Age-Related Changes of Aortic Hemodynamics Derived from 4D flow MRI in 60 Healthy Volunteers

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Introduction: It is well known that adult cardiovascular structure and function changes with age. Additionally, the ability to distinguish between age-related effects and disease becomes increasingly important, as age will increase the risk for aneurysm formation, atherosclerosis[1], and all-cause cardiovascular mortality[2]. Given this knowledge, it is important to establish normative values over a range of ages for a number of functional parameters. We performed 4D flow MRI in a large cohort of healthy volunteers (n=60) to measure the age dependency of aortic diameter and a number of hemodynamic factors in the entire thoracic aorta. Given that 4D flow allows for the measurement of the full time-resolved 3D blood flow velocity field in the aorta, specific attention was given to the use of spatial maps representing cohort-averages of the mean systolic aortic blood velocity, systolic wall shear stress (WSS) and velocity time-to-peak (TTP)[3]. We hypothesize that age-related significant differences in aortic hemodynamics exist that should be taken into account when comparing patient-specific hemodynamics to physiological norms.

Methods: ECG and navigator gated 4D flow MRI of the thoracic aorta was performed in 60 volunteers (age: 43±13 years, range: 19-78 year old, 42 men, 18 women) on MAGNETOM Aera, Espree and Skyra systems (Siemens Healthcare, Erlangen, Germany, spatial resolution = 2.50-3.19x1.77-2.34x2.4-2.6mm^3; temporal resolution = 38.4-41.6ms, TE/TR/FA = 2.4-2.8ms/4.8-5.3ms/7-15°; Venc = 150-250cm/s). All 4D flow MRI data was corrected for velocity aliasing, Maxwell terms and eddy currents[4]. 3D PC-MRA images were created by multiplying the phase contrast magnitude images with absolute velocity images averaged over all time frames[4]. The 3D PC-MRA data were used to semi-automatically segment the thoracic aorta using a commercial software package (MIMICS, Materialise, Leuven, Belgium). A volume centerline[5] was calculated based on the aortic 3D segmentation to automatically characterize the mid-ascending aortic diameter (MAA). The time frame with the maximum average absolute velocity within the segmentation was defined as peak systole. A region of interest was manually drawn in a maximum intensity projection of the absolute velocity to determine the maximum velocity at peak systole. TTP was calculated by multiplying the peak systolic cardiac time frame by the temporal resolution. Systolic 3D WSS along the entire aorta lumen surface was calculated using the algorithm developed by Potters et al.[6] In addition, mean velocity and mean systolic WSS were calculated in three aortic segments: 1) ascending aorta (AAo), aortic arch and descending aorta (DAo), see figure 1. For visualization purposes, spatially-resolved average velocities, WSS, and TTP maps for each age range shown in Table 1 and Fig. 1 were generated by: 1) creation of an idealized aorta geometry by rigid co-registration and determination of the maximum overlap of the aortas as previously described[7]. 2) Interpolation to the idealized geometry and subsequent averaging of all individual systolic 3D velocity, WSS and TTP fields over the cohort. A Kruskal-Wallis test was used to test for significant differences across age categories. Linear regression was performed to investigate relations between age, MAA diameter and hemodynamics in the entire aorta. P<0.05 was considered significant.

Table 1. Sex, age, peak velocity, mean velocity, WSS and TTP in the AAo, Arch and DAo of the volunteers categorized for age.

Age Category	Number of subjects	Mean age (years)	Peak velocity (m/s)	Mean Velocity (m/s)			WSS (Pa)			TTP (ms)			MAA (cm)
				AAo	Arch	DAo	AAo	Arch	DAo	AAo	Arch	DAo	
18-30 y	7M, 5W	25±4	1.35±0.15	0.67±0.12	0.69±0.13	0.86±0.13	0.78±0.15	0.84±0.16	0.98±0.13	24±3	25±2	28±3	2.9±0.3
31-40 y	8M, 4W	36±4	1.23±0.15	0.59±0.09	0.63±0.11	0.74±0.11	0.70±0.12	0.74±0.14	0.81±0.14	24±2	24±3	26±3	3.1±0.3
41-50 y	13M, 6W	46±3	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	23±3	22±2	24±2	3.3±0.4
51-60 y	11M, 2W	54±3	1.48±0.29	0.56±0.11	0.51±0.12	0.57±0.14	0.60±0.15	0.57±0.13	0.62±0.17	24±3	22±2	24±2	3.4±0.4
55-80 y	7M, 2W	64±9	1.51±0.28	0.51±0.08	0.49±0.06	0.53±0.08	0.55±0.10	0.56±0.08	0.58±0.11	25±2	23±3	25±3	3.6±0.3
P	-	<0.001	0.01	0.008	<0.001	<0.001	0.003	<0.001	<0.001	0.62	0.01	<0.001	<0.001

y=year, M=men, W=women, AAo=Ascending aorta, Arch=Aortic arch, DAo=Descending aorta, MAA = Mid-Ascending Aorta diameter

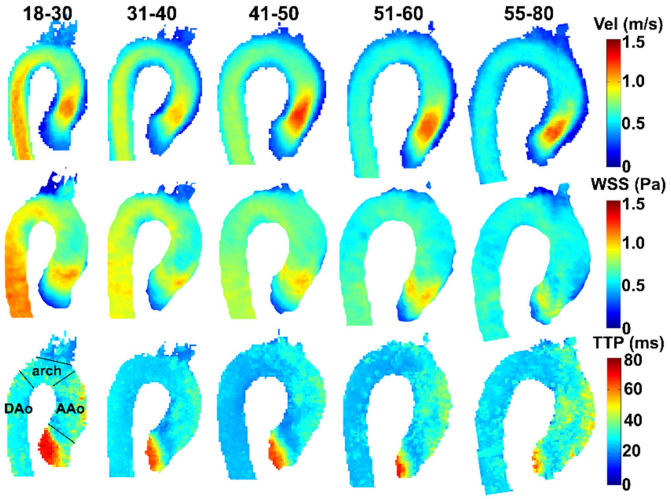

Fig 1. Cohort-averaged velocity (top row), WSS (center row) and TPS (bottom row) maps categorized for age.

Results: The post-processed 4D flow MRI data categorized according to age is found in table 1. In figure 1, the average 3D velocity for each age-category (top row), WSS (center row) and TTP (bottom row) maps are shown. As age increases, it is apparent that there is a significant reduction in mean velocity in the Arch and DAo (tables 1 and 2). A similar trend was seen as a function of age for WSS, which decreased significantly with age over the entire aorta (figure 1, tables 1 and 2). For TTP, a decrease over time is not apparent in figure 1; however, it can be seen in tables 1 and 2 that a significant decrease in TTP was found in the aortic arch and DAo. High TTP values due to mitral inflow were found in the aortic region before the valve. A significant increase in mid-ascending aorta diameter was found with age (table 2).

Table 2. Linear regression to age

	R	*P*	Slope
Peak velocity (m/s)	0.39	0.001	0.007
Mean velocity (m/s)	0.53	<0.001	-0.005
Mean WSS (Pa)	0.59	<0.001	-0.006
Mean TTP (ms)	0.39	0.001	-0.08
MAA Diameter (cm)	0.57	<0.001	0.02

Discussion/Conclusion: Despite an increase of peak velocity in the AAo with age, a significant decrease in mean velocity and WSS was found with increasing age, as hypothesized. The increase in peak velocity was not unexpected as the aortic valve calcifies with age and becomes stiffer. The resulting reduction in valve leaflet motility reduces the geometric orifice area and results in an increase in blood velocity immediately downstream from the valve. The decrease in mean velocity and WSS downstream may be related to the significant increase in aortic diameter with age. Note that the AAo of the 31-40 year cohort did not participate in the trend of increasing peak velocity/decreasing mean velocity with age, which may be due to a small sample size (i.e. low statistical power). TTP decreased significantly with age in the Arch and the DAo, which may indicate a stiffening of the aorta. These results are important to consider when comparing velocity and WSS in patients with cohort-averaged maps. While the technique allows for the easy identification of deviations from the physiologic norms, it is important to consider the age of the control population[8]. The results presented here show the importance of matching the patient age with an appropriate control group.

References: [1]O'Rourke, Staessen, *AJH* 2002 [2]Blacher et al. *Circulation* 1999 [3]Markl et al. *Magn Res Med* 2010 [4]Bock et al. *ISMRM* 2007 [5]Van Uitert et al. Med Phys 2007 [6]Potters et al. *J Magn Reson Imaging* 2013 [7]van Ooij et al. *Magn Res Med* 2014 [8]van Ooij et al. Ann Biomed Eng 2014

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