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Impact of Permanent Pacemaker Implantation on Clinical Outcome Among Patients Undergoing Transcatheter Aortic Valve Implantation

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Objectives This study sought to assess the impact of permanent pacemaker (PPM) implantation on clinical outcomes among patients undergoing transfemoral transcatheter aortic valve implantation (TAVI).

Background TAVI is associated with atrioventricular-conduction abnormalities requiring PPM implantation in up to 40% among patients treated with self-expanding prostheses.

Methods Between 2007 and 2010, 353 consecutive patients (mean age: 82.6 ± 6.1 years, log EuroSCORE: 25.0 ± 15.0%) with severe aortic stenosis underwent transfemoral TAVI at 2 institutions. Clinical outcomes were compared among 3 groups: (1) patients requiring PPM implantation after TAVI (PPM after TAVI), (2) patients without PPM before or after TAVI (no PPM), and (3) patients with PPM before TAVI (PPM before TAVI). The primary endpoint was all-cause mortality at 12 months, and an age-, sex-, and origin-matched standardized population served as controls.

Results Of 353 patients, 98 patients (27.8%) belonged to the PPM after TAVI group, 48 patients (13.6%) belonged to the PPM before TAVI group, and 207 patients (58.6%) belonged to the no PPM group. The PPM before TAVI patients had a significantly higher baseline risk compared with the PPM after TAVI and no PPM patients (coronary artery disease: 77.1% vs. 52.7% and 58.2%, respectively, $p = 0.009$; atrial fibrillation: 43.8% vs. 22.7% and 20.4%, respectively, $p = 0.005$). At 12 months of follow-up, all-cause mortality was similar in all 3 groups (PPM after TAVI group: 19.4%, PPM before TAVI group: 22.9%, no PPM group: 18.0%) in unadjusted analyses ($p = 0.77$) and adjusted analyses ($p = 0.90$). Compared with the standardized population, adjusted hazard ratios for death were 2.37 (95% confidence interval [CI]: 1.51 to 3.72) for the PPM after TAVI group, 2.75 (95% CI: 1.52 to 4.97) for the PPM before TAVI group, and 2.24 (95% CI: 1.62 to 3.09) for the no PPM group.

Conclusions Although prognosis remains impaired compared with an age-, sex-, and origin-matched standardized population, periprocedural PPM implantation does not seem to affect clinical outcomes adversely among patients undergoing transfemoral TAVI. (J Am Coll Cardiol 2012;60:493–501) © 2012 by the American College of Cardiology Foundation

Degenerative aortic valve stenosis is mediated by lipid retention, inflammation, and transformation of the tissue matrix resulting in calcification of valve leaflets with extension to the annulus and atrioventricular (AV) groove (1). Owing to the close spatial proximity of the aortic valve annulus, AV node, and bundle of His, this disease process can impair AV conduction and may require implantation of a permanent pacemaker (PPM) (2). Among patients under-

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Abbreviations and Acronyms

AV = atrioventricular
CI = confidence interval
ESP = Edwards Sapien/Sapien XT prosthesis
HR = hazard ratio
MCV = Medtronic CoreValve prosthesis
PPM = permanent pacemaker
TAVI = transcatheter aortic valve implantation

going surgical aortic valve replacement or transcatheter aortic valve implantation (TAVI), mechanical trauma at the level of the native valve and the adjacent subvalvular endocardial region may affect AV conduction further because of indirect mechanisms such as tissue edema and local inflammation, or direct pressure necrosis related to the implantation of the prosthesis or balloon valvuloplasty in case of TAVI. Thus, PPM implantation has been reported in 3% to 9% (3–8) of patients undergoing surgical aortic valve replacement, with lower rates in the past decade presumably resulting from improvements in surgical techniques (7,8). Conversely, PPM implantation rates of up to 40% have been observed in recently published series among patients undergoing TAVI (9–19), particularly when using a self-expanding prosthesis.

Although PPM implantation constitutes a significant proportion of procedure-related complications among patients undergoing TAVI, it is widely considered a benign event as compared with other major adverse cardiac and cerebrovascular events such as death, stroke, and myocardial infarction. Notwithstanding, PPM implantation not only requires an additional procedure, but also results in loss of physiological AV synchrony and altered hemodynamics and may predispose a patient to atrial fibrillation and cerebrovascular events. Moreover, AV-conduction disturbances usually are the expression of far advanced underlying cardiac disease, which may predispose patients to an adverse outcome, particularly among TAVI patients with frequent comorbidities and advanced age. To investigate the prognostic impact of TAVI-related PPM implantation, we compared the long-term clinical outcome of patients requiring PPM implantation after TAVI with that of patients without the need for PPM implantation, those with a PPM before TAVI, and an age-, sex-, and origin-based standardized control population.

Methods

Study design and patient population. The study population consisted of consecutive patients undergoing transfemoral TAVI for treatment of symptomatic native aortic valve stenosis using the Edwards Sapien/Sapien XT prosthesis (ESP; Edwards LifeSciences, Irvine, California) or the Medtronic CoreValve prosthesis (MCV; Medtronic, Minneapolis, Minnesota) at 2 institutions, Bern University Hospital, Bern, Switzerland, and Siegburg Heart Center, Siegburg, Germany. During the enrollment period, Siegburg Heart Center implanted only the MCV, whereas patients at Bern University were treated with both devices. Device selection was based on anatomic parameters and technical characteristics of the prostheses, as described elsewhere (15). Patients were accepted for TAVI after consensus obtained by the local heart team consisting of cardiologists and cardiac surgeons.

The TAVI procedure was performed using percutaneous femoral access, balloon predilation, and subsequent implantation of the prosthesis under conscious sedation or general anesthesia. A temporary pacemaker was used for rapid right ventricular pacing during balloon predilation as well as during implantation of the ESP and remained in place for 48 h after the procedure unless significant AV conduction disturbances were observed. Patients were monitored by continuous electrocardiography for 48 h in an intermediate care unit. Twelve lead electrocardiograms were obtained systematically at baseline, during the procedure, and daily after the procedure until hospital discharge. In case of procedure-related significant AV-conduction disturbances defined as high-degree AV block (third-degree or type II second-degree AV block), new-onset left bundle branch block with dynamic PR interval prolongation of more than 300 ms, or atrial fibrillation with inadequate ventricular escape rhythm, patients underwent PPM implantation.

Patients were categorized into 3 study groups: 1) patients requiring PPM implantation within 30 days after TAVI (PPM after TAVI group); 2) patients without PPM implantation up to 30 days before or after the procedure (no PPM group); and 3) patients with prior PPM implantation (PPM before TAVI group). The study complied with the Declaration of Helsinki and was approved by both institutional ethics committees. All patients provided written, informed consent.

Data collection and endpoints. Adverse events were assessed in the hospital, and regular clinical follow-up was performed at 30 days and 12 months by means of a clinic visit or a standardized telephone interview. All suspected events were adjudicated by an unblinded clinical event committee consisting of cardiac surgeons and interventional cardiologists. Baseline clinical and procedural characteristics and all follow-up data were entered into a dedicated database, held at an academic clinical trials unit (Clinical Trials Unit Bern, Bern University Hospital, Bern, Switzerland) responsible for central data audits and maintenance of the database. The primary study endpoint was all-cause mortality at 12 months. Secondary endpoints included stroke, transient ischemic attack, myocardial infarction, as well as the composite of these major adverse cardiac events. Observed rates of all-cause mortality at 12 months were compared with an age-, sex-, and country-

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matched standard population. Clinical adverse events were adjudicated according to the Valve Academic Research Consortium criteria (20).

Definitions. Acute device success was considered to be successful vascular access, delivery, and deployment of the device and successful retrieval of the delivery system, correct position of the device with adequate hemodynamic performance (mean aortic valve gradient <20 mm Hg and absence of moderate or severe prosthetic valve aortic regurgitation) in the proper anatomic location with only 1 device used. Stroke was defined as rapid onset of a neurologic deficit of 24 hours' duration or longer or an event necessitating either therapeutic intervention or documentation of a new intracranial defect using neuroimaging. Transient ischemic attack was defined as new focal neurological deficit with rapid symptom resolution within 24 h and without evidence of tissue injury in neuroimaging studies. Periprocedural myocardial infarction was defined as ischemic symptoms or signs combined with elevated cardiac biomarkers (peak value more than 10 times the upper reference limit or a peak value more than 5 times the upper reference limit with new pathologic Q waves in at least 2 contiguous leads) within 72 h after the index procedure.

Statistical analysis. Patient demographics and procedural and postprocedural data were collected prospectively and were entered in a dedicated database held at Clinical Trials Unit Bern, Bern University Hospital, Bern, Switzerland. All statistical analyses were performed by statisticians of an academic clinical trials unit (D.H. and P.J., Clinical Trials Unit Bern, Bern University Hospital, Bern, Switzerland) using Stata 12 software (StataCorp LP, College Station, Texas). Continuous variables are presented as mean ± SD and are compared by means of analysis of variance. Categorical data are expressed as frequency and percentages and are compared using the chi-square and Fisher exact tests. Survival curves were constructed for each endpoint according to the Kaplan-Meier method and were compared by Cox regression, and the corresponding hazard ratios (HRs, with 95% confidence intervals [CIs]) with p values were reported at the 30-day and 12-month follow-up visits, respectively (so-called crude Cox regression analyses). Endpoints with 0 events in 1 or more treatment groups were

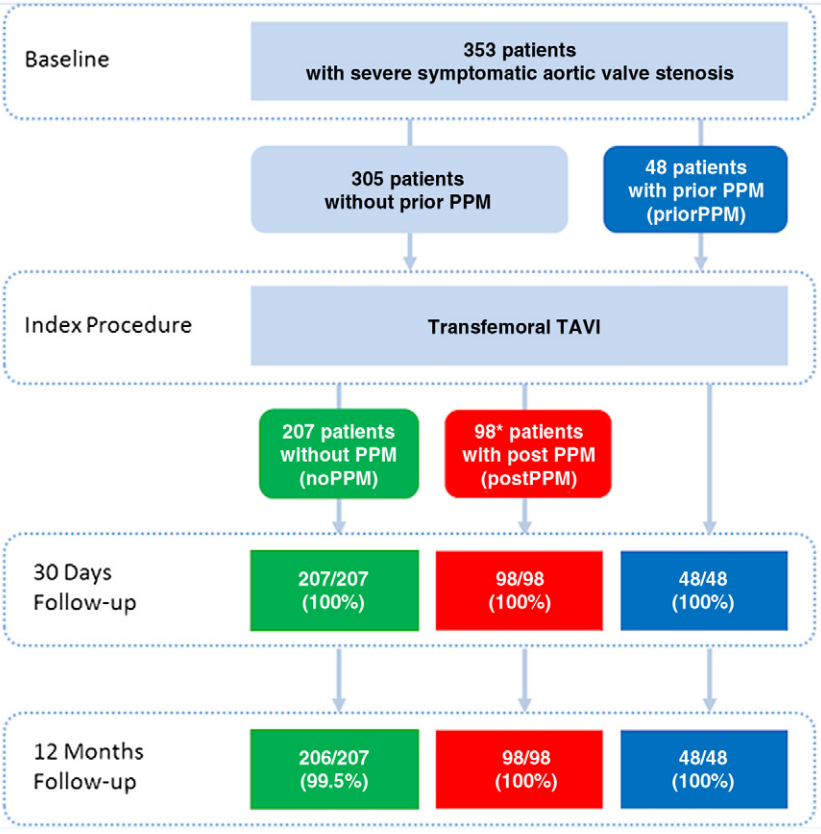

Figure 1 Diagram Showing Patient Flow

Diagram showing the flow of patients enrolled into the present study, including recruitment; allocation to the respective study group—patients with permanent pacemaker before transcatheter aortic valve implantation (TAVI) (PPM before TAVI), patients with new permanent pacemaker implantation after TAVI (PPM after TAVI), and patients without permanent pacemaker implantation (no PPM); and completeness of follow-up at 30 days and 12 months. *Including 3 patients with TAVI-associated PPM implantation on days 2, 3, and 7 prior to the TAVI procedure.

continuity corrected, and the corresponding risk ratios (with 95% confidence intervals) with Fisher exact tests and p values are reported at 30 days and 12 months of follow-up, respectively. The so-called adjusted Cox regression analyses of end points were performed by multinomial probit regression propensity score adjustment as follows (21). First, we fitted a multinomial probit regression model on the dependent variable treatment group (no PPM, PPM before TAVI, or PPM after TAVI) and the independent variables age, sex, type of prosthesis, hypertension, renal failure, prior stroke, and atrial fibrillation. Second, we extracted the estimated probability for each patient to fall into the no PPM group, based on these 7 independent variables. Third, this probability was entered as a propensity score covariate (degrees of freedom: 1) into the adjusted Cox regression analyses, and we report the adjusted HRs comparing treatment groups. Note that adjusted Cox regression analyses were possible only for end points with at least 1 event in each treatment group. Standardized mortality ratios were calculated for each treatment group, for males, for females, and for all patients separately using indirect standardization (i.e., compared with the Swiss and German national life tables per age and gender). All p values and confidence intervals are 2-sided. A p value <0.05 was considered statistically significant.

Results

Between August 2007 and March 2010, 353 consecutive patients underwent transfemoral TAVI at 2 institutions, with follow-up data available for 352 patients (99.7%) (Fig. 1). A total of 207 patients (58.6%) required no PPM during follow-up (no PPM group), and 48 patients (13.6%) already had a PPM before the procedure (PPM before TAVI group). The remaining 98 patients (27.8% of the overall study population, 32.1% of patients without PPM before TAVI) received a PPM within 30 days of TAVI (PPM after TAVI group, 29.2% of patients with MCV, 14.7% of patients with ESP). The indications for TAVI-related PPM implantation included high-degree AV block (62.2%), new-onset left bundle branch block with PR interval prolongation (21.4%), and slow atrial fibrillation (16.3%). Three patients included in the PPM after TAVI group had received a PPM immediately before undergoing TAVI in a prophylactic fashion because of the presence of left bundle branch block with marked PR interval prolongation in 2 cases and right bundle branch block with PR prolongation in 1 patient. The median preprocedural interval from pacemaker implantation to the index TAVI procedure in these patients was 3 days (range: 2 to 7 days). All 3 patients had complete AV block after the procedure. Postprocedural PPM implantation was performed at a median interval of 3 days (range: 0 to 22 days) (Fig. 2).

Patient population. Baseline characteristics according to PPM group are summarized in Table 1. The mean patient age was 82.6 ± 6.1 years, without significant differences between groups. Among patients in the PPM before TAVI group, comorbidities were more common compared with the other 2 groups, including presence of hypertension (PPM before TAVI group: 93.8%, no PPM group: 72.9%, PPM after TAVI group: 73.5%, p = 0.004), coronary artery disease (77.1%, 52.7%, and 58.2%, respectively, p = 0.009), prior myocardial infarction (31.3%, 14.5%, and 16.3%, respectively, p = 0.02), prior percutaneous coronary intervention (37.5%, 15.5%, and 19.4%, respectively, p = 0.002), renal failure (35.4%, 19.8%, and 19.4%, respectively, p = 0.049), and atrial fibrillation (43.8%, 22.7%, and 20.4%,

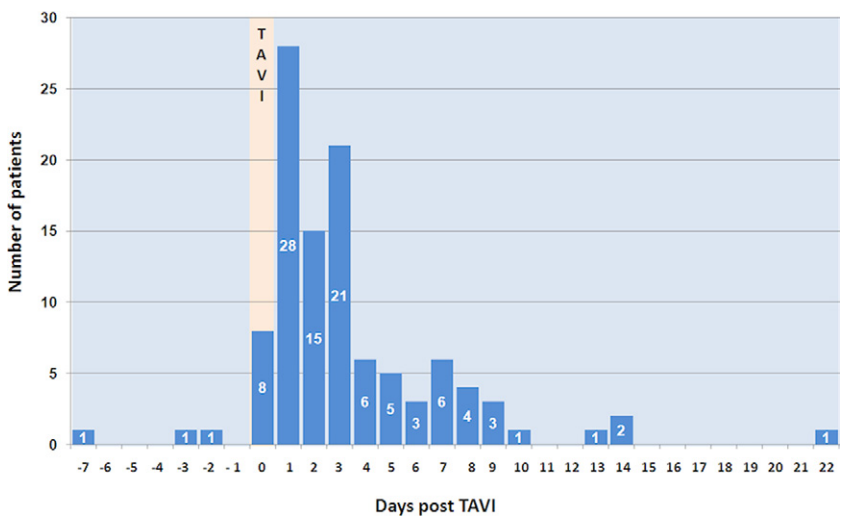

Figure 2 Frequency Distribution of Permanent Pacemaker Implantation Over Time

The **bars left of the beige bar** indicate preventive pacemaker implantation before trancatheter aortic valve implantation. Abbreviation as in Figure 1.

Table 1 Baseline Clinical and Echocardiographic Characteristics

	No PPM (n = 207)	PPM Before TAVI (n = 48)	PPM After TAVI (n = 98)	p Value
Age (yrs)	82.63 ± 6.22	82.61 ± 5.73	82.53 ± 5.99	0.99
Female	127 (61.4%)	24 (50.0%)	52 (53.1%)	0.21
Comorbidities				
Hypertension	151 (72.9%)	45 (93.8%)	72 (73.5%)	<0.004
Current smoker	27 (13.0%)	2 (4.2%)	14 (14.3%)	0.17
Diabetes	49 (23.7%)	15 (31.3%)	28 (28.6%)	0.45
Coronary artery disease	109 (52.7%)	37 (77.1%)	57 (58.2%)	<0.01
Pulmonary hypertension	42 (20.3%)	16 (33.3%)	30 (30.6%)	0.053
Renal failure	41 (19.8%)	17 (35.4%)	19 (19.4%)	0.049
Peripheral vasc. disease	37 (17.9%)	8 (16.7%)	25 (25.5%)	0.25
Prior MI	30 (14.5%)	15 (31.3%)	16 (16.3%)	0.021
Prior PCI	32 (15.5%)	18 (37.5%)	19 (19.4%)	<0.003
Prior CABG	39 (18.8%)	14 (29.2%)	29 (29.6%)	0.067
Prior stroke	13 (6.3%)	4 (8.3%)	10 (10.2%)	0.48
Atrial fibrillation	47 (22.7%)	21 (43.8%)	20 (20.4%)	<0.005
Symptoms				
NYHA functional class III/IV	146 (71.6%)	40 (83.3%)	77 (81.1%)	0.086
Risk assessment				
Log EuroSCORE	22.77 ± 14.42 (200%)	28.37 ± 15.91 (47%)	27.76 ± 15.23 (98%)	<0.01
Echocardiography before TAVI				
LVEF, %	52.21 ± 14.82 (207%)	48.50 ± 14.07 (48%)	49.27 ± 16.37 (98%)	0.15
Mean gradient, mm Hg	45.03 ± 16.62 (173%)	40.92 ± 17.12 (40%)	45.32 ± 14.97 (76%)	0.32
AVA, cm^2	0.62 ± 0.18 (177%)	0.64 ± 0.18 (41%)	0.62 ± 0.17 (83%)	0.83

Values are mean ± SD, n (%), mean ± SD (%).

CABG = coronary artery bypass graft; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PPM = permanent pacemaker; TAVI = transcatheter aortic valve implantation.

respectively, p = 0.005). Accordingly, the mean logistic EuroSCORE was somewhat higher in the PPM before TAVI group (28.4 ± 15.9%) compared with the no PPM and PPM after TAVI groups together (24.4 ± 14.9%, p = 0.09). There were no differences between the groups with regard to baseline symptom status and echocardiographic characteristics, including aortic valve area, mean valve gradient, and left ventricular ejection fraction.

Procedural results. Procedural characteristics and results are summarized in Table 2. All patients underwent transfemoral TAVI with either the MCV (90.4%, 319 of 353) or the ESP (9.6%, 34 of 353) prosthesis. Acute device success was similar in all 3 groups, ranging from 96.6% to 97.9%. In 1 patient, acute conversion to surgery was required after embolization of an ESP. Myocardial wire perforation occurred in 1 patient before device implantation, and sequential double-valve implantation was required in 9 patients to correct misplaced or functionally unsatisfactory results after implantation of the first prosthesis.

Clinical outcomes. Clinical outcomes at 30 days and 12 months of follow-up are shown in Table 3. All-cause mortality at 30 days and 12 months was 6.2% and 19.0%, respectively, without differences among the no PPM group

Table 2 Procedural Data and Acute Echocardiographic Outcomes

	No PPM (n = 207)	PPM Before TAVI (n = 48)	PPM After TAVI (n = 98)	p Value
Procedure				
Acute device success	200 (96.6%)	47 (97.9%)	95 (96.9%)	1.00
Conversion to surgery	1 (0.5%)	0 (0.0%)	0 (0.0%)	1.00
Valve in valve/sequential	4 (1.9%)	2 (4.2%)	2 (2.0%)	0.52
Type of prosthesis implanted				0.03
CoreValve	180 (87.0%)	46 (95.8%)	93 (94.9%)	
Edwards	27 (13.0%)	2 (4.2%)	5 (5.1%)	
After TAVI				
Mean gradient, mm Hg	8.56 ± 4.55 (188%)	7.13 ± 4.28 (46%)	8.92 ± 3.84 (96%)	0.06
Aortic regurgitation (2 or 3 grade)	49 (25.5%)	8 (16.7%)	20 (20.6%)	0.38
AVA, cm^2	1.69 ± 0.46 (139%)	1.66 ± 0.37 (39%)	1.70 ± 0.53 (69%)	0.90

Values are n (%) or mean ± SD (%).

Abbreviations as in Table 1.

Table 3 Clinical Outcomes at 30 Days and 12 Months of Follow-Up

	No PPM (n = 207)	Prior PPM (n = 48)	Post PPM (n = 98)	PPM Before TAVI vs. No PPM HR (95% CI)		PPM After TAVI vs. No PPM HR (95% CI)		p Value for Difference Between Groups	
				Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
30 days of follow-up									
All-cause death	14 (6.8%)	2 (4.2%)	7 (7.1%)	0.60 (0.14–2.64)	0.56 (0.12–2.53)	1.06 (0.43–2.62)	1.03 (0.41–2.56)	0.77	0.73
MI	2 (1.0%)	0 (0.0%)	0 (0.0%)	0.85 (0.04–17.37)	NA	0.42 (0.02–8.61)	NA	1.00	NA
Stroke	8 (3.9%)	0 (0.0%)	2 (2.0%)	0.25 (0.01–4.27)	NA	0.53 (0.11–2.43)	NA	0.48	NA
TIA	1 (0.5%)	1 (2.1%)	0 (0.0%)	4.29 (0.27–67.4)	NA	0.70 (0.03–17.0)	NA	0.33	NA
All-cause death or stroke	18 (8.7%)	2 (4.2%)	8 (8.2%)	0.46 (0.11–1.99)	0.38 (0.09–1.70)	0.93 (0.40–2.13)	0.86 (0.37–2.00)	0.58	0.45
All-cause death, stroke, or MI	19 (9.2%)	2 (4.2%)	8 (8.2%)	0.44 (0.10–1.87)	0.35 (0.08–1.54)	0.87 (0.38–1.99)	0.80 (0.35–1.84)	0.53	0.37
12 months of follow-up									
All-cause death	37 (18.0%)	11 (22.9%)	19 (19.4%)	1.28 (0.65–2.50)	1.18 (0.59–2.36)	1.09 (0.63–1.89)	1.06 (0.60–1.84)	0.77	0.90
MI	5 (2.4%)	0 (0.0%)	1 (1.0%)	0.39 (0.02–6.88)	NA	0.42 (0.05–3.55)	NA	0.6	NA
Stroke	8 (3.9%)	0 (0.0%)	2 (2.0%)	0.25 (0.01–4.27)	NA	0.53 (0.11–2.43)	NA	0.48	NA
TIA	2 (1.0%)	1 (2.1%)	1 (1.0%)	2.18 (0.20–24.09)	NA	1.05 (0.10–11.63)	NA	0.8	NA
All-cause death or stroke	40 (19.4%)	11 (22.9%)	20 (20.4%)	1.16 (0.59–2.25)	1.03 (0.51–2.05)	1.05 (0.61–1.79)	1.00 (0.58–1.72)	0.91	1.00
All-cause death, stroke, or MI	42 (20.4%)	11 (22.9%)	21 (21.4%)	1.09 (0.56–2.12)	0.94 (0.47–1.87)	1.04 (0.61–1.75)	0.98 (0.58–1.66)	0.97	0.98

Values are n (%) unless otherwise specified.
CI = confidence interval; HR = hazard ratio; MI = myocardial infarction; NA = not available; TIA = transient ischemic attack; other abbreviations as in Table 1.

(18.0%), PPM before TAVI group (22.9%, adjusted HR versus no PPM group: 1.18, 95% confidence interval [CI] 0.59 to 2.36), and PPM after TAVI group (19.4%, adjusted HR versus no PPM group: 1.06, 95% CI: 0.60 to 1.84) (Fig. 3). Strokes occurred in 2.8% of patients at 30 days and 12 months. The composite endpoint of death, stroke, or myocardial infarction at 12 months was 20.4% (no PPM), 22.9% (PPM before TAVI), and 21.4% (PPM after TAVI, p = 0.97). The rates for stroke, transient ischemic attack, and myocardial infarction were low, limiting the precision of estimates of HRs for these parameters (Table 3).

Comparing the HRs for death as well as the composite endpoints death or stroke and death, stroke, and myocardial infarction between PPM after TAVI and no PPM patients, respectively, we observed similar risks in crude and adjusted analyses. Results also were consistent among most subgroups, with the exception of atrial fibrillation, in which the subgroup patients with PPM after TAVI compared with those with no PPM trended to have a higher risk of death, stroke, and myocardial infarction in the adjusted analyses (HR: 2.26, 95% CI: 0.85 to 5.98, p = 0.08 for interaction).

Comparing the observed mortality of all study groups with an age, gender, and region-matched population, adjusted HRs for death were 2.24 (95% CI: 1.62 to 3.09) for the no PPM group, 2.75 (95% CI: 1.52 to 4.97) for the PPM before TAVI group, and 2.37 (95% CI: 1.51 to 3.72) for the PPM after TAVI group, with a trend for the highest risk among patients in the PPM before TAVI group (Fig. 4).

Discussion

The principal findings of the present study can be summarized as follows: 1) AV-conduction disturbances requiring PPM implantation after TAVI remain common, particularly after implantation of the self-expanding MCV prosthesis; 2) all-cause mortality and other major cardiac and cerebrovascular events were observed with similar frequency through 12 months among patients requiring PPM implantation after TAVI compared with patients without the need of PPM and those with a PPM before TAVI; and 3) regardless of PPM implantation, all-cause mortality increased more than 2-fold among patients with severe aortic stenosis who were undergoing TAVI as compared with an age-, sex-, and region-matched standardized population.

PPM implantation after transfemoral TAVI seems rather innocuous compared with other adverse events complicating TAVI. This finding is of importance because PPM implantation among patients undergoing TAVI is not uncommon. Recently reported PPM implantation rates range from 5% to 40% (9–19), with an increased incidence among patients receiving the self-expanding MCV prosthesis (18% to 43%) (10,12–15,18,19) as compared with patients treated with the balloon-expandable ESP (5% to 22%) (9–12,15–17,19). Differences in device designs may explain this finding, such as a deeper extension of the stent frame into the left

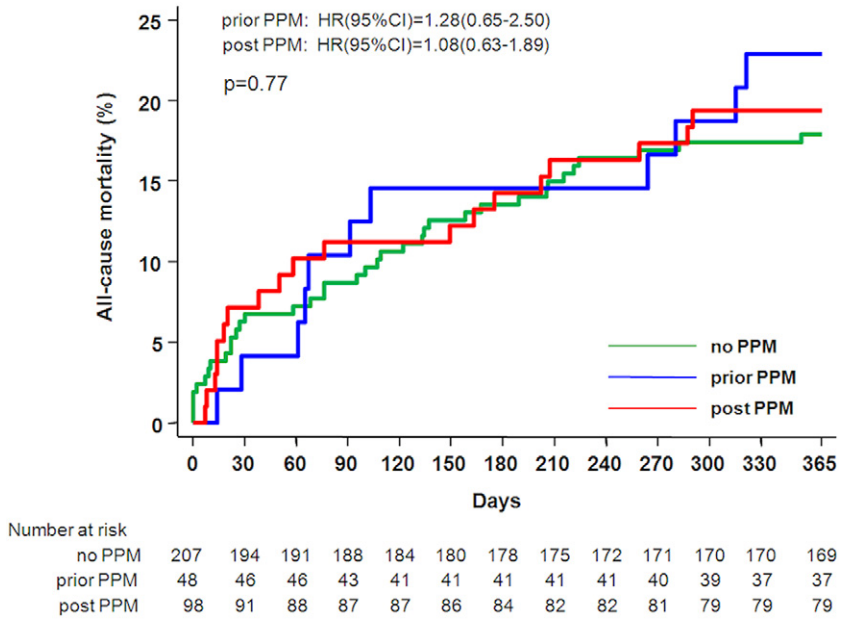

Figure 3 **Cumulative Incidence of All-Cause Mortality Through 1 Year According to Study Group**

The **blue line** represents outcomes of patients with permanent pacemaker implantation before TAVI, the **red line** represents patients with the need for permanent pacemaker implantation after TAVI, and the **green line** represents patients without permanent pacemaker implantation. CI = confidence interval; HR = hazard ratio; other abbreviations as in Figure 1.

ventricular outflow tract and the self-expanding properties of the MCV prosthesis, maintaining a steady radial force on the annular and subendocardial tissue. In addition, because of the lack of established and uniformly applied criteria for TAVI-related PPM implantation as well as heterogeneous implantation techniques (i.e., intended target depth of prosthesis implant, balloon and device sizing, and so on), the currently reported PPM rates differ substantially among different sites and studies. In our study, we observed a pacemaker rate of 27.8% (14.7% for ESP, 29.2% for MVP), which remains high but is well in line with previous reports. The predominant indication of TAVI-related PPM implantation was the development of a complete AV block, similarly consistent with previous findings (14).

Several predictors of severe AV-conduction disturbances necessitating PPM implantation after TAVI have been described, including right bundle branch block at baseline, deep valve implantation (>6 mm below the annular plane), increased septal wall thickness, noncoronary cusp thickness, and degree of calcification (12,22–24). However, the actual mechanisms are not understood fully. Left bundle branch block is the most commonly observed conduction disorder after TAVI (12,25), most likely induced by direct mechanical injury to the subvalvular region, which houses critical parts of the left-sided conduction system. Consequently, patients with pre-existing right bundle branch block are at particular risk of having complete heart block after TAVI. Prophylactic PPM implantation before TAVI in selected patients with predisposing electrocardiographic findings therefore is common practice in several centers and amounted to 3% of all TAVI-related PPM implantations in the present study.

Patients undergoing TAVI are a priori characterized by an exceptionally high risk profile because of the presence of severe cardiac pathological features in conjunction with other noncardiac comorbidities. Taking into account that the presence of AV-conduction disturbances is an expression of the severity of underlying cardiac disease predictive of adverse outcome (26), the occurrence of a conduction defect among patients undergoing TAVI theoretically may suggest a particularly harmful event. Indeed, in the present study, patients with previous PPM implantation before TAVI had a higher risk profile, with notable differences in various baseline characteristics, including hypertension, coronary artery disease, myocardial infarction, prior percutaneous coronary intervention, renal failure, and atrial fibrillation compared with patients without a history of PPM implantation. Notwithstanding, clinical outcome in terms of all-cause mortality through 12 months did not differ significantly among the 3 groups, regardless of the pacing status and compare favorably, with reported rates ranging from 24% to 31% in this type of high-risk population undergoing TAVI (16,17,27,28). Compared with a sex- and age-matched standardized population, patients with severe aortic stenosis undergoing transfemoral TAVI still had an increased risk of mortality that seemed to be more than twice as high as that in the general population, presumably because of the increased baseline risk profile. Interestingly,

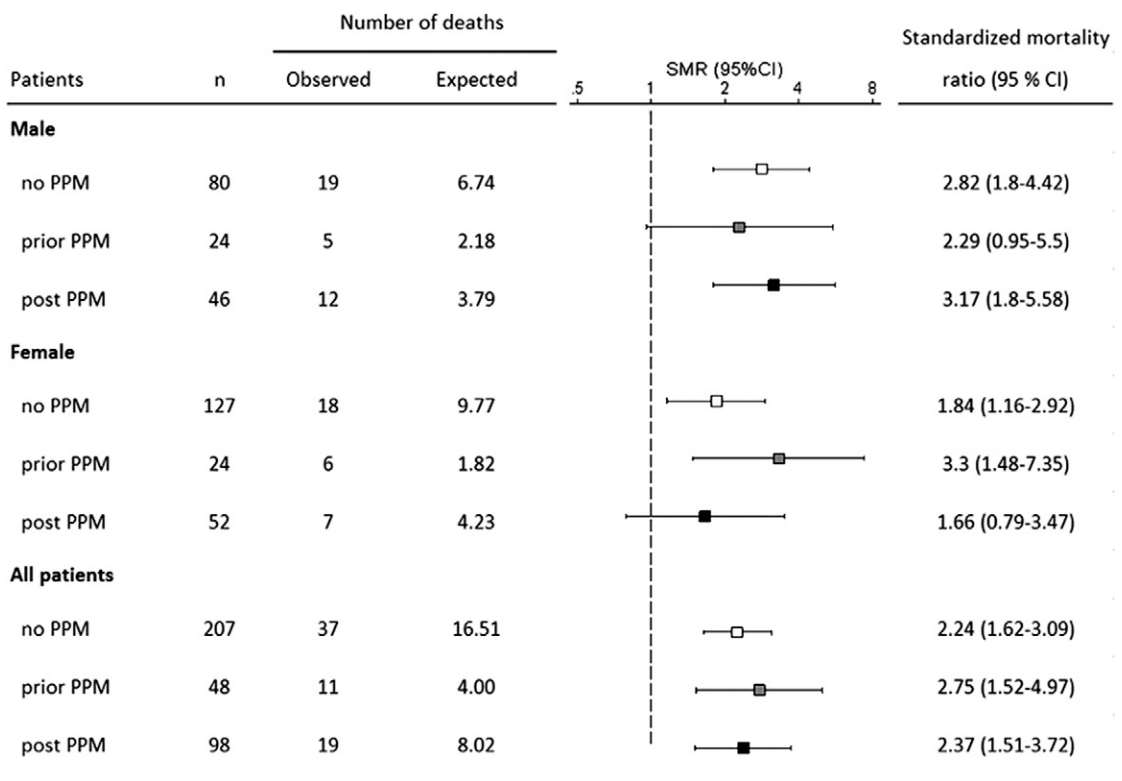

Figure 4 **Standardized Mortality Ratios With 95% CIs per Study Group for the Overall Population and According to Sex**

Standardized mortality ratio (SMR) is the ratio of observed to expected number of deaths comparing study patients with a reference population. SMR >1 indicates the group had higher rates of death than expected for an age-, sex-, and country-matched (Switzerland or Germany) reference population. Abbreviations as in Figures 1 and 3.

patients with previous PPM implantation, who had a significantly higher baseline risk than the other 2 study groups, showed the highest relative risk increase at 12 months in the present study. An extended follow-up period beyond 12 months may be necessary to reveal a significant difference for this particular population. Conversely, we did not find any indicators that patients without a history of PPM implantation who required permanent pacing after TAVI exhibit a different prognosis compared with patients without the need for pacing, which constitute 2 groups with similar baseline characteristics. It therefore may be speculated that spontaneous occurrence of AV-conduction disorders constitutes an indicator for adverse outcome driven by the extent of underlying cardiac disease, whereas procedure-related AV-conduction disorders after mechanical stress, as observed during various steps of the TAVI procedure, confers a more favorable long-term prognosis.

Several additional aspects associated with TAVI-related PPM implantations deserve consideration. PPM implantation adds technical complexity and considerable cost and may result in prolonged hospitalization (6). Apart from this, the impact of TAVI-related PPM implantation on outcomes such as functional patient status, atrial and ventricular remodeling, and rhythm profile deserves further detailed evaluation. Moreover, the implantation of single lead pacemakers with ventricular pacing modes in patients older than a certain age limit, which is common practice with supporting evidence (29), may be called into question in the TAVI patient population in view of the preload-dependent filling properties of the hypertrophic and restrictive ventricles, particularly in the presence of preserved atrial function.

Study limitations. Most patients enrolled in this study received the self-expanding MCV, whereas only 10% were treated with a balloon-expandable ESP. Therefore, the results may be affected by this unequal distribution, although we corrected for this confounder in adjusted analyses. In addition, only patients with transfemoral TAVI have been included in the present analysis, and similar studies may be necessary for alternative access routes such as transapical, subclavian, or direct aortic access. Furthermore, this study was not designed to prove the obvious benefit of pacing in patients with severe TAVI-related conduction disorders, comparing patients receiving a PPM versus those not receiving a PPM under this condition, but rather to analyze the impact of PPM implantation in patients with TAVI-related conduction disorders compared with patients without periprocedural PPM implantation resulting from an absence of TAVI-related PPM-requiring conduction disorders. Finally, one carefully has to interpret the negative results of the present study in the context of the event rates

within a relatively small, 2-center patient cohort, which certainly has to be confirmed in a larger patient population with a prolonged follow-up period.

Conclusions

Although prognosis remains impaired compared with an age-, sex-, and origin-matched standardized population, periprocedural PPM implantation does not seem to affect clinical outcomes adversely among patients undergoing transfemoral TAVI.

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Key Words: clinical outcome ■ pacemaker implantation ■ transcatheter aortic valve implantation.