Use of 4D Flow MRI to Investigate if Aortic Tissue Resection without an Open Distal and Hemi-Arch Procedure Addresses All Regions Suspected for Progression of Bicuspid Aortopathy

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Purpose: Bicuspid aortic valve (BAV) is associated with a high risk for aortopathy, including aortic dilation, aneurysm formation, and dissection (20-85% incidence)[1]. In cases with significant aortic disease, aggressive resection strategies of the ascending aorta are sometimes warranted. The American College of Cardiology and American Heart Association recommend surgical intervention in BAV subjects based on a consensus threshold for aortic diameter (>5.5 cm, or >4.5-5.0 cm with additional risk factors)[2]. However, there are no consensus recommendations as to the extent or type of surgery and no data to support the extent of aortic resection. Thus, the question remains: should the surgeon risk (1) hypothemic circulatory arrest with open beveled hemiarch anastomosis, thereby removing most of the ascending aorta native tissue, or (2) standard replacement of the proximal ascending aorta, leaving a remnant of the distal ascending aorta at the level of the cross-clamp. Option 1 presents a higher risk for near-term morbidity and mortality, but may completely remove tissue at risk for further complications. Option 2 is less risky in the near term, but may leave compromised tissue at risk for further aneurysm formation.

Recent data indicates that 4D flow MRI can identify regions of the aorta at risk of altered tissue architecture and signaling pathways through the use of wall shear stress (WSS) heatmaps[3, 4]. While additional validation is needed, it may be that regions of elevated WSS should be resected during aneurysm repair. Making this critical assumption, this study surveys the efficacy of standard aortic resection practices at our institution to include areas hypothesized to be at risk for disease progression, as determined by WSS measured from preoperative 4D flow MRI (i.e. time-resolved 3D phase contrast MRI with 3-directional velocity encoding).

Methods: 33 subjects were enrolled for this study with IRB approval and informed consent. 23 BAV patients (49±13 yrs) undergoing ascending aortic repair received preoperative standard of care CEMRA and a research 4D flow MRI exam. 4D flow MRI was implemented with prospective ECG gating and a free-breathing navigator to image the thoracic aorta at 1.5 and 3T (Espree, Avanto, Skyra, Aera, Siemens, Erlangen, Germany). Spatial resolution was 1.7-3.6x1.7-2.7x2.2-3.0 mm^3; temporal resolution was 36-43ms (13-23 timeframes); TE/TR/FA was 2.2-2.8ms/4.5-5.3ms/7-15° and the VENC ranged from 150-400cm/s depending on degree of valve disease. In addition, 10 age-matched normal subjects (50±14 yrs) with healthy tricuspid aortic valves were examined using the same 4D flow protocol (VENC=150 cm/s) and the data was used to compute the 95% confidence interval (CI) for physiologically normal WSS values[3]. The expression of WSS for individual BAV patients outside of the 95% CI was represented using heatmaps indicating abnormally high (Fig. 1, red regions) or low (blue regions). WSS above the healthy 95% CI classified tissue at risk (represented by dark gray shading, Fig 1). Risk was not classified outside of the region untreatable by open distal/hemi-arch repair. The surgeon was blinded to the WSS results and resected BAV tissue was labeled by aorta location and reserved for histology, biomechanical testing, and multiplex analysis (results reported in Guzzardi et al.[4]). Finally, standard of care postoperative CEMRA or CT angiography (CTA) identified the exact region of resection (Fig. 2). CTA imaging was performed on a dual-source 64 slice scanner (Somatom Definition, Siemens Medical Systems, Erlangen, Germany) with prospective ECG synchronization, and 110 mL of iodinated contrast was administered at 5 mL/msec, with scan initiation during the contrast bolus upslope in the ascending aorta. A Wilcoxon rank-sum test was used to test the significance of the remaining tissue at risk by surgical procedure.

Results and Discussion: Preoperative mean aortic diameter in the BAV sinus of valsalva (SOV) and mid-ascending aorta were 4.6±0.5 and 4.8±0.6 cm, respectively; the age-matched control diameters were 3.0±0.5 and 2.9±0.5 cm (P<0.001). 50% of patients had severe aortic stenosis or insufficiency. All patients had WSS above the physiologic norm (Fig. 1). All 12 patients with open distal and hemi-arch repair had complete removal of "at-risk" tissue as defined by elevated WSS. In all but one case, resection with clamp on would have resulted in residual at risk regions (1 case had 20% more tissue resected than at risk). Of the 11 patients with the occluding clamp left on: 4 had regions at risk that matched/were smaller than the resected regions (-9±6% of resection area) while 7 had remaining tissue at risk (33±18% of resection area). Between the two procedures, a significant difference existed regarding the absolute amount of at risk tissue remaining (p=0.02, Fig 3).

Conclusion: Preliminary results show evidence for a contribution of WSS to tissue dysfunction[4]. If WSS biomarkers are predictive for aortopathy progression, we set out to survey the efficacy of resection strategies to remove at risk tissue at our institution. The results show that in selected patients with BAV, aggressive resection using open distal/hemi-arch repair may be necessary. Less aggressive resections without an open distal anastomosis does not always completely remove "at risk" regions. With further validation, 4D flow MRI could be used to guide patient-specific resection strategies.

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References: **[1]** Verma, S, *et al.* J Thorac Cardiovasc Surg, 2013. 146(5): p. 1033-1040 e4. **[2]** Nishimura, RA*, et al.* Journal of the American College of Cardiology, 2014. **[3]** van Ooij, P, *et al.* Ann Biomed Eng, 2014. **[4]** Guzzardi, DG*, et al.*, in *AHA Scientific Sessions* 2014: Chicago.

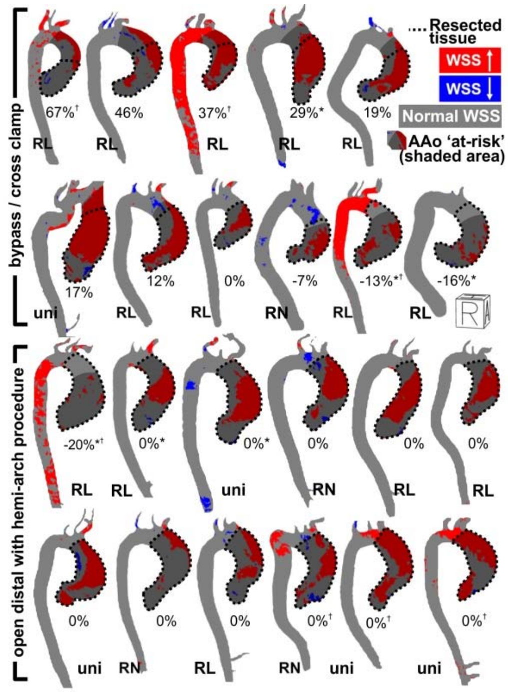

Fig. 1. 4D flow wall shear stress heatmaps (elevated WSS, red) indicate ascending aorta regions at risk for aortopathy (dark shading). At risk tissue regions are compared to surgically resected regions (dashed lines, see method, Fig. 2). The difference between the area at risk and the resected area are shown in percentages. [RL: right-left coronary leaflet fusion; RN: right-non coronary leaflet fusion; uni: unicuspid; *at risk region not fully visible in chosen view; †indicates notable at risk regions beyond hemi-arch repair.]

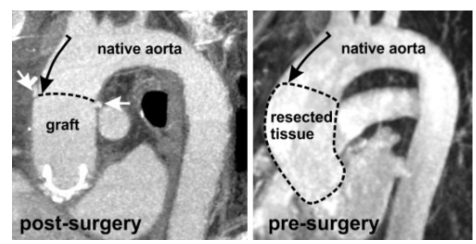

Fig. 2. The region of resected tissue was determined by pre- & post-surgical CE-MRA / CTA. The anastomosis (left, white arrows) and surgical notes indicated the type of procedure and the location of removed tissue. The distance of the anastomosis from the brachiocephalic (left, black arrow) was used to determine the resection region (right).

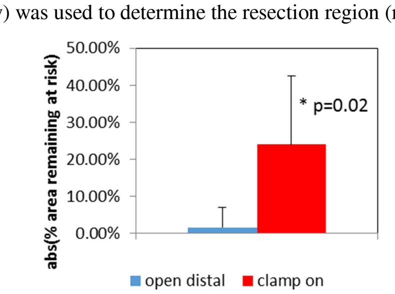

Fig. 3. Absolute remaining area of tissue at risk (as determined by WSS heatmap).