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Long-Term Outcomes in Patients With New Permanent Pacemaker Implantation Following Transcatheter Aortic Valve Replacement

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ABSTRACT

OBJECTIVES This study sought to evaluate the long-term clinical impact of permanent pacemaker implantation (PPI) after transcatheter aortic valve replacement (TAVR).

BACKGROUND Conduction disturbances leading to PPI are common following TAVR. However, no data exist regarding the impact of PPI on long-term outcomes post-TAVR.

METHODS This was a multicenter study including a total of 1,629 patients without prior PPI undergoing TAVR (balloon- and self-expandable valves in 45% and 55% of patients, respectively). Follow-up clinical, echocardiographic, and pacing data were obtained at a median of 4 years (interquartile range: 3 to 5 years) post-TAVR.

RESULTS PPI was required in 322 (19.8%) patients within 30 days post-TAVR (26.9% and 10.9% in patients receiving self- and balloon-expandable CoreValve and Edwards systems, respectively). Up to 86% of patients with PPI exhibited pacing >1% of the time during follow-up (>40% pacing in 51% of patients). There were no differences between patients with and without PPI in total mortality (48.5% vs. 42.9%; adjusted hazard ratio [HR]: 1.15; 95% confidence interval [CI]: 0.95 to 1.39; p = 0.15) and cardiovascular mortality (14.9% vs. 15.5%, adjusted HR: 0.93; 95% CI: 0.66 to 1.30; p = 0.66) at follow-up. However, patients with PPI had higher rates of rehospitalization due to heart failure (22.4% vs. 16.1%; adjusted HR: 1.42; 95% CI: 1.06 to 1.89; p = 0.019), and the combined endpoint of mortality or heart failure rehospitalization (59.6% vs. 51.9%; adjusted HR: 1.25; 95% CI: 1.05 to 1.48; p = 0.011). PPI was associated with lesser improvement in LVEF over time (p = 0.051 for changes in LVEF between groups), particularly in patients with reduced LVEF before TAVR (p = 0.005 for changes in LVEF between groups).

CONCLUSIONS The need for PPI post-TAVR was frequent and associated with an increased risk of heart failure rehospitalization and lack of LVEF improvement, but not mortality, after a median follow-up of 4 years. Most patients with new PPI post-TAVR exhibited some degree of pacing activity at follow-up. (J Am Coll Cardiol Intv 2018;11:301–10)

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

HR = hazard ratio

LVEF = left ventricular ejection fraction

PPI = permanent pacemaker implantation

TAVR = transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has become a therapeutic option for patients with severe symptomatic aortic stenosis who are at intermediate-to-high or prohibitive surgical risk (1–3). However, the occurrence of some periprocedural complications is still a concern. In particular, conduction abnormalities requiring permanent pacemaker implantation (PPI) are still the most frequent complications of TAVR, and its incidence has not been reduced by the introduction of the latest generation of transcatheter valve systems (4). This raises a major concern at a time when an expansion toward the treatment of lower-risk patients and of other aortic valve pathologies (bicuspid valves, aortic regurgitation) is expected (4). Thus, knowing the early and late clinical impact of PPI following TAVR is of high clinical relevance. In addition to the early and late local complications associated with PPI, chronic right ventricular pacing has been associated with negative effects on ventricular function and an increased risk of heart failure hospitalization and mortality at long-term follow-up in non-TAVR patients (5–7). However, to date studies evaluating the effects of PPI post-TAVR have provided controversial results and had a limited (<2 years) follow-up (3,8–19), precluding an accurate evaluation of the potential negative effects of PPI in the TAVR population. In addition, data on right ventricular pacing and pacemaker dependency are limited to a few studies with short-term (mainly 1 month) pacemaker interrogation. The aim of this multicenter study was to evaluate the impact of new PPI on long-term (>2 years) clinical outcomes in a large cohort of consecutive patients undergoing TAVR.

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METHODS

STUDY POPULATION. A total of 1,666 consecutive patients without prior PPI who underwent TAVR with either a balloon- or self-expandable valve in 9 centers between May 2007 and February 2015. Of these, 37 patients were excluded because of failure to valve implantation, conversion to open-heart surgery, or procedural death. The final study population consisted of 1,629 patients who had a minimum follow-up of 2 years. Patients were divided according to the need for PPI within the 30 days following TAVR (PPI vs. no-PPI post-TAVR groups). Patients were considered candidates for TAVR 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. 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.

INDICATIONS FOR PPI. In accordance with the American College of Cardiology/American Heart Association/Heart Rhythm Society recommendations (20), PPI was indicated either if third-degree or advanced second-degree atrioventricular block at any anatomic level occurred and was not expected to resolve or in the presence of sinus node dysfunction and documented symptomatic bradycardia. The indication for PPI in the presence of left bundle branch block with PR interval prolongation (>200 ms) not expected to normalize was at the discretion of the physician responsible for the patient. The selection of a single- or dual-chamber pacemaker and pacing mode followed the American College of Cardiology/American Heart Association/Heart Rhythm Society recommendations (20).

FOLLOW-UP. Follow-up was carried out through clinical outpatient visits or phone contacts at 30 days, 12 months, and yearly afterward. Long-term outcomes included overall and cardiac mortality, and heart failure rehospitalizations. Several sources of information were used to investigate endpoints: 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 (21). For patients with multiple hospitalizations resulting from heart failure, only the first episode was included in the analysis.

Echocardiographic examinations were available in all patients at baseline and discharge, and in 847 patients (67.4% of patients at risk) at ≥2-year follow-up. Left ventricular ejection fraction (LVEF) was calculated from the biplane modified Simpson method, and left ventricular dysfunction was defined as LVEF <50% (22). Pacemaker interrogation reports during follow-up were reviewed from different centers. The percentage of right ventricular pacing was recorded at the latest follow-up.

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 chi-square or Fisher exact test and 2-sided *t* test or Wilcoxon signed rank test as appropriate. All analyses were performed using a

hierarchical method to account for between-center variability. Late clinical outcomes were compared between the PPI and no PPI with the use of proportional hazards models (cumulative outcomes). Sensitivity analyses treating PPI as a time-varying covariate in Cox regression models were also performed. All multivariate models were adjusted for baseline differences in the univariate analysis including variables with a value of $p \leq 0.10$. Survival rates were summarized by use of Kaplan-Meier estimates. 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. The results were considered significant at values of $p < 0.05$. Analyses were conducted with the statistical package SAS version 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

A total of 322 (19.8%) patients had PPI following TAVR, and the clinical and procedural characteristics of these patients compared with those with no PPI are shown in **Table 1**. PPI patients were older (82 ± 6 years of age vs. 81 ± 7 years of age; $p = 0.011$), more likely to have prior coronary artery disease (44.1% vs. 42%; $p = 0.029$), and tended to have a higher risk profile (Society of Thoracic Surgeons Predicted Risk of Mortality score 7.4 ± 5.3% vs. 6.9 ± 5.4%; $p = 0.051$). Patients with PPI post-TAVR exhibited more frequently a right bundle branch block (26.0% vs. 6.5%; $p < 0.001$) at baseline electrocardiography. The incidence of 30-day PPI was higher among patients receiving a self-expanding CoreValve system (26.9%) (Medtronic, Minneapolis, Minnesota) compared with the balloon-expanding Edwards system (10.9%; $p < 0.001$) (Edwards Lifesciences, Irvine, California). There were no significant differences in the rates of balloon pre-dilation and post-dilation between the PPI and no-PPI groups.

TIMING AND CHARACTERISTICS OF 30-DAY PPI. The median time from TAVR to PPI was 2 days (interquartile range: 1 to 4 days) (**Figure 1**). The clinical indications for PPI, pacemaker type, and pacing mode are shown in **Table 2**. The most common indication for PPI was high-degree or complete atrioventricular block (71.4%), and most (56.8%) pacemakers implanted were dual chamber.

IN-HOSPITAL OUTCOMES. There were no significant differences between groups (PPI vs. no PPI) with respect to major complications post-TAVR (**Table 1**). However, PPI was associated with a longer hospital stay (7 [5–9] days vs. 6 [5–8] days; adjusted $p = 0.014$).

LONG-TERM CLINICAL OUTCOMES. At a median follow-up of 4 (interquartile range: 3 to 5) years, a total of 716 patients had died and 283 patients required rehospitalization due to heart failure. Late clinical outcomes according to the need for PPI following TAVR are shown in **Table 3**. PPI post-TAVR was associated with a higher mortality rate at follow-up (48.5% vs. 42.9%; $p = 0.044$), but differences were no longer significant after adjusting for baseline clinical differences between groups (adjusted hazard ratio [HR]: 1.15; 95% confidence interval [CI]: 0.95 to 1.39; $p = 0.152$). There were no differences between groups in cardiac mortality (PPI: 14.9%, no PPI: 15.5%; adjusted HR: 0.93; 95% CI: 0.66 to 1.30; $p = 0.662$). PPI was associated with a higher risk of heart failure rehospitalization (22.4% vs. 16.1%; adjusted HR: 1.42; 95% CI: 1.06 to 1.89; $p = 0.019$) and the combined endpoint of death or heart failure rehospitalization (59.6% vs. 51.9%; adjusted HR: 1.25; 95% CI: 1.05 to 1.48; $p = 0.011$). Similar results were obtained with sensitivity analyses treating PPI as a time-varying covariate for long-term outcomes. The 4-year follow-up Kaplan-Meier curves according to the need for PPI post-TAVR are shown in **Figure 2**.

There was no interaction between PPI or valve type and global or cardiac mortality at follow-up. In those patients who received a balloon-expandable Edwards valve, there were no differences between groups (PPI vs. no PPI) in global mortality (PPI: 52.6%, no PPI: 43.5%; adjusted HR: 1.33; 95% CI: 0.94 to 1.91; $p = 0.109$) and cardiac mortality (PPI: 17.9%, no PPI: 14.9%; adjusted HR: 1.29; 95% CI: 0.73 to 2.26; $p = 0.381$). In patients who received a CoreValve system, the incidence of global mortality (PPI: 46.8%, no PPI: 42.3%; adjusted HR: 1.14; 95% CI: 0.90 to 1.45; $p = 0.280$) and cardiac mortality (PPI: 14.4%, no PPI: 16.3%; adjusted HR: 0.81; 95% CI: 0.53 to 1.24; $p = 0.325$) was also similar between groups. The 4-year Kaplan-Meier curves, according to valve type, among those patients who required a PPI post-TAVR are shown in Online Figure 1.

CHANGES IN LVEF OVER TIME. Echocardiograms were analyzed in all surviving patients at discharge and in 847 (67.4% of patients at risk) patients at latest follow-up. LVEF changes over time according to the need for PPI are shown in **Figure 3**. Whereas LVEF increased over time in patients with no PPI, it decreased at follow-up in those patients who had PPI after TAVR ($p = 0.051$ for LVEF changes over time

TABLE 1 Baseline and Procedural Characteristics, and In-Hospital Outcomes of the Study Population, According to the Need for PPI Post-TAVR

	30-Day PPI			
	Yes (n = 322)	No (n = 1,307)	OR (95% CI)	p Value
Clinical characteristics				
Age, yrs	82 ± 6	81 ± 7	1.02 (1.01–1.04)	0.011
Male	181 (56.2)	768 (58.8)	0.84 (0.67–1.05)	0.130
Diabetes mellitus	104 (32.3)	457 (35.0)	1.03 (0.81–1.30)	0.816
COPD	78 (24.3)	361 (27.7)	0.81 (0.62–1.05)	0.115
NYHA functional class				
I–II	98 (30.4)	350 (26.9)	0.95 (0.73–1.24)	0.699
III–IV	223 (69.4)	953 (72.9)		
eGFR <60 ml/min/1.73 m^2	208 (64.6)	778 (59.5)	1.13 (0.88–1.43)	0.338
Coronary artery disease	142 (44.1)	549 (42.0)	1.29 (1.03–1.62)	0.029
Previous CABG	38 (11.8)	191 (14.7)	0.89 (0.62–1.27)	0.509
Previous valve surgery	14 (4.4)	60 (4.6)	0.92 (0.57–1.49)	0.738
Previous stroke	46 (14.3)	167 (12.8)	1.32 (0.96–1.81)	0.084
STS-PROM score, %	7.4 ± 5.3	6.9 ± 5.4	1.03 (0.99–1.05)	0.051
ECG characteristics				
Sinus rhythm	253 (78.8)	1,026 (78.6)	1.03 (0.77–1.37)	0.848
Atrial fibrillation/flutter	68 (21.2)	279 (21.4)		
Conduction disturbances				
First-degree AVB	52 (16.1)	162 (12.4)	1.22 (0.88–1.68)	0.229
LBBB	37 (11.4)	142 (10.9)		
RBBB	84 (26.0)	85 (6.5)	1.27 (1.18–1.38)	<0.001
Other conduction defect	47 (14.6)	165 (12.6)		

Continued on the next page

between groups) (Figure 3A). Differences between PPI and no-PPI groups in the evolution of LVEF over time were more marked in those patients with baseline left ventricular dysfunction (p = 0.005 for LVEF changes over time between groups) (Figure 3B).

PACING REQUIREMENT AT FOLLOW-UP. In patients with PPI post-TAVR, data on the percentage of right ventricular pacing collected at the latest available follow-up were available in 204 (86.4% of patients at risk) patients (Figure 4). Up to 86% of patients exhibited pacing >1% of the time at follow-up, and 51% of them were paced >40% of the time. A total of 56 (27.4%) patients were paced 100% of the time.

DISCUSSION

In a large cohort of patients without prior PPI undergoing TAVR, the need for PPI was a frequent complication that prolonged length of hospitalization. PPI post-TAVR was not associated with an increased risk of total mortality or cardiac mortality after a median follow-up of 4 years. However, patients with PPI post-TAVR had a higher risk of heart failure rehospitalization and a lesser improvement of left ventricular function over time. The vast majority of patients with PPI exhibited some degree of pacing (>1% pacing rate) and about one-half of them were paced >40% of the time at long-term follow-up.

The incidence of new PPI post-TAVR has been close to 6% and 20% with the use of the balloon-expandable Edwards valves and the self-expandable CoreValve system, respectively (23). The rates of PPI post-TAVR in the present report are slightly higher, and this may be partially due to the exclusion of patients with prior PPI. The vast majority of prior studies included patients with prior PPI when determining the incidence of PPI post-TAVR, and this has led to a systematic underestimation of the real incidence of new PPI following TAVR (24). Consistent with prior studies, advanced atrioventricular block was the most frequent reason for PPI and most pacemakers were implanted within 72 h following the procedure. This reflects the short delay between the occurrence of the conduction disturbance and PPI, a common practice in most TAVR centers, although this is not in accordance with current guidelines, which recommend longer observation periods before PPI (20,25). Future studies will need to determine whether longer periods of observation following the occurrence of the conduction disturbance would be

TABLE 1 Continued

	30-Day PPI			
	Yes (n = 322)	No (n = 1,307)	OR (95% CI)	p Value
Baseline echocardiography				
LVEF, %	57 ± 12	56 ± 13	1.00 (0.99–1.01)	0.851
LVEF <50%	72 (22.4)	322 (24.6)		
Mean gradient, mm Hg	47.2 ± 13.9	48.3 ± 15.0	0.99 (0.98–0.99)	0.032
Aortic valve area, cm^2	0.6 ± 0.2	0.7 ± 0.2	1.03 (0.65–1.64)	0.889
Aortic regurgitation				
None/trace/mild	290 (92.4)	1132 (85.9)	0.65 (0.43–1.00)	0.051
Moderate/severe	24 (7.6)	142 (11.2)		
Procedural variables				
Approach				
Transfemoral	278 (86.6)	1102 (84.9)	1.22 (0.98–1.53)	0.078
Transapical	27 (8.4)	145 (11.2)		
Transaortic	12 (3.7)	29 (2.2)		
Subclavian	4 (1.3)	23 (1.8)		
Prosthesis type				
SAPIEN	24 (7.5)	153 (11.7)	2.40 (1.75–3.28)	<0.001
Sapien XT	48 (14.9)	455 (34.9)		
Sapien 3	6 (1.9)	27 (2.1)		
CoreValve	139 (43.2)	372 (28.5)		
Evolut R	98 (30.4)	269 (20.6)		
Other	7 (2.2)	28 (2.1)		
Balloon valvuloplasty	278 (86.3)	1,087 (83.2)	1.14 (0.75–1.73)	0.529
Balloon post-dilation	66 (20.5)	219 (16.8)	1.29 (0.93–1.80)	0.131
Need for second valve	11 (3.4)	16 (1.2)	2.03 (1.10–3.78)	0.025
Discharge echocardiography				
LVEF, %	59 ± 12	58 ± 13	0.99 (0.98–1.00)	0.994
Mean gradient, mm Hg	9.5 ± 4.6	9.9 ± 5.2	0.99 (0.97–1.02)	0.996
Aortic valve area, cm^2	1.6 ± 0.5	1.7 ± 0.5	0.91 (0.65–1.27)	0.573
Aortic regurgitation				
None/trace/mild	303 (97.1)	1,212 (95.9)	1.03 (0.51–2.09)	0.935
Moderate/severe	9 (2.9)	52 (4.1)		
In-hospital outcomes				
Stroke	4 (1.4)	21 (1.6)	1.36 (0.99–1.89)	0.061
Myocardial infarction	6 (1.8)	22 (1.7)	0.79 (0.34–1.84)	0.581
Major vascular complications	29 (8.9)	103 (7.9)	0.88 (0.59–1.33)	0.550
Major bleeding	21 (6.5)	69 (5.3)	1.36 (0.85–2.16)	0.197
Hospitalization, days	7 (5–9)	6 (5–8)	1.02 (1.01–1.03)*	0.014

Values are mean ± SD or n (%). *Adjusted for baseline and procedural differences between groups.

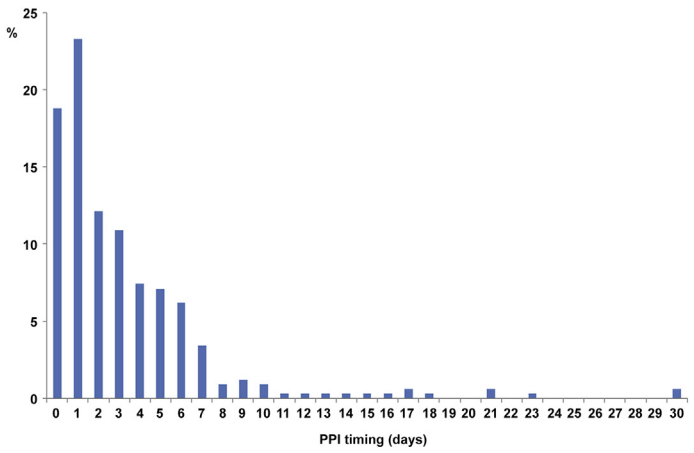
AVB = atrioventricular block; CABG = coronary artery bypass grafting; CI = confidence interval; COPD = chronic obstructive pulmonary disease; ECG = electrocardiography; eGFR = estimated glomerular filtration rate; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; OR = odds ratio; PPI = permanent pacemaker implantation; RBBB = right bundle branch block; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement.

associated with lower rates of PPI post-TAVR without compromising the patient's safety.

Although the need for PPI post-TAVR was not associated with an increase in early (30-day) complications, patients requiring PPI had a prolonged hospital stay, similar to what has been reported in previous studies (17,19). The longer length of hospitalization, along with the costs of PPI, has been associated with a significant increase in the costs of TAVR (26–28). Efforts to avoid the occurrence of conduction disturbances and limiting PPI to the well-established indications are therefore important for reducing the global costs and increasing the cost-efficacy value of the procedure.

LONG-TERM OUTCOMES. There has been some controversy in recent years regarding the impact of new PPI post-TAVR on mortality. The majority of studies

FIGURE 1 Time From Transcatheter Aortic Valve Replacement to PPI



The histogram displays frequency distribution of time to permanent pacemaker implantation (PPI).

have failed to show any association between PPI and mortality (total and cardiovascular), and this was confirmed in a recent meta-analysis (23). However, a substudy from the Society of Thoracic Surgeons Transcatheter Valve Therapy registry found an increase in late mortality, but not cardiovascular mortality, in those patients requiring PPI post-TAVR (19). The fact that increased mortality was not secondary to cardiac causes suggest a role of confounding factors in such an association. Also, the main limitation of the studies evaluating the late impact of new PPI to date is that follow-up was limited to ≤2 years (1-year follow-up in most of them) (8–19). Studies evaluating the effects of chronic right ventricular pacing on clinical outcomes have shown that a much longer follow-up is usually needed to demonstrate the negative effects of right ventricular pacing on mortality or heart failure rehospitalization (5–7,29). More recently, the SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation) trial failed to show any effect of new PPI post-TAVR on 2-year mortality (3). The present study, which is the first to provide data at 4-year follow-up in a large cohort of patients with PPI post-TAVR, showed the lack of association between PPI and total or cardiac mortality. Although a higher mortality rate was observed in PPI patients, differences did not remain significant after adjustment for baseline and procedural factors and no negative effect was observed regarding cardiovascular mortality. However, these results highlight the importance of longer-term studies with a close follow-up of these patients.

TABLE 2 Type, Pacing Mode, and Indications for 30-Day PPI

Type of pacemaker	
Single chamber	131 (40.7)
Dual chamber	183 (56.8)
Unspecified	8 (2.5)
Pacing mode	
DDD	132 (41.0)
VVI	170 (52.8)
Unspecified	20 (6.2)
Indications	
Complete or high-degree AVB	230 (71.4)
Sinoatrial node disease	18 (5.6)
Symptomatic bradycardia	10 (3.1)
LBBB + first-degree AVB	17 (5.3)
Unspecified	47 (14.6)

Values are n (%).
Abbreviations as in Table 1.

Chronic right ventricular pacing causes electrical and mechanical dyssynchrony, and this has been associated with a deleterious effect on ventricular function and an increased risk of heart failure hospitalizations, particularly in patients with pre-existing heart failure and left ventricular dysfunction (5,7,29–32). Multiple previous studies have shown a negative effect of PPI on ventricular function among TAVR patients as early as at 1-year follow-up (18,33–35). Our study confirms such a deleterious effect on ventricular function at longer-term follow-up, particularly in patients with reduced LVEF pre-TAVR. However, the vast majority of studies to date have failed to show an increased incidence of heart failure hospitalizations among TAVR patients with PPI (12,17–19,36), and this may be explained by the limited follow-up (<2 years). The present study showed, for the first time, an independent association between PPI post-TAVR and heart failure decompensations requiring hospitalization. In fact, PPI increased the risk for heart failure hospitalizations by close to 50% after a median time of 4 years post-TAVR. This finding has important clinical implications. First, such patients, particularly those with reduced LVEF, should have a closer follow-up, probably in heart failure clinics. In addition, the possibility of upgrading to a resynchronization therapy needs to be considered in those patients with high (>40%) right ventricular pacing who remain symptomatic and do not recover their ventricular function post-TAVR. In fact, there have already been some case reports of successful resynchronization therapy following TAVR (37,38). Future studies need to determine the potential benefits of a systematic implementation of such measures in these patients.

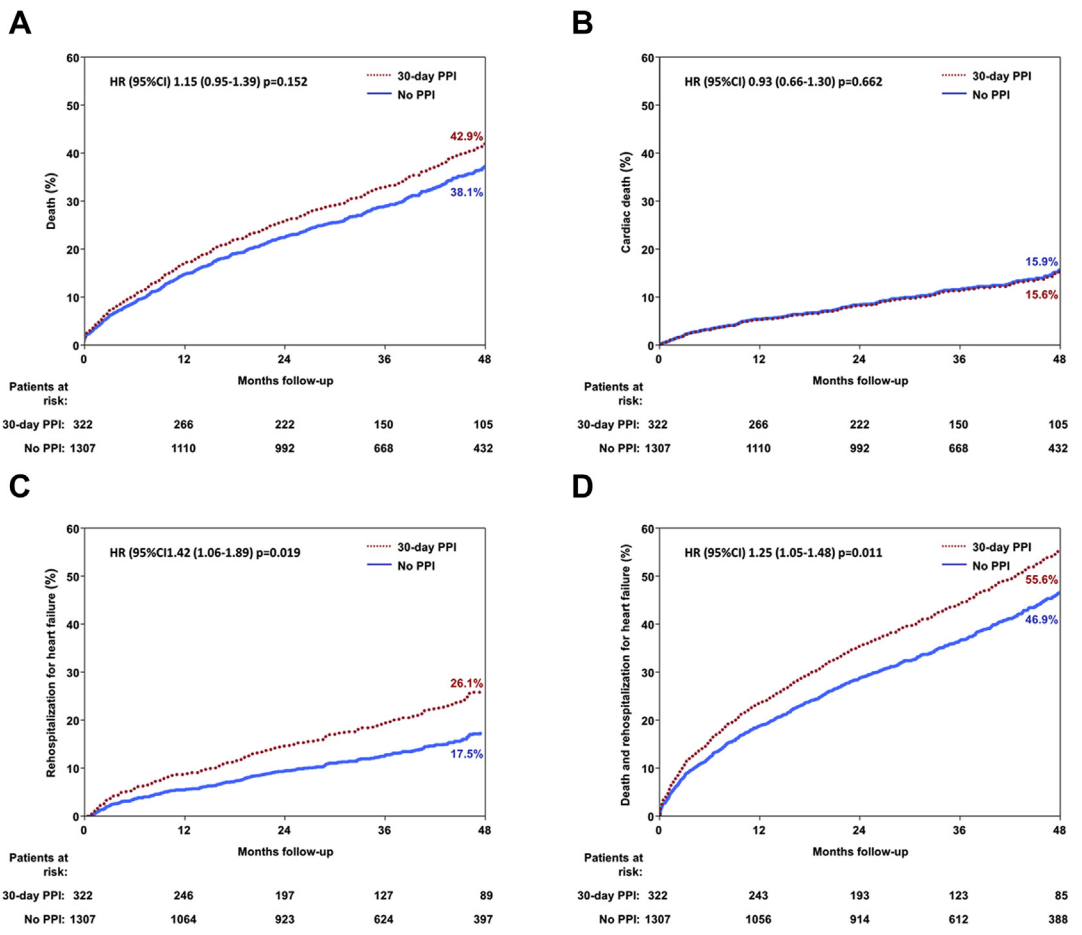
TABLE 3 Late Clinical Outcomes, According to the Need for PPI Post-TAVR

	30-Day PPI					
	Yes (n = 322)	No (n = 1,307)	HR (95% CI)	p Value	Adjusted HR* (95% CI)	p Value
Mortality	156 (48.5)	560 (42.9)	1.21 (1.01–1.45)	0.044	1.15 (0.95–1.39)	0.152
Sudden death	7 (2.2)	43 (3.3)	0.72 (0.31–1.64)	0.431	0.66 (0.28–1.57)	0.345
Cardiovascular death	48 (14.9)	202 (15.5)	1.01 (0.73–1.39)	0.976	0.93 (0.66–1.30)	0.662
Heart failure admission	72 (22.4)	211 (16.1)	1.48 (1.12–1.95)	0.006	1.42 (1.06–1.89)	0.019
Composite of mortality and heart failure	192 (59.6)	678 (51.9)	1.31 (1.11–1.55)	0.001	1.25 (1.05–1.48)	0.011
Composite of cardiovascular mortality and heart failure	101 (31.4)	354 (27.2)	1.27 (1.01–1.59)	0.039	1.21 (0.95–1.53)	0.124

Values are n (%). *Adjusted for baseline and procedural differences between groups.
HR = hazard ratio; other abbreviations as in Table 1.

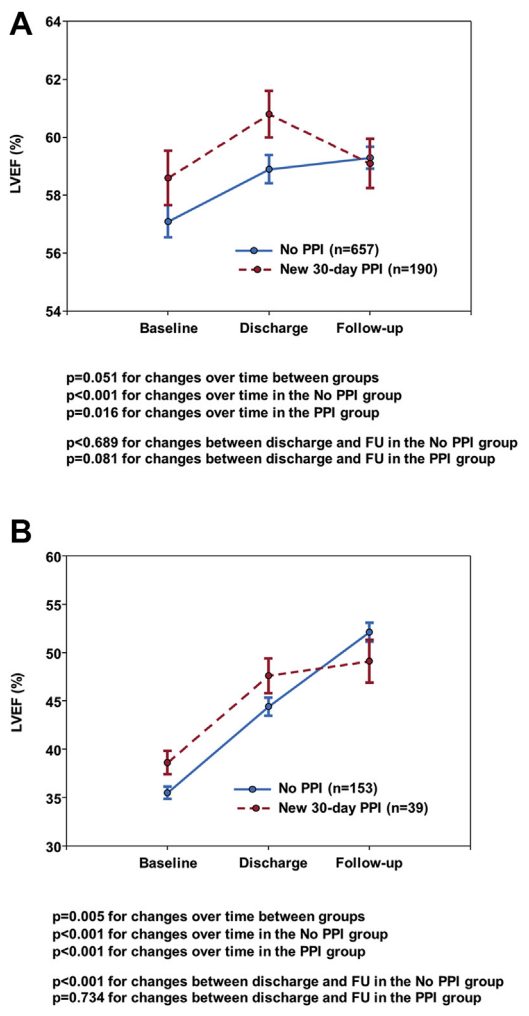
Several studies have evaluated the pacing rates and pace dependency in patients who required PPI following TAVR (39-44). The results of pacing requirement have varied among studies, from 29% to 44%. However, most studies have evaluated the pacing requirement post-TAVR at short (1 month) or midterm (1 year) follow-up, but none after a median follow-up of 4 years. Our study showed some degree

FIGURE 2 Long-Term Clinical Outcomes



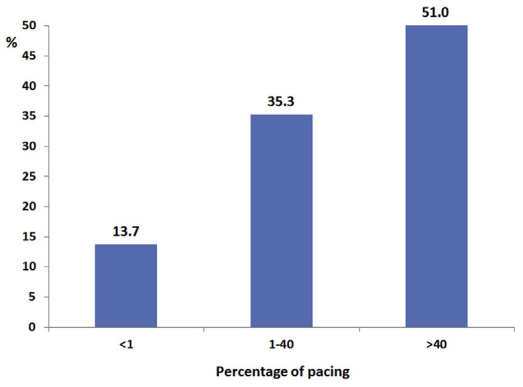
Cumulative incidence curves for **(A)** long-term (4-year) all-cause mortality, **(B)** cardiovascular death, **(C)** heart failure admission, and **(D)** composite of mortality and heart failure admission. CI = confidence interval; HR = hazard ratio; PPI = permanent pacemaker implantation.

FIGURE 3 Changes in Left Ventricular Function Over Time



Changes of left ventricular ejection fraction (LVEF) over time, according to the need for 30-day permanent pacemaker **(A)** in all patients, and **(B)** in patients with reduced left ventricular dysfunction at baseline (LVEF <50%). FU = follow-up; PPI = permanent pacemaker implantation.

FIGURE 4 Pacing Requirement at Follow-Up



The histogram displays percentage of right ventricular pacing at the latest follow-up.

of pacing in >80% of patients, with more than one-half exhibiting pacing rates >40%. This is higher than in prior studies, and suggests that patients developing advanced conduction disturbances post-TAVR have a high likelihood of requiring some pacing within the years following the procedure. Unfortunately, we do not have the pacing interrogation at different time points to evaluate the changes in pacing requirement over time. This will need to be determined in future studies.

STUDY LIMITATIONS. This report consists of a retrospective analysis of data collected prospectively and is subject to the limitations inherent to this study design. The missing data regarding echocardiography, physician's choice of pacemaker type, and pacing activity at follow-up may have had some influence on the final results.

CONCLUSIONS

PPI has an impact on the long-term clinical outcomes following TAVR. Although no association was found between PPI and mortality, there was a negative effect on LVEF and an increased risk of heart failure hospitalizations in these patients. Also, most patients exhibited some degree of pacing at long-term follow-up. Preventing conduction disturbances and following the guidelines regarding the indications for PPI post-TAVR are of major clinical relevance, particularly in an era when patients with a longer life expectancy (intermediate-risk patients) are starting to be treated with TAVR. Also, implementing specific protocols regarding the follow-up of such patients (heart failure clinic, considering resynchronization therapy) appears mandatory, particularly in the presence of reduced LVEF. TAVR is inevitably expanding toward the treatment of most patients with aortic stenosis, but conduction disturbances requiring PPI remains a major issue of this technology. This study providing evidence on the long-term clinical impact of this complication highlights the urgent need for further studies in this field.

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PERSPECTIVES

WHAT IS KNOWN? Conduction disturbances and PPI remain a frequent complication following TAVR. However, its association with adverse outcomes in the long term remains unclear.

WHAT IS NEW? PPI has a negative effect on long-term clinical outcomes following TAVR. PPI is associated with increased rates of heart failure readmission and lesser improvement in LVEF over time, but not total or cardiac mortality.

WHAT IS NEXT? Further studies are needed to better understand the impact of PPI and pacing dependency on cardiovascular mortality and adverse clinical outcomes post-TAVR. In addition, the role of resynchronization therapy in patients with chronic right ventricular pacing to prevent LVEF deterioration and heart failure admission should be examined.

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KEY WORDS aortic stenosis, left ventricular ejection fraction, pacemaker, transcatheter aortic valve replacement

APPENDIX For a supplemental figure, please see the online version of this article.