Thoracic Aorta 3D Wall Shear Stress as a Marker of Bicuspid Aortic Valve Disease in Pediatric Patients

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Background: Bicuspid Aortic Valve (BAV) has a prevalence of 0.5% to 2% and is the most commonly diagnosed congenital heart defect (1). Pediatric BAV patients are known to have larger aortic dimensions than children with trileaflet valves, and are prone to progressive ascending aorta (AAo) dilatation (2). As these patients progress into adulthood, they are at increased risk for aortic dissection as a result of the disease (3), however the risk of primary cardiac events in childhood is minimal (4). Still, when diagnosed at an early age, BAV patients frequently undergo surgical intervention to normalize valve function and alter thoracic aorta anatomy in hopes of reducing long term risk (5). Changes in aortic wall shear stress (WSS) have been shown to promote endothelial cell dysfunction and ultimately lead to vascular remodeling (6). Elevated AAo WSS resulting from high velocity, asymmetric outflow jets in BAV patients has been hypothesized to play a role in aneurysm growth and development in this cohort. Recent studies by Barker et al and Bissel et al. demonstrated that adults with BAV have systematically higher and more asymmetric WSS relative to normal controls(7,8). However, to our knowledge, a detailed analysis of aortic hemodynamics in a cohort of pediatric patients with BAV has not been presented. In this study, we report on the WSS in the aorta derived from 4D flow MRI in a group of n=26 pediatric BAV and evaluate correlation with age, body surface area, and aorta dimensions. Elevated WSS may increase the risk of progressive AAo dilatation and may be a useful tool in risk stratification in children with this disease.

Table 1: Correlations of patient findings with max and mean WSS_{sys} in the AAo.		Age		BSA		Root Z-score		Aortic Stenosis		Peak Vel_{sys}	
	Average	r	p	r	p	r	p	r	p	r	p
Max WSS_{sys}	1.31 ± 0.4 N/m^2	0.36	0.07	0.42	0.03	-0.35	0.08	0.63	0.001	0.93	0.001
Mean WSS_{sys}	0.69 ± 0.2 N/m^2	0.31	0.12	0.38	0.054	-0.52	0.01	0.37	0.07	0.83	0.001

Methods: Pediatric patients with known BAV (n = 26, age: 14.1 ± 5 (min: 3) years old, M:F =14:12) had 4D flow MRI included in a physician-ordered cardiac MR assessment as part of this IRB-approved study. MRI scans were performed at 1.5 T (MAGNETOM Avanto or Aera, Siemens, Germany) with spatial resolution = 2.2-3.5 x 1.7-2.5 x 2.0-4.0 mm^3, temporal resolution = 37.6-40.8 ms, TE/TR/ FA = 2.3-2.6 ms/ 4.7-5.1 ms/15°, and VENC = 150 – 400 cm/s. Data pre-processing included correction for eddy currents and velocity aliasing. In addition, a full 3D segmentation of the thoracic aorta was performed (MIMICS, Materlise, Belgium). Patient's aortic root z-scores were calculated from MRI measurements and body surface area (BSA) at time of scan using EchoIMS (Merge, Chicago, IL). 3D WSS along the entire vessel surface was calculated using the method described by van Ooij et al[2]. Peak systole was defined as the cardiac phase with highest average velocity in the aorta. Systolic values for WSS (WSS_{sys}) and velocity (vel_{sys}) were defined as the average over five systolic phases centered on peak systole (peak systolic phase ± 2 phases). The aorta was divided into AAo, arch, and descending aorta (DAo) regions (Figure 1B), and maximum and mean WSS_{sys} and vel_{sys} were calculated in each region. Maximum values were defined as the average of top 5% of all values in a region to account for noise within the data. WSS_{sys} maximum intensity projections (MIP) were mapped onto a sagittal view of each aorta for qualitative review (Figure 1B). All results were compared using Student's t-test or Mann-Whitney U test as appropriate. To identify relationships between hemodynamic parameters and age, BSA, z-score, and stenosis grade, linear regression was performed and Spearman (r_S) or Pearson (r) correlation coefficients were calculated. A $p<0.05$ was considered significant.
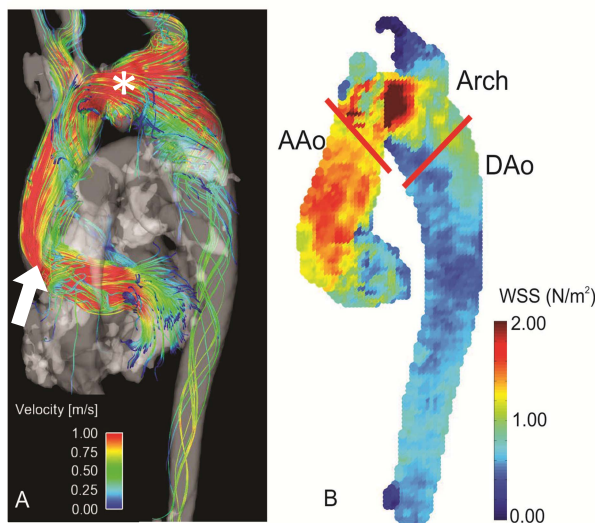

Figure 1: 4D flow findings in a pediatric BAV patient with a history of agothic arch and history of aortic coarctation repair. A) Pathline visualization of systolic blood flow. Note the high velocity outflow jet impinging on the lateral wall of the AAo (arrow) and well as high velocity flow within the arch of the aorta (*). B) Maximum intensity projection of WSS_{sys}, with high WSS values corresponding with regions of high velocity flow and jet impingement in A. Red lines – aortic region divisions.

Results: The BAV cohort included n = 22 right/left- coronary leaflet fusion patients and n = 4 right/non-coronary leaflet patients. Subjects had an enlarged aortic root with an average aortic root z-score of 2.64 ± 1.8. AAo mean and max WSS_{sys} in the AAo were 0.69 ± 0.2 N/m^2 and 1.31 ± 0.4 N/m^2, respectively, and AAo peak vel_{sys} was 1.27 ± 0.4 m/s. There was significant correlation between mean WSS_{sys} in the AAo and aortic root z-score (r = -0.52, p = 0.006) and peak AAo vel_{sys} (r = 0.8, p<0.001), indicating a structure-function relationship between aortic size and reduced systolic WSS and velocities. No significant relationships with aortic stenosis or BSA were found. Max WSS_{sys} did not correlated with aortic root z-score (r =-0.35, p = 0.08), but there was a strong significant relationship with peak AAo vel_{sys} (r = 0.93, p < 0.001) as well as aortic stenosis (r_S = 0.63, p = 0.001) and BSA (r = 0.42, p = 0.03). Neither AAo WSS_{sys} nor velocity correlated with age. (Table 1)

Conclusions: Our findings demonstrate the feasibility of non-invasive estimation of thoracic aorta 3D WSS using 4D flow MRI in pediatric patients with BAV, even at ages as young as 3 years old. Here we report the mean and max systolic 3D WSS in this cohort, but the challenge of capturing a control group of healthy pediatric patients for 4D flow CMR assessment makes acquiring appropriate comparison data difficult and, thus, inhibits us from reporting on the relative magnitude of these WSS values at this time. Of note, our results demonstrate that while max WSS_{sys} does not correlate with AAo diameter, mean WSS_{sys} decreases with increasing AAo diameter. This finding is intuitive but helps drive the hypothesis that the AAo in BAV patients may progressively dilate as a mechanism to normalize mean WSS levels. Early evaluation and quantification of WSS in young BAV patients may help to better risk stratify this group to help limit surgical intervention to only those patients at highest risk.

References: 1. Siu et al. *J. Am. Coll. Cardiol.* (2010). **2.**Holmes et al. *Am. J. Cardiol.* (2007). **3.**Tzemos et al. *JAMA.* (2008). **4.**Mahle et al. *J. Pediatr.* (2010). **5.**Fernandes et al. *J.Am. Coll. Cardiol.* (2007). **6.**Ben Driss et al. *Circulation.* (2000). **7.**Barker et al. *Circ Cardiovasc Imaging.* 2012. 8. Bissell et al. *Circ Cardiovasc Imaging.* (2013).