



Hemodynamic Performance of Pericardial Bioprostheses in the Aortic Position

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Background: This study was conducted to evaluate the hemodynamic performance and the incidence of prosthesis-patient mismatch (PPM) after aortic valve replacement (AVR) using bovine pericardial valves (Carpentier-Edwards Perimount Magana and Magna Ease).

Methods: In total, 216 patients (mean age, 70.0±10.5 years) who underwent AVR using stented bovine pericardial valves and had follow-up echocardiography between 3 months and 2 years (mean, 12.0±6.6 months) after surgery were enrolled. The implanted valve sizes were 19, 21, 23, and 25 mm in 32, 56, 99, and 29 patients, respectively.

Results: On follow-up echocardiography, the mean transvalvular pressure gradients for the 19-mm, 21-mm, 23-mm, and 25-mm valves were 13.3±4.4, 12.6±4.2, 10.5±3.9, and 10.2±3.7 mm Hg, respectively. The effective orifice area (EOA) was 1.25±0.26, 1.54±0.31, 1.81±0.41, and 1.87±0.33 cm², respectively. These values were smaller than those suggested by the manufacturer for the corresponding sizes. No patients had PPM, when based on the reference EOA. However, moderate (EOA index ≤0.85 cm²/m²) and severe (EOA index ≤0.65 cm²/m²) PPM was present in 56 patients (11.8%) and 9 patients (1.9%), respectively, when using the measured values.

Conclusion: Carpentier-Edwards Perimount Magna and Magna Ease bovine pericardial valves showed satisfactory hemodynamic performance with low rates of PPM, although the reference EOA could overestimate the true EOA for individual patients.

Keywords: Aortic valve, Surgery, Heart valves, Bioprosthesis, Hemodynamics

Introduction

The aim of treating patients with aortic valve (AV) disease is to relieve stenosis or regurgitation and to attain physiological transvalvular gradients. Prosthesis-patient mismatch (PPM) occurs when the effective orifice area (EOA) of the implanted valve is smaller than the patient's physiological needs, thereby generating higher transvalvular gradients. The poorer outcomes of patients with PPM following aortic valve replacement (AVR) have been thoroughly demonstrated in previous studies [1-5]. Thus, it is important to implant a prosthetic valve with a sufficiently large orifice area to meet the physiological requirements of the patient.

The Carpentier-Edwards Perimount Magna and Magna Ease (Edwards Lifesciences, Irvine, CA, USA) valves are

stented bovine pericardial bioprostheses that have been used worldwide. While each manufacturer provides a reference EOA for each valve size, *in vivo* Doppler echocardiographic results have shown variation of EOA in patients with the same prosthesis size. Also the *in vivo* reference values tend to be smaller than the *in vitro* values [3]. These differences are thought to be caused by biological variation, measurement errors, and underestimations or overestimations [2,6].

Therefore, this study was conducted (1) to evaluate the hemodynamic performance and the incidence of PPM after bioprosthetic AVR using bovine pericardial valves (Edward Perimount Magna and Magna Ease) and (2) to provide *in vivo* reference EOA values for these valves.



Methods

Study design

Between January 2005 and August 2018, 1,401 patients underwent AVR at our institution. Of these patients, 216 patients in whom Carpentier-Edwards Perimount Magna or Magna Ease valves were placed and who had echocardiographic evaluations before discharge and during follow-up between 3 months and 2 years after surgery were enrolled (Fig. 1). The study protocol was reviewed by the institutional review board, and was approved as a minimal-risk retrospective study (IRB approval no., 1912-030-1086) that did not require individual consent.

Operative data

All operations were performed using aortic and bicaval cannulation via median sternotomy by 1 of 4 surgeons at our institution. Prosthetic valves were implanted after removal of the AV leaflet and decalcification of the aortic annulus. The suture technique was identical in almost all study patients; non-everting mattress sutures buttress-reinforced with polytetrafluoroethylene as a tubule (so-called “spaghetti”) were used. One surgeon occasionally used several sutures with polytetrafluoroethylene as a pledget instead of a tubule. Another surgeon recently adopted a continuous suture technique, which was used in 11 study patients (5.1%).

Echocardiographic evaluation

Two-dimensional echocardiography and Doppler color-flow imaging were performed in the early postoperative period (8.5 ± 5.1 days) and 12.0 ± 6.6 months after surgery. The EOA was calculated as previously described [7]. Briefly, the left ventricular outflow tract (LVOT) diameter was measured in mid-systole from a parasternal long-axis view of the LVOT, with the inner to inner edge technique. The cross-sectional area (CSA) of the LVOT was calculated from the LVOT diameter by assuming it to be circular as follows: $LVOT\ CSA = \pi \times (LVOT\ diameter/2)^2$. The LVOT velocity time integral (VTI) was obtained using the pulsed-wave Doppler signal. From these measurements, the EOA was calculated using the continuity equation as follows: $EOA = (LVOT\ CSA \times LVOT\ VTI) / (VTI\ obtained\ from\ the\ continuous-wave\ Doppler\ signal)$ [7]. The VTI values obtained by pulsed-wave and continuous-wave Doppler were measured and averaged over 5 to 10 consecutive beats in

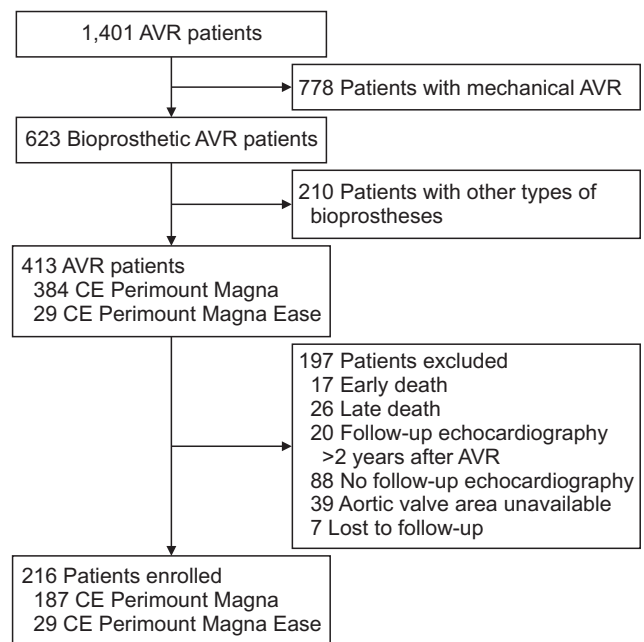


Fig. 1. Flowchart of patient selection. Patients who underwent AVR with CE Magna and Magna Ease between January 2005 to August 2018 with available postoperative follow-up echocardiography were selected. AVR, aortic valve replacement.

patients with atrial fibrillation. The effective orifice area index (EOAI, cm^2/m^2) was calculated by dividing the EOA by the body surface area of the patient, and moderate and severe PPM was defined as $EOAI \leq 0.85 \text{ cm}^2/\text{m}^2$ and $EOAI \leq 0.65 \text{ cm}^2/\text{m}^2$, respectively [1].

Anti-thrombotic management

Warfarin anticoagulation with a target international normalized ratio of 2.0–2.5 was maintained for 3–6 months and throughout the patient’s life after surgery in patients with sinus rhythm and in those with atrial fibrillation, respectively. However, since late 2014, antiplatelet therapy instead of warfarin anticoagulation has been used for patients with normal sinus rhythm.

Statistical analysis

Statistical analyses were performed using IBM SPSS ver. 25.0 (IBM Corp., Armonk, NY, USA). Data are expressed as means \pm standard deviation or proportions, as appropriate. Comparisons of paired data from continuous variables were performed using the paired t-test, and p-values < 0.05 were considered to indicate statistical significance.

Results

Patient data

Patients' mean age at surgery was 70.0 ± 10.5 years, and 116 patients (53.7%) were male. Carpentier-Edwards Perimount Magna and Magna Ease valves were used in 187 and 29 patients, respectively. The mean left ventricular ejection fraction at surgery was $58.7\% \pm 10.2\%$. Bicuspid AV (n=100, 46.3%) was the most common etiology (Table 1).

Valves sized 19 mm, 21 mm, 23 mm, and 25 mm were implanted in 32, 56, 99, and 29 patients, respectively. Concomitant procedures included arrhythmia surgery (n=20), aorta surgery (n=38), and coronary artery bypass grafting (n=29) (Table 2).

Table 1. Preoperative characteristics and risk factors (N=216)

Characteristic	Value
Age (yr)	70.0±10.5
Male	116 (53.7)
New York Heart Association class ≥ 3	50 (23.4)
Etiology	
Degenerative	88 (40.7)
Bicuspid	100 (46.3)
Rheumatic	23 (10.6)
Endocarditis	5 (2.3)
Left ventricular ejection fraction (%)	58.7±10.2
Risk factors	
Current smoker	33 (15.3)
Overweight (body mass index >25 kg/m ²)	45 (20.8)
Diabetes mellitus	52 (24.1)
Hypertension	116 (53.7)
History of stroke	12 (5.6)
Chronic obstructive pulmonary disease	8 (3.7)
Chronic kidney disease	50 (23.1)
Coronary artery disease	58 (26.9)
Atrial fibrillation	36 (16.7)
Emergency or urgency	1 (0.5)

Values are presented as mean±standard deviation or number (%).

Table 3. Transvalvular MPG and mEOA and rEOA of Carpentier-Edwards Magna and Magna Ease bovine pericardial valves on early postoperative (8.5±5.1 days after surgery) echocardiography

Size (mm)	No. of patients for MPG	MPG (mm Hg)	No. of patients for mEOA	mEOA (cm ²)	rEOA (cm ²)
19	32	15.8±4.8	30	1.17±0.35	1.58
21	56	14.7±5.3	43	1.39±0.38	1.90
23	99	12.4±4.3	84	1.63±0.42	2.07
25	29	12.2±5.0	24	1.73±0.38	2.33

Values are presented as mean±standard deviation, unless otherwise stated.

MPG, mean pressure gradient; mEOA, measured effective orifice area; rEOA, reference effective orifice area.

Early postoperative hemodynamic data

The transvalvular mean pressure gradient (MPG) and the EOA were measured in 216 and 181 patients, respectively. Overall, the transvalvular MPG on early postoperative echocardiography was 13.5 ± 4.9 mm Hg, and the transvalvular MPG values on early postoperative echocardiography for 19-mm, 21-mm, 23-mm, and 25-mm valves were 15.8 ± 4.8 , 14.7 ± 5.3 , 12.4 ± 4.3 , and 12.2 ± 5.0 mm Hg, respectively. The EOAs for those valves were 1.17 ± 0.35 , 1.39 ± 0.38 , 1.63 ± 0.42 , and 1.73 ± 0.38 cm², respectively. These values were smaller than those suggested by the manufacturer (Table 3).

Hemodynamic data on follow-up echocardiography and incidence of prosthesis-patient mismatch

On follow-up echocardiographic evaluations, the overall transvalvular MPG was 11.4 ± 4.2 mm Hg. The transvalvular MPG for 19-mm, 21-mm, 23-mm, and 25-mm valves were 13.3 ± 4.4 , 12.6 ± 4.2 , 10.5 ± 3.9 , and 10.2 ± 3.7 mm Hg, respectively. The EOAs for those valves were 1.25 ± 0.26 , 1.54 ± 0.42 , 1.81 ± 0.41 , and 1.87 ± 0.33 cm², respectively (Table 4). The MPGs on follow-up echocardiography were significantly lower than those on early postoperative echocardiography ($p < 0.001$) (Fig. 2). The EOAs on follow-up echocardiography were also significantly higher than the early

Table 2. Operative data (N=216)

Variable	Value
Cardiopulmonary bypass time (min)	190.0±75.1
Aortic cross-clamping time (min)	121.5±50.7
Concomitant procedures	
Arrhythmia surgery	20 (9.2)
Replacement of the ascending aorta	38 (17.6)
Coronary artery bypass grafting	29 (13.4)

Values are presented as mean±standard deviation or number (%).

Table 4. Transvalvular MPG and mEOA and rEOA of Carpentier-Edwards Magna and Magna Ease bovine pericardial valves on follow-up echocardiography performed at 12.0±6.6 months after surgery

Size (mm)	No. of patients ^{a)}	MPG (mm Hg)	mEOA (cm ²)	rEOA (cm ²)
19	32	13.3±4.4	1.25±0.26	1.58
21	56	12.6±4.2	1.54±0.42	1.90
23	99	10.5±3.9	1.81±0.41	2.07
25	29	10.2±3.7	1.87±0.33	2.33

Values are presented as mean±standard deviation, unless otherwise stated. MPG, mean pressure gradient; mEOA, measured effective orifice area; rEOA, reference effective orifice area.

^{a)}All study patients had both MPG and mEOA data.

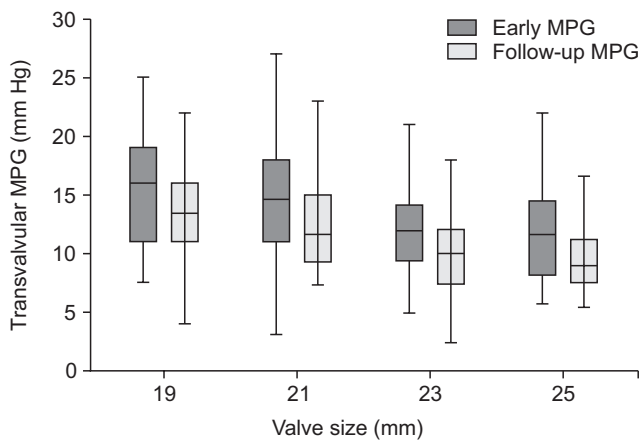


Fig. 2. Changes in the transvalvular MPG on early postoperative and follow-up echocardiography after aortic valve replacement using bovine pericardial valves. The central box represents the values from the lower to upper quartile and the middle line represents the median. A line extends from the minimum to the maximum value. MPG, mean pressure gradient.

postoperative values when those were compared in 181 patients who had both early postoperative and follow-up data for EOA ($p < 0.001$) (Fig. 3). However, the EOAs on follow-up echocardiography were still smaller than those suggested by the manufacturer for each size.

No patients had PPM when it was calculated based on the reference EOA. However, moderate and severe PPM was present in 56 patients (11.8%) and 9 patients (1.9%), respectively, when applying the measured values.

Discussion

The present study demonstrated 2 main findings. First, the currently available bovine pericardial valves had satisfactory hemodynamic performance with low rates of PPM. Second, the actual EOAs were smaller than the values supplied by the manufacturer.

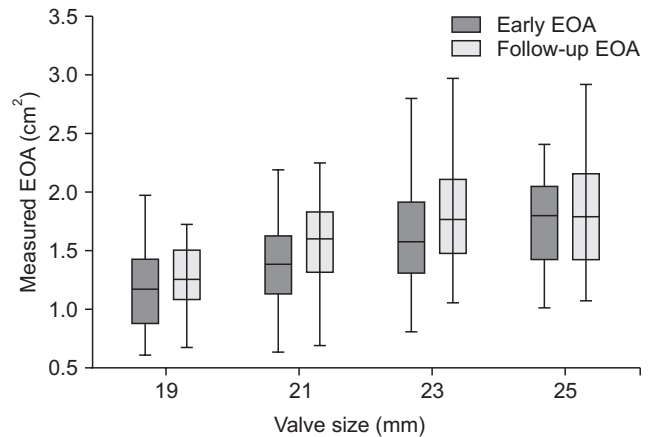


Fig. 3. Measured EOAs on early postoperative and follow-up echocardiography after aortic valve replacement using bovine pericardial valves. The central box represents the values from the lower to upper quartile and the middle line represents the median. A line extends from the minimum to the maximum value. EOA, effective orifice area.

The aim of AVR is to relieve stenosis or regurgitation and to implant AV prostheses that reach physiological transvalvular gradients. However, as parts of the sewing ring and the stent are positioned within the blood flow, a residual gradient may remain, especially for small valves [1-3]. PPM occurs when the EOA of the prosthesis is smaller than the patient's physiological needs, generating higher transvalvular gradients. PPM causes worse hemodynamic performance, which directly affects the clinical outcomes of AVR patients, resulting in less regression of left ventricular hypertrophy, higher incidence of cardiac events, and decreased long-term survival [1,4,5]. Thus, the most important goal in performing AVR is to implant a valve size that corresponds to the patient's needs [1-3].

Carpentier-Edwards Perimount Magna and Magna Ease are stented bovine pericardial bioprostheses designed to allow for complete supra-annular placement. Supra-annular placement allows the insertion of larger prostheses in the same aortic annular diameter. In addition, they have a smaller sewing ring, which is intended to increase the EOA or even to allow possible upsizing of the implanted valve, thereby improving hemodynamic status [3,8,9].

While each manufacturer provides an expected EOA for each valve size and surgeons usually follow this guidance, *in vivo* Doppler echocardiographic results have demonstrated variation of EOA in patients with the same prosthesis size, and the *in vivo* reference values tend to be smaller than the provided values [3,6,10]. Therefore, this study was conducted to evaluate the hemodynamic performance of these stented bovine pericardial valves and to provide in-

stitutional *in vivo* EOA data. Previous studies have recommended that the EOA should be based on *in vivo* data measured at 6 months to 1 year after surgery, as hemodynamic data may change during several months post-surgery [10,11]. In addition, measurements made too late might underestimate the actual EOA of the product because bioprosthetic valve failure could occur several years after surgery, although this is not a common event [12]. For these reason, patients who had only early postoperative echocardiographic data and who had data from more than 2 years after surgery were excluded from the present study, and only patients who had follow-up echocardiographic data between 3 months and 2 years after surgery were enrolled. The present study demonstrated significantly lower transvalvular MPG and larger EOA on follow-up echocardiography than on early postoperative echocardiography. These findings also support the possibility that the determination of the EOA of prosthetic valves and diagnosis of PPM might be incorrect if they are based on early postoperative echocardiographic data.

A previous study demonstrated EOAs of greater than 1.6 cm² even in 19-mm Perimount Magna valves [3]. Another study showed large EOAs in 21-mm to 25-mm Perimount Magna valves, although the EOA was 1.26±0.2 cm² for 19-mm valves [13]. The EOAs measured in the present study were smaller than those reported in previous studies. The relatively small number of patients in these studies, with the former and latter studies analyzing only 4 and 5 patients with 19-mm valves, respectively, might explain this difference. In addition, the actual EOAs in the present study were smaller than the values supplied by the manufacturer. Although the manufacturer indicates that their EOA chart was made based on *in vivo* data, it was drawn from only 1 study [14], which included a total of 40 patients (5 patients for 19-mm valves, 13 for 21-mm valves, 15 for 23-mm valves, and 7 for 25-mm valves), and more data from larger patient populations would appear to be mandatory. Therefore, when performing AVR, surgeons must consider the possibility that the actual EOAs could be smaller than the expected values provided by the manufacturer. Although these values are smaller than those reported by previous small-sample studies and those supplied by the manufacturer, the overall MPG and EOA were still favorable in the present study, and PPM was infrequent, with moderate and severe PPM rates of 11.8% and 1.9%, respectively. The improved hemodynamic performance of these bovine pericardial valves and the relatively small body size of Asians might explain the low proportion of PPM.

The present study has several limitations. First, this was

a retrospective observational study conducted at a single institution. Second, the timing of the echocardiographic follow-up was not identical. Third, adequate measurements of LVOT diameter—and consequently, EOA measurements—were not possible in certain patients in the early postoperative period because of a poor parasternal acoustic window related to recent sternotomy.

In conclusion, the Carpentier-Edwards Perimount Magna and Magna Ease bovine pericardial valves showed satisfactory hemodynamic performance with low rates of PPM, although the reference EOAs could overestimate the true EOA for each patient.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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