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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 5<sup>th</sup> to October 8<sup>th</sup>, 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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39

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  $73.4 \pm 9.5$  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  $56.8\% \pm 1.8$ . Freedom from SVD at 10 was  $96.5\% \pm 0.8$   
53 (Kaplan-Meier), and  $97.4\% \pm 0.6$  (competing risks) (28 SVD events after  $6.9 \text{ years} \pm$   
54  $3.3$ ). There were 15 reinterventions for SVD (redo-SAVR and TAVI); 10-year freedom  
55 from reintervention was  $97.8\% \pm 0.6$ . 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  $97.8\% \pm 0.5$  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<sup>®</sup> 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 2<sup>nd</sup>,  
105 2008 and December 31<sup>st</sup>, 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  $\leq 0.65$  cm<sup>2</sup>/m<sup>2</sup>, moderate when  
158 iEOA was  $\leq 0.85$  cm<sup>2</sup>/m<sup>2</sup>, or absent when iEOA was  $>0.85$  cm<sup>2</sup>/m<sup>2</sup> [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.

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### 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  $50.1 \pm 18.2$ , and  $66.8 \pm 8.7$  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  $\pm 0.58$ ) (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  $3.7 \pm 2$  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  $5 \pm 2$  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  $6.6 \pm 2.6$  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 10<sup>th</sup> 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  $8.5 \pm 3.9$  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  $\pm 9.5$  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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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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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 <sup>2</sup> )	1.80 $\pm$ 0.21
Creatinine ( $\mu$ mol/L)	97.2 $\pm$ 67.4
Male gender	577 (56.8)
<b><u>NYHA class</u></b>	
<b>NYHA I</b>	58 (5.7)
<b>NYHA II</b>	595 (58.7)
<b>NYHA III</b>	328 (32.4)
<b>NYHA IV</b>	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)
<b><u>Renal failure</u></b>	
- 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 <sup>2</sup> )	0.74 $\pm$ 0.24
<b><u>Aortic insufficiency</u></b>	
AI grade III	40 (3.9)
AI grade IV	34 (3.3)
<b><u>Etiology of aortic valve disease</u></b>	
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).

<b>Characteristic</b>	<b>N (%) or mean <math>\pm</math> SD</b>
<b>Timing</b>	
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
<b>Concomitant procedures</b>	
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)
<b>Discharge echocardiography</b>	
Mean Gradient (mmHg)	14 $\pm$ 5
Max Gradient (mmHg)	25.7 $\pm$ 8.8
EOA (mm <sup>2</sup> )	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)
<b>Coma</b>	
-transient	2 (0.2)
-permanent	4 (0.4)
<b>Stroke</b>	
-transient	5 (0.5)
-permanent	8 (0.8)
New Permanent Pacemaker	31 (3.0)
<b>Renal failure</b>	
- 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).

<b>Characteristic</b>	<b>N (%) or mean ± SVD</b>
<b><u>NYHA class</u></b>	
<b>NYHA I</b>	370 (46.7)
<b>NYHA II</b>	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 <sup>2</sup> )	1.46±0.42
<b><u>Aortic insufficiency</u></b>	
AI grade I	95 (21.0)
AI grade II	17 (3.8)
AI grade III	1 (0.2)
AI grade IV	1 (0.2)

558

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

<b>Characteristic</b>	<b>5 y</b>	<b>10 y</b>
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.

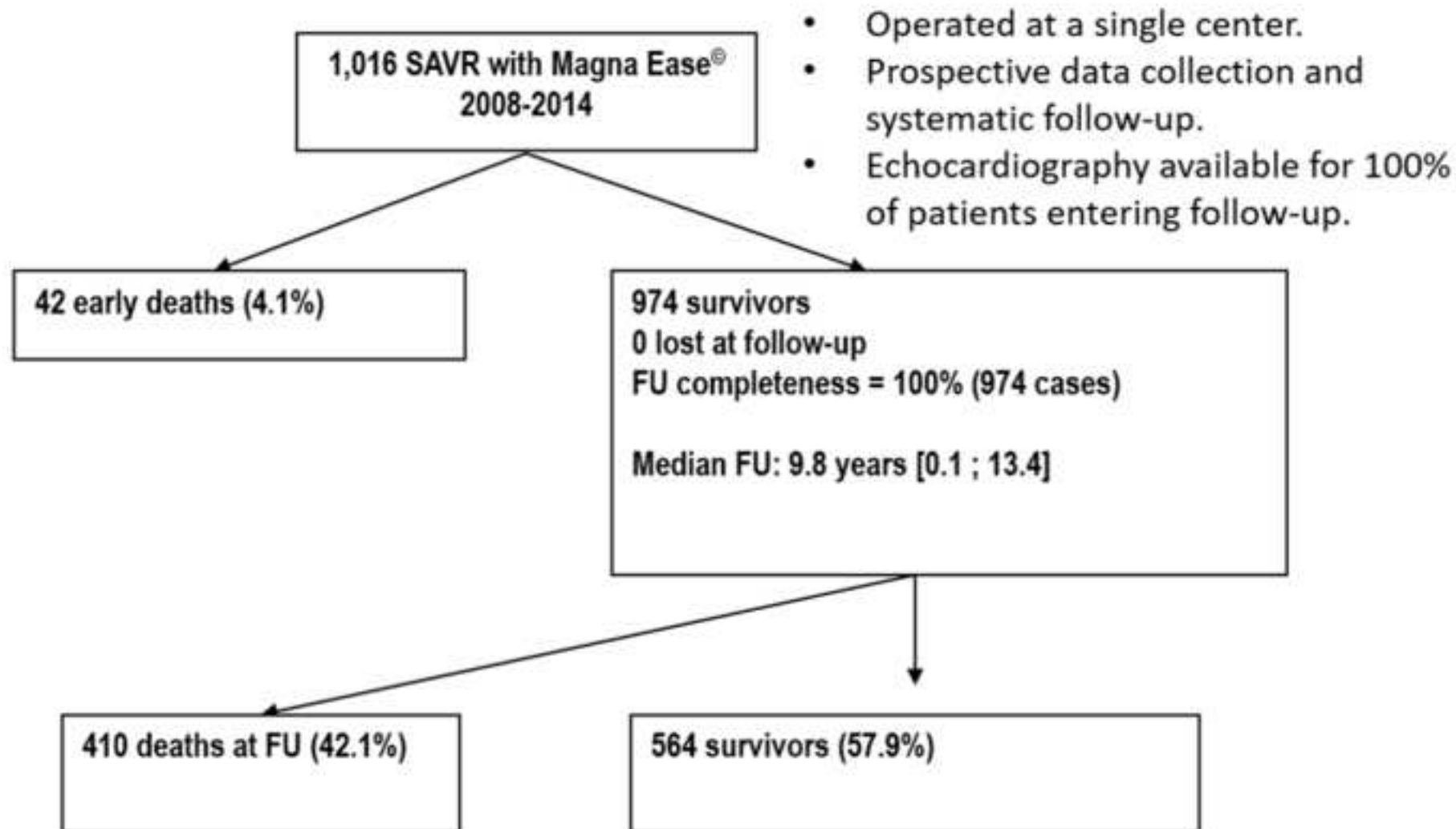
600 **Graphical Abstract legend.** Summary of the main study methods and findings  
601 concerning valve durability.

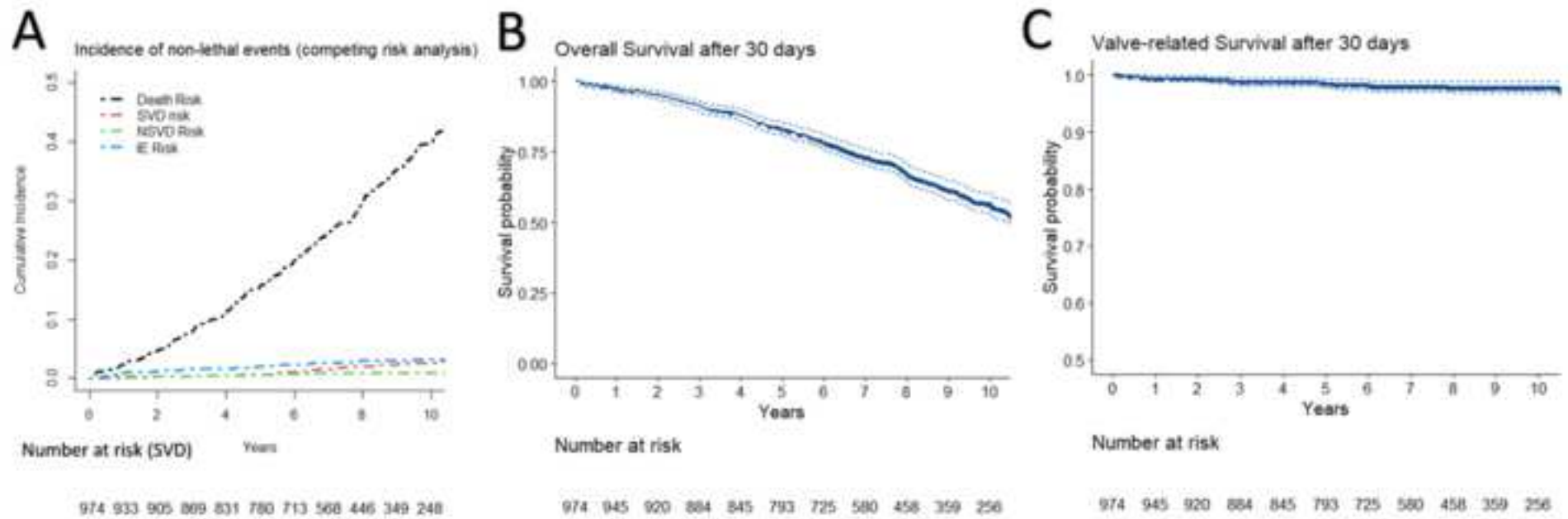
602 **Figure 1.** Study workflow. SAVR: Surgical Aortic Valve Replacement. FU: Follow-up.

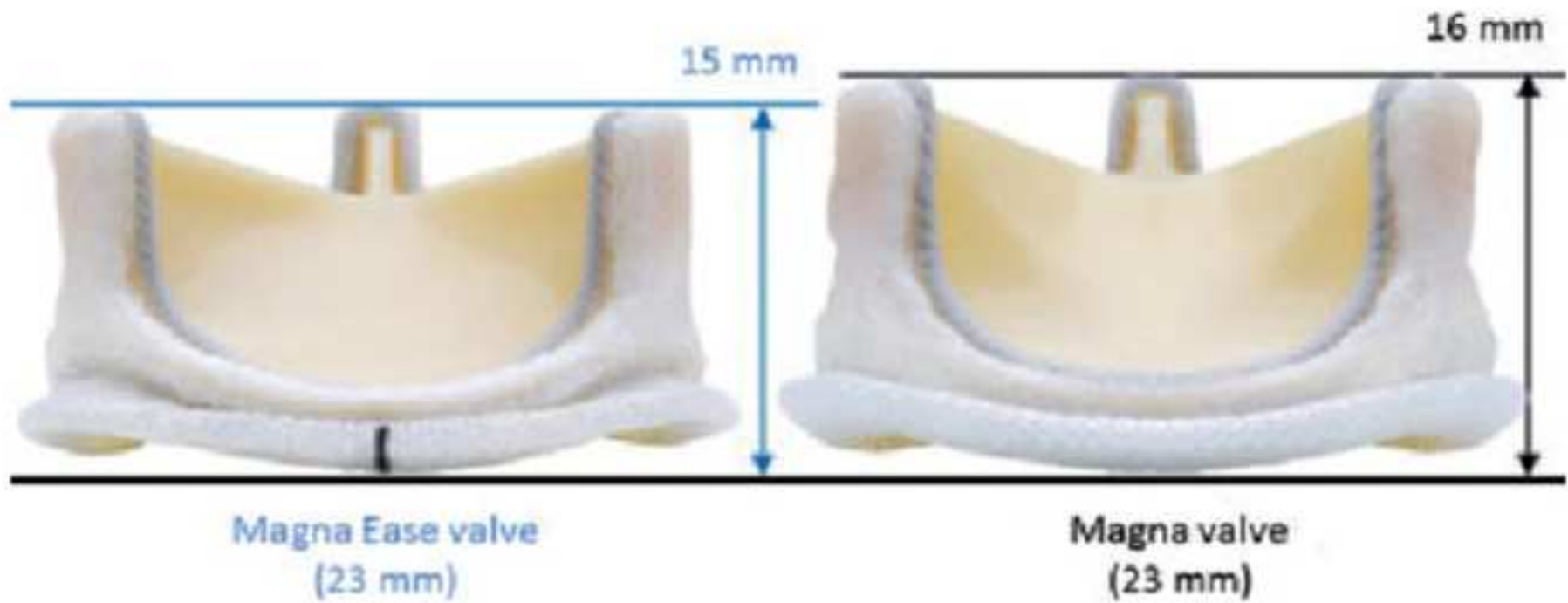
603 **Figure 2.** Incidence and Kaplan-Meier survival curves (operative mortality cases  
604 excluded). **A:** Incidence of non-lethal events. **B:** Overall survival. **C:** Survival free from  
605 any reintervention for SVD.

606 **Figure 3.** The Carpentier-Edwards Perimount Magna Ease<sup>®</sup> aortic bioprosthesis  
607 compared to its predecessor the Carpentier-Edwards Perimount Magna<sup>®</sup> aortic  
608 bioprosthesis.

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**Supplementary material**  
Supplementary Figure 3.tif

