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Systolic fluid-structure interaction model of the congenitally bicuspid aortic valve: assessment of modelling requirements.

A transient fluid-structure interaction model of a congenitally bicuspid aortic valve has been developed which allows simultaneous calculation of fluid flow and structural deformation. The valve is modelled during the systolic phase (the stage when blood pressure is elevated within the heart to pump blood to the body). The geometry was simplified to represent the bicuspid aortic valve in two dimensions. A congenital bicuspid valve is compared within the aortic root only and within the aortic arch. Symmetric and asymmetric cusps were simulated, along with differences in mechanical properties. A moving Arbitrary Lagrange-Euler mesh was used to allow fluid-structure interaction. The fluid-structure interaction model requires blood flow to induce valve opening and induced strains in the region of 10%. It was determined that bicuspid aortic valve simulations required the inclusion of the ascending aorta and aortic arch. The flow patterns developed were sensitive to cusp asymmetry and differences in mechanical properties. Stiffening of the valve amplified peak velocities, and recirculation which developed in the ascending aorta. Model predictions demonstrate the need to take into account the category, including any existing cusp asymmetry, of a congenital bicuspid aortic valve when simulating its fluid flow and mechanics.

Keywords: Bicuspid aortic valve, Congenital malformation, Fluid-Structure Interaction, Multi-physics modelling.

1. Introduction

The aim of this study was to simulate a type 0 (i.e. pure) congenitally malformed bicuspid aortic valve. The sensitivity of model predictions to symmetric and asymmetric cusps and to differences in mechanical properties were investigated. As the physical mechanism leading valve deformation is fluid flow (Bellhouse, 1972; Caro *et al*., 1978), a simultaneous and transient fluid-structure interaction (FSI) simulation was performed. A finite element (FE) method was used for simulations, including solution of computational fluid dynamics (CFD). We have previously used this method to investigate mitral valve mechanics (Al-Atabi *et al*., 2010; Espino *et al*., 2014).

The aortic valve is the semi-lunar, tricuspid, valve in the aorta that enables flow to the body during left ventricular systolic contraction. The valve opens during left ventricular systole to allow flow through the aorta. In up to 2% of the population the aortic, tricuspid, valve is congenitally malformed having only two cusps (rather than three) termed a bicuspid aortic valve (Roberts, 1970). Bicuspid aortic valves have associated problems such as a dilated aortic root, aortic dissection, stenosis, regurgitation and patients are at an increased risk of infection (Siu & Silversides, 2010).

The bicuspid aortic valve can be categorised as type 0, I or II (Sievers & Schmidtke, 2007). Type 0 refers to a pure bicuspid aortic valve which is composed of two distinctive cusps (figure 1). Types I and II refer to a valve in which three cusps can be distinguished but at least two cusps are joined together to form the bicuspid valve.

Simultaneous FSI solutions are well suited to heart valve modelling as instabilities may occur using iterative approaches (Peskin, 1972 & 1977). Briefly, simultaneous FSI simulations calculate the reaction force that the fluid exerts on the

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structure at the shared boundaries (Dowell & Hall, 2001; Wall *et al*., 2006; Van de Vosse *et al*., 2003). Simultaneous coupling is achieved by constraining the fluid velocity to be equivalent to the structural time-dependent deformation (Dowell & Hall, 2001; Wall *et al*., 2006; Van de Vosse *et al*., 2003). A moving Arbitrary-Lagrange-Euler (ALE) mesh enables both FE and CFD analysis (Donea *et al*., 1982; Formaggia & Nobile, 1999).

Several FSI aortic heart valve models have been developed (De Hart *et al*., 2000 & 2003). However, few computational models have investigated the bicuspid aortic valve (Robiseck *et al*., 2004; Viscardi *et al*., 2010; Weinberg & Kaazempur-Mofrad, 2008). Such studies have investigated flow through the aortic root (Weinberg & Kaazempur-Mofrad, 2008) or the aortic arch (Robiseck *et al*., 2004; Viscardi *et al*., 2010). However, FSI analysis of the bicuspid aortic valve is limited (Weinberg & Kaazempur-Mofrad, 2008). Computational models of the congenitally bicuspid aortic valve have not so far considered how differences in cusp length or mechanical properties might alter blood flow within a type 0 bicuspid aortic valve. Neither is it clear whether it is necessary to simulate the ascending aorta and aortic arch or whether simulating the aortic root suffices (figure 2). Hence, requirements for bicuspid aortic valve FSI modelling are unclear.

A simplified two-dimensional FSI model of the congenitally bicuspid type 0 aortic valve was created to assess the requirements for such models. A symmetric bicuspid valve that included the aortic arch was compared to one with only the aortic root. Subsequently, asymmetric cusps were considered. Finally, changes to cusp mechanical properties were assessed using an asymmetric cusp model. An asymmetric model was assessed for the final set of simulations as cusp length asymmetry has been reported in excised bicuspid aortic valves (Robiseck *et al*., 2004).

2. Methods

2.1 Geometry

The two-dimensional model simulated the cross-section of a type 0 bicuspid aortic valve

with anterior-posterior cusp alignment (see Sievers & Schmidtke, 2007). Such a type 0

bicuspid valve has an anterior or coronary cusp and a posterior or non-coronary cusp

(figure 2). Two symmetric cusp models of the bicuspid valve within the aorta were

simulated: (i) an aortic arch model, which included the ascending aorta, aortic arch, and

descending thoracic aorta and (ii) an aortic root model, which only modelled the aortic

root. Subsequently, two further models were simulated with asymmetric cusps: (iii) a

longer coronary cusp model and (iv) a longer non-coronary cusp model. Finally the

longer coronary cusp model was simulated with stiffened cusps (section 2.2) leading to a:

(v) stiffer non-coronary cusp model, (vi) stiffer coronary cusp model and (vii) stiffer

cusps model. Dimensions are defined in figure 3 and provided for all models in table 1.

The geometry used was based on published computational models (De Hart *et al*., 2003),

clinical measurements (Hager *et al*., 2002) and established literature (Levick, 1995).

2.2 Material properties

Cusps were considered to be isotropic, homogenous and to have a linear stress-strain

relationship (De Hart *et al*., 2000). Fluid properties assumed blood to be an

incompressible and Newtonian fluid; a valid assumption under large scale flow (Caro *et

al*., 1978). Blood was modelled with a density of 1000 kg/m^{-3} and viscosity of 4.3×10^{-3}

Pa s (De Hart *et al*., 2000). Cusp material properties (table 2) for initial models were

obtained from the literature (De Hart *et al*., 2000). Cusp stiffening was then simulated

(see section 2.1), this used an asymmetric model in which the coronary cusp was longer than the non-coronary cusp (table 2) because it approximated the asymmetry measured from excised valves (Robiseck *et al*., 2004). Models with either a stiffer non-coronary (model v; section 2.1) or coronary cusp (vi) were simulated along with a stiffer cusp model (vii) in which both cusps were stiffened (table 2). Stiffer non-coronary (v) and coronary (vi) cusp models simulated asymmetry in cusp material properties as it is not known whether these properties are similar or not. The Young's modulus of one cusp was doubled for these models (table 2) to assess the impact of such mechanical asymmetry on the model results. The stiffer cusps model (vii) simulated excess stiffening of both cusps, as might occur due to calcification or ageing. In the stiffer cusps model, the Young's modulus of both cusps was increased (to 5 MPa; table 2).

2.3 Boundary conditions

Boundary conditions for the fluid (figure 4) were set so as to approximate a physiological blood flow rate of 5 L/min and systolic timing (Levick, 1995). An inlet velocity, v_{in}, was applied perpendicular to the aortic inlet boundary (equation 1).

$$v_{in} = v_p \left(\frac{t}{T} \right) \qquad 1$$

where v_p, t and T refer to the peak velocity (0.175 m/s) parallel to the *y*-axis, time, and total solution time (0.3 s), respectively. The *x*- and *y*-axis define two orthogonal axes of a Cartesian coordinate system, in which the latter is perpendicular and the former parallel to inflow boundary of the aorta (figure 3).

Pressure was applied downstream from the aortic valve in all models. A time-dependent pressure, *P*, was applied at outflow boundaries (equation 2) to approximate

blood pressure in the aorta (Levick, 1995). For aortic arch models, this included the descending thoracic aorta and branching arteries, whereas for the aortic root model this condition was applied at the outflow of the aortic root (figure 4). The walls of the aorta were simulated using a no-slip wall conditions (i.e. 0 m/s).

$$P = P_o + P_p \left(\frac{t}{T}\right) \qquad 2$$

where P_o and P_p refer to initial pressure (80 mmHg; i.e. 10.7 kPa) and peak pressure rise (40 mmHg; i.e. 5.3 kPa), respectively.

Fluid at boundaries shared by a cusp and blood had constraints applied to ensure simultaneous fluid-structure interaction (see section 2.4). For the fluid, a velocity equivalent to that of the moving structure (i.e. that of the valve cusp) was applied according to equation 3.

$$u = \frac{dx}{dt}, \qquad v = \frac{dy}{dt} \qquad 3$$

where u, and v refer to x- and y-axis velocities, respectively.

Valve cusps were restricted from moving at their attachment to the aortic wall (figure 4b). The only forces acting on valve cusps were those induced by fluid dynamics. These forces were applied at boundaries shared by a cusp and blood (see section 2.4).

2.4 Solving Fluid-Structure Interaction

The constraints that couple simultaneous solution of fluid and structure, and their interaction have been explained previously (Espino *et al*., 2014). Briefly, the velocity constraint defined by equation 3 coupled fluid flow to structural changes. Similarly, equal and opposite reaction forces from the fluid on the structure ensured a two-way coupling. Fluid dynamics were solved using the continuity and incompressible Navier-Stokes

equations, assuming Newtonian flow, using a full stress tensor (Gunzburger, 1996). Anisotropic streamline diffusion (tuning parameter of 0.5) was applied. This stabilises the calculated results without the need for mesh refinement, and is applied along the streamlines (i.e. anisotropic application, as it is applied parallel but not perpendicular to the streamlines; Turek, 1999).

A moving Arbitrary Lagrange Euler (ALE) mesh was applied to boundaries shared by the valve cusps and blood. This enabled the mesh to follow cusp structural changes. No re-meshing was used but Winslow smoothing was applied to improve the resultant mesh. This mesh smoothing method optimizes uniform node spacing for quadratic elements in unstructured meshes (Winslow, 1966), such as those used in this study. The mesh used for the aortic arch and aortic root models are shown in figure 4; mesh details for all models are provided in table 3.

2.5 Analysis

The FE analysis package Comsol Multi-physics (v4.2, Comsol Ltd, Cambridge, UK), including the structural mechanics package, was used to solve the FSI model as reported previously (Espino *et al*., 2014). A PARDISO solver was used with free time-stepping; further details on time stepping are available elsewhere (Espino *et al*., 2013).

3. Results

3.1 Symmetric cusps within the aortic arch or aortic root

Peak stresses were predicted on the cusps towards their restrained base and lowest stresses towards their free edges (figures 5-7). Peak von Mises cusp stresses were in the region of 400 kPa (table 4, 5). Although the stresses predicted were of a similar order of magnitude, those predicted by the aortic arch model were generally greater than those predicted by the aortic root model (tables 4, 5; figures 5-7). For example, peak von Mises stress was greater by 35 kPa, peak *x*- and *y*-axis Cauchy stresses by 57 kPa and 42 kPa, respectively.

Greatest cusp deflection occurred at cusp free edges; however, the two cusps deformed more symmetrically in the aortic root model (figure 7). Similar strain values were predicted for both models, with peak strains of 9% (tables 4, 5).

Similar peak pressures and velocities were predicted by both models (tables 6, 7). For example, peak *y*-axis velocity was of the order of 0.75 m/s and 0.76 m/s for the aortic arch and aortic root models, respectively. The main difference in flow predictions included higher peak vorticity (the curl of the velocity field; Granger, 1985) predicted by the aortic arch model (602 s^{-1} compared to 494 s^{-1} for the aortic root model; tables 6, 7). The aortic arch model predicted recirculation in the ascending thoracic aorta, away from the aortic root (figure 5), a prediction not possible with the aortic root model.

3.2 Geometrically asymmetric cusps in an aortic arch

Stress distributions were not altered by geometric asymmetry with peak stresses predicted towards the base of cusps and lowest stresses towards their free edges (figures 8a, 8b, 9a,

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9b). The type of geometrical asymmetry determined whether stresses increased or decreased in the model when compared with the predictions of the symmetric model (table 4). The longer coronary cusp model experienced lower stresses than the symmetric (aortic arch) model, with peak von Mises, x- and y-axis Cauchy stresses being lower by 69 kPa, 106 kPa and 37 kPa, respectively (table 8). However, the longer non-coronary cusp model experienced higher stresses compared to the symmetric aortic arch model, with peak von Mises, x- and y-axis Cauchy stresses increasing by 78 kPa, 126 kPa, and 101 kPa, respectively (table 8).

The longer cusp underwent greater deflection than the shorter cusp in both asymmetric models (figures 9a, 9b). In the longer coronary cusp model such deflection led to a peak strain of 15% (table 8), this was greater than the peak strain predicted by the symmetric model (table 4). However, the longer non-coronary cusp model had a peak strain of 10% (table 8) comparable to the symmetric model peak strain (table 4).

Predicted flow parameters for asymmetric models (figures 8a, 8b; table 9) followed similar trends to the symmetric model (figure 5; table 6). However, the peak y-axis velocity increased by 0.11 m/s. Moreover, recirculation predicted at the ascending thoracic aorta was more pronounced in the longer coronary cusp model (figure 8a) but less pronounced in the longer non-coronary cusp model (figure 8b) as compared to the symmetric model (figure 5b). This might be partly a result of flow being better aligned with the y-axis in the longer non-coronary cusp model (figures 8a, 8b). Vorticity, at 0.3 s, increased in both asymmetric models as compared to the symmetric model (293 s^{-1}; table 6). However, vorticity was greater in the longer non-coronary cusp model (1043 s^{-1}) than in the longer coronary cusp model (385 s^{-1}; table 9).

3.3 Altered mechanical property models

Peak stresses for all stiffened models were located towards the restrained cusp base, with lowest stresses towards their free edges (figures 8c-e and 9c-e). In the stiffer cusps model, higher stresses went up to the mid-length of the cusp. Von Misses stress increased in all stiffened models as compared to the longer coronary cusp model (table 8). The greatest increase was the stress in the stiffer cusps model, increasing by 85 kPa. Cauchy stresses were greater for all models, when compared to the values for the longer coronary cusp model. For example, the stiffer cusps model experienced the highest x-axis Cauchy stress, increasing by 176 kPa. The stiffer non-coronary cusp model experienced the highest y-axis Cauchy stress, and x- and y-axis Cauchy stresses increasing by 94 kPa and 79 kPa, respectively.

The stiffer non-coronary cusp model predicted greater asymmetric deformation (figure 9c) than the longer coronary cusp model (figure 9a). The stiffer coronary cusp model rebalanced such asymmetric deformation (instead resembling the longer non-coronary cusp model; figures 9a, 9b, 9d) and experienced lower stresses than the stiffer non-coronary cusp model (figure 9c) and the stiffer cusps model (figure 9e). The stiffer non-coronary cusp and stiffer coronary cusp models experienced similar peak strains of around 8%, lower than the longer coronary cusp model strain of 15% (table 8). The stiffer cusps model underwent lower deformation with peak strain of 4%.

Predicted flow parameters (figures 8c-e; table 9) followed similar trends to the longer coronary cusp model (figure 8a; table 6). In all stiffened models, peak velocities increased, with the stiffer cusps model predicting highest velocities. For example, peak y-axis velocity in the stiffer cusps model increased to 1.25 m/s, compared to 0.86 m/s for

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the longer coronary cusp model (table 9). Vorticity increased in all models when compared to the longer coronary cusp model at 0.3 s (385 s^{-1}). The stiffer cusps model predicted the highest vorticity (969 s^{-1}).

The stiffer non-coronary cusp model predicted recirculation which extended up to the carotid arteries with a central jet of flow that was less centred along the ascending thoracic aorta (figure 8c) than the longer coronary cusp model. This recirculation appeared to interfere with the flow out of the ascending thoracic aorta (figure 8c). The stiffer coronary cusp model, however, experienced similar flow to the longer coronary cusp model (figure 8a, 8d).

In the stiffer cusps model, a region of high velocity blood flow appeared to reach the carotid arteries, with recirculation at the aortic arch (figure 8e). Such recirculation, along with the wall of the aorta, appeared to redirect blood flow in an opposing direction to the large recirculation established in the longer coronary cusp model (figure 8a). The result was a greater change in the blood flow trajectory than that of the longer coronary cusp model (figures 8a, 8e), consistent with the increased vorticity in the stiffer cusps model (table 9).

4. Discussion

4.1 Study findings

A transient, simultaneous, FSI model of a type 0 congenital bicuspid aortic valve (i.e. pure bicuspid aortic valve) with an anterior-posterior cusp alignment has been simulated during the systolic ejection phase. This study has led to the following findings:

- in order to predict flow and cusp deformation for the bicuspid aortic valve, it is necessary to simulate the aortic arch;

- resultant haemodynamics are sensitive to type of the geometrical cusp asymmetry of a pure bicuspid aortic valve;

- mechanically asymmetry bicuspid aortic valve cusps can either amplify, or attenuate, flow effects induced by geometrical asymmetry depending on which cusp is stiffer;

- stiffening of valve cusps increases the velocity through the aortic root, and amplifies detrimental haemodynamics, predisposing the aorta to unsteady flow downstream from the aortic root;

- stiffening of valve cusps reduces the strain but increases stresses experienced.

Limited experimental results are available to enable extensive model validation. However, our model results are in general agreement with available experimental results and computational models. Our longer coronary cusp model results are in agreement with the findings by Robiseck *et al*. (2004), who combined CFD results with an experimental model of a bicuspid aortic valve. The comparison is fair because in their study all three excised valve cusps had an equivalent cusp asymmetric. Our flow predictions are also consistent with available flow predictions from CFD studies (Robiseck *et al*., 2004;

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Viscardi *et al*., 2010). Therefore, model predictions are in agreement with available results, and conclusions obtained using our model are likely reliable (further discussion follows below).

Our findings demonstrate that when an aortic arch is included in simulations of a bicuspid aortic valve, changes to haemodynamics are more pronounced as compared to an aortic root model. Our simulations predict recirculation in the ascending aorta, with peak flow towards the free edge of valve cusps. Our flow predictions are similar to previous CFD studies that predicted similar areas of recirculation along the ascending thoracic aorta, away from the aortic sinuses (Robiseck *et al*., 2004; Viscardi *et al*., 2010). Such recirculation cannot be predicted by an aortic root model alone.

Robiseck *et al*. (2004) found valve cusps to be asymmetric in all three bicuspid aortic valves measured, subsequently modelling asymmetric models with a longer coronary cusp. Our study predicted that recirculation in the ascending aorta was either amplified or attenuated depending on which cusp was longer. Our longer coronary cusp model is in agreement with the findings by Robiseck *et al*. (2004). However, our longer non-coronary cusp model attenuated the recirculation induced by an equal cusp length model. Thus, our findings show that models are sensitive to cusp asymmetry, in particular as regards the flow predicted. Therefore, to understand bicuspid aortic valve mechanics not only must the category be identified (e.g. type 0 with anterior-posterior cusp alignment; Sievers & Schmidtke, 2007) but any cusp asymmetry must be modelled too.

Regardless of category and geometry, mechanical properties of cusps alter haemodynamics. This is important because collagen-reinforced tissues stiffen (Goh *et al*., 2008) with age, including heart valve tissues (Millard *et al*., 2011). The increased age-

related stiffness is likely attributable to age-related collagen cross-linking and structural changes in collagen fibres (Balguid *et al*., 2008; Goh *et al*., 2007 & 2012). Predictions from our simulations suggest that such age-related increased stiffness would increase stenosis, thereby: (i) increasing peak velocity through the aortic root which could predispose the aorta to unsteady flow downstream from the aortic root; (ii) reducing strain but increasing leaflet stress. However, our FSI results demonstrated that large scale flow effects were sensitive to differences in the mechanical properties of the two cusps. When the coronary cusp was stiffer recirculation was attenuated but when the non-coronary cusp was stiffened it was amplified. Unfortunately, differences in mechanical properties of cusps are not known, but models must account for this.

Robiseck *et al*. (2004) suggested that increased turbulence might cause fibrosis and calcification of bicuspid aortic valves. It is feasible, for example, that deposits are not washed from away from cusps in bicuspid aortic valve which could aid calcification. Calcification is associated with valve stiffening and subsequent stenosis (Schoen, 2005). In our model, equal stiffening of both cusps amplified turbulent flow. If turbulence does stiffen valves, further stiffening would induce greater turbulence, leading to a cycle of deterioration for both valve mechanics and haemodynamics. In our model, stiffer cusps experienced increased stresses but reduced strains. Excessive stress concentrations could damage the valve. It is difficult to compare such cusp stress findings with results from previous numerical studies that modelled the aortic arch and a bicuspid aortic valve (Robiseck *et al*., 2004; Viscardi *et al*., 2010). Such studies used CFD to predicted wall shear stresses on valve cusps, but predicted stresses do not account for cusp deformation which alters cusp stress. Moreover, a multi-scale FSI model of a bicuspid aortic valve

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(Weinberg & Kaazempur Mofrad, 2008) did not include the aortic arch. Therefore, changes are expected to the haemodynamics that subsequently load the valve, making comparison with our current study difficult. However, such multi-scale models may be a necessity in order to better understand the effects of fibrosis and/or calcification on valve mechanics.

Expansion of our current model requires three dimensional modelling of types 0, I and II. From this current study it is clear that flow predictions, in particular, will be sensitive to cusp asymmetry and differences in mechanical properties. The presence of an aortic arch is important as recirculation occurs outside the aortic root, but this also alters valve cusp loading.

The inclusion of an aortic arch in models may have a wider significance. Such models enable predictions of wall shear stresses along the aortic wall (Robiseck *et al*., 2004; Viscardi *et al*., 2010). This is important for bicuspid aortic valves due to the associated weakening of the aortic wall (Bauer *et al*., 2006). It is also feasible that the increased risk of infection associated with bicuspid aortic valves (Lamas & Eykyn, 2000) could be related to changes in haemodynamics or increased mechanical stress. For example, recirculation away from the aortic root could lead to blood which does not flow adequately through the aorta or may even stagnate. Regions where blood-flow is stagnant and/or turbulent could allow thrombus formation that encourages bacterial growth (Thiene & Basso, 2006). Such stagnant/turbulent flow could also impede immune cells from reaching sites of infection. Note, immune response has been implicated in degeneration of bicuspid aortic valves (Wallby *et al*., 2002). Alternatively, high stress

could damage a valve's endothelium and lead to platelet deposition (Thiene & Basso, 2006), enabling bacterial growth and calcification (Butcher & Nerem, 2007).

4.2 Limitations

A limitation in this study is the use of a two-dimensional model of the valve cross-section, to model a three-dimensional structure. However, two-dimensional FSI aortic valve models have been found to make predictions of systolic flow, such as cardiac output and stroke volume, only ≤15% lower than Doppler-derived flow measurements made clinically (Bahraseman *et al*., 2014a). Moreover, all predicted trends from the two-dimensional model were consistent with those derived from clinical measurements. The offset was reduced (≤11%) when comparing parameters such as peak velocity (Bahraseman *et al*., 2014a); furthermore, hydrodynamic predictions were consistent with wider literature (Bahraseman *et al*., 2014b). Predictions, including leaflet stress and strain, were also consistent with predictions from a corresponding three-dimensional FSI model (Bahraseman *et al*., 2013).

Using two-dimensional FSI models of the mitral valve, with its anatomically intricate three-dimensional geometry (Al-Atabi *et al*., 2012), we have found flow predictions to be consistent with experimental measurements (Al-Atabi *et al*., 2010). Peak stresses were also consistent with the range predicted through three-dimensional models and the predicted peak strain of 12.6% (Espino *et al*., 2014) compared to 14% peak strain measured experimentally (Chen *et al*., 2004).

Therefore, while the use of a two dimensional model may introduce limitations, the evidence is that two dimensional FSI heart valve model predictions are reliable.

Furthermore, the limitations introduced by using a two-dimensional model do not alter the conclusions from this study.

5. Conclusion

Haemodynamic predictions of FSI bicuspid aortic valve models are sensitive to the inclusion of the aortic arch, valve geometry (including any cusp asymmetry), and differences in cusp mechanical properties. The ascending aorta and aortic arch are necessary due to the recirculation induced away from the aortic root by bicuspid aortic valves. Both cusp geometrical asymmetry, and/or differences in mechanical properties, can either attenuate or amplify such recirculation, depending on which cusp is either longer or stiffer than the other.

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TABLES

Table 1. Dimensions of bicuspid aortic valve models (also see figure 3).

Model name	Aortic arch	Cusp symmetry	R_a (mm)	D_s (mm)	H_s (mm)	L_c (mm)	L_n (mm)	H_c (mm)	R_b (mm)	R_d (mm)
Aortic Arch	Yes	Yes	12.5	6	21	13.5	13.5	6	2	12.5
Aortic Root	No	Yes	12.5	6	21	13.5	13.5	6	n/a	n/a
Longer coronary cusp	Yes	No	12.5	6	21	14.5	12.5	6	2	12.5
Longer non-coronary cusp	Yes	No	12.5	6	21	12.4	15.0	6	2	12.5
Stiffer non-coronary cusp	Yes	No	12.5	6	21	14.5	12.5	6	2	12.5
Stiffer coronary cusp	Yes	No	12.5	6	21	14.5	12.5	6	2	12.5
Stiffer cusps	Yes	No	12.5	6	21	14.5	12.5	6	2	12.5

R_a, Aortic radius;
D_s, Sinus depth;
H_s, Sinus height;
L_c, Coronary cusp arc length;
L_n, Non-coronary cusp arc length;
H_c, Cusp height;
R_b, branching arteries radii;
R_d, descending thoracic aorta radius;
n/a, not applicable.

Table 2. Material properties of bicuspid aortic valve models.

Model name	Aortic arch	Cusp symmetry	E_c (MPa)	E_n (MPa)	Poisson's ratio
Aortic Arch	Yes	Yes	1.5	1.5	0.49
Aortic Root	No	Yes	1.5	1.5	0.49
Longer coronary cusp	Yes	No	1.5	1.5	0.49
Longer non-coronary cusp	Yes	No	1.5	1.5	0.49
Stiffer non-coronary cusp	Yes	No	1.5	3.0	0.49
Stiffer coronary cusp	Yes	No	3.0	1.5	0.49
Stiffer cusps	Yes	No	5.0	5.0	0.49

E_c, Coronary cusp Young's modulus;
E_n, Non-coronary cusp Young's modulus.

Table 3. Mesh and solver settings.

Model name	Total degrees of freedom solved	Number of Elements	Lagrange element type	BDF Maximum
Aortic Arch	7384	2325	Quadratic	5
Aortic Root	6241	1927	Quadratic	4
Longer coronary cusp	7262	2291	Quadratic	4
Longer non-coronary cusp	7185	2265	Quadratic	4
Stiffer non-coronary cusp	7162	2252	Quadratic	3
Stiffer coronary cusp	7162	2252	Quadratic	3
Stiffer cusps	7162	2252	Quadratic	5

BDF: backward differentiation formula; see Heath (1997).

Table 4. Maximum and minimum values for stress and strain under a given loading pressure, per time step for symmetric cusp aortic arch model.

Time (s)		von Mises stress (kPa)	Cauchy stress (kPa)		Green strain	
			σ_x	σ_y	ε_x	ε_y
0.1	max	64	84	47	0.03	0.03
	min	0	-88	-59	-0.03	-0.03
0.2	max	151	230	114	0.06	0.06
	min	4	-143	-92	-0.06	-0.06
0.3	max	278	438	266	0.09	0.09
	min	3	-186	-113	-0.08	-0.08

Table 5. Maximum and minimum values for stress and strain under a given loading pressure, per time step for symmetric cusp aortic root model.

Time (s)		von Mises Stress (kPa)	Cauchy stress (kPa)		Green strain	
			σ_x	σ_y	ε_x	ε_y
0.1	max	62	81	45	0.03	0.03
	min	0	-86	-58	-0.03	-0.03
0.2	max	140	213	10	0.06	0.06
	min	1	-137	-88	-0.06	-0.05
0.3	max	243	381	224	0.08	0.08
	min	6	-177	-108	-0.08	-0.07

Table 6. Maximum and minimum values for flow parameters for symmetric cusp aortic

arch model.

time (s)		Pressure (kPa)	x-velocity (m/s)	y-velocity (m/s)	velocity field (m/s)	Vorticity (1/s)
0.1	max	12.6	0.13	0.48	0.48	602
	min	12.4	-0.12	-0.05	0.00	0
0.2	max	14.4	0.21	0.64	0.64	342
	min	14.2	-0.20	-0.10	0.00	0
0.3	max	16.3	0.27	0.75	0.75	293
	min	15.9	-0.24	-0.14	0.00	0

Table 7. Maximum and minimum values for flow parameters for symmetric cusp aortic

root model.

time (s)		Pressure (kPa)	x-velocity (m/s)	y-velocity (m/s)	velocity field (m/s)	Vorticity (1/s)
0.1	max	12.6	0.12	0.45	0.45	494
	min	12.4	-0.12	-0.03	0.00	0
0.2	max	14.4	0.20	0.66	0.66	366
	min	14.2	-0.19	-0.05	0.00	0
0.3	max	16.3	0.24	0.76	0.76	297
	min	16.0	-0.23	-0.06	0.00	0

Table 8. Maximum values for stress and strain at 0.3 s for asymmetric cusp models with

an aortic arch.

Model name	von Mises Stress (kPa)	Cauchy stress (kPa)		Green strain	
		σ_x	σ_y	ε_x	ε_y
Longer coronary cusp	209	332	229	0.15	0.07
Longer non-coronary cusp	356	564	367	0.10	0.10
Stiffer non-coronary cusp	264	426	308	0.08	0.08
Stiffer coronary cusp	255	401	241	0.08	0.08
Stiffer cusps	296	508	286	0.04	0.04

Table 9. Maximum values for flow parameters at 0.3 s for asymmetric cusp models with

an aortic arch.

Model name	Pressure (kPa)	*x*-velocity (m/s)	*y*-velocity (m/s)	velocity field (m/s)	Vorticity (1/s)
Longer coronary cusp	16.3	0.30	0.86	0.86	385
Longer non-coronary cusp	16.3	0.35	0.86	0.86	1043
Stiffer non-coronary cusp	16.4	0.32	0.98	0.99	700
Stiffer coronary cusp	16.4	0.35	0.95	0.96	548
Stiffer cusps	16.7	0.37	1.25	1.25	969

FIGURES

Figure 1. Aortic valve cusps. (a) Tricuspid aortic valve, (b) Congenitally malformed bicuspid aortic valve (type 0, anterior-posterior bicuspid aortic valve). CC: Coronary cusp, NCC: Non-coronary cusp, LCC: Left coronary cusp, RCC: Right Coronary cusp. The two small circles represent the left and right coronary arteries.

Figure 2. Congenitally bicuspid aortic valve, including the ascending thoracic aorta (AT), aortic arch (AA) and descending thoracic aorta (DT). Also labelled is the aortic root (AR) including the sinus of the Valsalva (SV; also referred to as aortic sinus), the coronary cusp (CC) and non-coronary cusp (NCC).

Figure 3. Geometry of the pure bicuspid aortic valve including the ascending aorta, aortic arch and descending thoracic aorta. D_s denotes the sinus depth, H_c and H_s denote the starting cusp and sinus height respectively (also see figure 2), L_c and L_n denote the coronary (or anterior) and non-coronary (or posterior) cusp arc length respectively, and R_a, R_b, and R_d define radii of the aorta, branching arteries, and descending thoracic aorta, respectively.

Figure 4. Mesh and external boundary conditions applied to bicuspid aortic valve models of (a) aortic arch and (b) aortic root models. The hydrodynamic boundary conditions applied were the inlet velocity, v_{in}, (equation 1) and the outflow pressure, P, (equation 2).

Cusps were constrained at their aortic wall attachment (labelled *fixed* on the aortic root model).

Figure 5. Aortic arch model flow patterns (red lines), velocity field and valve cusp stress at (a) 0.1 s and (b) 0.3 s. Scale bars represent cusp stress (Pa) and blood velocity field (m/s), respectively. Note, maximum (above) and minimum (below) values are shown with scale bars.

Figure 6. Aortic root model flow patterns (red lines), velocity field and valve cusp stress at (a) 0.1 s and (b) 0.3 s. Scale bars represent cusp stress (Pa) and blood velocity field (m/s), respectively. Note, maximum (above) and minimum (below) values are shown with scale bars.

Figure 7. Deformation and cusp stress (Pa) at 0.3 s for models of the aortic (a) arch and (b) root. Note, maximum (above) and minimum (below) values are shown with scale bars.

Figure 8. Flow patterns (red lines), velocity field and valve cusp stress at 0.3 s for asymmetric valve models. (a) longer coronary cusp, (b) longer non-coronary cusp, (c) stiffer non-coronary cusp, (d) stiffer coronary cusp, and (e) stiffer cusps models. Scale bars represent cusp stress (Pa) and blood velocity field (m/s), respectively. Note, maximum (above) and minimum (below) values are shown with scale bars.

Figure 9. Deformation and cusp stress (Pa) at 0.3 s for asymmetric valve models. (a) longer coronary cusp, (b) longer non-coronary cusp, (c) stiffer non-coronary cusp, (d) stiffer coronary cusp, and (e) stiffer cusps models. Note, maximum (above) and minimum (below) values are shown with scale bars.