperscript{9,12,14,15}

2. The above restriction would also apply to those individuals in whom aortic diameters are approaching the threshold for intervention.

3. Individuals with bicuspid aortopathy can undergo aerobic or endurance exercise as these exercise is beneficial for blood pressure lowering\textsuperscript{16}

4. If patients wish to engage in vigorous aerobic exercise, such as running or basketball, one might consider performing a symptom-limited stress test to ensure that the patient does not have a hypertensive response to exercise.

5. Heavy weight lifting or competitive athletics involving isometric exercise may trigger aortic dissection and that such activities should be avoided.
References
