3D Aortic Blood Flow in Patients with Marfan Syndrome: Changes in Hemodynamics and Correlation with Aortic Geometry

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Introduction: Marfan syndrome is a connective tissue disorder, which affects the cardiovascular system, the skeleton, dural sac and eyes. The most devastating effects are those on the cardiovascular system causing complex aortic disease and mitral valve prolapse [1]. However, currently available tools for the characterization of cardiovascular manifestations of Marfan syndrome only rely on simple geometric parameters (e.g. aortic root diameter). A number of studies have shown that secondary flow patterns such as vortex or helix flow can induce unfavorable aortic wall shear forces which may facilitate the development of aortic disease [2,3]. The detection of such secondary flow patterns may thus help to identify risk factors for the development of complications in Marfan patients such as aneurysms or dissection. It was our aim to apply flow-sensitive 4D MRI for the characterizations of flow patterns in a cohort of clinically unsuspicious Marfan patients (without aortic aneurysms, dissections, and valve insufficiency). Results were compared to findings in healthy volunteers and patients with suspected Marfan syndrome.

Methods: 26 patients with Marfan syndrome (age=17.6±11.6 years) and 7 patients with suspected Marfan syndrome (age=13.9±2.8 years) were examined using 1.5T and 3T MR systems (Avanto & Trio, Siemens, Germany). Diagnosis was made according to the Ghent Nosology of 1996 [4]. Patients with suspected Marfan syndrome did not present with more than one main criterion. For comparison, 10 healthy volunteers (age=26.1±1.8 years) were included. For all 33 patients, aortic geometry was evaluated by MRI (diameter of ascending aorta (AAo), arch, and descending aorta (DAo)) and echocardiography (aortic valve and sinus).
ECG synchronized and respiration controlled (navigator gating) flow sensitive 4D MRI was performed covering the thoracic aorta (TE/TR = 2.6-3.5ms/5.1-6.1ms, flip angle=7-15°, temp. res.=40.8-48.8ms, spatial res.=1.7-2-4x2.0-2.5x2.2-3.0mm^3).[5] Aortic hemodynamics was evaluated by particle traces demonstrating time-resolved 3D blood flow in the aorta. Systolic 3D stream-lines visualized the 3D distribution of the 3-dir. velocities for individual time-frames (fig. 1). Flow visualization was evaluated (2 observers) regarding presence and extent of helix and vortex flow. These were defined as circular flow patterns with a rotation direction deviating by more than 90° from the physiological flow direction. Helicity was considered an overall corkscrew-like motion of blood along the direction of flow (figure 1, lower left), whereas vortices resembled recirculating areas within the vessel (figure 1, top right). Helix and vortex strengths were graded in 3 categories: none = 0, moderate (flow rotation <360°) = 1, pronounced (flow rotation >360°) = 2.

Results: Marfan patients had 3-25% larger aortic diameters compared to controls with suspected Marfan. Significant increases ($p<0.05$) were found for the aortic valve (23±3mm vs. 20±2mm) and aortic sinus (35±6mm vs. 28±2mm) diameters.
Flow grading results showed substantial inter-observer agreement ($\kappa=0.68$) and are summarized in table 1. The incidence and strength of helix and vortex formation in the AAo and arch was similar for all groups. In ~50% of subjects helix flow persisted in the aortic arch. Vortex flow was mostly absent from the ascending aorta and arch in all subjects. Conversely, helix flow in the DAo was more frequent and significantly increased for Marfan patients compared to both control groups. DAo vortex flow markedly more frequent in Marfan patients (13/26) compared to the suspected Marfan and volunteer group. Interestingly, in 7 patients (5 Marfan, 2 suspected Marfan) vortex formation in the branching region of the left subclavian artery (figure 1, top left) was observed. As summarized in figure 2, the existence of DAo vortex flow (n = 13, grading ≥ 1) in Marfan patients was associated with significantly increased valve and aortic diameters in these patients.

Discussion: Helix and vortex flow was markedly enhanced in the DAo of Marfan patients and associated with significant increases in valve and aortic diameters. The existence of vortex flow in the proximal left subclavian artery could provide an explanation for altered shear forces and subsequent formation of typical complications (aneurysm or Type-B dissection) originating at this site. Altough the most common pathologies in Marfan syndrome are located in the AAo, no obvious flow pattern changes were detected in this region. We speculate that in our patients with non-pathological aortic diameters, i.e. at an early disease stage, hemodynamic alteration may be subtler. Future studies should thus include a more quantitative evaluation of wall shear forces, which may provide more sensitive markers for the detection of the onset of disease. Longitudinal studies are necessary to correlate flow characteristics with the development and progression of the disease.

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References: **1.** Dean J, et al. Eur J Hum Genet 2007; 15: 724-733 **2.** Frydrychowicz A, et al. J Cardiovasc Magn Reson. 2008;10(1):30. **3.** Hope TA, et al. J Magn Reson Imaging. 2007;26(6):1471-1479. **4.** De Paepe, et al. Am J Med Genet 1996; 62: 417-426 **5.** Markl et al, J Magn Reson Imaging 2007;25:824-831

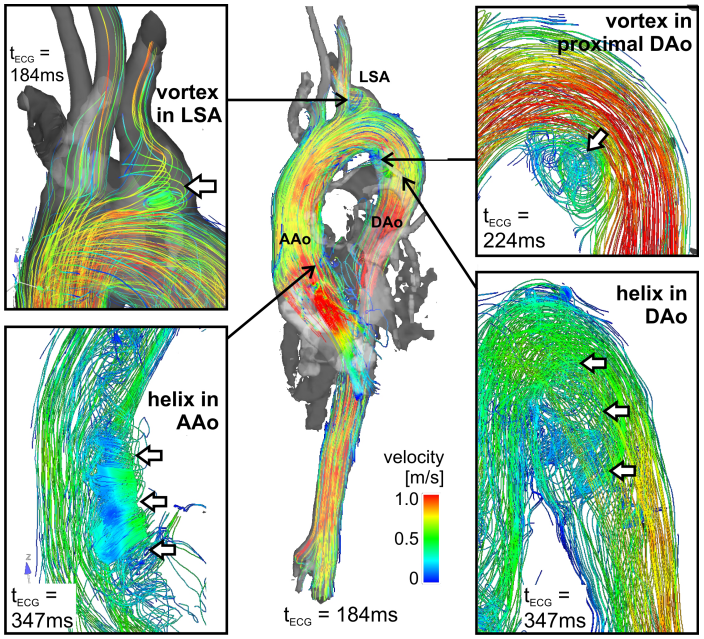

Fig. 1: 3D blood flow characteristics (systolic 3D stream-lines) in the thoracic aorta in a 19 year old Marfan patient. The images illustrate typical secondary flow patterns throughout systole such as helix flow in the AAo (grading = 1.5) and DAo (grading = 1), vortex flow in the proximal DAo (grading = 1), and vortex formation at the branching point of the left subclavian artery (LSA).

incidence [%]	helix			vortex flow		
ave. grading	AAo	arch	DAo	AAo	arch	DAo
Marfan	96%	42%	77%	none	4%	50%
(n=26)	1.2 ± 0.4	0.3 ± 0.4	**0.9 ± 0.7***		0.0 ± 0.0	0.5 ± 0.6
suspected	100%	57%	57%	none	none	14%
Marfan (n=7)	1.3 ± 0.4	0.4 ± 0.4	**0.4 ± 0.4****			0.1 ± 0.2
volunteers	100%	50%	40%	none	none	10%
(n=10)	1.1 ± 0.2	0.4 ± 0.5	0.3 ± 0.4			0.1 ± 0.2

* significant difference between Marfan patients & volunteers ($p < 0.05$)
** significant difference between Marfan patients & suspected Marfan syndrome

Table 1: Results of flow pattern grading in all 43 subjects.

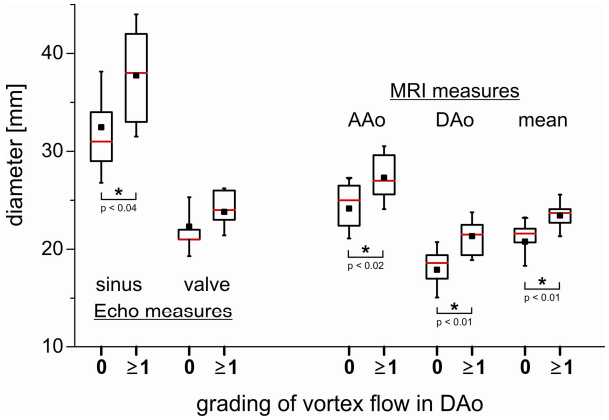

Fig. 2: Differences in aortic geometry between groups of Marfan patients with no visible vortex flow in the DAo (n = 13, grading = 0) compared to patients with moderate or pronounced vortex flow (n = 13, grading ≥ 1). Filled box = mean, red line = median; large box = lower and upper quartile; error bars = standard deviation. * statistically significant differences (t-test, $p < 0.05$).