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Predicting Aortic Regurgitation After Transcatheter Aortic Valve Replacement by Finite Element Method

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ABSTRACT Aortic regurgitation as a severe complication of transcatheter aortic valve replacement (TAVR) is usually due to the aortic valve leaflets that carry severity and inhomogeneous distribution of the calcification. However, it is difficult to precisely simulate the post-procedural biomechanical behavior on aortic tissue. This paper presents and validates a reliable system to predict which aortic stenosis patients may suffer aortic regurgitation after TAVR and to identify the best fit for TAVR valve. We randomly chose 22 patients (12 patients without regurgitation and 10 patients have regurgitation) who had been followed for at least 2 years after TAVR. An elastic model is designed to characterize the biomechanical behavior of the aortic tissue for each patient. After calculating the loading force on the tissue, the finite-element method (FEM) is applied to calculate the stresses of each tissue node. The support vector regression (SVR) method is used to model the relationship between the stress information and the risk of aortic regurgitation. Therefore, the risk of regurgitation and the optimal valve size can be predicted by this integrated model prior to the procedure. Leave-one-out cross-validation is implemented to assess the accuracy of our prediction. As a result, the mean prediction accuracy is 90.9% for all these cases, demonstrating the high value of this model as a decision-making assistant for pre-procedural planning of patients who are scheduled to undergo intervention. This method combines a bio-mechanical and machine learning approach to create a procedural planning tool that may support the clinical decision in the future.

INDEX TERMS Aortic regurgitation, transcatheter aortic valve replacement, finite element method, support vector regression.

I. INTRODUCTION

Aortic Stenosis (AS) is a common degenerative valvular disease in the aged population in the U.S. The number of patients with AS requiring aortic valve intervention is increasing every year. TAVR [1] is used to treat symptomatic patients with calcific AS. Although TAVR has many advantages, favorable outcomes require proper patient selection and meticulous procedural technique to avoid aortic insufficiency. Pursuant to S K. Kodali's reports [2], around 24.7% of patients need some revisions in 2 years after TAVR. The criterion for TAVR patients selection is severe circumferential calcification (porcelain aorta) or heavy atherosclerotic disease burden in the ascending aorta. However, in clinical practice, the severity and distribution of the calcification of valve leaflets are evaluated based on CT scans, which cannot identify the impairment of the TAVR efficacy. Calcium deposits in the native aortic valve might severely affect the expansion of the stent increasing the risk of TAVR failure leading to aortic regurgitation or restenosis as a result of the dysfunction of TAVR prostheses.

Reasons for aortic insufficiency after TAVR are complicated (e.g. displacement, loosening, progression of calcification, and paravalvular regurgitation) [2]–[4], and many of

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them are mechanically related. The mechanical behavior of aortic tissue varies with loading force, which is the contact force between the prosthetic stent and aortic root tissue. After TAVR, the loading force is primarily contributed from the altered stent expansion and calcium deposits in different patients. If the aortic valve leaflets carry severity and inhomogeneous distribution of the calcification, excessive stresses reacting upon the stent will block the function of prosthetic valvular leaflets and lead to early failure of TAVR. At 1 year, up to 75% of AS patients underwent TAVR still have mild or more paravalvular regurgitation [5]–[7]. Current selection of TAVR patients based on CT data may ignore pivotal information. Therefore, in this study, we established a statistical model to describe the relationship between the biomechanical properties of a patient's aortic tissue and aortic regurgitation. The novelty of the proposed approach lies in: [1]. calculation of the loading force on aortic tissue based on altered stent expansion and calcification of valve leaflet distribution [2]. design of elastic model in accordance with the volumetric portion of different tissue layers to characterize the biomechanical behavior of the aortic root and valve tissues; [3]. adoption of support vector regression (SVR) method to investigate relationships between biomechanical properties and the risk of aortic regurgitation after TAVR.

The purpose of this paper is to predict which AS patients have the higher risk of TAVR failure due to biomechanical factors and optimal valve size for AS patient. We hypothesize that severity and inhomogeneous distribution of the calcification of the aortic valve leaflets will block the function of periprosthetic valvular leaflets and lead to the deterioration of cardiac function. The biomechanical information of aortic tissue following virtual intervention can be accurately simulated by integrating a FEM with statistical learning model.

II. METHODS

This study presents an integrated approach to accurately simulate aortic tissue behavior for pre and post intervention respectively for the purpose of improving the aortic regurgitation after TAVR.

A. PARTICIPANTS

TAVR has been performed at Wake Forest Baptist Medical Center since 2011, all patients have the medical history and clinical outcomes information for this study. In this study, we took 22 patients randomly who underwent TAVR and had been followed for at least 2 years to assess risk of aortic regurgitation, among which 12 are males and 10 are females with average age of 80 yrs, ranging from 72 to 89 yrs, and average body mass index (BMI) of 27.7 kg/m^2, ranging from 20.4 to 40.1 kg/m^2. For the purpose of this analysis, post-procedural aortic regurgitation included aortic regurgitation reported immediately after the procedure, AR at 30-day follow-up, or AR at 1-year follow-up. Here we chose the degree of aortic regurgitation at 1-year follow-up as the clinical outcome for modeling, because many patients' regurgitations were improved by themselves after run-in period. Aortic regurgitation was graded none, trace, mild, or moderate according to the Valve Academic Research Consortium criteria [8]. We categorized these 22 cases into two Cohorts: Cohort A consists of 12 patients underwent TAVR only (none and trace regurgitation), while as the Cohort B consists of 10 patients underwent TAVR revision (mild and moderate regurgitation). In this study, we use follow-up study information for each patient as ground truth to confirm the patient selection. Preprocedural CT scans for 22 patients, echocardiography in the clinical database (followed by 12-24 months), were collected at Wake Forest Baptist Medical Center (IRB00012599 has been approved prior to the study).

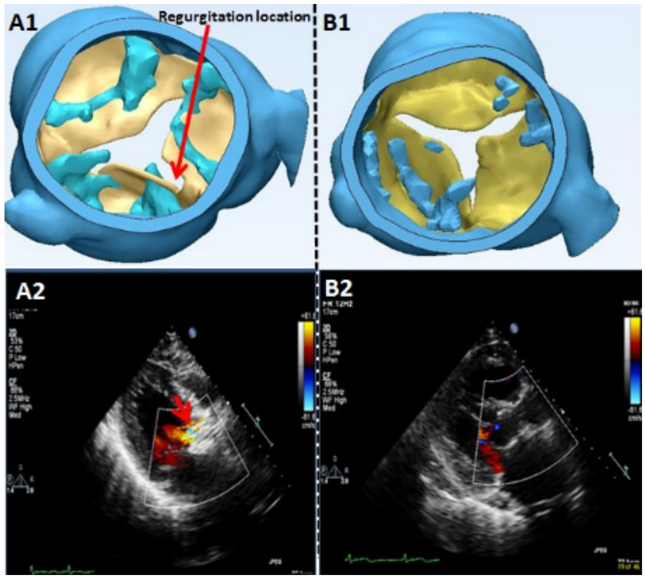

FIGURE 1. Aortic tissue segmentation (aortic root wall, valve and calcium deposits) and echocardiograms. (A1-2) With valvular regurgitation. (B1-2) No valvular regurgitation.

B. FEATURE EXTRACTION

1) AORTIC VALVE AND CALCIFICATION SEGMENTATION AND QUANTIFICATION

Twenty-two patients' CT images were used for valve segmentation. Multi-slice CT images were taken from a stenosis aortic root at peak diastole of the pre-procedural patient. Leaflet calcifications were present on the aortic leaflets, extending from the basal attachments up to the leaflet commissures. CT images were imported into Mimics 17.0 Imaging Software (Materialise, Leuven, Belgium). A 3D anatomically accurate model of the aortic root was created by manually thresholding image from 320-800 Hounsfield units chosen to most accurately preserve aortic root geometry. Segmentation via thresholding allowed for the separation of the aortic root beginning at the left ventricular outflow tract (LVOT) to the sino-tubular junction from the surrounding atria and ventricles [9]–[11]. Calcified aortic valve leaflets were also segmented for further assessment. **Fig.1** shows the segmented

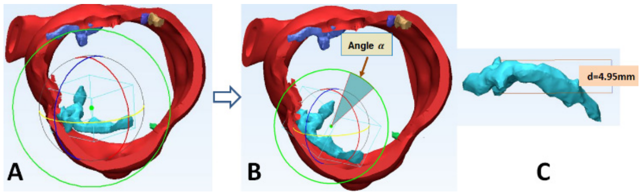

FIGURE 2. **Irregular calcium deposit rotation simulation. A: pre Procedural. B: postprocedural. C: calcium deposit thickness measurement, thickness d = 4.95mm.**

aortic roots with aortic valve and calcified regions from CT data and echocardiograms. To limit the area-of-interest and reduce computational complexity, we restricted the zone to the aortic roots of aorta because no tissue deformations appeared in other regions. **Fig.1 A1-2** demonstrates the case with valvular regurgitation after TAVR. **Fig.1 B1-2** indicates the case without valvular regurgitation after TAVR.

For TAVR, a preprocedural plan is meaningful only if it can be accurately transferred to a patient at the time of intervention. To this end, we have developed and validated the Computer-Aided Calcium Deposits Offset Simulation (CCDOS) system which can identify calcification area accurately pre and post-procedurally. The severity of calcification of valve leaflets can be evaluated by measuring the volume of all calcium deposits in the native aortic valve. Calcium deposits, varying in different size and density, are present within the native aortic valve. In TAVR, the aortic annulus allows for outward expansion (displacement) of prosthetic valve deployment. The prosthetic valve produces an expansive force to outspread aortic annulus. Assuming the distribution of calcium deposits would realign to the aortic wall of the annulus, each calcium deposit changes with displacement and rotation following virtual stent expansion can be calculated precisely. Position changes in calcium deposits with native aortic valve following balloon-expand/ self-expand during TAVR will generate different loading forces against the aortic root. We measured the thickness e of calcium deposits in each leaflet and the coordinate position changes of them using the Virtual Reality Valve Replacement Planning (VRVRP) system. The radial lines for aortic root were marked on a pre-procedural 3D model. The center of the aortic root was determined easily. Then, the calcium deposits shift along the virtual line generated by the centers of the deposit and aortic root, until contacting aortic wall. Rotation occurs in some irregular calcium deposit (**Fig. 2**). The angles of intersection between two centerlines were measured pre-and postprocedurally. Rotation in the calcium deposit after TAVR can be calculated by angle α, which will be used to simulate the contact area between the aortic wall and calcium deposit. Usually, a virtual rotation takes will make the both ends of calcium deposit contact the aortic wall. However, patients may still be at risk for early aortic insufficiency after TAVR because of the calcification of valve leaflets. Therefore, our system addresses the need to develop a reliable system for simulating tissue behavior in aortic valve stenosis patients with TAVR.

2) LOADING FORCE CALCULATION WITH THE POSTPROCEDURAL RADIAL CHANGE OF NATIVE VALVE

To study the mechanical behavior of aortic tissue after the intervention, we calculate the loading force to the 3D aortic root and valve tissue after the virtual valve replacement. The loading force is significantly increased due to calcium deposits following balloon-expand/ self-expand in TAVR. We denote d as the diameter of the largest size of calcium deposit in a native aortic valve, The stiffness of aortic wall (K), was determined by performing linear regression on the force-displacement data in [12]. This characteristic is a critical value defining the overall mechanical characteristics of the aortic tissue. The loading force F (i.e. contact force) is directed along the virtual line on the internal surface of the aortic wall, which is roughly equivalent to the expansive displacement e of the aortic root with the addition of calcium thickness d. Hence, $F = K \cdot (e + d)$ applies to the surface of aortic wall tissue. To reduce computational complexity, we restricted simulation to the biggest calcium deposit in each leaflet. Based on a 3D model of the aortic root wall, pre-procedural circumference C_{annu} of the aortic annulus can be measured precisely. When a TAVR prosthetic valve is deployed on the aortic native annulus, the expansive force produced from the not fully unfold stent with different prosthetic valve size r_{size} can cause the expansion/deformation responses of the aortic annulus. In general, all prosthetic valve sizes are designed slightly larger than the annuli of each TAVR patient. This expansion enables the prosthetic valves to have an expansive force to prevent dislodgement. The aortic annulus is a fibrous ring at the aortic orifice to the front and to the right of the atrioventricular aortic valve and is considered as the transition point between the left ventricle and aortic root. The annulus is part of the fibrous skeleton of the heart. It is at the level of the aortic sinus and is the site of prosthetic aortic valves. After prosthetic valve deployment, the aortic wall changes from irregular morphology to circularity, whose radius equals prosthetic valve size r_{size}, changing from the original radius (without loading force) r_{annu}. Original radius can be estimated as $r_{annu} = \frac{C_{annu}}{2\pi}$. Therefore, in each leaflet, expansive displacement e of aortic root can be calculated as $e = r_{size} - r_{annu}$. The thickness e of calcium deposits is measured in CCDOS system, therefore, the loading force F can be calculated by $F = K \cdot (r_{size} - \frac{C_{annu}}{2\pi} + d)$. The loading force is used to extract the biomechanical properties of the aortic wall tissue by FEM. After TAVR, the prosthetic valve creates a reactive force that works to immobilize it. This results in aortic valve replacement and improves clinical symptoms.

3) BIOMECHANICAL PROPERTIES OF AORTIC ROOT AND VALVE TISSUES

We developed an approach to generate a patient's 3D aortic tissue mesh model from his/her CT data. The segmented aortic roots with aortic valve and calcified regions were

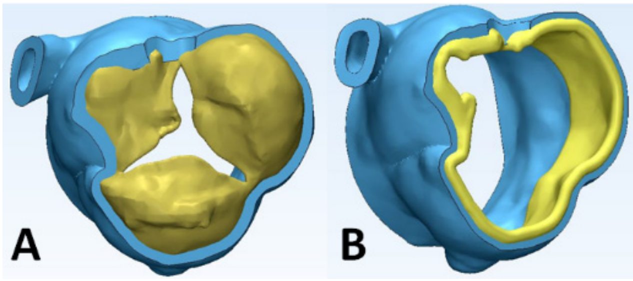

FIGURE 3. Aortic wall and native aortic valve. A: preoperation. B: postoperation, leaflets are extruded to the wall.

TABLE 1. Material parameters of aortic tissue.

	Young's Modulus [MPa]	Poisson's Ratio	Density [Kg/m3]
Aortic Root	2	0.45	2000
Aortic Valve	8	0.45	1100

first discretized the 3D object into small elements (called mesh). The mesh data were generated by using TrueGrid (XYZ Scientific Applications, Inc., Livermore, CA). It is composed of 6832 hexahedral elements and each element contains 8 mesh nodes. To limit the number of elements and reduce the computational complexity, FEM calculation was only restricted to the aortic annulus tissue which is the landing zone of the implanted prosthesis represents the most relevant anatomic structure with regard to aortic stenosis. The mesh nodes can be classified into the boundary and free nodes. The boundary nodes are located in the wall surface parts, which would be repositioned when the stent expands. The free nodes are subject to the displacement of boundary nodes. The displacement boundary condition [13], [14], consisting of the displacements of all the boundary nodes, will be simulated by FEM via adding a loading force on the internal surface of the aortic wall tissue.

4) DETERMINE MATERIAL PROPERTY OF THE AORTIC TISSUES

We incorporated anatomic details of the aortic tissues into the mesh data. **Fig. 3** shows the aortic wall and native aortic valve pre and post procedure. Different material parameters of these two layers were collected from previous studies (**Table 1**) [15]. Those material parameters of aortic tissues in terms of Young's modulus and Poisson's ratio were selected for our FEM calculation as shown in Table 1. To assign aortic tissue properties to FEM mesh data, we segment the tissue into the aortic root and native aortic valve layers. We simply defined the aortic tissue as a tissue with the homogenous and isotropic property. Using CCDOS in above section, we can measure the aortic wall and native aortic valve layers from the whole 3D tissue model. After TAVR deployment, the native leaflets were extruded and surrounded by the aortic root. Thus, the aortic tissue property was determined by weighting the tissue properties of aortic root wall and native aortic valve based on their volumetric proportion in the mesh data.

To do so, we began by measuring the volume of the aortic wall and native aortic valve tissue using Mimics software. Aortic tissue properties were then determined by weighting the tissue properties based on the volumetric proportion of each layer. The equivalent material properties were defined by the volumetric proportion of aortic wall P_{root} in each element of mesh data. Young's Modulus $E = E_{valve}(1-P_{root})+ E_{root}P_{root}$. We can similarly calculate Poisson's Ratio υ. These material parameters are included in the aortic tissue properties for simulating tissue behavior based on Hooke's law [16]. The heterogeneous properties of the aortic tissue will be examined in the proposed studies.

5) FORMULATION OF STRESSES ACCORDING TO LOADING FORCE AND TISSUE PROPERTIES

In TAVR, the aortic annulus allows for outward expansion (displacement) of prosthetic valve deployment. The prosthetic valve produces an expansive force to outspread the aortic annulus. Therefore, to precisely simulate a virtual intervention prior to the TAVR, we formulated the stresses according to the loading force and tissue properties.

We extracted stresses as one of the biomechanical properties from FEM by simulating a virtual prosthetic valve deployment. The stress for each mesh node varies according to different components of aortic annulus in FEM model. Young's modulus E and Poisson's ratio υ were determined in different tissues as tissue material parameters for FEM calculation on each mesh node. Since we mainly focused on the contact region of the prosthesis and aortic tissues, only nodes close to the annulus were selected for the calculation. To obtain a distribution of stress features, we first simulated valvular behavior (i.e., valvular stress from FEM) responding to loading force. Next, the stress vector σ_i was stacked together and employed as the feature of the i th patient. We denoted $\sigma_i = \sigma\left(F_i, E, \upsilon, A_i^{(n)}, P_i\right)$, where, F_i is the loading force of the i th patient. $A_i^{(n)}$ denotes cross-sectional area for the mesh node n *and* P_i is the prosthetic valve type. Finally, $\sigma(\bullet)$ represents the stress modeled by Hooke's law [12] with respect to these parameters. Here, FEM was implemented by the commercial FEM software ANSYS 12.0 (ANSYS Inc, PA). **Fig.4** shows the stress distribution in aortic tissue.

6) MODELING THE RELATIONSHIPS BETWEEN CLINICAL OUTCOME (PARAVALVULAR LEAKAGE OR AORTIC REGURGITATION) AND BIOMECHANICAL PROPERTIES

TAVR outcomes i.e. valvular leakage reflects the aortic regurgitation (AR) after intervention, which is closely related to the biomechanical properties such as stress induced by the prosthetic valve. In previous study [16], SVR was employed to model the relationship because this model can efficiently model any non-linear functions.

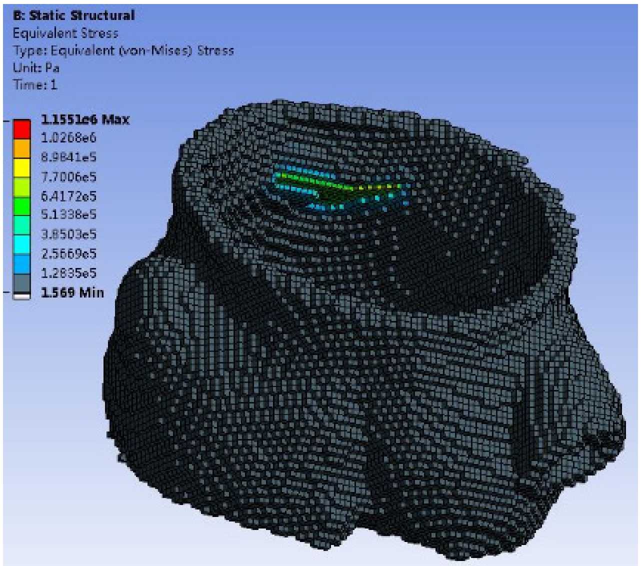

FIGURE 4. Stress distribution in aortic tissue.

Denote biomechanical features as $\sigma_i = \sigma(F_i, E, \upsilon, A_i^{(n)}, P_i)$, calcified volume as V_i, prosthetic valve type as P_i, and then the clinical outcome / aortic regurgitation (AR_i) of ith patient can be modeled as below: $AR_i = g\left[\sigma\left(F_i, E, \upsilon, A_i^{(1)}, P_i\right), \sigma\left(F_i, E, \upsilon, A_i^{(2)}, P_i\right), \ldots, \sigma\left(F_i, E, \upsilon, A_i^{(N)}, P_i\right), V_i, W\right]$.

N is the total number of mesh nodes and g is the support vector regression model $g(x) = \langle w, x\rangle + b$ with x as the input vector, $g(x)$ as output AR. W is the parameters [16] (the coefficients of the variables in g) to be determined by minimizing an objective function as $\hat{W}^* = \underset{W}{argmin}\left\|AR_i - g\left[\sigma\left(F_i, E, \upsilon, A_i^{(1)}, P_i\right), \ldots, \sigma\left(F_i, E, \upsilon, A_i^{(N)}, P_i\right), V_i, W\right]\right\|_{L2\ norm}$ which is calculated from the loading force F_i, the prosthetic valve type P_i, calcified volume V_i, and aortic regurgitation (AR_i). The optimal $\hat{W}^*$ is fixed for TAVR simulation for new patients. The numerical value of the coefficients can reflect which variables contribute mostly for the prediction model. We will design an adaptive learning model [17] for considering other clinical factors once new patients are added to the prediction model.

7) CLINICAL OUTCOME PREDICTION AND THE OPTIMAL VALVE SIZE ESTIMATION

The trained model becomes: $AR_i = g\left[\sigma\left(F, E, \upsilon, A^{(1)}, P\right), \ldots, \sigma\left(F, E, \upsilon, A^{(N)}, P\right), V, \hat{W}^*\right]$. When a new patient is considered for TAVR, the prosthetic valve type P is chosen by current selection criteria [18], loading force F, calcified volume V is calculated by CCDOS and VRVRP base on patient's CT data. $\hat{\theta}^*$ is known from training step. $E, \upsilon, A^{(1)}, \ldots, A^{(N)}$ are calculated from FEM. The risk of aortic insufficiency is predicted from the severity of aortic regurgitation AR. In addition, we employed a dynamic programming approach [19]–[21] to estimate the optimal loading force F for the new patient as below: $\hat{F}^* = \underset{F}{argmin}||AR - g\left[\sigma\left(F, E, \upsilon, A^{(1)}, P\right), \ldots, \sigma\left(F, E, \upsilon, A^{(N)}, P\right), V, \hat{W}^*\right]||$. Here, set $AR = 0$ (no aortic regurgitation). Thus, the optimal loading force can be estimated before TAVR to help in choosing optimal size r_{size} and type of valve, via $F = K \cdot (r_{size} - \frac{C_{annu}}{2\pi} + d)$ in VRVRP workbench developed to avoid excessive stress.

To identify the most relevant features with a high degree of discrimination between TAVR and TAVR revisions, we used the DX score feature selection method [22]. Its effectiveness and efficiency have been confirmed. Here, we selected the top 16 features as vector $[x_i^1, \cdots, x_i^{16}]^T$ with 93.5% impact percentage of all features that affect the outcome, for the ith patient, $i = 1, \ldots, N$. Some contact zone of the aortic tissue with high/excessive stresses will accelerate early deterioration and dysfunction of TAVR prostheses. Our model can underly the mechanism of aortic insufficiency consequently. For example, among biomechanical features $\{x^i\}_{i=1,}^{16}$ related coefficients $\{w^i\}_{i=1,}^{16}$ the $\{w^4, w^7, w^{12}, w^{15}\}$ are the biggest numbers that contribute mostly to the prediction model. These 4 coefficients represent the biomechanical features (excessive stresses) in the contact area of tissue and stent, which will block the function of periprosthetic valvular leaflets and leads to early deterioration and dysfunction of TAVR.

III. RESULTS

When a new patient comes to the hospital, we can accurately simulate the post-procedural biomechanical behavior on aortic tissue with FEM, and predict his/her the risk of regurgitation and optimal valve size with learned SVR model and the new patient's biomechanical information. Thus the procedural decision-making could be done prior to the intervention, reducing the medical cost and the risk related to mortality and unfavorable outcome of TAVR.

Leave-one-out (LOO) CV was implemented to assess the accuracy of our approach. One patient from all patients was used for model testing, while the remaining patients used for model training. The aforesaid procedures were repeated until each patient had been used once as a testing sample. We evaluated the performance based on the difference between the predicted clinical results (aortic regurgitation) and ground truth recorded in the clinical database by 2 years echocardiograms study post-procedurally. The average of prediction accuracy was 90.9% for all cases (20 out of 22).

By keeping the balance of the numbers in two Cohorts for TAVR patients, the receiver operating characteristic (ROC) curve is provided in the **Fig. 5**. The area under the curve (AUC) of prediction is 0.98, indicating our model performed well even with a smaller sample size. The prediction error in some cases may be caused by material nonlinearity.

Sensitivity analysis [16] was performed to explore the model output variation upon perturbation of variables [23], [24] such as loading force F, Young's modules E, Poisson's ratio υ, mesh related cross section area A,

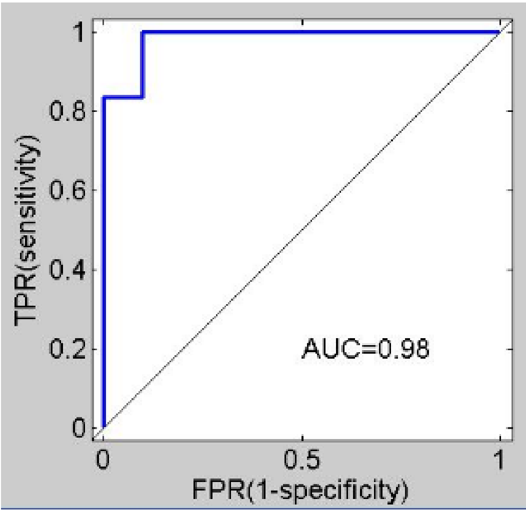

FIGURE 5. ROC curves of our model.

calcified volume V, prosthetic valve type P and parameters [16] such as 16 coefficients $\{w^i\}_{i=1}^{16}$ with 93.5% impact percentage of all features in training model. All of the factor values were perturbed over a range of 5%. Overall, the output variance of our model is bounded by 5%. Therefore, this model is quite stable. **Fig. 6** shows the effectiveness of various factors in our model. The risk factor of aortic insufficiency after TAVR for all patients is insensitive to some material related parameters, e.g., E, υ, (1.4%-1.9% upon 5% parameter perturbation), but is relatively more sensitive to other individual factors such as some biomechanical features and calcified volume V (2.8%-3.6% upon 5% parameter perturbation).

IV. DISCUSSION

Cases 1-12 in Cohort A underwent TAVR without regurgitation, and Cases 13-22 in Cohort B had aortic insufficiency after TAVR need revision due to Mild– or Severe regurgitation. **Table 2** represents the predicted performance of our approach. The average of prediction accuracy was 90.9% for all cases (20 out of 22). Certain cases failed for reasons cannot be attributed to the model. For example, Case # 4 failed because of prosthetic breakdown. It resulted in a central aortic regurgitation jet. Case # 18 failed because of displacement of the aortic prosthetic valve. This case required a novel stabilized valve. Our model indicated that excessive stress concentrations were observed around the calcified deposits in the aortic leaflets as well as at the aortic wall closed to the leaflets and the aortic sinuses. These excessive stress concentrations demonstrated that the aortic leaflets carried a large amount of loading force, thus, helped anchor the prosthesis in appropriate position. Unreliable deployment of prosthetic valves can lead to post-procedural aortic regurgitation due to a potential of aortic tissue tearing and breakdown of calcium deposits in calcified regions. More concerning was that even mild paravalvular leak cases after TAVR were associated with 10–15% higher mortality at 2 years than patients with none or trace paravalvular leak [25]. Many of the AS patients with mild regurgitation of the native aortic valve can remain asymptomatic and bear the specific condition for a long time, but TAVR patients do not appear to endure any regurgitation for unknown reasons. Postdeployment aortic regurgitation is usually paravalvular, and repeat ballooning may reduce leaks and is routinely used when they are severe.

TAVR depends on the calcified valve leaflets and annulus to anchor the apparatus, which means there will have an unavoidable risk for the inadequate seal between the valve stent and the irregular surface of the calcium deposits, native leaflets, and annulus. Underestimation of distribution of calcification can result in the placement of a TAVR valve that is too large with the increased risk of incomplete expansion of the construct or catastrophic annular rupture. Overestimation can lead to increased paravalvular leakage or unstable valve deployment. True annulus size must be segmented for measurement and without overlying calcium. The segmented calcium deposits may result in the dysfunction of periprosthetic valvular leaflets and lead to aortic regurgitation. The primary reason is that severity and distribution of calcification of valve leaflets can produce excessive stresses react upon the stent, which blocks the function of periprosthetic valvular leaflets and impair TAVR efficacy [26].

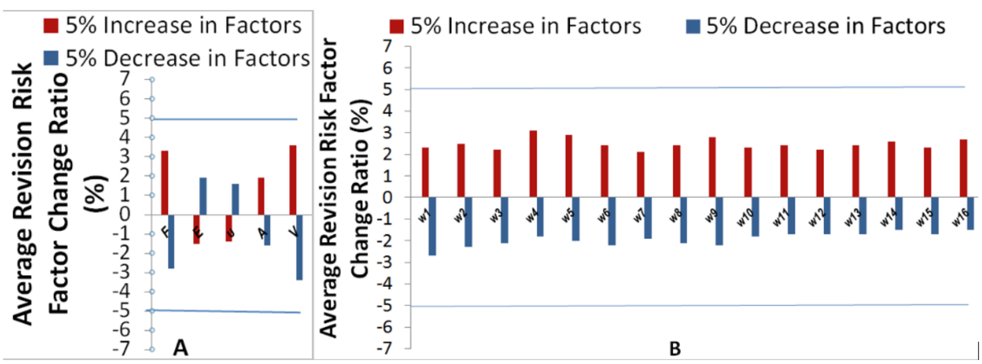

FIGURE 6. Sensitivity analysis for (A) the variables related Parameters and (B) model parameters: Coefficients $\{w^i\}_{i=1}^{15}$, and w^{16} (corresponding to calcified volume).

TABLE 2. Prediction performance on two groups.

No	True type for replacement	Calcified Volume (mm^3)	Aortic Regurgitation after TAVR	Predicted Results (0=TAVR without Regurgitation. 1=Regurgitation TAVR failure)	Applied Valve Size (mm)	Optimal Valve Size (mm)
1	TAVR	403	Trace	0.227	26	26
2	TAVR	425	No	0.151	29	29
3	TAVR	386	Trace	0.325	31	30
4	TAVR	445	Trace	0.607(TAVR)	23	24
5	TAVR	512	Trace	0.255	26	26
6	TAVR	683	Trace	0.234	23	24
7	TAVR	461	No	0.376	26	26
8	TAVR	442	No	0.189	26	26
9	TAVR	408	No	0.239	29	29
10	TAVR	392	No	0.468	29	29
11	TAVR	354	No	0.365	26	27
12	TAVR	362	No	0.272	23	23
13	TAVR failure	516	Mild	0.906	26	24
14	TAVR failure	532	Mild	0.784	23	25
15	TAVR failure	490	Moderate	0.835	23	25
16	TAVR failure	425	mild	0.621	26	28
17	TAVR failure	342	Mild	0.873	26	25
18	TAVR failure	556	Mild	0.389(Failure)	29	27
19	TAVR failure	432	Mild	0.915	26	27
20	TAVR failure	323	Mild	0.882	26	28
21	TAVR failure	472	Mild	0.725	29	27
22	TAVR failure	436	Mild	0.832	31	30

TAVR offers benefits to AS patients who are considered for inoperable or at a high risk of surgical valve replacement. However, complicated issues that adversely affect TAVR outcomes remain, and proper patient selection and apparatus design may help address current challenges. The optimal valve size estimation results from our model showed much consistence with the actual sizes in Cohort A. In Cohort B, the estimation results can reduce the excessive stress of aortic tissue, which may delay the early deterioration and dysfunction of TAVR prosthetic valve and leads to a favorable outcome.

On account of the complexity and variability of the aortic root anatomy, the incidence and severity of post-procedural aortic regurgitation are difficult to predict, indicating the need of a model that aid the cardiologist to select the optimal type and size of valve that best fits the individual patient. Accurate simulation of a TAVR procedure that is based upon the integration of the patient-specific anatomy, the biomechanical properties of the aortic tissue, and structure of prosthesis may serve this goal. In summary, our approach performed well in predicting aortic regurgitation for the aortic stenosis patients. The combination of biomechanical properties and machine learning method substantially improved prediction of clinical results. A nonlinear FEM approach will be used to improve the accuracy in the future.

The limitations of our study are that there are very small numbers and we do not have the capability of accounting for factors other than biomechanical. The limitations in this study cause aortic valve insufficiency after TAVR exclude stroke, malpositioning, valve migration/embolization, pacemaker implantation, blocking the coronary ostia, anterior mitral leaflet mobility, and atrioventricular conduction system dysfunction. Specific exclusion criteria are noted, in particular, native annular size <18 mm or >25 mm, bicuspid aortic valve, severe mitral regurgitation, left ventricular (LV) ejection fraction $<20\%$, renal failure, and estimated life expectancy <12 months.

V. CONCLUSION

In this work, we proposed a systematic approach to predict the risk of aortic regurgitation and the optimal valve size.

A 3D FEM of the aortic tissue was constructed to extract biomechanical stress information. The SVR method was used to model the relationships between the biomechanical stress information and the risk of aortic regurgitation. We have combined bio-mechanical and machine learning modeling to create a pre-procedural planning tool which may support clinical decision making reducing the medical cost and the risk related to mortality and unfavorable outcome of TAVR prior to the intervention in the future.

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