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Original article

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ABSTRACT

A computational fluid dynamics model of a bicuspid aortic valve has been developed using idealised three-dimensional geometry. The aim was to compare how orifice area and leaflet orientation affect the hemodynamics of a pure bicuspid valve. By applying physiologic material properties and boundary conditions, blood flow shear stresses were predicted during peak systole. A reduced orifice area altered blood velocity, the pressure drop across the valve, and the wall shear stress through the valve. Bicuspid models predicted impaired blood flow similar to a stenotic valve, but flow patterns were specific to leaflet orientation. Flow patterns developed in bicuspid aortic valves, such as helical flow, were sensitive to cusp orientation. In conclusion, the reduced opening area of a bicuspid aortic valve amplifies any impaired hemodynamics, but cusp orientation determines subsequent flow patterns which may determine the specific regions downstream from the valve most at risk of clinical complications.

Keywords: Bicuspid aortic valve, Computational fluid dynamics, Congenital malformation, Haemodynamics, Hemodynamics.

Introduction

The aortic valve is typically tricuspid, but 0.9% to 2% of the general population have a congenitally malformed bicuspid aortic valve.[1] Bicuspid aortic valves are associated with aortic stenosis, valve regurgitation, aortic dissection, and infective endocarditis.[2] Over 33% of those with bicuspid aortic valves develop serious complications, hence, it may be responsible for more morbidity and mortality than all other congenital heart defects.[3] Although bicuspid aortic valves may go undetected in some throughout their lifetime, interventions such as valve replacement may be necessary.[4] Bicuspid aortic valves have been categorised as type 0, 1 or 2.[5] Type 0 is referred to as "purely bicuspid"; whereas, type 1 and 2 have three differentiable cusps but with one or two fusions (i.e. raphes) between cusps, respectively.

The bicuspid aortic valve does not open fully, narrowing the valve morphologically,[6] it is stenotic and leads to high stresses in the valve.[7,8] The result is a rapid jet flow through the bicuspid aortic valve and high wall shear stress. Impaired hemodynamics may accelerate cusp calcification which would progressively increase aortic stenosis.[9] Whereas, aortic dilatation and aneurysm may result from high wall shear stress caused by asymmetric blood flow impacting on the aortic wall.[10-12] However, it is unclear

whether cusp orientation is important, or if stenotic opening area alone is responsible for impaired systolic hemodynamics.

Despite type 1 being the most common type of bicuspid aortic valve,[5] a pure bicuspid valve offers a unique physiological model. It is composed of two distinct cusps and is sub-classified according to cusp orientation as either anterior-posterior or lateral. Therefore, the main variable between these two clinically relevant sub-classifications is purely cusp orientation rather than opening area; type 1 and 2 bicuspid aortic valves may have further differences associated with aortic shape.[13] Computational Fluid Dynamics (CFD) could be used to obtain predictions which account for the viscosity of blood, and distinguish between the effects of fluid flow related to leaflet orientation, and those related directly to opening area (i.e. stenosis), which is otherwise challenging.[14-16] This could be achieved by comparing CFD models using the exact same conditions with the exception of either cusp orientation or opening area. The predictions made using the CFD model could then be verified against existing measurements to enable the reliability of the predictions to be assessed.

This study aimed to distinguish between the effects of opening orifice area and leaflet orientation on blood flow through a pure bicuspid aortic valve. CFD was used to model flow through bicuspid valves, and a tricuspid valve was modelled to provide a baseline

for comparison. The objectives were, to: (i) examine the effect of stenotic opening orifice area on the blood flow through aortic valve; (ii) determine whether cusp orientation alone (i.e. anterior-posterior and lateral) alters the predicted blood flow in a pure bicuspid aortic valve model; and (iii) compare model predictions from a tricuspid aortic valve to other model predictions and literature.

Methods

Geometry

All models were generated using Solidworks 2013 (Dassault Systemes, Waltham, MA, USA). Dimensions were based on previous bicuspid aortic valve models and included the ascending aorta, aortic arch, branching arteries and descending aorta.[7] All models shared the same idealised aortic root and aorta (Figure 1), with an aortic radius of 12.5 mm, commissural height of 10.5 mm, and 6.0 mm and 21.0 mm in sinus depth and height, respectively.[7,17-19] For simplification, the aortic inlet, ascending aorta, and descending thoracic aorta were assumed to have the same diameter. All three aortic arch branching arteries had a radius of 2 mm.[7] Models focused on the: (i) opening orifice area solely; (ii) bicuspid valve cusp orientation; and (iii) tricuspid valve for baseline comparison.

Two orifice area models were generated, a stenotic valve and a non-stenotic valve model. A nozzle-shaped valve was used, which ignored geometry features of independent cusps, and therefore cusp orientation, focusing solely on the level stenosis. The stenotic valve model was designed to be highly stenotic with an orifice area of 0.4 cm^2, and the non-stenotic valve model had a 1.7 cm^2 orifice area. The latter is equivalent to a mildly- or non-stenotic bicuspid aortic valve.[20]

Two bicuspid valve cusp orientation models were developed, simulating lateral and anterior-posterior pure bicuspid valves (Figure 1). These models were identical except for the cusp rotation, through 90°, about an axis passing through the centre of the valve and parallel to the length of the ascending aorta. An idealised tricuspid aortic valve model was generated to provide a baseline for comparison to the bicuspid aortic valve models. Models which included cusps were set so that these cusps were in a fully open position, simulating the aortic valve at peak systolic phase (Figure 1). Cusp dimensions were based on clinical measurements,[21,22] and other computational models[23] including predictions made through such simulations.[17,24,25] For key dimensions of the fully opened cusps, mean values of cusp free edge length of 27.5 mm and cusp height of 15 mm [21] were used.

Effective orifice area

The orifice area was measured for each modified valve, which were 3.6 cm^2 for the non-stenotic tricuspid model and 1.7 cm^2 for all other models other than a highly stenotic model (0.4 cm^2).[10,11,20] The effective orifice area, which has been used to clinically evaluate aortic stenosis severity, was calculated using Equation 1.[26]

$$A = \frac{F}{44.5 C_d \sqrt{\Delta p}} \qquad \text{Equation 1}$$

where A refers to effective orifice area (cm^2), F is the mean flow rate at peak systole (ml/s), C_d is a discharge coefficient equivalent to 1 in the human aorta,[26] and Δp is the instant pressure drop across the valve (mmHg). The pressure drop is estimated by either the simplified Bernoulli equation (Equation 2) or pressure distribution predicted computationally.

The simplified Bernoulli equation is widely used clinically to estimate transvalvular pressure gradient, with velocity mapping techniques such as Doppler ultrasound.[27] In this study, predicted velocity values were used to calculate an equivalent transvalvular pressure for comparison to clinical data. This was done solely to calculate a pressure gradient across the valve using the same simplified method, as is used clinically, which ignores the effects of blood viscosity in its calculations. Otherwise, this method was not used to predict the pressure of blood.

$$\Delta p = 4v^2 \qquad \text{Equation 2}$$

where v refers to blood flow velocity downstream from the valve in m/s.

Material properties

Blood was modelled as a homogeneous, isothermal, and incompressible Newtonian fluid at 37 ℃, a valid assumption for large geometries such as the aorta.[28,29] Blood flow was then solved by the continuity and Navier–Stokes equations for incompressible

fluids.[30] Blood density of 1.0×10^3 kg/m^3 and viscosity of 4.3×10^{-3} Pa.s were used.[17] The Navier–Stokes equation used ignored the body force term.

Boundary conditions

A combination of mass flow at an inlet and pressure at an outlet were applied along with no-slip wall conditions on rigid wall boundaries simulating valve cusps and the aorta (Figure 1). At the inlet boundary, a transient physiological flow was prescribed to approximate the blood pumped from the ventricle into the aorta.[11] This blood inflow was modelled with a spatially-uniform velocity profile. Linearisation (Equation 3) was used to represent the selected flow rate curve. This simplified the applied, transient, flow rate boundary condition and reduced the model solution time, while still approximating the physiological condition (Figure 2). Volume flow rates were translated into mass flow rate and imported into CFX-Pre (ANSYS INC, Canonsburg PA, USA).

$$Q(t) = \begin{cases} 50 + 2200t, & 0.00 \leq t < 0.15 \\ 785.9 - 2706t, & 0.15 \leq t < 0.32 \\ -400.1 + 1000.25t, & 0.32 \leq t \leq 0.40 \end{cases} \qquad \text{Equation 3}$$

where *Q(t)* is the time-dependent flow rate (cm^3/s) and *t* time (s).

A time-dependent pressure was applied to the outlet boundary, at the descending thoracic aorta and branching arteries (Figure 2), the same outlet pressure was defined for all branches. This simulated an outlet systolic blood pressure.[28]

Mesh & analysis

The geometry was meshed using a patch independent tetrahedron method (Ansys Meshing package, Ansys Inc., Canonsburg, PA, USA). Mesh convergence was performed for all models, with convergence achieved after a variation in peak velocity, pressure and wall shear stress of less than 0.5%. Mesh inflation was applied to the grid near the wall boundaries to enable local mesh refinement for improved boundary layer resolution (Figure 1d). Preliminary models showed that the wall shear stress obtained with the refined mesh increased by more than 30%, compared to those without local refinement. In preliminary models, mesh refinement was used to ensure a variation in wall shear stress of less than 0.5%. Final meshes used for the five different valve geometries ranged from 396,882 to 483,890 elements. The meshed geometry models were imported into Ansys CFX (CFX 14.5, Ansys Inc., Canonsburg, PA, USA). A transient simulation was run for the whole 0.4 s of systole. The advection scheme was set to high resolution for its numerical accuracy, and the transient scheme was set to second order backward Euler for the same reason.

The Reynolds number at the aortic inlet was 4418. This is larger than the suggested critical value of 2300 for Reynolds number during laminar flow.[30,31] The *k-Epsilon* mode with an initialized medium turbulence (intensity of 5%) was, therefore, selected to account for turbulence modelling.

Results

All results are presented at the peak systole (0.15 s), and odel predictions in tables are listed along with published values. The tricuspid valve hemodynamic model predictions for peak velocity, systolic pressure, and systolic transvalvular pressure gradient are within a range of values measured or predicted in the literature (Table 1). This was mostly the case for the shear stress predictions (Table 2), with the wall shear stress on valve cusps and blood viscous shear stress predictions falling within the literature range. However, the range of wall shear stresses on the aortic wall, predicted by our model was 2 Pa above another published study (Table 2).

The blood pressure and velocity predicted were highly sensitive to the opening orifice area. A 76% reduction in the opening orifice led to an increase in peak flow velocity, from 2.64 m/s to 9.66 m/s (Table 1). These values were greater than those for the tricuspid valve model (1.21 m/s). There was a higher transvalvular pressure gradient, measured as the pressure drop through the aortic root, predicted in the stenotic (310 mmHg) than in the non-stenosed valve (11.8 mmHg). A higher pressure near the aortic inlet was also predicted by the stenotic model (Table 1). The peak transvalvular pressure gradient and systolic pressures predicted by the stenosed and non-stenosed models were greater than those predicted by the tricuspid aortic valve model.

A reduced orifice area increased the magnitude of the wall shear stress. Peak values for the stenotic model (380 Pa) were much greater than for the non-stenotic model (27 Pa; Table 2). Likewise, the stenotic model also predicted much greater peak wall shear stresses on the aortic wall (740 Pa) than the non-stenotic model (20 Pa; Table 2). All wall shear stress values predicted were much greater than for the tricuspid valve model (8 Pa).

The peak velocity and peak systolic pressure and the trans-valvular pressure gradient were all higher in the bicuspid valve model than the tricuspid valve (Table 1). Peak velocity increased from 1.21 m/s in the tricuspid model to 3.17 m/s (anterior-posterior cusp orientation) and 3.21 m/s (lateral cusp orientation) in bicuspid models. Peak systolic pressure increased to 142 mmHg in both bicuspid models, compared to the tricuspid model (125 mmHg). The transvalvular pressure gradient increased in bicuspid models (22 mmHg) as compared to the tricuspid model (5 mmHg). Bicuspid models also predicted higher peak velocity and trans-valvular pressure gradient than the non-stenotic model with comparable opening area.

Bicuspid valve cusp orientation led to a minimal change in peak velocity predictions, (1.3% higher peak velocity in the lateral cusp orientation over the anterior-posterior

cusp orientation; Table 1). However, the turbulence which developed, affected distinct regions through the aorta. Unlike the tricuspid model, recirculation vortices in the bicuspid models were not limited to the sinus of the valsalva, but extended downstream (Figure 3). Both bicuspid models predicted a helical flow pattern in the ascending aorta, which was not observed in the tricuspid model (Figure 3d-f). A cross-sectional plane through such helical flow showed that the regions of the wall of the aorta exposed to blood recirculation differed between the anterior-posterior and lateral valve orientations (Figure 3e & 3f).

Wall shear stress was higher in bicuspid than tricuspid models (Table 2). The wall shear stress for the tricuspid model was mostly less than 4 Pa (Figure 4), peaking at 8 Pa on the aortic wall and 7 Pa on the leaflet cusps (Table 2). Bicuspid models, however, had high wall shear stress concentrations on the sinus wall, aortic arch (Figure 4) and valve cusps (Table 2). Valve cusp and aorta wall shear stresses increased to 35 Pa on the anterior-posterior cusp orientation and 50 Pa on the lateral cusp orientation. In the anterior-posterior cusp orientation the peak wall shear stress was comparable to the non-stenotic valve model with an identical opening orifice area (Table 2). Higher peak wall shear stress in the lateral cusp orientation were predicted, located at cusp commissures (Figure 4). Peak wall shear stress was induced at the tip of cusps, for all models, with higher wall shear stress on the ventricular surface. However, the wall shear stress

distribution through the aorta differed between the bicuspid and tricuspid valves as did the distribution between the later and anterior-posterior bicuspid valve orientations (Figure 4).

Discussion

CFD has been used to compare the effect of orifice area on stenosis and the effect of leaflet orientation on bicuspid aortic valve hemodynamics. Our three-dimensional bicuspid aortic valve models predicted blood flow recirculation extending downstream from the aortic root, demonstrating the need to include the aortic arch in such models, consistent with two-dimensional model findings.[7] The bicuspid valve models enabled separation of flow effects related to leaflet orientation to be distinguished from those due to opening area. Reduced opening area amplified impaired hemodynamics as expected, critically though, the effects of cusp orientation could be directly/quantitatively compared.

Compared to the tricuspid valve, a pure bicuspid valve had impaired hemodynamics due to both a reduced orifice area and leaflet orientation associated with its abnormal morphology. Blood velocity, transvalvular pressure and wall shear stress through the aortic valve were all sensitive to the opening orifice area. However, cusp orientation (lateral or anterior-posterior) of a pure bicuspid valve led to distinct flow features such as a helical flow pattern downstream from the valve and altered wall shear stress. For example, a peak wall shear stress of 7 Pa was predicted for the tricuspid valve, consistent with previous studies,[20] which increased in stenotic and bicuspid valve

models. However, for the lateral cusp orientation this value increased to 49 Pa as compared to 35 Pa for anterior-posterior cusp orientation. This is clinically relevant because endothelium may become damaged above 40 Pa.[28,32]

Predictions from orifice area models are consistent with *in vivo* measurements determining the severity of aortic stenosis both clinically[33,34] and through computational models.[35] Moreover, our tricuspid aortic valve model predictions were within known clinical,[14,15] experimental[36,37] and predicted computational[7] ranges from other studies. However, comparison of bicuspid aortic valve model predictions is limited by the available experimental and clinical evidence.

The reduced orifice area models demonstrate the effects of stenosis on hemodynamics. Stenosis is of consequence to patients with a bicuspid aortic valve as it is congenitally narrowed.[5] Reduced orifice area increases the pressure gradient across the valve.[35] Clinically, this leads to an increased transvalvular pressure gradient, used to assess aortic valvular performance. High transvalvular pressure gradient causes an increased left ventricular load which can lead to heart failure.[38] A transvalvular pressure gradient greater than 40 mmHg, or with an orifice area of less than 1.0 cm^2, [39] leads to the classification of severe aortic stenosis.

A stenotic valve causes an increase in wall shear stress experienced by the aortic arch. Our models demonstrated that cusp asymmetry will determine the affected aortic wall region, consistent with previous studies.[16,40] Wall shear stress changes experienced by the endothelium contribute to the local tissue regulation.[27,41,42] Thus, high wall shear stress along the aortic wall could play an important role in subsequent pathophysiology.[2,4,10-12,43,44] Our model predictions lead us to suggest that a reduced opening area magnifies parameters such as wall shear stress, with leaflet orientation determining which regions of the aorta are most at risk. However, in the stenotic model alone, without cusp orientation, a wall shear stress magnitude of 100-200 Pa was predicted along the aortic wall. This wall shear stress may induce endothelial damage.[28,32]

Our model with an effective opening area of 0.4 cm^2 led to peak wall shear stress in valve cusps of 485 Pa. This could lead to valve damage, or cusp calcification which would further increase stenosis.[45,46] However, leaflets undergo large deformation[47] which would alter predictions; hence, fluid-structure interaction may be more appropriate.[48,49,50,51] Regardless, the use of a pure bicuspid valve, in this study, has enabled the differences in predictions to be investigated due purely to valve orientation.

The greater ejection velocity and wall shear stress indicate lower valvular performance from a lateral, relative to the anterior-posterior, bicuspid aortic valve orientation. Consistent with CFD studies suggesting different flow patterns between bicuspid aortic valve categories,[10,11] but such models did not include valve cusps. Our models, however, predicted hemodynamics specific to cusp orientation. This included helical flow through the aorta. MRI studies have also reported abnormal helical systolic flow in the ascending aorta of patients with bicuspid aortic valves.[14,15] Such studies showed a left-handed helical flow in a right-non coronary cusp fusion and a right-handed helical flow in right-left coronary cusp fusion. If a lateral and anterior-posterior pure bicuspid aortic valve are considered as idealised, rapheless, fusions of right-non coronary cusps and right-left coronary cusps, respectively; then, our predictions are qualitatively in agreement with *in vivo* observations. Moreover, such hemodynamic differences highlight the need to further understand the relationship between bicuspid aortic valve category and pathology in patients.[36,37]

Conclusion

Cusp orientations of a pure bicuspid aortic valve, with the same opening orifice area, lead to distinct flow patterns. While effective opening area magnifies unwanted hemodynamic effects, cusp geometry is important in altering the specific regions most at risk, particularly along the ascending aorta.

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FIGURE CAPTIONS

Figure 1. Geometry of the aortic valve models which included cusps. The valve in isolation is shown for the (a) tricuspid valve, (b) lateral pure bicuspid valve, (c) anterior-posterior pure bicuspid valve, and (d) the full geometry including mesh and applied boundary conditions.

Figure 2. Time-dependent boundary conditions. (a) At the valve inlet, a standard inlet flow rate curve (curved, black line) was used,[11] and was approximated with a linearised model (straight, blue line). (b) An outlet pressure was downstream from the valve, based on literature.[28]

Figure 3. Blood flow through the aorta for a: (a) tricuspid, (b) lateral pure bicuspid, and (c) anterior-posterior pure bicuspid valve. The velocity and flow pattern through a cross-section of the ascending aorta is shown for a: (d) tricuspid, (e) lateral pure bicuspid, and (f) anterior-posterior pure bicuspid valve. Note, the flow profile in (d)-(f) are through a plane perpendicular to the long-axis of the ascending aorta.

Figure 4. Wall shear stress through an aorta, with a (a) tricuspid valve, (b) lateral pure bicuspid valve, and (c) anterior-posterior pure bicuspid valve.

TABLES

Table 1. Valvular performance for five aortic valve models.

	Healthy normal value[27,28]	Stenotic	Non-Stenotic	Tricuspid	Bicuspid lateral	Bicuspid anterior-posterior
Peak velocity (m/s)	1.0 - 1.7	9.66	2.64	1.21	3.21	3.17
Peak systolic pressure at aortic inlet (mmHg)	100 - 125	380	146	125	142	142
Peak systolic transvalvular pressure gradient / Valvular Resistance (mmHg)	< 10	310	12	5	22	22

Table 2. Systolic shear stress.

Model	Wall Shear Stress on Cusp (Pa)[20,36,37]	Wall Shear Stress on aortic wall (Pa)[20]	Viscous Shear Stress in blood (Pa)[27]
Stenotic	74-380	0-74	0–380
Non-Stenotic	4-26	0-20	0-26
Tricuspid	2-7	2-8	0-4
Bicuspid, lateral	10-50	10-50	2-8
Bicuspid, anterior-posterior	10-35	5-35	2-8
Normal healthy valve	2-8	0-6	<20