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ORIGINAL PAPER

Interval changes in aortic peak velocity and wall shear stress in patients with bicuspid aortic valve disease

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Abstract

Bicuspid aortic valve (BAV) is associated with abnormal valve-mediated hemodynamics including high velocity jets and elevated wall shear stress (WSS). This study investigated interval changes in flow and WSS in a multi-year follow-up study. This cross-sectional study included n = 44 patients with BAV (age = 44.9 ± 12 years), n = 17 patients with tricuspid aortic valve and thoracic aortic dilatation (TAV with dilation, age = 54.6 ± 16.5 years), and n = 9 healthy controls (age = 49.3 ± 14.7 years) underwent baseline and serial aortic 4D flow MRI (follow-up duration: BAV: 2.6 ± 0.7 years, TAV with dilation: 2.7 ± 0.5 years, controls: 1.1 ± 0.5 years). Data analysis included quantification of aortic dimensions, peak systolic velocities, as well as regional 3D WSS in the ascending aorta. At baseline, BAV patients demonstrated uniformly elevated peak velocity and WSS compared to TAV with dilation and control groups (peak velocity 2.2 m/s vs. 1.6 m/s vs. 1.5 m/s, $p < 0.004$; WSS: 0.74 Pa vs. 0.45 Pa vs. 0.55 Pa, $p < 0.001$). For BAV, peak velocity increased from baseline to follow up (2.2 ± 0.8 to 2.3 ± 0.9 m/s, $p < 0.001$) while WSS decreased (0.74 ± 0.22 to 0.65 ± 0.21 Pa, $p < 0.001$). Aortic growth was minimal for both BAV (0.05 cm/year) and TAV with dilation (0.03–0.04 cm/year) patients. For BAV patients, increase of ascending aorta peak velocities indicated worsening of valve function at follow-up. Compared to TAV with dilation patients, BAV patients demonstrated a reduction in WSS which may indicate a compensatory mechanism to reduce elevated WSS forces by aortic remodeling.

Keywords Bicuspid aortic valve · Flow imaging · 4D flow MRI · Aortic disease · Follow-up study

Introduction

Bicuspid Aortic Valve (BAV) affects 1 to 2% of the population and is associated with the development of aortopathy such as aortic dilatation, aneurysm, and dissection [1]. Recent studies suggest that BAV mediated changes in aortic blood flow patterns in the ascending aorta (AAO) may play an important role in disease progression [2, 3]. 4D flow MRI studies have demonstrated that BAV-induced eccentric transvalvular high-velocity flow jets may influence the development of aortic disease [4]. These flow jets exert a tangential viscous force at the arterial wall, or wall shear stress (WSS). The WSS is the drag force exerted by flowing blood on the vessel surface, and has been shown to be associated with altered endothelial cell function, including modulation of von Willebrand factor [5] and vessel wall remodeling [6] and wall tissue degeneration and elastic fiber thinning [7, 8].

However, most studies investigating abnormal blood flow patterns have been cross-sectional [9] and follow-up studies

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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are limited [10]. The slow aortic growth in BAV (0.4 to 0.6 mm/year) [11] and tricuspid aortic valve (0.4 mm/year) [12] patients with aneurysmal dilation makes study design challenging and underlines the need for a multi-year follow-up study to reliably detect disease progression. Hope et al. attempted to study the causality between aortic hemodynamics and growth, examining 13 BAV patients over an average follow-up time of 4 years [13]. Their study suggested that eccentric blood flow in the ascending aorta was associated with accelerated aortic growth, but findings were limited by semi-quantitative image analysis and by the small cohort size.

Therefore, the purpose of this study was to investigate longitudinal (> 2-year follow-up) changes in aortic hemodynamics (systolic peak velocities, WSS) in BAV patients compared to patients with tricuspid aortic valve (TAV) with thoracic aortic dilatation. We hypothesize that BAV patients will demonstrate more pronounced changes in metrics of aortic flow (WSS, peak velocities) compared to patients with TAV with dilation and controls.

Methods

Study design

This retrospective study enrolled patients with BAV or subjects with tricuspid aortic valve and thoracic aortic dilatation (TAV with dilation, defined as sinus of Valsalva (SOV) diameter > 4.0 cm) who underwent routine cardiothoracic MRI for surveillance of aortic dimensions including 4D flow MRI. BAV and TAV with dilation patients were included if they underwent two MRI exams (base line and follow-up MRI) with a minimum of two years between scans. Accordingly, 44 patients (31 males, mean age at baseline: 44.9 ± 12 years) with BAV and 17 patients (15 males, mean age at baseline: 54.6 ± 17 years) with TAV with dilation were included. In addition, 9 healthy controls, with a minimum follow-up duration of 1 year (8 males, mean age at baseline: 49.3 ± 15 years) with a tricuspid aortic valve and no aortic dilation (SOV diameter < 4.0 cm at both baseline and follow-up) were also included. This single center retrospective study was approved by the institutional review board (IRB). For the patient cohort, subjects were retrospectively included with waiver of consent. All healthy volunteers were prospectively included and written informed consent was obtained from all participants.

MR imaging

Patients underwent cardiothoracic MRI at baseline and follow-up using 1.5 T MRI systems (Magnetom Aera or Avanto, Siemens Healthcare, Erlangen, Germany). All BAV and TAV with dilation subjects underwent a standard-of-care thoracic cardiovascular MRI exam including 3D contrast-enhanced magnetic resonance angiography (3D CE-MRA) following the administration of contrast media (0.2 mmol/kg gadolinium-DTPA, Magnevist, Bayer Pharmaceuticals). Standard 2D ECG gated time-resolved (cine) balanced steady-state free-precession (SSFP) images covering the left ventricle and aortic valve were acquired to evaluate global cardiac function and aortic valve morphology (TR = 2.6–2.9 ms, TE = 1.2 ms, flip angle = 50°–8°, GRAPPA acceleration R = 2, spatial resolution = (1.8–2.3 mm)^2, slice thickness = 6 mm). In addition, three-dimensional (3D) cine phase-contrast MRI with three-directional velocity-encoding (4D flow MRI) was performed in a sagittal oblique 3D volume covering the thoracic aorta from the aortic valve annulus to the descending aorta. 4D flow MRI used prospective ECG gating and free-breathing with a respiratory navigator placed on the lung-liver interface (scan efficiency ranging from 60 to 80%) [14]. 4D flow pulse sequence parameters were as follows: spatial resolution = 2.2–4.2 mm × 1.7–2.9 mm × 2.2–4.0 mm; field of view = 320–470 mm × 234–382 mm × 66–120 mm; temporal resolution = 32.8–43.2; TE = 2.1–2.8 ms, TR = 4.1–5.4 ms, flip angle = 7°–15°, total scan time 8–12 min. Velocity encoding sensitivity (venc) was adjusted to minimize velocity aliasing (venc = 150–450 cm/s) based on 2D phase contrast MRI scout images.

Data analysis: 4D flow MRI

The 4D flow data analysis workflow is summarized in Fig. 1. Briefly, the 4D flow MRI images were first corrected for eddy current phase offset errors, noise, and velocity aliasing using custom built software programmed in Matlab (Natick, the Mathworks, USA, Fig. 1A) [15]. The magnitude-weighted velocity images were then used to calculate time-averaged 3D phase-contrast angiography (PC-MRA) images. Manual 3D segmentation of thoracic aorta was performed on PC-MRA images (Mimics, Materialise, Plymouth, MI, USA) as shown in Fig. 1B.

Data analysis: peak velocity

The aorta segmentation was used to mask the 4D flow velocity data and to calculate a maximum intensity projection (MIP) of the peak systolic absolute velocities in sagittal orientation as shown in Fig. 1C. This method has recently been introduced and has been proven valuable for fast and improved detection of regional peak systolic velocities frequently found in BAV patients [16]. Regions of interest in the peak velocity MIP covering the ascending aorta (AAO, from the aortic valve to the innominate vessel branching)

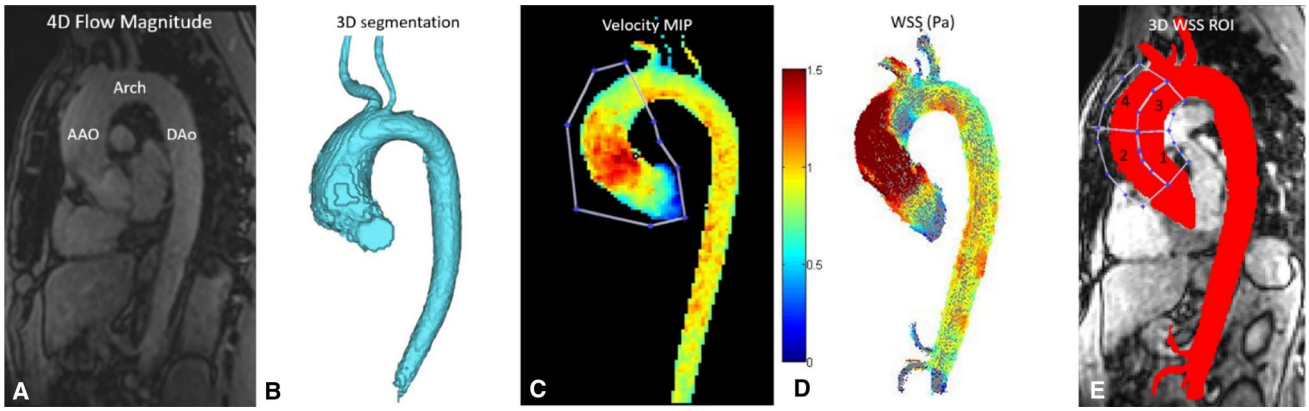

Fig. 1 Aortic 4D flow MRI data analysis workflow: Example of a magnitude image (AAO: ascending aorta) (**A**), Aortic volume segmentation (**B**), AAO peak velocity calculation from systolic maximum intensity projections (MIP) (**C**), systolic WSS 3D vectors (**D**) and manual division of the AAO into four segments (1: inner proximal AAO, 2: outer proximal AAO, 3: inner distal AAO, 4: outer distal AAO) (**E**)

were used to automatically extract maximum velocities in this aortic segment.

Data analysis: 3D WSS

The 3D distribution of WSS throughout the aorta was calculated from the 4D flow MRI dataset using an in house software developed in Matlab (The MathWorks, Natick, MA, USA) as previously described [17] (Fig. 1D). Local peak systolic absolute WSS was extracted and averaged within the following manually drawn aortic areas: (1) inner proximal AAO (2) outer proximal AAO (3) inner distal AAO (4) outer distal AAO (Fig. 1E).

Data analysis: aortic valve morphology and function

Tricuspid aortic valve and BAV morphology was confirmed using 2D cine SSFP images. Using the categorical method developed by Sievers et al., bicuspid valves were classified based on the presence or location of raphes [18]: type 0 = no visible raphe, type 1 = presence of a raphe based on fused portion of the leaflet (type 1 right-left coronary (RL), type 1 right-noncoronary (RN) or type 1 left-noncoronary (LN)); type 2 = presence of 2 raphes at locations RL and RN, RL and LN, or RN and LN. The degree of aortic stenosis (AS) was classified according to current guidelines in respect to ascending aortic peak velocity (< 2.0 m/s = No AS, 2.0 and 2.9 m/s = Mild AS, between 3.0 and 3.9 m/s = Moderate AS, ≥ 4.0 m/s = Severe AS) [19]. Peak velocity was quantified using 4D flow MRI in the AAO as described above according to strategies reported by Rose et al. [16]. Aortic regurgitation (AR) fraction was quantified using 2D cine phase-contrast MRI with planes above or below the valve (mild < 30%, moderate 30–59%, severe ≥ 60%) [20, 21].

Data analysis: aortic dimensions and global cardiac function

Mid ascending aortic (MAA) and sinus of Valsalva (SOV) diameters for both baseline and follow-up scans were measured based on 3D CE-MRA images using Vitrea (Vital Images, Inc., Minnetonka, MN). At the mid-ascending level, two measurements were taken orthogonal to the vessel and the higher value was considered as MAA diameter. Three measurements were taken at the SOV using the cusp-to-cusp method [22], and the maximum value of these three measurements was considered SOV. CE-MRA images were acquired directly after contrast bolus administration without EKG gating, so they represent an averaged view of the thoracic aorta over the cardiac cycle. Annual diameter growth was calculated as the change in the maximal SOV and maximal MAA diameter between baseline and follow-up while normalizing by follow-up time. Aortic dilation was defined as SOV diameter > 4.0 cm. Global cardiac function parameters (left ventricular ejection fraction, stroke volume) were obtained from standard 2D CINE SSFP images.

Statistics

All retrospective data analysis (aortic dimensions, peak velocity, WSS) was performed by a single observer. Statistical analysis was performed using commercially available software (SPSS, Armonk, NY:IBM Corp.). All variables were reported as mean ± standard deviation. A Shapiro–Wilk test was used to determine if the parameters were normally distributed. Comparisons across the three patient groups were performed using a one-way ANOVA test. If significant differences were detected ($p < 0.05$), post-hoc pair-wise test between individual groups as well as between baseline and follow-up exams were assessed

with two-sided, student's paired *t*-test (normal distribution) or a non-parametric equivalent test (non-normal distribution). A $p < 0.05$ was considered statistically significant.

Results

Study cohort

Patient baseline demographics are summarized in Table 1. Age at baseline was similar for all groups (BAV, TAV with dilation, controls) while less women were included (control, TAV with dilation and BAV patients: 11%, 12% and 30%, respectively). While stroke volume, heart rate and blood pressures were similar for BAV and TAV with dilation patients, there was a difference in left ventricular ejection fraction (58 ± 5% in TAV with dilation vs. 62 ± 6% in BAV, p = 0.02). The distribution of AR was similar between the two cohorts: 32% and 35% with no AR, 50% and 59% with mild AR, 18% and 6% with moderate-severe AR and 77% and 94% with no AS, 11% and 6% with mild AS, 11% and 0% with moderate-severe AS, respectively (Table 1). Distribution of cusp fusion types in the BAV group was as follows: 8 patients with type 0 fusion pattern, 3 with type 1-RN, 25 with type 1-RL, and 8 with type 2-RL/RN. The average follow-up time was similar for BAV and TAV with dilation patients (2.6 ± 0.7 and 2.7 ± 0.5 years) and 1.1 ± 0.5 years for controls (Table 1).

Regional aortic systolic 3D WSS and peak velocity

Examples of systolic aortic peak velocity and WSS distribution at baseline and follow-up for each group (BAV, TAV with dilation, control subjects) are illustrated in Fig. 2. At baseline, elevated peak velocity and WSS in the AAO is evident in the BAV patient compared TAV with dilation and control subjects. In contrast, AAO WSS is reduced in the TAV with dilation patient when compared to BAV and the control subject. These findings were representative of WSS and peak velocities in the entire cohort (Table 2): AAO peak velocity at baseline was significantly elevated for BAV patients compared to TAV with dilation (2.2 ± 0.8 m/s vs. 1.6 ± 0.6 m/s, p = 0.01) and control groups (2.2 ± 0.8 m/s vs. 1.5 ± 0.3 m/s, p = 0.03). In addition, BAV patients exhibited significantly increased baseline WSS compared to TAV with dilation patients averaged over the AAO (0.74 ± 0.22 vs 0.45 ± 0.12 Pa, $p < 0.001$). In contrast, baseline WSS averaged over the AAO in TAV with dilation patients was reduced compared to controls (0.45 ± 0.12 Pa vs 0.55 ± 0.11 Pa, p = 0.034).

Longitudinal changes in AAO WSS and peak velocity over the BAV, TAV with dilation and control cohorts are summarized in Table 2 and Fig. 3. Patterns of peak velocity and WSS remained stable from baseline to follow-up for all groups except for BAV patients who presented with a statistically significant decrease in WSS from baseline to follow-up in three regions of the ascending aorta (inner proximal, outer proximal, and outer distal). Peak velocities were significantly increased from baseline to follow-up in BAV ($P < 0.001$) but no change was noted in TAV with dilation or control groups. Compared to baseline WSS,

Table 1 Patient baseline characteristics

	Controls	TAV with dilation	BAV	p-value
N	9	17	44	–
% Female	11	12	30	–
Age (years)	49.3 ± 14.7	54.6 ± 16.5	44.9 ± 12	0.3
Follow up time (years)	1.1 ± 0.5	2.6 ± 0.4	2.6 ± 0.7	**< 0.0001**
Left ventricular ejection fraction (%)	–	58 ± 5	62 ± 6	**0.02**
Stroke volume / BSA (ml)	–	46 ± 7	49 ± 13	0.4
Systolic blood pressure (mmHg)	–	120 ± 12	121 ± 15	0.8
Diastolic blood pressure (mmHg)	–	72 ± 7	77 ± 10	0.07
Heart rate (bpm)	–	71 ± 9	72 ± 12	0.6
Aortic regurgitation (baseline) None/mild/moderate/ severe	–	6/10/1/0	14/22/7/1	–
Aortic regurgitation (follow-up) None/mild/moderate/severe	–	6/10/1/0	12/22/7/3	–
Aortic stenosis (baseline) None/mild/moderate/severe	–	16/1/0/0	34/5/3/2	–
Aortic stenosis (follow-up) None/mild/moderate/severe	–	16/1/0/0	32/5/4/3	–

Significant differences are indicated by bold type p-values

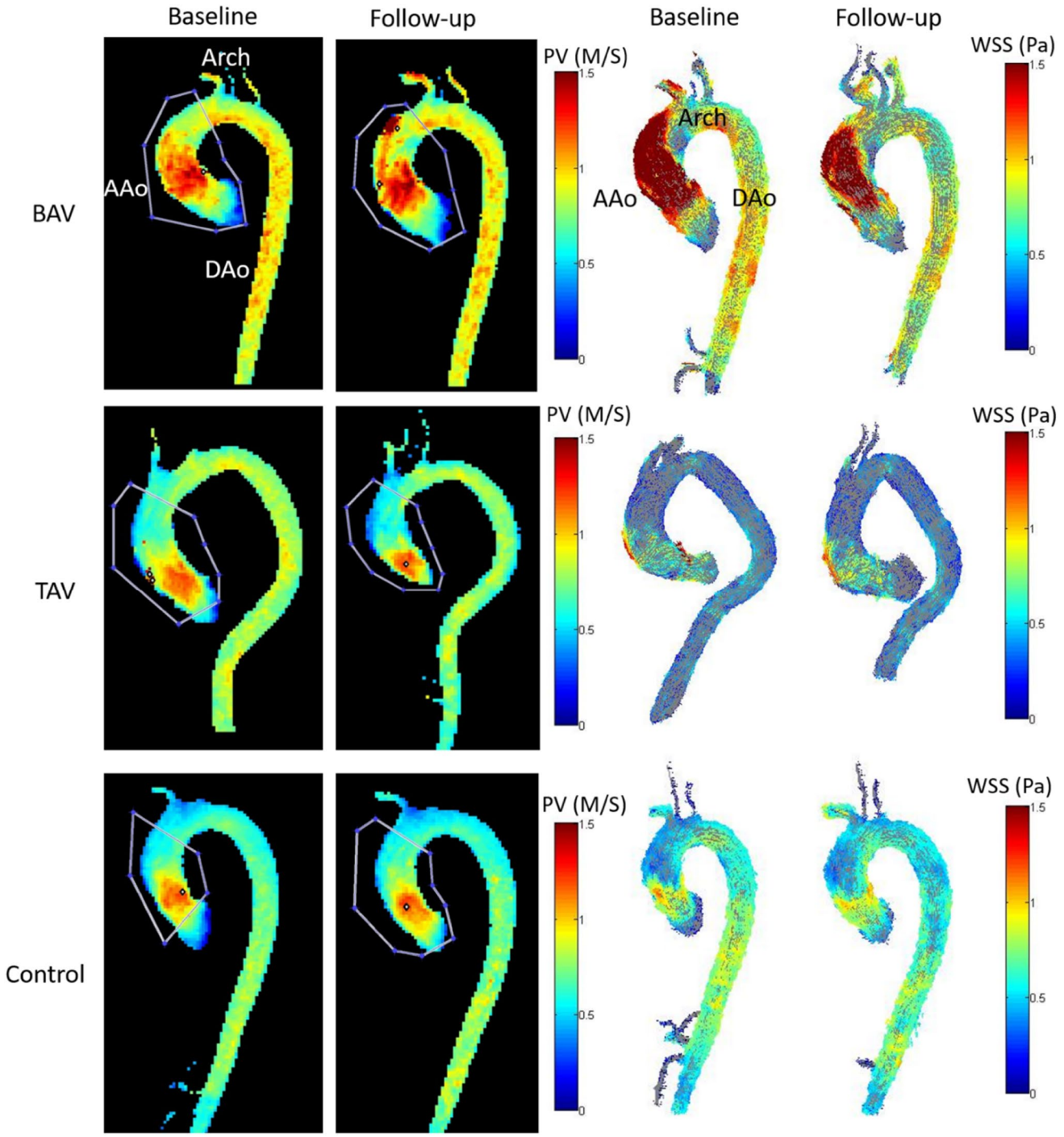

Fig. 2 Examples of baseline and follow-up aortic peak velocity (PV) maximum intensity projections (left), and systolic 3D WSS (right) for a patient with BAV (top row), TAV with dilation (mid), and control subject (bottom row). Regions of interest (white lines) show areas used for peak velocity quantification in the AAO. Elevated baseline peak velocity and WSS are seen in patients with BAV. In contrast, WSS calculation is lower in patients with TAV with dilation when compared to BAV and controls. Stable patterns for WSS are seen from baseline to follow-up scans for all cohorts, with reduced WSS pattern seen in BAV images

Table 2 Regional systolic wall shear stress (WSS) and peak velocity in the ascending aorta (AAO)

	WSS (Pa)				Peak velocity (m/s)
	Inner proximal AAO	Outer proximal AAO	Inner distal AAO	Outer distal AAO	AAO
BAV					
Baseline	0.73 ± 0.21	0.73 ± 0.23	0.71 ± 0.32	0.79 ± 0.30	2.2 ± 0.8
Follow-up	0.63 ± 0.21*	0.64 ± 0.18*	0.66 ± 0.35	0.69 ± 0.27*	2.3 ± 0.9*
TAV with dilation					
Baseline	0.44 ± 0.1†	0.40 ± 0.11†	0.46 ± 0.17†	0.51 ± 0.18†	1.6 ± 0.6†
Follow-up	0.44 ± 0.1	0.43 ± 0.15	0.49 ± 0.21	0.54 ± 0.22	1.6 ± 0.6
Controls					
Baseline	0.62 ± 0.18§	0.55 ± 0.10‡	0.52 ± 0.13	0.52 ± 0.10‡	1.5 ± 0.3‡
Follow-up	0.55 ± 0.13	0.51 ± 0.13	0.55 ± 0.15	0.52 ± 0.16	1.4 ± 0.3

*$p < 0.05$, baseline versus follow-up

†$p < 0.05$, baseline BAV versus TAV with dilation

‡$p < 0.05$, baseline BAV versus controls

§$p < 0.05$, baseline TAV with dilation versus controls

BAV patients demonstrated significantly decreased WSS at follow-up ($p < 0.002$) in all four AAO segments except the inner distal AAO.

Aortic dimensions

As summarized in Table 3, aortic diameters (SOV and MAA) at baseline were smallest in controls ($p < 0.001$ SOV, $p = 0.002$ MAA). SOV diameters were larger ($p < 0.001$) in the TAV with dilation group (4.3 ± 0.3 cm) compared to BAV patients (3.9 ± 0.3 cm) while MAA diameters were similar (3.9 ± 0.5 cm vs. 4.0 ± 0.5 cm, $p = 0.32$). BAV patients demonstrated only a mild increase in aortic dimensions between baseline and follow-up (annual growths rate of 0.05 cm/year for SOV and MAA). Even less pronounced changes in aortic dimensions were seen in TAV with dilation patients (annual growths rates: 0.04 cm/year for SOV, 0.03 cm/year for MAA).

Discussion

The main findings of our study were: (1) BAV patients demonstrated uniformly elevated peak velocity and WSS compared to TAV with dilation and control groups; (2) systolic peak velocity in the AAO significantly increased over time in BAV patients; and (3) AAO WSS significantly decreased in BAV patients at follow-up.

The propensity for patients with bicuspid aortic valve to develop both aortic stenosis and aortopathy is well described [23, 24]. Michelena et al. studied 416 BAV patients over 16 years using echocardiography to determine the incidence of aortopathy [24]. Comparison between the general population and BAV cohorts showed an increased incidence of aortic dilation or aneurysm development. Independent predictors of cardiovascular events or surgery for aortic dilation were described in a previous study of BAV subjects with normally functioning valves or minimally dysfunctional valves [25]. Age, sex, hypertension, ejection fraction, BAV type, presence of aortic regurgitation, total cholesterol, baseline ascending aortic diameter, and presence of valve degeneration were assessed for prognostic value. The most powerful predictor in this study was age, but valve degeneration and baseline aortic diameter were also important variables.

More recently, hemodynamic risk factors and flow displacement have also been shown to be correlated with aortic dilation [26]. For example, the longitudinal increase in peak velocity in the BAV cohort is likely a consequence of progressing valve disease [24]. It should be note that our study showed statistically significant, but small changes in peak velocity during the follow-up period available in out cohort. Nonetheless, we believe that these changes could become clinically significant over the more long-term progressive course of the disease. In addition, the flow patterns and angular jets as a result of BAV have been shown to be important factors in the development of high WSS [27, 28]. Complex hemodynamics may also play an important role in the development of aortopathy, with particular attention being given to WSS [29]. In our study we found higher mean baseline WSS in BAV (0.74 Pa) and healthy controls (0.55 Pa) compared to TAV with dilation patients (0.45 Pa) which corresponds well with previous studies [30, 31]. Guzzardi et al. found strong evidence for the association of WSS with the development of aortopathy, whereby histological architectural changes and extracellular matrix remodeling were found in the presence of high WSS [7]. Regeer et al. compared patients with BAV versus tricuspid aortic valve

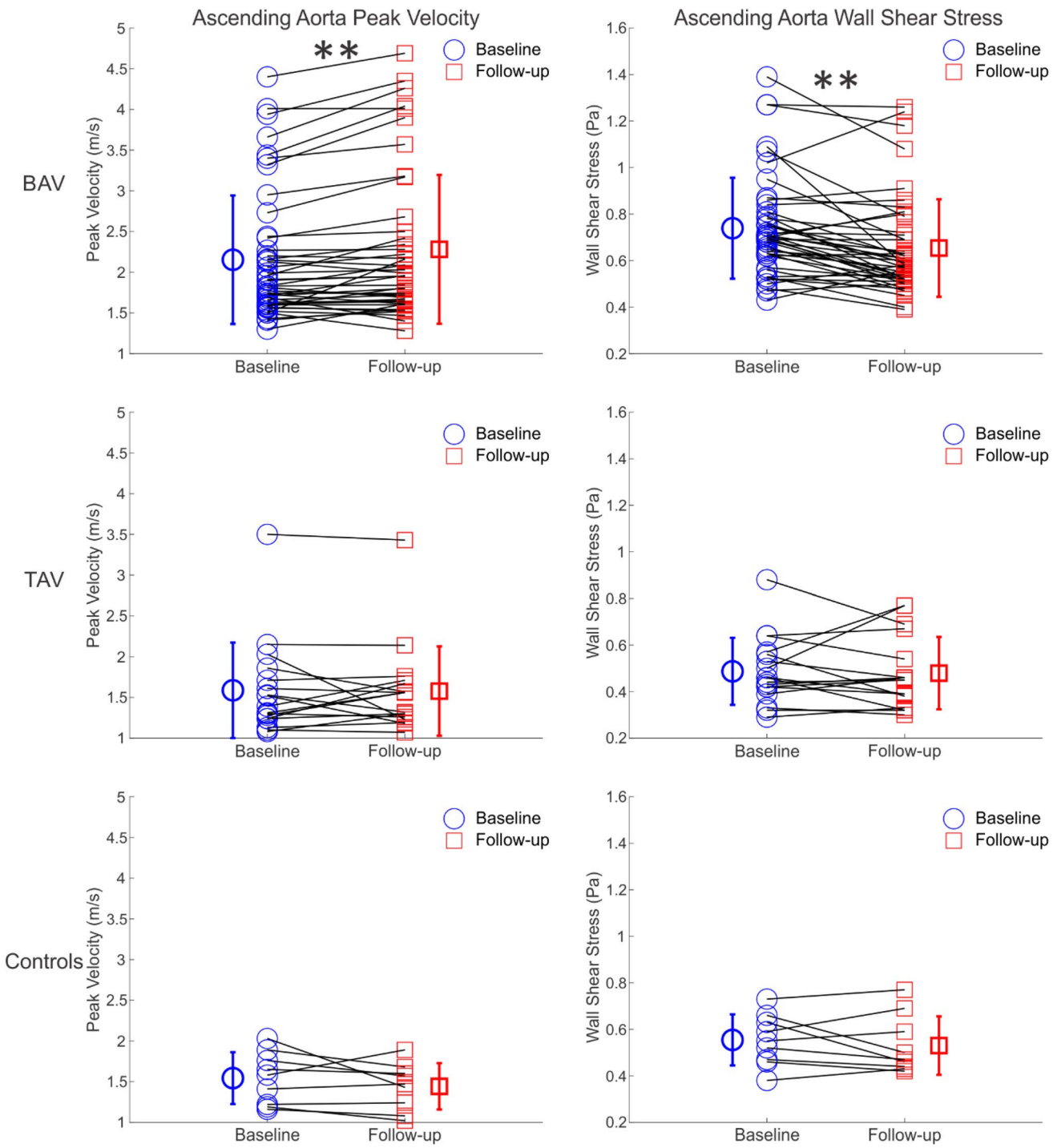

Fig. 3 Longitudinal changes in systolic peak velocity (left) and wall shear stress (right) averaged over the AAO from baseline to follow-up for Bicuspid Aortic valve (BAV), Tricuspid Aortic valve with dilation (TAV with dilation), and Tricuspid aortic valve without dilation (controls) cohorts. **Statistically significant $P < 0.001$ between baseline and follow-up

and valve dysfunction before and after surgery [32]. Findings from their study demonstrated faster progression of aortic dimensions before surgery and no differences after intervention - indicating that surgery-induced flow homogenization can remove the hemodynamic factor influencing the aortic growth.

Recent studies have shown that ascending aortic dilation in patients with BAV appears to be more gradual than previously described [11, 33]. While earlier studies demonstrated

Table 3 Aortic dimensions at baseline and follow-up

	MAA diameter (cm)	SOV diameter (cm)
BAV		
Baseline	4.0 ± 0.5	3.9 ± 0.3
Follow-up	4.1 ± 0.6*	4.1 ± 0.4*
TAV with dilation		
Baseline	3.9 ± 0.5	4.3 ± 0.3†
Follow-up	4.0 ± 0.6*	4.4 ± 0.4*
Controls		
Baseline	3.2 ± 0.4§‡	3.5 ± 0.3§‡
Follow-up	3.2 ± 0.5	3.5 ± 0.2

MAA mid ascending aorta, *SOV* sinus of Valsalva

*$p < 0.05$, baseline versus follow-up

†$p < 0.05$, baseline BAV versus TAV with dilation

‡$p < 0.05$, baseline BAV versus controls

§$p < 0.05$, baseline TAV with dilation versus controls

aortic dilation rates of 1 to 2 mm/year [5], few patients are found to exhibit such rapid growth. A recent study by Trinh et al. described diametric aortic growth of 0.06 cm/year [34]. This was corroborated by Detaint et al. who found average annual maximum growth rates of 0.04 cm/year (median 0.03 cm/year) as well as in Della Corte et al. with average annual maximum growth rates of 0.06 cm/year [11, 33]. The results of our study confirm these findings. The slow aortic growth rates found in our study indicate that the follow-up period of 2–3 years in this study maybe too short to identify aortic growth with sufficient discriminative power in order to determine if there is any prognostic value to 4D flow in the context of BAV.

The increase in peak velocities that we observed over time for our BAV patients may be related to calcification process and decreased motility of the aortic valve leaflets. However, somewhat counterintuitively, WSS decreased in the BAV patients even given the increased velocity across the valve. We suspect the decrease in WSS over time was possibly due to compensatory growth of the aorta. For example, previous studies have shown that there is an inverse cubic relation between WSS and vessel size [35]. Thus, even the small increase in the vessel size found in our study may impart a detectable reduction in WSS. Farag et al. showed that in BAV patients severity of aortic stenosis also contributes to increasing WSS in the thoracic aorta, and that WSS is increased in patients with non-dilated aortas [36]. Other factors could have contributed to the decreased WSS in this cohort over time, including decreased flow and altered aortic stiffness.

Previous studies at our center using the same methods have investigated WSS, peak velocity, and aortic diameter and demonstrated excellent inter-observer reproducibility for all parameters [16, 34, 37]. The test–retest variability for region of interest analysis of systolic peak velocity and 3D WSS showed good agreement (Intra-class correlation coefficient ICC = 0.9 for velocity, and ICC = 0.8 for WSS) and a maximum difference of 0.04 m/sec for velocity and 0.05 Pa for WSS in a previously published study [37]. Trinh et al., also showed excellent agreement between inter-observer aortic diameter measurements (ICC:0.83 for SOV, ICC:0.86 for MAA) [34]. In addition, the overall longitudinal stability of peak velocity and 3D WSS patterns as shown in Fig. 2 demonstrates the reproducibility of this technique.

This study has important limitations. First, subjects in this study underwent only MR imaging and did not undergo concomitant ultrasound. This precluded analysis of valve calcification, as well as calculation of global longitudinal strain as an alternative to ejection fraction. In addition, AS grading was performed based on guidelines developed for echocardiography. However, prior studies comparing 4D flow to echocardiography have shown excellent agreement between the two methods for when measuring peak velocity [16, 38].

Second, subjects received only ordinal grading of stenosis and regurgitation, and we do not report mitral valve status. 2D phase contrast MRI can also underestimate the degree of aortic regurgitation due to 2D PC MRI plane thickness, plane placement, or movement of the aortic valve plane relative to the placed plane during the cardiac cycle.

Third, the cohort size and follow-up duration were limited. This observational study showed BAV to be associated with increased systolic peak flow velocity and decreased WSS at follow-up but a causative relation between changes in aortic flow in BAV and increased growth of the aorta was not demonstrated. Larger patient cohorts with longer longitudinal follow up are thus needed to identify drivers of disease in the subgroup of patients who develop disease and to stratify analysis by aortic valve function and BAV cusp fusion type. There may also be a patient selection bias as the study design did not include BAV patients who did not undergo follow-up MRI because of progression of valve dysfunction and need for intervention. There may also be a bias due to a single observer performing all of the aorta diameter measurements, and longer follow up would improve the detection of diameter changes given the limited resolution of the CE-MRA studies. Future studies should also investigate the effects of medical therapies on aortic hemodynamics.

In conclusion, findings from this follow-up study demonstrated increased peak systolic velocity and WSS in BAV compared to tricuspid aortic valve patients with dilated aortas and healthy volunteers for reference. The increase in peak velocity was most likely a result of valvular disease, while the decrease in WSS may be a consequence of aortic remodeling. Future studies should aim for longer follow-up times

(> 5 years) to better understand this gradual disease process, and potentially apply WSS as a prognostic tool.

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