Flow Characteristics in Bicuspid Aortic Valve Relatives compared to normal controls using 4D flow MRI

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PURPOSE: Bicuspid aortic valve (BAV) is known as the most common congenital anomaly and its complications (ascending aortic aneurysm, dissection) can lead to noticeable morbidity and mortality. There is increasing evidence that, in addition to its genetic background, changes in aortic hemodynamics may play an important role in the development of aortopathy. Studies have shown that BAV can substantially alter aortic hemodynamics[1], but it is unclear if the genetic disposition can influence aortic properties and 3D blood flow in family members with normal tricuspid valves (BAV relatives). In a study with 34 subjects, we applied 4D flow MRI to evaluate changes in aortic 3D blood flow characteristics and wall shear stress (WSS) in 1st and 2nd degree relatives of BAV patients. The aim was to identify changes in 3D flow and regional WSS compared to normal controls and to investigate relationships between altered hemodynamics and aortic geometry.

METHODS: 15 controls and 3 families with one known BAV case in each family (Table 1) underwent contrast agent enhanced (BAV relatives: MultiHance, controls: Ablavar) MRI (1.5 or 3T, Siemens, Germany) for the evaluation of ascending aorta (AAo) dimensions, aortic valve morphology, aortic shape, and aortic 3D blood flow dynamics. To assess valve morphology and global cardiac function, breath-held, ECG-gated time-resolved (CINE) 2D balanced SSFP images were acquired. Aortic blood flow assessment was done using ECG and respiratory-gated 4D flow MRI with full volumetric coverage (VENC=150-250 cm/s, temporal resolution= 38.4-40.0ms). 4D flow data were pre-processed to correct for noise, eddy currents and velocity aliasing, and to calculate a 3D PC-MR angiogram (MRA) from the velocity data, as previously described[2]. 3D visualization was performed using commercial software (Ensight, CEI, Inc. Apex, NC). The presence and severity of helix and vortex flow was assessed by two readers at three analysis planes: the AAo (proximal to brachiocephalic trunk), Arch and descending aorta (DAo, level of left atrium) using a defined 3-point grading scale separately for helix and vortex flow in a blinded manner. Linear flow or flow rotation <90° was graded as 0, rotation of 90-180° was grade 1, grade 2: vortex/ helix flow 180-360°, and grade 3: flow rotation of >360. Morphology of aortic arch was visually evaluated based on three categories: gothic, cubic, and round (normal)[3]. For the quantification of regional aortic WSS, a 3D segmentation of the thoracic aorta geometry and subdivisions of AAo, Arch and DAo were created for each subject based on the 3D PC-MRA data (MIMICS, Materialise Inc., Belgium). Similar to previously reported strategies, systolic WSS vectors were calculated along the segmented vessel surface of the aorta[4] (Figure 1) and results were evaluated for all segments separately.

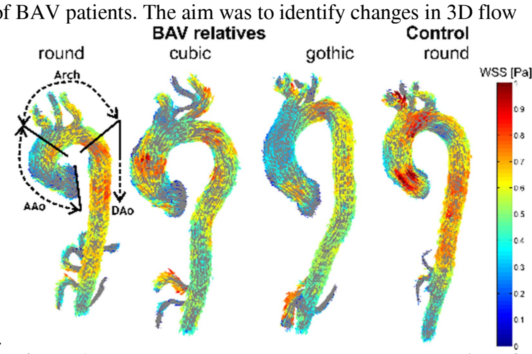

Figure 1: WSS vectors mapped on the 3D segmentation of the thoracic aorta for different aortic shapes in BAV relatives and in one control subject.

Table 1: Demographics, aortic dimensions, flow pattern, and systolic average WSS of study cohort. All BAV relatives' results are listed in the very left. In addition, the BAV three families (F1, F2, F3) are separately listed.

	BAV relatives				controls	p-value
	All	**F1**	**F2**	**F3**		
N (female)	19 (7)	14 (5)	2 (1)	3 (1)	15 (4)	-
age	41.7 ± 16.3	39 ± 15	42 ± 12	51 ± 25	37.2 ± 10.4	0.36*
SOV dia [mm]	31.3 ± 3.2	31.3 ± 3.5	29.5 ± 0.7	32.7 ± 2.5	29.6 ± 2.3	0.08*
MAA dia [mm]	28.6 ± 3.3	28.2 ± 2.2	25.0 ± 7.1	32.7 ± 1.2	17.2 ± 2.5	0.15*
ARCH dia [mm]	23.9 ± 2.7	23.9 ± 3.0	22.5 ± 0.7	25.0 ± 1.7	22.7 ± 2.7	0.20*
DAo dia [mm]	21.7 ± 2.1	21.4 ± 2.0	20.5 ± 0.7	24.0 ± 2.0	20.8 ± 3.2	0.31*
WSS Aorta [Pa]	0.39 ± 0.17	0.41 ± 0.17	0.25 ± 0.14	0.58 ± 0.23	0.43 ± 0.19	0.068†
aortic shape						**0.007‡**
round	10	8	1	2	14	-
cubic	7	5	-	1	-	-
gothic	2	-	1	1	1	-
Flow pattern						
vortex	1.0 ± 1.1	1.1 ± 1.1	0.8 ± 1.2	0.4 ± 0.9	0.2 ± 0.6	**< 0.001†**
helix	0.4 ± 0.7	0.5 ± 0.8	0.3 ± 0.8	0.2 ± 0.5	0.5 ± 0.9	0.62†

* paired t-test comparing controls and all BAV relatives, † Wilcoxon U-test comparing controls and all BAV relatives, ‡ Fisher's exact test comparing controls and all BAV relatives

RESULTS: Vortex and helix flow grading was performed with excellent inter-observer agreement (Cohen's kappa, κ=0.73). Vortex flow was significantly more frequent in BAV relatives compared to controls (Table 1, p<0.001). Specifically, vortex flow was increased in the AAo (p<0.004) and DAo (p<0.025). Helix flow was similar in BAV relatives and controls. 47% of all BAV relatives had a different (p<0.007) aortic shape than the typical round shape of the controls (93.3%). Systolic WSS was significantly higher for round aortas in the AAo (p=0.003) and DAo (p=0.016) compared to cubic shapes (Figure 2). Also, WSS was significantly increased for subjects with helix flow versus non-helix flow in the Arch (p = 0.004) (Figure 2). Compared to controls, systolic WSS was significantly lower in BAV relatives in the AAo (p=0.03).

DISCUSSION AND OUTLOOK: The findings demonstrate subtle but significant differences in aortic hemodynamics in BAV relatives compared to age-matched normal controls. Despite normal tricuspid valves, familial relationship with a BAV patient resulted in altered 3D flow and WSS compared to normal controls in a subgroup of BAV relatives with cubic shaped aortas. Only BAV relatives expressed cubic shaped aortas, which may explain the observed differences. In fact, the significant higher vortex flow in the BAV relatives in the AAo and DAo, as well as the significantly lower WSS was related to cubic aortic shape. Future longitudinal studies with larger cohorts matched for aortic shapes are warranted to better understand the dependence of blood flow characteristics on aortic shape, type of valve abnormality and relatives of BAV patients.

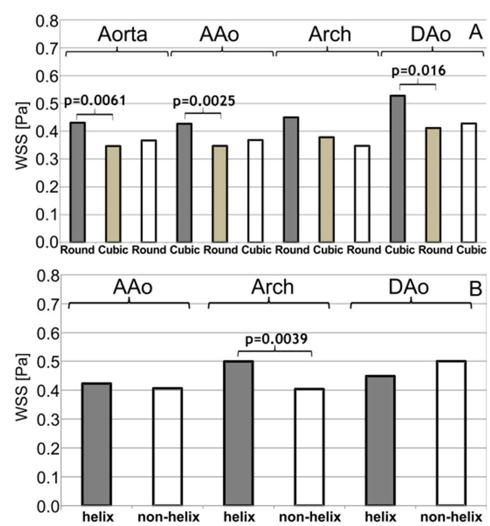

Figure 2: (A) Systolic WSS grouped for aortic shapes round (grey, n=24), cubic (light brown, n=7) and gothic (white, n=3) for the entire aorta, AAo, Arch and DAo. (B) Systolic WSS at the AAo, Arch and DAo for subjects with helix (n_{AAo}=7, n_{Arch}=8, n_{DAo}=9) versus non- helix flow (n_{AAo}=27, n_{Arch}=26, n_{DAo}=25).

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