Title: Computational Modeling of Patients Undergoing Aortic Valve and Mitral Valve Replacement Along with Tricuspid Repair

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Introduction: The field of cardiovascular research focuses on the heart, a complex muscular organ that transports blood and nutrients throughout the body (See Figure 1). The heart's network consists of chambers, valves, and blood vessels that provide proper circulation to maintain the human body's ability to function. The observed components in this research are the four chambers, which are the right atrium (RA), right ventricle (RV), left atrium (LA), and left ventricle (LV), three of the valves, the tricuspid valve (TV), mitral valve (MV), and aortic valve (AV), and the main vessels, which are the aorta and coronary arteries. The chambers work together to receive oxygen-rich or oxygen-poor blood before pumping blood along to the next area. The valves open and close to ensure that blood flows in a unilateral direction to prevent flow of blood into undesired areas. The aorta's role is to deliver blood to the rest of the body, while arteries supply blood and nutrients to the heart. These components work together to complete a full cardiac cycle, or heartbeat.

Dysfunction of these components can lead to heart failure and altered hemodynamic parameters, a term referring to the movement of blood. These can incur due to multiple factors, but this research studies the specific causes of valve failure. Valve failure occurs when diseased valves' ability to open and close is not properly regulated, inducing blood volume abnormalities which can lead to heart failure. To counteract heart failure, researchers have developed surgical procedures to replace failing valves with bioprosthetics. These surgical procedures are in high demand, with over 182,000 heart valve replacements being performed every year in the United States of America, making these procedures the most common procedure performed on the cardiac market [6]. Examples of current bioprosthetics include AV replacements, MV replacements, TV replacements, or TV repairs where the ring of the native heart valve is reinforced with an annuloplasty ring. In bioprosthetic AVs, the estimated life expectancy ranges from 12-15 years, leading to multiple valve replacements in younger patients [1]. In bioprosthetic MVs,

survival rates of patients who had undergone replacement was 62.4% after 10 years, portraying the need for design changes to increase survival rates [3]. TV repair is more successful in patients than TV replacement, but TV repair is understudied and lacks long-term results; further clinical trials are needed to discern long-term outcomes [11]. The increase in surgical procedures for bioprosthetic valve replacement has shifted the focus of clinicians to patients undergoing triple valve replacement to discern abnormal hemodynamic parameters and flow changes in patients. Due to lengthy "periods of cardiopulmonary bypass and aortic cross-clamp times," triple valve replacement surgery continues to pose a challenge for surgeons, with a reported mortality rate of 13% and 10-year survival rate of 61% [9]. The lack of successful outcomes has led current authors to gather data on one patient, known as the tricuspid aortic valve (TAV) patient, who had undergone triple valve replacement on the AV, MV, and TV.

The overall aim of this study is to consider current research of valve replacements and discover causes of valve failure in a single patient. The challenges of survival rate after 10 years, the restrictive 12-15 years of life for bioprostheses, and the abnormalities in hemodynamic parameters provided guidelines for authors to follow during analysis of results. The authors' focus on observing abnormalities in blood flow and blood volume, deformation of the three valves, and remodeling of the four chambers during the cardiac cycle provides insight to valve failure causation, tackling these challenges. The authors hypothesized abnormal blood volume would lead to remodeling of the chambers post-valve replacement, specifically present during the transition from systole, the contraction phase, to diastole, the relaxation phase, of the cardiac cycle. The authors also hypothesized that improper valve deformation would produce inadequate blood flow and blood volume in the four chambers. The specific aim of analyzation is to extend the longevity of bioprosthetic valves, increase triple valve replacement patient success, and produce accurate visualization of the heart functionality post-triple valve replacement.

Methods: To comprehend how valve failure may lead to heart failure, the authors performed three-dimensional modeling. They acquired cardiac-resolved computed tomography (CT) angiography images of a TAV patient at Yonsei University in Seoul, South Korea. The CT images arrived in ten sets for the

patient, each image representing 10% of the cardiac cycle, and were imported to three computer modeling softwares. The first set of components, the aorta, coronary arteries, and three replaced valves were modeled in SimVascular. SimVascular, a simulation software, allows users to import CT images and create 3D models to simulate different instances of a cardiac cycle. The models were created by initially importing CT images to SimVascular, which allowed users to view the images on four separate screens that represent three planes of axes (See Figure 2a). Paths were created by placing points along areas of lumen of a target vessel or valve (See Figure 2b). 2D contours were then segmented orthogonally on the paths, creating a circular feature (See Figure 2c). Finally, the segmented contours were lofted to create 3D surface models (See Figure 2d). The second set of components, the four chambers of the heart, were modeled in ITK-SNAP. This is a software application used to segment structures in 3D medical images, and to observe volume and statistics in 3D surface models. The CT images were imported to ITK-SNAP (See Figure 3a), and a legend was created for each chamber (See Figure 3b). The "snake" tool was activated to create bubbles in the precise target areas of each chamber and were given a threshold size to either enlarge or reduce in each chamber (See Figure 3c). Next the "paintbrush" tool was used to either brush away portions of the bubble overflow into separate chambers or fill in portions of chambers that were not segmented (See Figure 3d). To observe blood volume in these surface models, users accessed the "Volume and Statistics" feature included in ITK-SNAP software. Finally, the models for ITK-SNAP and SimVascular were imported into ParaView, which provided scientific visualization of combined models from each software (See Figure 4). These models provided a view into the movement of the chambers and vessels, blood volume in each chamber, and animation of valve deformations during the cardiac cycle (See Figure 5,6).

Results: The TAV patient had a variety of calculated results, which were used to observe altered hemodynamic parameters caused by triple-valve replacement. The blood volume results for each cardiac frame in the chambers are represented in Table 1 to help understand which frame caused abnormal blood volume. Table 1 portrayed the ten frames as percentages, where 10-40% represented systole, and 50-

100% represented diastole. Images of the four chambers during each cardiac cycle portrayed blood flow during each frame (See Figure 4). Three valve deformations were color-coded to accurately portray which frame caused specific deformation (See Figure 5,6).

Discussion: The results gathered insight into valve deformation and abnormal blood volume in the TAV patient's four chambers. In normal patients, ventricular volume increase begins as early as the last section of systole, continuing over the initial third of diastole [2]. In the results (See Table 1) authors noted this development of precise blood filling, leading them to assume valve replacement and repair were successful in the TAV patient. Unfortunately, according to a cross-sectional study observing age and gender-specific values of left ventricular volume, the mean end-diastolic volume (EDV) for males and females, age groups 11-80 years, ranged from 113-167 mL, which is higher than the 88.03 mL found in the TAV patient. Another study portrayed similar results in the RV, where the mean EDV in healthy patients was measured at 173 (±39) mL, compared to the measured 83.54 mL for the TAV patient [6]. In this study, end-systolic volume (ESV) for healthy patients was 69 (± 22) mL, compared to 37.6 mL of the TAV patient [6]. Concluded by physiological studies, "reduced diastolic filling and ejection fraction can lead to less blood leaving the heart into systemic circulation," and is a common cause of heart failure [2]. The reduced blood volume during EDV for the TAV patient led researchers to assume abnormal blood volume has occurred, potentially caused by any of the three bioprosthetic valves.

Upon further observance of blood volumes in the four chambers, researchers analyzed atrial volume to be skewed for the TAV patient. According to the study mentioned earlier, typical maximal LA volume is 97 (±27) mL, and minimal LA volume is 44 (± 13) mL [6]. The TAV patient's maximal LA volume reached 147.6 mL during ESV, portraying an abnormality in blood flow to cause a LA enlargement (LAE). According to a resource on cardiac physiology, LAE is "the hallmark of the structural remodeling process, which occurs in response to chronic pressure and volume overload" [8]. LAE can induce remodeling of the chambers of the heart and could've been caused by valve malfunction of any of the three valves, which supports the authors' hypothesis that abnormal blood volume was present during the

transition from systole to diastole. A recent scientific report supports the idea that "the direction and angle of aortic inflow and influence helical flow patterns and related hemodynamic features in the thoracic aorta" [5]. The authors' observed valve deformation in the AV, noting the most intense AV movement was observed during the transition from systole to diastole (See Figure 6a). This sudden movement occurs when the valve goes from TAV40 to TAV50, represented by a sudden influx of blood in the LV during TAV50 (See Table 1). This influx causes the AV to adjust quickly, causing the excess blood to leak back into the LA or flow into the aorta during diastole. Another instance of valve deformation was found during the TAV20 and TAV60 for the MV and TV (See Figure 6b). This corresponds to abnormal blood volume found in both atriums during TAV20 and TAV60 (See Table 1). These results relate to the authors' hypothesis that incorrect valve deformation will present abnormal blood volume and blood flow in the four chambers, specifically noted in the LA.

Conclusion & Study Limitations: The results for this study portrayed the effects of LAE, sudden AV deformation during the transition from systole to diastole, MV and TV deformation between 20% and 60%, and abnormal blood volume results during EDV for the TAV patient. This work will provide instances to understand bioprosthetic success and contribute to increasing the life of bioprosthetic valves. This study is currently ongoing, so as more valve replacement patient data becomes available to the authors, the more analysis can be carried out. A setback of this research is noted due to skewed CT images for cardiac frame TAV10, causing altered results of valve deformation, though blood volume was considered. Currently, the authors are continuing to observe other hemodynamic parameters during each cardiac frame via SimVascular, which induces boundary conditions on steady and deforming wall simulations. Authors are also modifying code to include geometric parameters of the three valves. For future work, the authors aim to model each valve's leaflets to increase understanding of leaflet degeneration caused by bioprosthetic valves. Analyzing these instances can further encourage bioprosthetic valve research, influence bioprosthetic valves longevity, and increase patient valve replacement success.

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Appendix:

Table 1: Calculated Volume (mm & mL) of TAV Patient's 10 Cardiac Frames

TAV10	Volume mm^3	Volume mL	TAV20	Volume mm^3	Volume mL	TAV30	Volume mm^3	Volume mL	TAV40	Volume mm^3	Volume mL	TAV50	Volume mm^3	Volume mL
LV	84407.6	84.4076	LV	59880	59.88	LV	46342.1	46.3421	LV	40413.2	40.4132	LV	48660	48.66
LA	47645.4	47.6454	LA	51454.7	51.4547	LA	59099.8	59.0998	LA	147600	147.6	LA	52626.8	52.6268
RV	61815.7	61.8157	RV	52726.9	52.7269	RV	33136.8	33.1368	RV	37600	37.6	RV	54046.9	54.0469
RA	137683	137.683	RA	138527	138.527	RA	147069	147.069	RA	62373.1	62.3731	RA	147340	147.34
TAV60	**Volume (mm^3)**	**Volume (mL)**	**TAV70**	**Volume (mm^3)**	**Volume (mL)**	**TAV80**	**Volume (mm^3)**	**Volume (mL)**	**TAV90**	**Volume (mm^3)**	**Volume (mL)**	**TAV100**	**Volume (mm^3)**	**Volume (mL)**
LV	59180	59.18	LV	70179.9	70.1799	LV	89456.7	89.4567	LV	86649.3	86.6493	LV	88026.2	88.0262
LA	139682	139.682	LA	139819	139.819	LA	139607	139.607	LA	136648	136.648	LA	139531	139.531
RV	51380	51.38	RV	50701.2	50.7012	RV	65952.8	65.9528	RV	74796.5	74.7965	RV	83535.2	83.5352
RA	51380	51.38	RA	44242.7	44.2427	RA	50601.6	50.6016	RA	42108.1	42.1081	RA	43721.6	43.7216

Figures:

Figure 1: Heart Diagram

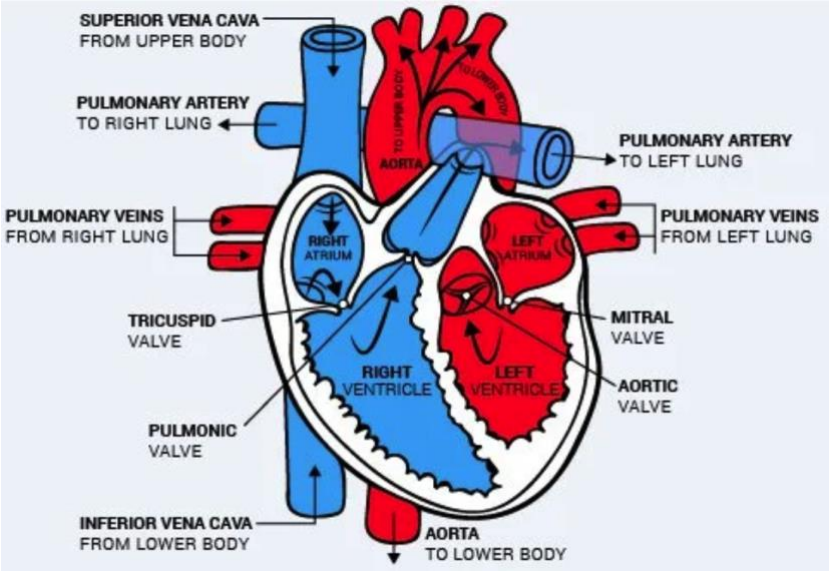

Figure 2: Computational Modeling of SimVascular

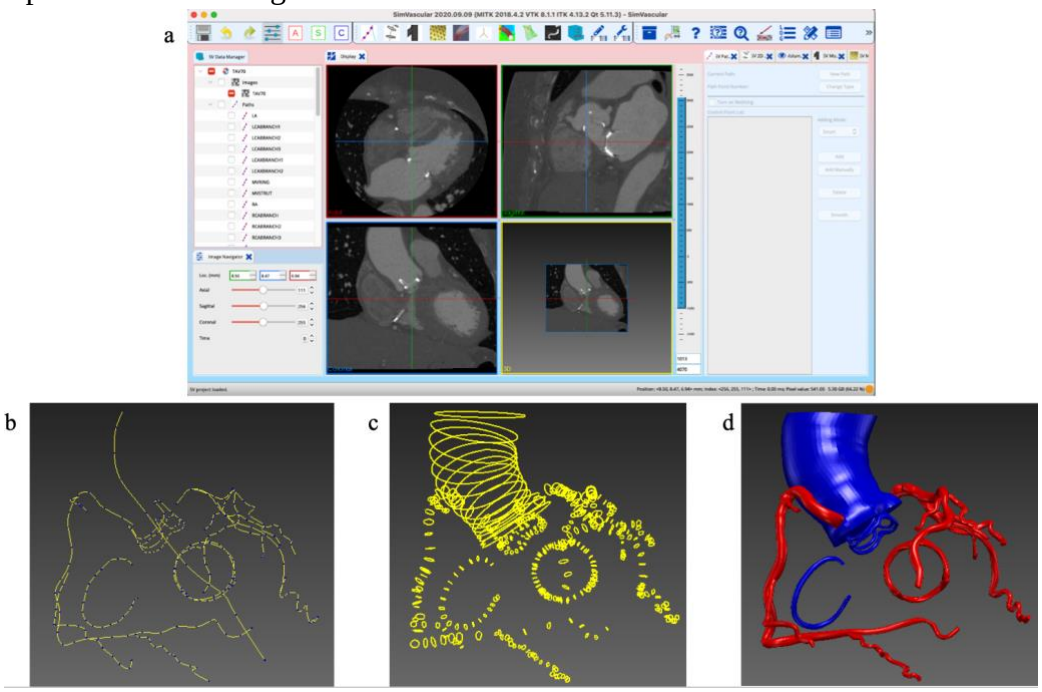

Figure 3: Computational Modelling of ITK-SNAP

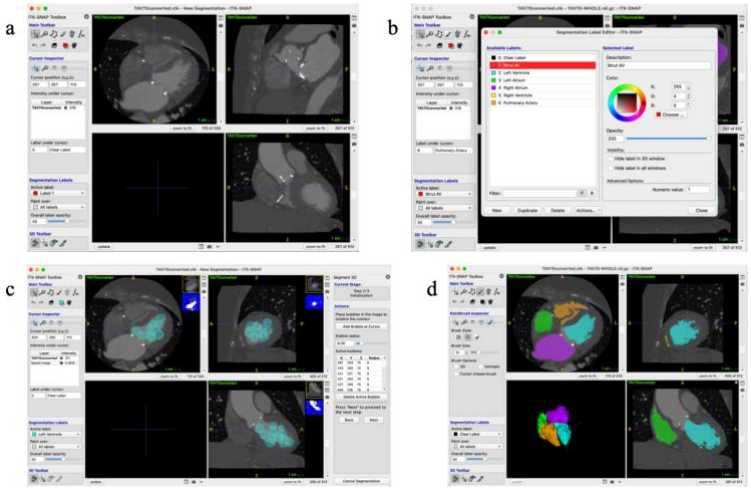

Figure 4: Joint Models in ParaView of Computational Models from SimVascular and ITK-SNAP

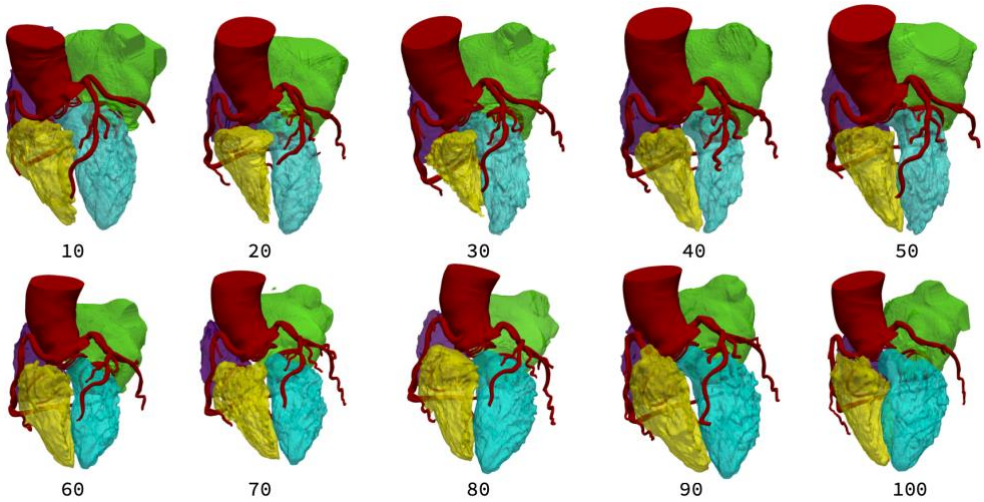

Figure 5: Tricuspid Valve (TV), Mitral Valve (MV), and Aortic Valve (AV) Through 10 Cardiac Frames

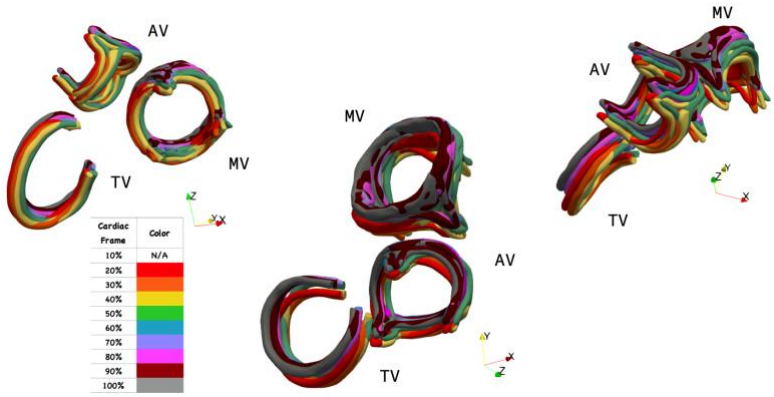

Figure 6a & 6b: Valve Deformation for TV & MV, 20 & 60% (left) and Deformation of AV, 40% & 70%