Valve-in-Valve Hemodynamics of 20-mm Transcatheter Aortic Valves in Small Bioprostheses

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Background. **Transcatheter aortic valve (TAV) implantation is a treatment for selected patients with failing bioprostheses. We previously showed that currently available SAPIEN (Edwards Lifesciences, Irvine, CA) TAV sizes did not yield acceptable valve-in-valve (VIV) hemodynamics in small degenerated bioprostheses because optimal TAV function requires full stent expansion to its nominal size. The study objective was to determine (1) if 20-mm TAVs provide acceptable hemodynamics in small degenerated bioprostheses and (2) the effect of TAV spatial orientation on valvular hemodynamics and coronary flows.**

Methods. **Twelve 20-mm TAVs were created for implantation within 19-mm and 21-mm degenerated Carpentier-Edwards Perimount (Edwards Lifesciences) and porcine bioprostheses. Degenerated valves were sutured into human homograft roots and mounted in a pulse duplicator. TAVs were implanted within bioprostheses as VIV in standard orientation, in which TAV and bioprosthetic commissures were aligned, and later with 60-degree rotation.**

Results. **The 20-mm TAVs migrated retrograde into the left ventricle after VIV in the 21-mm Perimount bioprostheses. However, 20-mm TAVs in 19-mm Perimount (54.9 ± 5.4 to 23.5 ± 3.9 mm Hg, $p = 0.006$) and 21-mm porcine bioprostheses (35.2 ± 8.9 to 16.8 ± 4.1 mm Hg, $p = 0.03$) significantly reduced mean gradients. No significant reduction in pressure gradient occurred after VIV in 19-mm degenerated porcine bioprostheses. Mild regurgitation was observed after VIV. VIV with standard and 60-degree TAV orientation did not significantly alter hemodynamics or coronary flows.**

Conclusions. **Valve-in-valve hemodynamics with 20-mm TAV improved for 19-mm Perimount and 21-mm porcine but not 19-mm porcine bioprostheses. No significant differences in hemodynamics were noted by orientation with TAV and bioprosthesis commissural alignment or 60-degree rotation.**

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Transcatheter aortic valve implantation (TAVI) is a viable treatment option for high-risk patients with severe native aortic stenosis [1, 2]. Furthermore, TAVI may be a promising option for patients with failing surgical bioprostheses [3–5], but limited clinical TAVI case series in failing bioprostheses have been reported [6, 7]. Bioprosthetic valves offer a well-distinguished circular landing zone with known dimensions for TAVI. However, we have previously demonstrated that TAVI within small surgical bioprostheses resulted in an increased valvular pressure gradient and impaired TAV leaflet coaptation, which potentially could result in reduced durability [4, 5, 8].

Optimal TAV function requires full stent expansion to TAV nominal size. Currently, TAVs are available in limited sizes and obtaining optimal valve-in-valve (VIV) hemodynamics requires a wider range of TAV sizes. The Edwards SAPIEN valve (Edwards Lifesciences, Irvine, CA), which was investigated in the Placement of Aortic Transcatheter Valve (PARTNER) trial in the United States and Conformité Européene-mark approved in Europe, is currently available in two sizes, 23 and 26 mm. Newer SAPIEN sizes with smaller diameters (20 mm) are under development, whereas larger diameters (29 mm) are available in Europe and may extend the range of bioprosthetic valves amenable to TAVI.

Our results have shown that implantation of currently available 23-mm TAVs within 23-mm degenerated Carpentier-Edwards PERIMOUNT bioprostheses significantly reduced the pressure gradient and improved the effective orifice area [5]. Transvalvular energy loss with TAVI was significantly higher, however, imposing a greater workload on the left ventricle than surgical repeat replacement with a normal 23-mm PERIMOUNT valve, comparable to that seen with a 21-mm valve [5]. A 23-mm TAVI within a 21-mm degenerated PERIMOUNT bioprostheses resulted in a significant residual pressure gradient, whereas a 23-mm TAVI within a 19-mm degenerated PERIMOUNT prosthesis was ineffective in relieving severe stenosis.

We hypothesized that VIV hemodynamics in 19-mm and 21-mm degenerated bioprostheses might be improved by using a smaller size-matched TAV or by developing new TAV designs, such as our supravalvular TAV [9]. The objective of this study was to determine if

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20-mm TAVs provide acceptable hemodynamics in 19-mm and 21-mm degenerated bioprostheses. We also investigated the effect of TAV spatial orientation on valvular hemodynamics and coronary flows.

Material and Methods

Transcatheter Aortic Valves

Twelve 20-mm TAVs were created based on the Edwards SAPIEN valve design for VIV within 19-mm and 21-mm degenerated Carpentier-Edwards PERIMOUNT (Model 2800TFX) and Carpentier-Edwards aortic porcine bioprostheses (n = 3 each). The 20-mm SAPIEN TAV is under development at Edwards Lifesciences but is not currently available clinically for testing. Our TAVs has been previously described in detail [4]. Briefly, 3 trapezoidal-shaped leaflets were cut from a flat piece of bovine pericardium (Edwards Bovine Pericardial Patch, Edwards Lifesciences). Lateral sides of the leaflets were sutured together and then sutured at the base to a Dacron (DuPont, Wilmington, DE) sheet. A 14-mm-long customized cylindrical stainless steel stent (W.L. Gore and Associates, Flagstaff, AZ) was dilated to an external diameter of 20 mm to anchor the leaflets and the Dacron sheet. Interrupted stitches were used at each intersection of the metal stent to attach the Dacron sheet to the stent (Fig 1).

Degenerated Bioprosthetic Valves

Acquiring explanted degenerated bioprostheses from patients is unpredictable with respect to transvalvular gradients as well as bioprosthetic valve type and sizes, and it is difficult to achieve a sufficient quantity of each size for statistical analyses at one institution. Thus for pericardial bioprostheses, we used our previously developed reproducible model to simulate degeneration [5]. The model provided consistent transvalvular pressure gradients and mimicked the in vivo pathology of the calcified valve.

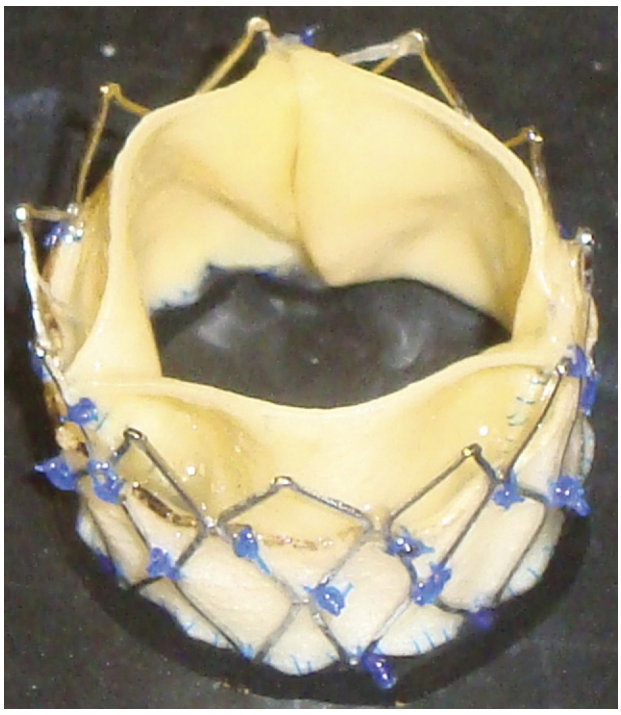

Fig 1. The 20-mm transcatheter aortic valve.

Briefly, BioGlue (CryoLife Inc, Kennesaw, GA) was applied to leaflets of a normal bioprostheses to stiffen the leaflets and imitate calcification. Three pieces of bovine pericardium (Edwards Bovine Pericardial Patch, Edwards Lifesciences) were cut in half-circles and sutured to the aortic side of each bioprosthetic leaflet to maintain BioGlue adherence and prevent dislodgement during balloon predilatation of the bioprosthesis before TAVI. A mean bioprosthetic gradient of 50 mm Hg was set as the goal, based on echocardiographic data, to reproduce hemodynamics of severe bioprosthetic stenosis [10, 11]. Degeneration of porcine bioprostheses is typically a combination of valvular stenosis and regurgitation. Echocardiographic data indicate that patients undergoing repeat replacement of porcine bioprosthetic aortic valve dysfunction have a mean bioprosthetic gradient of 36 ± 19 mm Hg and a regurgitation fraction of 52% ± 20% [11]. Porcine bioprosthetic degeneration was simulated by applying BioGlue on 2 leaflets and cutting the third leaflet in half along the bioprosthetic radius to induce regurgitation.

Pulse Duplicator System

An in vitro study provides a consistent and well-controlled environment to examine VIV hemodynamics. Valves were tested in a custom-built pulse duplicator system developed for TAVI and coronary flow measurements (ViVitro Systems Inc, Victoria, BC, Canada). The pulse duplicator has been previously described in detail [4]. Unlike previous experiments, the bioprostheses in this study were sutured into human homograft roots of matched annular sizes (Regeneration Technologies Inc, Cardiovascular, Alachua, FL). The roots were then mounted in the aortic position in the pulse duplicator, and physiologic flow was circulated at room temperature.

For coronary flow measurement, polytetrafluoroethylene tubes of appropriate diameter were connected to the coronary ostia, and the baseline flow rate was controlled using adjustable tube clamps (Fig 2). Heart rate, blood pressure, and cardiac output were used as control variables for the waveform generator controlling a servo pump. Recirculating fluid of 36% (by volume) of glycerin solution in normal saline was used as a blood analog fluid, which mimicked blood viscosity at 37°C when tested at room temperature. Pulse duplicator input variables were used to match International Organization for Standardization 5840 and U.S. Food and Drug Administration standards for testing heart valves: heart rate of 70 beats/min, 35% systolic duration of cycle period, mean atrial and aortic pressures of 10 and 100 mm Hg, and cardiac output 5 L/min [12, 13]. These hemodynamic variables were maintained constant throughout the study.

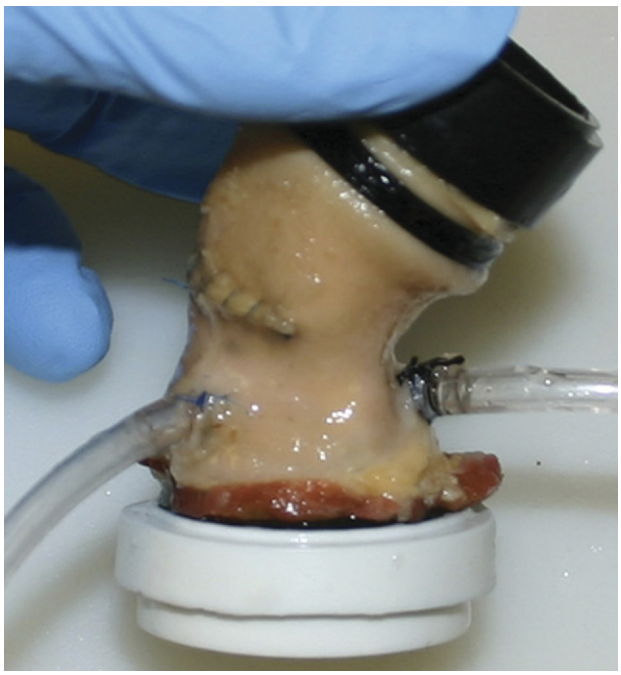

Fig 2. Human homograft roots were implanted in the pulse duplicator to study transcatheter aortic valve implantation.

Hemodynamic Measurements

Valve hemodynamics were evaluated by mean pressure gradient, effective orifice area, regurgitant volume, and transvalvular energy loss. Energy loss allowed assessment of valvular hemodynamics during the entire cardiac cycle, not just during forward flow. By this means, the ventricle became the focus of evaluation rather than the systolic function of the valve [8, 14]. Pressure was measured with strain gauge pressure transducers (Cobe Laboratories Inc, Lakewood, CO), and the effective orifice area was calculated using the Gorlin equation. An electromagnetic flowmeter (Carolina Medical Electronics Inc, East Bend, NC) was used to measure the flow rate and regurgitation volume of the aortic valve. The regurgitation fraction was calculated as aortic retrograde flow/systolic ejection flow. Transvalvular energy loss during forward, closing, and leakage flow was calculated based on the principle of conservation of energy. The energy loss calculation has been described previously in detail [8].

Two-dimensional echocardiography (ACUSON Sequoia C256, Siemens Medical Solutions USA Inc, Malvern, PA) was used to identify the location of valve leakage. Flow through coronary arteries was measured using ultrasound flow probes (Transonic Systems Inc, Ithaca, NY).

Data Acquisition and Analyses

First, TAVs were tested alone in the pulse duplicator before implantation. Data acquisition was run over 10 consecutive cardiac cycles. Then, normal Carpentier-Edwards aortic valves were mounted into human homografts and tested to obtain a hemodynamic baseline. Bioprostheses were degenerated and tested in the pulse duplicator to assess severity of bioprosthetic degeneration. After balloon predilatation of the degenerated bioprostheses was achieved, 20-mm TAVs were implanted with commissural alignment within the bioprostheses and measurements obtained for VIV hemodynamics. Finally, TAVs were explanted, recrimped, and reimplanted with a 60-degree rotation in the same degenerated bioprostheses to study the effect of TAV orientation on hemodynamics (Fig 3). All measurements were repeated for each of the 19-mm and 21-mm degenerated PERIMOUNT and porcine bioprosthetic valves ($n = 3$ each).

Individual paired t tests were used to compare measurements before and after TAVI. To compare VIV with surgical repeat replacement of the bioprostheses, VIV measurements were compared with measurements made in normal bioprostheses for each valve size using paired t test. The results had a normal distribution as determined by the Kolmogorov-Smirnov test. Statistical power analysis showed that sample size was adequate to evaluate two-sided standardized differences greater than 0.5 achieving a statistical power greater than 0.80. Values are reported as mean ± standard deviation, and statistical analyses were performed using SPSS 17 software (SPSS Inc, Chicago, IL).

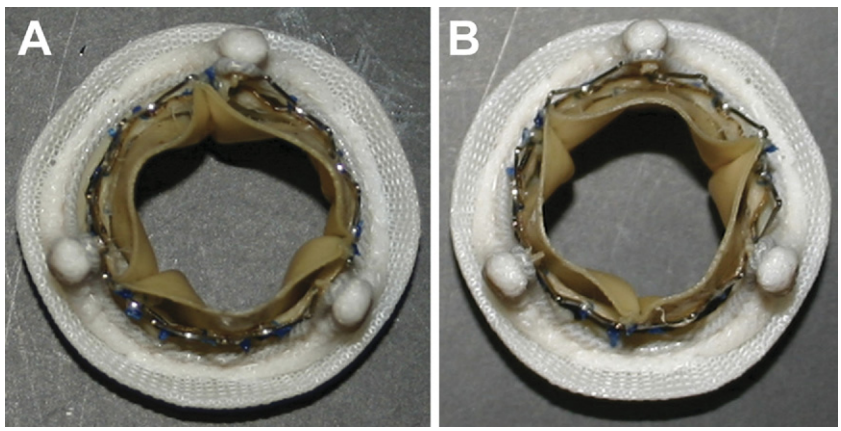

Fig 3. Transcatheter implantation of a 20-mm aortic valve within a 23-mm normal bioprosthesis is shown for illustration purposes. (A) Standard orientation. (B) Transcatheter aortic valves rotated 60 degrees.

Table 1. Hemodynamics Before and After Transcatheter Aortic Valve Implantation in 19-mm Degenerated PERIMOUNT Bioprostheses Compared With Normal 19-mm Bioprostheses

Variable	Degenerated Bioprosthesis (19-mm) Mean ± SD	Valve-in-Valve		Normal Bioprosthesis (19-mm) Mean ± SD
		Standard Orientation Mean ± SD	60-degree Rotated Mean ± SD	
Pressure gradient, mm Hg	54.9 ± 5.4	23.5 ± 3.9[a]	25.2 ± 5.4[a]	11.5 ± 2.0[b]
Effective orifice area, cm^2	0.69 ± 0.03	1.07 ± 0.10[a]	1.04 ± 0.14[a]	1.54 ± 0.13[b]
Regurgitation fraction, %	3.7 ± 1.8	16.8 ± 2.4[a]	16.9 ± 0.4[a]	4.8 ± 1.7[b]
Total energy loss, mJ/stroke	809.0 ± 52.1	582.3 ± 27.5[a]	610.0 ± 74.7[a]	248.7 ± 23.9[b]

[a] $p < 0.04$ between degenerated bioprostheses and valve-in-valve (both orientations). [b] $p < 0.05$ between valve-in-valve (both orientations) and normal bioprosthesis.

SD = standard deviation.

Results

The twelve 20-mm TAVs created in the laboratory had a mean pressure gradient of 8.1 ± 1.9 mm Hg when tested alone in the pulse duplicator. After VIV in 21-mm PERIMOUNT bioprostheses, 20-mm TAVs migrated retrograde into the left ventricle due to the large pressure gradient across the valve during diastole [15]. However, no TAV migration was observed after VIV within 19-mm PERIMOUNT and within 19-mm and 21-mm porcine bioprostheses. TAVI in 19-mm PERIMOUNT bioprostheses reduced the mean pressure gradient of degenerated valves significantly ($p = 0.006$; Table 1).

Next, VIV hemodynamics were compared with those of normal 19-mm PERIMOUNT bioprostheses. The VIV pressure gradient was significantly higher than in the normal 19-mm PERIMOUNT bioprostheses ($p = 0.037$; Table 1). Similarly, VIV in 21-mm porcine bioprostheses significantly reduced the mean pressure gradient of degenerated bioprostheses ($p = 0.03$), but here, the pressure gradient was comparable with normal 21-mm porcine bioprostheses ($p = 0.06$; Table 2). In contrast, no significant reduction in pressure gradient was obtained for VIV within 19-mm porcine bioprostheses, and the transvalvular gradient was significantly higher than in normal 19-mm porcine bioprostheses ($p = 0.04$; Table 3).

Before VIV implantation, 20-mm TAVs had an effective orifice area of 1.84 ± 0.20 cm^2. The effective orifice area significantly increased after VIV in degenerated 19-mm PERIMOUNT bioprostheses ($p = 0.02$; Table 1). However, because TAVs could not be dilated beyond the bioprosthetic annulus and were anchored inside the bioprosthesis, the VIV area was significantly lower than the effective orifice area of normal 19-mm PERIMOUNT bioprostheses ($p = 0.03$). Similarly, VIV in 21-mm porcine bioprostheses significantly increased effective orifice area ($p = 0.006$) but was comparable with normal 21-mm porcine bioprostheses (Table 2). However, VIV in 19-mm porcine bioprostheses was not effective, and the effective orifice area after TAVI was unchanged ($p = 0.80$; Table 3).

The regurgitant fraction of 20-mm TAVs alone was 7.4% ± 1.4% at baseline. After VIV in a 19-mm PERIMOUNT degenerated bioprostheses, the regurgitant fraction significantly increased ($p = 0.03$) and was significantly higher than that of the normal 19-mm PERIMOUNT bioprostheses ($p = 0.007$; Table 1). VIV did not significantly affect valvular regurgitation in 21-mm porcine bioprostheses ($p = 0.18$), and the regurgitant fraction was significantly higher than that of normal 21-mm porcine bioprostheses ($p = 0.03$; Table 2). In 19-mm porcine bioprostheses after VIV, valvular regur-

Table 2. Hemodynamics Before and After Transcatheter Aortic Valve Implantation in 21-mm Degenerated Porcine Bioprostheses Compared With Normal 21-mm Porcine Bioprostheses

Variable	Degenerated Bioprosthesis (21 mm) Mean ± SD	Valve-in-Valve		Normal Bioprosthesis (21 mm) Mean ± SD
		Standard Orientation Mean ± SD	60-degree Rotated Mean ± SD	
Pressure gradient, mm Hg	35.2 ± 8.9	16.8 ± 4.1[a]	17.5 ± 4.6[a]	11.7 ± 1.8
Effective orifice area, cm^2	0.87 ± 0.13	1.28 ± 0.15[a]	1.25 ± 0.16[a]	1.52 ± 0.11
Regurgitation fraction, %	25.2 ± 11.0	10.1 ± 2.0	9.6 ± 1.3	5.3 ± 0.9[b]
Total energy loss, mJ/stroke	1072.3 ± 213.4	381.0 ± 33.8[a]	387.3 ± 47.4[a]	255.0 ± 22.9[b]

[a] $p < 0.03$ between degenerated bioprostheses and valve-in-valve (both orientations). [b] $p < 0.03$ between valve-in-valve (both orientations) and normal bioprosthesis.

SD = standard deviation.

Table 3. Hemodynamics Before and After Transcatheter Aortic Valve Implantation in 19-mm Degenerated Porcine Bioprostheses Compared With Normal 19-mm Porcine Bioprostheses

Variable	Degenerated Bioprosthesis (19 mm) Mean ± SD	Valve-in-Valve		Normal Bioprosthesis (19 mm) Mean ± SD
		Standard Orientation Mean ± SD	60-degree Rotated Mean ± SD	
Pressure gradient, mm Hg	37.5 ± 0.6	43.9 ± 7.5	41.2 ± 2.6	18.1 ± 3.2[b]
Effective orifice area, cm^2	0.82 ± 0.01	0.78 ± 0.07	0.80 ± 0.04	1.22 ± 0.08[b]
Regurgitation fraction, %	22.6 ± 6.1	8.3 ± 1.3[a]	7.6 ± 1.3[a]	5.6 ± 0.8
Total energy loss, mJ/stroke	933.0 ± 147.2	726.3 ± 79.6	689.0 ± 35.4	348.7 ± 41.5[b]

[a] $p = 0.04$ between degenerated bioprostheses and valve-in-valve (both orientations). [b] $p < 0.05$ between valve-in-valve (both orientations) and normal bioprosthesis.

SD = standard deviation.

gitation reduced significantly ($p = 0.04$) and was comparable with that of 19-mm normal porcine bioprostheses ($p = 0.15$; Table 3).

From an energy standpoint, 20-mm TAVs tested alone in the pulse duplicator had a total energy loss of 220.3 ± 32.6 mJ/stroke: 184.2 ± 29.1 during forward, 5.4 ± 4.1 during closing, and 30.6 ± 10.8 during leakage flow. Total energy loss of the 19-mm PERIMOUNT degenerated bioprostheses was reduced significantly after 20-mm TAVI ($p = 0.004$; Fig 4). However, VIV implantation nonetheless imposed a significantly higher left ventricular workload than the normal 19-mm PERIMOUNT valves: 212.0 ± 23.0 mJ during forward, 11.0 ± 2.6 mJ during closing, and 26.0 ± 14.7 mJ during leak flow ($p = 0.005$; Table 1 and Fig 4). Implantation of a 20-mm TAV within the 21-mm porcine bioprosthesis reduced the transvalvular energy loss significantly ($p = 0.03$; Table 2 and Fig 4). However, transvalvular energy loss was not affected after VIV in 19-mm porcine valves ($p = 0.28$; Table 3 and Fig 4).

Transcatheter aortic valve spatial orientation did not significantly alter VIV hemodynamics (Tables 1, 2, and 3). After 60-degree rotation of TAVs within degenerated bioprostheses such that TAV commissures were located in the middle of bioprosthetic leaflets, no significant change in mean pressure gradient, effective orifice area, regurgitation fraction, or in total energy loss was observed when compared with standard VIV orientation where TAV and bioprosthetic commissures were aligned. Furthermore, TAVI in both orientations did not alter coronary flows significantly (Table 4). Before TAVI, time-average coronary flow rates were adjusted to 37 and 58 mL/min for the right and left coronary arteries, respectively, to match baseline flow rates that have been reported as normal coronary flow rates [16]. After TAVI, no substantial reduction in right or left coronary flow rates was observed (Table 4).

Comment

In this study, we evaluated the hemodynamic performance of 20-mm TAVs within 19-mm and 21-mm degenerated PERIMOUNT and porcine bioprostheses. Because the 21-mm bioprosthesis has a nominal internal diameter of 20-mm, TAVs migrated into the left ventricle after implantation due to the large pressure gradient across the valve during diastole [15]. Overexpansion and crowning of the 20-mm TAV within the 21-mm PERIMOUNT bioprostheses induced a significant amount of intravalvular regurgitation and TAV damage. However, no migration was observed after VIV within the 19-mm PERIMOUNT and within the 19-mm and 21-mm por-

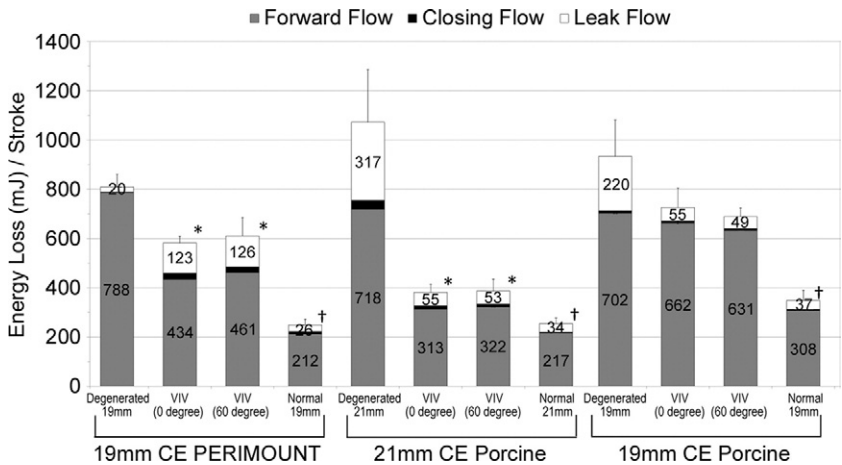

*Fig 4. Transvalvular energy loss during forward, closing, and leakage flow of degenerated, valve-in-valve (standard orientation), valve-in-valve (60-degree rotated), and normal 19-mm porcine, 19-mm PERIMOUNT, and 21-mm porcine Carpentier-Edwards (CE) bioprostheses (19-mm). * Indicates p ≤ 0.04 between degenerated bioprosthesis and valve-in-valve (both orientations). †Indicates p < 0.05 between valve-in-valve (both orientations) and normal bioprosthesis. Error bars show the standard deviation.*

Table 4. Time-Average Right and Left Coronary Flow Rates After 20-mm Transcatheter Aortic Valve Implantation at Standard and Rotated 60-degree Orientation[a]

	Standard Orientation		60-degree Orientation	
	Flow Rate, mL/min		Flow Rate, mL/min	
Variable[b]	Right Coronary	Left Coronary	Right Coronary	Left Coronary
19-mm PERIMOUNT[c]	36.0 ± 1.0	56.7 ± 0.6	36.3 ± 0.6	57.0 ± 1.0
21-mm porcine[c]	36.3 ± 0.6	57.3 ± 0.6	36.0 ± 1.0	57.0 ± 1.0
19-mm porcine[c]	36.6 ± 0.6	57.0 ± 1.0	36.3 ± 0.6	57.6 ± 0.6

[a] Before TAVI, the baseline right and left coronary arteries coronary flow rates were adjusted to 37 and 58 mL/min, respectively. [b] Data are presented as mean ± standard deviation. [c] Carpentier-Edwards, Edwards Lifesciences, Irvine, CA.

cine bioprostheses, whose inner stent diameters are 18, 17, and 19 mm, respectively. VIV implantation significantly reduced the mean pressure gradient of the 19-mm PERIMOUNT and 21-mm porcine degenerated bioprostheses. However, 20-mm TAVI within the 19-mm porcine bioprosthesis was ineffective, with no reduction in the pressure gradient.

Mild regurgitation was observed after deploying 20-mm TAVs within the degenerated bioprostheses. Two-dimensional echocardiographic assessment of valve leakage showed that the leakage was mainly paravalvular. Mild paravalvular leak is a common incidence after TAVI in patients with native or bioprosthetic valve dysfunction. However, regurgitation in our in vitro experiments might be reduced by using blood instead of blood analog fluid with no coagulation properties.

Transvalvular energy loss analysis demonstrated that TAVI within the 19-mm PERIMOUNT and 21-mm porcine bioprostheses significantly reduced left ventricular workload but was significantly higher than that from repeat replacement with normal bioprostheses of the same size. No significant changes in right or left coronary flow rates were observed after VIV implantation. Orientation of TAVI where TAV commissures were located at the center of bioprosthetic leaflets did not significantly alter mean pressure gradient, effective orifice area, regurgitation fraction, or total transvalvular energy loss. What we were unable to assess, however, was if TAV spatial orientation changed leaflet kinematics to impose higher stress on the leaflets, which may ultimately affect valve durability [17].

We recently demonstrated that implantation of currently available 23-mm-sized TAVs within the 19-mm PERIMOUNT bioprostheses yielded unacceptable hemodynamics, with no reduction in pressure gradient and energy loss [5]. VIV hemodynamics were improved using a new TAV design, such as our supravalvular TAV, where the valve within the TAV stent is situated above the bioprosthesis [9], but results using a smaller size-matched TAV were unknown. The results obtained in this study showed that implantation of 20-mm TAVs within degenerated 19-mm PERIMOUNT bioprostheses provided significantly better hemodynamics than the currently available 23-mm TAVs. Thus, the 20-mm TAV would be the size of choice for the 19-mm PERIMOUNT bioprosthesis. Because 20-mm TAVs in 21-mm PERIMOUNT bioprostheses migrated into the ventricle in this study, the 23-mm TAVs would be the size of choice for 21-mm degenerated PERIMOUNT valves. In addition, 20-mm TAV would be the size of choice for the 21-mm Carpentier-Edwards porcine bioprostheses, but it is not an effective treatment for 19-mm bioprosthesis.

Our studies demonstrate that use of 20-mm TAV within degenerated 19-mm PERIMOUNT and 21-mm porcine valves significantly reduces the mean pressure gradient and improves the effective orifice area; however, these VIV hemodynamics, including energy loss, are significantly worse than surgical repeat replacement with normal bioprostheses of matching size. The supravalvular valve design may be considered to improve upon these hemodynamics. Risks of reoperation based on patient comorbidities would be critical because higher mean gradients and energy loss may be acceptable, depending on the patient's comorbidities and expected length of survival.

The internal diameter of bioprosthetic valves varies by manufacturer, size, and model. Therefore, the nominal diameter of bioprosthetic valves could be misleading. Furthermore, bioprosthetic annulus and stent posts play a vital role in VIV. Carpentier-Edwards PERIMOUNT and porcine bioprostheses have a relatively rigid annulus and stent posts that constrain oversized TAVs. However, other bioprostheses, such as stentless models, may allow overexpansion by TAV. Overall, optimal VIV hemodynamics requires expansion of the TAV stent to its nominal size. Mean gradients of 17 to 18 mm Hg for VIV in 21-mm bioprostheses or 23 to 25 mm Hg in 19-mm bioprostheses are still much higher than surgical valves, with unknown consequences long-term. At the same time, some degree of oversizing is critical to avoid prosthesis migration. If VIV is considered future therapy for patients who would be predicted to have patient–prosthesis mismatch, a larger stentless xenograft root replacement or root enlargement may be considered at initial operation.

Clinical SAPIEN VIV Implantation

Limited clinical cases of VIV implantation for aortic bioprosthetic degeneration have been reported [3] in a subset examining SAPIEN VIV within degenerated Carpentier-Edwards valves [7, 18, 19]. Webb and colleagues

[7] reported 1 patient with a 21-mm stenotic bioprosthesis had a mean gradient of 24 mm Hg after 23-mm TAVI. Pampin and colleagues [19] reported another patient with a degenerated 21-mm PERIMOUNT bioprosthesis who was treated with a 23-mm TAV and had a 33 mm Hg mean gradient. No patients with VIV in 19-mm aortic bioprostheses to our knowledge have been reported. The VIV mean gradient for 23-mm SAPIEN VIV within 21-mm PERIMOUNT valve correlated with our in vitro data [5, 7]. Although our data cannot be directly extrapolated clinically, our in vitro data provide a reasonable guideline for what may be expected with VIV implantation, and we would not recommend use of 20-mm TAVs for 21-mm Carpentier-Edwards PERIMOUNT and 19-mm porcine bioprostheses.

Study Limitations

One minor limitation of the study was the inability to use the 20-mm SAPIEN valve, which is currently under development. Precise leaflet geometry and dimension are proprietary to Edwards Lifesciences Inc, which may affect valve function. The second limitation was our inability to acquire and use degenerated bioprostheses explanted from patients. It would be difficult to obtain sufficient numbers of explanted degenerated bioprostheses of an appropriate model and size with consistent transvalvular pressure gradients for comparison. Our degenerated bioprosthetic model provided consistent gradients in different sizes. Clinical VIV within degenerated bioprostheses may be complicated by irregular leaflet calcification, stent deformation, or pannus, which our study could not address.

The third study limitation was the ability to assess coronary flow obstruction based on orientation. Individual patients have coronary arteries that are different in size and location, which may affect coronary flow rates after TAVI. In homografts that we used in our experiments, we did not observe any coronary blockage from VIV. However, in individuals with low-lying coronaries, it is possible to imagine that VIV with TAV commissures in the middle of bioprosthetic leaflets could obstruct to coronary flow. Our results are based on a random sample of 6 homograft roots in the population.

Conclusions

Valve-in-valve intervention may be a promising option for elderly patients and those at high surgical risk with structural valve degeneration of previously implanted bioprostheses. The rigid bioprosthetic annulus and stent posts offer a suitable landing zone for TAVs. Currently, TAVs are available in limited sizes, and obtaining optimal VIV hemodynamics requires a wider range of TAV sizes. In this study, we investigated hemodynamics of VIV treatment for 20-mm TAV within 19-mm and 21-mm degenerated Carpentier-Edwards PERIMOUNT and porcine bioprostheses. We observed retrograde migration of 20-mm TAVs into the left ventricle after VIV within 21-mm PERIMOUNT bioprostheses. VIV within 19-mm PERIMOUNT and 21-mm porcine degenerated bioprostheses significantly reduced the pressure gradient and improved valve area. However, 20-mm TAVI within 19-mm porcine bioprosthesis yielded unacceptable hemodynamics. No significant change in coronary flow rates was observed after 20-mm TAVI. TAV spatial orientation did not significantly alter valvular hemodynamics.

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