Reproducibility of Advanced Velocity and Wall Shear Stress Quantification Techniques Derived From 4D Flow MRI in the Pathological Aorta

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Introduction: The decision to treat aortic dilatation is based on consensus guidelines and a diameter threshold of 5.5 cm for the ascending aortic of patients with or without bicuspid valves (BAV) [1,2]. However, some groups have proposed that these guidelines are too simplified, and that patient-specific strategies and new biomarkers are needed. Recently, our group developed a methodology, based on 4D flow MRI, to visualize abnormal hemodynamic blood velocity and wall shear stress (WSS) in the aorta as compared to physiological norms[3]. This strategy has the potential to aid in developing BAV phenotype or patient specific resection strategies. In this study, the reproducibility of the technique is investigated by comparing abnormal aortic velocity and WSS at baseline and follow-up 4D flow MRI in patients with BAV (BAV+D) or tricuspid aortic valves with aortic dilatation (TAV+D).

Methods: ECG and respiratory navigator gated baseline 4D flow MRI exams were performed in 24 BAV+D patients (mean age: 47±12 y/o, range: 29-76, 15 men, 9 women), 15 TAV+D patients (mean age: 62±12 y/o, range: 40-79, 9 men, 6 women) and 62 healthy controls (mean age: 44±12 y/o, range: 19-78) on 1.5 and 3T MAGNETOM Avanto, Espree, Aera and Skyra MRI systems (Siemens Healthcare, Erlangen, Germany). Follow-up scans were performed for the BAV+D (mean follow-up time: 324±121 days) and TAV+D patients (mean follow-up time: 333±136 days). For the controls, no follow-up scans were performed. Spatial resolution was 1.7-3.6x1.8–2.4x2.2–3.0 mm^3; temporal resolution was 37–42 ms resulting in 14 to 25 time frames; TE/TR/FA was 2.2-2.8 ms/4.6-5.3 ms/7-15^0 and the VENC was 1.5–4.5 m/s. All 4D flow MRI data were corrected for eddy currents, Maxwell terms and velocity aliasing using in-house built software in Matlab (Natick, The Mathworks, USA)[4]. 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[4]. The thoracic aorta was semi-automatically segmented using a commercial software package (Mimics, Materialise, Leuven, Belgium). The time frame with the maximum average absolute velocity in the segmentation was defined as peak systole. A maximum intensity projection (MIP) was created of the absolute velocity in the aorta. A region of interest was manually drawn in this MIP to determine the maximum velocity at peak systole. No, mild, moderate and severe aortic stenosis (AS) was defined as a peak velocity of <2m/s, 2.1-3m/s, 3.1-4m/s and >4m/s, respectively. Sinuses of Valsalva (SOV) and mid-ascending aortic (MAA) diameters were measured using contrast-enhanced MRA data. The regurgitation fraction (RF) was calculated by the quotient of the backward flow over the net flow over the cardiac cycle in a slice placed perpendicular to the aortic root. Mild aortic insufficiency (AI) was defined as a RF<30%. WSS was calculated with the method proposed by Potters et al.[5]. Five age cohorts (19-30 y/o, n=12, 31-40 y/o, n=12, 41-50 y/0, n=19, 51-60, n=13 and 55-78, n=11) were used to compute control cohort-averaged peak systolic velocity and WSS maps, as previously described, to understand physiological normal values and ranges for these hemodynamic parameters[6]. By comparing the velocity and WSS of an individual patient with the appropriate age-matched control map, individual maps for abnormal velocity (higher/lower than the mean+/-2SD control velocity, visualized by red/blue volumes) and WSS (higher/lower than mean+/-2SD control WSS, visualized by red/blue surfaces) maps were created. Abnormal velocity was quantified by the red and blue volume as a percentage of the aortic volume, whereas the surface with abnormal WSS was quantified as a percentage of the aortic surface. Differences in aortic diameter, peak velocity, RF and abnormal velocity or WSS

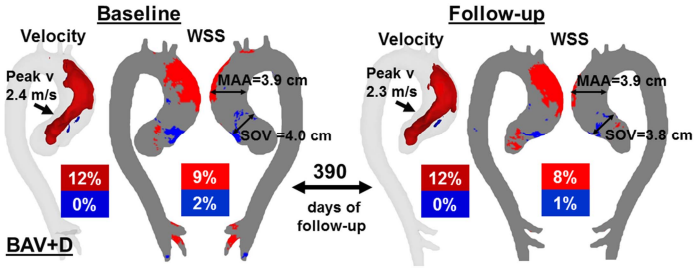

Fig 1. Aortic diameters, peak velocity, abnormal velocity and WSS maps and percentages for the baseline and follow-up scans of a typical BAV+D patient.

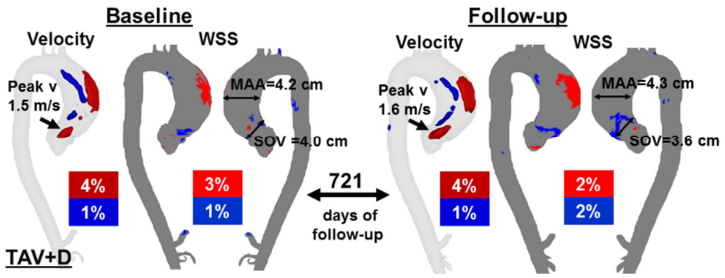

Fig 2. Aortic diameters, peak velocity, abnormal velocity and WSS maps and percentages for the baseline and follow-up scans of a typical TAV+D patient.

Table 1. Aortic diameters, peak velocity, abnormal velocity percentages and abnormal WSS percentages for the baseline and follow-up scans.

	SOV Diameter (cm)			MAA Diameter (cm)			Peak velocity (m/s)			Abnormal velocity red /blue (%)			Abnormal WSS red/blue (%)		
	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*
BAV+D	4.0±0.3	4.1±0.3	0.6	4.3±0.5	4.3±0.4	0.9	2.7±1.1	2.6±1.0	0.9	15±9/1±2	14±9/1±3	0.9/0.8	13±9/2±2	13±10/2±4	0.9/1.0
TAV+D	4.1±0.5	4.1±0.7	0.5	3.9±0.6	4.0±0.6	0.8	1.5±0.4	1.5±0.4	1.0	2±4/0±0	2±4/0±0	0.7/1	4±3/1±1	3±3/2±1	0.7/0.9

BAV+D = Bicuspid aortic valve with dilation, TAV+D = Tricuspid aortic valve with dilation, SOV = Sinus of Valsalva, MAA = Mid-ascending aorta

between the baseline and follow-up scans were established by a Wilcoxon rank sum test with P<0.05 considered significant.

Results: Eight BAV+D patients had no AS, 6 BAV+D patients had mild AS, 7 BAV+D patients had moderate AS and 3 BAV+D patients had severe AS. 2 TAV+D patients had mild AS, whereas 13 had no AS. One BAV+D and one TAV+D patient had mild AI; all other patients had no AI. Figures 1 and 2 show typical examples of abnormal velocity and WSS maps for a BAV+D and TAV+D patient, respectively. Peak velocity, aortic diameters and the days of follow-up are shown as well. The similarity of the baseline and follow-up maps with abnormal velocity and WSS can be appreciated. Table 1 shows that there were no significant changes in aortic diameters, peak velocity, abnormally elevated or decreased velocity, and abnormally elevated or decreased WSS for both the BAV+D and the TAV+D cohorts. Furthermore, no significant difference was found for RF (BAV+D, baseline: 3.7±4.0%, follow-up: 3.1±4.8%, *P*=0.2, TAV+D, baseline: 2.3±3.1%, follow-up: 1.8±3.7%, *P*=0.3).

Discussion/Conclusion: For both cohorts no significant changes were found in aortic diameters, peak velocity or regurgitation. Thus, no impact was anticipated for the long-term reproducibility of velocity and WSS measurements in the form of abnormal velocity and WSS maps. This study confirms that no significant differences were found for volumes of abnormally elevated velocity or abnormally elevated or decreased WSS. Therefore, we conclude that this technique to compare pathological aortic velocity and WSS with cohort-averaged velocity and WSS maps of healthy controls is stable over the long term in subjects with no change in AS, AI, or aortic size.

References: [1]Nishimura et al. *JACC* 2014 [2]Hiratzka et al. *JACC* 2010 [3]van Ooij et al. *Ann Biomed Eng* 2014 [4]Bock et al. ISMRM 2007 [5]Potters et al. *J Magn Res Imaging* 2014 [6]van Ooij et al. *Magn Res Med* 2014

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