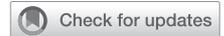


Durability of a bovine pericardial aortic bioprosthesis based on Valve Academic Research Consortium-3 echocardiographic criteria



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ABSTRACT

Objectives: The Carpentier-Edwards Perimount Magna Ease (Edwards Lifesciences) pericardial bioprosthesis has demonstrated satisfying hemodynamics at midterm follow-up, but its durability remains unclear. We report our 10-year experience with this third-generation valve implanted in the aortic position, with particular attention to structural valve deterioration.

Methods: From 2007 to 2016 at our center, 338 patients underwent aortic valve replacement using the Perimount Magna Ease pericardial bioprosthesis. Patients were prospectively followed (mean 6.6 ± 2.6 years) with clinical evaluation and yearly echocardiography. Follow-up was 98% complete (7 patients lost) for a total of 2238 valve-years. Bioprosthesis structural valve deterioration was determined by strict echocardiographic assessment based on the Valve Academic Research Consortium 3 criteria.

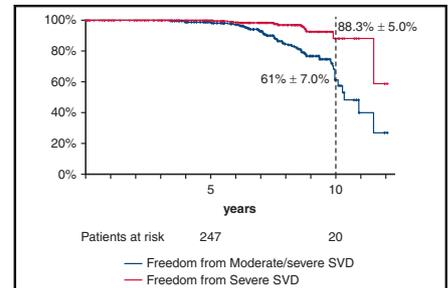
Results: Overall operative mortality was 1.2%. Actuarial survival including early deaths averaged $80.9\% \pm 2.2\%$ and $66.7\% \pm 4.4\%$ after 5 and 10 years of follow-up, respectively. Actuarial freedom from explantation due to structural valve deterioration at 5 and 10 years was $99.6\% \pm 0.4\%$ and $88.8\% \pm 5.0\%$, respectively, and actuarial freedom of structural valve deterioration at 5 and 10 years was $98.5\% \pm 0.7\%$ and $44.0\% \pm 6.4\%$, respectively. More precisely, actuarial freedom of structural valve deterioration stage 3 was $99.6\% \pm 0.4\%$ at 5 years and $88.3\% \pm 5.0\%$ at 10 years, whereas freedom of structural valve deterioration stage 2/3 was $98.5\% \pm 0.7\%$ and $60.9\% \pm 7.0\%$, respectively.

Conclusions: With a low rate of explantation due to structural valve deterioration events at 10 years, and particularly a low rate of moderate or severe structural valve deterioration based on echocardiographic Valve Academic Research Consortium 3 criteria, the Carpentier-Edwards Perimount Magna Ease pericardial bioprosthesis remains a reliable choice for a tissue valve in the aortic position. (JTCVS Open 2022;11:72-80)

The Carpentier-Edwards Perimount Magna Ease (CEPME) bioprosthesis (Edwards Lifesciences) is a trileaflet valve consisting of bovine pericardial leaflets mounted underneath a flexible cobalt-chromium stent. Compared with the previous Perimount and Magna valves, this model

differs primarily with a lower profile, a narrower sewing ring, and the addition of the Thermafix anticalcification process (Edwards Lifesciences). Multiple prior studies demonstrated the safety and efficacy of the Perimount valves,¹ but little is known regarding the midterm outcomes of the Magna Ease model 3300 TFX, especially regarding its risk of structural valve deterioration (SVD). Most studies have associated SVD with the need for reoperation, without providing any specific criteria to define SVD or the indication for reoperation.

The Valve Academic Research Consortium (VARC)² recently proposed an updated definition of SVD based on strict echocardiographic criteria and divided SVD into 3 stages (VARC-3). The aim of this study is to report midterm outcomes with the Magna Ease model 3300 TFX in the



Kaplan-Meier freedom from moderate/severe SVD and severe SVD.

CENTRAL MESSAGE

The CEPME bioprosthesis is a safe and durable bioprosthesis in the aortic position with few explantations due to SVD and few PPMs.

PERSPECTIVE

This study aimed to evaluate the CEPME bioprosthesis in the aortic position, using the new VARC-3 definitions to report clinical and hemodynamic outcomes. Following these standardized echocardiographic criteria for severe and moderate SVD in future studies would allow for more precise head-to-head comparisons between TAVR and surgical aortic valve replacement bioprosthesis performance.

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Abbreviations and Acronyms

AR	= aortic regurgitation
AVR	= aortic valve replacement
CEPME	= Carpentier-Edwards Perimount Magna Ease
EOA	= effective orifice area
PPM	= patient-prosthesis mismatch
SVD	= structural valve deterioration
TAVR	= transcatheter aortic valve replacement
VARC-3	= Valve Academic Research Consortium 3

aortic position, focusing on SVD based on systematic echocardiographic assessment using VARC-3 criteria.

PATIENTS AND METHODS

The CEPME bioprosthesis was first implanted in patients at the Tours University Hospital in January 2007. Indications of aortic valve replacement (AVR) with a bioprosthesis rather than a mechanical valve included all patients aged 60 years or older, as well as in younger patients if they met specific conditions (eg, endocarditis, short anticipated life expectancy because of comorbidities, contraindication to oral anticoagulant treatment, informed patient's choice). Multiple valve replacements were excluded from this study, but there was no exclusion for other concomitant operations. Operative techniques have been previously described.³ Postoperative anticoagulation therapy consisted of low-molecular-weight heparin enoxaparin 4000 IU once daily until hospital discharge. Warfarin sodium was prescribed only for atrial fibrillation. Antiplatelet agents were prescribed based on cardiac (coronary artery disease) or peripheral arterial diseases (cerebrovascular events or lower-extremity artery disease) indications only.

Data were recorded prospectively. Every year, questionnaires were mailed to all patients for a clinical evaluation and a transthoracic echocardiography was performed. In case of missing questionnaires or adverse events, telephone and in-person consults were conducted. At the time of follow-up, most recent echocardiographic data (<6 months) were included in our analysis. For deaths, the Social Security Death Index was used to confirm the date. The mean duration of follow-up was 6.6 ± 2.6 years for a total of 2238 valve-years. Follow-up including clinical and echocardiographic evaluations was 97.9% complete. The closing interval for this study was 12 months. Morbidity and mortality were defined according to the guidelines.^{4,5}

According to the VARC-3 document,² severe hemodynamic valve deterioration (SVD stage 3) was defined as an increase in mean transvalvular gradient 20 mm Hg or greater resulting in a mean gradient 30 mm Hg or greater with concomitant decrease in effective orifice area (EOA) 0.6 cm^2 or greater or 50% or greater or decrease in Doppler velocity index 0.2 or greater or 40% or greater compared with the reference echocardiographic examination performed 1 to 3 months postprocedure, or new occurrence or increase of 2 or more grades of intraprosthesis aortic regurgitation (AR) resulting in severe AR.

Moderate hemodynamic valve deterioration (SVD stage 2) was defined as an increase in mean transvalvular gradient 10 mm Hg resulting in a mean gradient 20 mm Hg or greater with concomitant decrease in EOA 0.3 cm^2 or greater or 25% or greater or decrease in Doppler velocity index 0.1 or greater or 20% or greater compared with the reference echocardiographic examination performed 1 to 3 months postprocedure, or new occurrence or increase of 1 or more grade of intraprosthesis AR resulting in moderate or greater AR.

Morphological SVD (stage 1) was defined as any morphological abnormality, including leaflet calcification, sclerosis, thickening, or new leaflet motion disorder, without significant hemodynamic changes.

PPM was categorized as severe (EOA index $\leq 0.65 \text{ cm}^2/\text{m}^2$), moderate (EOA index $0.66\text{--}0.85 \text{ cm}^2/\text{m}^2$), or nonsignificant (EOA index $>0.85 \text{ cm}^2/\text{m}^2$).²

This study was approved by the Ethical Committee of the French Society of Thoracic and Cardiovascular Surgery. The approval number for this study is CERC-SFCTCV-2013-12-5-21-30-57-BoTh, approved on December 31, 2013.

Statistical Analysis

Kaplan–Meier actuarial analyses are presented with the Greenwood formula for the variance. Survival curves were compared using the log-rank test. Life expectancy and expected valve durability are estimated by the median survival time and the area under the Kaplan–Meier curve. Univariate and multivariate Cox proportional hazards regression analyses were used to identify risk factors for death and SVD. For nonfatal events, competing risk analyses^{6,7} were performed using the R cmprsk package (R software, version 2.13.1).

RESULTS

From January 2007 to December 2016, 338 patients underwent AVR at Tours University Hospital with a CEPME bioprosthesis (Figure 1). The baseline characteristics are reported in Table 1. As many as 27% ($n = 92$) of patients were aged less than 65 years at the time of bioprosthetic AVR. At baseline, the type of valve disease was aortic stenosis in 91% of cases, whereas the etiology was degenerative in 85% of patients. Bicuspid anatomy was described in 80 patients (24%). Twenty procedures (5.9%) were redo surgeries. At least 1 concomitant procedure occurred in 55% of patients.

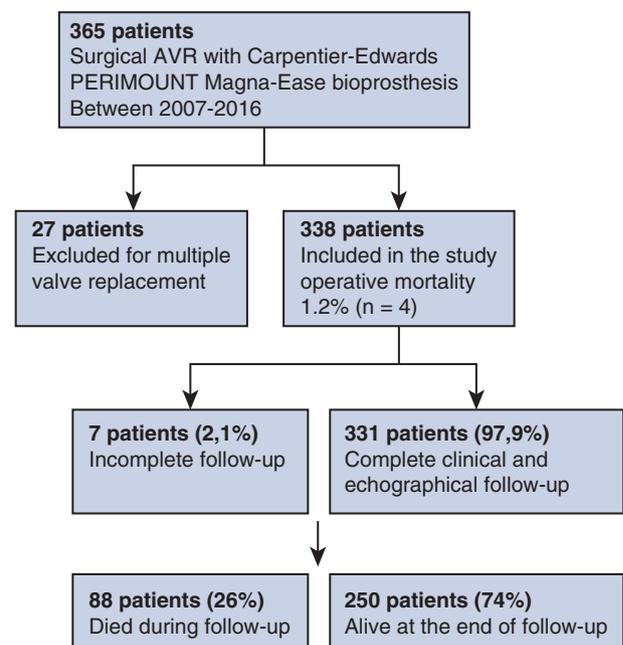


FIGURE 1. CONSORT diagram of the study. AVR, Aortic valve replacement.

TABLE 1. Baseline and operative characteristics

Characteristics	Values
Patients, n	338
Gender (female) n, %	153 (45.3%)
Age	
Mean \pm SD, y	70.6 \pm 11.5
Median (IQR)	73.7 (64.1; 78.6)
Range	21.8-89.2
Age \leq 60 y, n (%)	59 (17.5%)
NYHA class, n (%)	
I	20 (5.9%)
II	254 (75.1%)
III	60 (17.8%)
IV	4 (1.2%)
Left ventricular ejection fraction (mean \pm SD)	61.9 \pm 10.7
Atrial fibrillation	19 (5.6%)
Etiology, n (%)	
Degenerative	286 (84.6%)
Reoperative	20 (5.9%)
Endocarditis	13 (3.8%)
Rheumatic	13 (3.8%)
Inflammatory	1 (0.3%)
Congenital	3 (0.9%)
TAVI failure	1 (0.3%)
Bicuspid	80 (23.7%)
Arterial hypertension n (%)	204 (60.4%)
Family history of CVD n (%)	43 (12.7%)
Diabetes n (%)	88 (26.0%)
Dyslipidemia n (%)	181 (53.6%)
euroSCORE II %	2.54 \pm 2.18
Range	0.56-23.60
Procedure, n (%)	
Isolated AVR	151 (44.7%)
AVR + CABG	49 (14.5%)
AVR + CABG + other	12 (3.6%)
AVR + other	126 (37.3%)
Valve size, n (%)	
Mean \pm SD mm	21.8 \pm 1.9
19 mm	63 (18.6%)
21 mm	124 (36.7%)
23 mm	108 (32.0%)
25 mm	43 (12.7%)
PPM	
Nonsignificant (EOA index >0.85 cm ² /m ²)	158 (46.7%)
Moderate ($0.85 \leq$ EOA index <0.66 cm ² /m ²)	173 (51.2%)
Severe (EOA index ≤ 0.65 cm ² /m ²)	7 (2.1%)

SD, Standard deviation; IQR, interquartile range; NYHA, New York Heart Association; TAVI, transcatheter aortic valve implantation; CVD, cardiovascular disease; euroSCORE, European System for Cardiac Operative Risk Evaluation; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; PPM, patient-prosthesis mismatch; EOA, effective orifice area.

Operative Mortality and Survival

In the operative period, 4 deaths (1.2%) were reported. Eighty-four late deaths were noticed for linearized rate of 3.75%/valve-years. Valve-related deaths occurred in 25 patients and were attributed to the following outcomes: 1 endocarditis, 4 major bleedings, 2 thromboembolic events, and 18 sudden deaths or of unknown etiology.

At 5 and 10 years, the overall actuarial survival was 80.9% \pm 2.2% and 66.7% \pm 4.4%, respectively, and the valve-related actuarial survival was 92.5% \pm 1.5% and 86.0% \pm 6.1%, respectively (Figure 2).

A Cox regression analysis identified age at surgery, left ventricle ejection fraction (%), and New York Heart Association class III or IV as significant risk factors impacting survival (Tables E1 and E2).

Valve-Related Complications

Table 2 summarizes the main postoperative events.

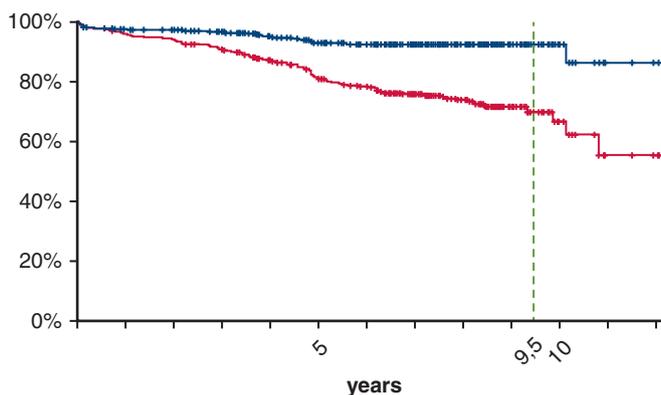
Hemodynamics and Patient-Prosthesis Mismatch

Prostheses size 19 mm and 21 mm were implanted in 19% and 37% of patients, respectively, whereas severe patient-prosthesis mismatch (PPM) was reported for 7 patients (2.1%) (Table 1). Main hemodynamic outcomes, recorded at discharge and at the end of follow-up, showed no significant differences at 10 years with a mean transprosthetic gradient of 12.6 \pm 3.0 mm Hg versus 15.0 \pm 5.4 mm Hg, respectively (Figure 3 and Tables E1 and E2). No patient in this series underwent an aortic annulus enlargement procedure.

Structural Valve Deterioration and Reintervention for Structural Valve Deterioration

At the end of follow-up (mean 6.6 \pm 2.6 years), SVD stage 3 was reported in 11 patients (3.3%) (mean time = 7.8 years), and stage 2 SVD was observed in 38 patients (mean time = 7.6 years). Actuarial freedom of SVD stage 3 was 99.6% and 88.3% at 5 and 10 years and freedom of SVD stage 2/3 was 98.6% and 61.1%, respectively (Figure 2). The expected valve durability, that is, the median survival time from the actuarial freedom from stage 3 SVD, could not be calculated in this cohort, because only 10 patients presented with SVD stage 3 after 10 years.

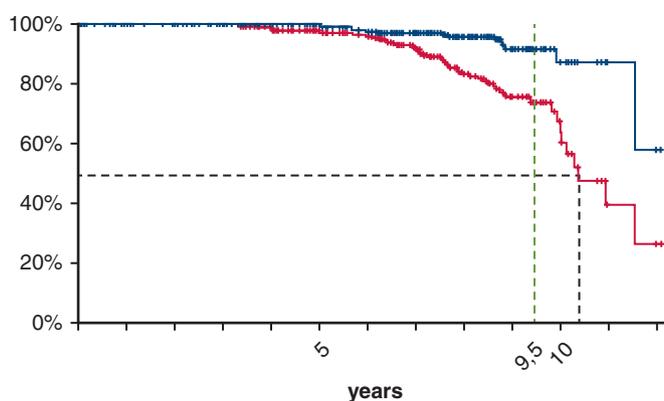
Patient's age at the time of valve implantation was a significant risk factor for SVD stage 3 (hazard ratio, 0.907; 95% confidence interval, 0.855-0.962; $P = .001$). No significant associations were observed with gender or valve size (Table 3). Nine patients required aortic valve reintervention due to SVD (mean time = 7.6 years), all of which were surgical procedures.



Patients, n	338	247	34	20
Overall survival, %		80.9 ± 2.2		66.7 ± 4.4
Valve-related Survival, %		92.5 ± 1.5		86.0 ± 6.1

— Valve-related survival — Overall survival

A



Patients at risk, n	338	247	34	20	Total
Moderate/severe, n		4		44	48
Freedom of moderate/severe SVD, %		98.5 ± 0.7		61 ± 7.0	26.7
Severe SVD, n		1		10	11
Freedom of severe SVD, %		99.6 ± 0.4		88.3 ± 5.0	58.9

— Severe SVD — Moderate/Severe SVD

B

FIGURE 2. A, Kaplan–Meier overall and valve-related survival. B, Kaplan–Meier freedom from moderate/severe SVD and severe SVD. SVD, Structural valve deterioration.

Competing risk analysis, including 3 distinct failures (nonvalve-related death, valve-related death, and reintervention due to SVD), was performed and is presented in Figure 4. The cumulative risk of valve explantation due to SVD at 10 years was 8.0% ± 3.4%, which is lower than the corresponding actuarial estimate (61.1%) and the corresponding probability of death (valve related 7.4% ± 1.5%; nonvalve related 25.4% ± 4.1%).

Other Valve-Related Outcomes

Additional valve-related events were reported during the follow-up: 6 thromboembolic events (no early event), 6 major bleeding events (2 early events), and 9 endocarditis events (3 early events). Kaplan–Meier estimates of the cumulative incidence of these valve-related complications are shown in Figure 4. Of note, no case of valve thrombosis was observed. Reinterventions, all consisting in surgical

TABLE 2. Summary of main events: Freedom from events with Kaplan–Meier estimates

Variable	Early events* n (rate)	Late events n (linearized rate)	95% CI linearized rate	Kaplan–Meier at 5 y	Kaplan–Meier at 10 y	MST (y)	AUC (y)
SVD Stage 1 (morphological)	0 (0%)	25 (1.12%/vy)	[0.74%-1.67%]	100 ± 0	72.3 ± 6.4	†	9.7
SVD Stage 2 (moderate)	0 (0%)	38 (1.70%/vy)	[1.22%-2.35%]	98.9 ± 0.6	69.0 ± 6.9	10.9	9.5
SVD Stage 3 (severe)	0 (0%)	11 (0.49%/vy)	[0.26%-0.90%]	99.6 ± 0.4	88.3 ± 5.0	†	9.8
SVD Stage 2-3 (moderate/ severe)	0 (0%)	49 (2.19%/vy)	[1.64%-2.91%]	98.5 ± 0.7	60.9 ± 7.0	10.3	9.3
SVD total	0 (0%)	74 (3.31%/vy)	[2.63%-4.16%]	98.5 ± 0.7	44.0 ± 6.4	9.9	9.1
Explantation due to SVD	0 (0%)	9 (0.40%/vy)	[0.19%-0.79%]	99.6 ± 0.4	88.8 ± 5.0	†	9.9
Mortality	4 (1.2%)	84 (3.75%/vy)	[3.04%-4.62%]	80.9 ± 2.2	66.7 ± 4.4	†	8.3
Valve-related mortality	4 (1.2%)	21 (0.94%/vy)	[0.62%-1.43%]	92.5 ± 1.5	86.0 ± 6.1	†	9.4
Not valve-related mortality	0 (0%)	63 (2.8%/vy)	[2.19%-3.62%]	87.5 ± 1.9	72.4 ± 4.6	†	8.8
Valve-related complications‡	7 (2.1%)	115 (5.14%/vy)	[4.28%-6.16%]	85.9 ± 2.0	36.6 ± 5.8	9.6	8.4
Endocarditis	3 (0.9%)	6 (0.27%/vy)	[0.11%-0.62%]	97.7 ± 0.9	95.7 ± 1.8	†	9.8
Thromboembolic events	0 (0%)	6 (0.27%/vy)	[0.11%-0.62%]	98.0 ± 0.8	98.0 ± 0.8	†	9.9
Major bleeding§	2 (0.6%)	4 (0.18%/vy)	[0.06%-0.49%]	98.4 ± 0.7	97.9 ± 0.9	†	9.8
Reintervention	0 (0%)	14 (0.63%/vy)	[0.36%-1.08%]	98.3 ± 0.8	86.2 ± 5.1	†	9.7

CI, Confidence interval; MST, median survival time; AUC, area under the curve; SVD, structural valve deterioration; vy, valve-years. *Defined as events occurring up to 30 days after surgery. †The survival curve does not cross the 50% line, MST not applicable. ‡Including endocarditis, thromboembolic events, bleeding, disinsertion, valve deterioration, and reintervention. §Including cerebral or life-threatening bleeding mortality.

procedures, were performed in 14 patients including 9 due to SVD and 5 due to endocarditis (no early event).

SVD (stage 3) was lower than 12% and risk of reintervention due to SVD was 8%.

DISCUSSION

In the present study, we evaluated the midterm durability of the CEPME pericardial bioprostheses in the aortic position based on VARC-3 criteria. We report an almost complete follow-up (97.9%) at 6.6 ± 2.6 years with this prosthesis in terms of echocardiographic structural valve description. At 10 years, the risk of severe hemodynamic

Survival

The overall 5-year and 10-year actuarial survivals were 80.9% ± 2.2% and 66.7% ± 4.4%, respectively, which compares favorably with previous series of Magna Ease implants.^{8,9} Moreover, the high valve-related actuarial survival, 92.5% ± 1.5% at 5 years and 86.0% ± 6.1% at 10 years, confirms an excellent long-term safety profile of

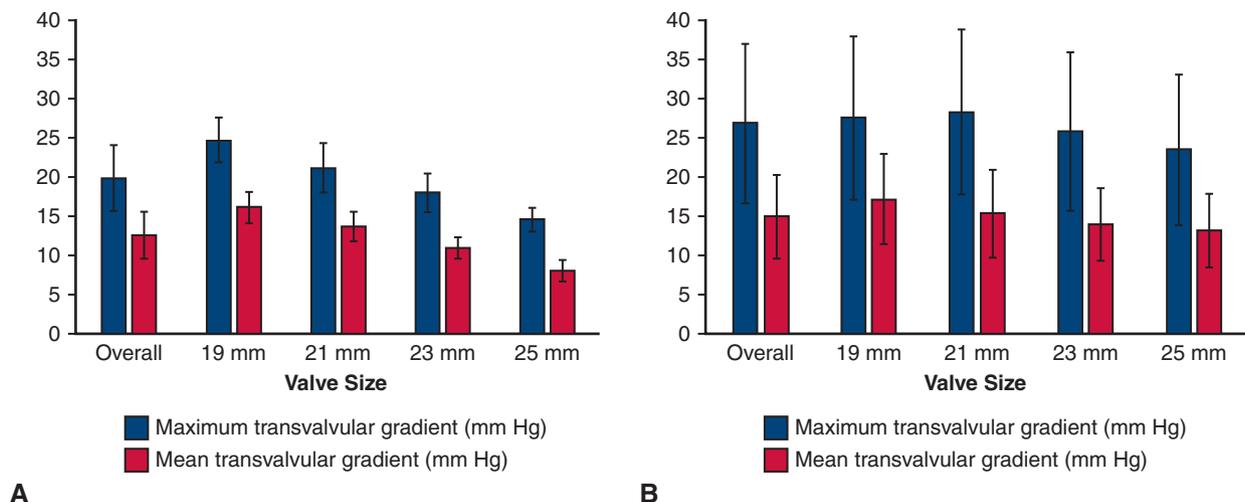


FIGURE 3. Hemodynamic outcome of CEPME bioprosthesis in aortic position at discharge (A) and end of follow-up (B).

TABLE 3. Cox regression analysis for identification of risk factors for structural valve deterioration

	HR (95% CI)
SVD total (stage 1 + 2 + 3)	
Age	0.968 (0.947-0.989)
Gender	1.071 (0.575-1.994)
Hypertension	1.285 (0.751-2.197)
Diabetes	1.078 (0.608-1.911)
Dyslipidemia	1.244 (0.760-2.037)
Renal function*	1.294 (0.925-1.811)
Valve size	0.883 (0.740-1.053)
SVD moderate/severe (stage 2/3)	
Age	0.951 (0.926-0.976)
Gender	1.578 (0.738-3.375)
Hypertension	1.728 (0.861-3.471)
Diabetes	1.207 (0.618-2.358)
Dyslipidemia	0.945 (0.518-1.726)
Renal function*	1.339 (0.886-2.024)
Valve size	0.894 (0.722-1.106)
SVD severe (stage 3)	
Age	0.907 (0.855-0.962)
Gender	0.751 (0.142-3.963)
Hypertension	6.104 (1.123-33.185)
Diabetes	0.383 (0.044-3.303)
Dyslipidemia	1.509 (0.347-6.556)
Renal function*	1.285 (0.507-3.260)
Valve size	0.714 (0.437-1.166)

Bold denotes statistical significance. HR, Hazard ratio; CI, confidence interval; SVD, structural valve deterioration. *Categorized as creatinine clearance greater than 85 mL/min, 50 to 85 mL/min, less than 50 mL/min and dialysis.

the prosthesis. Consistent with others,^{8,10} we found that long-term survival after surgery remains highly dependent on age at implantation.

Patient-Prosthesis Mismatch and Hemodynamic Outcomes

Overall mean transprosthetic gradients remained low even through 10-year follow-up (15.0 ± 5.4 mm Hg), compared with 12.6 ± 3.0 mm Hg observed at hospital discharge. Our data are consistent with prior studies^{11,12} and suggest that gradients observed with CEPME may be slightly higher than those reported for the Trifecta aortic valve. A recent meta-analysis of hemodynamic performance of CEPME and Trifecta valves concluded that gradients were lower in the Trifecta group; however, this study included few hemodynamic data beyond 1 year.¹³

Despite implanting small valve sizes (≤ 21 mm) in 55% of patients, we report only 2.1% of severe PPM. This is consistent with the study of Kume and colleagues,⁹ which did not report any severe PPM in a cohort of 282 Magna Ease AVR. These satisfying hemodynamic outcomes are particularly relevant, because severe PPM has been associated with increased all-cause and cardiac mortalities in

several studies.^{14,15} In addition, PPM-associated negative outcomes tend to occur at higher frequency in younger patients and in those with altered ejection fraction.¹⁶ Because selecting the right bioprosthesis size remains the cornerstone to prevent PPM, we suggest that the CEPME, with its supra-annular design and its lower profile, may be beneficial in patients with small aortic annulus.

Structural Valve Deterioration

In addition to hemodynamic performance, durability is another key requirement for bioprostheses, especially considering the younger age at implantation. In the era of transcatheter aortic valve replacement (TAVR), even in low-risk patients, durability is the area of interest when comparing outcomes. The mechanical performance of CEPME prostheses was first measured in vitro. Raghav and colleagues¹⁷ subjected the prostheses to 1 billion cycles, which is equivalent to 25 years of in vivo wear, and found excellent durability and hydrodynamic performance, with no episode of valve dysfunction. Although useful, in vitro experiments cannot fully replicate the in vivo blood environment and do not allow a reliable assessment of the SVD process. Until recently, SVD has been poorly defined in surgical AVR studies, and the need for reoperation has generally been used as a surrogate that does not necessarily take into account non-SVD indications for reoperation: Freedom from reoperation does not equate freedom from SVD. Biancari and colleagues¹⁰ compared Magna Ease and Trifecta bioprostheses in propensity score-matched pairs. They reported a 5.7% risk of repeat AVR for valve failure with Trifecta valves versus 0% with Magna Ease prostheses at 7 years. Our study confirms the durability of the CEPME prosthesis by showing that reoperation for SVD was only necessary in a minority of patients at 5 years (0.4%) and 11.2% at 10 years.

According to the new VARC-3 guidelines, severe hemodynamic SVD (stage 3) was present in only 3.3% of our population at 10-year follow-up. No severe SVD was reported during the first 5 years, but occurred after a mean time of 7.8 years. Valve deterioration was due to calcification causing progressive stenosis. This type of valve deterioration can be detected and allows for scheduled reintervention, which was not the case when implanting first-generation pericardial valves that unexpectedly tore resulting in severe acute AR and requiring emergency surgeries.¹⁸ Consistent with our findings, Anselmi and colleagues⁸ reported a 1.1% rate of SVD in a cohort of 849 CEPME implantations, occurring at an average of 4.5 ± 2.0 years after implantation. The 5-year actuarial freedom of SVD was $99.1\% \pm 0.5\%$, but the definition of SVD⁵ used by the authors of that study was not based on precise echocardiographic criteria.

Because valve deterioration is usually a gradual process, we also report moderate hemodynamic SVD (stage 2). In

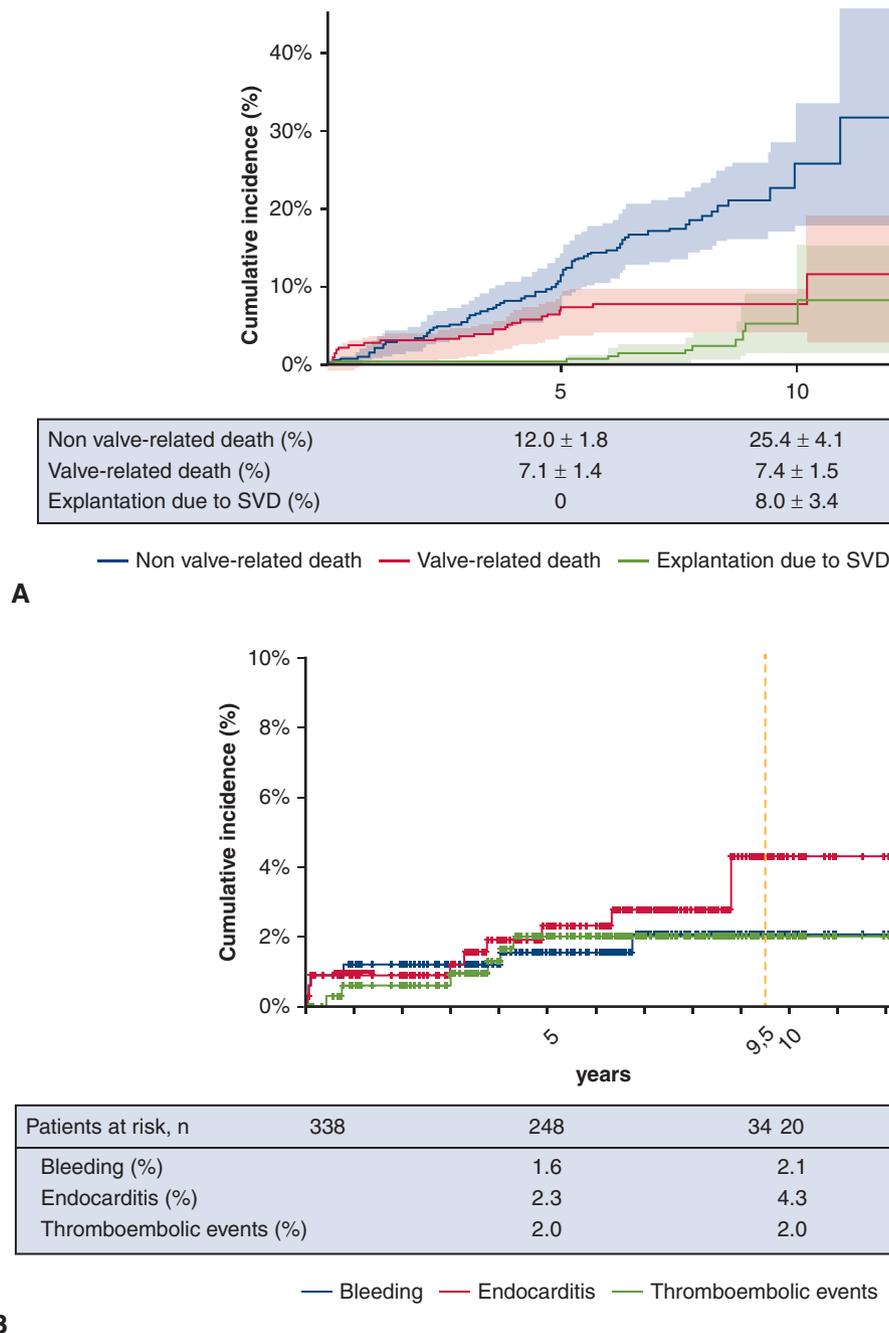


FIGURE 4. A, Competing risk analysis of valve-related death, nonvalve-related death, and explantation due to SVD. B, Kaplan–Meier estimates of cumulative incidence of valve-related complications. SVD, Structural valve deterioration.

1978, Rahimtoola¹⁹ reported that the majority of surgical bioprostheses may last more than a decade. First valve deterioration generally occurs after the first 5 years, and with the exception of a few specific models that behave particularly poorly,¹⁰ one may wait for several years before detecting severe hemodynamic consequences, and even longer for detecting symptoms. This represents a significant challenge in comparing different models of bioprostheses, and this

is even more critical to assess the durability of TAVR prostheses, characterized by a quick device turnover. We believe that the end point “moderate SVD” may be adapted to detect the initial signs of valve deterioration and may allow a relevant comparison between models regarding SVD, especially during the first 10 years. Moreover, although the diagnosis of severe SVD may result in reintervention, detection of moderate SVD may justify a closer clinical and

echocardiographic follow-up.²⁰ In our series, actuarial freedom from SVD stage 2 was 98.9% and 69% at 5 and 10 years of follow-up, respectively. The median survival time before the occurrence of stage 2 SVD was 11 years, confirming satisfying long-term durability, even when applying echocardiographic criteria of moderate deterioration. Following the standardized VARC-3 definitions for severe and moderate SVD in future studies would allow for more precise head-to-head comparisons between TAVR and surgical aortic valve replacement bioprosthesis performance across patient cohorts. This would ultimately increase our knowledge of the valve's long-term resilience in vivo and provide more meaningful answers to the durability question.

Study Limitations

This retrospective study was conducted at a single hospital with a medium-length period of observation. Although the data from a single center could also be regarded as an advantage in terms of consistent management, other centers may not have adopted our aggressive approach to reoperation even without symptoms, and combining data would be challenging. Second, this study might present a performance bias because all patients were not operated by the same surgeon. Third, the mode of patient follow-up by questionnaire also introduces a risk of ascertainment bias. Finally, larger cohorts of CEPME have been published.⁸ However, the present series focused on SVD and provides the longest follow-up of this prosthesis to date. Few patients were lost to clinical and echocardiographic follow-up (98%), and all events were reported in strict compliance with guidelines and VARC-3 criteria.

CONCLUSIONS

We found the CEPME to be a safe and durable bioprosthesis when implanted in the aortic position. Its use is associated with few severe PPMs, even when small size valves are implanted, and a low mortality at early and midterm. Applying VARC-3 definitions for valve deterioration, we report 12% of severe (stage 3) SVD and 31% of moderate (stage 2) SVD at 10 years. The median survival time before the occurrence of moderate SVD is 11 years.

Conflict of Interest Statement

T.B. reports speaker fees from Edward Lifesciences. All other authors reported no conflicts of interest.

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Key Words: aortic valve, bioprosthesis, cardiac surgery, patient-prosthesis mismatch, valve deterioration

TABLE E1. Hemodynamics of Carpentier-Edwards Magna Ease (Edwards Lifesciences) bioprosthesis in aortic position

	At discharge	At end of follow-up
Mean pressure gradient (mm Hg), mean \pm SD	12.6 \pm 3.0	15.0 \pm 5.4
EOA (cm ²), mean \pm SD	1.6 \pm 0.3	1.53 \pm 0.31
Indexed EOA (cm ² /m ²), mean \pm SD	0.87 \pm 0.17	0.82 \pm 0.17

SD, Standard deviation; EOA, effective orifice area.

TABLE E2. Cox regression analysis for identification of risk factors for overall mortality

	HR (95% CI)
Age [y]	1.033 (1.007-1.060)
Male gender	1.166 (0.754-1.804)
BMI [kg/m ²]	1.004 (0.960-1.050)
Hypertension	1.374 (0.842-2.241)
Diabetes	1.198 (0.730-1.968)
NYHA class III or IV	1.649 (1.010-2.692)
LVEF [%]	0.974 (0.958-0.990)
PPM severe	1.019 (0.228-4.549)

Bold denotes statistical significance. HR, Hazard ratio; CI, confidence interval; BMI, body mass index; NYHA, New York Heart Association; LVEF, left ventricle ejection fraction; PPM, patient-prosthesis mismatch.