The appreciation of prosthetic heart valves

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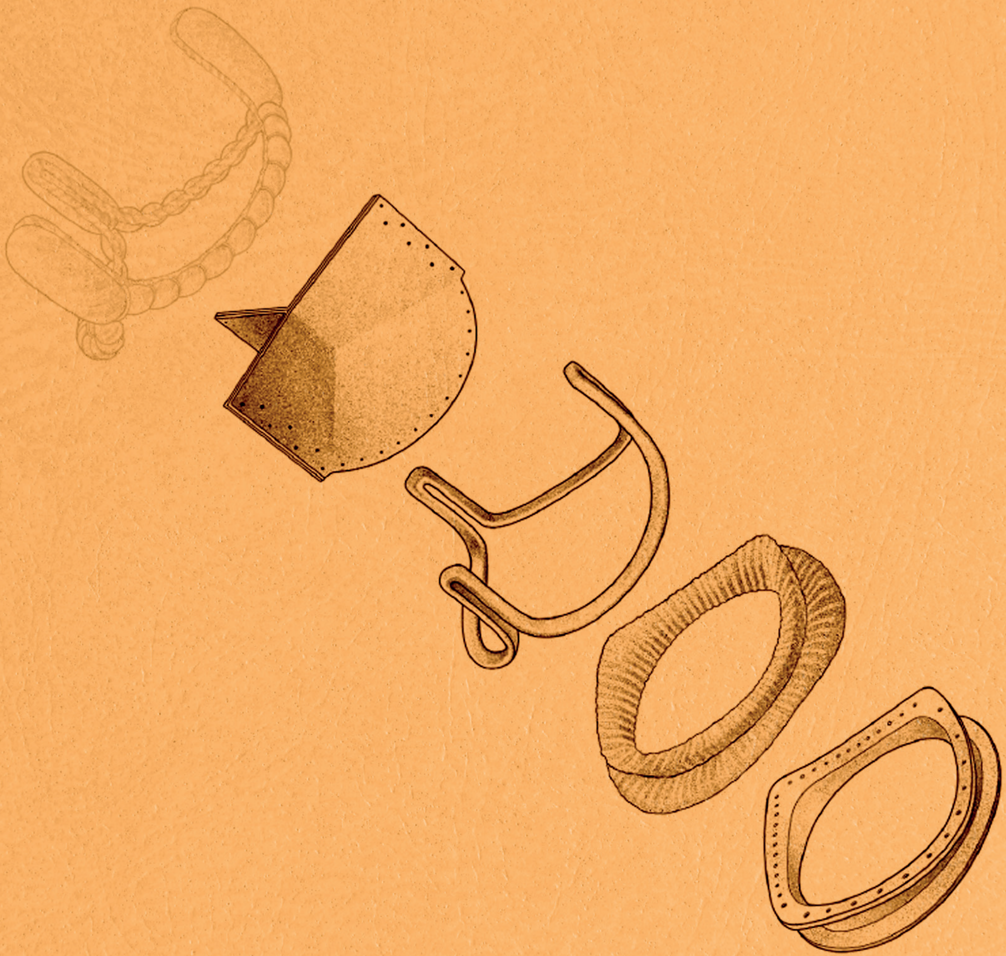

Chapter 6

An *in vitro* comparison of internally vs. externally mounted leaflets in surgical aortic bioprosthesis

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Abstract

Objectives:
To improve hemodynamic performance, design modifications of prosthetic valves have been proposed with each new generation of valves. These different designs also impact the amount of mechanical wear, as mechanical stresses are distributed differently. As long-term evidence for new prosthetic valves is lacking, this in vitro study compared hemodynamic performance and durability among three currently available bioprosthetic valves with internally (IMLV) or externally mounted leaflets (EMLV).

Methods:
Prostheses of the internally mounted Medtronic Avalus and Carpentier-Edwards Perimount Magna Ease valves were compared to prostheses of the externally mounted Abbott Trifecta valve. For each labelled size (e.g. 19, 21, and 23) of the three types, three valves underwent accelerated wear testing for up to 600 million cycles, corresponding to approximately 15 years of simulated wear. The valves underwent hydrodynamic testing and visual inspection.

Results:
EMLV had the largest EOA and lowest pressure gradient for each labelled size at baseline and 600 million cycles; EOA and pressure gradient was equivalent for the two types of IMLV. Five of nine EMLV had at least one hole or tear in the leaflet tissue around the stent posts, which resulted in severe regurgitation at 500 million cycles in two cases. All IMLV were intact at 600 million cycles with minimal tissue wear.

Conclusions:
EMLV demonstrated superior hydrodynamic performance but inferior mechanical durability compared to IMLV after 600 million cycles of testing. The primary failures were due to significant mechanical abrasion in the commisural region, which may warrant close monitoring of EMLV during long-term follow-up.

Introduction

For patients who undergo surgical aortic valve replacement, it is thought that the best results are achieved through optimal hemodynamic performance and durability of prosthetic valves. To improve hemodynamic performance, design modifications of prosthetic valves have been proposed with each new generation of valves. For example, bioprosthetic valves with externally mounted leaflets (EMLV) have been associated with a larger effective orifice area (EOA) and lower pressure gradient compared to valves with internally mounted leaflets (IMLV), as they allow for a more complete opening of the prosthesis(1,2).

Valve design also impacts the amount of mechanical wear, as mechanical stresses are distributed differently(3). Together with calcifications, mechanical wear is the most prevalent cause of primary failure of bioprosthetic valves(4). Although IMLV demonstrated good durability(5),(6), early versions of EMLV were known for tears at the commissures. This led to the withdrawal of the Ionescu-Shiley(7), Mitroflow A11(8), and Hancock pericardial(9) valves from the market.

Acute hemodynamic performance of valve designs can be distinguished relatively quickly, but understanding long-term hemodynamic performance and durability of valve designs requires 10 to 15 years of clinical follow-up. However, current commercial valves, such as the Abbott Trifecta valve (EMLV) and Medtronic Avalus valve (IMLV), have been introduced only recently. As there is a lack of long-term clinical follow-up, in vitro testing provides important insight into the differences between these valves. Although the ISO 5840 series of International Standards for Cardiac Valve Prostheses mandate in vitro testing of new bioprosthetic valves for commercial approval(10,11), there is no direct comparison of these data available in the literature. To improve our understanding of the impact of valve design, we compared the in vitro hydrodynamic performance and mechanical durability of IMLV versus EMLV.

Materials and methods

Valve selection

The selected valves for this study were the Trifecta valve (Abbott, Abbott Park, Illinois, USA), Perimount Magna Ease valve (Edwards, Irvine, California, USA), and Avalus valve (Medtronic, Minneapolis, Minnesota, USA). The Trifecta valve is an EMLV that gained commercial approval in 2011; the Perimount Magna Ease and Avalus valves are both IMLV and gained commercial approval in 2009 and 2017, respectively. Of each valve type, nine samples were used, three samples each of the 19, 21, and 23 labelled valve sizes.

Experimental Setup and Testing Methodology
In vitro methodology for the assessment of long-term mechanical durability of prosthetic tissue valves was conducted using accelerated wear testing (AWT) in accordance with the requirements of ISO 5840 (10,11). Valves were cycled between 10 and 20 Hz for 600 million cycles, which corresponds to 15 years of simulated use. Testing was conducted at a minimum differential pressure of 100 mmHg, where 5% of each cycle duration must be above this minimum. This resulted in a peak differential pressure of approximately 140 mmHg. To replicate physiologic leaflet motion, full leaflet excursion was ensured, with complete leaflet opening and closing based on leaflet motion assessment from the pulse duplicator under physiologic conditions. Testing was conducted in normal saline at body temperature with trace amounts of buffer and biocide to prevent non-physiologic pH and bacterial contamination.

Table 1. Hydrodynamic testing at baseline and 600 million cycles

	Baseline			600 Million Cycles		
Valve Size and Type	**EOA (cm^2)**	**MPG (mmHg)**	**RF (%)**	**EOA (cm^2)**	**MPG (mmHg)**	**RF (%)**
19 mm						
Avalus	1.40 ± 0.02	19.6 ± 0.6	2.0 ± 0.3	1.40 ± 0.02	19.2 ± 1.3	0.9 ± 0.2
Trifecta	1.73 ± 0.05	12.3 ± 0.5	1.4 ± 0.1	1.73 ± 0.05*	15.5 ± 0.7*	1.4 ± 0.5*
Magna	1.35 ± 0.03	19.7 ± 1.1	1.5 ± 0.4	1.35 ± 0.03	21.5 ± 1.4	0.8 ± 0.2
21 mm						
Avalus	1.59 ± 0.08	14.4 ± 1.3	2.5 ± 0.2	1.60 ± 0.08	16.9 ± 1.3	2.1 ± 0.2
Trifecta	2.15 ± 0.05	8 ± 0.4	1.9 ± 0.0	2.17 ± 0.01*	8.6 ± 1.0*	5.1 ± 4.4*
Magna	1.70 ± 0.08	12.7 ± 1.2	2.4 ± 0.6	1.69 ± 0.11	15.4 ± 1.8	1.6 ± 0.8
23 mm						
Avalus	1.87 ± 0.08	10.5 ± 0.8	2.8 ± 0.3	2.02 ± 0.13	10.9 ± 1.2	2.1 ± 0.4
Trifecta	2.65 ± 0.07	5.3 ± 0.3	3.0 ± 0.7	2.7 ± 0.05	5.7 ± 0.2	2.1 ± 0.1
Magna	1.95 ± 0.09	9.6 ± 1.0	2.6 ± 1.0	2.08 ± 0.14	10.1 ± 1.3	1.5 ± 0.4

EOA, effective orifice area; MPG, mean pressure gradient; RF, regurgitant fraction. Mean ± standard deviation. *At 600 million cycles one size 19 Trifecta valve and one size 21 Trifecta valve were excluded from hydrodynamic testing due to severe regurgitation at 500 million cycles.

Hydrodynamic performance testing was conducted using a pulse duplicator system that can be adjusted to simulate desired physiologic pressure and flow conditions. Parameters of EOA, mean pressure gradient, and regurgitant fraction (RF) were evaluated at cardiac conditions of 5 L/min, 70 beats per minute, 35% systolic duration, and 100 mmHg mean aortic pressure. Testing was conducted at baseline, intervals of 50 million cycles during the first 200 million cycles, and intervals of 100 million cycles thereafter. A high-speed camera was used to capture the leaflet kinematics during hydrodynamic testing. Valves with more than 10% RF at any time point were withdrawn from further testing as these were considered "primary failures".

Visual inspections of the valves were conducted by trained personnel at 10× magnification to assess wear. High-magnification images were captured to document all wear observations. Visual inspections were performed at baseline, intervals of 25 million cycles during the first 200 million cycles, and intervals of 50 million cycles thereafter. All continuous variables are expressed as mean ± standard deviation.

Results

Effective orifice area

The Trifecta valve had the largest EOA for each labelled size at baseline (Figure 1 and Table 1). The EOAs of the Magna Ease and Avalus valves were equivalent for each labelled size. The mean differences in EOA between the Avalus and Trifecta valves were 0.33 cm^2, 0.57 cm^2, and 0.78 cm^2 for, respectively, sizes 19, 21, and 23. At 600 million cycles, the EOA values for all types and sizes remained consistent with baseline; the mean differences between the Avalus and Trifecta valves were 0.19 cm^2, 0.57 cm^2, and 0.69 cm^2 for, respectively, sizes 19, 21, and 23. Two of the Trifecta valves were excluded from the measurements at 600 million cycles due to severe regurgitation at earlier stages.

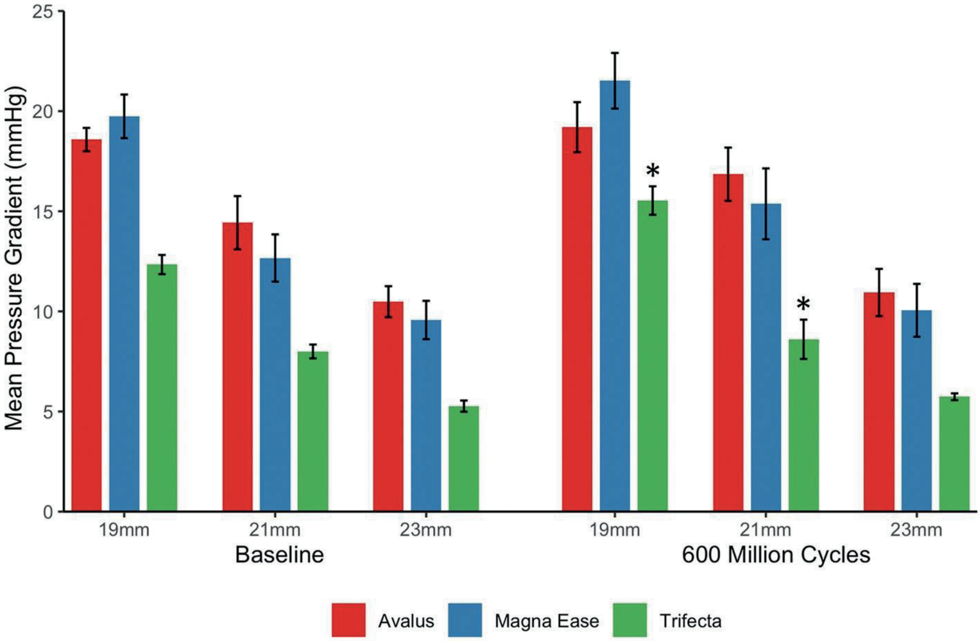

Figure 1. Mean effective orifice area (EOA, cm^2) at baseline and 600 million cycles. Error bars represent ± 1 standard deviation (SD). *At 600 million cycles one size 19 Trifecta valve and one size 21 Trifecta valve were excluded from hydrodynamic testing due to severe regurgitation at 500 million cycles.

Pressure gradient

The Trifecta had the lowest mean pressure gradient for each labelled size at baseline (Figure 2 and Table 1). The differences in mean pressure gradient between the Avalus and Magna Ease valves were 1.2 mmHg for the size 19, -1.8 mmHg for the size 21, and -0.91 mmHg for size 23. The differences in mean pressure gradient between the Avalus and Trifecta valves were 6.2 mmHg, 6.4 mmHg, and 5.2 mmHg for, respectively, sizes 19, 21, and 23. At 600 million cycles, the mean pressure gradients for all types and sizes remained consistent with baseline. Two of the Trifecta valves were excluded from the measurements at 600 million cycles due to severe regurgitation at earlier stages.

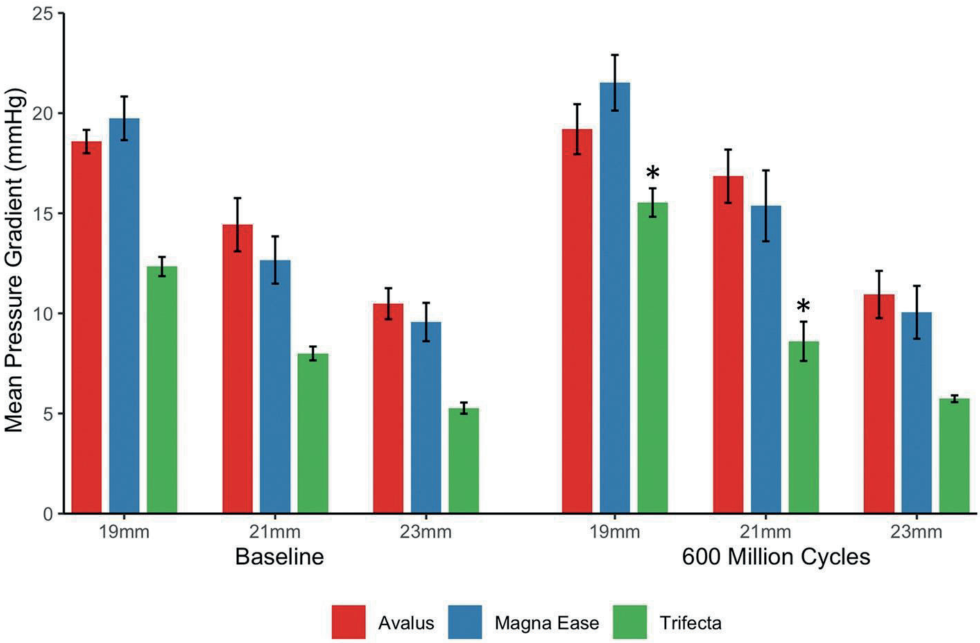

Figure 2. Mean pressure gradient at baseline and 600 million cycles. Error bars represent ± 1 standard deviation (SD). *At 600 million cycles one size 19 Trifecta valve and one size 21 Trifecta valve were excluded from hydrodynamic testing due to severe regurgitation at 500 million cycles.

Regurgitant fraction

The RF at baseline for the Avalus, Trifecta, and Magna Ease valves was 2.4% (± 0.4%), 2.1% (± 0.8%), and 2.1% (± 0.8%), respectively (Figure 3 and Table 1). From 400 million cycles onward, RF increased for three Trifecta valves. Two of these had severe regurgitation at 500 million cycles. With RFs of 31.3% and 45.9%, these valves were excluded from further hydrodynamic testing. Besides the two valves, there was another Trifecta prosthesis with a RF above 5% at 500 million cycles. This specific valve had a RF of 8.3% at 600 million cycles with a visible hole at the commissure on inspection.

None of the Avalus or Magna Ease valves developed significant regurgitation during testing, with RFs at 600 million cycles of 1.7% (± 0.7) and 1.3% (± 0.6), respectively.

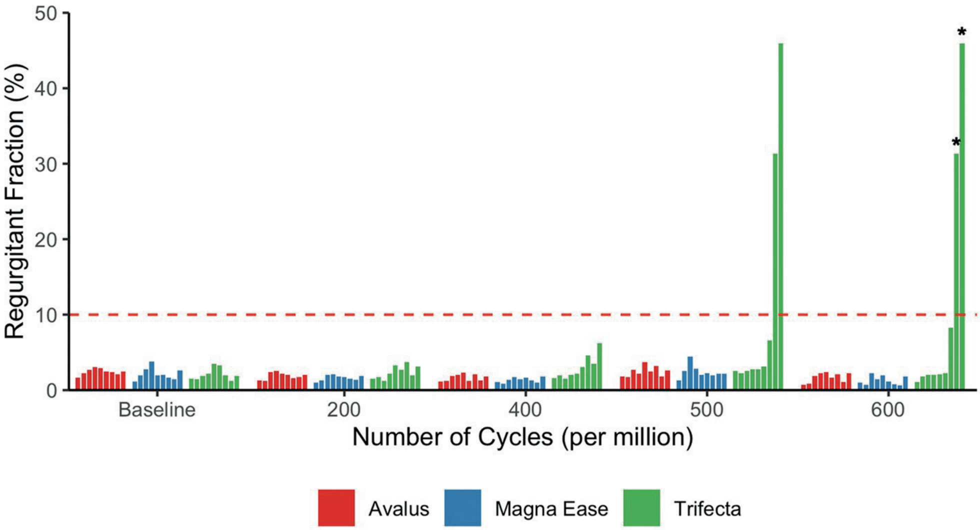

Figure 3. Mean regurgitant fraction (%) at baseline, 200, 400, 500, and 600 million cycles. *At 600 million cycles one size 19 Trifecta valve and one size 21 Trifecta valve were excluded from hydrodynamic testing due to severe regurgitation at 500 million cycles.

Visual inspection

Five of nine Trifecta valves had major abrasion damage resulting in at least one tear or hole around the commissures (Figure 4). Both valves that were excluded from further testing due to severe regurgitation had tears/holes at two commissures; the other three valves had tears/holes at only a single commissure. All Avalus and Magna Ease valves reached 600 million cycles with minimal tissue wear at the attachment of the pericardial leaflets (Figure 5). The leaflet kinematics of the Trifecta and Avalus valves, captured with high-speed camera at baseline, are shown in Videos 1 and 2, respectively.

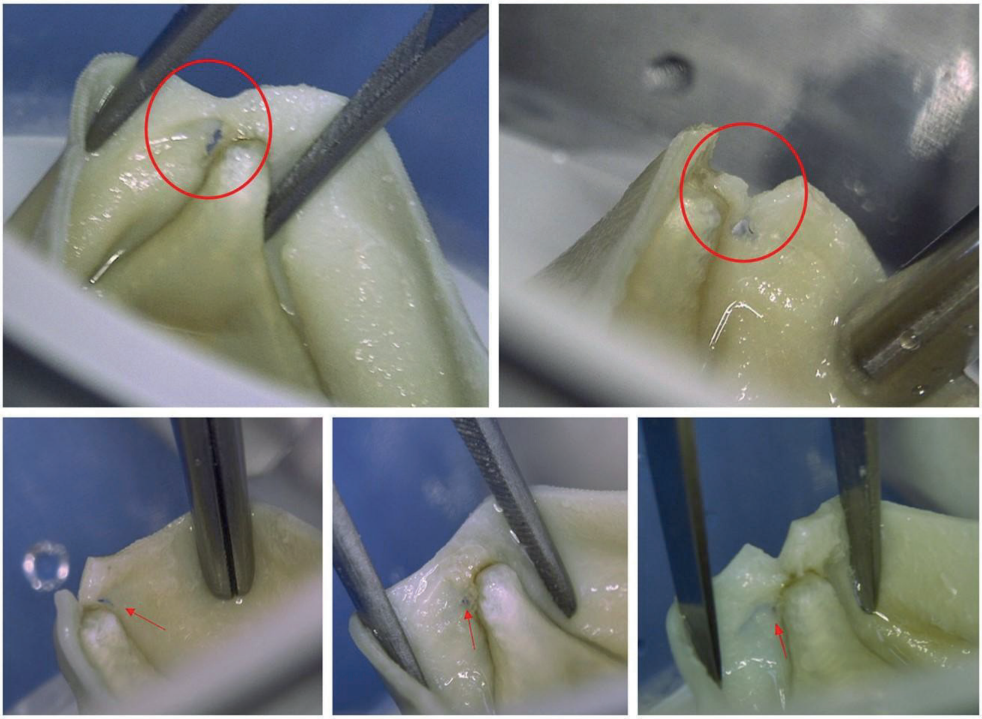

Figure 4: Five out of 9 Trifecta valves developed a tear or a hole at the commissure. Both upper valves failed hydrodynamic testing at 500 million cycles. The lower 3 valves had visible holes without severe regurgitation. The regurgitant fraction was respectively 8.4%, 2.3% and 2.0%, at 600 million cycles.

Discussion

In accordance with previous studies, EMLV have a higher EOA and lower pressure gradient than IMLV(12). However, our main finding is that the EMLV have a higher rate of mechanical failure compared to the IMLV. Of nine EMLV, two valves demonstrated severe regurgitation and one valve moderate regurgitation, all caused by wear in the commissural region. Furthermore, two valves showed severe wear in the commissural region without significant regurgitation at 600 million cycles.

Our findings are in line with those of Raghav et al., who did not find any major regurgitation after 1 billion cycles with six Perimount Magna Ease valves(13). They did find slightly lower EOA values at baseline; 1.60 cm^2 (± 0.08) for the size 21 mm and 1.70 cm^2 (± 0.08) for size 23 mm, in comparison to the 1.70 cm^2 (± 0.08) and 1.95 cm^2 (± 0.09) for size 21 and 23 mm in our study. This difference can be attributed to the well-established variation between test equipment and test laboratories for hydrodynamic performance testing(14). In addition, Raghav et al. found an increase of 10% to 12% of the EOA after 1 billion cycles, which was suggested to be potentially due to leaflets becoming more flexible over time from the repeated pressure loading in the AWT(13,15). In our study, we did not find any major differences in EOA or mean pressure gradient between baseline and the end of testing at 600 million cycles.

In the current study, the tears and holes in the EMLVs developed in the leaflet tissue around the commissural region. This location corresponds with the findings of the manufacturer during dynamic failure mode testing; "The failure mode observed was excessive regurgitation due to leaflet tear at the commissure apex. For Trifecta valves which failed, the failures occurred between 460 million and 1020 million cycles." To translate these findings to the clinical practice, 400 million cycles corresponds to about 10 years of simulated wear. Our hypothesis is that the failures of the EMLV are due to its closing mechanism. While the leaflets of the IMLVs are forced against the other leaflets at closing, the leaflet of the Trifecta wraps around the stent at each cycle (Video 1 & 2). This repeated leaflet-to-stent contact seem to cause tissue abrasion and ultimately tearing of the leaflet tissue. Although the Trifecta valve design includes a wrap of porcine pericardium over the stent to mitigate leaflet abrasion, this seems not to be sufficient to guarantee long-term mechanical durability.

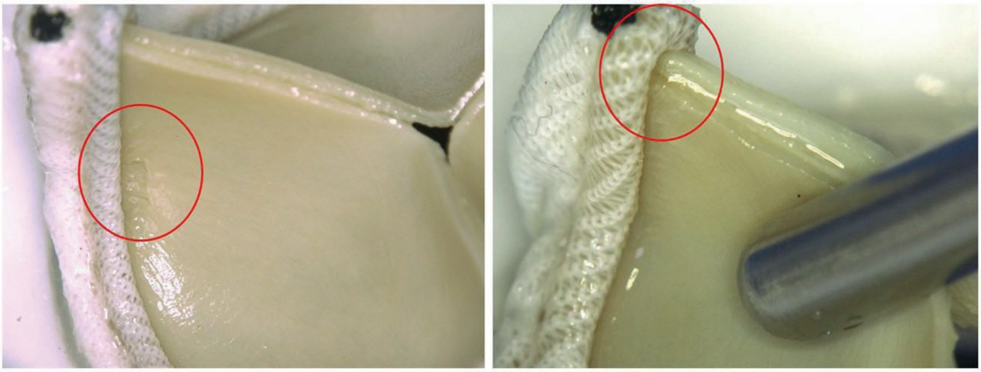

Figure 5. Minor abrasion wear of Magna Ease valve (left) and Avalus valve (right), the maximum regurgitant fraction at 600 million cycles was respectively 2.3% and 2.4%.

Leaflet tears or holes at the commisures are a known issue for externally mounted leaflet valves, first reported for the Hancock pericardial and Ionescu-Shiley valves in the 1980s. These valves had excellent hemodynamics, but the durability was limited in comparison to other porcine and pericardial valves(17). The reported mechanism of primary failure was high mechanical stress at the anchoring points or "alignment stitches" causing fatigue of the cusp tissue at the commisures(9,18). Non-calcific cuspal tears were also the dominant cause of structural valve deterioration (SVD) for the first-generation Mitroflow valve (11-A)(8,19), with a freedom from SVD as low as 39% for aortic valve

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replacement after 10 years(8). In comparison, the 10-year freedom from SVD for the internally mounted leaflet Carpentier-Edwards Perimount and Medtronic Hancock II valves was around 95%(5,6). To improve durability, the second-generation Mitroflow valve (12-A) was modified by reversing the polyester fabric covering the stent, so that the smooth side faced the pericardium(20). However, recent studies question the durability of this revised model(21),(22). Once again, pathologic evaluation demonstrated that tears occurred in the parastent post region in the majority of the explanted valves(23).

The Trifecta valve is the most recent valve with the externally mounted leaflet design, gaining FDA approval in 2011. Due to its recent introduction, there is limited long-term evidence on its durability. The reported durability at 6 years is within acceptable range, with a freedom from reoperation due to SVD of 97.3%(1). This is in agreement with our results as there were no primary failures at a roughly equivalent 300 million cycles. However, in recent years there have been numerous case reports published about the occurrence of leaflet tear(24,25,26). In combination with the current data, this may warrant close monitoring of Trifecta valves during follow-up, as the number of valves with >10 years of follow-up will increase in the next few years.

Limitations

This is an in vitro study using saline instead of blood as the test fluid. The conclusions cannot be applied directly to patients undergoing aortic valve replacement as our model did not simulate the immunologic reaction of the body to the prosthesis. Thus, we cannot assess the impact of calcifications on the durability of the prosthetic valves. In addition to not having the biological component, the test generates non-physiologic flow and pressure conditions due to the accelerated rate of testing.

Conclusions

Valves with externally mounted leaflets demonstrated superior hydrodynamic performance but inferior mechanical durability versus valves with internally mounted leaflets after 600 million cycles of testing. The primary failures were due to significant mechanical abrasion at the commisural region, which may warrant close monitoring of EMLV over the course of long-term follow-up.

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