Migration forces of transcatheter aortic valves in patients with noncalcific aortic insufficiency

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Objective: Transcatheter aortic valves have been successfully implanted into the calcified leaflets of patients with severe aortic stenosis. However, their stability in patients with noncalcified aortic insufficiency is unknown. Similar to thoracic and abdominal aortic stent grafts, transcatheter aortic valves are subjected to antegrade ejection forces during systole. However, retrograde migration forces into the left ventricle are also generated by the diastolic pressure gradient across the closed valve. It has been suggested that leaflet calcification anchors the prosthesis, and measurements of migration forces should be considered before clinical trials in noncalcified aortic insufficiency. The objective of this study was to use computational fluid dynamics simulations to quantify forces that could potentially dislodge the prosthesis.

Methods: A computational fluid dynamics model was developed to simulate systolic flow through a geometric mesh of the aortic root and transcatheter aortic valves. Hemodynamic measurements were made at discrete moments during ejection. Unsteady control volume analysis was used for calculations of force on the mesh.

Results: Results of the simulation indicate that a total force of 0.602 N acts on the transcatheter aortic valves during systole, 99% of which is in the direction of axial flow. The largest contributor to force was the dynamic pressure gradient through the transcatheter aortic valves. This antegrade force is approximately 10 times smaller than the retrograde force (6.01 N) on the closed valve during diastole.

Conclusion: Our model simulated systolic flow through a transcatheter aortic valve and demonstrated migration into the left ventricle to be of greater concern than antegrade ejection.

Transcatheter aortic valves (TAVs) represent a minimally invasive treatment for degenerative aortic stenosis as an alternative to open aortic valve replacement. In this procedure, TAVs are implanted via a retrograde femoral arterial or antegrade transapical approach. The results have proven effective in relieving symptoms of aortic stenosis. However, no attempt has been made to use TAV as treatment for aortic insufficiency or other valvular disease not involving degenerative calcification of the cusps. Unlike traditional bioprostheses, which are sutured to the annulus, stent valves are not secured within the aorta. The forceful ejection of blood during systole could lead to stent dislodgement and antegrade migration distally into the arch or descending thoracic

aorta. Such distal migration has been observed in some abdominal aortic stent grafts during long-term follow-up of abdominal aortic aneurysms.¹ However, unlike abdominal stent grafts, TAVs are subjected to retrograde forces during diastole because of the pressure gradient across the closed valve. This force could lead to stent migration into the left ventricle. To the authors' knowledge, no computational simulations have modeled TAV hemodynamics. This study seeks to use computational fluid dynamics (CFD) to investigate flow, wall shear stress, and total force acting on the device to assess TAV migration in noncalcific aortic insufficiency.

MATERIALS AND METHODS

Transcatheter Aortic Valve Geometry and Simulation

A 3-dimensional geometric model or mesh was generated, extending from the aortic annulus to the proximal descending thoracic aorta. The region to be studied in the greatest detail, the aortic root, contains geometry of the aortic sinuses developed from anatomic measurements available in literature.^{2,3} The ascending aorta and arch are modeled as a simple curved pipe, excluding the arterial branches. A second mesh was generated of the TAV and merged with the aortic mesh at the annulus. Assumptions were made about the geometry of the TAV for the sake of simplicity. The simulation represents TAV implantation within an incompetent valve, as opposed to a calcified, stenotic valve, and the native leaflets are presumed to have a negligible effect on flow. The TAV and annulus are circular and contiguous, allowing no paravalvular leak into the left ventricle. Second, the TAV mesh does not include the stainless steel or nitinol frame of the stent. When fully opened, the cusps of the TAV are flush with the frame and take

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Abbreviations and Acronyms

CFD = computational fluid dynamics
TAV = transcatheter aortic valve

the shape of the stent housing (Figure 1, A). An open cylinder was used to model this geometry; the cusps are not attached at the commissures and do not intrude into the sinus cavity (Figure 1, B).

This study models approximately 300 msec of systolic flow. Although in vivo, the opening of the TAV takes place over a finite time, the precise kinematics of the opening and closing of the cusps during this period are not simulated. As such, unsteady flow from the left ventricle is assumed to begin after instantaneous TAV opening, ignoring flow during the short period when the valve is partially opened. Throughout the simulation of systole the cusps remain static and fully open, fixed within the stent. The loading conditions driving flow through the mesh were taken from the literature and are representative of normal systolic pressures.⁴ CFD simulations are performed to study flows through the rigid mesh; aortic root dilation is not modeled.

Computational Fluid Dynamics

The CFD methodology used in this study has previously proven its efficacy characterizing flow in the aortic arch and bifurcations.^{4,5} This approach requires a detailed 3-dimensional and time-dependent description of flow through the aortic valve. The simulation is driven by a system of fluid flow equations, Navier–Stokes, which for an incompressible fluid in dimensionless control volume form are as follows:

$$\iint_S \vec{V} \cdot d\vec{A} = 0 \quad \text{Continuity} \quad (1)$$

$$\frac{\alpha^2}{\text{Re}} \iiint_V \frac{\partial \vec{V}}{\partial t} dV + \iiint_V (\vec{V} \cdot \vec{\nabla}) \vec{V} dV = - \iiint_V p \cdot d\vec{A} + \frac{1}{\text{Re}} \iiint_S \vec{\tau} \cdot d\vec{A} \quad \text{Momentum} \quad (2)$$

where p is the pressure, $\vec{\tau}$ is the viscous stress tensor, $\text{Re} = \frac{2R\bar{U}}{\nu}$ is the Reynolds Number, $\alpha = R(\frac{\omega}{\nu})^{1/2}$ is the Womersley parameter, R is the inlet radius of the aorta, $\bar{U}$ is the maximum inlet velocity, ν is the kinematic viscosity of the fluid, and ω is the inlet pulse frequency ($\omega = 2\pi f$ where f is the heart rate). Blood flowing through the aorta is modeled as a Newtonian fluid, appropriate for CFD simulations of arterial flow.⁶ Computational evaluations are made for discrete time intervals at a rate of 320 computational steps per second. Values for the maximum velocity and flow area are used as reference to nondimensionalize computations, allowing good estimation to be made over a significant Reynolds number and size range. These values are as follows:

$$U_{\max} = 60 \text{ cm/sec} \quad A_{\text{flow}} = \pi r^2 \quad r = 1.2 \text{ cm} \quad A_{\text{flow}} = 4.52 \times 10^{-4} \text{ m}^2 \quad (3)$$

The total force on the aortic valve is obtained by performing an unsteady control volume force analysis, and the control volume is defined by the mesh that surrounds the valve and the meshes across the inlet and exit areas of the valve.⁷ There are 4 contributions to the force: (1) the fluid momentum flux at the inlet and exit of the valve; (2) the unsteady change of momentum in the valve control volume; (3) the dynamic pressure force on the valve; and (4) the viscous shear stresses on the outer wall of the valve.

The dimensionless force coefficient, C_{force} , is defined as follows:

$$C_{\text{force}} = \frac{\text{Force}_{\text{real}}}{\rho U_{\max}^2 A_{\text{flow}}} \quad \text{where } \rho - \text{fluid density } U_{\max} - \text{Maximum flow velocity} \quad (4)$$

The values of pressure and shear stress in the figures have also been made dimensionless in the following manner:

$$p = \frac{P_{\text{dynamic}}}{\rho \left(\frac{U_{\max}}{2}\right)^2} \quad \tau = \frac{\tau_{\text{real}}}{\mu \frac{U_{\max}}{\text{Diameter}}}$$

$$\text{And } \rho \left(\frac{U_{\max}}{2}\right)^2 = 90 \text{ Pa} \quad \text{and } \mu \frac{U_{\max}}{\text{Diameter}} = 0.084 \text{ Pa} \quad (5)$$

RESULTS

Flow Through the Transcatheter Aortic Valve

The results of the simulation are presented first with velocity vectors and dynamic pressure contours (Figure 2). It should be mentioned that the dynamic pressure field is not the blood pressure, but rather it is determined from the local spatial gradient of the blood pressure caused by the flow. Velocity fields in the aortic arch and at points distal are essentially identical to those seen in unsteady flow analysis through a simple curved pipe, suggesting that implantation of the TAV has a negligible effect on hemodynamics downstream of the ascending aorta.⁸ Control of flow in the arch is dominated by the Womersley parameter, which is sensitive to changes in heart rate, as opposed to the geometry.

Unlike the flow seen in the aortic arch, the TAV alters hemodynamics in the root and ascending aorta considerably (Figure 3). Flow in the center of the aortic lumen continues to converge and accelerate after the valve. However, average velocity across the entire vessel decreases distal to the valve because of the increase in lumen area. If the leaflets remain fully open during ejection and the wall motion is neglected, the net fluid that flows in and out of the sinus cavity must be equal because of conservation of mass. Unsteady flow into and out of the sinus region is due to non-uniform fluid entrainment locally at the valve tip. The value of unitless flow presented in the figure is the axial component of flow, and the sinus bulge creates the movement of blood in both the positive and negative direction, as well as rotational flow around the leaflet. The geometric cause of the unsteady sinus flows is the non-axisymmetric shape of the sinus cavity, which influences the interaction with the flow in the valve.

Forces on the Transcatheter Aortic Valve

Throughout ejection, the largest component of force is pressure (Figure 4), followed by momentum flux force. Both the viscous force on the outside of the valve and unsteady flow forces in the valve are less than a few percent of the total force. Total force on the TAV is the magnitude or absolute value of the components of force in all 3 dimensions. However, approximately 99% of the total force is in the direction of axial flow. Total force peaks during maximum systolic flow at 0.602 Newtons. The pressure field observed corresponds with previous simulations and is dominated by the unsteady frequency parameter, α , in the large arteries.^{8,9}

FIGURE 1. TAV schematics. A, Schematic of an open TAV. B, Surface mesh of the TAV within the aortic root. TAV, Transcatheter aortic valve.

Wall Shear Stress

Figure 5 shows the magnitude or absolute value of the total wall shear stress on the ventricular TAV leaflet surfaces and the sinus surface. Shear stress on the TAV is larger than on the sinuses on average; however, at locations near the valve tip the sinus wall shear stress can approach more than 50% of valve wall shear stresses. At all times in the simulation, the maximum shear stress on the aortic sinus wall is located just distal to the bulge region of the sinus

FIGURE 2. Velocity vectors and dynamic pressure contours in the aortic arch. A, Maximum flow acceleration. B, Maximum flow. C, Maximum flow deceleration.

where the diameter is greatest. It seems that dynamic fluid entrainment caused by the sinus influences this profile of wall shear stress.

The greatest shear stress on the TAV occurs near the tip of the leaflets and peaks during maximum flow through the valve, corresponding to previous studies of shear in both the root and the aortic arch.⁴ Maximum shear stress on the valve leaflet tips is approximately 40 Pa (Equation 5).

Diastolic Force: Engineering Estimates

Considerable antegrade force acts on the TAV during ejection, pushing the prosthesis along the axis of flow. To determine the significance of this force, the entire cardiac cycle should be taken into consideration. At the beginning

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FIGURE 3. Velocity profile with velocity contours in the aortic root. A, Maximum flow acceleration. B, Maximum flow. C, Maximum flow deceleration.

of diastole, a small retrograde flow occurs during valve closure but likely generates negligible force. During left ventricular relaxation, however, the closed TAV is subjected to a large retrograde pressure gradient. A simple approximation can be made to estimate the resulting force on the TAV using left ventricular and ascending aortic pressure. The net pressure force occurs along the axis of flow and depends only on the projected area in that direction, as defined by the valve radius r_{valve} at the annulus. Considering the same size TAV used in the CFD simulation, area and force are:

$$r_{\text{valve}} = 12 \text{ mm} \quad A_{\text{projected}} = \pi r_{\text{valve}}^2 = 4.52 \text{ cm}^2$$

$$\text{Force} = \Delta p_{\text{valve}} A_{\text{projected}} = 6.01 \text{ N} = 1.36 \text{ lb}_f$$

Peak force during diastole is approximately an order of magnitude greater than peak force during systole.

DISCUSSION

CFD simulations in this study characterize for the first time flow through TAV and quantify the hemodynamics from the annulus to the descending aorta. Jet flow through the TAV leads to flow in the center of the lumen, converging distal

FIGURE 4. Force on the TAV. Magnitude of total force and pressure, the largest contributing component, during systole. Force and time are presented in dimensionless units from the simulation.

to the valve. A peak force of 0.602 N is exerted on the TAV, approximately 99% of which is in the direction of axial flow. The leaflet tips are subjected to a wall shear stress of approximately 40 Pa. Finally, a simple engineering estimate shows total force during diastole to be 6.01 N, approximately 10 times larger than force during ejection through the TAV.

Implantation of Transcatheter Aortic Valves

The first human percutaneous TAV implantation was performed in 2002 by Alain Cribier and colleagues.¹⁰ Overall, TAV has 73% to 100% implant success and procedural mortality of 2% to 14% in patients with predicted surgical mortalities of 12% to 31%. Surgical conversion was 0% to 2%, periprocedural stroke occurred in 0% to 10%, and 30-day mortality was 12% to 22%.¹⁰⁻¹⁹ Hemodynamically successful treatment of calcified aortic stenosis was achieved without major complications. Valve area significantly improved (0.5–0.7 to 1.5–1.7 cm²); transvalvular gradients substantially decreased (32–46 mm Hg to 9–11 mm Hg); and ejection fraction increased (45%–53% to 53%–60%). However, TAV implantation has never been attempted for treatment of aortic insufficiency in humans. Structural differences between a calcified, stenotic aortic valve and a dilated or prolapsing incompetent valve are significant. Patients requiring ascending aortic replacement or valve-sparing aortic root replacement to treat aortic insufficiency would not seem to be good candidates for TAV. Although the proportion of patients with isolated aortic insufficiency may not be substantial, once TAV technology becomes Food and Drug Administration approved, off-label use of TAV may potentially be expanded to patients without

FIGURE 5. Contours of wall shear stress on the transcatheter aortic valve and aortic root. A, Maximum flow acceleration. B, Maximum flow. C, Maximum flow deceleration.

significant calcification. Before consideration for clinical use, computational and experimental studies should be conducted to evaluate the safety of TAV under this pathology.

Predicting Stent Migration

Clinically, TAVs rarely migrate when seated correctly, despite large shear forces during systole and pressure gradients during diastole. One hypothesis is that calcification of the native leaflets anchors the stent in place because of a reduction in annular pliability.²⁰ Should this hypothesis be true, treatment of aortic insufficiency with TAV is likely not advisable. In Cribier's early experience of percutaneous treatment for severe aortic stenosis, 1 of the 6 enrolled patients died as a result of TAV migration.¹³ This patient had a highly irregular valve, with 1 leaflet torn away from the annulus during pre-TAV aortic balloon valvuloplasty, which resulted in massive aortic insufficiency. Because of the anatomy, the TAV was deployed but ejected distally during full balloon inflation, which the investigators believe led to its migration because of the absence of calcium for stent valve fixation.

Aortic stenosis cannot be readily re-created in an animal model, and thus *in vivo* animal studies more accurately simulate aortic insufficiency than stenosis. During a 2006 study of TAV implantation in pigs, 8 of 26 valves migrated (2 distal, 6 retrograde).²¹ Of these, 5 valves were cited to migrate into the left ventricle after a normal implantation when the

pig was weaned from cardiopulmonary bypass or rapid ventricular pacing. Another investigation of TAV deployment within pigs reported that 40% of the prostheses migrated shortly after being seated (6/15 total; 3 distal, 3 retrograde migrations).²⁰ The investigator cited the size and compliance of the normal, noncalcified root as a possible explanation for the dislodgement of the prosthesis. In light of these experimental results, patients with pure aortic insufficiency could present the same risk of migration, and additional means should be taken to secure the stent.

Securing the Stent

Migration is a known complication of all stent grafts but a clinical hazard and potential source of mortality for TAVs. Mechanically, migration is a device failure created when forces acting on the stent overcome the strength of the stent's attachment to the vessel wall. Studies using static pressurization of abdominal aortic stent grafts within cadaver and animal models have been used to quantify the force necessary for migration. Drag force, which holds the stent in place, is highly dependent on the outer surface of the device: 2 to 4 N for smooth stents and 7 to 12 N for stents with hooks and barbs.²² Newer designs have drag forces measured up to 25 N.²³ When implanting a self-expanding TAV in an animal model, both antegrade and retrograde migrations were problematic.²⁴ Initially, migration into the left

ventricle occurred during deployment, requiring the addition of retaining hooks to the design. In subsequent trials, the stent migrated antegrade after a successful deployment. Retaining hooks were added to prevent early retrograde migration, and increasing the radial force of the stent wire and oversizing the TAV were necessary to prevent migration into the ascending aorta.

Study Limitations

The simulation results were generated using a simplified, although physically reasonable, model of an implanted TAV during systole. For the purpose of comparison, we have made an engineering estimate of the closed TAV during diastole. A comprehensive study, incorporating the surface of the closed leaflets and the dynamic pressures in the aorta and left ventricle, is necessary for a more accurate prediction of diastolic force. As stated previously, this simulation does not model leaflet kinematics. The results show that peak shear stress and total force on the TAV both occur at maximum flow, indicating that the short period while leaflets are still opening is unimportant for TAV failure. The kinematics, however, are necessary to predict fatigue and long-term degeneration resulting from leaflet bending.²⁵ CFD simulation can calculate shear stress on TAV leaflets in detail that would be extremely difficult or impossible to determine experimentally. Nonetheless, future experimental and clinical investigation are necessary to validate the results. Last, the compliance of the aortic root and TAV is not incorporated in the model. We demonstrate that as blood exits the left ventricle during systole, it interacts with the distal edge of the TAV, and fluid entrainment creates complex vortical flow in the sinus cavity. Blood leaving the sinus along the aortic face of the TAV leaflet pulls new blood into the sinus from near the aortic root wall, creating regions of both positive and negative axial flow. Eddy currents and turbulence may be created in this region by interaction of the fluid at the boundaries of the TAV and the compliant aortic root. Realistic simulation of these complex phenomena requires the addition of fluid–structure interaction to the model, which may be performed in future studies.

CONCLUSIONS

CFD simulations in this study provide the first of its kind data quantifying hemodynamics of TAV within an incompetent aortic valve. The proposed treatment has not been attempted clinically and has shown only limited success in animals. Total force, likely the most significant result of this study, indicates that antegrade migration of TAV may not be a concern because it is in abdominal aortic stent grafts, when compared with retrograde migration. However, the drag force acting to prevent migration is unknown and possibly dependent on the direction of migration because of the irregular geometry.

Overall, CFD models are useful to investigate how a change in geometry leads to a change in hemodynamics. If the change is significant, a complete fluid–structure interaction model should be developed to investigate the deformation of the aortic root as well, and ultimately to estimate the drag force necessary to prevent stent migration. The TAV–root surface interaction will be the dominating parameter of drag, and a reliable model for testing specific surface geometries of both has 2 benefits. First, future TAV designs could be developed with anchoring elements, such as the hooks and barbs of abdominal aortic stents, to increase drag. Second, patients with certain valve disease, such as noncalcified incompetent leaflets, could be screened to predict whether TAV implantation is safe. These 2 benefits may lead to greater surgical success or an inclusion of patients not currently considered for TAV.

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