Pacemaker implantation after surgical aortic valve replacement and balloon-expandable transcatheter aortic valve implantation: Incidence, predictors, and prognosis

Davide Gabbieri, MD, PhD,[1] Italo Ghidoni, MD,[1] Greta Mascheroni, MD,[1] Matteo Chiarabelli, RN, MSN,[2] Giuseppe D'Anniballe, MD,[1] Paolo Pisi, MD,[1] Marco Meli, MD,[1] Clorinda Labia, MD,[1] Alice Barbieri, CP,[3] Francesca Spina, CP,[3] Federico Giorgi, MD[4]

From the [1]Cardiac Surgery Unit, Department of Medical-Surgical Cardiology, Hesperia Hospital Modena, Modena, Italy, [2]Edwards Lifesciences, Milan, Italy, [3]Hospital Solutions, Bologna, Italy, and [4]Cardiac Surgery Unit, Department of Surgical, Medical and Molecular Pathology and Critical Care, Azienda Ospedaliero-Universitaria Pisana, University of Pisa, Pisa, Italy.

BACKGROUND Permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI) remains a significant challenge despite new-generation devices.

OBJECTIVES This study aimed to identify predictors of PPI during preoperative evaluation and assess its mid-term impact in a single-center, real-world setting.

METHODS From 2010 to 2020, 1486 patients with aortic stenosis underwent surgical aortic valve replacement or TAVI using balloon-expandable transcatheter heart valves. The PPI rate was estimated using the hospital discharge record for each patient in the Emilia-Romagna region.

RESULTS The 30-day incidence of PPI in the TAVI group was 3.4%. While 30-day PPI did not affect overall survival (log-rank, P = .494 NS), it predicted rehospitalization due to cardiac causes (hazard ratio 10.28; 95% confidence interval [CI] 95% 3.41–31.00; P <.001). Calcifications in the leaflet (odds ratio [OR] 4.66; 95% CI 1.41–15.47; P = .012), left ventricular outflow tract (OR 4.51; 95% CI 1.48–13.76; P = .008), and device landing zone (OR 2.52; 9% CI 0.86–7.40; P = .093) were associated with a higher risk of PPI.

CONCLUSION A low 30-day PPI incidence was observed, primarily because of the exclusive use of balloon-expandable SAPIEN transcatheter heart valves and high implantation techniques. Baseline factors such as leaflet, left ventricular outflow tract, and device landing zone calcifications, as well as right bundle branch block, highlight the need for comprehensive preoperative analysis to reduce PPI incidence and mitigate its associated longer hospital stays and rehospitalizations due to cardiac causes.

KEYWORDS TAVI; SAVR; Permanent pacemaker implantation; Leaflet; LVOT; DLZ; Calcifications

(Heart Rhythm O2 2025;6:259–272)

Introduction

Over the last decade, transcatheter aortic valve implantation (TAVI) has revolutionized the management of symptomatic severe aortic valve stenosis (AS). Initial TAVI trials demonstrated its effectiveness in inoperable and high-risk patients. Subsequently, excellent results in intermediate- and low-risk patients have broadened TAVI indications. The current European and American guidelines recommend both transfemoral TAVI and surgical aortic valve replacement (SAVR) as class I treatments for most patients with severe symptomatic AS.[1,2]

However, from the outset, it became apparent that new-onset conduction disturbances were more frequent with TAVI than with surgery, making postprocedural pacemaker (PM) implantation the "Achilles' heel" of the TAVI procedure.[3] The development of new-generation devices has significantly reduced this gap, though it still exists.[4] Available data are insufficient to determine whether PM implantation affects patients' mid- and long-term outcomes.[5,6] As TAVI use expands to younger and low-risk patients with longer life expectancies, understanding the impact of permanent PM implantation (PPI) after TAVI becomes increasingly

Address reprint requests and correspondence: Dr Federico Giorgi, Cardiac Surgery Unit, Department of Surgical, Medical and Molecular Pathology and Critical Care, Azienda Ospedaliero-Universitaria Pisana, University of Pisa, Via Paradisa 2, 56126 Pisa, Italy. E-mail address: giorgifederico97@gmail.com.

2666-5018/

https://doi.org/10.1016/j.hroo.2025.01.001

KEY FINDINGS

- Balloon-expandable SAPIEN (Edwards Lifesciences, Irvine, CA) transcatheter heart valves have resulted in a low 30-day permanent pacemaker implantation (PPI) rate of 3.4%. In addition, performing a high implantation technique has been confirmed to reduce the risk of PPI.
- PPI has been strongly associated with rehospitalizations due to cardiac causes during follow-up; its influence on overall survival has not been reported; and it might require further investigation.
- Preoperative computed tomography scan factors, such as leaflet, left ventricular outflow tract, and device landing zone calcifications quantified using a quantitative method, have emerged as predictive for PPI.

important. Recently, some authors have argued that early PM implantation after TAVI may be unnecessary, showing a low rate of PM stimulation during follow-up.[7]

In this retrospective study, we analyzed mid- and long-term mortality after SAVR and TAVI with balloon-expandable (BE) technology. In addition, we investigated the anatomical and echocardiographic predictors of 30-day PM implantation after TAVI and the influence of PM implantation on patient outcomes.

Methods

Patient source and data collection

In Hesperia Hospital Modena, Italy, 1486 consecutive patients with native AS underwent SAVR with all types of commercially available biological and mechanical prostheses or TAVI with BE SAPIEN (Edwards Lifesciences, Irvine, CA) transcatheter heart valves (THVs) from February 2010 to December 2020. Exclusion criteria were active endocarditis, previous SAVR or TAVI, mild or moderate AS, asymptomatic AS, or isolated aortic valve regurgitation. Since 2010, inoperable or high-risk patients, after Heart Team discussion, were selected for TAVI, similarly to PARTNER 1A and 1B[8,9]; moderate- or low-risk patients were considered for TAVI in case of multiple comorbidities or severe frailty. Demographic data, comorbidities, preoperative status, procedural and in-hospital outcomes, and postoperative and long-term outcomes were collected in a mean follow-up of 5.7 years. All patients signed written informed consent, and the research reported in this article adhered to Helsinki Declaration.

Preoperative variables

Data were collected from RERIC Hesperia Hospital. The "Regione Emilia Romagna Interventi Cardiochirurgia Registry" is a prospective regional database collecting preoperative, intraoperative, and postoperative data from patients undergoing cardiac surgical procedures in the 6 regional cardiac surgery departments (academic hospitals: n=2; private hospitals: n=4). The registry management is centralized; every 3 months, the Cardiac Surgery Department, Hesperia Hospital, is required to dispatch the data to the Regional Health Care Agency for quality/completeness control and to monitor cardiac surgery results in the Emilia-Romagna region. Demographic data, such as sex, age, and residency region at the time of the procedure, and clinical data, such as medical history, including other cardiovascular risk factors (diabetes mellitus, obesity, hypertension, dyslipidemia, and smoking habit) or other extracardiac conditions (chronic obstructive pulmonary disease [COPD], frailty, chronic kidney disease, whether on dialysis or not, cerebrovascular events, and extracardiac arteriopathy), were considered.

Preoperative, procedural, and postoperative variables are listed in Tables 1, 2 and 3, respectively.

The length of stay, 30-day mortality, and in-hospital mortality were recorded. Using the ANPR (Anagrafe Nazionale della Popolazione Residente) database, we were able to obtain the date and cause of death. Follow-up of the patients living in Emilia-Romagna was possible because of the affiliation of Hesperia Hospital Modena to the UNIMORE TAVI-nAVEN study (Sostituzione valvolare aortica per via percutanea TAVI – Area Vasta Emilia Nord), approved by the Institutional Review Board of Area Vasta Emilia Nord on January 4, 2019, with protocol AOU 0000184/19. Using the hospital discharge record (scheda dimissione ospedaliera), the cardiovascular disease diagnosis ICD 9 codes (390–459), and cardiovascular procedure ICD 9 codes (35–39), especially 37.8 "Insertion, replacement, removal, and revision of pacemaker device," and excluding Emilia-Romagna residents who underwent PPI at the time of the index procedure, we could freedom from PM implantation estimate for each patient living in Emilia-Romagna (Figure 1). The impact of PM implantation on rehospitalizations for stroke, heart failure, and all-cardiac causes (Valve Academy Research Consortium 3 definitions[10]) was evaluated. Angiographic and computed tomography parameters were identified and evaluated for their influence on PM implantation after TAVI.

Protocols for angiographic analysis and computed tomography analysis are reported in the Online Supplement.

Leaflet (global and by cusp), left ventricular outflow tract (LVOT), and device landing zone (DLZ) calcifications were categorized as significant or not, according to other previous studies.[11–13] Leaflet calcification was considered significant if >235 mm^3 and if >4528 Agatston unit (AU). A >10-mm^3 threshold was used for LVOT calcification, while DLZ calcification had a >1000-AU cutoff.

Statistical analysis

Continuous variables are reported as mean ± SD or as median, while categorical variables are expressed as frequency and percentage. Differences between groups for continuous variables were tested using the Student *t* test (unpaired 2-tailed *t* test) or Mann-Whitney test, as appropriate, while

Table 1 Baseline parameters

Preoperative variable	TAVI (n = 437 [29.4%])	SAVR (n = 1049 [70.6%])	*P*
EuroSCORE I (logistic)	15.9 ± 9.4	7.0 ± 4.9	<.001
EuroSCORE II	5.2 ± 4.0	2.0 ± 1.7	<.001
STS-PROM score	4.5 ± 2.8	2.0 ± 1.2	<.001
Age (y), mean	82.2 ± 6.2	72.7 ± 9.7	<.001
Age (y), median	83.2	75.0	<.001
Female	235 (53.8)	498 (47.5)	.027
BMI (kg/m^2)	27.3 ± 5.0	27.5 ± 5.0	.4292
BSA (m^2)	1.7 ± 0.2	1.8 ± 0.2	<.001
Diabetes	101 (23.1)	194 (18.5)	.042
Hypertension	433 (99.1)	993 (94.7)	<.001
Hypercholesterolemia	296 (67.7)	659 (62.8)	.072
Dialysis	6 (1.4)	8 (0.8)	.267
Preoperative creatinine (mg/dL)	1.5 ± 7.5	1.1 ± 3.6	.145
Stroke	19 (4.4)	21 (2)	
TIA	23 (5.3)	32 (3.1)	.004
Smoking habit	167 (38.2)	544 (51.9)	<.001
COPD	76 (17.4)	60 (5.7)	<.001
Extracardiac arteriopathy	118 (27.0)	152 (14.5)	<.001
Bicuspid anatomy of the aortic valve	7 (1.6)	182 (17.4)	<.001
Previous cardiac surgery	61 (14.0)	29 (2.8)	<.001
Previous CABG	49 (11.2)	6 (0.6)	<.001
Previous surgery of cardiac valves	14 (3.2)	18 (1.7)	.072
Previous PCI	216 (49.4)	111 (10.6)	<.001
History of myocardial infarction	63 (14.4)	37 (3.5)	<.001
Recent myocardial infarction (EuroSCORE II definition)	14 (3.2)	18 (1.7)	.072
CAD	260 (59.5)	150 (14.3)	<.001
Preoperative AF	83 (19.0)	100 (9.5)	<.001
NYHA class III or IV	383 (87.6)	304 (29.0)	<.001
EF < 30%	113 (25.9)	185 (17.6)	<.001
Aortic regurgitation	82 (18.8)	119 (11.3)	<.001
Mitral regurgitation	76 (17.4)	52 (5.0)	<.001
Tricuspid regurgitation	69 (15.8)	27 (2.6)	<.001
Pulmonary hypertension	22 (5.0)	11 (1.1)	<.001
PM dependency	30 (6.9)	13 (1.2)	<.001
Liver cirrhosis	3 (0.7)	5 (0.5)	.700
Active cancer	5 (1.1)	11 (1.1)	.871
Senile aortic valve degeneration	431 (98.6)	1009 (96.2)	.019
Degeneration of the tricuspid valve	3 (0.7)	33 (3.1)	<.001
Degeneration of the bicuspid valve	3 (0.7)	7 (0.7)	<.001
Aortic valve area (cm^2)	0.7	0.7	ns
Mean aortic transvalvular gradient (mm Hg)	49	48.5	ns

Values are presented as mean ± SD, median, or n (%).

AF = atrial fibrillation; BMI = body mass index; BSA = body surface area; CABG = coronary artery bypass graft; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; EF = ejection fraction; NS = not significant; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PM = pacemaker; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; TIA = transient ischemic attack.

comparisons for categorical variables were done using the χ^2 test or Fisher exact test, as appropriate.

All preoperative and intraoperative variables were first analyzed using univariate analysis (unpaired 2-tailed *t* test, Mann-Whitney test, χ^2 test, or Fisher exact test, when appropriate) to determine whether any single factor influenced mortality. Variables that achieved $P < .05$ in the univariate analysis were examined using multivariable analysis by forward stepwise logistic regression to evaluate independent risk factors for mortality. Survival curves were estimated at 1, 2, 5, and 8 years using the Kaplan-Meier method and compared using the log-rank test. To adjust survival outcomes for possible influencing factors, Cox models were built and hazard ratios (HRs) have been calculated.

Univariate logistic regression analysis was then applied to the TAVI cohort to relate a broad range of preoperative parameters to the study end point (ie, 30-day PM implantation after TAVI). Variables with a *P* value of <.05 were selected and included in a multivariable regression model using forward stepwise selection to identify the covariates with the highest predictive value. The associations were expressed as odds ratio (OR) with their 95% confidence interval (CI). All tests were 2-sided, and *P* values < .05 were considered statistically significant.

Table 2 Procedural variables

Procedural variable	TAVI (n = 437 [29.4%])	SAVR (n = 1049 [70.6%])
Mechanical valve		62 (5.9)
Bioprosthetic valve		987 (94.1)
Cross-clamp time (min)		60.3 ± 17.9
ECC time (min)		83.0 ± 21.8
Edwards SAPIEN THV	9 (2.1)	
Edwards SAPIEN XT THV	123 (28.1)	
SAPIEN 3 THV	213 (48.7)	
SAPIEN 3 Ultra THV	92 (21.1)	
Transfemoral approach	266 (60.9)	
Transapical approach	105 (24)	
Transaortic approach	60 (13.7)	
Transaxillary approach	6 (1.4)	
20-mm THV	6 (1.4)	
23-mm THV	173 (39.6)	
26-mm THV	187 (42.8)	
29-mm THV	71 (16.2)	

Values are presented as mean ± SD or n (%).

ECC = extracorporeal circulation; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; THV = transcatheter heart valve.

To evaluate the discriminatory utility of some features, a sensitivity analysis using a receiver operator characteristic curve (ROC curve) for the risk of PPI after TAVI was performed. The area under the curve was used to summarize the performance into a single measure. An area under the curve >0.70 was considered good. Statistical analysis was performed using STATA software (StataSE.19, StataCorp, College Station, TX).

Results

Preoperative variables

The mean EuroSCORE I, EuroSCORE II, and STS-PROM score in TAVI and SAVR were 15.9% vs 7%, 5.2% vs 2%, and 4.5% vs 2%, respectively. The mean age of TAVI and SAVR populations were 82.2±6.2 vs 72.7±9.7 years, respectively. Pulmonary hypertension (pulmonary artery pressures ≥60 mm Hg), COPD, coronary artery disease, extracardiac arteriopathy, PM implantation, previous cardiac surgery, permanent atrial fibrillation, moderate-severe mitral regurgitation, worse New York Heart Association (NYHA) class (III or IV), and reduced ejection fraction (EF < 30% and/or 30% < EF < 50%) were more frequent in the TAVI cohort. In the SAVR cohort, smoking habit and bicuspid anatomy of the aortic valve were more frequent. Regarding aortic valve area (0.7 cm^2 vs 0.7 cm^2; P = .65) and mean aortic transvalvular gradient (48.5 mm Hg vs 49 mm Hg; P = .73), no differences were observed (Table 1).

Intraoperative variables

The SAPIEN 3 THV was implanted in about half the cases (n=213 [48.7%]), followed by the Edwards SAPIEN XT THV (n=123 [28.2%]), the SAPIEN 3 Ultra THV (n=92 [21.1%]), and the Edwards SAPIEN THV (n=9 [2.1%]). We chose the 26-mm THV in 42.8% of cases (n=187),

Table 3 Postoperative variables

Postoperative variable	TAVI (n = 437 [29.4%])	SAVR (n = 1049 [70.6%])	*P*
Blood transfusion	166 (38.0)	529 (50.4)	<.001
Mechanical ventilation time (h)	13.1 ± 58.8	14 ± 62.4	<.001
ICU length of stay (d)	1.7 ± 3.5	2.2 ± 6.6	.129
Acute renal failure stage 1	9 (2.1)	25 (2.4)	.751
Acute renal failure stage 2	2 (0.5)	5 (0.5)	
Acute renal failure stage 3	2 (0.5)	11 (1.1)	
Minor bleeding	4 (0.9)	5 (0.5)	.017
Major bleeding	17 (3.9)	17 (1.6)	
Minor vascular complications	31 (7.1)	0 (0)	<.001
Major vascular complications	9 (2.1)	0 (0)	
Percutaneous vascular complications	13 (3.0)	0 (0)	
All stroke	2 (0.5)	8 (0.8)	.732
TIA	1 (0.2)	4 (0.4)	.999
Postoperative AF	12 (2.8)	332 (31.7)	<.001
PM implantation	10 (2.3)	24 (2.3)	.999
In-hospital length of stay days, mean	9.6 ± 12.0	11.6 ± 11.9	.004
In-hospital length of stay days, median	7	9	<.001
Valve embolization	1 (0.23)		
Annular injury	2 (0.46)		
Coronary obstruction	3 (0.69)		
More than moderate perivalvular leak	9 (2.1)		

Values are presented as mean ± SD, median, or n (%).

AF = atrial fibrillation; ICU = intensive care unit; PM = pacemaker; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; TIA = transient ischemic attack.

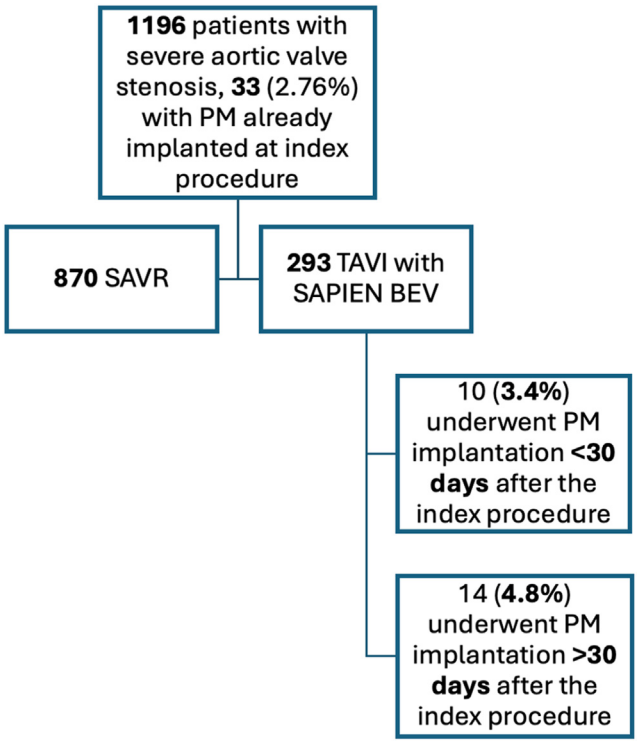


Figure 1 Study population and pacemaker (PM) implantation incidence. SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

the 23-mm THV in 39.6% (n=173), the 29-mm THV in 16.2% (n=71), and the 20-mm THV in 1.4% (n=6) (Table 2).

Postoperative variables

The TAVI cohort was characterized by mean mechanical ventilation time, mean intensive care unit length of stay, mean in-hospital stay, need for blood transfusion, and postoperative atrial fibrillation incidence statistically significantly lower than that in the SAVR cohort. By contrast, minor vascular complications and major bleeding were more common. Regarding the incidence of postoperative kidney failure, transient ischemic attack, stroke, and PM implantation, no differences between the 2 cohorts were observed (Table 3).

Mortality

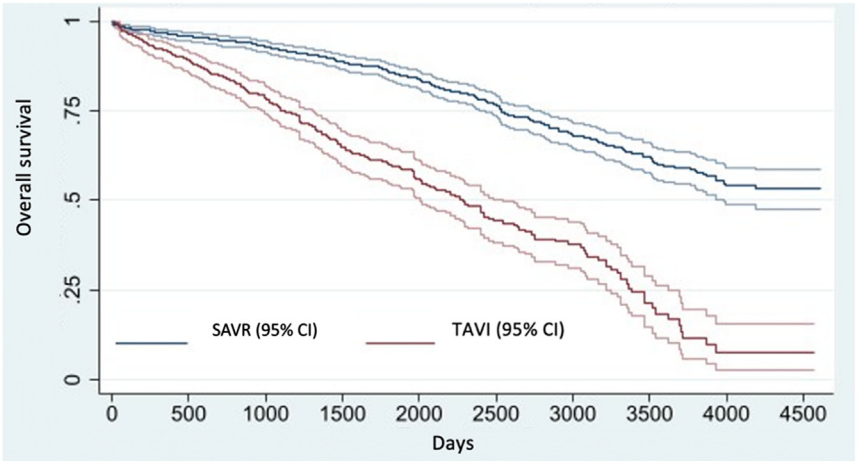
In the overall population, a 30-day mortality and in-hospital mortality of 1.2% (n=18) and 1.6% (n=24), respectively, were found: 0.9% (n=4) and 2.1% (n=9) in the TAVI cohort and 1.3% (n=14) and 1.4% (n=15) in the SAVR cohort, with no statistically significant differences between the 2 procedures. Worse NYHA class, major blood procedural transfusion rate, major or minor bleeding, higher risk scores (EuroSCORE I, EuroSCORE II, and STS-PROM), more than moderate mitral regurgitation, and chronic kidney disease whether on dialysis or not were statistically significantly higher in a bivariate analysis.

All-cause mortality (classified in cardiac vs noncardiac)

The 30-day, 1-year, 2-year, 5-year, and 8-year freedom from all-cause mortality was 98.9%, 94.9%, 78.2%, and 61.3%, respectively (Figures 2 and 3).

PM implantation

Excluding Emilia-Romagna residents who underwent PPI at the time of the index procedure (n=33 [2.76%] of the study population from Emilia-Romagna), we could estimate freedom from PM implantation for each patient living in Emilia-Romagna (n=1163). Permanent PM implantation rates at 30 days and after 30 days were 3.4% (n=35) and 2.9% (n=34), respectively, with no statistically significant difference (P = .081 NS). In the TAVI cohort (n=293), permanent PM implantation rates at 30 days and after 30 days were 3.4% (n=10) and 4.8% (n=14), respectively. In the SAVR cohort (n=870), permanent PM implantation rates at 30 days and after 30 days were 2.9% (n=25) and 2.3% (n=20), respectively. When comparing the permanent PM implantation rate between the SAVR and TAVI cohorts, no statistically significant difference was found (P = .640 NS). In patients who underwent TAVI (n=293), we evaluated PM implantation for each Edwards BE THV used, founding a rate of 0%, 5.7%, 3.8%, and 0% for SAPIEN (n=8), SAPIEN XT (n=88), SAPIEN 3 (n=133), and SAPIEN 3 Ultra (n=64), respectively, with no statistically significant difference (P = .265 NS). When comparing the first-generation Edwards BE THVs (SAPIEN and SAPIEN XT, n=96) with the new-generation Edwards BE THVs (SAPIEN 3 and SAPIEN 3 Ultra, n=197), the permanent PM implantation rate at 30 days was 5.2% and 2.5%, respectively, with no statistically significant difference (P = .237 NS). Overall survival in patients who underwent or not permanent PM implantation in the first 30 days after TAVI was not statistically significantly different (log-rank, P = .494 NS) (Figure 4). Also, in patients who underwent SAVR, the impact of 30-day PM implantation on overall survival was not found statistically significantly different (log-rank, P = .446 NS) (Figure 5). In the TAVI subset, COPD and preoperative atrial fibrillation were more statistically significantly prevalent in patients not implanted after the index procedure while conduction disorders, such as right bundle branch block (RBBB), were more common in implanted patients, similarly to postoperative longer weaning time (Tables 4 and 5). In the same population, 49% of patients underwent nontransfemoral TAVI (29% transapical [n=7] and 20% transaortic [n=5]). The most common THV size in patients requiring PM implantation after TAVI was 26 mm in 45% of cases, followed by 23 mm in 29% and 29 mm in 25%, respectively. The univariate analysis showed preoperative RBBB as an independent predictor of PM implantation (OR 6.74; 95% CI 2.65–17.15; $P < .001$). Undergoing PM implantation was found to be statistically significantly related to rehospitalizations due to all cardiac causes (HR 10.28; 95% CI 3.41–31.00; $P < .001$).

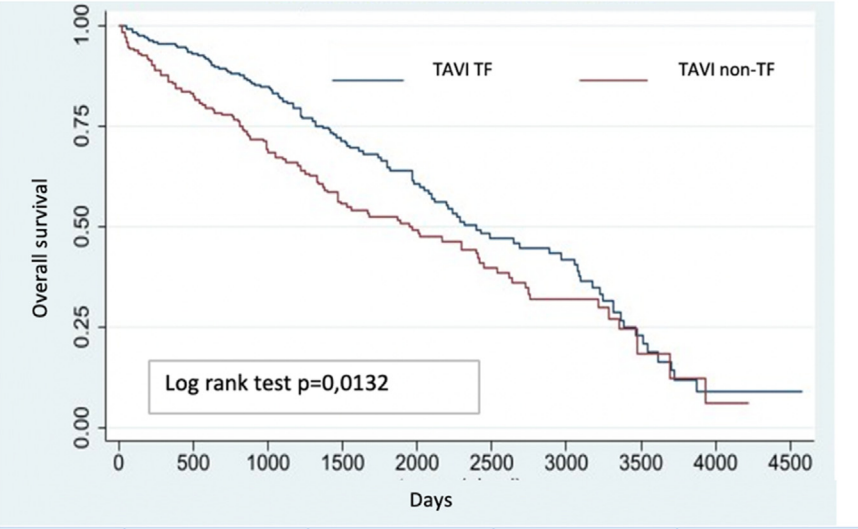


	t =30 days		t =1 year		t = 5 years		t = 8 years	
	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %
SAVR	1038	98,86	1011	96,28	651	85,74	295	69,48
TAVI	436	99,31	402	91,76	146	59,45	54	38,45

Figure 2 Overall survival after surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI).

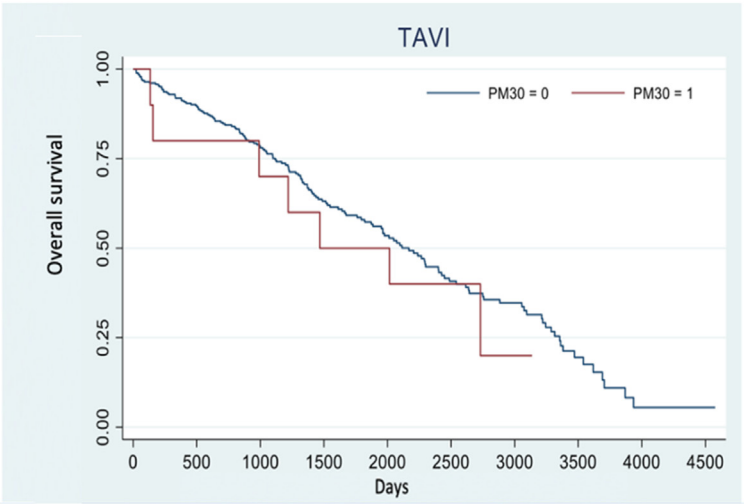
Calcium analysis showed overall leaflet calcification as an independent predictor of PM implantation (OR 4.66; 95% CI 1.41–15.47; $P = .012$), as well as LVOT calcification (OR 4.51; 95% CI 1.48–13.76; $P = .008$). The Agatston score analysis evidenced DLZ calcifications (OR 2.52; 95% CI 0.86–7.40; $P = .093$) as a postoperative PM implantation predictor. The multivariable regression model showed high implantation as a protective factor (OR 0.32; 95% CI 0.12–0.90; $P = .030$), while LVOT (OR 4.05; 95% CI 1.44–11.42; $P = .008$) and leaflet (OR 4.78; 95% CI 1.71–13.37; $P = .003$) calcifications were both associated with a higher risk of PM implantation after TAVI (Tables 6 and 7).

ROC curve analysis showed a 77% specificity and 55% sensitivity for total leaflet calcification with a 203-mm^3 cutoff value. The same sensitivity and specificity emerged considering the Agatston score analysis for the same region, with a 3732-AU cutoff value. Considering the calcium analysis



	t =30 days		t =1 year		t = 5 years		t = 8 years	
	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %
TAVI TF	266	99,99	255	95,49	82	64,02	33	43,17
TAVI non-TF	170	98,25	148	85,96	65	52,40	22	31,93

Figure 3 Overall survival after transfemoral (TF) transcatheter aortic valve implantation (TAVI) and non-TF TAVI.



	t =30 days		t = 1 year		t = 5 years		t = 8 years	
	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %
no PPI <30 days	282	98,94	261	91,87	94	57,30	39	34,72
PPI <30 days	10	90,0	9	80,0	6	50,00	1	20,00

Figure 4 Overall survival in patients who underwent or not pacemaker (PM) implantation in the 30 days after transcatheter aortic valve implantation (TAVI). PPI = permanent pacemaker implantation.

by cusp (analysis of calcium performed considering the single cusps) right coronary cusp calcification reached a 70% specificity with a 80.5-mm^3 cutoff value. Evaluating the calcification impact on PM implantation using the Agatston score, the sensitivity and specificity for left, right, and noncoronary cusp calcifications were 70% and 60% (cutoff 856.5 AU), 75% and 68% (cutoff 808 AU), and 65% and 77% (cutoff 1620 AU), respectively. DLZ calcification reached an 80% sensitivity with a 64% specificity for PM implantation, with a 20-mm^3 cutoff value (Figures 6–11). The membranous septum length showed neither a relevant sensitivity nor specificity for PM implantation.

Discussion

The American and European guidelines now recommend TAVI as a class I treatment for AS, highlighting its central role.[1,2] Initially, TAVI was reserved for inoperable and high-risk patients. However, recent trials have demonstrated its excellent performance in moderate- and low-risk patients,[14,15] suggesting a potential expansion of the eligible population for this procedure.

Given that new-onset conduction disturbances are more frequently associated with TAVI than with SAVR,[3] it is crucial to determine the true incidence of PM implantation with new-generation devices and to assess the impact of permanent PM implantation on patient outcomes.

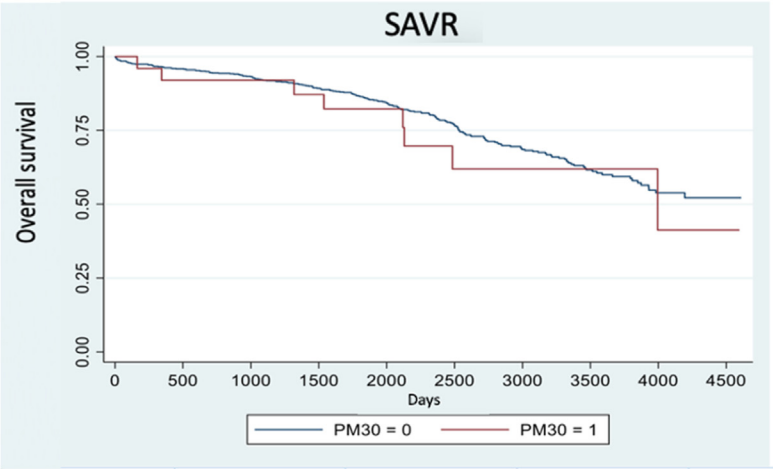
In the second decade of the 21st century, TAVI was primarily used for inoperable or high-risk patients.[8,9] Today, the screening process includes younger and intermediate-risk patients.[14] Data from Hesperia Hospital Modena confirm this trend, showing that patients who underwent TAVI tend to be older and have a higher burden of comorbidities (eg, extracardiac arteriopathy, COPD, coronary artery disease, worse NYHA class, previous cardiac surgery) than did patients who underwent SAVR. Age-related conditions such as preoperative atrial fibrillation and PM implantation are also more common in the TAVI cohort.

The Heart Team at Hesperia Hospital Modena, consisting of a heart surgeon, an interventional cardiologist, 2 clinical cardiologists, and an anesthetist, remained consistent throughout the 2010–2020 decade. Patients were typically referred by local cardiologists and screened by the Heart Team. Those deemed inoperable or high risk for surgery were considered for TAVI. All TAVI procedures were performed by the same team, which had extensive experience in transcatheter procedures from the outset, resulting in a favorable learning curve.

Mortality

In our experience, the overall 30-day mortality rate of 1.2% is lower than that reported in the PARTNER 1A trial (4%), PARTNER 2A trial (3.9%), and the US Nationwide Readmissions Database (3.5%).[9,14,16] However, the 30-day mortality rate for each procedure was similar to that reported in other real-world studies: 0.9% for SAVR and 1.3% for TAVI. Di Eusanio et al, the UK national database, and Takeji et al reported 30-day mortality rates of 2.2%, 1.9%, and 1.3% for SAVR, respectively.[17–19] For TAVI, the UK TAVI Registry and the Nationwide Inpatient Sample Registry reported 30-day mortality rates of 1.8% and 3.17%, respectively.[20,21]

The overall 5-year survival rate was 78.2% for both SAVR and TAVI. All-cause mortality has already been discussed previously.[22]



	t =30 days		t = 1 year		t = 5 years		t = 8 years	
	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %	Patients at risk	Survival %
no PPI <30 days	836	98,82	814	96.21	518	86.23	226	69.51
PPI <30 days	25	96	24	92	16	82.32	7	61.91

Figure 5 Overall survival in patients who underwent or not pacemaker (PM) implantation in the 30 days after surgical aortic valve replacement (SAVR). PPI = permanent pacemaker implantation.

PM implantation

New-onset conduction disturbances requiring PM implantation are among the most common complications of TAVI, with an incidence of 9.3%–42% for self-expandable THVs and 2.5%–11.5% for BE THVs.[23] SAVR can also lead to PM implantation, with rates ranging from 3.2% to 8.5%.[24–30]

Table 4 Baseline TAVI and SAVR parameters for patients who underwent PPI

Baseline parameter	Overall study population (N = 1163)	PPI after SAVR (n = 45 [65.2%])	PPI after TAVI (n = 24 [34.8%])	*P*
EuroSCORE I (logistic) (%)	9.4 ± 7.7	6.7 ± 0.7	18.8 ± 2.5	<.001
EuroSCORE II (%)	2.9 ± 2.9	1.8 ± 0.2	5.3 ± 0.8	<.001
STS-PROM score (%)	2.6 ± 2.1	1.8 ± 0.2	4.3 ± 0.5	<.001
Age (y)	75.0 ± 9.6 (median 77)	71.6 ± 1.2 (median 72)	83.6 ± 0.8 (median 83.5)	<.001
Female	572 (49.2)	19 (42.2)	11 (45.8)	.773
Body mass index (kg/m^2)	27.4 ± 5.0	28.1 ± 0.8	28.0 ± 0.9	.449
Surface body area (m^2)	1.8 ± 0.2	1.9 ± 0.3	1.8 ± 0.4	.015
Diabetes	232 (19.9)	14 (31.1)	7 (29.2)	.867
Hypertension	1120 (96.3)	44 (97.8)	24 (100)	.462
Dyslipidemia	750 (64.5)	31 (68.9)	17 (70.8)	.867
Dialysis	11 (1.0)	1 (2.2)	0 (0)	.462
Previous stroke	37 (3.2)	1 (2.2)	2 (8.3)	.097
Previous TIA	33 (2.8)	1 (2.2)	3 (12.5)	.097
Smoking habit	562 (48.3)	30 (66.7)	11 (45.8)	.093
COPD (EuroSCORE)	95 (8.2)	2 (4.4)	0 (0)	.295
Extracardiac arteriopathy (EuroSCORE)	206 (17.7)	9 (20.0)	6 (25.0)	.632
Bicuspid anatomy	144 (12.4)	7 (15.6)	0 (0)	.042
Previous cardiac surgery	67 (5.8)	0 (0)	3 (12.5)	.015
Previous PCI	245 (21.1)	4 (8.9)	13 (54.2)	<.001
Previous AMI	76 (6.5)	4 (8.9)	4 (16.7)	.336
Coronary artery disease	313 (26.9)	8 (17.8)	15 (62.5)	<.001
Preoperative atrial fibrillation	135 (11.6)	1 (2.2)	0 (0)	.462
NYHA class III or IV	516 (44.4)	12 (26.7)	20 (83.3)	<.001
Reduced EF (30%–50%)	221 (19.0)	7 (15.6)	8 (33.3)	.077
Severely reduced EF (<30%)	22 (1.9)	0 (0)	1 (4.2)	.077

Values are presented as mean ± SD or n (%).

AMI = acute myocardial infarction; COPD = chronic obstructive pulmonary disease; EF = ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PPI = permanent pacemaker implantation; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; TIA = transient ischemic attack.

Table 5 Baseline and postoperative parameters in patients who underwent or not PM implantation after TAVI

Parameter	TAVI (n = 293 [25.2%])		
	No PPI after TAVI (n = 269 [91.8%])	PPI after TAVI (n = 24 [8.2%])	*P*
Baseline parameters			
EuroSCORE I (logistic) (%)	15.9 ± 0.6	18.8 ± 2.5	.926
EuroSCORE II (%)	5.3 ± 0.3	5.3 ± 0.8	.482
STS-PROM score (%)	4.4 ± 0.2	4.3 ± 0.5	.417
Age (y)	81.8 ± 0.4	83.6 ± 0.8	.914
Female	146 (54.3)	11 (45.8)	.427
Body mass index (kg/m^2)	27.0 ± 0.3	28.0 ± 0.9	.817
Surface body area (m^2)	1.7 ± 0.1	1.8 ± 0.1	.416
Diabetes	59 (21.9)	7 (29.2)	.867
Hypertension	268 (99.6)	24 (100)	.765
Dyslipidemia	184 (68.4)	17 (70.8)	.806
Dialysis	5 (1.9)	0 (0)	.501
Previous stroke	14 (5.2)	2 (8.3)	.072
Previous TIA	9 (3.4)	3 (12.5)	.072
Smoking habit	100 (37.2)	11 (45.8)	.402
COPD (EuroSCORE)	44 (16.4)	0 (0)	.032
Extracardiac arteriopathy (EuroSCORE)	73 (27.1)	6 (25.0)	.821
Bicuspid anatomy	3 (1.1)	0 (0)	.603
Previous cardiac surgery	41 (15.2)	3 (12.5)	.719
Previous PCI	133 (49.4)	13 (54.2)	.657
Previous AMI	40 (14.9)	4 (16.7)	.813
Coronary artery disease	163 (60.6)	15 (62.5)	.855
Preoperative atrial fibrillation	59 (21.9)	0 (0)	.010
NYHA class III or IV	240 (89.2)	20 (83.3)	.382
Reduced EF (30%–50%)	63 (23.4)	8 (33.3)	.475
Severely reduced EF (<30%)	7 (2.6)	1 (4.2)	
Preoperative first-grade BAV	32 (11.9)	9 (37.5)	.001
Preoperative RBBB	22 (8.2)	10 (37.5)	<.001
Preoperative LBBB	17 (6.3)	6 (25)	.001
Preoperative LAFB	26 (9.7)	4 (16.7)	.278
Postoperative parameters			
Mechanical ventilation hours 1–5	27 (10.0)	3 (12.5)	.027
Mechanical ventilation hours 6–12	41 (15.2)	2 (8.3)	
Mechanical ventilation hours 13–24	195 (72.5)	18 (75.0)	
Mechanical ventilation hours 25–48	1 (0.4)	0 (0.0)	
Mechanical ventilation hours >48	0 (0.0)	1 (4.2)	
ICU length of stay 1–24 h	220 (81.8)	20 (83.3)	.877
ICU length of stay 25–48 h	23 (8.6)	2 (8.3)	
ICU length of stay >48 h	19 (7.1)	2 (8.3)	
Acute renal failure stage 1	261 (97.0)	24 (100.0)	.693
Acute renal failure stage 2	6 (2.2)	0 (0.0)	
Acute renal failure stage 3	2 (0.7)	0 (0.0)	
Minor bleeding (VARC 2)	2 (0.7)	1 (4.2)	.190
Major bleeding (VARC 2)	9 (3.4)	0 (0.0)	
Stroke (VARC 2)	0 (0.0)	0 (0.0)	–
TIA (VARC 2)	1 (0.4)	0 (0.0)	.765
New-onset atrial fibrillation	7 (2.6)	0 (0.0)	.424
In-hospital stay (d), mean	7.7 ± 0.41	11.9 ± 2.5	.996
In-hospital stay (d), median	6	7	.541

Values are presented as mean ± SD, median, or n (%).

AMI = acute myocardial infarction; BAV = atrio-ventricular block; COPD = chronic obstructive pulmonary disease; EF = ejection fraction; ICU = intensive care unit; LAFB = left anterior fascicular block; LBBB = left bundle branch block; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PPI = permanent pacemaker implantation; RBBB = right bundle branch block; TAVI = transcatheter aortic valve implantation; TIA = transient ischemic attack; VARC 2 = Valve Academy Research Consortium 2.

Table 6 PPI predictors

PPI predictor	OR	95% Confidence interval	*P*
Total leaflet calcification (>235 mm^3)	0.70	0.22–2.19	.535
LVOT calcification (>10 mm^3)	4.51	1.48–13.76	.008
Total leaflet calcification (>4528 AU)	4.66	1.41–15.47	.012
DLZ calcification (>1000 AU)	2.52	0.86–7.40	.093
High TAVI implantation (>80:20)	1.13	0.05–28.02	.940
High TAVI implantation (>70:30)	0.30	0.02–4.07	.367
Preoperative RBBB	6.74	2.65–17.15	<.001

AU = Agatston unit; DLZ = device landing zone; LVOT = left ventricular outflow tract; OR = odds ratio; PPI = permanent pacemaker implantation; RBBB = right bundle branch block; TAVI = transcatheter aortic valve implantation.

Bagur et al[25] reported a permanent PM implantation rate of 7.3% after TAVI with SAPIEN and SAPIEN XT in a population of 411 patients with AS and similar preoperative electrocardiographic characteristics. This rate was higher, though not statistically significant, than the 3.4% rate after SAVR. Conduction disturbances after TAVI and SAVR included complete atrioventricular (AV) block (5.6% vs 2.7%; $P = .039$) and symptomatic severe bradycardia (1.7% vs 0.7%; $P = .097$). Preoperative RBBB was an independent predictor of PM implantation after TAVI (OR 8.61; 95% CI 3.14–23.67; $P < .0001$), but not after SAVR.[25]

The introduction of new-generation Edwards BE devices, SAPIEN 3 and SAPIEN 3 Ultra, was initially not associated with a lower incidence of permanent PM implantation. In the PARTNER 3 trial, PM implantation and left bundle branch block rates were higher in the TAVI group than in the SAVR group, though not statistically significant (6.6% vs 4.1%; HR 1.65; 95% CI 0.92–2.95 and 22.0% vs 8.0%; HR 1.65; 95% CI 2.13–4.72, respectively).[15]

The strong association between preoperative conduction disturbances, especially RBBB, and postprocedural PM implantation has led to the inclusion of RBBB in preoperative risk scores, such as the Emory risk score[31] and the Midas strategy.[32] In our study, RBBB was a consistent independent predictor of PM implantation after TAVI (OR 6.74; 95% CI 2.65–17.15; $P < .001$). This may be due to an increased incidence of bradyarrhythmia and high-grade AV block in cases of left bundle branch injury during valve deployment.[33]

Table 7 PPI predictive risk score

Predictive PPI risk score	OR	95% Confidence interval	*P*
High TAVI implant (>70:30)	0.32	0.12–0.90	**.030**
LVOT calcification (>10 mm^3)	4.05	1.44–11.42	**.008**
Total leaflet calcification (>4528 AU)	4.78	1.71–13.37	**.003**

AU = Agatston unit; LVOT = left ventricular outflow tract; OR = odds ratio; PPI = permanent pacemaker implantation; TAVI = transcatheter aortic valve implantation.

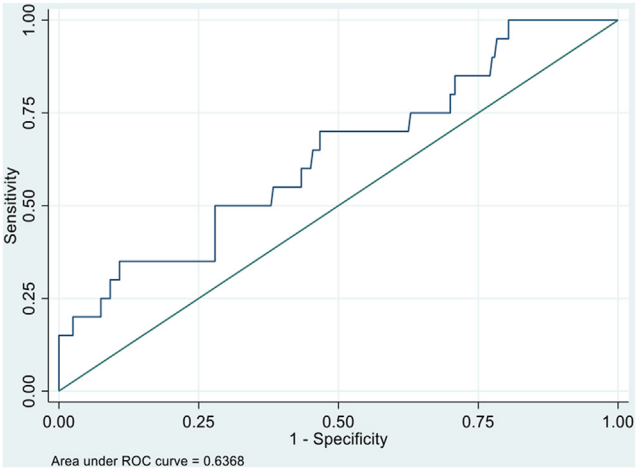


Figure 6 Receiver operator characteristic (ROC) curve for total leaflet calcification.

Recent years have seen the adoption of a different implantation strategy for new-generation Edwards BE devices, SAPIEN 3 and SAPIEN 3 Ultra, which involves reducing the implantation depth.[34–39] This approach aims to reduce the THV frame in the LVOT by positioning the balloon marker a few millimeters above the virtual basal ring. Mailey et al[40] found that a high implantation strategy, using the radio-transparent line on the THV crimped frame as a reference, resulted in a permanent PM implantation rate of 4.4%. However, the effectiveness of this strategy needs further confirmation in clinical practice, as it may affect coronary reaccess and valve-in-valve feasibility.

In our population, the permanent PM implantation rate was 3.4% for TAVI and 2.9% for SAVR, with no statistically significant difference. When comparing the old-generation Edwards BE THVs (SAPIEN and SAPIEN XT, n=96) with the new-generation devices (SAPIEN 3 and SAPIEN 3 Ultra, n=197), the 30-day PM implantation rates were 5.2% and 2.5%, respectively, with no statistically significant difference ($P = .237$). The introduction of new-generation

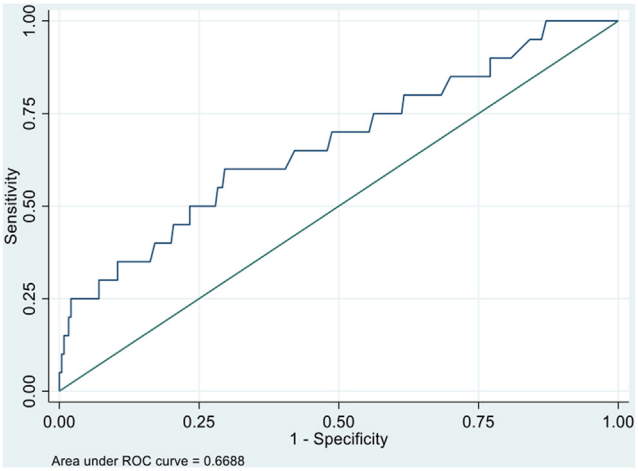


Figure 7 Receiver operator characteristic (ROC) curve for right coronary cusp calcification.

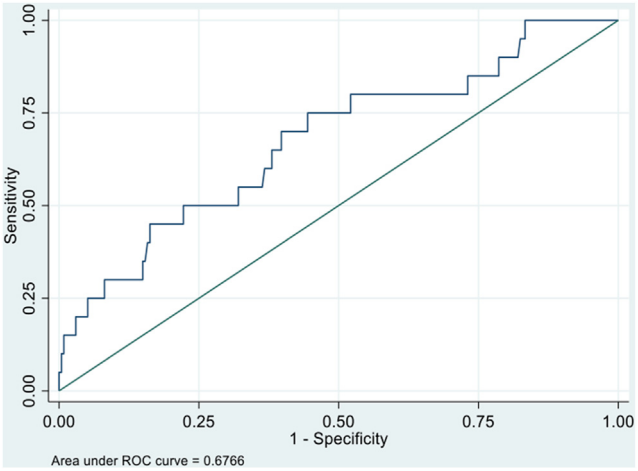


Figure 8 Receiver operator characteristic (ROC) curve for left coronary cusp calcification Agatston score.

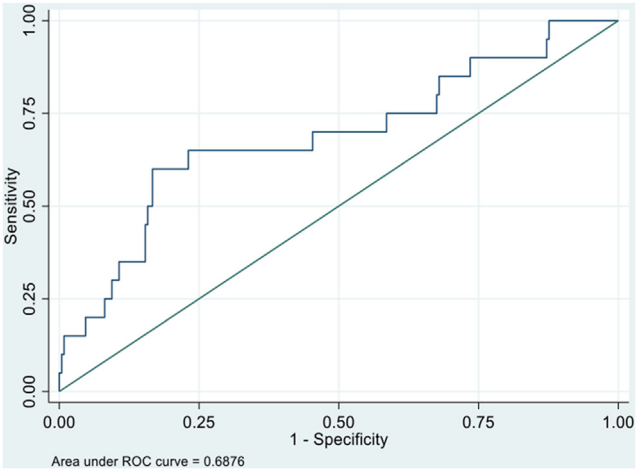


Figure 10 Receiver operator characteristic (ROC) curve for noncoronary cusp calcification Agatston score.

devices led to a reduction in the 30-day PM implantation rate (2.5%), possibly because of higher THV implantation techniques.

In the last decade, the depth of TAVI implantation has become a crucial topic of discussion. Initially, an implantation depth ratio of <70:30 was recommended by industry standards.[41] However, recent studies have highlighted the benefits of more aortic implantation.[32,40]

In our analysis, we categorized THV implantation depth into 2 subsets: one with a ratio of >80:20 and another with a ratio of >70:30. The statistical analysis showed no significant difference for the >80:20 class, while the >70:30 ratio was identified as a protective factor, reducing the risk of PM implantation by up to 68% in our predictive risk model. Ramanathan et al[42] and Jilaihawi et al[32] reported similar findings, supporting the evidence that higher implantation acts as a protective factor for PPI.

This technique reduces the need for a PM because the valve is deployed high in the aortic annulus, with only a minimal portion of the valve in the LVOT, thereby avoiding the conduction system. The AV node is located in the right atrium, near the septal part of the tricuspid valve and the muscular ventricular septum, which is continuous with the aortic valve cusps. At a lower level, the LVOT is closely related to the left bundle branch.[43] Direct mechanical trauma or compression of the AV node or the left bundle branch by balloon dilation or prosthesis implantation can cause a high-degree AV block or left bundle branch block during or after TAVI. Preexisting damage to the conduction system, such as RBBB, increases the risk of advanced conduction abnormalities after TAVI, necessitating PPI.

Analyzing overall survival with and without 30-day PM implantation after SAVR and/or TAVI showed no statistically significant differences. The literature reports conflicting results on this topic. Some studies associate 30-day PM implantation with worse overall survival and more frequent rehospitalizations due to heart failure,[44,45] while others do not find a negative impact on patient prognosis.[46] In our

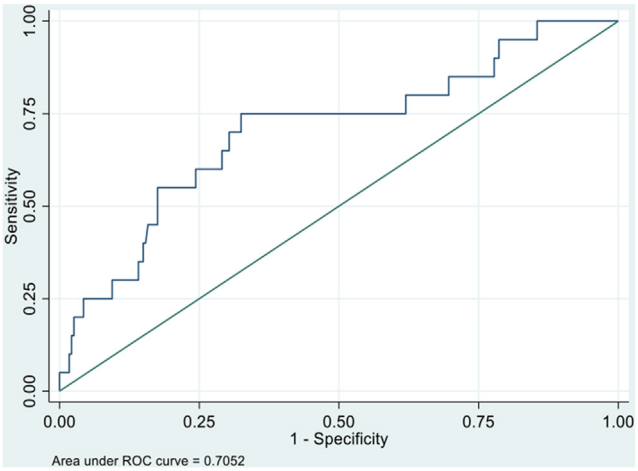


Figure 9 Receiver operator characteristic (ROC) curve for right coronary cusp calcification Agatston score.

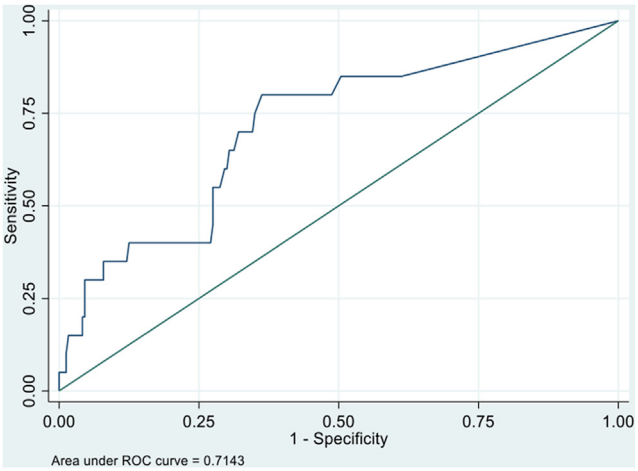


Figure 11 Receiver operator characteristic (ROC) curve for device landing zone calcification.

study, PM implantation did not significantly affect overall survival but was associated with a higher risk of rehospitalizations due to cardiac causes (HR 8.65; 95% CI 4.87–15.36; $P < .001$). This trend, observed by Sá et al,[44] was confirmed in our population. The higher rehospitalization rate may be related to PM implantation, as right ventricular pacing can lead to dyssynchronous systolic left ventricular function, higher degrees of heart failure, and lower left ventricular EF.[47] The absence of mechanical synchrony after afterload relief (induced by preprocedural left ventricular hypertrophy) combined with ventricular dyssynchrony (electrically induced by right ventricular pacing) may not only compromise the postprocedural normalization of cardiac function but also cause further decline in function.[44]

The impact of aortic valve calcification on procedural success and outcomes is a well-discussed topic in the literature. Its association with annular rupture[48] and paravalvular aortic regurgitation[12,49] has been established. However, the role of aortic valve calcification in PPI remains unclear.

Nai Fovino et al[50] found that patients who received a PM had a higher grade of LVOT calcifications (36% vs 32%; $P = .045$) using a qualitative calcification grade. Latsios et al[51] proposed DLZ calcification, using a semiquantitative method, as a predictor of PPI (OR 1.06; 95% CI 1.02–1.11; $P = .004$). Fujita et al,[52] using a quantitative method, found an association between left coronary cusp calcification (>209 mm^3) and a higher rate of PPI after TAVI. However, Gama et al,[53] in a quantitative calcium analysis, failed to prove any correlation between aortic root calcification and PPI.

In our experience, using a quantitative calcium grading system, overall leaflet calcification $>$ 4528 AU, LVOT calcification $>$ 10 mm^3, and DLZ calcification $>$1000 AU (even if with $P = .093$) were identified as independent predictors of PM implantation. However, we did not find a correlation between regional calcium location and 30-day PM implantation.

We also failed to prove any correlation between membranous septum length and 30-day PM implantation after TAVI, unlike other authors. However, we did find a correlation between a high implantation technique and a lower PM implantation rate. Chen et al[54] analyzed the preprocedural assessment of membranous septum length in coronal view compared with infra-annular membranous septum length from the stretched vessel image, highlighting the need to determine the optimal implantation depth to mitigate conduction disturbances after TAVI. Jung et al,[55] in a large cohort of consecutive patients, confirmed the significantly independent predictive value of membranous septum length for the occurrence of postprocedural AV block with the need for PPI.

Using ROC curve analysis, we were unable to identify any variable with relevant sensitivity or specificity. For isolated sensitivity, left coronary cusp (70%), right coronary cusp (75%), and DLZ (80%) calcifications were significant, while for specificity, total leaflet (77%), right coronary cusp (70%), and noncoronary cusp (77%) calcifications were adequate.

Our results support the need for further investigation into the impact of aortic valve calcification on PM implantation rates. If confirmed, this should become part of routine preprocedural evaluation.

Study limitations

The study presents all the intrinsic limitations of observational retrospective studies, such as discrepancy in data collection, changes in definitions of comorbidities, and loss of patients during follow-up. However, between 2010 and 2020, all data were collected by the same physician, comorbidity definitions did not change, and patients were registered in the same database (RERIC). Moreover, adopting the Italian ANPR database and the hospital discharge record (scheda dimissione ospedaliera) system for Emilia-Romagna residents, no patients were found to be lost at follow-up, regarding mortality and rehospitalizations during follow-up. During the study period, the choice of TAVI or SAVR, made by the local heart team, was influenced by outcome data from PARTNER trials 1A and 1B.[1,2] Inoperable and high-risk patients were selected for TAVI, while SAVR was performed in all others, introducing selection bias, which can be observed considering the remarkable heterogeneity of our 2 populations. All patients who underwent TAVI were treated with BE THVs, allowing the comparison with procedural outcomes from PARTNER trials, but preventing from translating our outcomes with self-expandable THVs.

During the first 2 years of the study, electrocardiogram-gated computed tomography scans were not available, introducing a possible bias in imaging analysis.

Conclusion

Mechanical trauma during TAVI can injure the conduction system, leading to permanent PM implantation. Anatomical features, particularly the variation in the length and location of the penetrating segment of the bundle of His and the depth of the proximal portion of the left bundle, affect susceptibility to injury.

In our population, a 3.4% permanent PM implantation rate was reported. This outcome is likely due to the exclusive use of Edwards BE devices and thorough preoperative evaluation. However, given the negative impact of PPI on patient prognosis, it is essential to explore new tools in preoperative screening and operative techniques, such as high implantation, to further reduce this event.

While the impact of PPI on mortality remains debated, it is still associated with the increased length of hospital stay and rehospitalizations. A comprehensive preoperative evaluation, considering factors such as the amount of calcium in the LVOT (LVOT calcification $>$10 mm^3) and aortic root (overall leaflet calcification $>$ 4528 AU), the length of the membranous septum, the implantation depth in the LVOT, and a precise computed tomography–scan simulation before the procedure,

could be crucial in lowering the PPI incidence and preserving the benefits of TAVI.

Acknowledgments

The authors express their deepest gratitude to Edwards Lifesciences for their research grant and support during all the study.

Funding Sources: This study was funded by a research grant from Edwards Lifesciences (Nyon, Switzerland; grant number THV-I23-092). The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Disclosures: Dr Gabbieri declares his role of consultant for Edwards Lifesciences. Mr Chiarabelli is an Edwards Lifesciences employee. The other authors declare no conflict of interest.

Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent: All patients signed written informed consent.

Ethics Statement: The research reported in this article adhered to Helsinki Declaration and was approved by the Institutional Review Board of Area Vasta Emilia Nord.

References

1. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol 2021;77:450–500.
2. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2022;43:561–632.
3. Huang HD, Mansour M. Pacemaker implantation after transcatheter aortic valve replacement: a necessary evil perhaps but are we making progress? J Am Heart Assoc 2020;9:e016700.
4. Kempfert J, Holzhey D, Hofmann S, et al. First registry results from the newly approved ACURATE TA™ TAVI system†. Eur J Cardiothorac Surg 2015; 48:137–141.
5. Nazif TM, Dizon JM, Hahn RT, et al. Predictors and clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve replacement: the PARTNER (Placement of AoRtic TraNscathetER Valves) trial and registry. JACC Cardiovasc Interv 2015;8:60–69.
6. Weber M, Brüggemann E, Schueler R, et al. Impact of left ventricular conduction defect with or without need for permanent right ventricular pacing on functional and clinical recovery after TAVR. Clin Res Cardiol 2015;104:964–974.
7. Baldi E, Compagnone M, Errigo D, et al. Long-term percentage of ventricular pacing in patients requiring pacemaker implantation after transcatheter aortic valve replacement: a multicenter 10-year experience. Heart Rhythm 2020; 17:1897–1903.
8. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010; 363:1597–1607.
9. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–2198.
10. Généreux P, Piazza N, Alu MC, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. J Am Coll Cardiol 2021;77:2717–2746.
11. Jilaihawi H, Makkar RR, Kashif M, et al. A revised methodology for aortic-valvar complex calcium quantification for transcatheter aortic valve implantation. Eur Heart J Cardiovasc Imaging 2014;15:1324–1332.
12. John D, Buellesfeld L, Yuecel S, et al. Correlation of device landing zone calcification and acute procedural success in patients undergoing transcatheter aortic valve implantations with the self-expanding CoreValve prosthesis. JACC Cardiovasc Interv 2010;3:233–243.
13. Seiffert M, Fujita B, Avanesov M, et al. Device landing zone calcification and its impact on residual regurgitation after transcatheter aortic valve implantation with different devices. Eur Heart J Cardiovasc Imaging 2016;17:576–584.
14. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016;374:1609–1620.
15. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019; 380:1695–1705.
16. Saad AM, Kassis N, Isogai T, et al. Trends in outcomes of transcatheter and surgical aortic valve replacement in the United States (2012-2017). Am J Cardiol 2021;141:79–85.
17. Takeji Y, Taniguchi T, Morimoto T, et al. Transcatheter aortic valve implantation versus conservative management for severe aortic stenosis in real clinical practice. PLoS One 2019;14:e0222979.
18. Di Eusanio M, Fortuna D, De Palma R, et al. Aortic valve replacement: results and predictors of mortality from a contemporary series of 2256 patients. J Thorac Cardiovasc Surg 2011;141:940–947.
19. Jahangiri M, Bilkhu R, Embleton-Thirsk A, et al. Surgical aortic valve replacement in the era of transcatheter aortic valve implantation: a review of the UK national database. BMJ Open 2021;11:e046491.
20. Krittanawong C, Kumar A, Wang Z, et al. Predictors of in-hospital mortality after transcatheter aortic valve implantation. Am J Cardiol 2020;125:251–257.
21. Ludman PF. UK TAVI Registry. Heart 2019;105:s2–s5.
22. Gabbieri D, Giorgi F, Mascheroni G, et al. Coronary revascularization after transcatheter and surgical aortic valve replacement. J Clin Med 2023;12:7257.
23. Abdel-Wahab M, Landt M, Neumann FJ, et al. 5-Year outcomes after TAVR with balloon-expandable versus self-expanding valves: results from the CHOICE randomized clinical trial. JACC Cardiovasc Interv 2020;13:1071–1082.
24. Bagur R, Manazzoni JM, Dumont É, et al. Permanent pacemaker implantation following isolated aortic valve replacement in a large cohort of elderly patients with severe aortic stenosis. Heart 2011;97:1687–1694.
25. Bagur R, Rodés-Cabau J, Gurvitch R, et al. Need for permanent pacemaker as a complication of transcatheter aortic valve implantation and surgical aortic valve replacement in elderly patients with severe aortic stenosis and similar baseline electrocardiographic findings. JACC Cardiovasc Interv 2012; 5:540–551.
26. Keefe DL, Griffin JC, Harrison DC, Stinson EB. Atrioventricular conduction abnormalities in patients undergoing isolated aortic or mitral valve replacement. Pacing Clin Electrophysiol 1985;8:393–398.
27. Totaro P, Calamai G, Montesi G, Barzaghi C, Vaccari M. Continuous suture technique and impairment of the atrioventricular conduction after aortic valve replacement. J Card Surg 2000;15:418–422. discussion 423.
28. Koplan BA, Stevenson WG, Epstein LM, Aranki SF, Maisel WH. Development and validation of a simple risk score to predict the need for permanent pacing after cardiac valve surgery. J Am Coll Cardiol 2003;41:795–801.
29. Limongelli G, Ducceschi V, D'Andrea A, et al. Risk factors for pacemaker implantation following aortic valve replacement: a single centre experience. Heart 2003;89:901–904.
30. Dawkins S, Hobson AR, Kalra PR, Tang AT, Monro JL, Dawkins KD. Permanent pacemaker implantation after isolated aortic valve replacement: incidence, indications, and predictors. Ann Thorac Surg 2008;85:108–112.
31. Kiani S, Kamioka N, Black GB, et al. Development of a risk score to predict new pacemaker implantation after transcatheter aortic valve replacement. JACC Cardiovasc Interv 2019;12:2133–2142.
32. Jilaihawi H, Zhao Z, Du R, et al. Minimizing permanent pacemaker following repositionable self-expanding transcatheter aortic valve replacement. JACC Cardiovasc Interv 2019;12:1796–1807.
33. Sammour Y, Krishnaswamy A, Kumar A, et al. Incidence, predictors, and implications of permanent pacemaker requirement after transcatheter aortic valve replacement. JACC Cardiovasc Interv 2021;14:115–134.
34. De Torres-Alba F, Kaleschke G, Diller GP, et al. Changes in the pacemaker rate after transition from Edwards SAPIEN XT to SAPIEN 3 transcatheter aortic valve implantation: the critical role of valve implantation height. JACC Cardiovasc Interv 2016;9:805–813.
35. Tarantini G, Mojoli M, Purita P, et al. Unravelling the (arte)fact of increased pacemaker rate with the Edwards SAPIEN 3 valve. EuroIntervention 2015; 11:343–350.
36. Schwerg M, Fulde F, Dreger H, Poller WC, Stangl K, Laule M. Optimized implantation height of the Edwards SAPIEN 3 valve to minimize pacemaker implantation after TAVI. J Interv Cardiol 2016;29:370–374.
37. Eliav R, Elitzur Y, Planer D, et al. Predictors for permanent pacemaker implantation following transcatheter aortic valve implantation: trends over the past decade. J Interv Card Electrophysiol 2021;62:299–307.
38. Droppa M, Rudolph TK, Baan J, et al. Risk factors for permanent pacemaker implantation in patients receiving a balloon-expandable transcatheter aortic valve prosthesis. Heart Vessels 2020;35:1735–1745.

39. Tretter JT, Mori S, Anderson RH, et al. Anatomical predictors of conduction damage after transcatheter implantation of the aortic valve. Open Heart 2019;6:e000972.
40. Mailey JA, Brennan PF, Kearney A, et al. Reframing optimal implantation of the Sapien 3 transcatheter heart valve. J Invasive Cardiol 2022;34:E380–E389.
41. Sammour Y, Banerjee K, Kumar A, et al. Systematic approach to high implantation of SAPIEN-3 valve achieves a lower rate of conduction abnormalities including pacemaker implantation. Circ Cardiovasc Interv 2021;14:e009407.
42. Ramanathan P, Kasi P, Nazir S, et al. Novel method for implantation of balloon expandable transcatheter aortic valve replacement to reduce pacemaker rate—line of lucency method. Struct Heart 2020;4:427–432.
43. Piazza N, de Jaegere P, Schultz C, Becker AE, Serruys PW, Anderson RH. Anatomy of the aortic valvar complex and its implications for transcatheter implantation of the aortic valve. Circ Cardiovasc Interv 2008;1:74–81.
44. Sá MP, Jacquemyn X, Sun T, et al. Late outcomes of permanent pacemaker implantation after TAVR: meta-analysis of reconstructed time-to-event data. J Soc Cardiovasc Angiogr Interv 2022;1:100434.
45. Glaser N, Persson M, Dalén M, Sartipy U. Long-term outcomes associated with permanent pacemaker implantation after surgical aortic valve replacement. JAMA Netw Open 2021;4:e2116564.
46. Rück A, Saleh N, Glaser N. Outcomes following permanent pacemaker implantation after transcatheter aortic valve replacement: SWEDEHEART observational study. JACC Cardiovasc Interv 2021;14:2173–2181.
47. Yu CM, Chan JY, Zhang Q, et al. Biventricular pacing in patients with bradycardia and normal ejection fraction. N Engl J Med 2009;361:2123–2134.
48. Barbanti M, Yang TH, Rodès Cabau J, et al. Anatomical and procedural features associated with aortic root rupture during balloon-expandable transcatheter aortic valve replacement. Circulation 2013;128:244–253.
49. Feuchtner G, Plank F, Bartel T, et al. Prediction of paravalvular regurgitation after transcatheter aortic valve implantation by computed tomography: value of aortic valve and annular calcification. Ann Thorac Surg 2013;96:1574–1580.
50. Nai Fovino L, Cipriani A, Fabris T, et al. Anatomical predictors of pacemaker dependency after transcatheter aortic valve replacement. Circ Arrhythm Electrophysiol 2021;14:e009028.
51. Latsios G, Gerckens U, Buellesfeld L, et al. "Device landing zone" calcification, assessed by MSCT, as a predictive factor for pacemaker implantation after TAVI. Catheter Cardiovasc Interv 2010;76:431–439.
52. Fujita B, Kütting M, Seiffert M, et al. Calcium distribution patterns of the aortic valve as a risk factor for the need of permanent pacemaker implantation after transcatheter aortic valve implantation. Eur Heart J Cardiovasc Imaging 2016;17:1385–1393.
53. Gama F, Teles RC, Oliveira A, et al. Predicting pacemaker implantation after TAVR with procedural CT. Eur Heart J 2020;41. ehaa946.0192.
54. Chen YH, Chang HH, Liao TW, et al. Membranous septum length predicts conduction disturbances following transcatheter aortic valve replacement. J Thorac Cardiovasc Surg 2022;164:42–51.e2.
55. Jung S, Ammon F, Smolka S, Moshage M, Marwan M, Achenbach S. Membranous septum length as predictor for permanent pacemaker implantation after TAVI. Eur Heart J 2022;43:ehac544.1607.