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Original Article

PORCINE OR BOVINE TISSUE VALVES: WHICH ARE BETTER FOR SURGICAL AORTIC VALVE REPLACEMENT?

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Summary

The choice between mechanical and bioprosthetic aortic valve implants is affected by relatively clear criteria. However, the choice between porcine or pericardial valve is more complex regarding bioprosthetic devices. We aimed to elucidate any hemodynamic and clinical difference between two widely used bioprosthetic valves: the Sorin Mitroflow bovine pericardial valve and the St. Jude Medical Epic Supra porcine valve. We retrospectively studied 71 consecutive patients separated into two groups based on the valve they received. Clinical outcomes included patient survival and hemodynamic performance of the implanted prostheses. Patients were assessed at one and five years postoperatively. Mean transprosthetic pressure gradients were used as a marker of hemodynamic performance. The Mitroflow valve exhibited lesser mean transvalvular gradients than the Epic valve for all labelled sizes at one and five years postoperatively. The 5-year survival was equal between groups. Both prostheses demonstrated a small but significant increase in mean pressure gradients in the fifth year. Most patients enjoyed significant clinical improvement as assessed by NYHA functional class. Both bioprostheses performed very well with excellent hemodynamic parameters. The pericardial valves are a safe and appropriate choice for surgical bioprosthetic aortic valve replacement.

Keywords: aortic valve, bioprosthesis, pericardial valve, porcine valve, hemodynamics

Introduction

In the era of ever-growing experience with transcatheter aortic valve replacement (TAVR), the role of surgical aortic valve replacement (SAVR) is nonetheless a major one in the treatment of aortic valve disease [1]. There are established guidelines for the choice of proper valve substitute following the clinical scenario [2]. Bioprosthetic valves are generally preferred over mechanical prostheses in elderly patients because they avoid the necessity

for lifelong anticoagulation and, thence, the inherent bleeding/thrombotic risks and imposed restrictions on lifestyle [2]. Also, biological prosthetic valves show delayed structural deterioration in senior patients compared to younger recipients [3]. However, no particular recommendations exist as to the type of bioprosthesis. The decision to implant either a porcine or bovine pericardial valve is still equivocal, and in most circumstances, it is up to the individual surgeon.

Bioprosthetic valves have gained favour worldwide due to their improved design, better hemodynamics, and reduced degeneration rates. Pioneering bioprostheses were created by assembling equal-sized porcine aortic valve leaflets mounted on a metal frame. The Hancock porcine bioprosthesis was the first commercially available heart valve for clinical use. It was first inserted in 1970 and was derived from the experimental work of Carpentier et al. [4]. However, one animal provides one valve at most. In search of a more resourceful material, inventors developed bioprosthesis from bovine pericardium. M. Ionescu is credited for the first clinical use of pericardial implants [5]. The main drawback of early tissue valves was greatly diminished durability. The early attempts at improving valve durability used antimineralization treatments. Generally, the current generation of porcine and bovine valves has demonstrated increased durability rates over previous versions due to better preservation and anticalcification treatments [6], and choosing between porcine and bovine valves proves to be an uneasy task. Although various studies suggest some hemodynamic advantage to pericardial valves, no conclusive data indicate that these valves are more durable or confer a survival advantage over porcine valves [7]. Also, a recent study showed that minor hemodynamic differences amongst current-generation porcine and bovine pericardial valves do not translate into disparities in clinical outcomes and left ventricular mass regression at one year [8].

Porcine bioprostheses have been used more extensively and have a longer history than bovine pericardial bioprostheses. Consequently, they can be considered the gold standard for comparative analyses with other bioprostheses, particularly valve durability. But is that gold standard really gold?

Materials and Methods

Bioprostheses

The present study is a retrospective review of two current-generation stented biologic prosthetic valves: the Sorin Mitroflow™ bovine pericardial valve (Sorin Group, LivaNova PLC, London W2 1AY, UK) and the St. Jude Medical Epic™ Supra porcine valve (St. Jude Medical Inc., St. Paul, Minnesota, USA). We aimed to compare these prostheses regarding early and mid-term postoperative hemodynamic performance and clinical outcomes.

The *Sorin Mitroflow™*–bovine pericardial valve was first introduced into the European market in 1982 and in 2007 in the United States. Over the years, it has undergone several design changes that addressed failure modes in clinical practice [9]. It is a second-generation bioprosthesis constructed of glutaraldehyde-fixed bovine pericardium sutured onto a flexible acetyl homopolymer stent covered with polyester cloth. A piece of bovine pericardium, placed outside the stent, forms the Mitroflow valve leaflets. The sewing ring is composed of a tungsten-impregnated silicone elastomeric insert for radiographic opacity. The Mitroflow prosthesis in the aortic position has been subject to many prospective and retrospective analyses with favourable mid- and long-term durability, superb hemodynamics, and freedom from adverse events, including death[10]. Recent evaluations revealed that the Mitroflow valve provides superior hemodynamics, particularly for patients with small left ventricular outflow tract (LVOT) diameter [10].

The *St. Jude Medical Epic™ Supra* valve is a tricomposite porcine bioprosthesis formulated from three selected, size-matched porcine valve leaflets. It comprises a low-profile co-polymer flexible stent with a pericardial shield on the struts, providing tissue-to-tissue contact as the valve opens and closes. The valve undergoes low-pressure fixation and proprietary anticalcification treatment [11]. Valve distribution began in 2003 and 2007 in Europe and USA, respectively. The *Epic™ Supra* is available in labeled sizes of 19, 21 and 23 mm. The manufacturer recommends the standard *SJM Epic* heart valve for larger annulus diameters.

Study subjects

The present study included 71 consecutive patients divided into two groups. All data were obtained from a single institution after approval by the institutional ethics committee. From January 2010 to August 2014, all elective AVR cases with the bioprostheses mentioned above were included in the study. Exclusion criteria were age younger than 18 years, pregnancy, patient refusal to receive one of the two prostheses, patients presenting in shock, severe neurologic disease (a debilitating stroke), end-stage renal failure, immunocompromised patients and/or immunosuppressive therapy, or severe calcification of the aortic root or ascending aorta ("porcelain aorta"). Patients undergoing concomitant procedures (e.g. coronary artery bypass grafting, repair/replacement of other valves, etc.) and re-operative cases remained eligible for inclusion.

Group A (Mitroflow group) comprised 37 patients (43% female) who received AVR with the Sorin Mitroflow™ pericardial valve. The mean age was 71±11 years. Eighteen patients (49%) had isolated aortic stenosis (AS), and 4 (11%) had isolated aortic regurgitation (AR). Thirteen patients (35%) had significant mitral regurgitation (MR), and four patients (11%) had mitral stenosis (MS). Twelve patients (32%) also had coronary artery disease (CAD). Three patients (8%) were diagnosed with aortic valve endocarditis (by echocardiographic and blood culture criteria), one of whom had prosthetic valve endocarditis. Twenty patients (55%) were classified into NYHA functional class III or IV. Six patients (16%) had severe left ventricular (LV) dysfunction (ejection fraction (EF) <30%), whereas 26 patients (70%) had preserved LV function (ejection fraction>50%). Eighteen patients (49%) were considered high-risk, according to the logistic EuroSCORE calculation (16.6±3.7%). Nine patients (24%) had a documented atrial fibrillation. Fourteen patients (38%) reported neurologic symptoms – syncope in 6 patients (16%), transient ischemic attacks in 5 patients (14%), and stroke in three patients (8%).

Group B (Epic group) comprised 34 patients (26% female) who received the St. Jude Medical Epic™ Supra porcine valve. The mean age was 68±14 years. Fourteen patients (41%) were diagnosed with isolated AS; six (18%) had isolated AR; the remainder had a mixed lesion. Two patients (6%) had aortic valve endocarditis. Additional cardiac pathology was severe MR in 14 patients (41%), MS in 4 patients (11%), and CAD in 11 patients (32%). Twenty-eight patients (82%) had NYHA functional class III or IV symptoms. Twenty-two patients were rated high-risk based on EuroSCORE calculation (42.8±11.4%). Nine patients had documented chronic atrial fibrillation. Fourteen patients (41%) had experienced neurologic events – syncope in 5 patients (15%), transient ischemic attacks in 4 patients (11%), and stroke in 6 patients (18%). The preoperative characteristics and the concomitant diseases and risk factors of all patients are displayed in Table 1 and Table 2, respectively.

Surgical procedures

All patients underwent standard cardiopulmonary bypass and crystalloid cardioplegic arrest. Following aortotomy, native valve excision and annular decalcification were performed. The native valve annulus and LVOT were measured by the manufacturer's prosthesis-devoted sizers and Hegar dilators. In both groups, the valve prostheses were implanted by the supraannular technique using non-everything pledgeted mattress sutures. No root enlargement procedures were performed in the current series.

Clinical evaluation and follow-up

The primary end-point of the study was the postoperative hemodynamic performance of the implanted prostheses. The secondary end-point was patient survival. Clinical follow-up was performed at one and five years after surgery. Both groups were examined by echo at three time points: at hospital discharge (100% complete), one year after surgery (95.5% complete or 64 patients) and five years after surgery (82.1% complete or 55 patients). The patients were contacted and invited for a clinical and echocardiographic check-up. In both groups, we focused our interest on the patient's general status, NYHA functional class, and echocardiographic parameters of prosthesis function.

Echocardiography

Echocardiography was performed by a single experienced sonographer using standard acquisition protocols and multiple acoustic windows. Patients underwent comprehensive transthoracic echocardiography before discharge from the hospital and on follow-up. Continuous-wave Doppler ultrasound was implemented for the assessment of prosthetic function. Transvalvular mean pressure gradients (ΔP_m) were calculated automatically with the modified *Bernoulli equation*. They were used as a marker of the hemodynamic performance of the implanted bioprostheses. EF was used as a surrogate marker of left ventricular systolic function.

Statistical Analysis

The statistical analysis was performed by an independent certified statistician using SPSS 11.0.1, Version 11 (SPSS Inc. Chicago, IL, USA) statistical software. All quantitative data were checked for normal distribution using the non-parametric Kolmogorow-Smirnow test. Continuous variables were summarized as means±standard deviation. The variables lacking normal distribution were assessed with the Mann-Whitney U-test. Cox regression analysis was applied to establish if there were any differences in survival between the two groups. Relationships between categorical variables were sought with Fisher's exact test and the χ^2-test. Student t-test was applied to test the equality of normally distributed data. A p-value < 0.05 was considered significant.

Results

Both groups were comparable concerning preoperative characteristics and comorbid disease (Table 1 and Table 2).

There were significantly more females in the Mitroflow group. The Epic group presented more often with mixed stenosis/ regurgitation pathology, a higher chronic kidney disease rate and a higher overall EuroSCORE.

Table 1. Preoperative patient data.

Patient characteristics	Group A	Group B	*p*
Number	37	34	NS
Male/female	21/16	25/9	<.05
Age (mean ± standard deviation)	71±11	68±14	NS
Aortic valve pathology			
Aortic stenosis	18 (49%)	14 (41%)	NS
Aortic regurgitation	4 (11%)	6 (18%)	NS
Mixed	4 (11%)	12 (35%)	<.05
Infective endocarditis	3 (8%)	2 (6%)	NS
Congenital	1 (3%)	–	NS
Native valve hemodynamics			
Peak gradient (mmHg)	62±27	68±26	NS
Mean gradient (mmHg)	42±21	57±17	NS
Effective orifice area (sq.cm.)	0.7±0.18	0.56±0.22	NS
Associated disease			
Coronary artery disease	12 (32%)	11 (32%)	NS
Previous myocardial infarction	6 (16%)	8 (24%)	NS
Mitral regurgitation	13 (35%)	14 (41%)	NS
Mitral stenosis	4 (11%)	4 (11%)	*NS*
Pulmonary hypertension	7 (19%)	13 (35%)	NS
Chronic atrial fibrillation	9 (24%)	9 (26%)	NS
Redo surgery	1 (3%)	2 (6%)	NS
Ejection fraction	52±15	48±18	NS
<30%	6 (16%)	5 (15%)	NS
30-50%	11 (30%)	15 (44%)	NS
>50%	20 (54%)	14 (41%)	NS

Table 2. Associated disease and risk factors.

Concomitant disease & risk factors	Group A	Group B	*p*
Hypertension	23 (74%)	27 (79%)	NS
Cigarette smoking	11 (35%)	27 (79%)	NS
Diabetes mellitus	14 (45%)	18 (53%)	NS
Dyslipidemia	17 (55%)	21 (62%)	NS
Obesity (*BMI>30*)	7 (23%)	7 (22%)	NS
Neurological disorders			
Cerebral vascular disease	–	11 (32%)	–
Syncope	6 (16%)	5 (15%)	NS
Transitory ischemic attack	5 (14%)	4 (11%)	NS
Previous stroke	3 (8%)	6 (18%)	NS
Peripheral vascular disease	6 (19%)	3 (10%)	NS
Chronic kidney disease	2 (6%)	13 (38%)	<.05
Chronic obstructive pulmonary disease	4 (13%)	11(32%)	NS
Neoplastic disease	2 (6%)	1 (3%)	NS
Gastroesophageal reflux disease	7 (23%)	4 (11%)	NS
Logistic EuroSCORE (*mean ± SD*)	14.7 ± 4.2	9.8 ± 3.4	NS
NYHA class			
I	–	–	–
II	14 (45%)	6 (18%)	NS
III	12 (39%)	24 (71%)	NS
IV	5 (16%)	4 (11%)	NS

Patient survival

Early and late postoperative death were defined according to the updated guidelines for reporting morbidity and mortality after cardiac valvular operations [12]in this document the term 'operated valve' indicates prosthetic and bioprosthetic heart valves of all types: operated or repaired native valves and allograft and autograft valves. The term 'operated valve' includes any cardiac valve altered by a surgeon during an operation. Much morbidity and mortality is a direct consequence of the interaction between the patient and operated valve(s. Operative mortality includes all patients who succumbed within thirty days of their surgery regardless of patient's location (e.g. death in the operating room, intensive care unit, home or nursing centre) or within the same hospital stay. All

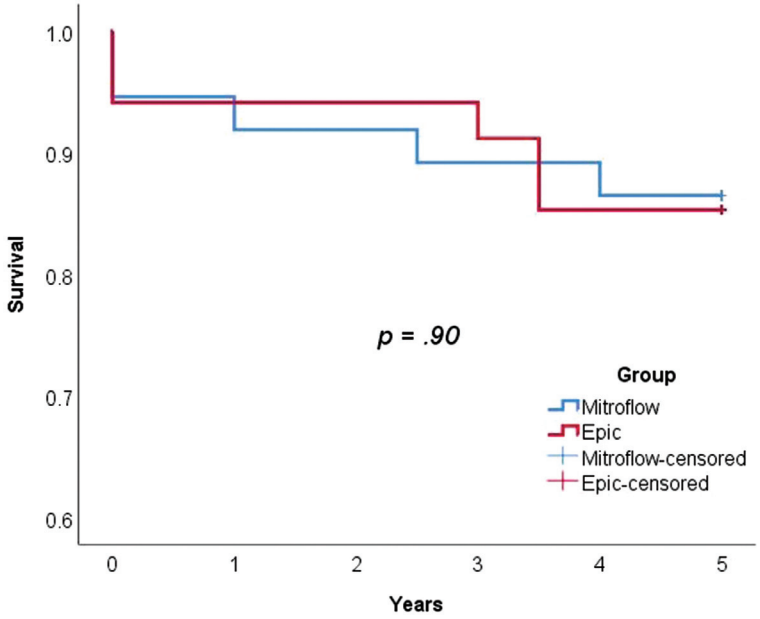

Figure 1. Survival functions of the Mitroflow and Epic group.

early deaths occurred in the intensive care unit during the index hospital stay. Mortality in group A was 5.4% (2 patients). In both cases, the cause of death was low cardiac output syndrome, unrelated to valve performance. Mortality in group B was 5.9% (2 patients). One was operated on for acute aortic valve endocarditis and died of overwhelming sepsis. The other patient died of progressive heart failure in the setting of complex multivalvular disease and high-grade pulmonary hypertension. There was no statistically significant difference in early mortality between both groups ($p = 1.0$). *At* one year, one patient (2.7%) from the Mitroflow group died of pneumonia. At five years, two more patients (5.4%) from group A and three (8.8%) from group B were found to have died. None of the fatal events was attributed to the implanted prosthetic valve. One patient died of a stroke in each group. The remaining patients experienced sudden cardiac death caused by acute myocardial infarction or rhythm/conduction disturbances of the heart. Thus, overall five-year survival in the Mitroflow group was 86.5% and 85.3% in the Epic group. Cox regression analysis showed no difference in survival between the two groups, $p = .90$ (Figure 1).

Prosthetic valve performance

Valve function was assessed by standard echocardiographic measurements. All patients were evaluated before discharge. At one year, 97% of the discharged patients (34 patients) of the Mitroflow group and 94% (30 patients) of the Epic group were seen for echocardiographic evaluation. At five years, follow-up dropped to 83% and 81% for the Mitroflow and Epic groups, respectively.

The Mitroflow valve performed better than the Epic valve one year after surgery for all labelled sizes. This favourable outcome persisted throughout the follow-up period (Figure 2 and Figure 3).

Table 3 below summarizes those differences in calculated mean transvalvular pressure gradients.

A paired-sample T-test was applied to check for any statistically significant difference in pressure gradient between the two follow-up time points for each group. The Mitroflow and Epic group showed a 2.1±0.1 mmHg increase in mean gradients at five years $p< 0.05$ (Figure 4).

Clinical status

The clinical status and physical capabilities were assessed in all patients who were followed up. Only 16 patients (43%) were in NYHA functional class I or II before the operation in group A. One year later, their number grew to 27 (73%). In group B, the results were analogous. Before the operation, six patients (18%) were in NYHA class I or II, whereas postoperatively, they expanded to 23 (85%), $p<0.05$.

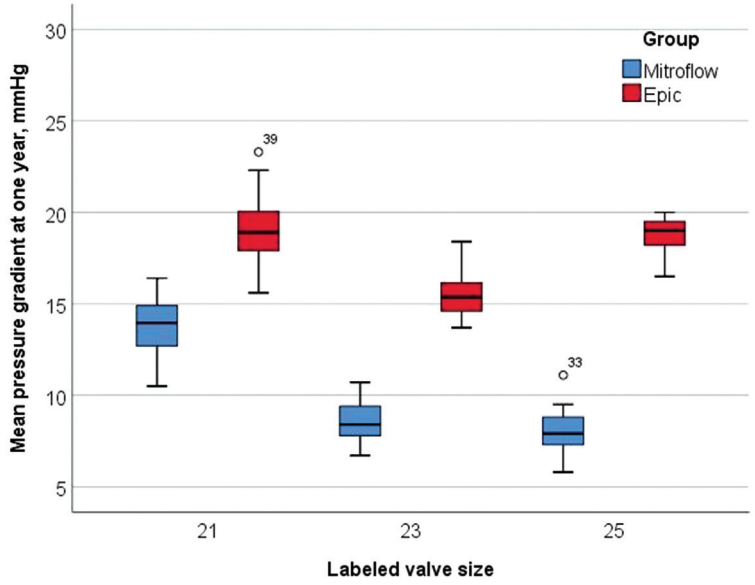

Figure 2. Boxplot chart demonstrating the difference in pressure gradients between Mitroflow and Epic valves at one year echo examination.

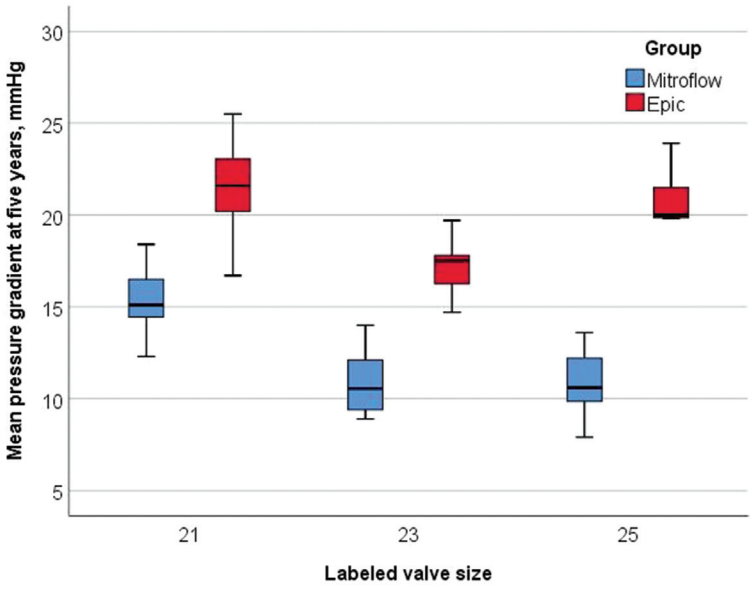

Figure 3. Boxplot chart demonstrating the difference in pressure gradients between Mitroflow and Epic valves at five years echo examination.

Table 3. Comparison of mean transprosthetic pressure gradients (ΔP_m, mmHg) for various sizes at two time points.

One year				
Valve size/Group	Mitroflow	Epic	Mean difference	p
21	13.7±1.6	19.2±2.0	5.5±0.6	<.001
23	8.6±1.1	15.5±1.4	6.9±0.5	<.001
25	8.1±1.7	18.7±1.2	10.6±0.8	<.001
Five years				
Valve size/Group	Mitroflow	Epic	Mean difference	p
21	15.3±1.6	21.6±2.4	6.3±0.7	<.001
23	10.9±1.7	17.2±1.3	6.3±0.6	<.001
25	10.9±2.0	20.9±1.5	10.0±0.9	<.001

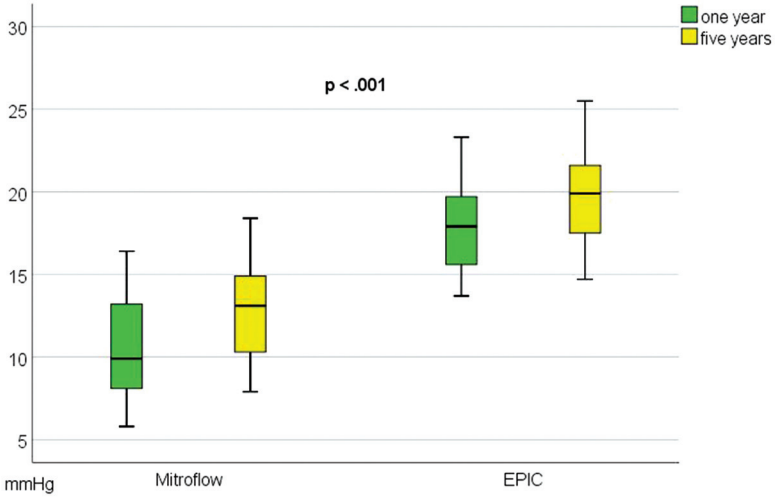

Figure 4. Gradient rise throughout the follow-up due to early bioprosthetic degeneration.

Discussion

Advancing the life expectancy in developed countries leads to an increased incidence of degenerative valve disease. In the current era, the implantation of bioprostheses has become more common, and manufacturers constantly refine their devices. Choosing an appropriate bioprosthesis is a responsible and important decision that can influence the long-term results of valve replacement. For decades, porcine bioprostheses have been the first choice for most surgeons. During the last two decades, bovine pericardial valves were established firmly into clinical practice due to improved fixation methods and anticalcification treatment. Currently, they stand along porcine valves in the surgeon's armamentarium.

The present study retrospectively reviewed the early and mid-term results after implantation of two different bioprosthetic valves: the Sorin Mitroflow™ pericardial valve and the St. Jude Medical Epic™ Supra porcine valve. All data were gathered at a single institution between January 2010 and August 2014.

Operative mortality in group A (5.4%) and group B (5.9%) was lower than expected based on logistic EuroSCORE estimate – 14.7±4.2% for group A and 42.8±11.4% for group B (p<0.05). Like in other studies, comparing the two valves did not find a significant difference in mortality [8]St Paul, Minn. The early and mid-term survival results corresponded to those reported by other authors [13]as appropriate. Results: The median age was 80 years (range, 49-96.

Prosthetic valve size and design are the prime determinants of its hemodynamic function. According to Poiseuille's law, the flow through a cylinder depends mainly on its radius. Thus, the larger the inner diameter of the valve, the lower the impedance and the greater the flow. This relationship explains the effort of every surgeon to insert the largest possible prosthesis.

The Mitroflow and Epic valves both demonstrated excellent hemodynamic profiles, and patients enjoyed significant clinical improvement. However, actual instrumental function measurements showed lesser transprosthetic gradients through the pericardial valves for all sizes throughout the follow-up period. As transprosthetic gradient is in inverse relationship with effective orifice area, pericardial valves were suggested to be less obstructive than porcine valves, which would favour left ventricular mass reduction and long-term prognosis.

To better understand the hemodynamic function of the studied bioprostheses, we searched for studies comparing two other commonly used bioprostheses: Medtronic Mosaic™ Ultra – a stented porcine valve, and Carpentier-Edward Perimount™ Magna – a stented pericardial valve. In one study, the Perimount valve performed better than the Mosaic valve [14], like our results, comparing another pericardial with another porcine prosthesis. Another study showed that pericardial valves were less obstructive to flow than porcine valves, although similar improvements in exercise ability and left ventricular mass regression were noted in the short term [15]. A prospective randomized study showed that a pericardial valve (Carpentier Edwards Perimount) was significantly superior to a porcine valve (Medtronic Mosaic) concerning hemodynamic performance, the incidence of patient-prosthesis mismatch, and left ventricular mass regression that became more evident with time [16]. A recent study has demonstrated that porcine valves are linked to a risk of prosthetic hemodynamic deterioration and a chance of reintervention in time [17].

Calculation of left ventricular mass regression was not included in our echocardiographic protocol. Thus, we cannot say whether the more favourable hemodynamic parameters of the Mitroflow valve had translated into better left ventricular reverse remodelling. Considering the results of a study mentioned above [16] and our patients' well-being, this would have been the case.

Over the first year following AVR, none of the prostheses from all sizes demonstrated significant changes in the transvalvular gradients. However, it was recognized that in the long term, bioprosthetic function deteriorates. Between the first and fifth years, the mean pressure gradient in both bioprosthetic valves in our series increased by 2 mmHg on average. Nevertheless, those changes were not clinically relevant, as demonstrated in other studies [18].

Asch et al. shared their 5-year experience

with the Mitroflow valve and concluded that long-term morbidity rates were low and valve durability was stable in the elderly population with a high prevalence of comorbid conditions [18]"ISSN":"00034975","abstract":"Backgrou nd: The Mitroflow valve (Sorin Group, Milan, Italy.

Conclusion

The current stented pericardial valves exhibit smaller gradients and larger effective orifice areas than size-matched stented porcine bioprostheses. However, there is no significant difference in mid-term patient survival and morbidity. Thus, pericardial bioprostheses are an excellent choice for AVR, especially in senior patients.

Acknowledgements

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Limitations

1. The present study is a non-randomized retrospective analysis, and the patient data were obtained from chart records and partially incomplete hospital documentation.

2. The number of patients is relatively small, which may underestimate the value of our results. Also, the follow-up was relatively short for adequate assessment of patient survival and prosthesis function and durability.

3. The labelled sizes of many heart valve prostheses do not always correlate to the diameter of the native valve annulus and the labelled sizes of other valves. Therefore, the published literature data regarding pressure gradients, valve orifice area and PPM could be, in some cases, misleading and non-comparable to our results.

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