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Permanent Pacemaker Implantation After Transcatheter Aortic Valve Implantation

Impact on Late Clinical Outcomes and Left Ventricular Function

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Background—Very few data exist on the clinical impact of permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation. The objective of this study was to assess the impact of PPI after transcatheter aortic valve implantation on late outcomes in a large cohort of patients.

Methods and Results—A total of 1556 consecutive patients without prior PPI undergoing transcatheter aortic valve implantation were included. Of them, 239 patients (15.4%) required a PPI within the first 30 days after transcatheter aortic valve implantation. At a mean follow-up of 22±17 months, no association was observed between the need for 30-day PPI and all-cause mortality (hazard ratio, 0.98; 95% confidence interval, 0.74–1.30; *P*=0.871), cardiovascular mortality (hazard ratio, 0.81; 95% confidence interval, 0.56–1.17; *P*=0.270), and all-cause mortality or rehospitalization for heart failure (hazard ratio, 1.00; 95% confidence interval, 0.77–1.30; *P*=0.980). A lower rate of unexpected (sudden or unknown) death was observed in patients with PPI (hazard ratio, 0.31; 95% confidence interval, 0.11–0.85; *P*=0.023). Patients with new PPI showed a poorer evolution of left ventricular ejection fraction over time (*P*=0.017), and new PPI was an independent predictor of left ventricular ejection fraction decrease at the 6- to 12-month follow-up (estimated coefficient, −2.26; 95% confidence interval, −4.07 to −0.44; *P*=0.013; R^2=0.121).

Conclusions—The need for PPI was a frequent complication of transcatheter aortic valve implantation, but it was not associated with any increase in overall or cardiovascular death or rehospitalization for heart failure after a mean follow-up of ≈2 years. Indeed, 30-day PPI was a protective factor for the occurrence of unexpected (sudden or unknown) death. However, new PPI did have a negative effect on left ventricular function over time. **(*Circulation*. 2014;129:1233-1243.)**

Key Words: aortic stenosis ■ aortic valve ■ death, sudden, cardiac ■ heart valves ■ pacemaker, artificial

Transcatheter aortic valve implantation (TAVI) has become the treatment of choice for patients with aortic stenosis who are considered to be nonoperable and a good alternative for those at high surgical risk.[1] However, the occurrence of some periprocedural complications remains a concern. The need for permanent pacemaker implantation (PPI) after the procedure is one of the most frequent complications associated with TAVI, with an overall incidence of ≈15% (≈25% and 7% after TAVI with self-expandable valves [SEVs] and balloon-expandable valves [BEVs], respectively).[1]

Clinical Perspective on p 1243

Strong evidence supports the potential negative impact of right ventricular apical pacing, which has been associated with an increased rate of the combined end point of mortality and rehospitalization for heart failure in patients with left ventricular dysfunction,[2–4] ventricular tachyarrhythmias,[5,6] and pacing-induced cardiomyopathy in patients without overt structural heart disease.[7] However, evidence for the clinical impact of PPI after TAVI remains scarce and based on small

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studies with limited (≤1 year) follow-up.[8–11] Although these studies did not find any impact of PPI on mortality, concerns that they may have been underpowered as a result of inadequate sample size have been raised.[12] In addition, no studies to date have evaluated the impact of PPI on rehospitalizations resulting from heart failure, left ventricular function changes, and sudden death. Finally, the vast majority of patients included in studies evaluating the impact of PPI after TAVI had received a SEV,[8–11] and very few data exist on patients who received a BEV. Therefore, the aims of this study were to assess in a large cohort of patients undergoing TAVI with BEV and SEV the impact of new PPI on late outcomes (including mortality and rehospitalization for heart failure) and left ventricular function and functional status changes after the intervention.

Methods

Study Population

A total of 1811 consecutive patients who underwent TAVI with either a BEV or an SEV in 8 centers between January 2005 and February 2013 were screened. Of these, 233 patients were excluded because of preexisting pacemaker implantation and 22 patients because of an unsuccessful procedure without valve implantation. The final study population consisted of 1556 patients (BEV, 858 patients; SEV, 698 patients).

Patients were considered candidates for TAVI if they were at high or prohibitive predicted perioperative risk as evaluated by a heart team composed of cardiac surgeons and interventional cardiologists at each center. TAVI procedures were performed as previously described.[1] The study was conducted in accordance with the institutional ethics committee of each participating center, and all patients provided signed informed consent for the procedures. Data were collected prospectively in each center. Procedural complications for the purpose of this study were defined according to Valve Academic Research Consortium-2 criteria.[13]

Indications for PPI

In agreement with the American College of Cardiology/American Heart Association/Heart Rhythm Society recommendations, PPI was indicated if third-degree or advanced second-degree atrioventricular block (AVB) at any anatomic level occurred and was not expected to resolve or in the presence of sinus node dysfunction and documented symptomatic bradycardia.[14] The indication of PPI in the presence of left bundle-branch block (LBBB) with PR prolongation (>200 milliseconds) not expected to normalize was at the discretion of the physician. The selection of a single-chamber or dual-chamber pacemaker was left to the implanter.

Follow-Up

Follow-up was carried out through clinical outpatient visits or phone contacts at 30 days, 6 months, and 12 months and yearly afterward. No patient was lost during the follow-up period. Echocardiographic examinations at baseline were available in all patients, in 1279 patients at hospital discharge, and in 902 patients at the 6- to 12-month follow-up (83% of patients alive at that point of time, 89% and 78% in the BEV and SEV groups, respectively; P=0.002). Left ventricular ejection fraction (LVEF) was calculated from the biplane modified Simpson method, and left ventricular dysfunction was defined as LVEF ≤50%.[15]

End Points and Definitions

The primary end point was defined as a composite of all-cause mortality and hospitalization resulting from heart failure at last follow-up. Secondary end points were all cause-mortality, cardiovascular mortality, sudden cardiac death, composite of sudden cardiac death and death resulting from an unknown cause, rehospitalization for heart failure, functional class changes, and LVEF changes. Several sources of information were used to investigate end points: outpatient clinical visits; phone contacts with patients, families, or physicians; and review of medical records to determine causes of death when necessary. All events were defined according to the Valve Academic Research Consortium-2 criteria.[13] Sudden cardiac death was defined as any unexpected death caused by cardiac disease occurring within 1 hour after of the onset of symptoms.[16] Death was classified as resulting from an unknown cause if the unexpected death failed to meet the confirmation criteria of sudden cardiac death and the cause of death could not be determined after contact with the responsible physician or the patient's family. Death resulting from an unknown cause was classified as cardiovascular death.[13] Only readmissions with a primary diagnosis of heart failure at hospital discharge were considered as rehospitalizations resulting from heart failure. For patients with several hospitalizations resulting from heart failure, only the first episode was included in the analysis.

Statistical Analysis

Qualitative variables are expressed as percentages and quantitative variables as mean±SD or median (interquartile range) according to variable distribution and were compared by use of the χ^2 or Fisher exact test and 2-sided t test or Wilcoxon signed-rank test as appropriate. The primary composite end point and secondary end points were compared between the PPI and no PPI and the BEV and SEV groups with the use of proportional hazard models (cumulative outcomes). All multivariate models were adjusted for baseline differences in the univariate analysis including variables with a value of P≤0.10. A landmark analysis with a landmark cutoff at 30 days was used to further investigate the impact of PPI on study outcomes. Thirty-day outcomes were assessed with a logistic regression model. Survival rates were summarized by use of Kaplan-Meier estimates, and the log-rank test was used for comparison between groups. A linear general model for repeated measures with interaction was used to compare the changes in LVEF at different time points between the PPI and no PPI groups. Further comparisons were performed with the Tukey technique. Predictors of LVEF changes over time were analyzed by use of a univariate and a multivariate linear regression model. The results were considered significant at values of P<0.05. Analyses were conducted with the statistical package SAS version 9.2 (SAS Institute Inc, Cary, NC).

Results

A total of 239 patients (15.4%) received a PPI within 30 days after TAVI (25.5% versus 7.1% in the SEV and BEV groups, respectively; P<0.001). Baseline and procedural characteristics of the study population according to the need for PPI after TAVI are shown in Table 1. The timing, clinical indications, and pacemaker models implanted overall and according to the type of transcatheter valve (SEV or BEV) are shown in Table 2. The 30-day outcomes according to study group (PPI versus no PPI) are shown in Table 3. There were no differences between groups in 30-day mortality or major complications after TAVI (P>0.20 for all).

A resting ECG was performed at the 6- to 12-month follow-up in 133 patients with 30-day PPI (62% of patients at risk, 61.7% and 62.5% in the SEV and BEV groups, respectively; P=0.707) with the aim of assessing the presence of pacemaker activity. Pace rhythm was observed in 89 of these patients (66.9%), and it was more frequent in patients who had received an SEV (72.8% versus 46.7% in patients with a BEV; P=0.007).

30-Day PPI and Late Outcomes

Cumulative late clinical events grouped according to the need for PPI within 30 days after TAVI are shown in Table 4. After

Table 1. Baseline and Procedural Findings According to the Need for 30-Day New Pacemaker Implantation After Transcatheter Aortic Valve Implantation (n=1556)

	No Pacemaker (n=1317)	30-d Pacemaker Implantation (n=239)	*P* Value
Clinical characteristics			
Age, y	80±8	81±5	0.074
Male, n (%)	629 (47.8)	111 (46.4)	0.708
Body mass index, kg/m^2	26 (23–29)	27 (24–30)	0.134
NYHA class ≥3, n (%)	1014 (77.0)	175 (73.2)	0.206
Hypertension, n (%)	1067 (81.0)	199 (83.3)	0.354
Diabetes mellitus, n (%)	418 (31.7)	67 (28.0)	0.282
COPD, n (%)	409 (31.1)	73 (30.5)	0.864
eGFR <60 mL/min, n (%)	741 (56.3)	141 (59.0)	0.433
Paroxysmal/chronic atrial fibrillation, n (%)	372 (28.2)	62 (25.9)	0.499
Coronary artery disease, n (%)	765 (58.1)	112 (46.9)	0.001
Porcelain aorta, n (%)	192 (14.6)	29 (12.1)	0.246
Logistic EuroSCORE, %	20.5±14.0	20.3±14.0	0.776
STS-PROM score, %	7.7±5.4	7.2±4.9	0.237
Echocardiography			
LVEF, %	55±14	56±13	0.283
LVEF ≤50%, n (%)	397 (30.2)	70 (29.3)	0.785
Mean gradient, mm Hg	47±16	49±16	0.085
Aortic valve area, cm^2	0.60 (0.50–0.80)	0.64 (0.50–0.79)	0.178
Procedural findings, n (%)			
Procedural success* n (%)	1128 (85.6)	198 (82.8)	0.261
Approach			
Transapical/transaortic	362 (27.5)	32 (13.4)	<0.001
Transfemoral/subclavian	955 (72.5)	207 (86.6)	
Prosthesis type			
Self-expandable	520 (39.5)	178 (74.5)	<0.001
Balloon-expandable	797 (60.5)	61 (25.5)	
Prosthesis size			
20–23 mm	368 (27.9)	32 (13.4)	<0.001
26 mm	678 (51.5)	118 (49.4)	
29–31 mm	271 (20.6)	89 (37.2)	
Need for a second valve	32 (2.4)	15 (6.3)	0.001
Moderate or greater AR	174 (13.2)	40 (16.7)	0.187

Values are expressed as mean (±SD) or median (25th–75th percentile) when appropriate. AR indicates aortic regurgitation; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and STS-PROM, Society of Thoracic Surgeons predicted risk of mortality.

*Following Valve Academic Research Consortium-2 criteria.

a mean follow-up of 22±17 months, a total of 525 patients (33.7%) either had died or required a rehospitalization for heart failure, with no differences between the PPI and no PPI groups (34.1% versus 31.8%; hazard ratio [HR], 1.00; 95% confidence interval [CI], 0.77–1.30; *P*=0.980). There were no differences between groups in the secondary end points of late overall and cardiovascular mortality or rehospitalization for heart failure (Table 4). There was, however, a lower rate of unexpected (sudden or unknown) death among patients who had a PPI within 30 days after TAVI (HR, 0.31; 95% CI, 0.11–0.85; *P*=0.023). This protective effect of 30-day PPI on unexpected death persisted after a landmark analysis with a cutoff at 30 days (Table 4).

Table 2. Timing, Type, and Indications for 30-Day Permanent Pacemaker Implantation Overall and According to Transcatheter Valve Type

	Overall (n=239)	Self-Expandable Valve (n=178)	Balloon-Expandable Valve (n=61)	*P* Value
Time after TAVI, d	3 (1–6)	2 (1–6)	3 (2–6)	0.188
PPI timing, n (%)				
≤24 h	86 (36.0)	71 (39.9)	15 (24.6)	0.025
24 h–7 d	128 (53.6)	93 (52.2)	35 (57.4)	
>7 d	25 (10.4)	14 (7.9)	11 (18.0)	
Indications, n (%)				
Complete or high-degree AVB	180 (75.3)	135 (75.8)	45 (73.8)	0.030
Sinoatrial node disease	17 (7.1)	14 (7.9)	3 (4.9)	
Symptomatic bradycardia	19 (7.9)	9 (5.1)	10 (16.4)	
LBBB+first-degree AVB	23 (9.6)	20 (11.2)	3 (4.9)	
Type of pacemaker, n (%)				
Single-chamber	96 (40.2)	78 (43.8)	18 (29.5)	0.051
Dual-chamber	143 (59.8)	100 (56.2)	43 (70.5)	

Values are expressed as median (25th–75th percentile) when appropriate. AVB indicates atrioventricular block; LBBB, left bundle-branch block; PPI, permanent pacemaker; and TAVI, transcatheter aortic valve implantation.

The Kaplan-Meier curves at the 3-year follow-up according to the study group (PPI versus no PPI) are shown in Figure 1.

The individual characteristics of the 76 patients who suffered sudden or unknown death are detailed in Table I in the online-only Data Supplement. Clinical, echocardiographic, and ECG univariate and multivariate predictors of unexpected (sudden and unknown) death and sudden cardiac death in the study population are shown in Table 5. New-onset persistent LBBB (NOP-LBBB) was observed in 269 patients

Table 3. Thirty-Day Outcomes According to the Need for Permanent Pacemaker Implantation Within the First 30 Days After the Procedure

30-d Outcomes	No PPI (n=1317), n (%)	30-d PPI (n=239), n (%)	OR	*P* value
Death	92 (7.0)	16 (6.7)	0.96 (0.55–1.66)	0.892
Stroke	38 (2.9)	10 (4.2)	1.49 (0.73–3.03)	0.274
Myocardial infarction	25 (1.9)	3 (1.3)	0.59 (0.14–2.60)	0.485
Major vascular complications	95 (7.2)	22 (9.2)	1.31 (0.80–2.12)	0.282
Major or life-threatening bleeding	206 (15.6)	33 (13.8)	0.85 (0.57–1.27)	0.434

OR indicates odds ratio; and PPI, permanent pacemaker.

Table 4. Risk of Mortality and Heart Failure According to the Need for 30-Day Permanent Pacemaker Implantation

Outcome	No PPI, n (%)	30-d PPI, n (%)	Univariate HR (95% CI)	*P* Value	Multivariate HR* (95% CI)	*P* Value
All patients						
Patients	1317	239				
Primary outcome						
Death or rehospitalization for heart failure	449 (34.1)	76 (31.8)	0.81 (0.64–1.04)	0.097	1.00 (0.77–1.30)	0.980
Secondary outcomes						
Death resulting from any cause	364 (27.6)	62 (25.9)	0.83 (0.63–1.09)	0.178	0.98 (0.74–1.30)	0.871
Death resulting from cardiovascular causes	254 (19.3)	37 (15.5)	0.72 (0.51–1.02)	0.063	0.81 (0.56–1.17)	0.270
Sudden cardiac death	26 (2.0)	1 (0.4)	0.19 (0.03–1.39)	0.101	0.15 (0.02–1.08)	0.059
Sudden cardiac death/unknown death	72 (5.5)	4 (1.7)	0.27 (0.10–0.75)	0.011	0.31 (0.11–0.85)	0.023
Rehospitalization for heart failure	134 (10.2)	24 (10.0)	0.86 (0.55–1.32)	0.482	1.16 (0.73–1.85)	0.529
>30 d to maximum						
Patients	1225	223				
Primary outcome						
Death or rehospitalization for heart failure	357 (29.1)	60 (26.9)	0.78 (0.60–1.03)	0.082	1.05 (0.78–1.40)	0.762
Secondary outcomes						
Death from any cause	272 (22.2)	46 (20.6)	0.80 (0.58–1.09)	0.160	1.02 (0.74–1.42)	0.895
Death from cardiovascular causes	162 (13.2)	21 (9.4)	0.61 (0.39–0.96)	0.034	0.79 (0.49–1.27)	0.331
Sudden cardiac death	17 (1.4)	1 (0.4)	0.27 (0.04–2.07)	0.209	0.19 (0.03–1.47)	0.112
Sudden cardiac death/unknown death	63 (5.1)	4 (1.8)	0.31 (0.11–0.85)	0.022	0.36 (0.13–1.00)	0.047
Rehospitalization for heart failure	132 (10.8)	24 (10.8)	0.87 (0.56–1.34)	0.521	1.17 (0.74–1.87)	0.500

CI indicates confidence interval; HR, hazard ratio; and PPI, permanent pacemaker implantation.
*Adjusted for baseline differences between groups.

(20.4% of patients without 30-day PPI, 39.5% and 10.2% in the SEV and BEV groups, respectively; $P<0.001$). The mean QRS at discharge in patients with NOP-LBB was 145±19 milliseconds. Preexisting paroxysmal/chronic atrial fibrillation (HR, 1.76; 95% CI, 1.09–2.86; $P=0.021$) and lack of 30-day PPI (HR, 3.22; 95% CI, 1.16–9.09; $P=0.024$) were the independent predictors of unexpected death. The occurrence of NOP-LBBB (HR, 2.77; 95% CI, 1.09–7.07; $P=0.033$) and a lower LVEF at baseline (5.25 for each 5% decrease; 95% CI, 5.15–5.45; $P<0.001$) were the independent predictors of sudden cardiac death. No association was observed between NOP-LBBB and overall mortality (HR, 1.30; 95% CI, 0.86–1.89; $P=0.226$) or cardiovascular mortality (HR, 1.31; 95% CI, 0.74–2.34; $P=0.357$).

Subgroups Analyses (Low LVEF, Transcatheter Valve Type)

Late outcomes according to the need for PPI after TAVI in patients with low (≤50%) and normal (>50%) LVEF at baseline are shown in Table 6. There were no differences in all-cause mortality and rehospitalization for heart failure, all-cause mortality, cardiovascular mortality, and sudden cardiac death between patients with and without LVEF ≤50% ($P>0.10$ for all). However, a higher rate of unexpected (sudden or unknown) death was observed in patients with no PPI and normal left ventricular function ($P=0.043$). In addition, no negative impact of PPI was encountered in patients with at least moderate left ventricular dysfunction (LVEF ≤40%; $P>0.10$ for all), with a protective effect on unexpected death in patients with normal or mildly depressed left ventricular function ($P=0.023$).

Baseline clinical characteristics and procedural findings and clinical outcomes during the follow-up period according to the type of valve implanted are given in Tables II and III in the online-only Data Supplement, respectively. Death or heart failure, death resulting from any cause and from cardiovascular causes, sudden cardiac death, sudden/unknown death, and hospitalizations for heart failure were similar in the SEV and BEV groups ($P>0.10$ for all).

The late outcomes according to the need for PPI after TAVI for the patients who had received a BEV or an SEV are shown in Table 7. There were no differences in any of the late outcomes between patients with and without PPI in each of the transcatheter valve type groups. In the SEV group, a trend toward a lower rate of sudden cardiac/unknown death was observed in patients with PPI (HR, 0.30; 95% CI, 0.09–1.02; $P=0.053$). In the BEV group, the risk of sudden cardiac/unknown death was similar in patients with and without PPI (HR, 0.28; 95% CI, 0.04–2.05; $P=0.212$). However, no significant interaction was found between the need of PPI and the type of valve implanted for unexpected death ($P=0.997$) and sudden cardiac death ($P=0.984$).

PPI, LVEF, and Functional Status

Changes in valve hemodynamics according to the need for PPI are shown in Figure I in the online-only Data Supplement. LVEF significantly increased in the overall population at 6- to 12-month follow-up (from 56±13%

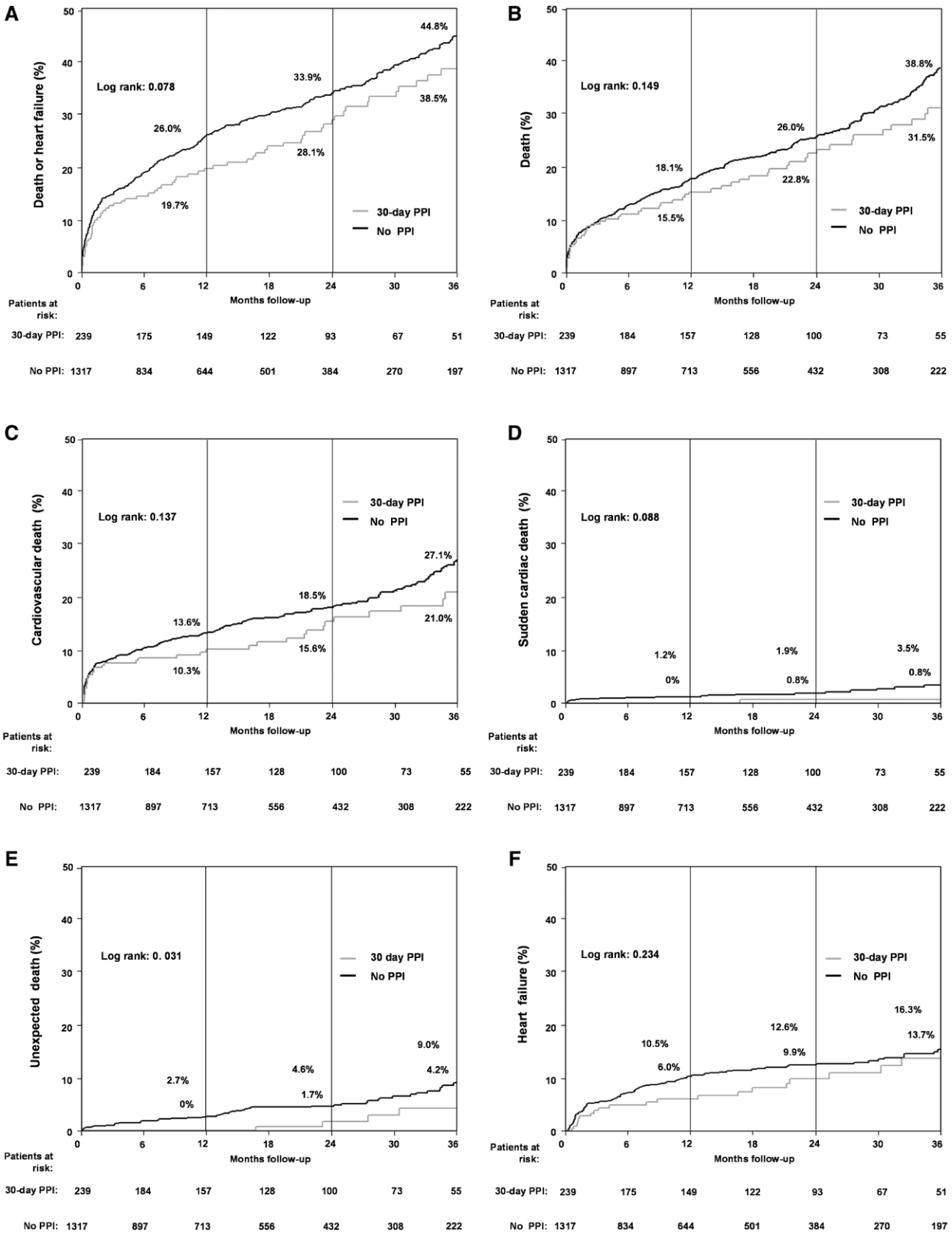

Figure 1. Kaplan-Meier curves at the 1-year follow-up for the combined end point of all-cause mortality and rehospitalization for heart failure (**A**), all-cause mortality (**B**), cardiovascular mortality (**C**), sudden cardiac death (**D**), sudden cardiac death or death resulting from an unknown cause (**E**), and rehospitalization for heart failure (**F**). PPI indicates permanent pacemaker implantation.

to 59±11%; $P<0.001$). LVEF changes over time according to the need for PPI are shown in Figure 2A. Whereas LVEF increased over time in patients with no PPI, LVEF decreased at follow-up in those patients who had PPI after TAVI ($P=0.017$ for comparison between groups), without differences between the BEV and SEV groups ($P=0.668$;

Table 5. Univariate and Multivariate Predictive Factors of Unexpected (Sudden/Unknown) Death and Sudden Death in the Study Population (n=1556)

	Unexpected (Sudden/Unknown) Death				Sudden Cardiac death			
	Univariate HR (95% CI)	*P* value	Multivariate HR (95% CI)	*P* Value	Univariate HR (95% CI)	*P* Value	Multivariate HR (95% CI)	*P* Value
Clinical and echocardiographic variables								
Age	1.02 (0.99–1.06)	0.260			0.97 (0.93–1.02)	0.292		
Male	1.09 (0.69–1.71)	0.717			1.34 (0.63–2.86)	0.446		
Hypertension	0.71 (0.42–1.18)	0.191			1.07 (0.41–2.82)	0.893		
Diabetes mellitus	0.85 (0.51–1.42)	0.542			1.87 (0.87–4.00)	0.107		
COPD	1.11 (0.67–1.82)	0.677			0.83 (0.35–1.97)	0.671		
eGFR <60 mL/min	1.11 (0.70–1.76)	0.646			1.31 (0.60–2.86)	0.502		
Paroxysmal/chronic atrial fibrillation	1.71 (1.06–2.74)	0.027	1.76 (1.09–2.86)	0.021	1.02 (0.43–2.41)	0.972		
Coronary artery disease	1.88 (1.14–3.09)	0.013	1.61 (0.95–2.74)	0.079	1.19 (0.55–2.58)	0.660		
LVEF*	5.10 (5.05–5.15)	0.027	5.05 (5.00–5.25)	0.060	5.20 (5.10–5.30)	0.001	5.25 (5.15–5.45)	<0.001
STS-PROM score	1.04 (1.00–1.08)	0.061	1.02 (0.98–1.07)	0.330	0.96 (0.87–1.05)	0.353		
Procedural findings								
Balloon-expandable valve	1.51 (0.95–2.41)	0.083	1.04 (0.62–1.73)	0.881	0.34 (0.14–0.81)	0.014	0.47 (0.17–1.33)	0.154
Moderate or greater AR	1.43 (0.78–2.61)	0.248			2.09 (0.83–5.26)	0.119		
Lack of 30-d PPI	3.70 (1.33–10.00)	0.011	3.22 (1.16–9.09)	0.024	5.26 (0.71–3.84)	0.101		
NOP-LBBB	1.00 (0.57–1.74)	0.994			2.51 (1.13–5.60)	0.024	2.77 (1.09–7.07)	0.033

AR indicates aortic regurgitation; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; NOP-LBBB, new-onset persistent left bundle-branch block; PPI, permanent pacemaker implantation; and STS-PROM, Society of Thoracic Surgeons predicted risk of mortality.

*For each decrease of 5% in LVEF.

Figure II in the online-only Data Supplement). The poorer evolution of LVEF in patients who needed PPI was observed in those patients who received a dual-chamber (versus single-chamber) PPI (P=0.043; P=0.023 after adjustment for the presence of atrial fibrillation; Figure 2B). The variables associated with LVEF changes over time are given

Table 6. Risk of Mortality and Hospitalization for Heart Failure According to the Need for 30-Day Permanent Pacemaker Implantation in Patients with Normal and Low Left Ventricular Ejection Fraction

Outcome	No PPI, n (%)	30-d PPI, n (%)	Univariate HR (95% CI)	*P* Value
LVEF >50%				
No. of Patients	920	169		
Primary outcome				
Death or rehospitalization for heart failure	296 (32.2)	52 (30.8)	0.83 (0.62–1.12)	0.218
Secondary outcomes				
Death resulting from any cause	235 (25.6)	43 (25.4)	0.87 (0.63–1.20)	0.385
Death resulting from cardiovascular causes	158 (17.2)	22 (13.0)	0.67 (0.43–1.10)	0.081
Sudden cardiac death	13 (1.4)	1 (0.6)	0.36 (0.05–2.75)	0.324
Sudden cardiac death/unknown death	46 (5.0)	3 (1.8)	0.30 (0.09–0.98)	0.043
Rehospitalization for heart failure	87 (9.5)	16 (9.5)	0.87 (0.51–1.48)	0.603
LVEF ≤50%				
No. of Patients	397	70		
Primary outcome				
Death or rehospitalization for heart failure	152 (38.3)	24 (34.3)	0.78 (0.51–1.20)	0.259
Secondary outcomes				
Death resulting from any cause	128 (32.2)	19 (27.1)	0.77 (0.47–1.24)	0.277
Death resulting from cardiovascular causes	95 (23.9)	15 (21.4)	0.81 (0.47–1.40)	0.447
Sudden cardiac death	13 (3.3)	0	…	…
Sudden cardiac death/unknown death	26 (6.5)	1 (1.4)	0.20 (0.03–1.47)	0.114
Rehospitalization for heart failure	47 (11.8)	8 (11.4)	0.85 (0.40–1.79)	0.663

CI indicates confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction; and PPI, permanent pacemaker implantation.

Table 7. Risk of Mortality and Rehospitalization for Heart Failure After TAVI With Balloon-Expandable and Self-Expandable Valves According to the Need for 30-Day Permanent Pacemaker Implantation

Outcome	No PPI, n (%)	30-d PPI, n (%)	Univariate HR (95% CI)	*P* Value
Balloon-expandable valve				
Patients	797	61		
Primary outcome				
Death or hospitalization for heart failure	313 (39.3)	26 (42.6)	1.11 (0.75–1.66)	0.600
Secondary outcomes				
Death resulting from any cause	251 (31.5)	22 (36.1)	1.08 (0.70–1.67)	0.737
Death resulting from cardiovascular causes	174 (21.8)	13 (21.3)	0.93 (0.53–1.64)	0.803
Sudden cardiac death	7 (0.9)	0	…	…
Sudden cardiac death/unknown death	45 (5.6)	1 (1.6)	0.28 (0.04–2.05)	0.212
Hospitalization for heart failure	102 (12.8)	7 (11.5)	0.92 (0.43–2.00)	0.840
Self-expandable valve				
Patients	520	178		
Primary outcome				
Death or hospitalization for heart failure	136 (26.2)	50 (28.1)	0.99 (0.72–1.37)	0.965
Secondary outcomes				
Death resulting from any cause	113 (21.7)	40 (22.5)	0.97 (0.68–1.39)	0.859
Death resulting from cardiovascular causes	80 (15.4)	24 (13.5)	0.82 (0.52–1.29)	0.386
Sudden cardiac death	19 (3.7)	1 (0.6)	0.15 (0.2–1.09)	0.060
Sudden cardiac death/unknown death	26 (5.0)	3 (1.7)	0.30 (0.09–1.02)	0.053
Hospitalization for heart failure	32 (6.2)	17 (9.6)	1.41 (0.78–2.54)	0.252

CI indicates confidence interval; HR, hazard ratio; and PPI, permanent pacemaker implantation.

in Table 8. LVEF at baseline and the need for PPI within 30 days were the only independent predictors of an LVEF decrease over time (estimated coefficient, −3.44; 95% CI, −4.11 to −2.77; $P<0.001$; and −2.26; 95% CI, −4.07 to −0.44; $P=0.013$, $R^2=0.121$, respectively).

Changes in New York Heart Association class over time are shown in Figure 3. A marked improvement in New York Heart Association class was observed in patients with and without 30-day PPI ($P<0.001$ for both groups) without differences in New York Heart Association class changes between the PPI and no PPI groups ($P=0.672$).

Discussion

Injury to the conduction system is one of the more frequent complications of TAVI.[17] Although there is wide variability in the incidence of pacing requirements across studies,[17] an analysis of the literature showed that 1 of 7 patients (<10% and up to ≈25% when using BEV and SEV, respectively) require a PPI periprocedurally,[18] which is consistent with the results of the present study. Also in accordance with prior studies,[18] almost 90% of PPIs at 30 days were implanted within the first week after the procedure, with a much lower risk thereafter, and 75% were secondary to high-degree or complete AVB.

PPI After TAVI and Clinical Outcomes

There is strong evidence that the need for a paced rhythm increases the risk of late mortality and heart failure.[2–4,19–21] In contrast to these results, we failed to find any deleterious effect of PPI on mortality or heart failure status in patients undergoing TAVI, even in patients with left ventricular dysfunction at baseline. However, these finding are consistent with prior studies in the cardiac surgery field,[22] as well as with some prior smaller TAVI series.[8–11]

Results from the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial, Mode Selection Trial (MOST), and Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) showed that the deleterious impact of pacing on heart failure or mortality depends on cumulative percent time of ventricular pacing. Specifically, a right ventricular pacing during ≥40% to 50% of the time was associated with increased risk of heart failure or mortality.[2,3,23] Several studies on TAVI have shown that new conduction disturbances after TAVI may resolve over time in ≈50% of patients,[24,25] especially with the use of BEV. Indeed, it has been shown that >50% of patients requiring periprocedural PPI are not pacing dependent at follow-up.[8,26,27] In the present study, more than one third of patients with PPI (>50% in patients who had received a BEV) did not exhibit pacing activity on the ECG performed at the 6- to 12-month follow-up. Because most PPIs were implanted as a result of a high degree of or complete AVB, this observation suggests that a significant proportion of AVBs have resolved over time. This is consistent with the situation observed after surgical aortic valve replacement,[28,29] and in fact, current surgical guidelines recommend the implantation of a permanent pacemaker in patients with postoperative AVB only if the conduction abnormality persists at least 7 days after cardiac surgery or is not expected to resolve.[14] Interestingly, Simms

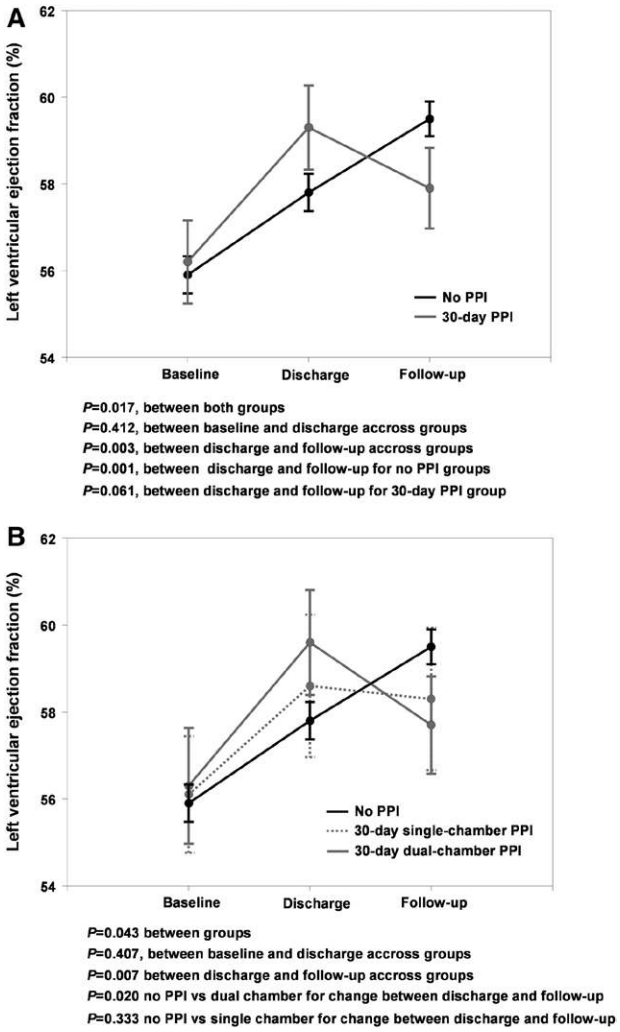

Figure 2. Left ventricular ejection fraction changes between baseline and the 6- to 12-month follow-up according to the need for 30-day permanent pacemaker implantation (**A**) and the type of pacemaker implanted (**B**). Of note, only the 855 patients with echocardiographic exams at the 3 points of time have been included. PPI indicates permanent pacemaker implantation.

et al[26] reported similar rates of late pacing dependency in patients undergoing SAVR and TAVI.

It has been suggested that the deleterious impact of PPI might differ between younger and older patients[30]; whereas a poorer survival has been observed in younger patients requiring PPI, some studies have shown that PPI has no impact on mortality in octogenarians and nonagenarians,[31] who in fact represent the vast majority of patients undergoing TAVI nowadays. In addition, the presence of left ventricular dysfunction has been reported as an independent predictor of a deleterious clinical impact of PPI,[32,33] whereas LVEF remained stable over time in most patients without structural heart disease receiving a PPI.[34] However, we did not find differences between patients with and without PPI when analyzing the data by subgroups according to left ventricular function. The severity of comorbidities and concomitant structural heart disease in patients undergoing TAVI led to a high rate of death and heart failure, and this might mitigate the potential negative effect of PPI in these patients. Furthermore, the immediate hemodynamic improvement attributable to aortic stenosis release resulted in significant improvement of left ventricular function in patients with preexisting ventricular dysfunction (36±8% to 50±13%; $P \leq 0.001$), as previously reported,[35] and this may have compensated for the potential deleterious effect of ventricular pacing in such patients.

The fact that PPI after TAVI resulted in a significant decrease in unexpected (sudden cardiac and unknown) death during the follow-up period merits further evaluation. Preexisting atrial fibrillation and the lack of 30-day PPI were predictors of unexpected death, and the occurrence of NOP-LBBB and a lower LVEF at baseline predicted the occurrence of sudden death. Left ventricular dysfunction and atrial fibrillation are well-recognized predictors of sudden death,[36,37] and NOP-LBBB after TAVI has been associated with an increased risk of late overall and cardiac mortality,[38] although this has not been confirmed in other studies.[24,25] In this study, the occurrence of NOP-LBBB was not associated with overall or cardiac death, but it increased by >2 times the risk of sudden death during the follow-up period. NOP-LBBB after TAVI has been associated with a higher risk of PPI and complete AVB,[24] which in turn, might lead to sudden death if a pacemaker is not implanted. However, the number of sudden death events in the present study was relatively low; therefore, these results need to be interpreted with caution. Future studies are needed to assess the impact of NOP-LBBB after TAVI on sudden death and to evaluate the potential predictors of increased death in these patients.

PPI and LVEF

After an initial improvement in LVEF immediately after valve obstruction relief, those patients who required PPI exhibited a significant decrease in LVEF over time compared with a continuous improvement in ventricular function in the rest of the study population. In fact, PPI was the only factor determining a deleterious effect on ventricular function after TAVI. Importantly, this negative effect of PPI was more pronounced in those patients receiving a dual-chamber (versus single-chamber) PPI. It is well known that pacing induces electric and mechanical dyssynchrony, which in turn, may lead to an adverse left ventricular remodeling and ultimately to the development of heart failure.[7,39,40] The occurrence and extent of pacing-induced heart disease have been associated with ventricular pacing burden and duration,[33] and dual-chamber pacemakers have been associated with a higher percentage of cumulative pacing, leading to a higher risk of rehospitalization for heart failure.[3,7] Interestingly, the implantation of a biventricular pacemaker in patients with preserved LVEF and symptomatic bradycardia and in those with AVB and left ventricular dysfunction has been shown to prevent the adverse effects of pacing on LVEF.[40,41] The potential usefulness of biventricular pacing in patients requiring PPI after a TAVI procedure should be evaluated in future studies.

The negative impact of PPI on LVEF did not translate into a deleterious effect on the heart failure status, which may be related to the mild degree of LVEF deterioration in most

Table 8. Univariate and Multivariate Predictors of Left Ventricular Ejection Fraction Changes Over Time (Hospital Discharge and 6- to 12-Month Follow-Up)

	Univariate		Multivariate	
	β Coefficient (95% CI)*	*P* Value	β Coefficient (95% CI)*	*P* Value
Clinical variables				
Age	0.23 (–0.51 to 0.97)	0.534		
Male	0.94 (–0.49 to 2.37)	0.197		
Hypertension	–0.50 (–2.27 to 1.28)	0.584		
Diabetes mellitus	0.11 (–1.42 to 1.63)	0.892		
eGFR <60 mL/min	–0.53 (–1.96 to 0.90)	0.470		
Paroxysmal/chronic atrial fibrillation	–1.54 (–3.13 to 0.50)	0.058	–1.32 (–2.82 to 0.18)	0.084
Coronary artery disease	1.57 (0.15 to 2.99)	0.030	0.29 (–1.09 to 1.66)	0.681
Echocardiography				
LVEF	–3.49 (–4.15 to –2.83)	<0.001	–3.44 (–4.11 to –2.77)	<0.001
Mean gradient	–0.50 (–1.21 to 0.21)	0.170		
Aortic valve area	0.04 (–0.64 to 0.72)	0.914		
Procedural variables				
Transapical/transaortic approach	1.76 (0.17 to 3.34)	0.030	0.67 (–0.87 to 2.21)	0.395
Moderate or greater AR	–1.21 (–3.29 to 0.87)	0.253		
30-d PPI	–2.63 (–4.52 to –0.74)	0.006	–2.26 (–4.07 to –0.44)	0.013

AR indicates aortic regurgitation; CI, confidence interval; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; and PPI, permanent pacemaker implantation.

*Per 1-SD increase or categorical change.

patients and the positive hemodynamic effects related to aortic stenosis release.

Limitations

Although data were collected prospectively in each center, data analyses were performed retrospectively, and there was no event adjudication committee for the study. Echocardiographic examinations at follow-up were not completed in ≈15% of patients, and this may have had an impact on the results concerning LVEF changes over time. Pacing dependency and right ventricular pacing burden were not systematically evaluated. Finally, a bias cannot be ruled out in a comparison of outcomes between the BEV and SEV groups because of the lack of randomization.

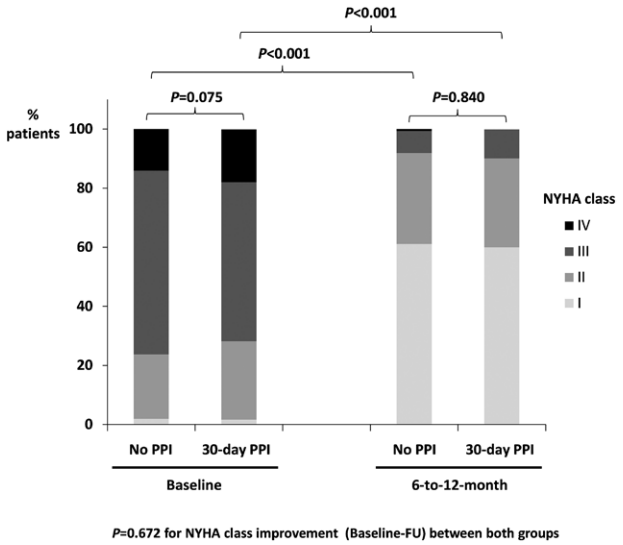

Figure 3. Changes in New York Heart Association (NYHA) class over time according to the need for permanent pacemaker implantation (PPI) within the first 30 days after transcatheter aortic valve implantation. FU indicates follow-up.

Conclusions

This study including a large cohort of patients undergoing TAVI with BEV and SEV showed that periprocedural PPI remains a frequent complication of TAVI. The need for PPI periprocedurally had no impact on overall and cardiovascular death or on functional status and heart failure decompensation requiring rehospitalization after a mean follow-up of ≈2 years. Indeed, 30-day PPI was a protective factor for the occurrence of unexpected (sudden cardiac or unknown) death during the follow-up period, which indirectly raises questions about the most appropriate management of new conduction disturbances that do not meet the criteria for PPI after TAVI. However, PPI, particularly with a dual-chamber pacemaker, was associated with a negative effect on left ventricular function. Further efforts will be important to determine the long-term impact of this decrease in LVEF and the potential benefits of resynchronization therapies in some patients.

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Disclosures

Dr Rodés-Cabau is a consultant for Edwards Lifesciences and St. Jude Medical. Drs Webb and Dumont are consultants for Edwards Lifesciences. Dr Tamburino is a consultant for Edwards, Medtronic, CeloNova, and Abbott. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

The need for permanent pacemaker implantation (PPI) is a frequent complication after transcatheter aortic valve implantation. However, evidence of the clinical impact of PPI after transcatheter aortic valve implantation remains scarce. This study assessed the impact of new PPI after transcatheter aortic valve implantation on late outcomes in a cohort of 1556 patients undergoing balloon-expandable and self-expandable valves. The incidence of 30-day PPI was 15.4%, mostly as a result of complete atrioventricular block. Thirty-day PPI was not associated with all-cause mortality, cardiovascular mortality, and all-cause mortality or rehospitalization for heart failure ($P>0.20$). Moreover, 30-day PPI was a protective factor for the occurrence of unexpected (sudden or unknown) death (hazard ratio, 0.31; $P=0.023$). The occurrence of new-onset persistent left bundle-branch block and a lower left ventricular ejection fraction at baseline were independent predictors of sudden cardiac death. The need for PPI had a negative effect on left ventricular function over time (estimated coefficient, −2.26; $P=0.013$). This study provides new and important insight into the impact of new conduction disturbances after transcatheter aortic valve implantation and urges further evaluation of the most appropriate management of new-onset left bundle-branch block that does not meet the criteria for PPI after transcatheter aortic valve implantation.

SUPPLEMENTAL MATERIAL

Supplemental Table 1. Individual Characteristics of the 76 Patients Having Unexpected Death (Sudden Cardiac Death or Death of Unknown Cause)

Age (years)	Gender	STS-PROM (%)	LVEF (%)	Prosthesis type	30-day PPI	QRS morphology at baseline	QRS morphology at discharge/death	Cause of death	Days after TAVI
63	female	2.4	65	BEV	no	RBBB + LAHB	RBBB + LAHB	unknown	963
65	female		72	SEV	no	IVCD	unknown	sudden cardiac death	1
67	male	7.5	50	BEV	no	normal	LBBB	unknown	1624
68	male	7.0	63	SEV	no	normal	LBBB	sudden cardiac death	93
69	female	3.5	55	SEV	no	LAHB	LAHB	sudden cardiac death	1158
69	female	2.2	20	SEV	no	normal	normal	sudden cardiac death	18
70	female	3.0	35	SEV	no	LBBB	LBBB	sudden cardiac death	406
71	female	2.5	30	SEV	no	normal	LBBB	sudden cardiac death	168
72	female	2.5	60	SEV	yes	LIBBB	LBBB	unknown	915
73	male	6.4	45	BEV	no	IVCD	IVCD	sudden cardiac death	25
73	female	6.5	58	SEV	no	normal	unknown	sudden cardiac death	1
74	male	5.6	60	BEV	no	normal	normal	unknown	1461
75	male	14.1	30	BEV	no	IVCD	IVCD	unknown	94
75	male	26.8	35	BEV	no	IVCD	IVCD	unknown	395
76	male	4.3	40	SEV	no	RBBB	RBBB	sudden cardiac death	3
76	male	3.5	56	SEV	no	normal	LBBB	unknown	1631
78	female	4.5	60	BEV	no	normal	normal	unknown	300
78	female	7.9	50	BEV	no	normal	LBBB	unknown	440
79	male	12.2	45	BEV	no	IVCD	IVCD	sudden cardiac death	3
79	male	6.3	20	SEV	no	normal	LBBB	sudden cardiac death	35
79	male	14.7	65	SEV	no	RBBB	RBBB	unknown	168
79	female	4.2	55	SEV	no	normal	normal	unknown	726
79	female	22.0	45	BEV	no	normal	normal	unknown	356
79	female	3.7	54	BEV	no	normal	normal	unknown	1105
79	female	11.9	25	BEV	no	LBBB	LBBB	unknown	476
80	male	3.8	65	SEV	no	normal	LAHB	sudden cardiac death	819
80	male	4.6	55	SEV	no	IVCD	LBBB	sudden cardiac death	746
80	female	15.1	54	SEV	yes	normal	paced	unknown	825
80	female	5.1	58	SEV	no	normal	LBBB	unknown	1071
81	female	2.8	37	SEV	no	normal	LBBB	sudden cardiac death	92
81	female	6.5	10	SEV	no	LBBB	LBBB	sudden cardiac death	1

81	female	2.7	60	BEV	no	normal	normal	unknown	1422
81	male	5.3	65	BEV	no	normal	normal	unknown	219
81	male	4.7	50	BEV	no	RBBB	RBBB + LAHB	unknown	149
81	male	5.3	25	BEV	no	RBBB	RBBB	unknown	1039
82	male	11.2	20	BEV	no	RBBB + LAHB	RBBB + LAHB	sudden cardiac death	3
82	male	2.1	50	SEV	no	normal	LBBB	sudden cardiac death	895
82	female	4.3	60	SEV	yes	IVCD	paced	sudden cardiac death	501
82	male	3.7	60	SEV	no	normal	LBBB	sudden cardiac death	1031
82	male	6.5	55	BEV	no	normal	normal	unknown	853
82	male	6.8	30	BEV	no	IVCD	IVCD	unknown	169
82	male	5.3	65	BEV	no	normal	normal	unknown	219
83	female	2.6	58	SEV	no	normal	LBBB	sudden cardiac death	9
83	female	22.4	70	BEV	no	normal	normal	unknown	1782
83	female	8.3	60	BEV	no	normal	normal	unknown	1273
83	female	4.7	59	SEV	no	normal	normal	unknown	1034
84	male	10.2	40	BEV	no	IVCD	IVCD	sudden cardiac death	387
84	male	15.1	25	BEV	yes	RBBB	paced	unknown	692
85	male	7.1	60	BEV	no	IVCD	LBBB	sudden cardiac death	1610
85	female	8.1	62	SEV	no	normal	LAHB	sudden cardiac death	1765
85	male	6.2	60	SEV	no	IVCD	IVCD	unknown	2158
85	female	16.8	25	BEV	no	normal	LAHB	unknown	31
86	female	9.4	54	SEV	no	normal	LAHB	sudden cardiac death	659
86	male	6.5	58	SEV	no	normal	LBBB	sudden cardiac death	486
86	female	5.1	60	BEV	no	normal	normal	unknown	1382
86	female	5.6	65	BEV	no	normal	normal	unknown	1137
86	male	10.3	75	BEV	no	normal	normal	unknown	1171
86	male	11.4	35	BEV	no	normal	LBBB	unknown	458
86	male	9.3	65	BEV	no	RBBB + LAHB	RBBB + LAHB	unknown	105
86	female	17.5	45	BEV	no	IVCD	IVCD	unknown	343
87	female	7.1	60	BEV	no	normal	normal	unknown	1905
87	female	31.7	65	BEV	no	LBBB	LBBB	unknown	402
88	male	13.2	55	BEV	no	LBBB	LBBB	sudden cardiac death	253
88	female	7.9	65	BEV	no	normal	normal	unknown	1257
88	male	9.7	60	BEV	no	normal	normal	unknown	856
88	female	5.5	78	SEV	no	normal	normal	unknown	996
89	male	5.2	65	BEV	no	normal	normal	unknown	423

89	female	6.9	68	BEV	no	normal	normal	unknown	428
90	female	7.1	60	BEV	no	normal	normal	unknown	67
91	female	12.3	65	BEV	no	RBBB + LAHB	RBBB + LAHB	unknown	467
92	female	14.8	65	BEV	no	normal	normal	unknown	1972
92	female	7.9	65	BEV	no	normal	normal	unknown	1423
92	male	10.4	65	BEV	no	normal	normal	unknown	822
92	female	13.7	45	BEV	no	RBBB	RBBB	unknown	1795
93	male	8.0	60	BEV	no	LAHB	LAHB	unknown	215
97	female	21.9	50	BEV	no	RBBB + LAHB	RBBB + LAHB	sudden cardiac death	946

STS-PROM: Society of Thoracic Surgeons predicted risk of mortality, LVEF: left ventricular ejection fraction, PPI: permanent pacemaker implantation, TAVI: transcatheter aortic valve implantation, LBBB: left bundle branch block, LAHB: left anterior hemiblock, RBBB: right bundle branch block, IVCD: intraventricular conduction delay, LIBBB: left incomplete bundle branch block

Supplemental Table 2. Baseline and Procedural Findings According to the Type of Valve Implanted (n=1556)

	Balloon-expandable valve (n=858)	Self-expandable valve (n=698)	*P* value
Clinical Characteristics			
Age (years)	81 ± 8	80 ± 6	0.199
Male	423 (49.3)	317 (45.4)	0.127
Body mass index (kg/m^2)	26 (23-29)	27 (24-30)	0.004
NYHA class ≥3	644 (75.1)	545 (78.1)	0.163
Hypertension	699 (81.5)	567 (81.5)	0.999
Diabetes mellitus	259 (30.2)	226 (32.3)	0.315
COPD	228 (26.6)	254 (36.1)	<0.001
eGFR <60 ml/min	473 (55.1)	409 (58.6)	0.170
Paroxysmal/chronic atrial fibrillation	286 (33.3)	148 (21.2)	<0.001
Coronary artery disease	590 (68.8)	286 (41.0)	<0.001
Logistic EuroScore (%)	21.3 ± 14.4	19.5 ± 13.2	0.014
STS-PROM score (%)	8.0 ± 5.0	7.2± 5.6	0.006
Echocardiography			
LVEF (%)	55 ± 13	56 ± 14	0.055
LVEF≤40%	149 (17.4)	120 (17.2)	0.932
Mean gradient (mmHg)	46 ± 17	50 ± 17	<0.001
Aortic valve area (cm^2)	0.60 (0.50-0.78)	0.62 (0.41-0.79)	0.358
Procedural findings			
Procedural success*	769 (89.6)	557 (79.8)	<0.001
Approach			
Transapical/Transaortic	385 (44.9)	9 (1.3)	<0.001
Transfemoral/Subclavian	473 (55.1)	687 (98.7)	
Prosthesis size (mm)			
20-23	388 (45.2)	12 (1.7)	
26	425 (49.5)	371 (53.2)	<0.001
29-31	45 (5.2)	315 (45.1)	
Need for a second valve	18 (2.1)	29 (4.2)	0.018
≥Moderate AR	82 (9.6)	132 (18.9)	<0.001
30-day PPI	61 (7.1)	178 (25.5)	<0.001
30-day mortality	61 (7.1)	47 (6.7)	0.772

*According VARC-2 criteria

NYHA: New York Heart Association, COPD: chronic obstructive pulmonary disease, eGFR: estimated glomerular filtration ratio, STS-PROM: Society of Thoracic Surgeons predicted risk of mortality, LVEF: left ventricular ejection fraction, AR: aortic regurgitation, NOP-LBBB: new-onset persistent left bundle branch block

Supplemental Table 3. Cumulative Outcomes of the Study Population According to the Type of Valve Implanted (n=1556)

	Univariate HR* (95% CI)	*P* value	Multivariate HR*† (95% CI)	*P* value
Death or hospitalization for heart failure	1.96 (1.64-2.35)	<0.001	1.26 (0.75-2.13)	0.382
Death from any cause	1.76 (1.45-2.15)	<0.001	0.99 (0.55-1.77)	0.960
Death from cardiovascular causes	1.72 (1.35-2.19)	<0.001	0.94 (0.45-1.99)	0.807
Sudden cardiac death	0.34 (0.14-0.81)	0.014	0.19 (0.02-1.94)	0.163
Sudden death/unknown death	1.51 (0.95-2.41)	0.083	0.76 (0.27-2.13)	0.598
Hospitalization for heart failure	2.42 (1.72-3.39)	<0.001	1.65 (0.63-4.31)	0.311

*Compared to self-expandable valve group; † Adjusted for baseline and procedural differences.
HR: hazard ratio, CI: confidence interval

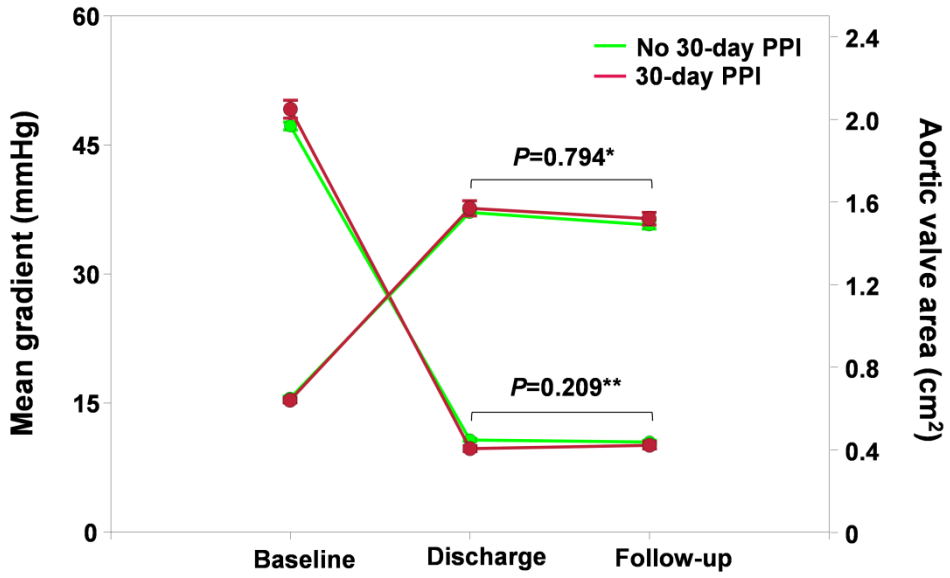
SUPPLEMENTAL FIGURES

Supplemental Figure 1

Changes in valve hemodynamics (mean aortic valve gradient and aortic valve area) according to the need for permanent pacemaker implantation within 30-day following transcatheter aortic valve implantation

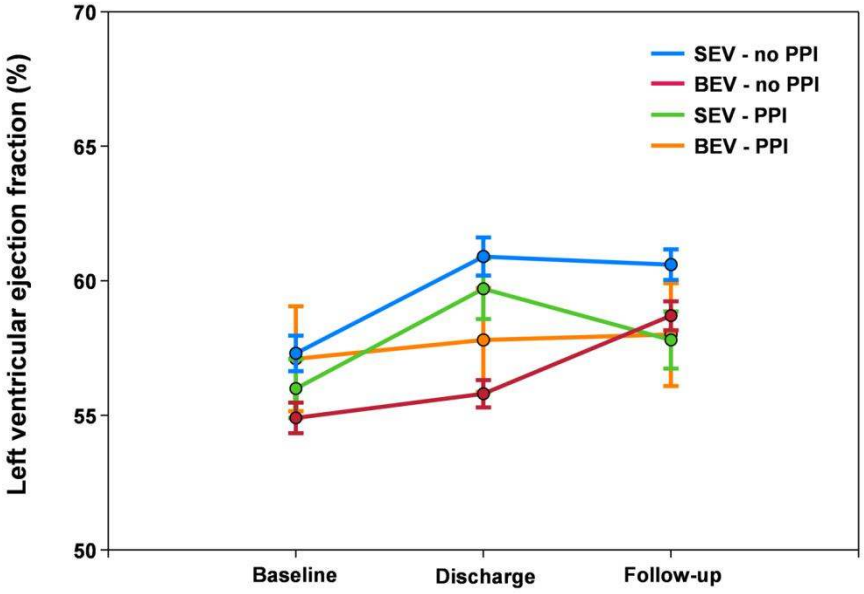
Supplemental Figure 2

LVEF changes between baseline and 6- to- 12 month follow-up according to the need for 30-day permanent pacemaker implantation and the type of valve implanted



*AVA changes over time between groups

**Mean gradient changes over time between groups



P<0.002, between baseline and follow-up for SEV–no PPI group
P<0.001, between baseline and follow-up for BEV–no PPI group
P=0.354, between discharge and follow-up for SEV–PPI group
P=0.996, between discharge and follow-up for BEV–PPI group
P=0.114, between SEV–no PPI and BEV–no PPI groups
P=0.688, between SEV–PPI and BEV–PPI groups