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Simulation of Altered Blood Flow in Bicuspid Aortic Valve Disease: *A Proof of Concept Study*

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Abstract: Background: Bicuspid aortic valve (BAV) is a common congenital heart disease which is associated with aortic dilatation. There is controversy in the literature regarding the various measures of the biomechanical properties of the aorta in these patients and their relationship to aortic dilatation. The present study aimed to assess both conventional 2D Cardiac Magnetic Resonance Imaging (CMRI) measurements of aortic biomechanics (compliance and distensibility) and a computational fluid dynamics (CFD) approach in patients with BAV and either normal or dilated ascending aorta. Methods: 2D CMRI was performed in 18 patients (6 controls, 6 BAV with dilated ascending aorta and 6 BAV with normal ascending aorta i.e. <36mm diameter) and ascending aortic compliance and distensibility was calculated. CFD was performed with *ANSYS Fluent software* using 2D CMRI derived parameters to simulate the hemodynamic relationships between blood and the aortic wall. Results: The groups were similar in terms of demographics (mean age 38±13 years, 56% male, pulse pressure 56±15mmHg). There was a numerically lower but not significant difference in aortic compliance between dilated BAV and the other groups. Aortic distensibility was no different between groups. Using CFD, at the mid-ascending aorta pressure was significantly higher in patients with dilated BAV (147.6 ± 24.1 mmHg) than non-dilated BAV (118.6 ± 16.2 mmHg) and controls (124.5 ± 14.4 mmHg), p=0.04. Conclusions: We demonstrate that is possible to estimate regional aortic pressure from 2D CMRI derived parameters using a CFD approach. These novel parameters may add value to surveillance strategies in aortic disease.

Keywords: Cardiac Magnetic Resonance Imaging, Bicuspid Aortic Valve, Aortic Disease, Aortic Compliance

1. Introduction

Bicuspid aortic valve (BAV) is a common congenital heart disease associated with progressive ascending aortic dilatation and/or catastrophic rupture [1]. Current guidelines recommend regular surveillance of thoracic aortic aneurysm/dilatation in these patients [2, 3]. Determining which patients are more predisposed to an adverse aortic event is problematic, with insufficient evidence regarding the timing of prophylactic operative intervention [4]. The proposed mechanisms for aortic dilatation in BAV include genetic factors, defects of the aortic wall as well as altered flow from the bicuspid valve independent of the degree of aortic valve stenosis. These mechanisms are eventually likely to lead to increased aortic stiffness predisposing to aneurysm formation. There is controversy in the literature regarding the various measures of aortic bio-mechanical properties (stiffness, compliance, elasticity, distensibility and wall shear stress) and how they relate to eventual complications. For example, studies using echocardiography have demonstrated reduced aortic elasticity in patients with both stenotic and nonstenotic BAV [5-7], and that reduced elasticity is associated with accelerated aneurysm growth [8]. However, Guala et al reported similar stiffness between BAV and tri-leaflet aortic valve (TAV) patients with and without aortic dilatation using 4D flow [9]. We sought to assess the ability of clinically generated standard 2D Cardiac Magnetic Resonance Imaging (CMRI) data to simulate the pressure distribution across the entire thoracic aorta using a computational fluid dynamics (CFD) approach in patients with BAV. Regional aortic bio-mechanical properties were examined both by conventional methods and CFD.

2. Methods

Patients with BAV presenting to a cardiology practice specializing in CMRI between June 2016 and July 2018 were retrospectively included in the study. The patients needed to have MRIs of adequate quality to assess 2D compliance and CFD, as well as having had non-invasive brachial blood pressure measured at the time of scanning by sphygmomanometer. Patients were excluded if they had previous surgical repair of or other procedures to the aorta or aortic valve. Patients were also excluded if they had greater than mild aortic stenosis (Vmax >2m/sec on 2D echocardiogram), or any degree of aortic regurgitation. The BAV patients were separated into two groups based on whether they were dilated with a cut off ascending aortic diameter >36mm.

Two-dimensional, standard MRI measurements were obtained using a 1.5T MR scanner (GE medical system). The protocol included retrospectively gated balanced steady-state free precession (bSSFP) cine MR images, fluoro-triggered gadolinium 3D MRA timed for the thoracic aorta and through plane phase contrast imaging to map flow/velocities in the proximal ascending aorta at the sino-tubular junction and the descending aorta at the level of diaphragm.

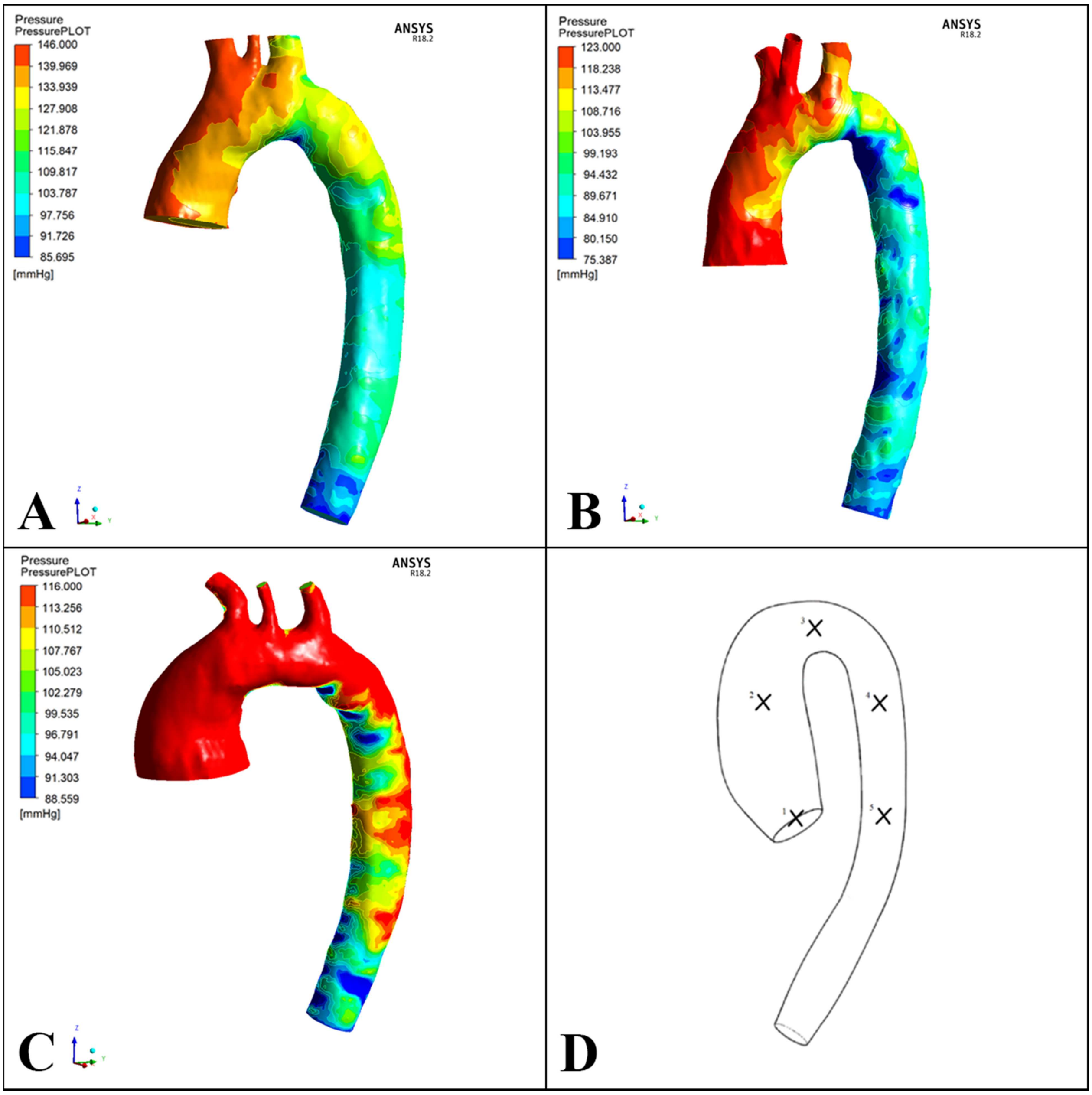

Figure 1. A: Control Patient Pressure Distribution; B: Normal sized BAV Patient Pressure Distribution; C: Dilated BAV Patient Pressure Distribution; D: Location of Simulated Pressure Probes.

2D CMRI measurements were obtained and 2D measurements of the aorta were calculated using OsiriX MD (V 11.0.03) by an experienced investigator (RP). The parameters were obtained in the ascending aorta at the level of the bifurcation of the main pulmonary artery, and aortic compliance and distensibility were calculated as previously described [10].

CFD was performed using the software *ANSYS Fluent*. *ANSYS Fluent* has been shown to be a reliable predictor of peak systolic pressure drops in CoA when compared to diagnostic catheterization [11]. Computational methods such as fluid-structure interactions have been used previously to evaluate hemodynamic predictors and wall stresses in the aorta [12]. Further, a paper by Rojczyk et al [13] shows how *ANSYS Fluent* can be used to recreate blood flow in an aorta with a velocity profile as an inlet condition and an outlet pressure boundary condition to mimic the human cardiac cycle.

Bolus tracked 3D gadolinium based aortic MR angiographic data was processed in the software *ScanIP* to create anatomically correct 3D aortic models. These models were then imported into *ANSYS Fluent* in which the haemodynamic relationship between blood and the aortic wall was simulated. This allowed for the visualization of pressure distribution across the entire thoracic aorta. The fluid simulated was characterized as an incompressible Newtonian fluid and material properties were set to those of human blood. The pressure in the ascending aorta was set to use a velocity inlet as a fluid condition, which was sourced from the single breath-held through-plane phase contrast 2D MRI aortic flow acquired at the sino-tubular junction. The brachiocephalic artery, the left common carotid artery and the left subclavian artery were all set to behave as pressure outlets for this simulation. The values for the "gauge" pressure at these three locations was set to the systolic blood pressure, which was measured at the time of the scan.

The descending aorta was set to be a pressure outlet with a value equal to the ascending aortic pressure multiplied by the ratio of the descending aortic blood volume over the ascending aortic blood volume also sourced from phase contrast 2D MRI aortic flow data. *ANSYS Fluent* was then used to run until a solution converged to set criteria before displaying a pressure gradient map along the original 3D model. Simulated pressure probes can be placed into the model to attain pressure values at five locations along the aortic arch. The values obtained were used for the statistical analyses. Representative examples of each of the three patient categories are presented in figure 1 A-C, with the locations of the simulated pressure probes shown in panel D.

Data for aortic dimensions, compliance and distensibility, pressure, and demographic data except for body mass index (BMI) and gender were normally distributed. One-way ANOVA was used for continuous variables, and Chi-square test for categorical variables (gender). When one-way ANOVA was significant, the differences were further explored with the post-hoc Tuckey procedure. The Kruskal-Wallis H test was used to compare BMI.

3. Results

A total of 6 control patients (mean age 36 ± 13 years, 33% male), 6 patients with BAV and normal aortic dimensions (mean age 35 ± 12 years, 66% male), and 6 patients with BAV and dilated aorta (mean age 44 ± 13 years, 66% male) were assessed. There was no significant difference in age, gender, pulse pressure or BMI between the groups. All BAV patients had type 1 BAV with right-left coronary cusp fusion. By design, the ascending aortic diameter was significantly larger in the dilated BAV group (40.3 ± 6.7mm) compared to the normal sized BAV (29.7 ± 3.2mm) and control groups (29.5 ± 5.4mm), p=0.004.

Conventional 2D techniques demonstrated patients with dilated BAV had a numerically lower, but not statistically significantly different, aortic compliance (1.6 ± 1.2 mm^2mmHg^{-1}) than non-dilated BAV (2.6 ± 1.4 mm^2mmHg^{-1}) and controls (2.2 ± 1.5 mm^2mmHg^{-1}), p=0.482. Aortic distensibility was not different between the groups (p=0.149).

Using our novel CFD approach, we noted at the mid ascending aorta (point 2), aortic pressure was significantly higher in patients with dilated BAV (147.6 ± 24.1 mmHg) than non-dilated BAV (118.6 ± 16.2 mmHg) and controls (124.5 ± 14.4 mmHg), p=0.04. There was no statistically significant difference in aortic pressures throughout the rest of the measured aorta.

4. Discussion

This study provides the "proof of concept" that from standard 2D CMRI it is possible to simulate regional aortic pressure measurements in the aorta through the use of CFD methods. This technique detected significantly elevated ascending aortic pressure in patients with BAV with aortic dilatation, where conventional 2D measurements of compliance and distensibility could not demonstrate significant differences. The additional value of aortic pressure parameters, beyond defining aortic size alone, may assist in clinical risk stratification where conventional 2D measurements are not significantly different.

The clinical challenge with aortic disease is the lack of reliable imaging data to predict adverse events such as development of aneurysm and/or rupture. Our findings indicate that patients with increased regional aortic pressure may be predisposed to progressive dilatation, and therefore may require more frequent surveillance.

4D flow MRI has been proposed as a potential important and novel method to map aortic wall shear stress in patients with BAV. Our results correspond to these studies which demonstrated elevated wall shear stress at the proximal and mid-ascending aorta in RL-BAV patients [14, 15, 16]. We conclude that our method of CFD modelling has advantages over 4D flow MRI as it involves less intensive data acquisition, which may make it more feasible to include in the clinical setting. Although 4D flow will have more optimal spatio-temporal resolution, the acquisition of such data can add 5-15 minutes to the scan time i.e. in our current protocol increasing scan times by up to 50%. We demonstrate that it is possible to describe regional aortic pressure with boundary conditions based on 2D CMRI, where parameters were acquired with only three single breath-holds of 10-15 seconds. Furthermore, post-processing using our methodology results in reduced analysis time compared with 4D flow, allowing improved efficiencies, more likely enabling clinicians to utilize these pressure data sets in conjunction with standard structural parameters.

There are a number of limitations to this study. The measurements are dependent on the systolic pressure, which has been obtained from brachial pressure, which only indirectly relates to central aortic pressure. The small numbers of patients in this pilot study may predispose to type 2 error and need to be confirmed in a larger patient cohort. Furthermore, the clinical utility of measuring regional aortic pressure has yet to be determined and further studies assessing the impact of pressure on patient outcomes need to be performed.

5. Conclusion

This study demonstrates that it is possible to derive regional aortic pressure measurements from 2D MRI techniques using a CFD approach. This data is relatively straightforward to acquire and may have implications for aortic disease pathogenesis and monitoring. Further investigation in a larger cohort and across a spectrum of conditions is required.

Conflicts of Interest

The authors declare that they have no competing interests.

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