ORIGINAL ARTICLE

The necessity of applying 3D printing technique to the preoperative evaluation of transcatheter aortic valve replacement: Re-analysis of 4 death cases

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Transcatheter aortic valve replacement (TAVR) has already been used as a standard treatment for patients with symptomatic severe aortic stenosis (AS). Pre-procedural cardiac computed tomography (CT) is required to simulate the annulus sizing. However, limitations of CT should be highlighted: 1. The valve annulus structure could only be measured through the certain plane, three-dimensional structure is not fully reflected; 2. It cannot assess the situation after implantation, such as relative movement of calcification and annulus, and the changes of the coronary ostium direction and height; and 3. It cannot predict intraoperative and postoperative complications accurately. Three-dimensional (3D) printing could establish individualized anatomy models for pre-operative planning. This study aimed at determining whether 3D printed models could be used for predicting the complications which other pre-procedural imaging techniques failed to.

Key Words: *3D Printing; Preoperative evaluation*

INTRODUCTION

Patients with aortic valve stenosis accepted in our vascular center who died after TAVR between June 2011 and June 2016 were enrolled in the study. In total, 4 patients were retrospectively collected, whose pre- TAVR cardiac CT were available and indicated no fatal complications. The causes of the death were preliminarily proved to be 2 coronary obstructions and 2 annular ruptures (Table 1).

MATERIALS AND METHODS

All patients in the study received balloon-expandable Edwards Sapien XT valve treatment. Prosthesis size was selected by SAPIEN sizing calculator, based on the annulus diameter calculated from annular cross-sectional area (CSA) measured by cardiac CT (1-3).

Pre-procedural cardiac CT

All patients' cardiac CT were performed under an inspiratory breath-hold while the electrocardiogram (ECG) was recorded simultaneously to allow retrospective through the heart over a complete R-R interval (0-99%) by every 5%-time phase, using a 320 × 0.5 mm detector row scanner CT (Toshiba Aquilion ONE Dynamic Volume CT). Patients received about 50 ml iodinated contrast, followed by 40 ml normal saline solution at a rate of 5 ml per second (4-6).

Creation of 3D models

Aiming at better preoperative assessment and more accurate forecast for postoperative complications, 4 cases died during TAVR procedure were re-analyzed by 3D models based on CTA data. These 3D models were created by selecting the template at the R-R interval 30%-40% (systolic phase), during the maximal opening of the aortic valve (7).

The CT datasets of the patients were imported into 3D construction software (Mimics, Materialize). The corresponding threshold values for each patient were adjusted to capture the individual contrast range, and to semi-automatically exclude the calcium. The blood pool included aortic root, annulus and left ventricular outflow tract. The calcium was segmented manually. Segmented model were then imported into the computer aided design software (3-matic, materialize) to reconstruct the blood vessel wall and aortic valve, a 2 mm thick wall was added to the outside of the blood pool in all models, and a 1 mm aortic valve was added to aortic root; this strategy was necessary because the true aortic wall and valve leaflets were too thin to segment. Finally, the blood vessel wall, valve leaflets and calcium were combined into one model named aortic root model. After all, the aortic root models were converted to 3D printable standard tessellation language (STL) files.

Aortic models were 3D printed using a 3D printer and blood vessel and valves were printed with flexible material (Heart Print Flex) and calcium

TABLE 1

Study population

Patient	CSA (mm²)	Annulus diameter (mm)	Distance between annulus and coronary ostium (mm)		Valve size (mm)	Complication	Cause of death
			left	right			
1	618	28	11.1	16	29	Left coronary obstruction	Acute myocardial infarction
2	276	18.7	19.9	12	23	Left coronary obstruction	Acute myocardial infarction
3	491	25	9.47	11.2	26	Annular rupture	Acute pericardial tamponade
4	607	27.8	11.5	14.4	29	Annular rupture	Acute pericardial tamponade

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was printed with a rigid white material. As both Young's modulus and distensibility of the HreatPrint Flex model were in compliance with human arterial tissue properties, the designed model thereafter not only offers the correct geometry of the aorta, but also mimics the material behavior of the real anatomy.

Release test in 3D models

We designed a release test using the non-valve stent mode that was consistent with Edwards Sapien XT valve in size and radial support force, to predict complications during and after operations. A 0.035-inch guide wire from the ascending aorta was put into the left ventricular outflow tract through the aortic valve, the pre-dilation balloon in the corresponding size was selected to the annulus and was placed at the annulus level, and then valvuloplasty was performed. The stent model was delivered to the annulus level and implanted by injecting the balloon with the same amount of normal saline as used in the actual operation.

The whole process was observed and recorded by endoscope, especially the valve leaflets and annulus, so that we can know the anatomic relationships between the prosthetic valve and the aortic valve complex such as coronary ostia, calcification, etc., after the operation.

The presence of coronary occlusion was confirmed when the edge of the prosthetic was higher than the coronary ostia, or when the calcification was pushed towards the coronary ostia. As the HreatPrint Flex printed model biomimetically imitated the aorta, the presence of aortic annulus rupture was defined as the rupture of the model during or after the process.

RESULTS

Patient 1

<u>Pre-operation</u>

The calcification was obviously seen in the left ventricular outflow tract side of the valve; the calcification ridge was observed in the junction of non-coronary and right coronary valves and the calcification was seen attached to the edge of the left coronary valve leaflet.

<u>Intro-operation</u>

It could be seen after the balloon valvuloplasty, the left and right coronary ostia (red arrows) were intact Figure 1.

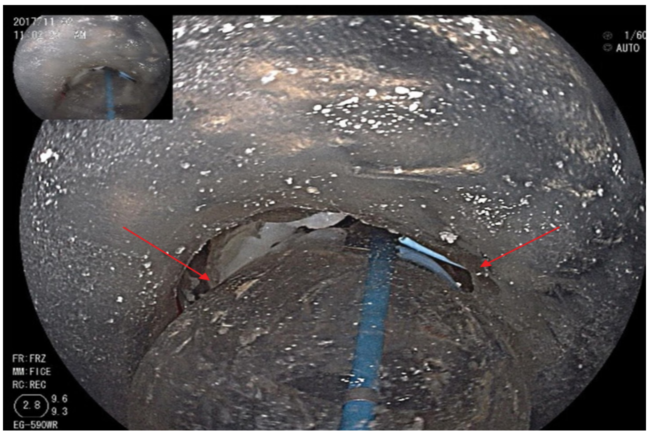

Figure 1) *After the balloon valvuloplasty, the left and right coronary ostia (red arrows) were intact*

<u>Post-operation</u>

After implanting the stent, it was clearly observed from the ascending aorta side that the left coronary valve was pressed towards the annulus after stent expansion; the calcification clump of the leaflet obviously blocked the left coronary ostium Figure 2a, while the right ostium was not affected Figure 2b.

Patient 2

<u>Pre-operation</u>

The calcification was evidently in the side of the valve leaflet which faced towards the ascending aorta, especially in the right coronary valve. Calcification was not observed in the left ventricular outflow tract Figure 3.

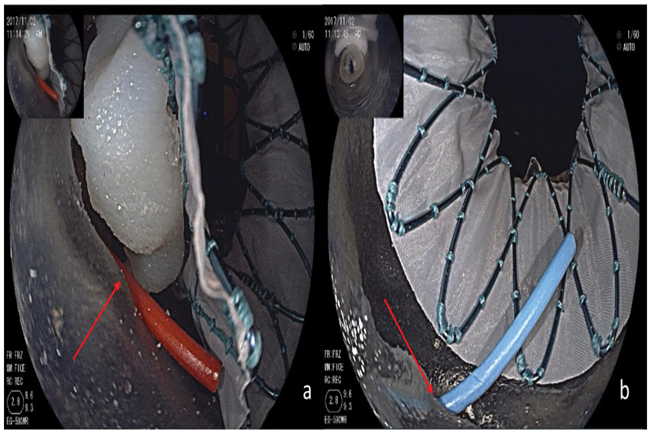

Figure 2) *After the THV was implanted at the annulus plane, the calcification clump of the leaflet obviously blocked the left coronary ostia (a), while the right ostia were intact (b)*

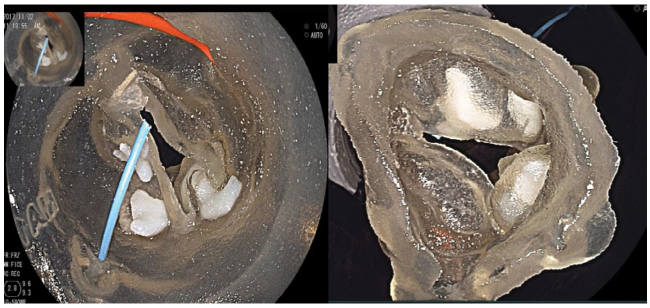

Figure 3) *The calcification was evidently in the side of the valve leaflet which faced towards the ascending aorta, especially in the right coronary valve (red wire came from the left coronary ostia; blue wire came from the right coronary ostia)*

<u>Intro-operation</u>

The valve structure remained intact after the balloon valvuloplasty.

<u>Post operation</u>

The stent was accurately positioned. The distal edge of the stent could be harmful to the left coronary ostium, which was partially covered after the implantation Figure 4a. The right coronary ostium was not influenced by the stent structure Figure 4b. The in vitro test by 3D model compares favorably with the DSA during the operation Figure 4c.

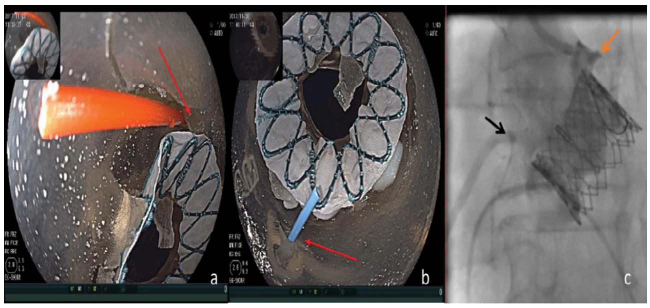

Figure 4) *The left coronary ostia were partially covered by the distal edge of prosthesis (a), the right coronary ostium was not influenced (b), compares favorably with the DSA during the operation (c)*

Patient 3

<u>Pre-operation</u>

The valve was in a good condition observed from the ascending aorta side Figure 5a.

The patient could be defined as bicuspid, Type 0 from the left ventricular outflow tract. The calcification plaques could be seen at the left coronary leaflet Figure 5b.

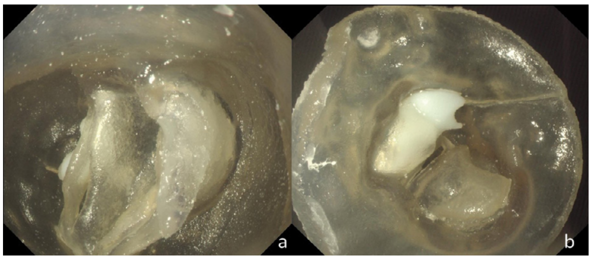

Figure 5) *The patient could be defined as bicuspid with two leaflets from the ascending aorta (a) and the left ventricular outflow tract (b)*

Intro-operation

The annulus displayed rupture to a certain degree after the pre-expanding balloon inflated to the largest extent, while the overall shape of the valve can remain after the balloon withdrawal Figure 6.

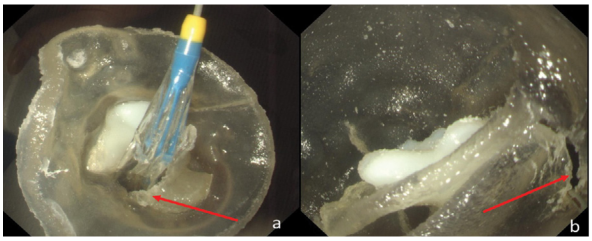

Figure 6) *After the balloon valvuloplasty, the annulus was rupture at a slight degree (red arrows)*

Post-operation

The stent was well embedded, the valve avulsion was clear, while the shape was changed. Stent displacement occurred due to the annulus rupture, both left and right coronary arterial openings were partially covered. Five minutes after releasing, the annulus model was torn from the annulus to the ascending aorta Figure 7.

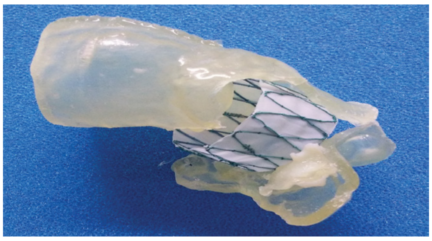

Figure 7) *There was annular rupture after the THV was implanted*

Patient 4

Pre-operation

The patient was clearly defined as bicuspid Type I. Calcification was also apparent in the surrounding area of the valve annulus and the junction of the left and right coronary valve, where the calcification ridge was formed Figure 8.

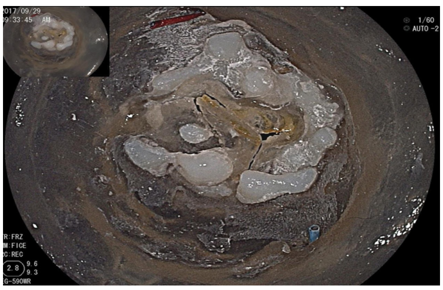

Figure 8) *Calcification was apparent in the surrounding area of the annulus and the junction of the left (blue wire) and right (red wire) coronary valve*

Intro-operation

The annulus did not show obvious rupture after the pre-expanding balloon inflated to the largest extent, and the overall shape of the valve can remain after the balloon withdrawal.

A 29 mm non-valve stent was successfully transferred to the annulus by the guiding wire through the delivery system. After injecting 33cc water by the pressure pump, the balloon expands successfully. The junction of the right and left coronary valve showed the evidence of tear, and the partial tear also appeared between non-coronary and right coronary valve. The stent was released at the annular plane Figure 9.

Figure 9) *The THV was decentration after implanted, cause of the calcification. The left (blue wire) and right red wire) coronary ostia were intact*

Post-operation

The stent was well placed. The red guiding wire barely entered the aorta through the left coronary artery, which was partially covered by the stent and the valve. While the blue guiding wire entered the aorta root via the right coronary artery which was also partially covered, it can barely pass through the gap between the stent and the coronary sinus. The original partial tear at the junction of right and non-coronary valve led to the annulus rupture that pointed from the annulus to the ascending aorta due to the persistent existence of the stent.

DISCUSSION

The advantages of 3D model in pre-operation evaluation. CTA assesses the annulus structure in a plane that is formed by the aortic cusp hinge points of the three valve leaflets (8). This method can only realize the planar evaluation instead of 3-dimensional evaluation, thus cannot accurately assess the pathological structure of annulus and leaflets (9). For instance, patient 3 was Type 0 bicuspid that only has two valve leaflets, which cannot form a plane with their aortic cusp hinge points, thus the planar measurement by CTA cannot be realized (10).

The valve and annulus of the patient are pathological tissues; the asymmetry and the eccentricity of the aortic cusp hinge points that caused by the structural or calcification, supravalvular aortic stenosis, valve hypertrophy, and sub valvular obstruction, all can lead to the narrowest plane to be off the annulus after the stent release. Therefore, the actual conditions of the narrowest plane in the surrounding area of the aortic valve cannot be fully assessed by CT.

3D model can precisely mimic related structures from the aortic root to the left ventricular outflow tract (11). Besides depending on the diameter, circumference and the area, it takes various factors and in vitro releasing results into consideration, and the valve annulus structure can be measured under directly observation. Integrating the valve condition after releasing, 3D model takes measurement on the selected anchoring panel and reminds the potential complications caused by the discrepancy in shape (the diameters are the same) in and after the operation.

Furthermore, it is unable to carry out the intro-operation and post-operation evaluation by CTA, because the location and direction of the coronary ostia would change after placing the prosthesis into the annulus due to the structure itself and the calcification.

3D model can reflect the complex structures of annulus and leaflets. Combining with in vitro release, it can simulate the operation, imitate the relative movement of the coronary ostia and calcification, and predict the intra and postoperative complications. The advantage of 3D model in reminding the potential risk of the coronary artery obstruction.

CTA evaluates the risk of coronary artery by comparing the prosthesis height with the vertical distance from the coronary ostia to the annulus plane. Although the annulus will expand in the parallel level, the study showed that the possibility of annulus expansion is very small (2). However, the relative distance between coronary ostia and the annulus plane and the angle between its flow direction and the aorta will change after implantation, which further influences the blood supply.

3D printed model can appropriately elongate the printed length of the coronary artery to observe the artery flow direction and shape, and to analyze the relationship between the coronary artery and the aorta root. Incorporating the in vitro experiment results, the 3D model can predict the coronary artery change after implantation and its condition in and after the operation.

Calcification related risk analysis by 3D model

The calcification around the annulus is an important factor in causing the annulus rupture, coronary artery obstruction, displacement of prosthesis and other severe complications (12,13). Especially, the risk caused by the calcification after implantation cannot be evaluated by the traditional imaging. At present, CTA can only realize the initial assessment via parameters like calcification score, size, ridge height and location. It is indicated by the previous TAVR surgeries and the in vitro release test in this study that calcification is a risk factor in TAVR, especially the calcification with sharp morphology, wide range and high ridge, which are easy to cause the annulus rupture, coronary ostia obstruction and other sever complications.

The application of 3D model in the *in vitro* release is very beneficial in observing the relative motion of calcification and the annulus in and after the operation. Based on the observation in this study, two situations were presented in terms of calcification movement: Affected by the stent radial supporting force, the calcification combined loosely with the surrounding tissues, and moved outward with the stent expansion Figure 10a.

Due to loose connection between the calcification and surrounding tissue, the calcification stayed relatively static during the stent expansion process. At the same time, the calcification blocked the stent expansion and led to the outward movement of the annulus tissue on two sides, which was pushed by the expanding stent, as a result, the calcification relatively moved inward Figure 10b.

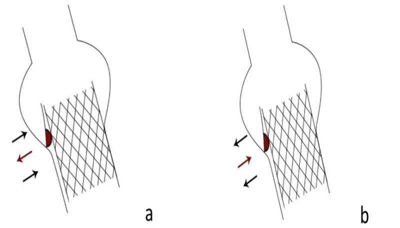

Figure 10) *The calcification was pushed outward(a) and inward(b) relative to the annulus*

We can also find that the calcification clump of the leaflet may be pushed towards the coronary sinus, causing the coronary ostium obstruction. The correlation of the mode of calcification motion and annulus rupture requires further mechanical experimental analysis and in vitro experiment to demonstrate. However, it is undoubted that 3D model can better restore the relative motion of the calcification.

Application of 3D model

As reported by previous literature and in this study, 3D model has significant advantage over CTA in terms of the assessment in important factors such as abnormal calcification, annulus plane and coronary artery risks, it can as well predict the complications in and after the operation (14,15). 3D model is applicable to surgeries with higher risks, especially to patients with complex annulus and leaflet structures, severe calcification and poor coronary artery conditions.

Incorporating the in vitro experiment, we may find that the size of prosthesis is larger than the theoretical value, the risk of the coronary artery obstruction, and then try to avoid risks by reducing the prosthesis size, changing the surgical path or the type of prosthesis. These trial methods can also be verified in in vitro experiments.

CONCLUSION

The heart should be kept at systolic state using temporary pace maker when expanding the balloon and placing the stent during the operation. The 3D model, similarly, was constructed and printed based on the systolic phase. As a result, it can simulate the morphological conditions in the operation. The 3D model was constructed with HeartPrint Flex material, whose Young's modulus and distensibility were close to that of human arterial tissue. The designed model, therefore, not only simulated the geometry of the aorta, but also mimicked the material behavior of the real anatomy. The 3D model could predict the obstruction of coronary artery and the rupture of valve annulus in the in vitro releasing process. These risks were consistent with DSA observations in the operation but not detected in the preoperative CT.

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