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COMPUTATIONAL SIMULATIONS OF VENTRICULAR OUTFLOW TRACT OBSTRUCTIONS ASSOCIATED WITH VARIED REPLACEMENT VALVE GEOMETRIES

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BACKGROUND

Transcatheter replacement therapies for the atrioventricular (AV) valves are considered as the next frontier for the treatment of valvular regurgitation. The AV valves, tricuspid and mitral, are the regulators of blood flow from the atria into the ventricles. During diastole, blood flows through the open tricuspid and mitral valves to fill the right and left ventricles, respectively. During systole, the ventricles contract, closing the AV valves, and forcing the blood to exit through their respective ventricular outflow tracts (VOTs) to the arterial circulations. Although the current gold standard for the treatment of valvular regurgitation is surgical replacement or repair, the field of transcatheter therapies is rapidly expanding as new treatment options for patients; especially for those individuals considered to be at greater risks for surgical complications. Market released bioprosthetic devices for replacing the aortic and pulmonary valves have shown great promise and success. However, the advancement of similar therapies for either the mitral and tricuspid valves remain in the early stages of development. This slower progress is attributed to the high complexities and variabilities of the AV valves, which present challenges for both device design and post-implantation functions.

Transcatheter replacement valves typically consist of a metal stent frame, which supports the biological tissue leaflets. Often when replacing native AV valves with a bioprosthetic, the potential VOT obstruction is a high risk factor to consider. Further, the proximities and anatomical relationships between the tricuspid and mitral valves with the right ventricular outflow tract (RVOT) and left ventricular outflow tract (LVOT), are critical when implanting potentially protruding devices in the native valvular positions. Currently, quantification and pre-screening of VOT anatomies and obstructions are performed using echocardiography and computerized tomography (CT). However, these methods are limited to anatomical measurements without bioprosthetic simulations.

In this study, a novel and feasible method to simulate a valve bioprosthetic implant in reconstructed ventricular anatomies was developed and used to both quantify and predict a projected VOT obstruction. Hearts were imaged using magnetic resonance imaging (MRI) and reconstructed using a medical image segmentation software. A novel MATLAB script was developed to simulate the implantation of varying height sized replacement devices in either a reconstructed mitral and tricuspid annulus. The relative amount of a given VOT that might be obstructed by the implanted valve was quantified for both the left and right sides of these hearts. Three-dimensional (3D) printing and prototyping were also employed to accompany these computational simulations.

METHODS

We created simulations utilizing MRI, computational modeling, and 3D printing, of fixed human heart specimens to better understand valve implantations with varying geometries so to quantify the potential for VOT obstructions. Human heart specimens were studied to obtain clinically relevant anatomical structures of both the AV valves, as well as VOTs. These

specimens were obtained from The Human Heart Library of the Visible Heart® Laboratory (Department of Surgery, University of Minnesota), which to date, has preserved 470 human hearts: those deemed non-viable for transplant[1]. The library contains an extensive range of perfusion-fixed heart specimens with multiple forms of heart disease: including valvular regurgitation cases. These hearts were fixed in end-diastolic states with the VOTs and valvular annuli dilated open. These hearts were next prepared by gelling them in agarose and imaged using MRI. The generated DICOM data sets were used to generate 3D reconstructed heart models that accurately depicted both the valve and ventricle anatomies.

Mimics and 3matic (Materialize NV; Leuven, Belgium), medical image processing and modeling software programs, were both utilized to reconstruct the anatomies of the imaged hearts. The Mimics software permits the segmentation of specific heart anatomies and components. Analyses of the resultant 3D models of the heart structures provided unique perspectives for visualizing the proximities and relationships between these valves and their associated VOTs. Although the uses of Mimics and 3matic software allows for the accurate reconstructions of the valve and ventricular anatomies, their applications leave two major inadequacies for studying the effects of replacement valve devices. Their uses have minimal or no abilities to accurately simulate varying replacement valve frame geometries, in either mitral or tricuspid valve annuli and/or allows one to quantify the percentages of VOT obstructions. Therefore, we developed a novel MATLAB interface that allowed us to appropriately reconstruct these ventricular and valve anatomies, as well as to simulate the implantations of multiple frame depth sizes to evaluate the potential for causing VOT occlusions.

For this project, a given heart specimen was imaged with MRI; then the spline, or coordinate points, of the mitral and tricuspid annuli were marked and obtained utilizing the Mimics software. The RVOT and LVOT structures were also accurately reconstructed. Representative reconstructed VOTs and associated AV valvar apparati were illustrated in Figure 1.

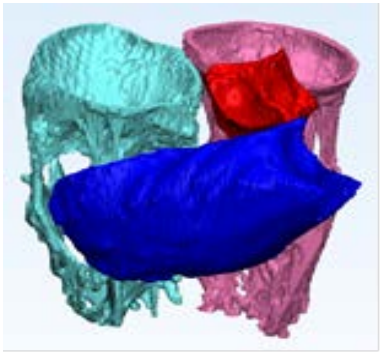

Figure 1: Computational 3D reconstructions of the tricuspid valve (green), the RVOT (blue), the mitral valve (pink), and the LVOT (red) of HH108 (see: Atlas of Human Cardiac Anatomy; http://www.vhlab.umn.edu/atlas/).

The valve annuli splines and VOT structures were subsequently imported into the developed MATLAB interface. This computation interface was then used to simulate a replacement valve frame extended down from the imported valve annuli. A range of 5 to 25 mm in frame depths were tested and this range typically represents the frame sizes in transcatheter replacement valve devices currently being developed. The resulting valve frame depths and VOT structures were simulated and computationally displayed. The relative amounts of VOT obstructions were determined as the amount of overlap between the edges of the simulated valve frame placements and the interfaces with the VOT structures. The directions best representing the VOT axes were chosen as the paths of valve frame obstructions; as this simulates the blood flow exiting the ventricles during systole. VOT obstructions were calculated as the percentages of VOT areas obstructed, over the total surface areas of the VOT starting plane. Figure 2 illustrates a typical simulation of relative valve frame depths and the resultant percentages of obstructions on the VOT starting plane surfaces: for both the right and left side of an imaged heart.

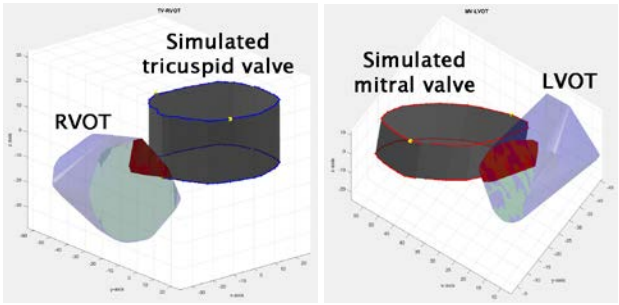

Figure 2: Left – Simulated valve frame (25 mm depth) in the tricuspid valve annulus and RVOT obstruction (red). Right – Simulated valve frame (10 mm depth) in the mitral valve annulus and LVOT obstruction (red).

Following the computational simulations, 3D printing was used to create representative models of the ventricular anatomies, outflow tracts, AV valves, and frame stents. The valve frame stent was printed to the size and height dimensions of a given market TMVR device: i.e., being investigated for mitral valve replacement. The valve frame models were placed in the 3D printed AV valves and its effect on the associated VOT was directly visualized. The use of these prints to accompany the computational simulations aids one to better identify the soft tissue-device interactions and visualize the potential severities of VOT obstructions. Figure 3 demonstrates the implantation of a constructed valve frame stent into the tricuspid valve annulus and its projected RVOT obstruction.

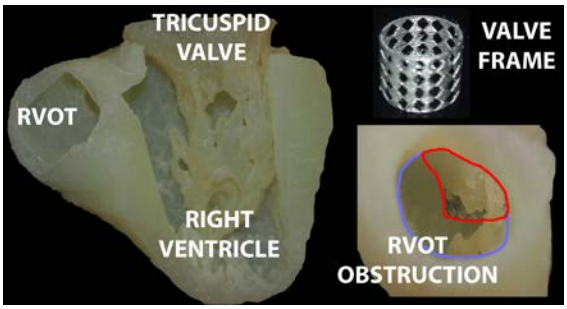

Figure 3: A 3D print of the right ventricular anatomy from an imaged heart specimen (HH108, Left). The valve frame (18 x 23 mm) was implanted in the tricuspid valve annulus and viewed from the pulmonary artery with the entire RVOT marked (purple). The RVOT obstruction (red) was highlighted.

RESULTS

For both RVOT and LVOT anatomies, a range of valve frame depths were simulated and the percentages of VOT obstructions were calculated. Figure 4 plots these relationships for both simulated replacement valve frames in either the mitral and tricuspid annuli.

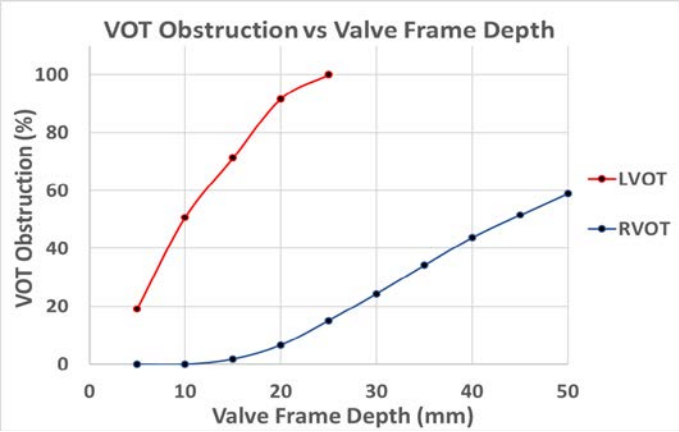

Figure 4: LVOT (red) and RVOT (blue) obstruction plots for increasing valve frame depths.

Preliminary results from these AV valves and VOT simulations of a given representative human heart scan, shows the proportional relationships between the valve frame depths and respective VOT obstructions. From computational modeling, one could estimate that for the mitral valve in this heart, a frame depth of 20 mm would obstruct approximately 91.7% of the LVOT interface. For comparison, the same frame depth simulated for a tricuspid valve implant would obstruct approximately 6.6% of the RVOT. Interestingly, a valve frame depth less than 10 mm, would predictively not induce a RVOT obstruction, but if placed in the left heart it would obstruct approximately 50.7% of the LVOT.

INTERPRETATION

These computational simulations allow one to more critically predict how anatomical variations between the AV valves and associated VOTs would affect optimizations for valve implantations. For example, with the mitral anterior leaflet and aortic valve being in near proximity, there is greater concern and prevalence of LVOT obstructions for mitral valve replacements. The results from our study confirm that for a given valve frame depth, the potential for LVOT obstructions are greater than those would be for the RVOT.

A single VOT obstruction computation, from reconstruction to valve frame depth simulation, was approximately in less than half an hour. The most time-consuming parts in this process were the Mimics anatomy reconstructions and manual selections of spline points from the heart MRI images.

The future direction for this project is to perform these computational simulations in a large number of human heart scans with known pathologies. The derived simulations from each heart could be further validated by analyzing multi-phase CT imaging of actual valve implants as well as to 3D print various heart/valve interfaces[2]. Additional physical models of various valve frame geometries/designs could be 3D printed and then implanted into these actual fixed heart specimens; those from which the computation models were developed. Subsequently, CT imaging of these hearts with implanted 3D valve prints, could be used to further validate the predicted VOT obstructions. In other words, CT imaging of various 3D valve prints implanted within fixed human hearts, would establish better correlations between valve geometries and percentage of VOT obstructions over a broad range of patient demographics. This would be a critical means to validate our computational approach and provide additional means for studying these device/tissue interactions.

We consider here that our simulations of these device-tissue interactions, using the described methodologies is a novel approach compared to currently employed expensive imaging modalities[2,3,4]. Current techniques used to predict LVOT obstruction require the use of CT imaging and computer-aided design (CAD) modeling[2,5]. The ongoing consensus within the dynamic transcatheter mitral valve replacement field is to best define the patient's VOT anatomy, such as the elongated LVOT post-implant as "neo-LVOT", and/or validate using multi-planar CT imaging. Note that these assessment tools require contrast-enhanced CT screenings (exposure to radiation and contrast agents) and prolonged reconstruction of CAD models. Hence one aims to improve on these validations.

Our developed simulation and modeling techniques have the potential to address the concerns with currently employed CT-CAD prediction tools. Our approach utilizes MRI imaging of hearts within our large library of specimens so to reconstruct patient specific anatomies. Additionally, transesophageal echocardiography (TEE) could be used validate the measurements from MRI-Mimics reconstructions and MATLAB implant simulations. Thus in future studies,

depending on the acquisition and quality of TEE imaging, the pre-implant AV valvular annuli and VOT dimensions could be used for such described simulations as well. Today, the clinical uses of MRI and TEE present fewer patient complications, are readily available in most major interventional valve implant centers, and are standardized for cardiac assessment. Overall, the novel computational assessment approaches we describe here will hopeful aid one to better determine the optimized implantation depths and frame size ranges; that should aid to minimize VOT obstructions. This work has the potential to impact the fields both device development and clinical deployments of transcatheter AV valve replacement; since significant VOT obstructions of blood flow can be detrimental to a given patient.

ACKNOWLEDGMENTS

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