

1 **Long-term outcomes with balloon-expandable and self-expandable prostheses**
2 **in patients undergoing transfemoral transcatheter aortic valve implantation for**
3 **severe aortic stenosis**

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31

32 **Keywords**

33 Transcatheter aortic valve implantation (TAVI), Valvular heart disease, Outcome, Structural valve
34 deterioration, Self-expanding prosthesis, Balloon-expandable prosthesis

35

36 **2 Tables and 2 Figures**

37 **Table 1:** Baseline clinical characteristics.

38 **Table 2:** Echocardiographic imaging characteristics.

39 **Figure 1:** (A) Cumulative incidence including landmark analysis of all-cause mortality according to
40 transcatheter aortic valve type up to 5 years of follow-up. (B) Cumulative incidence including
41 landmark analysis of cardiac mortality according to transcatheter aortic valve type up to 5 years of
42 follow-up. (C) Cumulative incidence including landmark analysis of major stroke according to
43 transcatheter aortic valve type up to 5 years of follow-up.

44 **Figure 2:** Cumulative incidence of structural valve deterioration up to 5 years of follow-up.

45

46 **ABSTRACT**

47 Background

48 Data on long-term outcomes in patients undergoing transcatheter aortic valve implantation (TAVI) is
49 scarce.

50 Methods

51 We investigated long term outcomes of consecutive patients undergoing TAVI with balloon- and self-
52 expandable bioprostheses (Edwards SAPIEN (ESV), Edwards Lifesciences Inc., Irvine, CA, USA;
53 Medtronic Corevalve system (MCS), Medtronic Inc., Minneapolis, MN, USA).

54 Results

55 Among 628 patients (mean age 82.4±5.8 years, 55% female), 489 (77.8%) underwent transfemoral
56 TAVI. 309 (63.2%) patients received a MCS prosthesis, whereas 180 (36.8%) patients were treated
57 with an ESV prosthesis. The median duration of follow-up amounted to 5.2 years (range 3.4–8.3
58 years). All-cause mortality did not differ between the two groups (MCS 46.9%, ESV 53.4%, CI 95%: RR
59 1.21 [0.93–1.57], P = 0.15), whereas cardiac mortality was higher in the ESV cohort after 5 years of
60 follow-up (MCS 35.1%, ESV 45.4%, CI 95%: RR 1.37 [1.01–1.86], P = 0.04). Structural valve
61 deterioration, which was on average diagnosed 41.9 months (range 18–60 months) after TAVI,
62 occurred in 8 cases (1.6%), resulting in one repeat intervention.

63 Conclusions

64 While half of all patients died within 5 years after TAVI with no significant differences in all-cause
65 mortality, structural valve deterioration was documented in 2% of cases.

66 **INTRODUCTION**

67 Transcatheter aortic valve implantations (TAVI) are rapidly expanding towards the low risk spectrum
68 of patients with severe aortic stenosis. Randomized controlled trials showed comparable safety and
69 efficacy of both, self- and balloon-expandable prostheses, as compared to surgical aortic valve
70 replacement [1–3]. Regarding the use of TAVI in younger patients, the question of long-term
71 outcomes and in particular of valve durability becomes of major importance. However, there is a
72 significant lack of data regarding these factors, which can also be seen as directories regarding the
73 decision making in favor of TAVI or surgical aortic valve replacement (SAVR) in patients with a lower
74 operative risk profile. The aim of the present analysis was to evaluate the long-term outcomes
75 regarding the performance of the two most widely used TAVR systems: the balloon-expandable
76 Edwards SAPIEN valve (ESV) (Edwards Lifescience Inc., Irvine, CA, USA) and the self-expandable
77 Medtronic Corevalve system (MCS) (Medtronic Inc., Minneapolis, MN, USA) in patients undergoing
78 TAVI for severe symptomatic aortic valve stenosis.

79

80 **METHODS**

81 **Study population**

82 Between July 2007 and January 2013, all patients undergoing TAVI at the Swiss Cardiovascular
83 Center of Bern University Hospital in Switzerland were consecutively recorded in a prospective
84 registry held at the Clinical Trials Unit of the University of Bern in Switzerland. Inclusion criteria
85 consisted of a) symptomatic, severe aortic stenosis (AS) with an echocardiographic mean gradient
86 >40 mm Hg or a calculated aortic valve area <1 cm² and b) age ≥ 80 years with a high operative risk
87 score (logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) >15%). Patients
88 <80 years of age were eligible if at least one of the following comorbid conditions were present:
89 previous cardiac surgery, liver cirrhosis, chronic pulmonary disease (forced expiratory volume <1 l/s),
90 severe pulmonary hypertension, porcelain aorta, history of mediastinal radiotherapy, severe
91 connective tissue disease with contraindication for surgery, or frailty. Additionally, anatomical

92 prerequisites consisted of an aortic annulus diameter in the range of 18 to 27 mm and a vascular
93 access site suitable for transfemoral TAVI. Exclusion criteria included degenerated aortic valve
94 prostheses and severe aortic regurgitation in the absence of AS. An interdisciplinary team of cardiac
95 surgeons and interventional cardiologists reviewed all cases and formed a consensus on treatment
96 allocation (TAVI or SAVR). The registry as well as the study have been approved by the local cantonal
97 ethics committee and comply with the Declaration of Helsinki. All patients enrolled in the database
98 provided written informed consent.

99

100 **Definitions and procedures**

101 Patients undergoing TAVI underwent comprehensive multimodal assessment using transthoracic and
102 transesophageal echocardiography, right and left heart catheterization, and contrast computed
103 tomography. TAVI was performed according to standard protocols via transfemoral approach using
104 both balloon-expandable ESV (Sapien THV and XT) and self-expandable MCS. Device selection was
105 based on anatomical and technical characteristics as described previously [4]. Pre- and postdilatation
106 were performed according to the operators' discretion. Postinterventional antithrombotic and
107 antiplatelet treatment was prescribed according to the discretion of the operator. For definitions of
108 outcome variables see Supplemental File 1. Procedural success was defined as device success in the
109 absence of major adverse cardiovascular and cerebral events during the first 48 h after device
110 implantation. Device success was defined according to VARC-2 criteria. Bioprosthetic valve
111 dysfunction, including valve deterioration, thrombosis, and endocarditis, was defined according to
112 the consensus statement from the European Association of Percutaneous Cardiovascular
113 Interventions (EAPCI).

114

115 **Data collection**

116 Demographic characteristics, imaging parameters, hemodynamic measurements, and procedural
117 variables were prospectively recorded in a web-based database. All patients underwent sweep

118 follow-up between April and November 2017 which was performed by means of standardized
119 telephone interviews. In addition, medical records, discharge summaries, and documentation of
120 hospitalization were systematically collected from general practitioners, referring cardiologists as
121 well as referring hospitals for verification of clinical endpoints. For a validated calcification score
122 analysis [5], measurements were done at theHU-850 threshold in Contrast CT images. All endpoints
123 were defined according to the updated version of the Valve Academic Research Consortium (VARC-
124 2) definitions [6], and adjudicated by a clinical event committee, which consists of interventional
125 cardiologists and cardiac surgeons from different institutions.

126

127 **Statistical analysis**

128 Continuous data are reported as mean \pm standard deviation (SD) if their distribution is approximately
129 normal and as median/range otherwise. The means were compared using analysis of variance and
130 differences in medians were analysed with Mann-Whitney test. Categorical variables are expressed
131 as number of patients (% of patients). Survival was estimated using the Kaplan-Meier method and
132 differences in estimates were compared by means of the log-rank test. The at-risk time span was
133 derived from the date of intervention and the last available data of the patient, determined either
134 by the last follow-up, the time of death, or information coming from referring hospitals and/or
135 practitioners. Survival estimates were calculated using univariate and multivariate Cox proportional
136 hazard models including landmark analyses. Reported are crude hazard ratios (HR; with 95%
137 confidence intervals) with p-values from Wald chi-square tests, or continuity correct risk ratios with
138 p-values from Fisher's exact tests. P-values <0.05 were considered statistically significant. For
139 adjusted analyses, baseline and pre-TAVI characteristics were included that showed a difference
140 between the two groups with a p-value \leq 0.1 (TAVI device, sex, body mass index, previous CABG,
141 previous stroke or TIA, prior permanent pacemaker, EuroScore, aortic valve area, LV ejection
142 fraction, and calcification score). All analyses were performed with Stata version 14 (StataCorp,
143 College Station, TX, USA).

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146

147 RESULTS

148 Among 628 patients (mean age 82.4 ± 5.8 years, 54.6% female), 489 patients (77.8%) underwent
149 transfemoral TAVI for native aortic valve stenosis. Patients undergoing transapical (N = 124, 19.7%)
150 or trans-subclavian (N = 9, 1.4%) TAVI, as well as patients with a transcatheter-valve-in-surgical-valve
151 procedure (N = 6, 1%) were excluded from the present analysis. 309 (63.2%) patients were treated
152 with a MCS whereas 180 (36.8%) patients received an ESV (ESV THV in 27 (5.5%) cases, ESV XT in 153
153 (31.3%) cases). Baseline clinical characteristics at the time of intervention are summarized in Table 1.
154 Both, patients in the MCS and the ESV cohort, were comparable with respect to cardiovascular risk
155 factors, clinical features, symptom status, and preinterventional antithrombotic therapy. While more
156 female patients underwent implantation of a MCS (MCS 46.3% vs. ESV 35%, $P = 0.0148$), patients in
157 the ESV cohort had more frequently experienced a previous stroke or transient ischemic attack (TIA)
158 as compared with MCS patients (ESV 10.8% vs. MCS 4.8%, $P = 0.0136$). Echocardiographic imaging
159 characteristics are outlined in Table 2. No significant preinterventional differences between the two
160 treatment arms could be noted except a higher left ventricular ejection fraction (LVEF) within the
161 ESV group (ESV 56.6% vs. MCS 51.8% vs., $P=0.0004$). Furthermore, measurements from left/right
162 heart catheterization were comparable between the two groups (Supplemental Table 1).

163

164 Procedural outcomes

165 Procedural data are depicted in Supplemental Table 2. Procedure time did not significantly differ
166 between MCS and ESV and took on average 67.5 min ($P = 0.52$). Implantation of a MCS valve
167 required more contrast dye (MCS 266.7 ± 102.7 ml, ESV 225.7 ± 96 ml, $P \leq 0.001$) and was less
168 frequently performed with a balloon predilatation as compared with the implantation of an ESV
169 (MCS 92.6% vs. ESV 99.4%, $P=0.0007$). After intervention, patients treated with an ESV had a higher

170 mean aortic valve gradient (MCS 7.2 ± 3.7 mm Hg, ESV 8.5 ± 4.0 mm Hg, $P = 0.0003$) whereas the
171 need for permanent pacemaker implantation was higher in the MCS cohort (MCS 29.8% vs. ESV
172 14.4%, $P = 0.0001$). Postprocedural moderate to severe aortic regurgitation occurred more
173 frequently among patients treated with a MCS valve (MCS 19.1% vs. ESV 4.5%, $P \leq 0.0001$). The mean
174 hospital duration was 9.1 (7.2 ± 12.3) days with a longer duration for patients treated with a MCS
175 prosthesis (MCS 9.1 (8.4 ± 12.4) days, ESV 8.3 (7.3 ± 11.1) days, $P = 0.02$). In 11 cases, all of which
176 occurred within the MCS cohort (3.6%, $P = 0.01$), the implantation of more than one valve in series
177 was required.

178

179 **Clinical outcomes**

180 Comparisons of clinical outcomes are descriptive. The median duration of follow-up amounted to 5.2
181 years (range 3.4–8.3 years). None of the patients was lost to follow-up. Event rates with crude
182 hazard ratios for all major clinical endpoints according to VARC through 30 days, 3 years, and 5 years
183 are provided in Supplemental Table 3. All-cause mortality throughout 5 years of follow-up did not
184 differ between the two groups (MCS 46.9%, ESV 53.4%, RR 1.21 [0.93–1.57], $P = 0.15$) whereas
185 cardiac mortality was higher in the ESV cohort, taking effect after 3 years (30 days: MCS 3.9%, ESV
186 5.6%, RR 1.59 [0.67–3.75], $P = 0.29$; 3 years: MCS 21.6%, ESV 24.5%, RR 1.18 [0.8–1.75], $P = 0.4$; 5
187 years: MCS 35.1%, ESV 45.4%, RR 1.37 [1.01–1.86], $P = 0.04$). Fig. 1 shows cumulative event rates for
188 all-cause mortality, cardiac mortality, and major stroke throughout 5 years stratified for MCS and
189 ESV and including landmark analyses (0 to 30 days, 31 days to 5 years) with the aforementioned
190 described significant difference in long-term cardiac mortality ($P = 0.04$) between the two groups.
191 The landmark analyses as such did not show any further significant differences between the two
192 valve types (Supplemental Table 4). Adjusted univariable analyses showed an association between
193 all-cause mortality and female gender (HR 0.73, 95% CI 0.57–0.95; $P = 0.0183$), previous CABG (HR
194 1.60, 95% CI 1.03–2.49; $P = 0.0355$), logistic EuroScore (HR 1.02, 95% CI 1.01–1.03; $P = 0.001$), and
195 LVEF (HR 0.99, 95% CI 0.98–1.00; $P = 0.0052$), between cardiac mortality and the implantation of an

196 ESV (HR 1.37, 95% CI 1.01–1.86; P=0.0409), logistic EuroScore (HR 1.03, 95% CI 1.02–1.04; P <0.001),
197 and LVEF (HR 0.98, 95% CI 0.97–0.99; P = 0.0006), whereas major stroke was associated with
198 previously occurred strokes or transitoric ischemic attacks (HR 3.27, 95% CI 1.23–8.72; P = 0.0177).
199 Univariable and multivariable adjusted analyses are illustrated in Supplemental Tables 5 and 6.

200

201 **Echocardiographic follow-up and time-related valve safety**

202 Post-procedural echocardiographic data relate to the last available transthoracic echocardiographic
203 follow-up performed at the university center or at an outpatient cardiology center. After three years,
204 echocardiographic data amounted to 72% of cases; after five years echocardiographic follow-up data
205 was available in 65% of cases. While mean and peak aortic valve (AV) gradients as well as LVEF were
206 higher in the ESV cohort (mean AV gradient: MCS 8.85 ± 4.75 mm Hg; ESV 10.25 ± 4.52 mm Hg, P =
207 0.0033; peak AV gradient: MCS 16.23 ± 9.4 mm Hg; ESV 18.59 ± 8.69 mm Hg, P = 0.0277; LVEF: MCS
208 55.55 ± 12.43 mm Hg; ESV 57.83 ± 10.94 mm Hg, P = 0.0543), severe pulmonary hypertension (MCS
209 40.4% vs. ESV 26.9%, P=0.0335) and moderate or severe aortic regurgitation (MCS 19% vs. ESV 9%, P
210 = 0.0055) were more frequently observed in patients treated with a MCS valve. Regarding relevant
211 aortic regurgitation, no significant change could be seen over time after TAVI in both, MCS and ESV
212 treated patients (MCS: P = 0.1384, ESV: P=0.0621). The degree and changes in aortic regurgitation
213 before and after treatment have been depicted in Supplemental Figs. 1 and 2. In total, 8 cases (1.6%)
214 of structural valve deterioration (SVD) (3 MCS (1%), 5 ESV (2.8%)) occurred during the follow-up
215 time. On average, prosthetic SVD was diagnosed 41.9 months (range 18–60 months) after TAVI.
216 Moderate SVD occurred in 7 cases (ESV: 4 (2.2%), MCS: 3 (1%)), whereas severe SVD was only found
217 in one patient (ESV, 0.6%). Details are shown in Supplemental Tables 7 and 8 as well as in Fig. 2. A
218 repeat procedure due to SVD was performed in only one case 4.6 years after implantation of an ESV
219 XT 26 mm (mean AV gradient 64 mm Hg, aortic valve area (AVA) 0.6 cm^2) with a successful valve-in-
220 valve procedure using a MCS valve. All other cases of SVD were treated conservatively. In addition to
221 the SVD case, valve-related repeat interventions were performed in another four patients (0.1%). In

222 two patients, who were primarily treated with a MCS-valve, a balloon dilatation of the transcatheter
223 valve was performed due to relevant paravalvular regurgitation 13 days and 14 days after the index
224 procedure. One patient with a MCS valve developed severe paravalvular aortic regurgitation after
225 1.3 years and was treated with another MCS prosthesis. Another patient was diagnosed with an
226 aorto-right ventricular fistula 1.3 months after implantation of an ESV prosthesis resulting in a fistula
227 occlusion with a coil [7]. In total, two cases of prosthetic valve endocarditis were diagnosed. One
228 with an ESV XT 26 mm valve 2.6 years after implantation and the other one with an ESV XT 23 mm
229 4.8 years after implantation. No case of manifest prosthetic valve thrombosis occurred during the
230 follow-up.

231

232 **DISCUSSION**

233 We present long-term clinical outcomes of patients with a symptomatic severe AS treated with
234 transfemoral TAVI using either a balloon-expandable (ESV) or a self-expandable (MCS) prosthesis.
235 The key findings can be summarized as follows: (1) >50% of patients died within 5 years after TAVI;
236 there were no differences in all-cause mortality and major stroke between patients treated with
237 either a balloon-expandable ESV or a self-expandable MCS prosthesis; (2) Structural valve
238 deterioration occurred in <2% of survivors and was diagnosed on average 3.5 years after the index-
239 procedure; (3) Repeat interventions for prosthetic heart valve related problems were rare.
240 Our results of a high efficacy of both, the balloon-expandable ESV and the self-expandable MCS
241 valve, can be confirmed through various studies [8–10]. However, valve-specific drawbacks have
242 been previously described as well. In patients treated with a MCS prosthesis, we observed a higher
243 need for permanent pacemaker implantation (29.8% vs. 14.4% at 30 days, $P = 0.0001$), which was
244 consistent with previous reports [11–14]. This fact is most likely due to the deeper extension of the
245 valve into the left ventricular outflow tract in addition to the self-expanding nature of its frame
246 applying constant pressure on the atrioventricular conductance system. Regarding rates of
247 atrioventricular conduction disturbance and potential impact on long-term mortality, conflicting

248 evidence exists. While data from our cohort suggested that preprocedural pacemaker implantation
249 does not adversely affect clinical outcomes, data of the PARTNER study showed that the presence of
250 a pacemaker (pre- or periprocedural) was independently associated with increased 1-year mortality
251 [15,16]. However, further technical developments, such as adjustments of the valve frame and
252 additional modifications of the catheter, which allows a more accurate positioning of the valve, may
253 further reduce the likelihood of a pacemaker dependency [17,18].

254 In addition, patients treated with MCS more commonly had paravalvular regurgitation as compared
255 to patients treated with ESV (19.1% vs. 4.5%, $P \leq 0.001$), which has previously been associated with
256 worse long-term clinical outcomes [19]. Our results are in line with reported rates of relevant AR
257 after TAVI with early generation devices ranging from 15% to 20% [20–24]. Most of the cases of
258 no/mild aortic regurgitation at baseline that worsened were worsening from mild to moderate aortic
259 regurgitation. Improved valve positioning and stabilisation resulting in predictable implantation
260 depth in combination with refinements of the prosthesis with skirts, cuffs, and seals, have
261 significantly reduced the rate of paravalvular regurgitation [25,26]. Despite the higher rates of
262 moderate to severe paravalvular regurgitation, valve in series procedures, and permanent
263 pacemaker implantation in the MCS group, there was no excess mortality in this cohort, even though
264 all of these complications have been associated with worse outcomes as described above. This
265 paradoxon may be partially explained by the moderate sample size of this study as well as by
266 “background” events of death occurring in octogenarians as already hypothesized by the one year
267 results of the CHOICE trial [27].

268 The observed all-cause mortality rate of 30.8% for MCS and 32.9% of ESV prosthesis in our cohort as
269 well as the cardiac mortality rate of 21.6% for the MCS and 24.5% for the ESV cohort at 3-year
270 follow-up is within the range of previous reports, albeit at the lower end [28–31]. Outcome data
271 beyond 3 years in terms of comparison of the two most widely used TAVI systems is scarce. Bouleti
272 et al. showed a 5-year event-free survival rate of $28\% \pm 4\%$, however, the study cohort was small (N
273 = 123) and in >90% of patients, an ESV prosthesis was used [32]. In the study of Tarantini and

274 colleagues, 171 patients were treated (MCS: N = 87, ESV: N = 84) with an overall survival rate of
275 44.9% at 5 years without a difference between valve types [33]. Data of the UK TAVI Registry with an
276 almost balanced implantation rate between MSC and ESV prostheses, presented a 5 year all-cause
277 mortality rate of 53.1% being in line with our findings (MCS 46.9%, ESV 53.4%). Valve type
278 differences at 5 years as well as data on cardiac mortality were not presented. Our results showed a
279 statistically higher cardiac mortality in the ESV group (MCS 35.1% vs. ESV 45%, P=0.04) taking effect
280 after 3 years. Crude cardiac mortality rates of patients treated with an ESV prosthesis were lower as
281 compared with the 5-year results from the PARTNER trial (45.4% vs. 57.5%) [30]. Of note, no
282 relevant difference in calcification volume could be found within the two cohorts. Due to the
283 observational nature of this single center study these results have to be interpreted with caution.
284 Notwithstanding, and with the knowledge that a lot of morbidities unrelated to cardiovascular
285 disease heavily contribute to death in the long-term, this effect requires further scrutiny and needs
286 to be considered for further analyses comparing the two valve systems. The incidence of adverse
287 events including stroke at 3 and at 5 years were comparable to other reports and showed no
288 differences between the valve types.

289 The low incidence of time-related valve safety events according to VARC is reassuring and
290 comparable to other long-term TAVI studies [29,34,35]. Structural valve deterioration occurred in 8
291 patients (1.6%) in both, patients treated with an ESV or MCS-valve. Referring to the consensus
292 statement from the European Association of Percutaneous Cardiovascular Interventions [36],
293 moderate SVD occurred more frequently as compared with severe SVD, underlined by data from the
294 NOTION trial [37]. While reported rates of structural valve deterioration in surgically implanted
295 aortic valve prostheses requiring reoperation range from 6–47% by 12 to 29 years after
296 implantation, reports of transcatheter valve durability are needed to safely expand TAVR to the low
297 risk spectrum of younger patients [38–42]. The observation of subclinical leaflet thrombosis (SLT)
298 has recently raised concerns and may affect long-term clinical outcomes, in particular rates of

299 cerebrovascular events [41,42]. Further research is crucial in order to evaluate if actual rates of
300 bioprosthetic valve dysfunction also relate to newer generation valves.

301 The present analysis has to be interpreted against the background of several limitations. First, the
302 number of patients included into the analysis was modest. Conversely, no patient was lost to clinical
303 follow-up and reports on long-term outcome of patients undergoing TAVI are scarce. Second, data
304 was acquired at a single center, thus not being generalizable to institutions with different referral
305 patterns. Third, allocation to treatment with MCV and ESV was non-randomized; differences in
306 clinical outcomes are therefore open to bias. Fourth, current data on long-term follow-up includes
307 treatment with older generation valves resulting in a possible impact on generalizability.

308 Furthermore, the assessment of long-term structural valve deterioration might be limited in high-risk
309 populations with rather high mortality rates in the early TAVI era. Additionally, the lack of uniformity
310 of echocardiography and the low follow-up data of echocardiography over time might have
311 introduced a bias in addition to a possible bias of underestimation of valve thrombosis in the
312 absence of routine multisliced computed tomography in SVD patients. However, the analyses
313 represent treatment decisions and outcomes of consecutive patients as encountered in routine
314 clinical practice.

315

316 **CONCLUSION**

317 More than 50% of patients undergoing TAVI died within 5 years of the procedure with no significant
318 differences in all-cause mortality between MCS and ESV. Structural valve deterioration was
319 documented in <2% of patients.

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441 **TABLES**442 **Table 1:** Baseline clinical characteristics.

443 Depicted are means \pm SD with p-values from t-tests or counts (%) with p-values from Fisher's tests
 444 (two categories) or chi-square tests (more than two categories). BMI = Body mass index; CABG=
 445 Coronary artery bypass grafting; GFR = Glomerular Filtration Rate; MI=Myocardial infarction;
 446 IQR=Interquartile range; NYHA=New York Heart Association; PCI = Percutaneous coronary
 447 intervention; TIA = Transient ischemic attack; STS = Society of Thoracic Surgeons.

	Overall	Medtronic CoreValve	Edwards Sapien	P value
	N = 489	N = 309	N = 180	
<i>Demographics</i>				
Age, years	82.9 \pm 5.2	82.8 \pm 5.1	83.0 \pm 5.6	0.7534
Female gender, n (%)	206 (42.1)	143 (46.3)	63 (35.0)	0.0148
BMI, kg/m ²	26.2 \pm 4.9	25.9 \pm 4.8	26.7 \pm 5.0	0.0740
<i>Cardiac risk factors</i>				
Diabetes mellitus, n (%)	130 (26.6)	78 (25.2)	52 (28.9)	0.3787
Hypercholesterolaemia, n (%)	303 (62.0)	187 (60.5)	116 (64.4)	0.3884
Arterial Hypertension, n (%)	417 (85.3)	259 (83.8)	158 (87.8)	0.2334
<i>Past medical history</i>				
Previous MI, n (%)	72 (14.7)	48 (15.5)	24 (13.3)	0.5077
Previous PCI, n (%)	119 (24.3)	82 (26.5)	37 (20.6)	0.1371
Previous CABG, n (%)	35 (7.2)	17 (5.5)	18 (10.0)	0.0627
Previous stroke or TIA, n (%)	33 (7.0)	14 (4.8)	19 (10.8)	0.0136
Peripheral vascular disease, n (%)	70 (14.3)	50 (16.2)	20 (11.1)	0.1226
Chronic obstructive pulmonary disease, n (%)	80 (16.4)	56 (18.1)	24 (13.3)	0.1673
<i>Clinical features</i>				
Pulmonary artery hypertension, n (%)	417 (85.3)	259 (83.8)	158 (87.8)	0.2334
Renal failure (GFR < 60 mL/min/1.73 m ²), n (%)	337 (69.1)	218 (70.8)	119 (66.1)	0.2818
Coronary artery disease, n (%)	297 (60.7)	191 (61.8)	106 (58.9)	0.5232
Atrial fibrillation, n (%)	156 (31.9)	100 (32.4)	56 (31.1)	0.7746
Prior permanent pacemaker, n (%)	45 (9.2)	34 (11.0)	11 (6.1)	0.0711
Calcification score, mm ³ ; median (IQR)	259 (129–466)	290 (125–484)	246 (134–400)	0.5139
<i>Symptoms</i>				
NYHA Functional Class				0.5640
I, n (%)	33 (6.8)	19 (6.2)	14 (7.8)	
II, n (%)	121 (24.8)	81 (26.3)	40 (22.2)	
III, n (%)	276 (56.6)	169 (54.9)	107 (59.4)	
IV, n (%)	58 (11.9)	39 (12.7)	19 (10.6)	
<i>Risk assessment</i>				
Logistic EuroScore, %	22.3 \pm 13.7	23.5 \pm 14.8	20.2 \pm 11.4	0.0113
STS score, %	6.8 \pm 4.4	6.9 \pm 4.8	6.6 \pm 3.5	0.4705
<i>Antithrombotic therapy at baseline</i>				
Aspirin, n (%)	295 (60.6)	188 (61.2)	107 (59.4)	0.6959
Clopidogrel, n (%)	96 (19.7)	59 (19.2)	37 (20.6)	0.7203
Oral anticoagulation, n (%)	129 (26.5)	78 (25.4)	51 (28.3)	0.4800

449 **Table 2:** Echocardiographic imaging characteristics.450 Pre- and post TAVI assessments via transthoracic echocardiography. Depicted are means \pm SD with

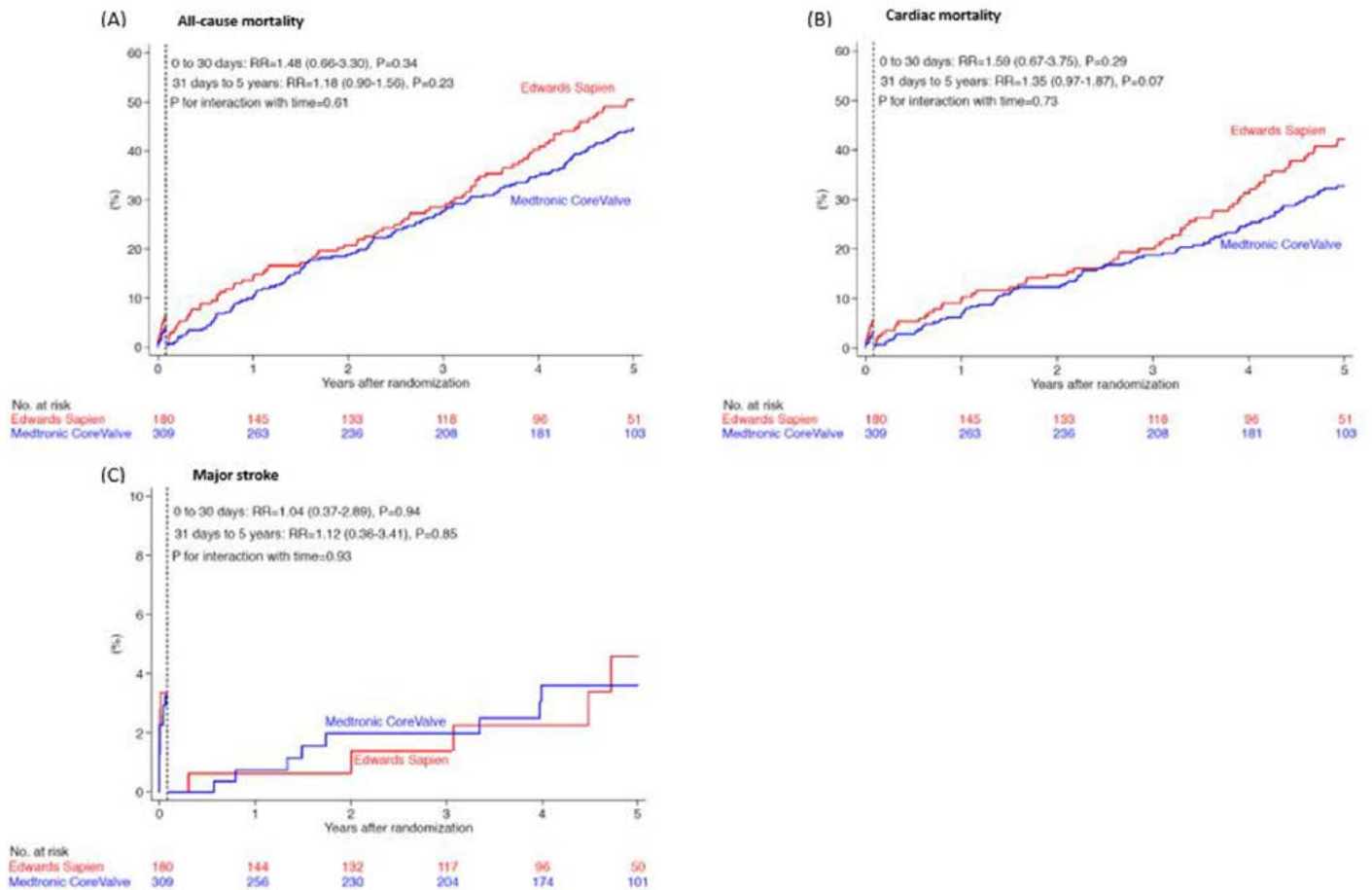
451 p-values from t-tests or counts (%) with p-values from Fisher's tests (two categories) or chi-square

452 tests (more than two categories). LV = Left ventricle; TAVI= Transcatheter aortic valve implantation.

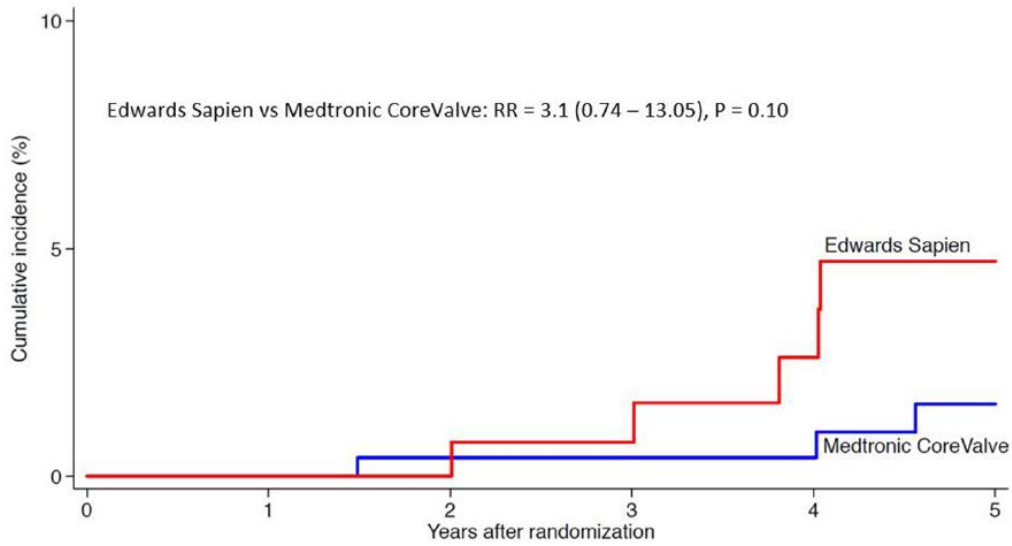
	Overall N = 489	Medtronic CoreValve N = 309	Edwards Sapien N = 180	P value
<i>Pre-TAVI assessment</i>				
<i>Aortic stenosis severity</i>				
Aortic valve area, cm ²	0.70 \pm 0.23	0.69 \pm 0.23	0.72 \pm 0.22	0.0901
Indexed aortic valve area, cm ² /m ²	0.39 \pm 0.12	0.38 \pm 0.13	0.40 \pm 0.12	0.1289
Mean gradient, mm Hg	43.70 \pm 17.60	44.16 \pm 18.42	42.99 \pm 16.28	0.5155
Peak gradient, mm Hg	71.39 \pm 26.98	72.02 \pm 27.89	70.26 \pm 25.35	0.5958
<i>Left ventricular assessment</i>				
LV ejection fraction, %	53.52 \pm 14.34	51.76 \pm 15.11	56.61 \pm 12.35	0.0004
LV ventricular mass index (g/m ²)	152.14 \pm 42.03	153.50 \pm 47.00	151.13 \pm 38.47	0.8112
LV enddiastolic diameter (LVEDD, mm)	48.19 \pm 9.46	48.03 \pm 10.63	48.33 \pm 8.44	0.8829
LV endsystolic diameter (LVESD, mm)	32.80 \pm 10.60	33.42 \pm 11.65	32.21 \pm 9.63	0.6281
<i>Right ventricular assessment</i>				
Decreased right ventricular function	26 (21.5)	15 (25.4)	11 (17.7)	0.3038
Severe pulmonary hypertension	42 (28.2)	28 (29.5)	14 (25.9)	0.6436
<i>Associated valvular abnormality</i>				
Aortic regurgitation moderate or severe, n (%)	43 (9.9)	32 (11.3)	11 (7.2)	0.1653
Mitral regurgitation moderate or severe, n (%)	112 (24.7)	75 (26.0)	37 (22.6)	0.4214
Tricuspid regurgitation moderate or severe, n (%)	27 (12.1)	15 (13.8)	12 (10.4)	0.4447
<i>Post-TAVI assessment</i>				
<i>Aortic stenosis severity</i>				
Aortic valve area, cm ²	1.84 \pm 0.56	1.81 \pm 0.49	1.88 \pm 0.62	0.2658
Indexed aortic valve area, cm ² /m ²	1.02 \pm 0.32	1.01 \pm 0.29	1.03 \pm 0.34	0.5163
Mean gradient, mm Hg	9.43 \pm 4.70	8.85 \pm 4.75	10.25 \pm 4.52	0.0033
Peak gradient, mm Hg	17.18 \pm 9.18	16.23 \pm 9.40	18.59 \pm 8.69	0.0277
<i>Left ventricular assessment</i>				
LV ejection fraction, %	56.50 \pm 11.87	55.55 \pm 12.43	57.83 \pm 10.94	0.0543
LV ventricular mass index (g/m ²)	153.55 \pm 87.81	152.70 \pm 45.45	154.43 \pm 116.71	0.8926
LV enddiastolic diameter (LVEDD, mm)	46.90 \pm 8.45	47.20 \pm 9.10	46.57 \pm 7.69	0.6079
LV endsystolic diameter (LVESD, mm)	30.82 \pm 9.10	31.52 \pm 10.14	29.95 \pm 7.58	0.2675
<i>Right ventricular assessment</i>				
Decreased right ventricular function	70 (21.7)	70 (42.7)	36 (22.6)	0.6771
Severe pulmonary hypertension	75 (33.8)	46 (40.4)	29 (26.9)	0.0335
<i>Associated valvular abnormality</i>				
Aortic regurgitation moderate or severe, n (%)	61 (15.0)	46 (19.0)	15 (9.0)	0.0055
Mitral regurgitation moderate or severe, n (%)	51 (16.4)	31 (19.7)	20 (13.0)	0.1075
Tricuspid regurgitation moderate or severe, n (%)	0.18 \pm 0.39	0.23 \pm 0.42	0.14 \pm 0.35	0.0675

455 **FIGURES**

456 **Figure 1:** (A) Cumulative incidence including landmark analysis of all-cause mortality according to
 457 transcatheter aortic valve type up to 5 years of follow-up. (B) Cumulative incidence including
 458 landmark analysis of cardiac mortality according to transcatheter aortic valve type up to 5 years of
 459 follow-up. (C) Cumulative incidence including landmark analysis of major stroke according to
 460 transcatheter aortic valve type up to 5 years of follow-up.
 461 Medtronic CoreValve (blue line), Edwards Sapien (red line). (For interpretation of the references to
 462 colour in this figure legend, the reader is referred to the web version of this article.)



464 **Figure 2:** Cumulative incidence of structural valve deterioration up to 5 years of follow-up.
465 Medtronic CoreValve (blue line), Edwards Sapien (red line). (For interpretation of the references to
466 colour in this figure legend, the reader is referred to the web version of this article.)



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