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Late Clinical and Echocardiographic Results with the Magna Ease© Pericardial Aortic Bioprosthesis

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1 **Late Clinical and Echocardiographic Results with the Magna Ease®**
2 **Pericardial Aortic Bioprosthesis**

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26 Meeting to be held in Milan, Italy, from October 5th to October 8th, 2022.

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29 **Visual Abstract.**

30 Key Question: Which are the long-term outcomes with the Perimount Magna Ease®
31 bioprosthesis for SAVR?

32 Key Findings: In 1,016 SAVRs after median 9.8 years, clinical outcomes were optimal
33 and freedom from SVD (10-yrs) was 96.5% and 97.4% (Kaplan-Meier and competing
34 risks).

35 Take-Home message: The Magna Ease® bioprosthesis can be safely employed for
36 SAVR in patients with life expectancy of at least 10 years. Continued investigation is
37 required for further follow-up timepoints.

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40 **Abstract.**

41 **Objectives.** The population of candidates to surgical aortic valve replacement (SAVR)
42 is evolving. The Perimount Magna Ease© bioprosthesis has been introduced relatively
43 recently in the practice. We aimed at evaluating its long-term results.

44 **Methods.** Single-center cohort of 1,016 consecutive SAVRs with the Magna Ease©
45 valve (2008-2014), all-comers population. Prospective collection of in-hospital data,
46 systematic clinical and echocardiographic follow-up. Evaluation of valve-related
47 events: SVD, (structural valve deterioration, according to modified definition criteria),
48 NSVD (nonstructural valve dysfunction), PPM (patient-prosthesis mismatch).

49 **Results.** Age at SAVR was 73.4±9.5 years; calcified aortic stenosis was the indication
50 to surgery in 59.6%. 974 patients entered the follow-up, 564 were alive at last follow-
51 up (median duration: 9.8 years) (up to 13.4 years). NYHA class was I or II in 92.1%.
52 Overall survival at 10 years was 56.8%±1.8. Freedom from SVD at 10 was 96.5%±0.8
53 (Kaplan-Meier), and 97.4%±0.6 (competing risks) (28 SVD events after 6.9 years ±
54 3.3). There were 15 reinterventions for SVD (redo-SAVR and TAVI); 10-year freedom
55 from reintervention was 97.8% ± 0.6. Moderate and severe PPM occurred in 26.8%
56 and 5.4%, respectively; without association with late mortality (p=0.12 for moderate
57 and p=0.70 for severe PPM). Freedom from valve-related mortality was 97.8%±0.5 at
58 10 years.

59 **Conclusions.** In this follow-up of the Magna Ease bioprosthesis for SAVR, data
60 indicate good late outcomes (30-days outcomes are excluded). Continued follow-up is
61 required to further support its use in patients with life expectancy greater than 10-12
62 years.

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68 **Introduction.**

69 Surgical Aortic Valve Replacement (SAVR) remains the treatment of choice for
70 severe aortic stenosis in patients younger than 75 and presenting acceptable operative
71 risk, and for operable patients affected by severe aortic regurgitation [1]. While older
72 patients are preferentially treated through transcatheter aortic valve replacement
73 (TAVR), the population of candidates to SAVR is being characterized by younger age.
74 Additionally, societal evolutions and the importance attributed to lifestyle trigger
75 frequent demands from informed patients younger than 60 to receive a bioprosthesis
76 when SAVR is required [2], in order to avoid the limitations associated with
77 anticoagulant therapy after implantation of a mechanical valve. Therefore, the
78 appreciation of long-term durability of bioprostheses acquires a growing importance.
79 The Perimount Magna Ease© bioprosthesis is widespread in the clinical practice. It
80 has been the object of investigations focusing on its mid-term durability and clinical
81 outcomes [3] even in comparison to other pericardial bioprostheses. Nonetheless, its
82 introduction following its predecessor Perimount Magna© valve is relatively recent. In
83 this context, the aim of the current study is to evaluate the long-term outcomes of SAVR
84 with this valve device under the profiles of overall survival, freedom from SVD and from
85 other valve-related outcomes.

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91 **Patients and Methods.**

92 Ethical Statement.

93 The institutional database, ensuring consecutiveness and completeness of the
94 cohort, is declared in the CNIL (*Commission Nationale des Informatiques et Libertés*)
95 under the number 1207754, according to compliance regulations and to the French
96 law. Patients signed an informed consent for the employment of personal data for
97 research purposes, and all data were analyzed anonymously.

98

99 Criteria of inclusion and management of data.

100 We performed a retrospective recall of data about 1,017 SAVR procedures
101 performed with the Perimount Magna Ease[®] bovine pericardial bioprosthesis in 1,016
102 patients. We considered only the first procedure for the single patient with twice
103 procedures in the database. Although this device is implanted in our department even
104 during current years, we enrolled patients undergoing SAVR between January 2nd,
105 2008 and December 31st, 2014 in order to focus on long-term follow-up. Combined or
106 reoperative procedures did not represent an exclusion criterion. The electronic
107 database of Rennes University Hospital, entailing prospective collection of in-hospital
108 data of all patients undergoing cardiac surgery at our department since 1978, has been
109 used as the source of all pre, intra- and early postoperative variables. Surgical methods
110 for SAVR were homogeneous across the study period; bioprostheses were implanted
111 using a supra-annular technique with a series of non-everting U-shaped pledgetted or
112 non-pledgetted sutures.

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113 Systematic follow-up of the included patients was performed in 2020 and 2021. At
114 first, we interrogated the INSEE (*Institut National de la Statistique et des Etudes*
115 *Economiques* – National Institute of Statistics and Economical Studies) database to
116 obtain the patients' vital status and the date of death. Following collection of the
117 available in-house follow-up data, questionnaires were sent by surface mail to general
118 practitioners and/or cardiologists. Such questionnaires enquired about the results of
119 the last available echocardiography, NYHA class and causes of death, if applicable.
120 Questionnaires inquired about any adverse event occurring during the follow-up; both
121 death and adverse events were categorized as valve- or non-valve related.
122 Controversies were adjudicated by consensus. Any alteration related to the
123 bioprosthesis as assessed by echocardiography, clinical examination or reoperation
124 was recorded. Echocardiography date were interpreted according to standard criteria.
125 When the questionnaire was not informative or when we had no response, the
126 cardiologists or referring physicians were directly contacted, or even the
127 patients/families. For individual patients to be considered not lost at follow-up,
128 echocardiography results had to be available; the date of the last available
129 echocardiography was considered as the date of last follow-up.

130

131 Outcomes and definitions.

132 Definitions of valve-related events were formulated with the basis of the 2008 Akins
133 guidelines and of more recent consensus documents as well [4, 5, 6]. SVD was defined
134 as a persistent dysfunction or deterioration of the bioprosthesis evident at
135 echocardiography and/or reoperation, but exclusive of infection or thrombosis. SVD
136 could be under the form of stenosis, with significant and persistent increase in average
137 gradient (>10 mmHg increase in average gradient vs. reference echocardiography,

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138 unless attributable to other transient causes such as anemia or abnormally increased
139 cardiac output), and/or decrease in effective orifice area (EOA) compared to reference
140 echocardiography. SVD could otherwise be under the form of intraprosthetic leak \geq
141 grade 2/4. Morphologic valve deterioration was therefore a component of the definition
142 of SVD (“Bioprosthetic Valve Dysfunction” in a previous consensus paper [7]). Recent
143 granular definitions have been proposed for SVD. These comprise the evidence of
144 average gradient at any timepoint >20 mmHg to define SVD [6, 8, 9]. In the view of the
145 Authors, and consistently with a large body of previous literature, elevated
146 transvalvular gradient evident at hospital discharge (reference echocardiography) in
147 absence of bioprosthetic dysfunction and corresponding to PPM (patient-prosthesis
148 mismatch), persisting during the follow-up with no significant change in the average
149 transvalvular gradients or the EOA, and with no evidence at
150 echocardiography/reoperation of evolutive structural dysfunction, does not constitute
151 an SVD event. These events were computed as PPM. Additionally, we distinguished
152 between SVD and reintervention for SVD: such outcome measures are presented
153 separately. Reintervention for SVD included both redo aortic valve surgery and
154 transcatheter Valve-in-Valve procedure. NSVD (Non-Structural Valve Deterioration) is
155 any dysfunction in valve function not linked to a structural failure, including
156 periprosthetic leak, thrombosis, hemolysis, pannus. PPM was categorized as severe
157 when the indexed Effective Orifice Area (iEOA) was ≤ 0.65 cm²/m², moderate when
158 iEOA was ≤ 0.85 cm²/m², or absent when iEOA was >0.85 cm²/m² [4, 10]. Infectious
159 endocarditis (IE) was any infection involving the bioprosthesis. Early post-operative
160 mortality was death within 30 days following surgery or later if during the index
161 hospitalization. We defined valve-related mortality as due to SVD, NSVD, IE or
162 reintervention on the index bioprosthesis leading to death, or as due to embolism,

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163 hemorrhage and cardiac insufficiency as well, unless the cause-effect relationship with
164 any failure of the index bioprosthesis could be excluded.

165

166 Endpoints

167 The primary endpoint was the freedom from SVD at follow-up, using both actuarial
168 (Kaplan-Meier) and actual (competing risks) methods.

169 The secondary endpoints were the overall follow-up survival, the freedom for
170 reintervention for SVD, the rate of PPM and its impact on late survival, the freedom
171 from NSVD, the freedom from IE.

172

173 Statistical analysis

174 Continuous variables were described as mean \pm standard deviation (SD) in case
175 of normal distribution, or as median in case of non-normal distribution. The
176 Kolmogoroff-Smirnoff test was used to assess normality. Categorical variables were
177 expressed as percentages. Time-to-event analyses for non-lethal valve-related events
178 were built employing both the Kaplan-Meier (“actuarial”) and competing risks (“actual”)
179 methodologies in complementary manner [5, 11]. Non-lethal events at follow-up (such
180 as SVD) were also analyzed with the ‘actual’ method (competing risks). In fact, the
181 description of SVD using the “actuarial” (Kaplan-Meier) method alone would provide
182 excessively pessimistic estimations for the purposes of counseling individual patients
183 concerning the expected risk of SVD, since death due to other causes censors the
184 occurrence of SVD itself. On the contrary, the Kaplan-Meier method is appropriate to
185 compare outcomes among different models of bioprostheses. In the graphical

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186 representation of Kaplan-Meier curves, confidence intervals were shown as dotted
187 lines corresponding to each curve. For the purposes of the analysis of late survival,
188 early mortality was excluded from Kaplan-Meier curves. The median follow-up duration
189 was also estimated using reversed Kaplan-Meier method. To study the impact of PPM
190 on late survival, a Fine and Gray model was used. We performed stratified analysis by
191 size of implanted prosthesis. Intergroup comparison was conducted with ANOVA for
192 continuous data and chi-square test for categorical data. Opposed Kaplan-Meier
193 curves were compared with the log-rank statistic. The alpha level was set at 0.05. The
194 analyses were conducted using IBM SPSS Statistics 27.0 (IBM Inc., New York, USA)
195 and *survminer* and *cmprsk* packages for R 4.0 (The R Foundation for Statistical
196 Computing Platform, Vienna, Austria), within an external, independent and academic
197 Biostatistics Department (JM).

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205 **Results.**

206 The dataset comprised 1,016 patients receiving SAVR with the Magna Ease® valve;
207 Figure 1 displays the study workflow. The baseline characteristics are summarized in

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208 Table 1; the population is mainly represented by patients affected by calcified aortic
209 stenosis, while isolated aortic regurgitation or infectious endocarditis were markedly
210 less frequent. Table 2 reports the early in-hospital findings. There was a considerable
211 rate of concomitant procedures to SAVR (34.2%) (concomitant coronary bypass in
212 23.1%, other valve surgery in 5.7%, ascending aortic replacement in 47 pts 4.9%),
213 while redo surgery occurred in 3.4% of instances. Operative mortality was 4.1% with
214 42 deaths. No early death was valve-related. The rate of implantation of a new
215 permanent pacemaker was 3% in this cohort including patients affected by infectious
216 endocarditis and undergoing reoperative valvular operations.

217 Stratified analysis by prosthesis size suggested that the recipients of smaller sized
218 valves tended to be older, to be female, to have smaller BSA and higher baseline
219 LVEF, to present more frequently calcified aortic stenosis and less frequently bicuspid
220 aortic valve (Supplementary Table 1). At discharge, recipients of smaller-sized valves
221 presented higher average and peak aortic gradients, and lower EOA. They also
222 displayed a higher rate of new permanent pacemaker implantation (Supplementary
223 Table 2).

224

225 Follow-up Results

226 Of the 974 patients discharged alive from the hospital, none was lost at follow-up
227 (100% completeness); median follow-up duration was 9.8 years according to reversed
228 Kaplan-Meier method (up to 13.4 years). During the follow-up period, we noted 410
229 deaths (42.1%); therefore, 564 patients were alive at the end of the follow-up. The
230 functional result was NYHA class I or II in 92.1% of patients; in the entire population.
231 Overall survival (Table 4 and Figure 2B) was $83.2\% \pm 1.2$ at 5 years and $56.8\% \pm 1.8$

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232 at 10 years. At last echocardiography, mean average transvalvular gradient in the
233 entire population was $14.4 \text{ mmHg} \pm 7.5$, and average EOA was $1.46 \text{ cm}^2 \pm 0.42$; aortic
234 regurgitation was noted to be of grade 3 or 4 in 0.4% of cases. Recipients of smaller-
235 sized prostheses presented higher average and peak gradients, and lower EOA than
236 recipients of larger-sized valves (Supplementary Table 3). At follow-up, we observed
237 no statistically significant differences in valve-related events by size of implanted
238 prosthesis (Supplementary Table 4). We observed a total of 28 SVD events during the
239 follow-up, occurring after $6.9 \text{ years} \pm 3.3$ (longest interval: 12.7 years); freedom from
240 SVD was $96.3\% \pm 0.8$ (Kaplan-Meier) and $97.2\% \pm 0.6$ (competing risks) at 10 years
241 (Table 4 and Figure 2A). Of the 28 SVD events, 15 were treated with reintervention
242 (10 redo-SAVR and 5 Valve-in-Valve TAVR); the remainders were not treated due
243 either to moderate SVD with limited clinical impact, or to severely compromised clinical
244 conditions in very aged patients. The average age of redo-SAVR patients was
245 50.1 ± 18.2 , and 66.8 ± 8.7 for valve-in-valve TAVR patients ($p=0.077$). Freedom from
246 reintervention (any) for SVD was $97.8\% \pm 0.6$ at 10 years (Kaplan-Meier) (Table 4).
247 Freedom rates from other valve-related events (NSVD, IE) are reported in Table 4; of
248 note, there were a total of 20 late valve-related late deaths (10-years freedom: 97.8%
249 ± 0.58) (Figure 2C). There were no significant intergroup differences at stratified
250 Kaplan-Meier analysis by size of implanted prosthesis, in terms of freedom from late
251 valve-related events (Supplementary Figure 1). At last echocardiography, data about
252 EOA allowing estimation of PPM were available in 88 patients (90.5% of patients
253 entering the follow-up). Among these, no PPM was noted in 567 (85.2%), moderate
254 PPM in 261 (26.8%), and severe PPM in 53 (5.4%). In Fine & Gray model, PPM was
255 not identified as a significant predictor of late mortality ($p=0.12$ for moderate PPM;
256 $p=0.70$ for severe PPM). From discharge echocardiography to last follow-up, we noted

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257 no statistically significant difference in average aortic gradient, but a statistically
258 meaningful decrease in peak aortic gradient and in EOA (Supplementary Figure 2).

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272 **Discussion.**

273 Surgical aortic valve replacement (SAVR) is still the treatment of choice for severe
274 aortic valve disease, in younger patients (aged <75 according to the recent
275 ESC/EACTS recommendations) [1] with low and intermediate operative risk.
276 Therefore, the average age of candidates to SAVR is decreasing. Additionally, there is

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277 a diffusing tendency towards the employment of bioprostheses for SAVR over
278 mechanical valves in patients younger than 60 years after appropriate patients'
279 information. Given the employment of bioprostheses in patients with important life
280 expectancy, often beyond 15 or 20 years, the appreciation of very late reliability and
281 valve-related outcomes acquires greater significance in the current era. The device
282 investigated herein is one of the last-generation stented pericardial bioprostheses with
283 inner-mounted pericardial leaflets. It can be distinguished from its predecessor
284 (Magna© valve) by a lower profile, sleek commissure posts and a low stent base,
285 aimed at facilitating implantation namely in smaller root anatomies (Figure 3). It entails
286 a flexible cobalt–chromium alloy stent, designed to absorb energy changes during the
287 cardiac cycle and reduce leaflet stress. It mounts three independent bovine pericardial
288 leaflets. Given its relatively recent introduction in clinical practice (2007) and its
289 widespread diffusion, it is important to evaluate its late performance in the current
290 context. In previous investigations, we have showed the optimal hemodynamic
291 performance of the Magna Ease bioprostheses in small aortic annuli (19 to 23 mm
292 nominal size valves) [2], which is a distinguished feature over porcine valve devices.
293 Nonetheless, the aforementioned investigation was limited by a 3.7 ± 2 years average
294 follow-up. Previous studies with large sample size have been so far performed to
295 evaluated mid-term durability (ex. Thorp and associates, reporting a 0.3% rate of
296 reoperation for SVD in 1,126 recipients after a mean follow-up time of 5 ± 2 years) [12].
297 Such investigation was further limited, in the Authors' view, by the use of VARC-2
298 criteria for definition of SVD (including average transprosthetic gradient >20 mmHg
299 irrespective of the cause), leading to an excessively pessimistic 28.7% SVD rate in this
300 mid-term study [9]. An important series [3] comprised 1,365 recipients of Magna Ease©
301 valve, but presented a 4.3 years only average follow-up time. Additionally, this paper

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302 presented only freedom from SVD requiring reintervention, which likely underestimates
303 the true SVD burden. In the view of the Authors, elevated transvalvular gradient should
304 be adjudicated between PPM, valve thrombosis (or other potential causes such as
305 subvalvular pannus) vs. SVD, based on transthoracic and transesophageal
306 echocardiography evidence, morphology and movement of leaflets, evolution of
307 gradients / EOA over time. Thereof, we herein considered as SVD only cases with
308 valve dysfunction due to inherent structural failure (such as, but not limited to, fracture,
309 poppet escape, calcification, leaflet tear, stent creep, and suture line disruption inside
310 the prosthetic valve). The SVD definition herein corresponds to the “Structural
311 Bioprosthetic Valve Dysfunction” in the 2020 consensus paper [7], which confirms the
312 importance to distinguish between SVD and PPM, and between echocardiographically
313 evident SVD and its clinical consequences (with or without reintervention). Our
314 approach is, therefore, essentially consistent with the consensus document. We
315 described event-freedom rates which actually correspond to the outcome required for
316 appropriate patient information at the time of preoperative counseling. More recently,
317 other studies have addressed the 10-year durability of the Magna Ease© valve (mean
318 6.6 ± 2.6 years follow-up) [13], but was based on a limited cohort of 338 patients. With
319 1,016 included SAVR cases, our study features one of the largest cohorts and one of
320 the longest follow-up (average 8,9 years among survivors). We report good late
321 durability and reliability in terms of freedom from valve-related adverse events with the
322 investigated device, supporting its reasonable employment in patients whose life
323 expectancy is 10 to 12 years. The current study, yet one of the largest in terms of
324 cohort and follow-up duration, cannot provide robust indications about longer follow-
325 up (i.e. with respect to patients with longer life expectancy), since after the 10th follow-
326 up year less than one fourth of the initial cohort is still at risk. Continued investigation

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327 is required to this purpose. To this respect, we underline the originality of the current
328 series which provides a longer follow-up than previous studies with a comprehensive
329 assessment of valve-related events. This rationally supports clinical decision-making
330 on the basis of demonstrated durability at longer timepoints.

331 Structural valve deterioration is a relatively infrequent event often occurring after
332 several years after implantation. Therefore, sufficient sample size and follow-up
333 duration are required for appropriate appreciation [14]. Also, the features, timing of
334 appearance and modalities of clinical presentation of SVD can be often associated with
335 individual models of bioprostheses. In example, noncalcified leaflet tear potentially
336 occurring 3 to 5 years after implantation with abrupt clinical manifestation has been
337 associated to some devices with externally mounted pericardium [4, 15], and
338 accelerated calcification to others [16]. In the current study, the form of SVD was more
339 frequently represented by progressive leaflet calcification leading to stenosis. Porcine
340 bioprostheses feature lesser hemodynamic performance than pericardial valves
341 (notably in smaller annuli) but SVD seems to occur more frequently under the form of
342 progressive, indolent calcification and to show longer delay until occurrence (ex. $9.3 \pm$
343 4.9 years after implantation in a third-generation device followed up during an average
344 8.5 ± 3.9 years period [17]). Similar considerations can be done for other porcine
345 xenografts [18]. Such average time to appearance of SVD is greater that observed in
346 the current study ($6.9 \text{ years} \pm 3.3$); this point deserves particular attention and possibly
347 comparative investigations for the very long-term follow-up (15 to 20 years). Therefore,
348 appropriate evaluation of the burden of SVD and of its clinical consequences need to
349 be considered when discussing the late effectiveness of SAVR as a therapy vs.
350 transcatheter techniques (TAVR). Similarly, such comparative evaluation cannot be

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351 based only on the rate of freedom from valve-related reintervention, which excludes
352 SVD cases not undergoing reoperation or valve-in-valve TAVI [19].

353 The clinical significance of PPM remains object of debate. Some Authors have
354 associated PPM with increased overall and cardiac mortality, mainly in patients with
355 baseline impaired left ventricular ejection fraction [20, 21]. The appreciation of PPM
356 depends on individual model of bioprostheses [22]. In the present large cohort, we
357 failed to identify a significant association between PPM and overall late mortality (Fine-
358 Gray model), although no subgroup-based analysis was performed. Given the known
359 very good hemodynamic characteristics of the investigated bioprosthesis [2], in our
360 center we tended to its frequent employment in patients with small annuli (19-21 mm),
361 thus leading to a potential overestimation of the rate of PPM in the overall population
362 herein (28.4% and 5.9%, respectively for moderate and severe PPM). Stratified
363 analysis described that the distribution of other valve-related events than PPM across
364 subgroups by prosthesis size. Our series is homogeneous in technical aspects
365 potentially impacting the hemodynamic results (all valves implanted supra-annular).

366 Age at surgery influences the lifetime likelihood of incurring in SVD due to longer life
367 expectancy. Herein, we observed a significantly higher risk of SVD or reoperation for
368 SVD among patients younger than 65 at surgery (Supplementary Table 5). This further
369 underlines the usefulness of the competing risks method when addressing non-lethal
370 valve-related events. Additionally, we observed a significant association at Kaplan-
371 Meier analysis between mean aortic gradient >20 mmHg at discharge and occurrence
372 of SVD (Supplementary Figure 3). This can be interpreted as a consequence of smaller
373 'reserve' in EOA predisposing to evident SVD in case of evolution towards leaflet
374 calcification.

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375 The current investigation is limited by its single-center nature. Although the included
376 patients were identified retrospectively, their in-hospital clinical data had been collected
377 prospectively. Although no patient was lost at follow-up and control echocardiography
378 was available for all of them, causes of death at follow-up remained unknown for 17.8%
379 of cases, with a potential underestimation of the rate of valve-related death. We missed
380 EOA information for 9.5% of followed-up patients, which should be considered in the
381 interpretation of PPM results. The average age at SAVR in the current population (73.4
382 ± 9.5 years) is potentially higher and therefore less representative of the population of
383 patients undergoing SAVR in the current era. Nonetheless, good life expectancy in a
384 large proportion of our patients facilitated the performance of long-term investigations.
385 In the interpretation of long-term results, the exclusion of immediate postoperative
386 events from Kaplan-Meier curves (as we focused herein on late valve-related events)
387 should be considered. Therefore, the current conclusions can only be applied to late
388 outcomes.

389 In conclusion, we herein report the long-term valve-related outcomes with the
390 Perimount Magna Ease© bioprosthesis for SAVR. Durability of this device is good at
391 10 to 12 years, with a 2.9% rate of SVD. The hemodynamic characteristics are optimal,
392 with low rates of PPM; rates of other valve-related adverse events (NSVD, IE) are
393 limited. It is to be considered that early (30-days) events are excluded from this
394 analysis. Continued evaluation (up to 15 and 20 years) is required for appropriate
395 decision-making in the currently evolving population of candidates to SAVR.

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401 of interest. The Authors sincerely thank Mrs. Sylvie Marie for her work.

402

403 **Data Availability Statement.**

404 The current database's data are available from the corresponding author upon
405 reasonable request.

406

407 **Authors' contribution statement.**

408 Conceptualization: AA, JPV

409 Data curation: AA, MA, JT, GDA

410 Formal analysis: AA, GDA, JM

411 Funding acquisition: AA, JPV

412 Investigation: AA, MA, JT, GDA, JM, JPV

413 Methodology: AA, JM, JPV

414 Project administration: AA, JPV

415 Resources: GDA

416 Software: JM

417 Supervision: JPV, HC, TL, EF

418 Validation: MA, JT, EF

419 Visualization:

420 Writing – Original draft: AA

421 Writing – Review & Editing: AA, MA, JT, GDA, JPV, TL, HC, EF

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429 **Conflict of Interest statement.**

430 This work was partially supported by an unrestricted research grant from Edwards
431 Lifesciences inc.

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541 **Table 1.** Baseline characteristics in the entire study population (N=1,016).

Characteristic	N (%) or mean \pm SD
Age (years)	73.4 \pm 9.5
BSA (m ²)	1.80 \pm 0.21
Creatinine (μ mol/L)	97.2 \pm 67.4
Male gender	577 (56.8)
<u>NYHA class</u>	
NYHA I	58 (5.7)
NYHA II	595 (58.7)
NYHA III	328 (32.4)
NYHA IV	32 (3.2)
Syncope	72 (7.1)
Previous stroke	35 (3.4)
Systemic hypertension	623 (61.3)
Smoker: past or present	203 (20)
Dyslipidemia	562 (55.3)
Diabetes mellitus	156 (15.4)
<u>Renal failure</u>	
- not requiring hemodialysis	45 (4.4)
- requiring hemodialysis	7 (0.7)
COPD	109 (10.7)
Cancer : past or present	86 (8.5)
LVEF (%)	60.5 \pm 11.2
LV end-Diastolic diameter (mm)	49.7 \pm 7.9
SPAP (mmHg)	36.9 \pm 11.2
Average Aortic Gradient (mmHg)	49.3 \pm 16.2
Aortic surface (cm ²)	0.74 \pm 0.24
<u>Aortic insufficiency</u>	
AI grade III	40 (3.9)
AI grade IV	34 (3.3)
<u>Etiology of aortic valve disease</u>	
Calcified aortic stenosis	606 (59.6)
Bicuspid morphology	120 (11.8)
Prolapse/annular dilation	1 (0.1)
Endocarditis	40 (3.9)
Other	28 (2.9)

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543 *NYHA: New York Heart Association. BSA: Body Surface Area. COPD: Chronic*
544 *Obstructive Pulmonary Disease. LVEF: Left Ventricular Ejection Fraction. SPAP:*
545 *Systolic Pulmonary Artery Pressure. AI: Aortic Insufficiency.*

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550 **Table 2.** In-hospital results in the entire study population (N=1,016).

Characteristic	N (%) or mean \pm SD
Timing	
Elective	966 (95.1)
Non-elective	50 (4.9)
CPB time (min)	75 \pm 36.7
Cross-clamp time (min)	59.9 \pm 30.3
Concomitant procedures	
Any	347 (34.2)
CABG	235 (23.1)
Other valve	58 (5.7)
Thoracic aorta	50 (4.9)
Other	25 (2.5)
Redo surgery	35 (3.4)
Prosthesis diameter (mm)	22.2 \pm 1.82
Early mortality	42 (4.1)
Discharge echocardiography	
Mean Gradient (mmHg)	14 \pm 5
Max Gradient (mmHg)	25.7 \pm 8.8
EOA (mm ²)	1.67 \pm 0.4
Aortic insufficiency grade I	111 (10.9)
Aortic insufficiency grade II	19 (1.9)
Aortic insufficiency grade III	2 (0.2)
Revision for bleeding	4 (0.4)
Gastrointestinal bleeding	5 (0.5)
Coma	
-transient	2 (0.2)
-permanent	4 (0.4)
Stroke	
-transient	5 (0.5)
-permanent	8 (0.8)
New Permanent Pacemaker	31 (3.0)
Renal failure	
- Not requiring hemodialysis	91 (9.0)
- Requiring hemodialysis	12 (1.2)

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552 *CPB: Cardiopulmonary Bypass. CABG: Coronary Artery Bypass Grafting. EOA.*
553 *Effective Orifice Area.*

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557 **Table 3.** Follow-up results (N=974).

Characteristic	N (%) or mean ± SVD
<u>NYHA class</u>	
NYHA I	370 (46.7)
NYHA II	361 (45.4)
NYHA III	60 (7.5)
NYHA IV	3 (0.4)
LVEF (%)	61.4±9.7
LV end-Diastolic diameter (mm)	49.2±12.4
SPAP (mmHg)	34.3±9.9
Average Aortic Gradient (mmHg)	14.4±7.5
Max Aortic Gradient (mmHg)	24.8±10.6
EOA (mm ²)	1.46±0.42
<u>Aortic insufficiency</u>	
AI grade I	95 (21.0)
AI grade II	17 (3.8)
AI grade III	1 (0.2)
AI grade IV	1 (0.2)

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559 *NYHA: New York Heart Association. LVEF: Left Ventricular Ejection Fraction. SPAP:*
560 *Systolic Pulmonary Artery Pressure. EOA: Effective Orifice Area. AI: Aortic*
561 *Insufficiency.*

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569 **Table 4.** Follow-up results in time-to-event analyses (overall survival, freedom from
 570 SVD and from any reintervention for SVD, freedom from NSVD and from IE) (N=974).
 571 Actuarial (Kaplan-Meier) rates are provided; if applicable, freedom rates calculated
 572 according to the competing risks method are provided in *italics*.

N (%)		
	5 y	10 y
Deaths : 410 (42.1)	83±1.2	56.8±1.8
SVD : 28 (2.9)	99.3±0.3 <i>99.4±0.3</i>	96.5±0.8 <i>97.4±0.6</i>
Reintervention for SVD : 15 (1.5)	99.4±0.3	97.8±0.6
NSVD : 10 (1)	99.2±0.3	99±0.4
IE : 29 (3)	97.8±0.5	96.2±0.7
Valve-related death : 20 (2.1)	98.6±0.4	97.8±0.5
N at risk	793	256

573 *SVD: Structural Valve Deterioration. NSVD: Nonstructural Valve Dysfunction. IE:*
 574 *Infectious Endocarditis.*

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583 **Table 5.** Follow-up valve-related events described as cumulative incidence (competing
584 risks).

Characteristic	5 y	10 y
SVD	0.6±0.3	2.6±0.6
Reintervention for SVD	0.5±0.2	1.6±0.4
NSVD	0.6±0.3	0.8±0.3
IE	2.1±0.5	3.2±0.6
Any reintervention	1.4±0.4	3.5±0.6
Valve-related death	1.3±0.4	1.9±0.5

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596 **Figure Legends.**

597 **Central Image Legend.** Summary of SVD results: number of events, time to
598 occurrence, freedom rates according to both the Kaplan-Meier and competing risks
599 methods.

600 **Graphical Abstract legend.** Summary of the main study methods and findings
601 concerning valve durability.

602 **Figure 1.** Study workflow. SAVR: Surgical Aortic Valve Replacement. FU: Follow-up.

603 **Figure 2.** Incidence and Kaplan-Meier survival curves (operative mortality cases
604 excluded). **A:** Incidence of non-lethal events. **B:** Overall survival. **C:** Survival free from
605 any reintervention for SVD.

606 **Figure 3.** The Carpentier-Edwards Perimount Magna Ease[®] aortic bioprosthesis
607 compared to its predecessor the Carpentier-Edwards Perimount Magna[®] aortic
608 bioprosthesis.

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