Magn Reson Imaging. Author manuscript; available in PMC 2016 June 01.

Published in final edited form as:
Magn Reson Imaging. 2015 June ; 33(5): 695–700. doi:10.1016/j.mri.2015.02.020.

Extended 3D Approach for Quantification of Abnormal Ascending Aortic Flow

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Abstract

Background—Flow displacement quantifies eccentric flow, a potential risk factor for aneurysms in the ascending aorta, but only at a single anatomic location. The aim of this study is to extend flow displacement analysis to 3D in patients with aortic and aortic valve pathologies.

Methods—43 individuals were studied with 4DFlow MRI in 6 groups: healthy, tricuspid aortic valve (TAV) with aortic stenosis (AS) but no dilatation, TAV with dilatation but no AS, and TAV with both AS and dilatation, BAV without AS or dilatation, BAV without AS but with dilation. The protocol was approved by our institutional review board, and informed consent was obtained. Flow displacement was calculated for multiple planes along the ascending aorta, and 2D and 3D analyses were compared.

Results—Good correlation was found between 2D flow displacement and both maximum and average 3D values (r>0.8). Healthy controls had significantly lower flow displacement values with all approaches ($p<0.05$). The highest flow displacement was seen with stenotic TAV and aortic dilation (0.24±0.02 with maximum flow displacement). The 2D approach underestimated the maximum flow displacement by more than 20% in 13 out of 36 patients (36%).

Conclusions—The extended 3D flow displacement analysis offers a more comprehensive quantitative evaluation of abnormal systolic flow in the ascending aorta than 2D analysis.

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Competing Interests
No conflicts to disclose.

Differences between patient subgroups are better demonstrated, and maximum flow displacement is more reliable assessed.

Keywords

MRI; Aorta; Valves; BAV; Eccentric Jets

Background

Eccentric systolic flow is widely reported in patients with bicuspid aortic valves (BAVs) using 4D Flow imaging [1–5]. Altered hemodynamics related to eccentric flow have been investigated as potential risk factors for progressive valve-related aortic disease. Many different quantitative parameters have been proposed in this context, but consensus has not been reached about which parameter is best. Some groups have calculated the degree of helicity caused by eccentric systolic flow [6,7], whereas others have looked at the flow jet angle [8], or the restriction in aortic valve leaflet excursion that causes deviation of flow away from the aortic midline [9]. Another approach has been to estimate changes in wall shear stress (WSS) caused by flow eccentricity. While some reports have shown gross differences in WSS estimates between different patients groups [3,4], others have shown that WSS estimates are less reproducible than other markers and may become less reliable for higher WSS values [10,11].

Flow displacement is a simple parameter developed for reliable quantification of the degree of flow eccentricity for a cross-sectional plane [12]. It is defined as the distance between the anatomic center of the aorta for a given cross-section and the “center of velocity” of forward flow, normalized by the luminal diameter. Flow displacement has been shown to be reproducible and correlate with aortic growth in a preliminary study [10,13], but it only offers information for a single anatomic level. A 3D approach for flow displacement analysis is preferable as it would better reflect the original visual observations of abnormal flow patterns, and ensure that the location of maximum flow displacement is captured. The aim of the current work is to extend the analysis of flow displacement to 3D, and to compare 2D and 3D analysis in patients with aortic and/or aortic valve pathologies.

Materials and Methods

Study Population

The study was institutional review board approved and was in compliance with Health Insurance Portability and Accountability Act regulations. All participants provided written informed consent.

Patients referred by the Department of Cardiology and Cardiothoracic Surgery for evaluation of aortic and/or aortic valve morphology at our institution between 2011 and 2013 were retrospectively included in the study. A total of 48 consecutive patients were studied with MRI in 5 separate groups: tricuspid aortic valve (TAV) with aortic stenosis (AS) but no dilatation, TAV with dilatation but no AS, and TAV with both AS and dilatation, BAV without AS or dilatation, BAV without AS but with dilation. Aortic valve pathologies were determined from prior echocardiography and/or cardiac magnetic resonance (CMR) studies, and aortic diameters were obtained from prior contrast-enhanced MRI or computed tomographic angiography studies. Degree of aortic stenosis was determined by standard echocardiography criteria [14], and for simplicity only those patients with moderate or severe AS were deemed to have AS. A group of 7 healthy individuals underwent the same MRI protocol and were used as controls. Exclusion criteria were: poor quality MRI data, absent or insufficient evaluation of the aortic valve by echocardiogram, severe aortic insufficiency, complex congenital heart disease, and any contraindication to MRI.

MR Imaging

MR imaging was performed at 1.5T on a Signa CV/i system (GE, Milwaukee, WI) and on an Avanto system (Siemens Healthcare, Erlangen, Germany). To assess blood flow, an oblique-sagittal slab encompassing the thoracic aorta was imaged using a time-resolved 3D Phase-Contrast MRI (4D Flow) pulse sequence with respiratory compensation and ECG gating (retrospective for GE and prospective for Siemens). The 4D Flow MRI protocols used at the different scanner platforms have been described previously [15,16]. Imaging parameters for the GE system were as follows: VENC = 160–250 cm/s, fractional FOV= (300 × 270) mm^2, slab thickness = 78 mm, matrix = (256 × 192 × 30), spatial resolution = (1.17 × 1.56 × 2.60) mm^3, temporal resolution = 74–77 ms. Parallel imaging (GRAPPA) with an acceleration factor of 2 was used. 735 heartbeats were required for data acquisition, resulting in scan times of 8 to 15 minutes. Imaging parameters for the Siemens system were as follows: VENC = 200–280 cm/s, Parallel imaging (GRAPPA) reduction factor = 2, FOV= (240–360 × 240–360) mm^2, slab thickness = 55–80 mm, matrix = (96–144 × 96–144 × 22–32), spatial resolution = (2.5 × 2.5 × 2.5) mm^3, temporal resolution = 35 ms. 528–1240 heartbeats were required for data acquisition, resulting in nominal scan times of 8–18 minutes.

Data Analysis

Three different measures of flow displacement were evaluated: 1) 2D flow displacement, 2) maximum flow displacement and 3) average 3D flow displacement. The 3D flow displacement analysis developed in this study is presented in Figure 1. First, peak systole was identified as the time-point of maximum average speed in the ascending aorta. Next, peak-systole PC-MRA datasets were computed from the 4D Flow data using Matlab (The MathWorks Inc, Natick, MA). The PC-MRA images were imported in Amira (Visage Imaging, Germany) for semi-automatic segmentation of the ascending aorta from the aortic valve to the origin of the brachiocephalic artery, and vessel centerline computation. The AsAo segmentation and centerline were exported for subsequent automated flow displacement analysis written in Matlab. The automated analysis placed equally spaced cross-sectional planes along the AsAo centerline. The normalized flow displacement parameter, described previously [12], was calculated for each cross-sectional plane at peak systole. The normalized flow displacement is defined as the distance between the anatomical center of the lumen and the "center of velocity" (C_{vel}) of forward flow, normalized by the lumen diameter: $FlowDisplacement = {C_{vel}}/{Vessel\ Diameter}$, where $C_{vel,j} = \frac{\sum_i r_{i,j}|v_i|}{\sum_i |v_i|}$, i =

lumen pixels, j = x,y,z. For simplicity, the term ***flow displacement*** will be used from now on to designate the normalized peak systolic flow displacement parameter.

Conventional 2D flow eccentricity analysis was performed by using a standardized plane-positioning approach [12,13]. An experienced observer placed a cross-sectional plane in the ascending aorta just distal to the sinotubular junction and the "***2D flow displacement***" was calculated based on this plane and the previously defined ascending aorta segmentation. The ***maximum flow displacement*** in the AsAo was calculated as the maximum value of flow displacement among all planes along the ascending aorta centerline. The percentage difference between the 2D flow displacement and the maximum flow displacement was calculated for each patient. ***Average 3D flow displacement*** was calculated as the area under the curve of normalized flow displacement along the AsAo, normalized by the length of the investigated segment. Additionally, the flow displacement values of each plane along the centerline were plotted against the distance along the centerline for a visual representation of 3D flow displacement, and the length of displacement > 0.15 along the AsAo was computed.

Finally, the maximum velocity (Vmax) in the AsAo was obtained from the segmented 4D Flow data set for each patient.

Statistics

To evaluate differences between the groups of subjects in terms of 2D flow displacement, maximum flow displacement and average 3D flow displacement, one-way analysis of variance (ANOVA) on 6 independent samples was performed, using Tukey's least significant difference post-hoc test to evaluate individual differences between groups. A cut-off value of 0.05 was considered statistically significant. Correlation between the 2D analysis and the extended 3D analysis was evaluated using the Pearson's correlation coefficient. Additionally, correlation between each of the 3 flow displacement parameters with the ascending aortic diameter, and between the flow displacement parameters, the length of the flow displacement > 0.15 and Vmax, were also evaluated using the Pearson's correlation coefficient.

Results

4D Flow data quality was evaluated in terms of presence of aliasing. Correction of aliasing was performed in 10 patients, minimizing the extent of the artifact. However, a separate group of 10 patients had to be excluded because of severe aliasing that could not be corrected. An additional 2 patients were excluded for severe aortic insufficiency. Flow displacement analysis was thus performed on 36 patients (28 males, 8 females, mean age 51±23 years) and on all of the healthy subjects (6 males, 1 female, mean age 29±5). The number of subjects per group was as follows: healthy subjects = 7, TAV with AS but no dilatation = 8, TAV without AS but with dilatation = 6, and TAV with both AS and dilatation = 5, BAV without AS or dilatation = 10, BAV without AS but with dilation = 7. Patient demographics are presented in Table 1.

2D analysis

The average values of 2D flow displacement per group of subjects were as follows: 0.04±0.02 were for healthy subjects, 0.17±0.07 for TAV with AS but no dilation, 0.14±0.07 for TAV with dilatation but no AS, 0.19±0.08 for TAV with both AS and dilatation, 0.15±0.06 for BAV without AS or dilation, and 0.16±0.06 for BAV without AS but with dilatation. Flow displacement values for healthy subjects were significantly lower than for all patient groups (p=0.01). However, no significant differences were shown between any of the patient groups with 2D analysis.

3D analysis

The maximum flow displacement values per group were as follows: 0.07±0.01 for healthy subjects, 0.20±0.03 for TAV with AS but no dilation, 0.17±0.04 for TAV with dilatation but no AS, 0.24±0.02 for TAV with both AS and dilatation, 0.17±0.05 for BAV without AS or dilation, 0.19±0.06 for BAV without AS but with dilatation. For the average 3D flow displacement, the mean values per group were: 0.04±0.01 for healthy subjects, 0.13±0.02 for TAV with AS but no dilation, 0.08±0.02 for TAV with dilatation but no AS, 0.15±0.02 for TAV with both AS and dilatation, 0.10±0.04 for BAV without AS or dilation, 0.12±0.03 for BAV for BAV without AS but with dilatation.

Maximum flow displacement values were significantly different between healthy subjects and all of the patient groups (p<0.001). TAV with both AS and dilatation showed significantly higher maximum flow displacement values compared to TAV patients without AS and the BAV patients without dilatation (p=0.05). The presence of AS resulted in the highest overall flow displacement values (0.24±0.02 and 0.20±0.03). However, no significant differences were shown between any of the other patient groups using the maximum flow displacement parameter.

Average 3D flow displacement values were significantly different between healthy subjects and all of the patient groups (p=0.01). Higher values were seen with average 3D flow displacement for patients with AS compared to those without AS (p=0.05), except the BAV with dilatation group. Additionally, a significant difference was seen between TAV with dilation but not AS and BAV patients with dilation but not AS (p<0.05). Average values per subject group for the three investigated parameters (2D flow displacement, maximum flow displacement and average 3D flow displacement) are presented in Figure 2.

Flow Pattern Analysis

Representative plots of the flow displacement values from cross-sections along the AsAo as a function of distance are presented in Figure 3 for each group (individual plots for each subject are provided as Supplemental Data). Healthy controls had low flow displacement values that were relatively constant along the AsAo. Generally, the presence of AS resulted in the highest flow displacement values that remained high for longer distances along the AsAo. Patients with BAV had characteristic 3D displacement plots with a sharp increase to proximal high peak values, followed by a smooth tapering distally through the ascending aorta.

2D versus 3D

Strong correlations were found between the 2D flow displacement and both the maximum flow displacement (r=0.84) and the average 3D flow displacement (r=0.77). The 2D flow displacement analysis underestimated the maximum displacement by more than 20% in 36% of the patients (13 out of 36). Four of these patients were in the TAV with dilatation but no AS group. Out of the remaining 9 patients, 3 were in the BAV without AS or dilation group, 3 in the TAV with AS but no dilation group, 2 in the BAV with dilatation group, and 1 in the TAV with AS and dilatation group, which was the patient with the largest difference of 81%.

Diameter and Flow Displacement

No correlation was found between maximum AsAo diameter and any of the flow displacement parameters. Pearson's correlation coefficients were 0.1 for the 2D flow displacement, 0.2 for maximum flow displacement and −0.01 for average 3D flow displacement. Figure 4 presents the scatter plots for each of the flow displacement parameters and the maximum AsAo diameter of the aorta.

Maximum velocity and Flow Displacement

A small and not statistically significant correlation was found between Vmax and the 2D displacement ($r = 0.276$, $p = 0.07$). However, moderate and statistically significant correlations were found between Vmax and maximum flow displacement ($r = 0.458$, $p < 0.01$), and Vmax and the area of normalized displacement ($r = 0.462$, $p < 0.01$). The highest correlation was found between Vmax and the length of flow displacement ($r = 0.57$, $p < 0.001$).

Discussion

Abnormal flow displacement is demonstrated in the ascending aortas of all patients studied with aortic and/or aortic valve pathologies using both 2D and 3D approaches. Differences between patient subgroups, however, are better revealed with the 3D flow displacement analysis we have introduced.

Flow displacement quantifies the degree of flow eccentricity for a cross-sectional plane [12]. Increasing evidence demonstrates that flow displacement is reproducible, correlates with aortic growth [10,13], and distinguishes between BAV phenotypes [17]. However, in these previous studies, flow displacement has been evaluated at specific anatomic levels in 2D. In our present study, we have extended the flow displacement analysis to a 3D approach and demonstrated improved detection of flow abnormalities.

The maximum flow displacement parameter allows detection of the most pronounced systolic flow abnormalities. The highest flow displacement values were seen in patients with stenotic TAV with or without dilated aortas (0.24±0.02 and 0.20±0.03). 2D analysis performs well in most cases, but can grossly underestimate regions of abnormal flow (up to 81% error). Overall, 2D underestimated the maximum flow displacement by more than 20% in 36% of patients.

3D flow displacement analysis allows objective evaluation of ascending aortic flow patterns, and more importantly it allows detection of specific flow characteristics related to different aortic pathologies. Strong evidence seems to point toward the hypothesis that the orientation of the flow jet is related to the shape of the aortic valve [17]. Highly eccentric flow has previously been related to the presence of aortic stenosis, even in the absence of dilatation [18]. The proposed 3D flow displacement analysis showed characteristic flow displacement profiles related to aortic stenosis in which displacement remained high for longer distances along the AsAo. This is potentially a direct result of the high jet velocity, also indicated by the good correlation between Vmax and the length of flow displacement. While this eccentricity subjects the vessel wall to abnormal stress, there may certainly be other important factors at play. Pressure differences may be a cause and consequence of flow eccentricity. Detailed interpretation of the eccentricity profiles along the ascending aorta would require a more complete study of the underlying hemodynamics and may best be performed with Computational Fluid Dynamics simulations.

The average 3D flow displacement parameter can distinguish between patients with and without aortic stenosis, whereas the 2D displacement parameter does not. Patients without aortic stenosis but with BAV showed lower flow displacement relative to stenotic TAV only with the average 3D flow displacement parameter (0.10 versus 0.13 ($p=0.016$), and versus 0.15 ($p=0.004$)). 2D and maximum flow displacement values are comparable between nonstenotic BAV and stenotic TAV. Only slightly and nonsignificantly higher displacement values were seen if a dilated aorta was present with nonstenotic BAV. These findings support the idea that a BAV causes abnormal systolic flow, and that abnormal flow is seen without aortic stenosis by standard criteria. Yet it is also at odds with the report from den Reijer et al. [8] that shows that flow jet angle is associated with larger aortic sizes. This may be partially explained by the fact that flow displacement is normalized for aortic size in all cases, whereas flow jet angle is not. In our analysis, no correlation between diameter and flow displacement is demonstrated in either 2D or 3D (Figure 4).

The proposed method for semi-automatic quantification of aortic flow displacement is in line with ongoing efforts in the field MR blood flow imaging. Recent reports have highlighted the advantages of using the volumetric nature of 4D Flow data to minimize the degree of user-interaction and subjectivity of visualization [16,19]. The proposed 3D flow displacement analysis does just this by using a semi-automatic, 3D segmentation (Amira software, 5 minutes per patient) to generate quantitative measurements of abnormal aortic flow. Fully automatic segmentation of 4D PC-MRI is anticipated in the near future [20].

This study has several limitations. First, not all parameters for quantification of abnormal aortic flow were included in the analysis, only flow displacement. Our emphasis was the differences between 2D and 3D approaches, and the relative advantages of a comprehensive 3D analysis, rather than the comparison of parameters that has been performed in other reports [10]. Second, the number of patients per group was relatively small therefore the results are potentially not representative for aortic blood flow in other patients. Third, a BAV subgroup with aortic stenosis was not included. As discussed, however, flow displacement values for nonstenotic BAV patients are comparable to stenotic TAV patients, making the BAV subgroup we have targeted of unique clinical interest, as the abnormal systolic flow would otherwise go unrecognized by standard imaging. Due to the retrospective nature of the study, the MRI scans were performed with slightly different temporal and spatial resolutions. The clinical and independent predictive value of flow displacement descriptors such as the ones presented here for future dilatation or plaque development will need to be identified by follow-up studies.

Conclusions

In conclusion, abnormalities of systolic blood flow can be quantified with MRI using flow displacement. All patients with aortic and/or aortic valve disease have elevated flow displacement values compared to healthy controls using both 2D and 3D approaches. Maximal values are more reliably captured with 3D analysis, and differences are more pronounced between subgroups when the parameter of average 3D flow displacement is used. We propose that this parameter be considered in future studies aimed at evaluating flow eccentricity in the ascending aorta.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Sources

Covidien/Radiologic Society of North America Research Scholar Grant 2012–2014 (MDH), National Institutes of Health (grant NS059944) (DS), Veterans Affairs Merit Review Grant (DS), Swedish Research Council (PD).

Abbreviations

AsAo	ascending thoracic aorta
BAV	bicuspid aortic valve
TAV	tricuspid aortic valve
MRI	magnetic resonance imaging
3D	three-dimensional
4D Flow	3D, time-resolved phase contrast MRI
WSS	wall shear stress

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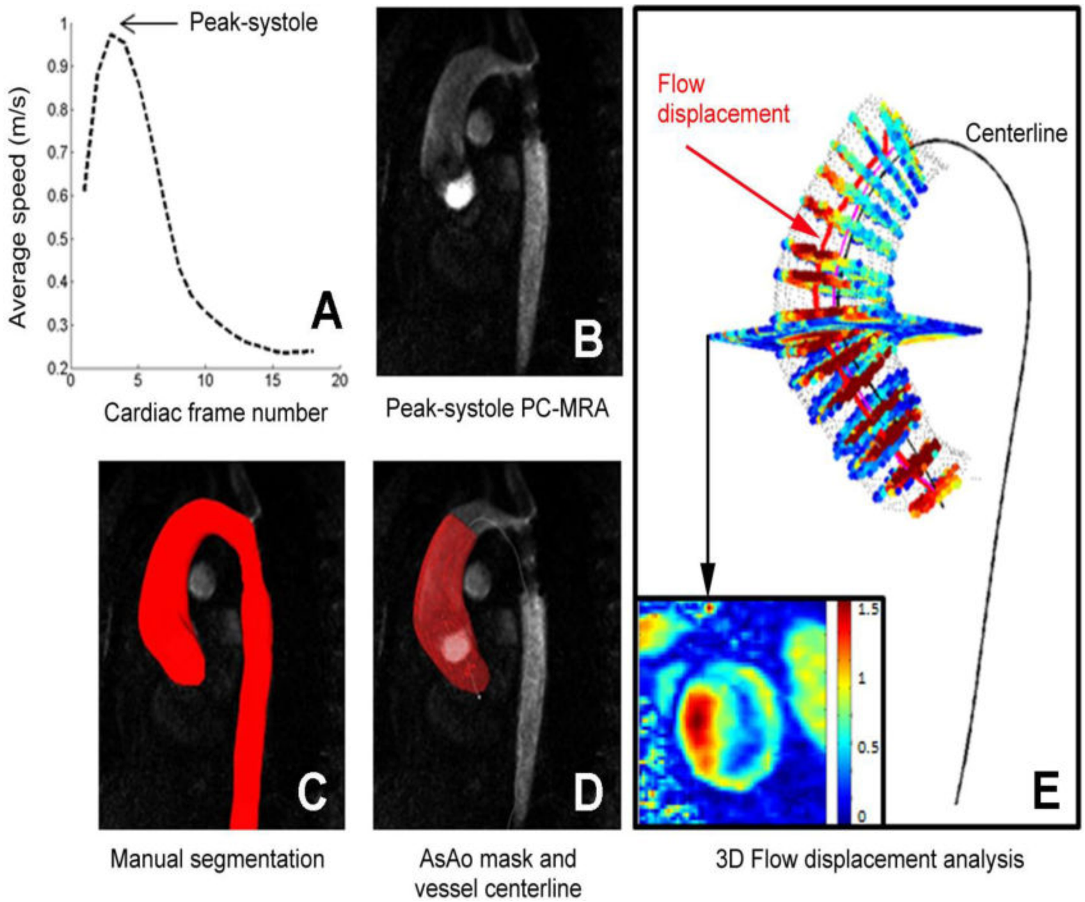

Figure 1.

3D analysis workflow: detection of peak systole (**A**), manual segmentation of peak-systole PC-MRA and centerline calculation (**B**, **C**, **D**), and example of the 3D flow displacement analysis results (**E**): cross-sections containing speed information are automatically placed along the vessel centerline (black), normalized displacement is calculated for each cross-section (red line), and velocity map of the standard plane presenting an eccentric flow pattern (Inset).

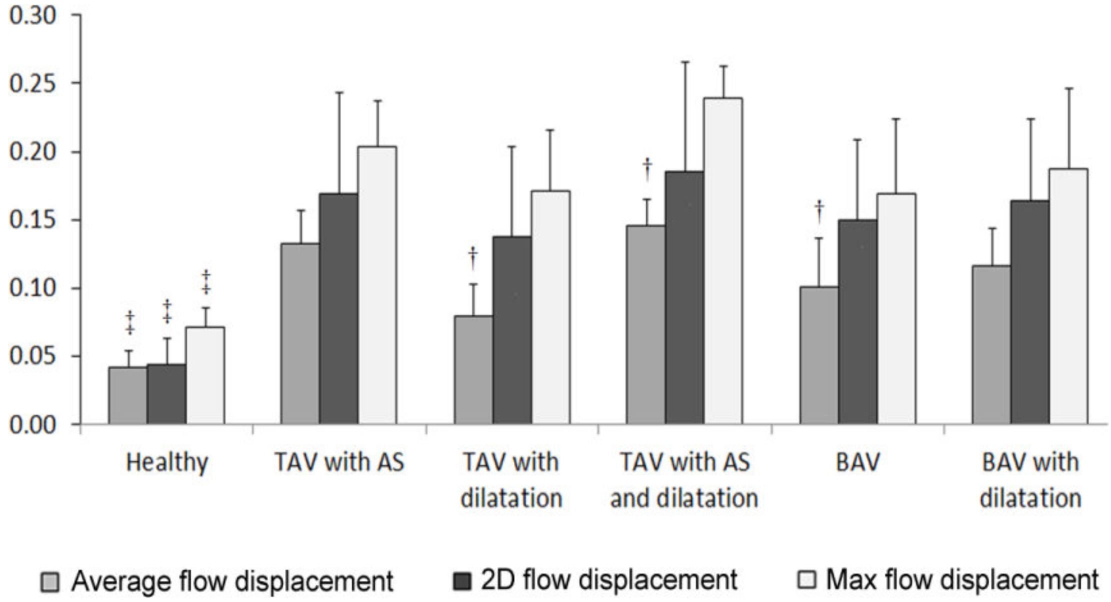

Figure 2.

Mean values of the three flow displacement parameters for each of the 6 groups. Healthy subjects have the lowest flow displacement values (‡ p=0.01). Only average 3D flow displacement reveals higher flow displacement values for patients with aortic stenosis compared to those without aortic stenosis († p=0.05).

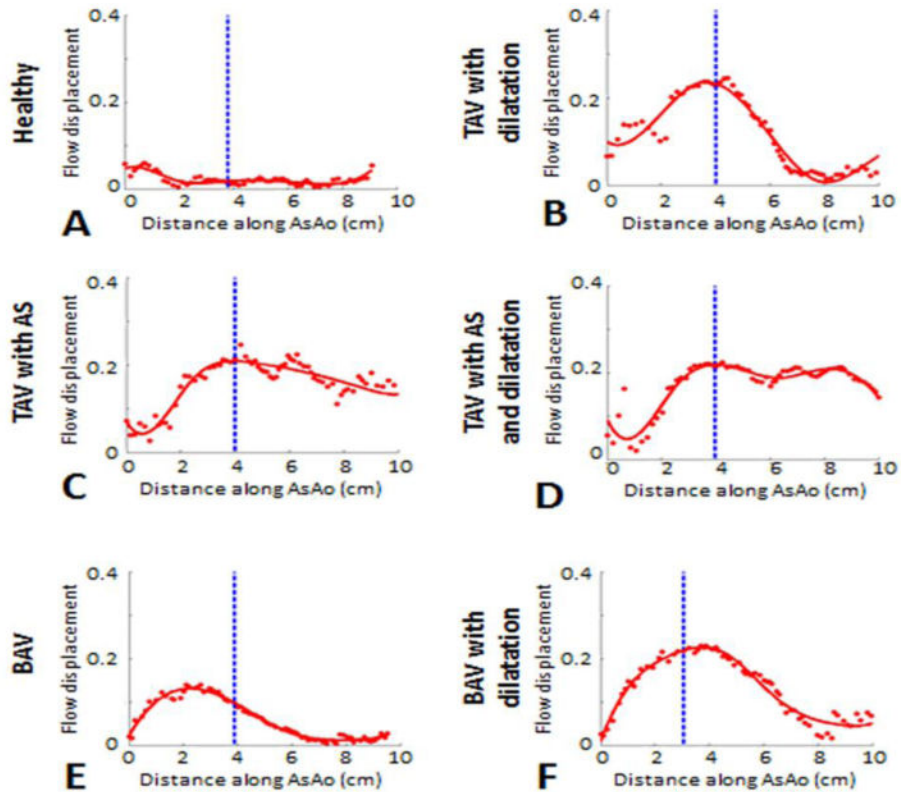

Figure 3.

Representative plots of flow displacement from each of the cross-sections (red dots, red curve – spline fit) as a function of distance along the AsAo for each of the 6 groups. The dotted blue line indicates the location of the 2D plane, which was placed just distal to the sinotubular junction. No high flow displacement was observed for the healthy control group (**A**). Generally, the presence of AS resulted in the highest flow displacement values that remained high for longer distances along the AsAo (**C**, **D**). Patients with BAV had characteristic 3D displacement plots with a sharp increase to proximal high peak values, followed by a smooth tapering distally through the ascending aorta (**E**, **F**).

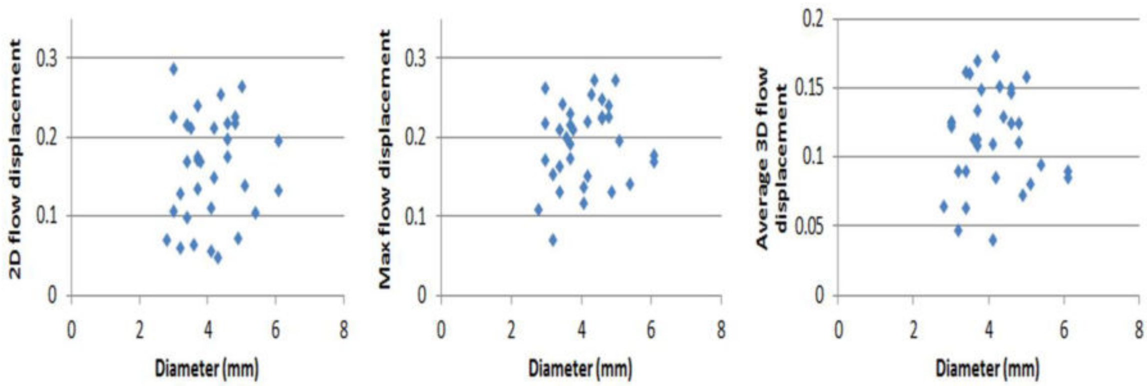

Figure 4.

Correlation analysis of each of the 3 flow displacement parameters with the diameter of the ascending aorta (2D flow displacement (r=0.1) – left, maximum flow displacement (r=0.2) – center, and average 3D flow displacement (r=−0.01) – right).

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Table 1

Patient Demographics

Patient group	N	Mean Age	Diameter	AS
TAV with dilatation but no AS	6	67±7	5.2±0.8	Mild, n=1
TAV with AS but no dilation	8	71±7	3.5±0.3	Critical, n=3 Severe, n=5
TAV with AS and dilatation	5	72±5	4.4±0.2	Moderate/Severe, n=4 Severe, n=1
BAV without AS or dilation	10	30±7	3.4±0.3	Mild, n=3
BAV with dilatation but no AS	7	29±19	4.7±0.5 (*)	Mild, n=1

*For one pediatric patient (age 8 years), the diameter was not used in the average calculation.