Published in final edited form as:

Magn Reson Med. 2015 September ; 74(3): 817–825. doi:10.1002/mrm.25466.

Assessment of Altered 3D Blood Characteristics in Aortic Disease by Velocity Distribution Analysis

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Abstract

Purpose—To test the feasibility of velocity distribution analysis for identifying altered 3D flow characteristics in patients with aortic disease based on 4D flow MRI volumetric analysis.

Methods—Forty patients with aortic (Ao) dilation (mid ascending aortic diameter MAA=40±7 mm, age=56±17 yr, 11 females) underwent cardiovascular MRI. Four groups were retrospectively defined: mild Ao dilation (n=10, MAA<35 mm); moderate Ao dilation (n=10, 35<MAA<45 mm); severe Ao dilation (n=10, MAA>45 mm); Ao dilation+aortic stenosis AS (n=10, MAA>35 mm and peak velocity >2.5m/s). 3D PC-MR angiograms were computed and used to obtain a 3D segmentation of the aorta which was divided into four segments: root, ascending aorta, arch, descending aorta. Radial chart displays were used to visualize multiple parameters representing segmental changes in the 3D velocity distribution associated with aortic disease.

Results—Changes in the velocity field and geometry between cohorts resulted in distinct hemodynamic patterns for each aortic segment. Disease progression from mild to Ao dilation+AS resulted in significant differences ($P<0.05$) in flow parameters across cohorts and increased radial chart size for root and ascending aorta segments by 146% and 99%, respectively.

Conclusion—Volumetric 4D velocity distribution analysis has the potential to identify characteristic changes in regional blood flow patterns in patients with aortic disease.

Keywords

4D flow MRI; aortic dilation

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors contributed to the design and realization of the study, interpretation of the data and preparation of the manuscript. JG collected and analyzed the data and wrote the first draft of the manuscript. All authors read and approved the final version of the manuscript.

INTRODUCTION

Time-resolved 3D PC-MRI with three-directional velocity encoding (4D flow MRI) has been successfully applied for the analysis of altered hemodynamics in patients with aortic disease (1-3). Data analysis, however, can be time-consuming and often relies on the manual placement of 2D analysis planes at user defined vascular regions of interest or standardized anatomic landmarks (4,5). The analysis of flow parameters and derived hemodynamic metrics are thus limited by observer variability. In addition, when analysis of 4D flow MRI data is performed using 2D planes, the full 3D volumetric coverage of the vasculature provided by 4D flow MRI is not utilized and additional volumetric information remains to be exploited.

Nevertheless, using traditional 2D plane analysis methods, a number of 4D flow MRI studies have evaluated the impact of common aortic pathologies such as aortic dilation/aneurysm (2,4,6,7) or aortic valve disease on aortic hemodynamics changes (1-3) considering flow hemodynamic metrics. However, planar data analysis strategies can be limited by error propagation or the need for exact definition of vessel boundaries. A more robust analysis can be performed using the volume surface (7,8) and full volumetric information from 4D flow MRI data as proposed in recent studies (3,9,10).

We hypothesized that the full volumetric velocity distribution analysis may identify changes in 3D blood flow characteristics over a range of patients with aortic dilation, without the need for the manual definition of 2D analysis planes. Thus, the purpose of this study was to test the feasibility of a novel automated 3D blood flow analysis based on the velocity distribution in entire 3D vessel segments.

METHODS

Study population

To investigate the feasibility of the proposed automated full volume blood flow velocity distribution analysis 40 subjects were identified via an IRB-approved retrospective chart review from an existing database of 161 subjects who underwent a 4D flow MRI between November 2011 and February 2013. Inclusion criteria consisted of mild to severe aortic dilation (mid-ascending aortic diameter MAA = 40 ± 7 mm, age = 56 ± 17 years, females = 11), trileaflet aortic valve morphology, no/mild aortic regurgitation and no known connective tissue disorder (i.e. Marfan's syndrome). Contrast-enhanced MR angiography images in a sagittal oblique slab were used to measure aortic dilation at sinus of Valsalva and mid-ascending aorta (MAA). Aortic valve stenosis (AS) was graded by aortic valve peak velocity (PV) measured from 4D flow MRI downstream from the aortic valve at the vena contracta region (where velocities reach their maximum during peak systole, as found using the ascending aorta volume). Peak systole was defined as the time step in the cardiac cycle where the velocity averaged over the entire volumetric aorta was maximal. The time-resolved masked aorta velocity field was then used to generate a velocity magnitude (*i.e.* $= \sqrt{V_x^2 + V_y^2 + V_z^2}$) maximum intensity projection (MIP) in an oblique sagittal plane (Fig. 2), averaged over three cardiac time frames centered on peak systole. Each subject was

classified into four groups: mild Ao dilation controls (n=10, MAA<35 mm and PV<2.5 m/s); moderate aortic (Ao) dilation (n=10, 35<MAA<45 mm and PV<2.5 m/s); severe Ao dilation (n=10, MAA>45 mm and PV<2.5 m/s); Ao dilation + AS (n=10, MAA>35 mm and PV>2.5 m/s). Due to database size and retrospective study's inclusion criteria a minimum common group size (n=10) was used. Subject characteristics are summarized in Table 1.

Magnetic resonance imaging

MR Imaging was performed on 1.5T and 3T systems (Magnetom Avanto, Aera, and Skyra, Siemens AG, Erlangen, Germany). All subjects underwent a standard-of-care thoracic cardiovascular MRI exam including dynamic 2D cine SSFP imaging of the heart and aortic valve, contrast-enhanced MRA following the administration of contrast media (Magnevist, gadopentate dimeglumine, 0.1 mmol/kg) to provide a comprehensive evaluation of aortic morphology and valve function as previously reported (11,12). In addition, 4D flow MRI was acquired in a sagittal oblique 3D volume covering the thoracic aorta using prospective ECG gating and a respiratory navigator placed on the lung-liver interface (13). 4D flow MRI was performed with full 3D coverage of the thoracic aorta (spatial resolution=1.97-2.62×1.97-2.62×2.5-4 mm³; temporal resolution=36-40 ms). Pulse sequence parameters were as follows: 1.5 T scan parameters ranged from TE/TR=2.1-2.5/4.5-4.9 ms, flip angle α =15° and a field of view of 128-160×196-150; 3T scans used TE/TR =2.4/2.5 ms, flip angle α =10-15°, and a field of view of 160-192×130-156. Velocity encoding was adjusted to minimize velocity aliasing (1.5-4.5 m/s) based on the 3CH view of in-plane 2D PC MRI scout images. Velocity encoding selection resulted in value changes for TE and TR settings. Acquisition time varied from 8 to 15 min depending on heart rate and navigator gating efficiency.

Data analysis

MR images of the heart were evaluated to quantify global left ventricular systolic function calculating the ejection fraction, end-systolic/diastolic volume, stroke volume, left ventricular mass and the sagittal oblique slab of the aorta was used to measure aortic diameters (sinus of Valsalva and MAA) using dedicated software (Argus, Siemens Medical Systems, Germany).

All 4D flow MRI data were corrected for eddy currents, Maxwell terms, and velocity aliasing using custom built software programmed in Matlab (Mathworks, Natick, Ma, USA). 3D PC-MR angiograms were computed for the 4D flow data as described previously (13) and used to obtain a 3D segmentation of the aorta (Mimics, Materialise, Leuven, Belgium). Based on the 3D segmentation, four aortic sub-regions were analyzed (see Fig. 1), including: Segment 1 (aortic root): from the left ventricular outflow tract to the sino-tubular junction; Segment 2 (ascending aorta), from the sino-tubular junction to the brachiocephalic trunk; Segment 3 (aortic arch): from the brachiocephalic trunk to the left subclavian artery; and Segment 4 (descending aorta): from the proximal to the distal descending aorta. Each segment was generated with a 3D segmentation software (Mimics) using a multi-planar and 3D viewer. The segments were manually defined by anatomic landmark (5) and cut planes perpendicular to the aortic vessel were used to define the extent of each segment. Once the local segment was created it was subtracted from the 3D full aorta segmentation allowing

consistency between volumes and avoiding segment volume overlaps. The generation of four segments required 1-2 min after 3D full aorta segmentation. A 3D penalized least square filter was applied to the 4D velocity field to mitigate noise in 7/10 cases in the Ao dilation + AS group. The four vascular 3D segments were used to compute a masked 4D velocity field (3 spatial dimensions + time) for each aortic segment.

In addition, the velocities for all voxels and cardiac time-frames inside an aortic segment were plotted in histogram form and normalized by the total number of voxels in each segment. The aim was to create a subject-specific velocity histogram that can be compared across subjects and cohorts. The normalized histograms were averaged over all subjects in each of the four groups (Fig. 3). Further, segment volume, local peak velocity by averaging the top 5% maximum values, the normalized number of voxels >1m/s (incidence) as well as velocity histogram characteristics such as mean, median, standard deviation, skewness (asymmetry of the distribution) and kurtosis (peak shape of the distribution) were calculated with Matlab. As shown in Figure 1, the velocity distribution analysis in the radial chart display graphically summarizes the volumetric blood flow velocity histogram characteristics (i.e. mean, median, standard deviation, skewness and kurtosis) and local segment characteristics (i.e. volume, incidence of pixels above 1 m/s, and local peak velocity for an aortic segment). The inner area of the radial chart (as computed from all parameters) was also calculated.

A sensitivity analysis was conducted to identify which fractions of the velocity distribution (number of time frames and top percent of velocities) were most sensitive to differences in flow distribution between patient groups (14). This analysis consisted of a statistical assessment covering the full range of velocities within the segment volume over all time steps for all parameters included in the radial chart display. At each threshold (i.e. steps of 10% of velocities), a t-test was conducted to evaluate the significance of differences between groups for each parameter included in the radial chart display. It was determined that the first 8 time steps of the cardiac cycle (spanning 280-320ms) and 100% of the data were optimal to detect cohort differences. Thus, the data within this optimal threshold was used for further analysis.

Statistical analyses

All continuous variables are expressed as mean $\pm$ SD. Probability distribution was assessed by Q-Q plots for all hemodynamic velocity distribution parameters. ANOVA was used to compare all groups and, if a significant difference existed, two-tailed Student's *t*-tests were used to compare individual groups. Correlations between disease characteristics (MAA and PV) and 4D flow-derived velocity parameters were assessed by the use of the Pearson's correlation coefficient. Inter- and intra- observer variability for full aorta segmentation in a subset of 10 patients (Ao Dilation + AS group) was assessed using Bland-Altman analysis for all parameters included in the radial chart display. Percentage absolute error was defined

by $\delta x = \frac{|x_0 - x|}{x} \times 100$. Statistical analysis was performed with SPSS 17 (SPSS, Chicago, IL).

RESULTS

Patient characteristics

Patients with moderate Ao dilation, severe Ao dilation and severe Ao dilation + AS were significantly ($P<0.05$) older than patients with mild Ao dilation. All subjects had normal left ventricular systolic function with an average ejection fraction of $60\pm6\%$. The global left ventricular systolic function parameters and mass were similar for all groups (ANOVA, Table 1). Severe Ao dilation and Ao dilation + AS groups showed a non-significant trend towards higher values compared to mild and moderate Ao dilation groups.

Pre-processing and segmentation

4D flow MRI pre-processing and aortic 3D segmentation required manual user interaction for defining thresholds and for the definition of aortic region and anatomic landmarks (Fig. 1). Pre-processing and 3D segmentation, including sub-regions, required 10-20 minutes for each subject. Subsequent velocity distribution analysis to generate velocity histograms and MIPs was fully automated.

Peak systolic velocity Maximum Intensity Projection (MIP)

Velocity MIPs for the 40 subjects included in this study are shown in Fig. 2 and illustrate disease specific differences in the aortic velocity patterns and distribution. Compared to subjects with mild Ao dilation, patients with moderate Ao dilation, severe Ao dilation as well as Ao dilation + AS demonstrated more focal variation in the velocity magnitude MIPs. The majority of patients in these three groups (27 of 30, 90%) demonstrated localized outflow jets and high flow regions (red color) which were only seen in one mild Ao dilation subject (case #6, see top row in Fig. 2). Regionally confined velocity jets were present and most pronounced in all patients with severe Ao dilation and for Ao dilation + AS. PV and Ao dilation groups showed a positive correlation to MAA ($r=0.36$, $P<0.05$), whereas PV and Ao dilation + AS showed a negative correlation to MAA ($r=-0.61$, $P<0.05$).

Velocity distribution analysis

To quantify cohort differences in 4D aortic hemodynamics, vessel size and velocity distribution analysis for the four aortic segments was performed in all subjects. Q-Q plots indicated normal distributions for all velocity distribution parameters (i.e. plotted points fall on or near the line $y=x$) (15). Figure 3 shows a direct comparison of cohort-averaged velocity histograms between all four groups for the aortic root (segment 1). Changes in velocity distribution, in particular for the patient group with Ao dilation + AS, are clearly evident and illustrate the potential of volumetric flow analysis to detect hemodynamic differences between groups.

Radial chart displays for all aortic segments and patient groups are shown in Fig. 4. Differences in hemodynamic metrics resulted in cohort specific shapes for each aortic segment that reflect disease induced changes in aortic volume and blood flow. Most pronounced differences in radial chart display size and shape between cohorts can be observed for the aortic root (segment 1) and ascending aorta (segment 2). Progressive worsening of aortic disease from mild to Ao dilation + AS resulted in increased chart display

size for segment 1 of 146% and segment 2 of 99%. In addition, changes in shape were accompanied by significant differences in individual parameters across cohorts (ANOVA, $P<0.05$ indicated by * in Fig. 4). Segment volume, PV, velocity standard variation, skewness and kurtosis were significantly different in all four aortic segments. Incidence showed a significant difference ($P<0.05$) between groups only for segment 4. Mean velocity was significantly different ($P<0.05$) between groups for segments 1 and 4. Median velocity showed a significant difference ($P<0.05$) between groups for segments 2 and 3.

Correlation analysis revealed a significant association of PV with segment volume in the aortic root ($r=0.54$, $P<0.001$). In segment 1, there was a significant relationship between PV and other velocity distribution parameters such as velocity incidence ($r=0.47$, $P<0.01$) and mean velocity ($r=0.56$, $P<0.001$). In both segments 1 and 2, a significant relationship was found for PV to standard deviation ($r=0.85$, $P<0.001$; $r=0.86$, $P<0.001$), skewness ($r=0.75$, $P<0.001$; $r=0.61$, $P<0.001$), and kurtosis ($r=0.79$, $P<0.001$; $r=0.4$, $P<0.01$), respectively.

Velocity distribution variability

Inter- and intra- observer variability for all parameters included in the radial chart display are summarized in figures 5 and 6. All parameters showed small inter- intra- observer variability and absolute error: volume = $4\pm2\%$, incidence = $7\pm7\%$, mean velocity = $4\pm4\%$, median velocity = $3\pm2\%$, velocity standard deviation = $2\pm2\%$, skewness = $5\pm4\%$, and kurtosis = $6\pm5\%$. PV measurement presented no variability.

DISCUSSION

The findings of our study demonstrate the feasibility of a volumetric velocity distribution analysis to identify hemodynamic alterations associated with different aortic pathologies. The analysis did not require the calculation of derived parameters or the application of fluid dynamics concepts but was solely based on the measured 4D (3D + time) velocity vector field and easy to obtain, robust descriptors of the spatio-temporal velocity distribution inside the aorta (e.g. mean, median, standard deviation, skewness, kurtosis). The separation into easily identifiable sub-regions permitted the automated characterization of changes in regional aortic hemodynamics in subjects with aortic disease.

One caveat regarding automation is the need for 3D segmentation of the aortic lumen, which requires user interaction and resulted in total analysis times of 10-20 minutes per case. Importantly, our results showed small inter- and intra-observer absolute error for volume segmentation. Nevertheless, the remaining velocity distribution analysis of blood hemodynamics was fully automated. It is important to note that in the clinical environment, individual measurements are not examined in a vacuum, i.e. they form a clinical picture representing the overall function and pathology of the patient (e.g. PV vs. MAA, PV vs. stroke volume, etc...). The presented radial chart display summarizes the aortic disease information in a brief snapshot, taking all parameters into account.

The results of our study indicate that radial chart display is sensitive to detect altered aortic hemodynamics in patients with aortic disease based on easy derived metrics of aortic geometry and blood flow.

Current clinical assessment

Current guidelines recommend the measurement of aortic diameter for grading Ao dilation and the assessment of peak systolic velocity and effective orifice area for evaluating aortic valve stenosis (5,16). These biometrics, along with considerations for size (height, weight, body surface area) and flow range (increased, normal, low) are important prognostic indicators for disease progression and outcome (17,18). In particular, MRI is used to corroborate or substitute other diagnostic imaging modalities (i.e. Echo-Doppler and/or CT).

A recent study from Della Corte et al. (19), suggested that any degree of AS may be a predictive factor for aortic root dilation. Similar to findings in their study, the results from this study showed a negative relationship of PV to MAA diameter ($r = -0.61$), for the Ao dilation + AS patient group. These findings may be driven by the aggressive surgical management of patients with concomitant Ao dilation and AS. It has been reported that 61% of aortic valve replacement/repair and supra-coronary replacement surgeries are performed in combination with Ao dilation (20). Thus, care must be taken when interpreting the negative correlation, as it may represent a surgical referral selection bias.

Current 4D flow assessment

Most investigators evaluate 4D flow data by positioning multiple 2D analysis planes in different regions of interest (2,4,6,7,9). In our study, patients with Ao dilation presented PV in a range from 0.9 to 1.95 m/s which is considered as non-stenotic by the guidelines (5,16) and corresponded with previous reported ranges (~0.7 to 1.7 m/s) using 4D flow with healthy volunteers (21). Since 4D flow analysis is generally performed using a single plane, the site of PV may not be interrogated (upstream or downstream of the plane) resulting in underestimation of true peak velocity value. This issue also applies to the standard through-plane encoded 2D PC-MRI currently used in the clinical practice, with added challenges due to eccentric flow patterns and/or elevated helical flow, as is especially common in the presence of AS (22). For example, AS can cause complex 3D flow patterns which may produce lower values when only the through-plane longitudinal velocity is measured. This, in part, may be the reason a recent 4D flow study demonstrated higher PV values than those obtained from 2D analysis and echo-Doppler (23). However, the effect of intravoxel phase dispersion and moderate spatial resolution (~ 2 mm) in aortic 4D flow data may also alter PV measurement (24). In this study the transvalvular PV was 2.9 m/s in patients with Ao dilation + AS, which was similar to the PV (3.3 m/s) reported in patients with moderate AS using 4D flow (21). In addition, Dyverfeldt et al. used a similar volumetric approach to measure transvalvular PV and mean velocity (3) in a population with severe AS (i.e. PV > 4m/s) using 4D flow. Additional examples of volumetric and 3D surface measurements with 4D flow include those which assessed velocity (3,9,10), turbulent kinetic energy (3), viscous energy loss (9), wall shear stress (7,25), and pressure gradients (26).

Flow visualization

There are several ways to visualize flow patterns using 4D flow data. Most studies use vector graphs, streamlines or time-resolved 3D particle traces in the region of interest (1-3,6), and, more recently, color-coded charts (27) and isovolumes (3). In this study, we used 4D flow-derived MIPs to visualize aortic flow patterns in a fast and simple manner.

This visualization approach allowed the identification of localized flow differences within and between groups. For example, transvalvular flow appears fairly homogeneous in the mild Ao dilation group shown in Figure 2. Flow impingement regions are apparent in many of the subjects at the aortic wall in groups with Ao dilation and AS. A similar approach was used in a recent work from our group (9), our results suggest that MIP visualization has particular promise for translation to clinical practice.

Data analysis strategy

4D flow MRI data preprocessing was performed using software tools developed by our group which included the correction for phase offset errors and calculation of 3D-PC-MRA data as a basis of the 3D segmentation of the aorta. An important component is the volumetric segmentation of the aorta and the definition of its sub-regions at specific anatomic landmarks using multi-planar and 3D viewers. To better utilize the 4D flow velocity data, a sensitivity analysis was conducted to identify the fraction of the 4D flow velocity data most optimally reflecting the hemodynamic impact caused by aortic diseases. Velocity distribution analysis was then performed for 4D flow velocity data based on this threshold (i.e. time frame 1-8). It should be noticed that the selected cut-off excluded diastolic velocities and potential hemodynamic changes during this cardiac period were not reflected in our data. Since none of our subjects had aortic valve insufficiency, the omitted data most likely included low diastolic velocities. It is important to mention that local velocity distribution has been used in previous studies (10,28) for diverse pathologies but not in the context of aortic disease and the proposed radial chart display.

Radial chart display approach

As a visual summary concept, we used the pictorial representation of geometric and velocity distribution parameters to generate radial chart displays. An advantage of the proposed radial chart display approach is the easy visual differentiation between parameters by a single plot. The findings from our study indicate that relatively simple flow distribution parameters are sufficient to detect different expressions of aortic disease which were most prominent for the Ao Dilation + AS group. These differences may be due to the severity of Ao dilation and helical flow in groups with Ao dilation (2,29).

The radial chart display concept is flexible and other descriptors such as age, height, weight, body surface area and flow range (i.e. increased, normal, low), ejection fraction, LV function parameters or medication may be added to establish treatment thresholds. Moreover, derived 4D flow parameters such as wall shear stress (4,7,8,30), pulse wave velocity (31), viscous energy loss (9), and turbulent kinetic energy (3) could be included. This approach may be useful for comparing individual trends with an averaged reference cohort including tolerance ranges. However, an increase in the number of parameters may result in complex shapes that may be difficult to interpret. Further studies, such as those incorporating pattern recognition methods or eigenvector decomposition, are thus warranted to systematically investigate different parameter combinations and their sensitivity to identify patients with aortic disease.

Study Limitations

The main limitation of this feasibility study is the small number of subjects ($n=10$) included in each group. However, on the basis of previous studies and theoretical expected results (3,4,10,22,23,32,33), we defined $\sigma=50 \text{ mm}^3$ and a minimum expected difference (D) of 50 mm^3 for volume, a $\sigma=0.5 \text{ m/s}$ and a $D=0.5 \text{ m/s}$ for peak velocity, $\sigma=10 \%$ and a $D=10 \%$ for incidence, $\sigma=0.5 \text{ m/s}$ and a $D=0.5 \text{ m/s}$ for mean, median and standard deviation, $\sigma=0.5$ and a $D=0.5$ for skewness and kurtosis. A two-tail significance criterion of 0.1 and a sample size of 10 per group yield a minimum power of 0.9 (34). Nevertheless, results for velocity distribution analysis differentiated flow velocity and anatomical alterations within groups. Due to the retrospective nature of this study some acquisition parameters differed in the included patients. In particular the spatial resolution showed an important variation (up to a factor of 3) in the evaluated population. A sub-analysis was performed to evaluate the impact of degradation due to spatial resolution effect (high resolution volume of $1 \times 1 \times 1 \text{ mm}$ versus low resolution volume of $3 \times 3 \times 3 \text{ mm}$) on parameters included in the radial chart display. When comparing the high vs. low resolution case, volume and peak velocity measurements showed only small absolute errors of 1%. The velocity distribution parameters also showed small absolute error values: incidence 2%, mean velocity 1%, median velocity 0.4%, standard deviation of velocity 0.2%, skewness 1% and kurtosis 1%. For this feasibility study inter- and intra-observer variability demonstrated a minor impact on velocity distribution analysis of blood hemodynamics (Fig. 5 and 6) using the optimal threshold obtained from the sensitivity analysis. An additional limitation is the lack of velocity distribution comparison between 2D velocity analyses at defined anatomic landmarks with the proposed volumetric approach. This assessment may provide further understanding about obtained results and how those compare with the standard 2D analysis for different pathologies. Another important point is the selection of velocity encoding for 4D flow acquisition, especially with high velocity acquisition (e.g. aortic stenosis). It should be considered that the use of velocity filters in stenosis patients may contribute to the differences observed within patients and groups. This issue may be solved by using multi-encoding strategies during 4D flow acquisition (35).

The proposed radial chart display approach showed differences between cohorts included in this study but it remains unclear how these differences could be used for improving patient risk stratification for progression of aortic disease. It should be noted that the effect of clinical empiric prognostic factors such as aortic diameter growth rate, age-matching and aortic shape on the velocity distribution analysis was not analyzed in this study. Further studies with larger number of patients and pathologies are thus necessary to confirm the incremental diagnostic and prognostic value of the proposed velocity distribution analysis and to investigate its association with other factors such as age.

In conclusion, the systematic velocity distribution analysis of 4D flow velocity data may identify altered characteristics of blood flow patterns in aortic diseases. Further studies are needed to evaluate the association of velocity distribution derived metrics with progression of aortic disease and ultimately patient outcome.

Acknowledgements

This work was supported by NIH R01HL115828 and K25HL119608, AHA 13SDG14360004, AHA 14POST18350019, CONACyT (grant 203355), SIR Pilot Study grant and a DFG (grant SCHN 1170/1-1). Authors thank Alex Powell for his technical assistance.

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FIGURE 1. Workflow of hemodynamic velocity distribution analysis

4D flow MRI data (time-resolved magnitude images and velocity vector components along (X, Y, Z)) were used to generate a 3D PC-MR angiogram and a 3D segmentation of the aorta which was divided into four segments: Segment 1 (aortic root in yellow) left ventricular outflow tract to the sino-tubular junction; Segment 2 (ascending aorta in orange) sino-tubular junction to the aortic arch; Segment 3 (aortic arch in magenta) aortic arch; Segment 4 (descending aorta in green) proximal to distal descending aorta. Segments were used to mask 4D flow velocity field in order to perform volumetric velocity distribution analysis. An example of the velocity distribution analysis for Segment 2 is shown in a patient with severe aortic dilation (patient #4, Fig. 2). Segmental aortic volume and velocity histogram characteristics are used to generate a radial chart display. sd: standard deviation; kur: kurtosis; ske: skewness.

FIGURE 2. Systolic velocity maximum intensity projection
The masked aorta velocity fields of three highest systolic velocity frames were used to generate a maximum intensity projection (MIP) in an oblique sagittal plane for all n=40 subjects. AS: aortic stenosis.

FIGURE 3. Cohort averaged histograms for Segment 1

Illustration of flow characteristic differences between the four patient cohorts is provided in panel A-D. Panels A-C show the cohort averaged histogram for the entire cohort for mild Ao dilation, moderate, and severe Ao dilation, respectively. Panel D shows the cohort averaged histogram for the entire cohort for Ao dilation + AS. The red line represents the median velocity, the green line represents the mean velocity, and the pink line represents the incidence threshold set at 1 m/s. Ao: aortic; AS: aortic stenosis; sd: standard deviation; kur: kurtosis; ske: skewness.

FIGURE 4. Radial chart display of the histogram characteristics

Radial chart displays provide a visual impression of the histogram characteristics for each aortic segment (1-4) using averaged values for each cohort and standard deviation (SD). Charts are in arbitrary units (AU). Blue band: SD for mild Ao Dilation; Green band: SD for moderate Ao Dilation; Yellow band: SD for severe Ao Dilation; Red band: SD for Ao Dilation + AS; Ao: aortic; AS: aortic stenosis. *: $P < 0.05$ between groups using ANOVA.

FIGURE 5. Bland-Altman for intra-observer variability for all parameters included in the radial chart display

Panel A-G show the plots for segment volume, median velocity, mean velocity, standard deviation velocity, incidence above 1 m/s, skewness and kurtosis, respectively.

FIGURE 6. Bland-Altman for inter-observer variability for all parameters included in the radial chart display

Panel A-G show the plots for segment volume, median velocity, mean velocity, standard deviation velocity, incidence above 1 m/s, skewness and kurtosis, respectively.

Table 1
Subject Characteristics

	All	Mild Ao Dilation	Moderate Ao Dilation	Severe Ao Dilation	Ao Dilation + Aortic Stenosis	ANOVA P-value
n	40	10	10	10	10	
Age (yrs)	58 ± 16	41 ± 16	63 ± 11	62 ± 10	64 ± 14	0.001
Female (n)	11	2	4	4	1	0.358
Ejection fraction (%)	60 ± 6	57 ± 6	59 ± 8	64 ± 4	60 ± 6	0.122
Left ventricle mass (gr)	135 ± 44	106 ± 19	122 ± 26	137 ± 10	170 ± 57	0.078
End-diastolic volume (ml)	158 ± 46	150 ± 26	145 ± 32	161 ± 64	176 ± 52	0.517
Stroke Volume (mL)	93 ± 30	85 ± 13	84 ± 21	100 ± 47	102 ± 26	0.102
Sinus of Valsalva Diameter (mm)	41 ± 5	39 ± 9	41 ± 3	42 ± 5	39 ± 4	0.652
Mid Ascending Aorta Diameter (mm)	40 ± 7	30 ± 4	41 ± 3	47 ± 2	42 ± 3	0.001
Peak Velocity (m/s)	1.78 ± 0.98	1.2 ± 0.4	1.3 ± 0.3	1.35 ± 0.15	3.3 ± 0.66	0.001