An In Vitro Model of Aortic Stenosis for the Assessment of Transcatheter Aortic Valve Implantation

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A significant number of elderly patients with severe symptomatic aortic stenosis are denied surgical aortic valve replacement (SAVR) because of high operative risk. Transcatheter aortic valve implantation (TAVI) has emerged as a valid alternative to SAVR in these patients. One of the main characteristics of TAVI, when compared to SAVR, is that the diseased native aortic valve remains in place. For hemodynamic testing of new percutaneous valves and clinical training, one should rely on animal models. However, the development of an appropriate animal model of severe aortic stenosis is not straightforward. This work aims at developing and testing an elastic model of the ascending aorta including a severe aortic stenosis. The physical model was built based on a previous silicone model and tested experimentally in this study. Experimental results showed that the error between the computer-aided design (CAD) file and the physical elastic model was <5%, the compliance of the ascending aorta was 1.15 ml/mm Hg, the effective orifice area (EOA) of the stenotic valve was 0.86 cm², the peak jet velocity was 4.9 m/s and mean transvalvular pressure gradient was 3.1 mm Hg, consistent with severe aortic stenosis. An EDWARDS-SAPIEN 26 mm valve was then implanted in the model leading to a significant increase in EOA (2.22 cm²) and a significant decrease in both peak jet velocity (1.29 m/s) and mean transvalvular pressure gradient (3.1 mm Hg). This model can be useful for preliminary in vitro testing of percutaneous valves before more extensive animal and in vivo tests. [DOI: 10.1115/1.4026576]

Keywords: transcatheter valve replacement, stenotic aortic valve, hemodynamic performance, surgical training, rapid prototyping model

1 Introduction

Aortic stenosis is a disease characterized by a narrowing of the aortic valve orifice, mostly due to calcification and stiffening of valve cusp. If symptoms appear in patients with aortic stenosis, the only solution is to remove the native calcified valve and replace it with a biological or mechanical prosthetic heart valve. However, this procedure requires an open-heart surgery. As a consequence, a significant number of patients, especially the patients over 80 years and those with severe comorbidities are denied aortic valve replacement due to high operative mortality risk. The number of these patients will continue to grow as a result of population aging. The recent development of transcatheter aortic valves provides a valid alternative to surgical aortic valve replacement in this category of patients. A transcatheter aortic valve consists of prosthetic valve leaflets and a metallic stent. Its implantation relies on a minimally invasive technique, preventing the need for an open-heart surgery. It is predicted that the number of TAVI will increase exponentially during the upcoming decades [1]. It is then important to develop dedicated facilities for testing the performance of such valves and contribute to a better training of future physicians involved in TAVI.

Of primary importance here is to design and develop an adequate experimental model of severe aortic stenosis allowing TAVI. Some work has already been dedicated to the development of elastic models of left heart cavities using rapid prototyping for TAVI applications. Kalejs and von Segesser designed an anatomical silicone model of the aortic root and ascending aorta [2]. The main objective of the model was to train interventional cardiologists for the positioning and deployment of transcatheter valve. The same group (Abdel-Seyed et al.) further developed their model by adding an anatomical model of the left ventricle (LV) and the left atrium from CT-scan images [3]. The new model allowed training on TAVI through a transapical access. It should be noted, however, that these models had important limitations: (1) they did not include a stenotic aortic valve, and (2) they were not tested under physiological flow conditions. The only experimental model of aortic stenosis reported in the literature was designed by our group and tested in vitro in Ref. [4]. However, the model was hand-made and built using multiple layers of silicone. It is therefore hardly reproducible.

The objective of this work was to develop a reproducible experimental model of the ascending aorta including a severe aortic stenosis. The performance of this model was evaluated under realistic physiological conditions and the implantation of a transcatheter valve inside the model was performed.

2 Materials and Methods

The original non-stenotic Computer-Aided Design (CAD) model of the stenotic aortic valve was based on a previously published model [5,6]. The model is symmetric and includes three leaflets, three commissures, three sinuses, and three interleaflet triangles, which is consistent with Sutton et al.’s description of the normal aortic valve [7]. The model was modified to include a severe aortic stenosis. In order to create the model of aortic stenosis, two parameters have been altered—(1) Leaflet material properties: several models of the aortic stenosis have been built using 3D stereolithography (by Axisprotoype; Montreal, QC, Canada) with the same material (Digital Materials™) but different durometers; (2) Leaflet thickness: in order to mimic the “atherosclerotic-like” process of degenerative aortic stenosis, the thickness of
valve leaflets has been increased. A combination of a durometer of 65 with a leaflet thickness of 2 mm led to hemodynamic results that are consistent with clinical findings. The material used, Digital Materials TM, is formed by the combination of a Tango plus (tensile strength at break: 211 MPa, elongation at break: 218%) and Vero plus material (tensile strength at break: 55 MPa, elongation at break: 15%).

The dimensions of the final model are displayed in Figs. 1(a) and 1(b). An STL file of the model can be freely downloaded from http://users.encs.concordia.ca/~kadem/Research.html. The dimensions of the model can be modified to allow for patient-specific tests by varying, within certain limits, the geometry of the aorta and the severity of the aortic stenosis. The resulting physical model is displayed in Fig. 1(c). The maximal error in dimensions between the CAD file and the physical model was 5% (mean error: 3.5%). The model was then easily installed in a ViVitro cardiac simulator (ViVitro Labs Inc., Victoria, BC, Canada) for the evaluation of its hemodynamic performance (Fig. 1(d)). The working fluid contained 75% water and 25% glycerol in volume, leading to a density of 1080 kg/m³ and dynamic viscosity of 3.5 cP. A second set of tests consisted in implanting an EDWARDS-SAPIEN 26 mm valve inside the model and test its hemodynamic performance. For this purpose, a transcatheter valve was implanted in the model using a balloon (Fig. 1(e)).

Experimental measurements included: (1) pressure measurements upstream and downstream of the stenotic valve using Millar catheters MPC-500 with an accuracy of ±0.025% on the full scale; (2) transvalvular flow rate using an electromagnetic flowmeter Carolina Medical (FM501) with an accuracy of ±0.10% on the full scale; (3) instantaneous valve geometrical area using a Phantom v 4.2 high-speed camera (Vision Research Inc., NJ, USA) at 1000 frames per second; (4) doppler derived parameters—valve effective orifice area (EOA) using continuity equation, peak, and mean transvalvular pressure gradients (TPGpeak and TPGmean) using the simplified Bernoulli equation, Doppler Velocity Index (DVI) defined as the ratio of the peak flow velocity in the left ventricular outflow tract to the maximum jet velocity at downstream of the aortic valve [8]. All Doppler measurements were performed using an Acuson 128 XP/10 Echo Doppler machine. The evaluation of the performance of the model was done for three different stroke volumes (40, 50, and 60 ml) at a constant heart rate of 70 bpm and under normal physiological aortic pressure conditions.

3 Results

Figure 2(a) shows the instantaneous LV and aortic pressure waveforms obtained using our stenotic valve model for a stroke volume of 60 ml. These waveforms are similar to those found in...
patients with severe aortic stenosis. The estimated compliance of the aortic model was 1.15 ml/mm Hg which falls within the range of compliance values for patients with severe aortic stenosis (0.89–1.49 ml/mm Hg) [9]. Interestingly, the model as mounted on the ViVitro system also allowed for an axial elongation of the aortic root by 15% of the sino-tubular junction diameter. Such elongation has already been reported in vivo by Beller et al. [10] and Labrosse et al. [11]. Figure 2(b) shows the pressure waveforms obtained after TAV implantation. A clear reduction in the LV pressure and the transvalvular pressure gradient can be observed.

Figures 3(a) and 3(b) show the stenotic aortic valve model and transcatheter aortic valve in closed position and at maximal geometrical opening as recorded by the high-speed camera. Instantaneous geometrical orifice area is displayed in Fig. 4. A delayed opening of the stenotic valve can clearly be seen as well as an incomplete coaptation of the thick leaflets of the valve during diastole. These findings are consistent with in vivo observations [12]. Peak jet velocity downstream of the stenotic valve, as determined by echo-Doppler measurements, was 4.87 m/s and the corresponding TPGpeak was 94 mm Hg for a stroke volume of 60 ml. TPGmean across the valve was 50 mm Hg. Valve EOA and DVI were 0.86 cm² and 0.18, respectively. All these values correspond to a severe aortic stenosis as defined by both the European Association of Echocardiography and the American Society of Echocardiography guidelines [8,13]. As a consequence, a hypothetical patient with an aortic valve similar to the model developed in this study should be referred, in the presence of symptoms, to aortic valve replacement and if not eligible, to TAVI. After implanting the percutaneous heart valve, the hemodynamic parameters are significantly improved—Peak jet velocity: 1.29 m/s (TPGpeak = 6.6 mm Hg); TPGmean = 3.1 mm Hg; EOA = 2.22 cm²; and DVI = 0.6. The instantaneous geometrical orifice area after TAV implantation is shown in Fig. 4 in comparison with the one for stenotic valve.

Although the experimental model of a severe aortic stenosis developed in this study is capable of well reproducing clinical situations, some limitations are still associated with the model. First, several studies have shown that the normal aortic root expansion is asymmetric and rotates and tilts during the cardiac cycle [14,15]. Note, however, that there is no evidence that these findings are still applicable to a calcified aortic annulus. Second, the current model does not include coronary ostia. Since the model is elastic, adding coronary ostia at various locations reproducing different clinical scenarios is straightforward. The upgraded model with coronary ostia could then be connected to an in vitro experimental model of coronary arteries flow [16].

4 Discussion and Conclusions

In this study, we demonstrated the feasibility of developing an experimental model of a severe aortic stenosis. The in vitro tests showed that the results were consistent with clinical data and observations in patients with severe aortic stenosis. The dimensions of the model and the material properties can be modified depending on the user’s needs in terms of severity. The model can be useful for the development of new TAV or medical devices related to TAVI. Currently, patients with non-optimal positioning of coronary ostia or patients with bicuspid aortic valve, with a
prevalence up to 30% among the patients with aortic stenosis, are not referred to TAVI. The next generation of TAV will probably have to target such populations. The model developed in this study can easily be modified in order to generate a bicuspid valve, by a fusion of two leaflets for example, or can be combined to an experimental model of coronary flow to evaluate the impact of TAV on coronary circulation. Also, a device aiming at percutaneous aortic valve resection prior to TAVI can be tested on the model developed in this work [17]. Furthermore, the model can be useful for training, in vitro, surgeons on good positioning of TAV during implantation. This is very important since a non-optimal positioning of TAV can result in significant paravalvular leaks, one of the current major limitations of TAVs. Finally, future development of the model can include multimaterial stereolithography to simulate localized calcium spots on the valve leaflets.

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References