Hemodynamics of the Edwards Sapien XT transcatheter heart valve in noncircular aortic annuli

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Objectives: During implantation of transcatheter aortic valves into severe calcified aortic annuli, misdeployments due to asymmetric shapes of the target region were reported. Whether the resultant stent deformations influence valve performance has not been quantified. The objective of this study was to investigate in vitro hemodynamics of the Edwards Sapien XT (Edwards Lifesciences, Irvine, Calif) after valve deployment in noncircular aortic annuli.

Methods: Six Edwards Sapien XT valves were implanted into a model of the aortic annulus with different shapes (elliptical, triangular, and bulged compared with ideal circular) and investigated in a pulsatile flow simulator. Leakage was determined by ultrasonic flow measurements, and leaflet coaptation was visualized by high-speed video. In addition, the origin of leakage was investigated under static pressure.

Results: The lowest amount of leakage occurred in the ideal circular shape, whereas in most of the noncircular configurations increased transvalvular leakage due to paravalvular leaks and folds at the free edges of the leaflets was found, more often by implantation of the valve within a triangular annulus shape. Implantation of the valves into the elliptical configuration with the prosthesis commissure directed to the longitudinal axis of the annular plane showed similar values compared with the circular annulus. Pressure gradients were not influenced by the valve distortion.

Conclusions: Implantation of the Edwards Sapien XT transcatheter valve into non–circular-shaped aortic annuli leads to increased leakage. Annulus shape and relative position of the prosthesis are main determinants of leakage. Implantation into elliptical annuli, as found in bicuspid aortic valves, seems feasible. (J Thorac Cardiovasc Surg 2014;148:126-32)

ACD

Aortic stenosis (AS) is the most frequent valvular heart disease. The gold standard of therapy for patients with AS is aortic valve replacement; however, patients with severe calcification of the aorta and elderly patients with serious comorbidities are at risk with conventional open surgery.

For these patients, the transcatheter aortic valve implantation (TAVI) has emerged as an attractive alternative since 2002. The advantage of this technique is the reduced invasiveness, which holds true for both TAVI techniques, the transfemoral and transapical approaches. The number of TAVI procedures increased rapidly during the last years, up to 5083 procedures in Germany in 2011.[1] Initial clinical results of the technique are promising, but in addition to other procedure-related morbidity, such as vascular complications, strokes, and arrhythmias, post-interventional transvalvular and paravalvular leaks frequently are diagnosed and residual aortic regurgitation was found in 50% to 72.4% of cases.[2,3] Recent findings from the Placement of Aortic Transcatheter Valves trial suggest that even mild transvalvular leaks are associated with higher mortalities at 2 years,[4] underlining the importance of this residual hemodynamic lesion.

Not only the valve phenotype (tricuspid and bicuspid) but also the nonuniform distribution of the calcification within the surrounding tissue (ie, the leaflets and aortic annulus) can provoke uneven expansion of the prosthesis stent and inadequate adaptation of the stent to the target region. Investigations with multidetector computed tomography confirmed such nonuniform calcifications in patients. The locations of the calcification were the hinge points between the leaflets and the annulus, the commissures and the free edge of the leaflets. Also, an aortic valve annulus with an eccentric shape showed a higher degree of regurgitation after TAVI.[5,6]

In a recent investigation, Zegdi and colleagues[7] described typical deformations of valve stents in simulated TAVI. In normal tricuspid aortic valves, a circular shape was found most frequently after stent implantation, but elliptical and triangular configurations also became visible, which affected the stent symmetry. The aortic annulus of patients with a bicuspid aortic valve showed an elliptical shape in the majority of cases and occasionally local irregularities

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Abbreviations and Acronyms
AS = aortic stenosis
TAVI = transcatheter aortic valve implantation

such as prominent plaques influenced the geometry. Consequently, Zegdi and colleagues were able to confirm the incidence of some kind of distortion of the prosthesis after the stent deployment, which may impair the function of an implanted valve.

However, the investigation by Zegdi and colleagues[7] was conducted qualitatively. The aim of this study was to quantify the hemodynamics of a frequently used transcatheter valve, the Edwards Sapien XT prosthesis (Edwards Lifesciences, Irvine, Calif) after TAVI in different noncircular aortic annuli in an in vitro setup.

MATERIALS AND METHODS

In this study, 26-mm Edwards Sapien XT transcatheter aortic valves (n = 6) were used in a model of an aortic root composed of a vascular prosthesis incorporating plastic inserts simulating different annulus shapes (Figure 1). The mean inner diameters of these artificial annuli were 24 mm. The shapes of the annuli were circular, representing an ideal aortic annulus as reference (R); elliptical (E), which is often found in patients with a bicuspid aortic valve (EK, commissure of the valve prosthesis on the short axis; EL, commissure on the longitudinal axis of the annular plane), with a ratio of 1.2 between the long and short axis; triangular (T) as a simulation of severely calcified valve leaflets in combination with a less calcified annulus (TK, commissure of the prosthesis on the commissural area of artificial annulus; TL, commissure of the prosthesis on valve leaflet position), and a circular shape with bulge (B) as a simulation of a prominent atherosclerotic plaque (BK, commissure of the prosthesis on plaque; BL, commissure shifted apart from plaque).

First, valves were implanted and tested in the regular circular configuration and subsequently implanted into the noncircular annuli in both commissural orientations. The sequential arrangement of the different annuli was randomly varied to minimize the influence of the necessary multiple folding of the valves. The implantation was performed in transapical fashion in accordance with the clinical implantation procedure of the Edwards Sapien XT using the Ascendra+ system (Edwards Lifesciences). The post-procedural adaption to the artificial annulus was examined and a redilatation was performed if necessary, with the same balloon filling as initial.

Pressures were measured via capacitive pressure sensors (Endress+Hauser, Maulburg, Germany), and the volume flow through the valve was measured with an ultrasonic flowmeter (Transonic Inc, Ithaca, NY). A high-speed camera (Motionscope HR-1000; Redlake Imaging Corp, Morgan Hill, Calif) was mounted above the valve to record the movements of the valves leaflets at 500 frames per second. The measurements were performed under conventional physiologic conditions in the pulse duplicator, the details of which have been described.[8] The data were analyzed according to the international standard for the testing of heart valves (ISO 5840[9]).

In addition, 2 valves were exemplarily investigated under static pressure while implanted into the triangular shape in both configurations to obtain more information about the location of the leakage. In this regard, the contact area between prosthesis and annulus was sealed with silicon to exclude paravalvular leaks.

Statistical analysis of the hemodynamic parameters was performed by the Friedman rank-sum test and subsequent Wilcoxon tests.

RESULTS

The results of the hemodynamic measurements are shown in Table 1. Significance could not be ascertained at mean and peak pressure and in closing volumes. A significant increase in leak volume was found in most of the noncircular configurations (R vs EK with $P = .0464$; R vs TK with $P = .0277$; R vs TL with $P = .0464$; R vs BL with $P = .0464$), except the elliptical shape (with the commissure of the prosthesis on the longitudinal axis of the annular plane) and the circular shape with bulge (with the commissure of the prosthesis on plaque). We have proven the significance in leak volumes between the 2 commissure positions of the elliptical annulus (EL vs EK with $P = .0277$).

The evaluation of the video recordings showed pronounced buckling and folding of the leaflet edges in nearly all noncircular configurations. The implantation of the valves within the triangular annulus shape showed areas at which the prostheses did not completely adapt to the aortic annulus, also in case of the circular shape with plaque the valve stents did not adapt to the annulus in the vicinity of the plaque (Figure 2, *top*).

Within the elliptical configuration, different behaviors of the valves could be detected between both orientations of the commissure. In the configuration with the prosthesis commissure orientated on the short axis of the annulus plane, similar deformations of the leaflet edges as described earlier became obvious (Figure 2, *bottom*), whereas with the commissure in the longitudinal axis a nearly unaffected valve configuration was observed. Under static pressure, valvular leakage flow was distinctly visible at the marked folds, both medial and in the field of coaptation area (Figure 3).

DISCUSSION

TAVI is rapidly emerging as a new therapy option for patients with severe AS and high surgical risk. In addition to the excellent results in most patients, there is still a risk of complications, such as vascular injuries, strokes, arrhythmias, and leakage.[10] The latter may be caused because TAVI usually leaves calcium deposits behind, which leads to irregular shapes of the anchoring site. The present study showed that TAVI in noncircular aortic annuli results in an increase of leakage depending on the different shapes of the annulus.

The main reason for AS is calcium deposition into the tissue, which obviously does not proceed homogenously, even more because of the different types of tissue of the aortic annulus.[11] The irregular distribution of the calcification induces a large variability in annular shapes, as described by other authors.[7,12] In most cases, these shapes are asymmetric, which may lead to deformation of the valve stents and thus may influence the hemodynamics after TAVI.

During measurements, we could not demonstrate significance between the groups' mean and peak pressure

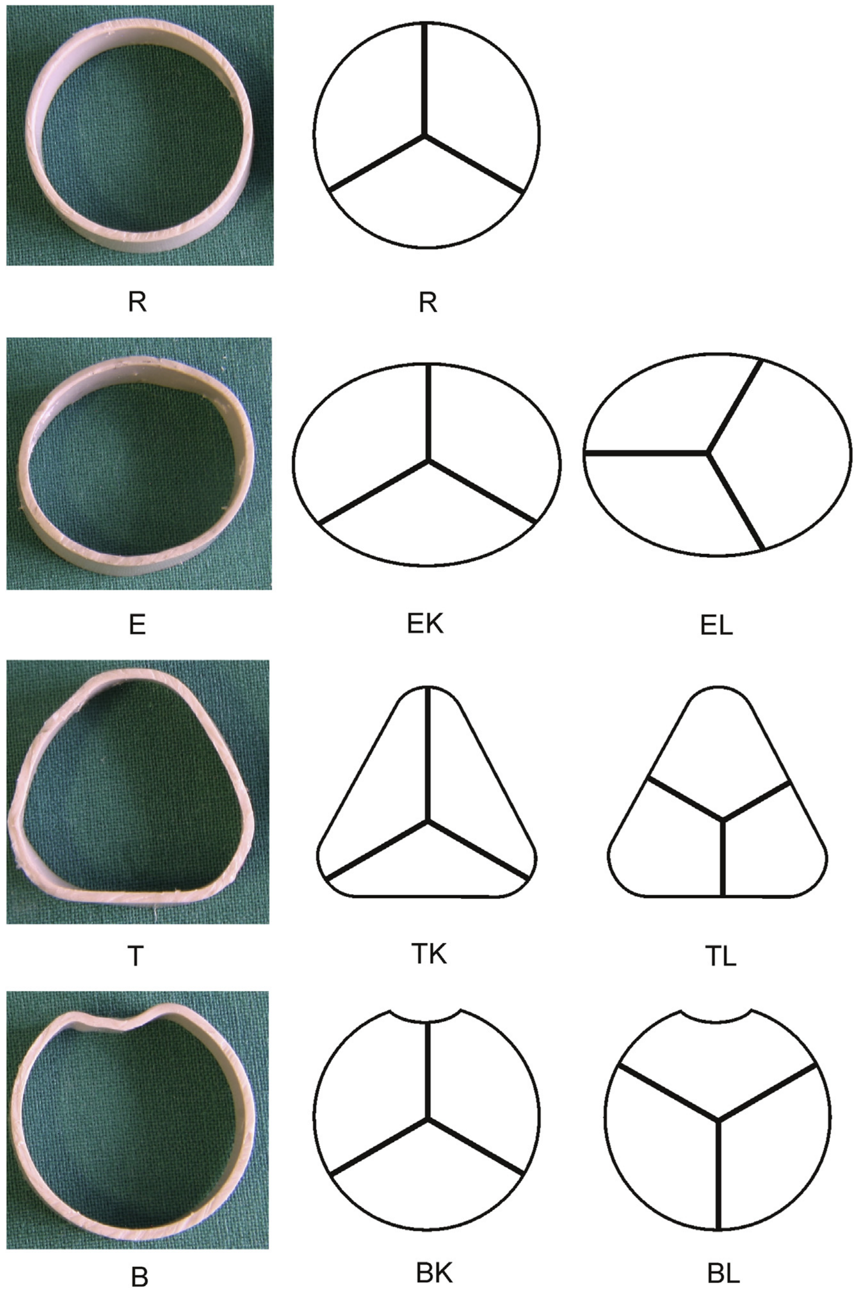

FIGURE 1. Different shapes of annulus configuration used in this study (from *top* to *bottom*: circular [*R*], elliptical [*E*], triangular [*T*], circular with bulge [*B*]). The schemes on the right depict the 2 commissure directions. *EK*, Commissure of the valve prosthesis on the short axis; *EL*, commissure on the longitudinal axis of the annular plane; *TK*, commissure of the prosthesis on the commissural area of the artificial annulus; *TL*, commissure of the prosthesis on valve leaflet position; *BK*, commissure of the prosthesis on plaque; *BL*, commissure shifted apart from the plaque.

gradients and closing volume. This was an expected finding because the valves opened completely and closing motions were unaffected regardless of deformations, as the video records showed.

However, in most of the noncircular configurations we could detect an increase of leak volume in comparison with the circular configuration, except the elliptical configuration with the prosthesis commissure orientated on the longitudinal axis of the annular plane. This was also true for the circular-shaped annulus with bulge and the commissure of the prosthesis orientated on the plaque. Leaks may be caused by the deformation of the valve stents appearing as paravalvular leakage, as well as malcoaptation of the leaflet edges probably inducing transvalvular leakage. The video records showed corresponding deformations at the stent and the leaflet free edges, which are differently

TABLE 1. Hemodynamic measurements of the Sapien XT in different annulus configurations

	Mean pressure (mm Hg)	Peak pressure (mm Hg)	Closing volume (mL)	Leakage volume (mL)
Regular				
R	5.26 ± 0.34	13.12 ± 1.34	5.35 ± 1.45	12.66 ± 1.00
Elliptical				
EK	5.39 ± 0.63	11.54 ± 0.72	5.20 ± 1.34	17.63 ± 3.70
EL	5.73 ± 0.64	13.15 ± 2.38	5.23 ± 1.27	14.47 ± 2.67
Triangular				
TK	5.98 ± 0.69	12.47 ± 0.86	4.73 ± 1.24	19.38 ± 3.29
TL	5.67 ± 0.77	11.92 ± 1.43	5.17 ± 1.06	18.82 ± 5.05
Bulged				
BK	5.68 ± 0.76	12.30 ± 0.90	5.43 ± 1.65	17.38 ± 5.06
BL	5.88 ± 0.72	12.60 ± 1.21	4.70 ± 1.48	16.17 ± 3.22

Significance was found between R and EK with $P = .0464$; R and TK with $P = .0277$; R and TL with $P = .0464$; R and BL with $P = .0464$, and EL and EK with $P = .0277$. *R*, Reference; *EK*, commissure of the valve prosthesis on the short axis; *EL*, commissure on the longitudinal axis of the annular plane; *TK*, commissure of the prosthesis on the commissural area of artificial annulus; *TL*, commissure of the prosthesis on valve leaflet position; *BK*, commissure of the prosthesis on plaque; *BL*, commissure shifted apart from plaque.

pronounced and arranged in the annuli configurations used in this study.

The implantation of the valves in the triangular-shaped annulus particularly showed distortions of the stent and the leaflet edges in both commissural orientations (Figure 2). The stents did not properly attach to the annuli, which implies paravalvular regurgitation; on the other hand, the distinct deformations of the leaflet's free edges possibly led to transvalvular leaks. The measurements showed an increase of leak volume up to −18.82 ± 5.05 mL and −19.38 ± 3.29 mL per cycle, respectively, for these configurations. Because of these results, TAVI in triangular configuration should be further investigated to clarify whether such difficulties also occur in aortic annuli that are less calcified.

In the circular-shaped annulus with bulge, deformations of the stent with incomplete adaption to the annulus also could be found adjacent to the bulge (Figure 2, *middle row, point 1*), and likewise deformations of the leaflet edges in both configurations. In most of the cases, the valves implanted into the configuration with the prosthesis commissure shifted apart from the plaque showed more irregularities.

One might assume that a possible alternative may be a smoother stent material that allows for better adaption of the stent to the calcified annulus preventing paravalvular leaks. With the Sapien XT, the manufacturer has already provided a smoother stent material than the previous version, and the design of the stent has changed regarding this aspect.[13] Obviously, these changes might be of some advantage, but the particular effect of different stent configurations, including the self-expanding transcatheter valves, should be investigated in more detail. From our findings, an even more elastic stent material probably decreases paravalvular leakage flow by more tightly fitting to the shape of the annulus, but the deformation of the valve itself may be stronger in this case, possibly leading to additional transvalvular leaks.

In this context, we exemplarily investigated the impact of the observed deformations of the free edges of the leaflets on transvalvular leakage under static pressure and actually found such leaks. During these experiments, the valves were completely sealed with silicon between the prosthesis stent and the annulus so that the origin of leakage could only be transvalvular (Figure 3). These findings suggest that such folds in the free edge of leaflets may induce transvalvular leaks in many cases. A similar situation has been described after reimplantation of aortic valves into inadequate small vascular prostheses during the "David" procedure, in which decentral foldings in the coaptation area due to the redundant leaflet material lead to mild valve insufficiency.[6,14] The experiments showed that the observed reflux did not build straight downward jets but run along the ventricular aspect of the fold in the leaflet, directed to the valve annulus (Figure 3, *blue arrows*). In this respect, it sometimes may be difficult to distinguish transvalvular from paravalvular leakage with echocardiography.

One of the major findings of this study is that the elliptical configuration with 1 prosthesis commissure orientated in the longitudinal axis of the annular plane showed less deformation of the edges of the leaflets and less leak volume. The results were similar to those of the implantation of the transcatheter valves into an ideal circular-shaped annulus. Such an elliptical shape is often found in patients with a bicuspid aortic valve and is usually mentioned as a contraindication for TAVI.[15,16] However, from the described results, the implantation of transcatheter aortic valves seems to be feasible in the elliptical annulus, particularly in that configuration with the prosthesis commissure on the longitudinal axis of the annular plane, if no other contraindications (eg, position of the coronary arteries) suggest otherwise.[15]

Study Limitations

Some limitations of the setup should be taken into account. The applied annulus models were rigid and thus did not completely reflect the anatomic situation in vivo. The deformations of the valves might be less in moderately

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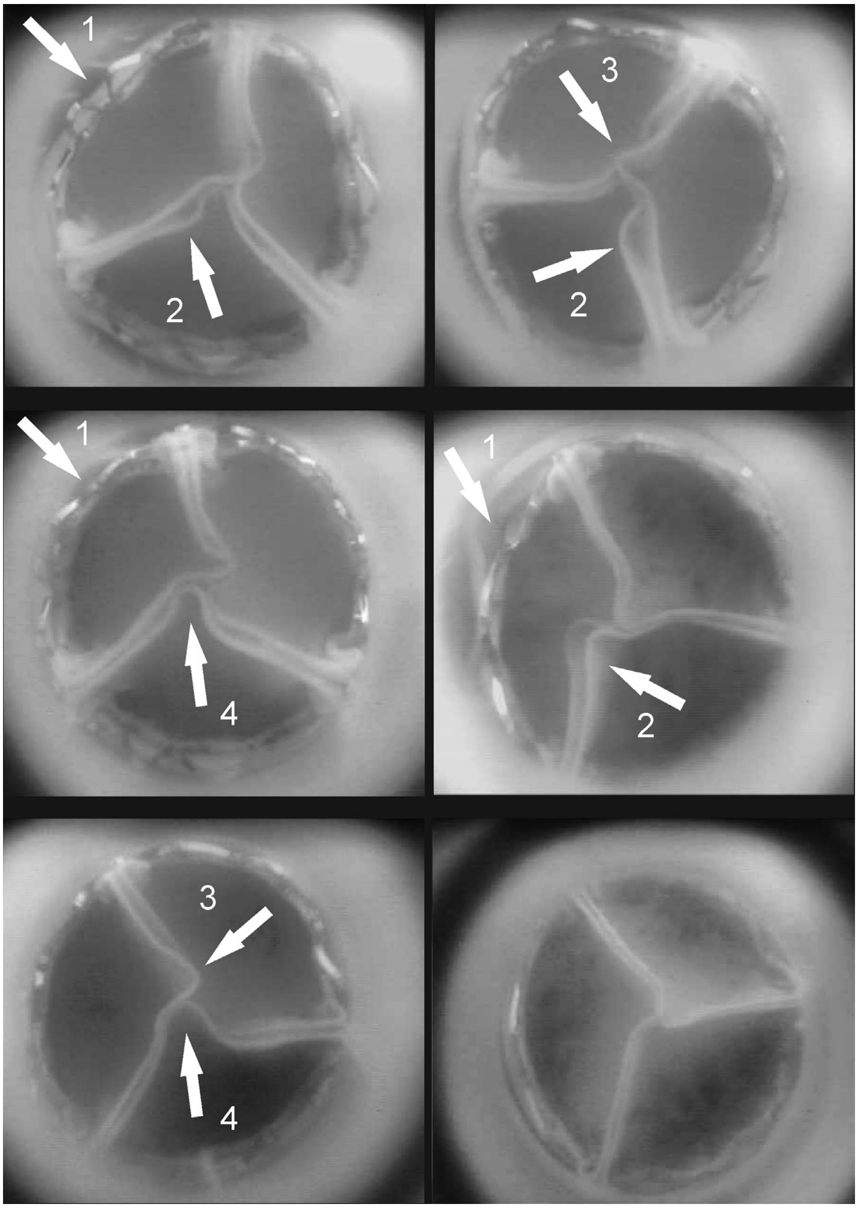

FIGURE 2. Edwards Sapien XT implanted in the different annulus models. *Top*: triangular model. *Left*: with commissure of the prosthesis on commissure of the valve (TK) and right on valve leaflets (TL). *Middle row*: the circular model with bulge. *Left*: with commissure of the prosthesis on plaque (BK). *Right*: with commissure shifted apart from the plaque (BL). *Bottom*: elliptical model. *Left*: with commissure of the valve prosthesis on the short axis (EK). *Right*: on the longitudinal axis of the annular plane (EL). The *arrows* indicate areas at which the prosthesis did not completely adapt to the aortic annulus (*1*) and the leaflet edges did not attach properly (*2*), overlapped (*3*), or were strongly folded (*4*).

calcified aortic annuli; however, in severe AS a similar rigidity of the annulus structure can be expected. Adhesion of the valves also may be influenced by the rigidity of the models, so we add a thin silicon film to the inner surface. However, remaining leakage could be observed even in the ideal circular configuration, which probably does not comply with the situation in vivo, but more silicon may distort the results. In this regard, not the absolute values but rather the differences between groups should be taken into account.

The models also lacked native leaflet material, which may influence the stabilization and adhesion of the transcutaneous aortic valve. On the other hand, the shapes of the models are typical for the particular kind of calcification, reflecting the resulting geometry if valves were implanted in such aortic roots.[7]

Our annulus models also provide an ideal size of the annulus in relation to the applied valve size. The observed leakages will be different in patients' annuli with variant dimensions; thus, paravalvular insufficiency may increase

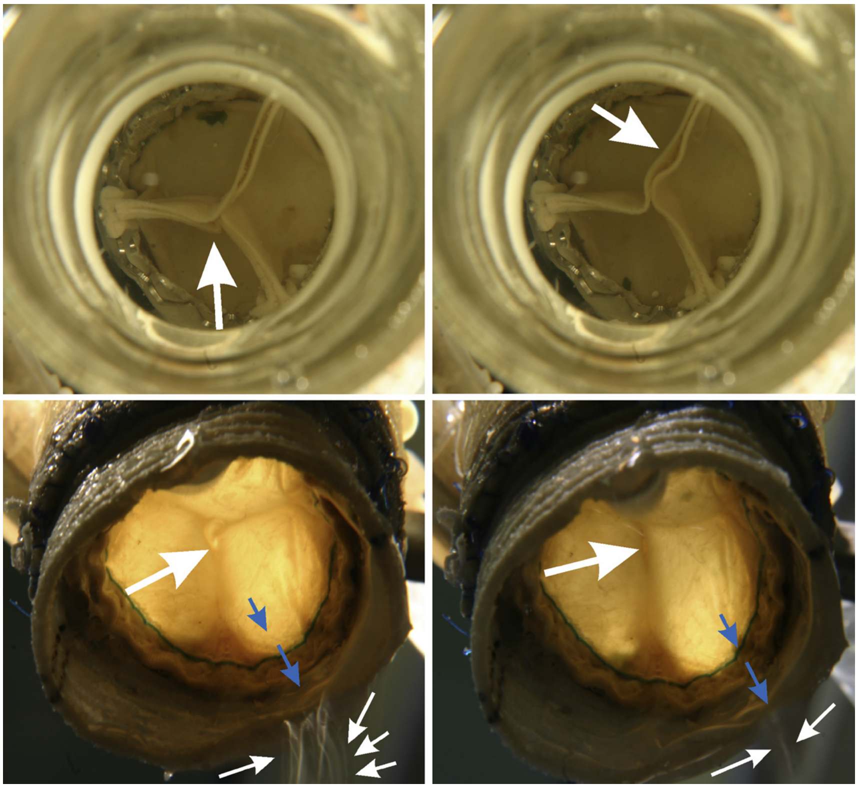

FIGURE 3. Edwards Sapien XT under static pressurization. The valve was mounted in the triangular model with tight sealing of the deployment area. *Top*: view from the aortic side showing the leaflet deformations (*white arrows*). *Bottom*: view from the ventricular side. *White arrows* indicate the respective fold of the leaflet's free edge representing the origin of the leakage. *Blue arrows* mark the course of the leakage flow running along the ventricular side of the leaflet toward the annulus.

for the greater diameters and transvalvular insufficiency may increase for the smaller diameters. Further investigations are needed regarding this.

Another possible limitation is the multiple use of the valves, which may change the stent geometry and expansion behaviors and the structural integrity of the pericardial leaflets.[6] However, we randomly arranged the implantation sequence in the different tests and did not fully crimp the stents, but only reduced the size so that it fit into the model. The results do not differ along the measurements, so one might assume that the possible structural modification is not significant.

CONCLUSIONS

This study shows that the annulus shape has a determinant influence on paravalvular and transvalvular leaks after TAVI. Stent deformation causes inadequate adaption to the native annulus and leaflet malcoaptation, both potentially leading to paravalvular or transvalvular leakage. The mean and peak pressure gradients and the closing volume remain unaffected. TAVI in elliptical shapes of the annulus, which are often found in patients with a bicuspid aortic valve, seems feasible, particularly if one prosthesis commissure is orientated on the longitudinal axis of the annulus plane. These findings may be of some interest for clinical TAVI regarding pre-implantation diagnosis of valve phenotype and the arrangement of calcium deposits to predict the post-interventional shape of the anchoring site and the positioning of the prosthesis to the particular valve pathology.

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