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Age-Related Changes in Aortic 3D Blood Flow Velocities and Wall Shear Stress: Implications for the Identification of Altered Hemodynamics in Patients with Aortic Valve Disease

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Abstract

Purpose—To investigate age-related changes in peak systolic aortic 3D velocity and wall shear stress (WSS) in healthy controls and to investigate the importance of age-matching for 3D mapping of abnormal aortic hemodynamics in bicuspid aortic valve disease (BAV).

Methods—4D flow MRI (fields strengths=1.5–3T; resolution=2.2–3.9×1.7–2.6×2.2–4.0mm³; v_{enc} =150–250cm/s; TE/TR/FA=2.3–2.8ms/4.7–5.4ms/7–15°) was performed in 56 controls (age range: 19–78 years) and in two BAV patient groups each consisting of 10 subjects (group 1: 20–29 years, group 2: 52–57 years). Heat maps showing abnormal 3D velocity and WSS were created for the BAV patients by comparison with an age-matched and with an unmatched control group. The fraction of the aorta exposed to abnormal velocity/WSS was calculated relative to the total aortic volume/surface.

Results—Significant inverse relationships between age and healthy velocity/WSS were found ($R^2=0.32/0.39$, $P<0.001$). For BAV group 1, abnormally elevated velocity/WSS was overestimated when compared with older controls (51–60 years) than when correctly age-matched ($\sim 25\pm 14\%$ vs. $\sim 8\pm 5\%$). For BAV group 2, abnormally decreased velocity/WSS was overestimated when compared with younger controls (21–30 years) than when correctly age-matched ($\sim 9\pm 7\%$ vs. $1\pm 1\%$).

Conclusion—Significant correlations exist between age and peak systolic velocity and WSS. Therefore, robust age-matching is important when creating abnormal 3D aortic velocity and WSS maps for patients with BAV.

Keywords

4D flow MRI; wall shear stress; healthy controls; bicuspid valve disease

INTRODUCTION

4D flow MRI (time-resolved three-dimensional phase contrast MRI with three-directional velocity encoding) has been used to investigate 3D blood flow patterns in patients with diseases of the thoracic aorta (1–7). Previous studies have demonstrated that 4D flow MRI can be used to visualize and quantify changes in 3D blood flow velocities that are associated with aortic pathologies such as dilatation, aneurysm, dissection, or aortic valve dysfunction (8–10). In addition, wall shear stress (WSS), a biomarker for endothelial cell dysfunction that has been implicated in aortic remodeling, can be derived from 4D flow MRI (11–14). Recent developments permit the quantification of full 3D velocity fields in the aortic lumen and 3D WSS along the entire aorta wall (14–16).

It is known that arterial wall stiffness increases with age, which has been linked to changes in aortic geometry (17–19). For example, it was determined by echocardiography and CT that aortic diameter increases with age (20,21). Furthermore, Doppler flow measurements revealed that aortic net flow decreased with increasing age (22,23). Although studies have been performed to investigate aortic pulse wave velocity for aortic stiffness assessment (19,24,25), the comprehensive evaluation regarding the impact of age on aortic 3D velocity fields and 3D WSS patterns has not been performed and reference data across age groups is lacking.

We have recently developed tools to compute regional geometric and hemodynamic confidence intervals for cohort groups (hereafter referred to as aortic ‘atlases’). In this study, we aim to investigate regional age-related changes in aortic 3D velocity fields and 3D WSS in a cohort of 56 healthy controls, ranging in age from 19 to 78 years. The importance of age-matching for the detection of abnormal 3D velocities and 3D WSS was analyzed by investigating the impact of the use of age-matched versus unmatched cohorts for the identification of regions with abnormal 3D velocity and 3D WSS in 20 patients with bicuspid aortic valve (BAV).

METHODS

Subject Enrollment

Fifty-six healthy control subjects (37 men, 44 ± 13 years, range = 19 – 78 years), subdivided in five age groups: 19–30 years ($n = 11$), 31–40 years ($n = 10$), 41–50 years ($n = 19$), 51–60 years ($n = 12$) and 61–78 years ($n = 4$) were enrolled in the study. To investigate the influence of age-matching, ten younger BAV patients (group 1, 7 men, mean 25 ± 3 years, range = 20 – 29 years) and ten older BAV patients (group 2, 6 men, 54 ± 2 years, range = 52 – 57 years) with non-stenotic bicuspid valves were selected from a database of subjects who underwent 4D flow MRI at Northwestern University between 2012 and 2014. All subjects for this HIPAA compliant study were included in the study according to procedures approved by the Northwestern University Institutional Review Board. Informed consent was obtained from all controls and the 5 patients who were recruited for research MRI scans. Fifteen BAV patients undergoing standard-of-care MRI were enrolled via retrospective chart review.

MR Imaging

4D flow MRI with prospective ECG gating and respiratory navigator gating was performed in all subjects in a sagittal oblique volume covering the entire thoracic aorta. All exams were performed on 1.5 T and 3 T MAGNETOM Avanto, Espree, Aera and Skyra systems (Siemens Medical Systems, Erlangen, Germany). Pulse sequence parameters for all subjects were: spatial resolution = $2.2 - 3.9 \times 1.7 - 2.6 \times 2.2 - 4.0 \text{ mm}^3$; field of view = $320 - 450 \times 240 - 341 \times 66 - 120 \text{ mm}^3$; temporal resolution = $38 - 43 \text{ ms}$ (10 – 30 time frames); TE/TR/FA = $2.3 - 2.8 \text{ ms}/4.7 - 5.4 \text{ ms}/7 - 15^\circ$; Venc = $150 - 250 \text{ cm/s}$ in all three velocity encoding directions.

BAV morphology was assessed using routinely acquired balanced ECG gated breath held 2D CINE steady state free precession (SSFP) scans acquired at the level of the valve and categorized according to the Sievers scheme by a cardiovascular and interventional radiologist (J.D.C with 10 years of experience) (26,27). Aortic insufficiency (AI) was characterized as mild for regurgitant fraction $<30\%$, moderate for $31\% - 49\%$, and severe 50% (28).

4D flow MRI pre-processing and 3D segmentation

All 4D flow MRI data (figure 1a) were corrected for eddy currents, Maxwell terms and velocity aliasing using in-house software programmed in Matlab (Natick, The Mathworks, USA) (29). 3D Phase contrast (PC) magnetic resonance angiography (MRA) images were created by voxel-wise multiplication of the magnitude data with absolute velocities averaged over all cardiac time frames (29). Next, a 3D segmentation of the thoracic aorta was semi-automatically obtained based on the 3D PC-MRA data (Mimics, Materialise, Leuven, Belgium) (figure 1b).

For the controls, the mid-ascending aorta (MAA) diameter was automatically characterized by calculating a centerline from the 3D segmentation (30). Subsequently, a plane normal to the centerline direction at the level of the right pulmonary artery was generated and the MAA diameter was derived assuming a circular area (figure 1c) (31). For the patients with BAV, the diameters at the level of the Sinus of Valsalva (SOV) and the MAA were measured by a cardiovascular and interventional radiologist (J.D.C with 10 years of experience) on routinely acquired contrast-enhanced magnetic resonance angiography exams.

Peak systole was defined as the time frame with the highest absolute mean velocity in the aortic volume defined by the aorta 3D segmentation (figure 1b). In addition, peak systolic velocity in the proximal ascending aorta was extracted from a maximum intensity projection image of the absolute velocity at peak systole (figure 1c) (28).

WSS was calculated as previously described (figure 1c) (15,32). To calculate segmental aortic mean velocity and WSS, each aorta was manually subdivided in three regions: 1) the ascending aorta (AAo, from the sinotubular junction to the origin of the innominate artery), 2) the aortic arch (from the origin of the innominate artery to the proximal descending thoracic aorta approximately 2 cm distal to the left subclavian artery and 3) the descending aorta (DAO, from the proximal descending aorta to the descending aorta approximately 2 cm proximal to the celiac trunk) (figure 1c).

Normal Controls - Aortic 3D velocity and 3D WSS atlases for different age groups

For all five age groups, cohort-averaged 3D velocity fields and WSS atlases (figure 2a and 3a, respectively) were created as described previously (32). Briefly, for each age group a shared aortic geometry was created by maximizing the overlap of all aortic 3D segmentations (32). To calculate the normal velocity atlases (figure 2a), the absolute velocities inside the aortic segmentation of each individual subject were interpolated to the voxels of the shared geometry and averaged over all subjects in the respective age groups. In addition, absolute WSS of each individual subject was projected onto the wall points of the shared aortic geometry and averaged over all subjects in the respective age group (figure 3a). Furthermore, standard deviations (SD) of velocities in each voxel and WSS in each wall point across all subjects of each age group were calculated.

BAV patients - heat maps for the assessment of changes in aortic blood flow velocities and WSS

For each individual BAV patient, 3D velocity and 3D WSS heat maps were calculated to quantify the fraction of the aortic volume and surface area exposed to elevated or reduced (i.e. abnormal) velocity and WSS as described previously (33) (figures 2b and 3b). Briefly, the 3D segmentation of the individual BAV aorta was co-registered to the shared aortic geometry of a normal control age group. Subsequently, the velocity and WSS atlases were interpolated to the aortic segmentation of the BAV patient. Next, volumes and surfaces with velocity and WSS elevated above the 95% confidence interval for normal velocity and WSS in this age group (as defined by the mean $\pm$ 1.96 * SD map) were delineated in red. Regions in the aortic volume and on the surface exposed to velocity and WSS below the 95% confidence were labeled blue (figure 2d). The fraction of the aorta exposed to abnormal velocity or WSS was calculated relative to the total aortic volume or aortic wall surface, respectively.

To investigate the impact of age on the detection of altered aortic velocity and WSS, two series of heat maps were calculated for each BAV patient by 1) selecting the appropriate age-matched control group, and by 2) selecting an unmatched control group (control age group 51–60 years for younger BAV group 1 and control age group 19–31 years for older BAV group 1).

Statistical Analysis

All continuous parameters were expressed as mean $\pm$ SD. Differences in MAA diameter, peak velocity, regional mean velocity and regional mean WSS between the five age groups were determined using a Kruskal-Wallis test. Linear regression with age was performed for MAA diameter, peak velocity and velocity and WSS averaged over the entire segmentation. A Wilcoxon rank sum test was used to test for significance between abnormal velocity/WSS percentages created with the two different age-matching methods. A Wilcoxon rank sum test was used to test for significance between abnormal velocity/WSS percentages between the BAV cohort aged between 20–29 years and the BAV cohort aged between 52–57 years. For all tests, $P < 0.05$ was considered statistically significant.

RESULTS

Study cohort

Demographics for the control cohort and the five age sub-groups are summarized in table 1. All controls had no history of cardiovascular disease and normal valve function (no stenosis: peak systolic velocity < 2 m/s).

Demographics of BAV patients are summarized in table 2. Both BAV patient groups (group 1: 20–29 years, group 2: 52–57 years) had identical distribution of aortic valve morphology: 5 patients with no raphe and opening in anterior-posterior direction (Sievers 0 AP), 2 patients with no raphe and opening in lateral direction (Sievers 0 LAT) and 3 patients with one raphe and fusion of the right and left cusps (opening in anterior-posterior direction, Sievers 1 RL) (26). SOV and MAA diameters were significantly larger for the older patient cohort than the young, see table 2. The distribution of aortic valve insufficiency was similar between groups. In addition, the peak velocity was similar for both groups of BAV patients and for the BAV patients and the healthy controls ($P=0.65$).

Normal Controls - Influence of Age on Aortic 3D Hemodynamics

Figure 4 shows the resulting 3D velocity (MIPs) and 3D WSS atlases for the five different volunteer age groups. A decrease in mean 3D velocity and 3D WSS with increasing age and differences in the spatial distribution of the velocity field with age can be appreciated.

The MAA diameter ($P=0.001$) and peak velocity ($P=0.03$) were significantly different between age cohorts, see table 1. Regression analysis demonstrated significant relationships of elevated MAA diameter and peak velocity with increased age ($R^2=0.35$, slope= 0.02 cm/year, $P<0.001$, and $R^2=0.09$, slope= 0.005 m/s/year, $P=0.03$, respectively). In addition, mean velocity and mean 3D WSS were significantly different between age groups for all three aortic segments (AAo: $P=0.01$, arch: $P=0.002$, DAo: $P<0.001$, see table 1). Both segmental 3D mean velocity and 3D WSS decreased with increasing age. There were significant inverse relationships between 3D velocity and 3D WSS averaged over the entire aorta and age ($R^2=0.32$, slope= -0.005 m/s/year and $R^2=0.39$, slope= -0.007 , $P<0.001$, respectively). Furthermore, significant correlations were found for mean velocity and MAA diameter ($R^2=0.21$, $P<0.001$) and mean WSS and MAA diameter ($R^2=0.27$, $P<0.001$). A near perfect correlation was found between mean aortic velocity and WSS ($R^2=0.97$, $P<0.001$).

BAV Patients - Changes in Aortic Hemodynamics and Impact of Age Matching

Table 3 summarizes the fraction of the aorta exposed to abnormal 3D velocity and 3D WSS in patients with BAV. The extent of elevated or decreased 3D velocities and 3D WSS was similar for both BAV groups if appropriately age-matched normal control atlases were selected, except for regions with abnormally decreased 3D WSS ($P=0.007$). Notably, the calculation of abnormal 3D velocities and 3D WSS based on unmatched control groups significantly impacted the result. Specifically for young BAV patients (group 1, 20–29 years), the selection of an older control group (51–60 years) resulted in substantial overestimation of abnormally elevated 3D velocities and 3D WSS ($P=0.002$ and $P<0.001$,

respectively, see table 3). Furthermore, for the BAV group aged between 52 and 57 years old, the selection of a younger control group (21–30 years) resulted in substantial overestimation of abnormally decreased 3D velocities and 3D WSS (both $P < 0.001$, table 3).

For a subgroup of five patients from each BAV cohort, figures 5 and 6 show the series of individual 3D velocity and 3D WSS heat maps, respectively. Differences in the extent and distribution of abnormal hemodynamics between heat maps based on appropriately age-matched and unmatched control groups can clearly be appreciated. Specifically, calculation of abnormal 3D velocity and 3D WSS heat maps based on unmatched control atlases showed substantial and significant differences with appropriately age-matched 3D velocity and 3D WSS heat maps. For the example subgroup of young BAV patients displayed here, there was an increase in abnormally elevated velocity/WSS from $9 \pm 5\%/6 \pm 4\%$ to $21 \pm 7\%/27 \pm 10\%$ ($P=0.03/0.01$). For the exemplary subgroup of older BAV patients displayed here, an increase in abnormally decreased velocity/WSS from $1 \pm 0\%/1 \pm 1\%$ to $10 \pm 8\%/16 \pm 9\%$ ($P=0.01/0.01$) was found. A good correlation was found between percentages of abnormally elevated velocity and abnormally elevated WSS ($R^2=0.75$, $P < 0.001$).

DISCUSSION

In this study, we investigated age-related changes in peak systolic 3D velocity fields and 3D WSS in the thoracic aorta of 56 healthy volunteers. The decrease in velocity and WSS with age had a significant effect on the visualization and quantification of the 3D velocity and 3D WSS heat maps in BAV patients. BAV patients were chosen as an example group since these patients have abnormal blood flow, even at normal peak velocities, that can be visualized comprehensively with the heat map technique, as we have shown previously (34).

As has been previously reported, a significant positive correlation of MAA diameter was found with age (24). The change in velocity and WSS fields with age are most likely related to the geometric size changes which occur in the aorta with age, as well as changes known to occur in the compliance and elasticity of the aorta (18,35).

Recently, we presented a technique for creating patient-specific WSS heat maps for investigating aortopathy in BAV disease. The process involved comparing a patient with a healthy WSS atlas (33). In that study, a control cohort was used with a fairly wide range of ages (33 – 76 years old). In the current study, we show here that care must be taken when using a control cohort with a wide range of ages as WSS will vary with age. Given the larger standard deviations experienced with a wide range of age (and thus wider 95% CI), the identification of abnormal WSS in an individual patient will be minimized. Here we demonstrate this concept by examining the heat map results when using two age groups. Note that the code to create atlases and heat maps is freely available and can be obtained by sending an e-mail to the first author.

Few studies have investigated regional age-related changes in aortic velocity with MRI. In the first study where 2D phase contrast MRI (2D PC-MRI) was employed to investigate aortic hemodynamics in healthy controls, pulse wave velocity was studied, and a trend toward decreased mean aortic velocity with age was suspected (19). Bogren et al. employed

2D PC-MRI in a sagittal slice through the aorta with three-directional velocity encoding to detect a decrease in peak velocity with age (4). In contrast, we found a weak positive correlation between peak velocity and age, which may be explained by the fact that more subjects were included here than in Bogren et al. (56 vs. 16 controls) and that 4D flow MRI encompassing the entire aorta was used rather than one sagittal slice through the aorta, prone to miss true peak velocity. Notably, a decrease in peak velocity for the 31–40 year and 51–60 year old control cohorts was found. This was contrary to the general trend and is suspected to be due to physiologic noise between the cohorts. Peak velocity mainly increased with age, which is most likely due to progressive valve calcification, reduced valve mobility, a reduced geometric orifice area and thus increasing the blood velocity immediately downstream from the valve (36). Kröner et al. measured a decrease in flow volume per minute with older age, which could also indicate a decreased mean velocity. However, they focused on pulse wave velocity and aortic stiffness like most other studies investigating age-related hemodynamic changes (37) (24) (25).

Another finding of our study was the increased MAA diameter with age, which was previously reported by Rogers et al (24). The decrease in mean velocity and WSS with age in our study could be related to an increase in aortic diameter.

Three-dimensional velocity heat maps are comprehensive yet simple visualizations that provide insight in the aortic locations where velocity is abnormally higher or lower than healthy controls, even when technically not stenotic. In this context, note that when compared with age-matched controls, each of the BAV patients included had regions of abnormally elevated velocity, even up to 17% of the total aortic volume, despite having stenosis-free BAV's. This supports the notion of BAV-related abnormal eccentric flow patterns (38–41) result in a regional deviation of velocity as compared to healthy subjects. Abnormally elevated velocity was predominantly found in the right-anterior part of the ascending aorta. Note that with correct age-matching, the amount of abnormally elevated velocity was identical for the young and old BAV cohorts.

WSS is closely related to velocity since the former is a derivation of the latter. This is illustrated by the near perfect correlation between mean velocity and mean WSS in all segmentations of the entire aorta in the control cohort. Furthermore, this is supported by the good correlation between abnormal velocity and abnormal WSS in the BAV patient cohort. Yet, it is important to add the WSS analysis alongside the velocity analysis, since WSS is a shear force acted on the wall of aorta, and therefore potentially a direct biomarker for aortic wall dysfunction. In previous work, we showed in a cohort of BAV patients that regions of abnormally elevated WSS exhibited increased expression of matrix metalloproteinases (MMP's) and elastin degradation than regions of normal WSS (42). Thus, abnormal WSS may have more predictive value for dilation progression than abnormal velocity. Future follow-up data will allow for the investigation of aortic growth in relation to abnormal hemodynamic maps.

4D flow MRI-estimated WSS values decrease with the spatial resolution of the acquisition (11,15). Thus, the absolute WSS values are underestimated when compared with different techniques such as computational fluid dynamics (43,44). In this context, it is important that

all 4D flow MRI acquisitions were performed with similar spatial resolution. In this study, the voxel size varies widely from 8 – 41 mm³. However, the 41 mm³ voxel size was used in only one subject in the BAV patient group of 52–57 years old. With exclusion of this patient, the statistical results did not change. Furthermore, for perfect parabolic flow, Stalder et al showed that differences in WSS were on the order of 0.1 Pa for pixel lengths within this range and Potters et al. showed a smaller variation on the order of 0.05 Pa. Thus, a comparison of WSS between controls and patients is valid here.

In this study, inter-observer variability was not taken into account, since only one observer performed the aortic segmentations. We recently showed that the inter-observer variability in quantification of 3D velocity and WSS and abnormal velocity and WSS was low (45).

As a result of different SNR levels for 1.5T and 3T scanner systems, some variance in velocity and WSS values may be present. However, it was shown by Strecker et al. (46) that such differences were not significant between 1.5T and 3T systems.

Although a relatively large control cohort of 56 patients was used, age-matching for the creation of abnormal hemodynamic maps necessitated subdivision in smaller groups of ~14 subjects per cohort, limiting the statistical power of each group. However, when a difference in WSS between control and non-stenotic BAV patients of 0.5 ± 0.3 Pa is assumed (13), only the 61–78 year-old cohort did not comprise a sufficient number of subjects. This age-group was therefore not used in the analysis for the abnormal hemodynamic maps. The statistical power can be increased by combining all volunteers in one group. Nonetheless, as we demonstrated in this study, the trade-off between increasing statistical power and robustness of age-matching may favor the latter.

Ideally, 3D velocity and 3D WSS atlases created in this study were not only stratified for age, but for gender as well. However, the limited number of subjects did not allow for the investigation of the influence of gender as it has been performed in aortic diameter nomograms (47,48). Future work will consist of analyses such as those presented here of 4D flow MRI data acquired in women.

In conclusion, we demonstrated in 56 healthy controls that significant correlations exist between age and the hemodynamic parameters velocity and WSS at peak systole. Therefore, robust age-matching is important when creating abnormal 3D aortic velocity and WSS maps for patients with bicuspid valves.

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Figure 1.

Post-processing pipeline for the healthy controls: (a) 4D flow MRI data, (b) Data analysis: 1. Creation of an angiogram (displayed as a maximum intensity projection [MIP]) that is used for 2. 3D segmentation of the aorta. (c) Calculation of parameters of interest: 1. the mid-ascending aortic diameter (MAA), 2. 3D velocity field (MIP) and peak velocity, and 3. 3D WSS along the aorta wall.

Figure 2.

(a) Creation of the velocity atlas. (b) Creation of the velocity heat map. All aortic images are presented in the right-anterior view.

Figure 3.

(a) Creation of the WSS atlas. (b) Creation of the WSS heat map. All aortic images are presented in the right-anterior view.

Figure 4. Peak systolic 3D velocity (maximum intensity projection, top row) and 3D WSS (bottom row) atlases categorized for age. All images are presented in the right-anterior view

Figure 5.

3D velocity heat maps for a selection of five patients from the two BAV cohorts (left column: 20–29 years, right column: 52–57 years) created with the appropriately age-matched group of normal controls (left column) and the unmatched group of controls (right column). The red volume indicates abnormally elevated velocity, whereas the blue volume indicates abnormally decreased velocity. BAV morphology as well as the fraction (in %) of abnormally elevated/decreased velocity are shown. AP = anterior-posterior, RL = right-left, LAT = lateral. All images are presented in right-anterior and left-posterior view.

Figure 6.

3D WSS heat maps for a selection of five patients from the two BAV cohorts (left column: 20–29 years, right column: 52–57 years) created with the appropriately age-matched group of normal controls (left column) and the unmatched group of controls (right column). The red surface indicates abnormally elevated WSS, whereas the blue surface indicates abnormally decreased WSS. BAV morphology as well as the fraction (in %) of abnormally elevated/decreased WSS are shown. AP = anterior-posterior, RL = right-left, LAT = lateral. All images are presented in right-anterior and left-posterior view.

Table 1

Demographics, MAA diameter, peak and regional mean velocity and WSS in 56 healthy controls subdivided in five age groups

Age group	Number of subjects	Mean age (years)	MAA diameter (mm)	Peak velocity (m/s)	Mean Velocity (m/s)			WSS (Pa)		
					AAo	Arch	DAo	AAo	Arch	DAo
19–30 y	4M, 7W	25±4	28±4	1.37±0.14	0.67±0.13	0.70±0.13	0.87±0.14	0.79±0.16	0.84±0.17	0.98±0.14
31–40 y	8M, 2W	35±3	31±3	1.21±0.16	0.59±0.10	0.63±0.12	0.73±0.12	0.68±0.13	0.73±0.15	0.81±0.14
41–50 y	13M, 6W	46±3	33±4	1.50±0.23	0.63±0.10	0.60±0.10	0.68±0.15	0.70±0.15	0.69±0.13	0.74±0.17
51–60 y	10M, 2W	54±3	35±4	1.43±0.24	0.54±0.11	0.50±0.12	0.55±0.13	0.59±0.15	0.56±0.13	0.59±0.15
61–78 y	2M, 2W	70±6	37±2	1.50±0.21	0.46±0.09	0.45±0.09	0.44±0.06	0.48±0.11	0.50±0.11	0.46±0.07
<i>P-value</i> *	-	-	0.001	0.03	0.013	0.002	<0.001	0.005	<0.001	<0.001

y = year, M = men, W = women, MAA = mid-ascending aorta, AAo = Ascending Aorta, DAo = Descending Aorta

*Kruskal-Wallis test (significant for $P < 0.05$)

Table 2

BAV Patient demographics.

	BAV group 1: 20–29 years		BAV group 2: 52–57 years		P-value
N (female)	10 (3)		10 (4)		-
Age (mean ± SD)	25 ± 3		54 ± 2		-
BAV morphology	Sievers 0 AP	5	Sievers 0 AP	5	-
	Sievers 0 LAT	2	Sievers 0 LAT	2	-
	Sievers 1 RL	3	Sievers 1 RL	3	-
SOV diameter (cm)	3.7 ± 0.5		4.5 ± 0.3		0.003 *
MAA diameter (cm)	3.6 ± 0.6		4.3 ± 0.5		0.02 *
Peak velocity (m/s)	1.6 ± 0.2		1.5 ± 0.2		0.16
Aortic Insufficiency	None	8	None	9	-
	Mild	1	Mild	0	
	Moderate	1	Moderate	1	

BAV=Bicuspid Valve SOV=Sinus of Valsalva, MAA=Mid-ascending Aorta,

*Wilcoxon rank sum test, P<0.05

Table 3

Fraction of the aorta exposed to abnormal velocity and WSS in patients with BAV.

Age-matching	Elevated velocity (%)			Elevated WSS (%)			Decreased velocity (%)			Decreased WSS (%)		
	Matched	Unmatched	P-value*	Matched	Unmatched	P-value*	Matched	Unmatched	P-value*	Matched	Unmatched	P-value*
BAV group 1: 20–29 years	8±5	22±14	0.002	8±5	28±14	<0.001	2±2	0±0	0.01	3±3	1±1	0.006
BAV group 2: 52–57 years	7±6	5±4	0.57	6±5	3±3	0.07	1±1	7±6	<0.001	1±1	11±8	<0.001
P-value*	0.47	0.001	-	0.57	<0.001	-	0.15	<0.001	-	0.007	<0.001	-

*Wilcoxon rank sum test (significant for P<0.05)