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Predictors of Permanent Pacemaker Implantations and New-Onset Conduction Abnormalities With the SAPIEN 3 Balloon-Expandable Transcatheter Heart Valve

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ABSTRACT

OBJECTIVES This study investigates the influence of implantation depth and prosthesis oversizing on conduction abnormalities (CA) and permanent pacemaker implantation (PPI) after SAPIEN 3 (Edwards Lifesciences, Irvine, California) implantation.

BACKGROUND CA and PPIs are frequent complications after transcatheter aortic valve replacement with a next-generation balloon-expandable transcatheter heart valve (SAPIEN 3). The potential underlying mechanisms are incompletely understood.

METHODS Of 244 patients treated with SAPIEN 3,208 without a previous pacemaker and 184 without baseline CA were analyzed. We assessed the association of angiographic implantation depth (% of frame height below the annulus) and degree of oversizing with PPI and CA.

RESULTS New PPI and new or worsened CA or PPI occurred in 16% (34 of 208) and 31% (57 of 184), respectively. Patients requiring PPI had a higher prevalence of atrial fibrillation (44% vs. 24%; $p = 0.017$), complete right bundle branch block (27% vs. 5%; $p = 0.001$), and bradycardia (<60 beats/min, 38% vs. 21%; $p = 0.034$). In patients with new CA or PPI, implantation depth was lower (at septal side: 29 ± 8% vs. 25 ± 7%; $p = 0.003$), and rate of oversizing was higher (19% [11 of 57] vs. 6% [8 of 126]; $p = 0.007$). Independent predictors of new or worsened CA or PPI were implantation depth at septal side (odds ratio [OR]: 1.063 [95% confidence interval (CI): 1.017 to 1.110]; $p = 0.006$ per % of frame below the aortic annulus), oversizing (OR: 3.489 [95% CI: 1.236 to 9.848]; $p = 0.018$), and QRS duration (OR: 1.033 [95% CI: 1.011 to 1.056]; $p = 0.003$ per ms).

CONCLUSIONS Implantation depth and prosthesis oversizing were associated with a higher rate of new CA or PPI using the SAPIEN 3. Thus, avoidance of deep implantation and extreme oversizing may reduce these complications.
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Post-procedural new or worsened conduction abnormalities (CA) and permanent pacemaker implantation (PPI) after transcatheter aortic valve replacement (TAVR) remain a serious concern.

The incidence of new or worsened CA, in particular complete left bundle branch block (LBBB) and PPI with balloon-expandable valves has been reported to be between 8% and 30% (1-5) and 5% and 12% (6-8), respectively. Although PPI does not seem to affect survival (9,10), overall costs and hospital stay are increased (11) and symptomatic benefit may be limited (12). New or worsened CA may negatively affect left ventricular function recovery and increase the risk for PPI during follow-up (13,14).

Recently, a balloon-expandable prosthesis (SAPIEN 3, Edwards Lifesciences, Irvine, California) (15) has been introduced featuring a higher metal frame with an outer skirt designed to avoid paravalvular leakage. The clinical experience with this device is limited, but first results are excellent (16). However, regarding post-procedural PPI, preliminary studies report a relatively high rate, ranging from 13% to 25.5% (16-18).

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The development of new devices should weigh potential improvements, like minimizing paravalvular leakage and vascular complications, against an increase in PPI and CA. Minimizing these complications is mandatory for further improvement in TAVR outcome, especially in intermediate-risk patients. Therefore, determinants of PPI and CA need to be identified. Possible causes include technical issues, but also the appropriateness of sizing algorithms.

We aimed to examine potential determinants of new PPI and CA with the SAPIEN 3 valve using clinical, electrocardiographic, angiographic, and CT-morphological parameters.

METHODS

PATIENT POPULATIONS. We treated 244 consecutive patients with the SAPIEN 3 valve at our institution. TAVR was performed in a hybrid operation suite under general anesthesia or conscious sedation using the transfemoral approach. All patients provided written informed consent for the procedure.

To determine the incidence of new PPI after TAVR, patients with previous pacemaker (n = 23, 9%), atypical valvular anatomy (bicuspid valve; n = 5, 1%) or degenerated biological prostheses (n = 8, 3%) were excluded, resulting in 208 patients. Of these patients, those with complete bundle branch blocks at baseline were excluded (n = 24) to analyze the incidence of new or worsened CA or PPI after TAVR, leaving 184 patients (Figure 1).

MULTISLICE COMPUTED TOMOGRAPHY DATA ANALYSIS. Aortic annulus measurements were assessed in diastole using multiple plane reconstruction according to the guidelines of the Society of Cardiovascular Computed Tomography (19). Area and perimeter of the aortic annulus were obtained by direct planimetry. An approximation of the minimal and maximum diameters was manually obtained (Figure 2) to calculate the eccentricity of the aortic annulus as the eccentricity index using the formula: 1 − (minimum diameter/maximum diameter). The closer this index comes to zero, the more circular the aortic annulus.

Calcification of the valvular apparatus was assessed at the height of the aortic cusps, annulus, and left ventricular outflow tract and was visually graded as none = 0, mild = 1, moderate = 2, and severe = 3. Dedicated Food and Drug Administration-approved software (OsiriX MD 3.9.4, Pixmeo, Switzerland) was used.

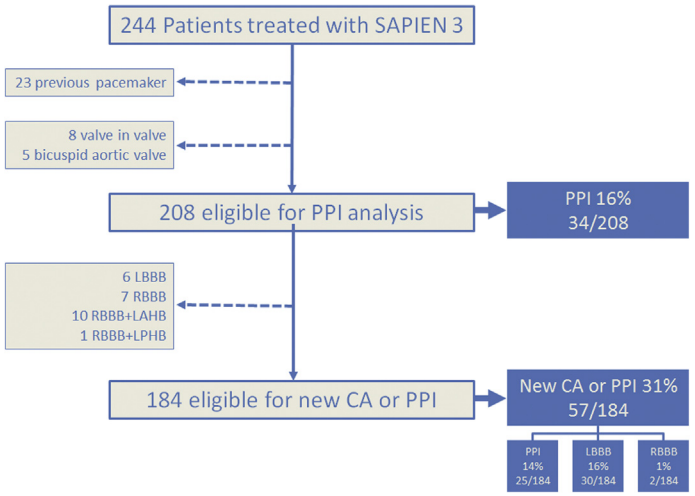
PROSTHESIS SIZE SELECTION. The SAPIEN 3 valve is available in 23-, 26-, and 29-mm sizes. The dimensions of a nominal expanded SAPIEN 3 and the manufacturer's sizing recommendations are given in Table 1. The final decision on prosthesis size was left to the discretion of the physicians performing the procedure and was mainly based on multislice computed tomography (MSCT)-derived annular area and taking into account other anatomical features like presence and distribution of calcification, eccentricity of the aortic annulus, and also the patient anatomy in case of borderline sizing ranges. Percentage of oversizing according to area and perimeter were calculated using the formula: (nominal prosthesis dimension/patient anatomy − 1)·100. The adherence to the manufacturer's sizing guidelines by annular area was categorized as "undersized," "within sizing range," and "oversized."

DETERMINATION OF IMPLANTATION DEPTH. Angiographic data were transferred to a separate workstation and assessed offline using Food and Drug Administration-approved software (OsiriX MD 3.9.4, Pixmeo, Switzerland). The implantation plane was identified using previously described techniques, by either calculation from the MSCT (20) or by combination of angiographic and fluoroscopic guidance (21). A pigtail was placed in the right coronary cusp, and an orthogonal view on the 3 aortic cusps was confirmed by aortic angiography. The final

ABBREVIATIONS AND ACRONYMS

CA = conduction abnormalities
CI = confidence interval
LBBB = left bundle branch block
OR = odds ratio
PPI = permanent pacemaker implantation
RBBB = right bundle branch block
TAVR = transcatheter aortic valve replacement

FIGURE 1 Patient Flow, Reasons for Exclusion From Analyses, and Incidence of PPI and New or Worsened CA



CA = conduction abnormalities; LAHB = left anterior hemiblock; LBBB = left bundle branch block; LPHB = left posterior hemiblock; PPI = permanent pacemaker implantations; RBBB = right bundle branch block.

post-deployment aortic angiogram was selected showing the prosthesis in an orthogonal view. The native aortic annulus was marked by intersecting the sinuses of Valsalva. The entire prosthesis frame height and the portion below the aortic annulus were measured at the septal (i.e., noncoronary cusp) and nonseptal (i.e., left coronary cusp) sides. Implantation depth was expressed as the percentage of frame height below the aortic annulus (Figure 3).

ELECTROCARDIOGRAPHIC ANALYSIS. Electrocardiograms (ECGs) were recorded on admission and before discharge and were reviewed by 2 physicians blinded to clinical data according to recommendations issued by the American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society (22). Doubtful cases were solved by consensus. Rhythm, heart rate (beats/min), PQ and QRS intervals (ms), atrioventricular conduction disturbances, and intraventricular conduction abnormalities were recorded. Due to potential interference of pacemaker stimulation, intraventricular conduction was not evaluated in patients who underwent PPI after TAVR and was instead denoted as "pacemaker."

DEFINITION OF ENDPOINTS. Endpoints of the study were PPI before discharge in patients without previous pacemaker (n = 208) and new or worsened CA or PPI in patients without bundle branch blocks or pacemaker at baseline (n = 184) (see Figure 1 and previous section).

The treating physicians made the final decision for PPI, and the indication was recorded in every case. New or worsened CA was defined as new complete LBBB or right bundle branch block (RBBB) at discharge.

All data were prospectively collected. In-hospital outcome, device success, and procedural complications were categorized according to the Valve Academic Research Consortium (23).

STATISTICAL ANALYSIS. Continuous variables are expressed as mean ± SD or as the median (interquartile range [IQR]) and were compared using the unpaired Student *t* test or Mann-Whitney *U* test as appropriate. Discrete variables were compared with the chi-square test or Fisher exact test as appropriate. To identify independent predictors for PPI and new or worsened CA, multivariable logistic regression models were applied, adjusted by variables yielding a $p < 0.1$ in univariate analyses or variables known to influence either endpoint. To assess the impact of oversizing by area and implantation depth, these variables were included in the models. Odds ratios (ORs) with the respective 95% confidence intervals (CIs) were computed. A 2-sided p value <0.05 was considered to be statistically significant. SPSS Statistics version 22 (IBM, Armonk, New York) was used for analyses.

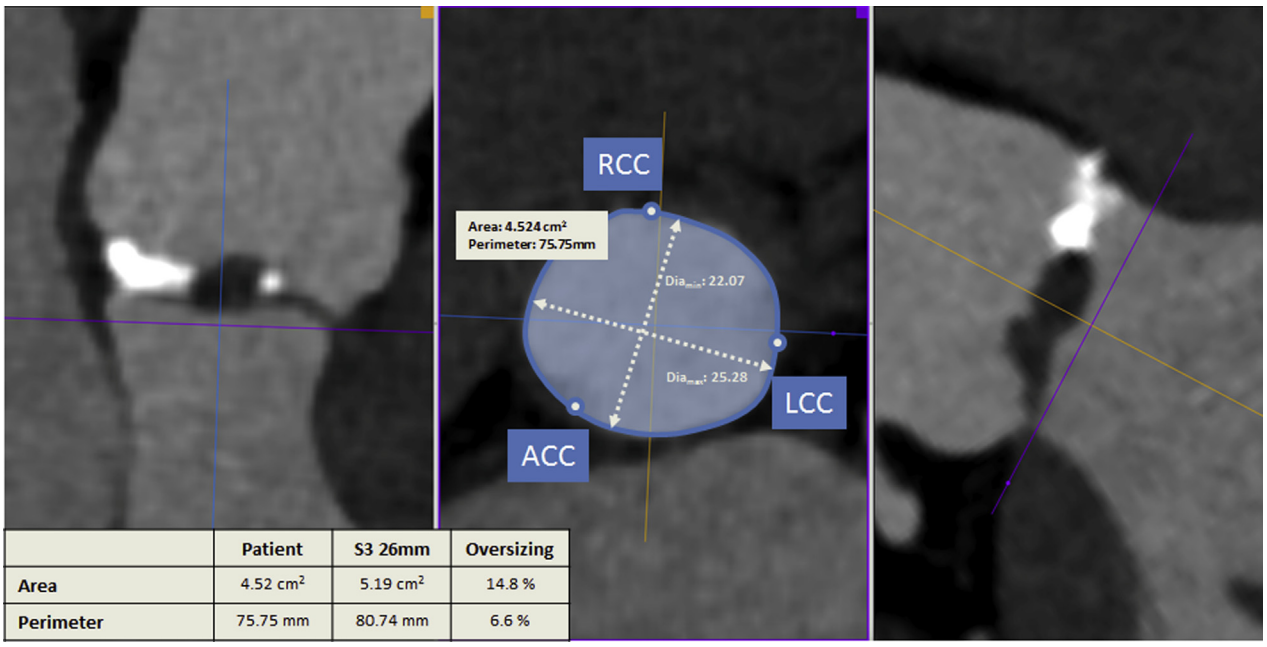
RESULTS

Clinical baseline, electrocardiographic, and procedural characteristics of the study population are displayed in Tables 2 and 3. Mean age was 81 years with a logistic EuroSCORE of 16%. TAVR was performed using the 23-, 26-, and 29-mm SAPIEN 3 valve in 44%, 38%, and 18% of cases, respectively. Device success was achieved in 98%, with post-procedural paravalvular insufficiency ≥2 in 2% of cases. Conscious sedation was used in 39% of cases. Median hospital stay was 5 days, and there was no in-hospital death.

Implantation depth (% of frame height below the aortic annulus) was evaluated in 207 patients (1 case was performed under echocardiographic guidance without contrast administration due to pre-operative severe renal failure). Mean implantation depth was 26 ± 7% (range 6% to 48%, Table 3).

MSCT data and degree of oversizing are displayed in Tables 4 and 5 and are available for 206 patients, as 2 patients did not undergo MSCT due to renal failure. The median percentage of oversizing according to annular area and perimeter was 7% and 2%, respectively. Prosthesis selection was within range in 77% (159 of 206), undersized in 12% (24 of 206), and

FIGURE 2 MSCT Analysis and Calculation of Oversizing



	Patient	S3 26mm	Oversizing
Area	4.52 cm²	5.19 cm²	14.8 %
Perimeter	75.75 mm	80.74 mm	6.6 %

Example of multislice computed tomography (MSCT) analysis and calculation of oversizing in a patient with a 26-mm SAPIEN 3 (Edwards Lifesciences, Irvine, California). Nominal area of a 26-mm SAPIEN 3 (5.19 cm^2) was divided by patient anatomy (4.52 cm^2) to obtain the degree of area oversizing (14.8%). Note that minimal and maximal diameters were not automatically obtained but were manually drawn to allow for an approximation of annulus eccentricity. For details, see the Methods section. ACC = non (a-)coronary cusp; LCC = left coronary cusp; RCC = right coronary cusp.

oversized in 11% (23 of 206) of cases. Mean oversizing by area and implantation depth in these categories was 7.3 ± 6.6% and 26 ± 8%, −9.3 ± 3.8% and 24 ± 6%, and 26.7 ± 5.2% and 28 ± 6%, respectively.

NEW PPIS AFTER SAPIEN 3 IMPLANTATION. After TAVR with the SAPIEN 3, 16% (34 of 208) underwent PPI before discharge (**Figure 1**). Indication and timing for PPI is provided in Online Table 1. Intraventricular conduction at baseline and discharge is displayed in **Figure 4A**. Patients undergoing PPI had a higher prevalence of atrial fibrillation (44% vs. 24%; p = 0.017), complete RBBB (27% vs. 5%; p = 0.001), and bradycardia (<60 beats/min, 38% vs. 21%; p = 0.034) (**Table 2**) at baseline.

Depth of implantation and its association with PPI are displayed in **Table 3**. Patients with PPI had a trend toward deeper implantation, especially at the nonseptal side, without statistical significance. Postdilation was not associated with PPI (32% vs. 35%; p = 0.762).

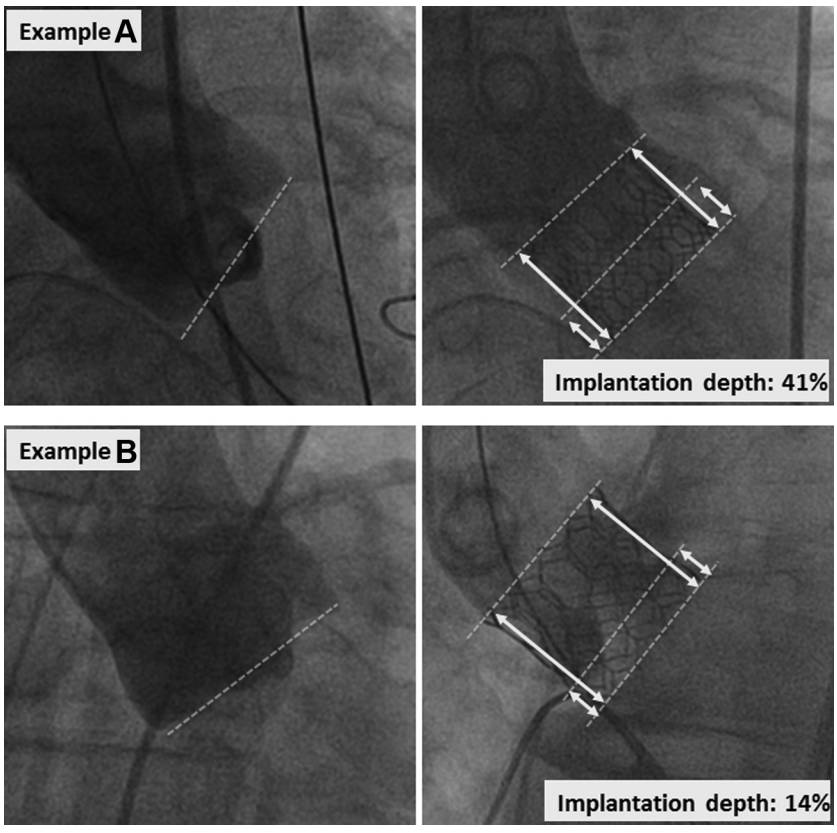
In MSCT data, the degree of oversizing and adherence to sizing recommendations are displayed in **Tables 4 and 5**. There was no difference in the degree of median area oversizing in patients with or without PPI after TAVR (6% [IQR: 2% to 11%] vs. 8% [IQR: 1% to 15%]; p = 0.566) nor was there a difference in degree of calcification or eccentricity index between both groups.

In a multivariable analysis, independent predictors of PPI were previous RBBB (OR: 11.965 [95% CI: 3.406 to 42.026]; p < 0.001), atrial fibrillation (OR: 3.996 [95% CI: 1.567 to 10.192]; p = 0.004), heart rate on admission (OR: 0.941 [95% CI: 0.907 to 0.977]; p = 0.001, per beat/min increase), previous unspecific intraventricular conduction abnormality (OR: 10.022 [95% CI: 1.644 to 61.083]; p = 0.012), COPD (OR: 4.660 [95% CI: 1.513 to 14.405]; p = 0.007), and implantation depth at the nonseptal side (OR: 1.066

TABLE 1 SAPIEN 3 Nominal Prosthesis Dimensions and Sizing Recommendations

	23 mm	26 mm	29 mm
Frame height, mm	18	20	22.5
Outer diameter, mm	22.75	25.71	28.75
Outer perimeter, mm	71.47	80.74	90.32
Outer area, cm^2	4.06	5.19	6.48
Recommended range (area), cm^2	3.38–4.30	4.30–5.46	5.40–6.80
Recommended range (area-derived diameter), mm	20.7–23.4	23.4–26.4	26.2–29.4

FIGURE 3 Determination of Implantation Depth



Example of deep **(A)** and high **(B)** implanted SAPIEN 3 (Edwards Lifesciences, Irvine, California). Final post-deployment aortic angiogram shows the prosthesis in an orthogonal view. The native aortic annulus was marked by intersecting the sinus of Valsalva. The entire prosthesis frame height **(long arrows)** and the portion below the aortic annulus **(short arrows)** were measured at the septal (i.e., noncoronary cusp) and nonseptal (i.e., left coronary cusp) sides. Implantation depth was expressed as percentage of frame height below the aortic annulus.

[95% CI: 1.066 to 1.127]; p = 0.022, per % of frame below annulus), but not prosthesis oversizing (OR: 0.217 [95% CI: 0.026 to 1.780]; p = 0.155). No difference in incidence of PPI was observed across the tertiles of consecutive cases (p for trend 0.327) (Online Figure 1).

NEW-ONSET OR WORSENED CA OR PPI AFTER SAPIEN 3 IMPLANTATION. The overall incidence of new or worsened CA or PPI was 31% (57 of 184) (**Figure 1**): PPI in 14% (25 of 184), LBBB in 16% (30 of 184), and RBBB in 1% (2 of 184). Intraventricular conduction at baseline and at discharge is displayed in **Figure 4B**. At baseline, patients with new CA or PPI had a longer QRS duration (100 ± 24 ms vs. 93 ± 11 ms; p = 0.006) and a higher prevalence of nonspecific intraventricular conduction abnormalities (9% vs. 1%; p = 0.011; **Table 2**).

Implantation depth was lower in patients with new or worsened CA or PPI, especially at the septal side (29 ± 8% of frame height below annulus vs. 25 ± 7%; p = 0.003). Patients in the upper quartile of mean implantation depth (range 30% to 48% of frame below annulus) exhibited a significantly higher rate of new or worsened CA or PPI as compared with lower quartiles (46% [21 of 46] vs. 26% [36 of 138]; p = 0.013). New CA or PPI were more frequent under conscious sedation (51% vs. 35%; p = 0.037), but there was no association with post-dilation (33% vs. 38%; p = 0.561).

Percentages of oversizing, valvular calcification, or annulus eccentricity were not significantly different in patients with new or worsened CA or PPI compared with those without (**Table 4**). However, in case of out-of-range prosthesis oversizing, the rate of new or worsened CA or PPI was significantly higher (58% [11 of 19] vs. 28% [46 of 164]; p = 0.007).

TABLE 2 Baseline and ECG Characteristics

	All Patients (n = 208)	New Permanent Pacemaker			PPI and New or Worsened CA		
		Yes (n = 34)	No (n = 174)	p Value	Yes (n = 57)	No (n = 127)	p Value
Clinical characteristics							
Age, yrs	81 ± 6	82 ± 6	81 ± 6	0.194	82 ± 6	80 ± 6	0.012
Female	94 (45)	11 (32)	83 (48)	0.100	28 (49)	59 (47)	0.738
Logistic EuroSCORE, %	16 ± 12	19 ± 15	15 ± 12	0.106	17 ± 13	14 ± 10	0.065
NYHA functional class III/IV	135 (65)	28 (79)	108 (62)	0.053	41 (72)	76 (60)	0.115
COPD	27 (13)	8 (24)	19 (11)	0.045	8 (14)	14 (11)	0.560
PAD	28 (14)	4 (12)	24 (14)	0.999	8 (14)	16 (13)	0.789
Extracardiac arteriopathy	58 (28)	9 (27)	49 (28)	0.841	16 (28)	33 (26)	0.767
GFR, ml/min	54 ± 37	49 ± 29	55 ± 39	0.409	49 ± 27	58 ± 43	0.162
Coronary artery disease	137 (66)	23 (68)	114 (66)	0.811	41 (72)	83 (65)	0.379
Myocardial infarction	19 (9)	3 (9)	16 (9)	0.999	5 (9)	13 (10)	0.757
PCI	81 (39)	15 (44)	66 (38)	0.499	22 (39)	52 (41)	0.764
CABG	12 (6)	3 (9)	9 (5)	0.419	4 (7)	6 (5)	0.503
Diabetes mellitus	59 (28)	11 (32)	48 (28)	0.573	14 (25)	35 (28)	0.671
Stroke	20 (10)	1 (3)	19 (11)	0.209	4 (7)	14 (11)	0.398
LVEF <35%	21 (10)	4 (12)	17 (10)	0.756	7 (12)	10 (8)	0.340
Electrocardiographic data							
Atrial fibrillation	57 (27)	15 (44)	42 (24)	0.017	15 (26)	31 (24)	0.782
Heart rate, beats/min	72 ± 14	68 ± 15	73 ± 14	0.073	69 ± 13	73 ± 14	0.107
Bradycardia <60 beats/min	50 (24)	13 (38)	37 (21)	0.034	19 (33)	27 (21)	0.080
PQ interval, ms	181 ± 37	197 ± 44	179 ± 35	0.035	182 ± 43	181 ± 34	0.955
AVB I°	34 (16)	8 (24)	26 (15)	0.216	12 (21)	19 (15)	0.307
QRS duration, ms	100 ± 22	115 ± 31	98 ± 19	<0.001	100 ± 24	93 ± 11	0.006
LAHB	20 (10)	3 (9)	17 (10)	0.999	5 (9)	15 (12)	0.540
Incomplete RBBB	3 (1)	0 (0)	3 (2)	0.999	1 (2)	2 (2)	0.999
Nonspecific IVCA	6 (3)	3 (9)	3 (2)	0.057	5 (9)	1 (1)	0.011
RBBB	18 (9)	9 (27)	9 (5)	0.001	–	–	–
LBBB	6 (3)	0 (0)	6 (3)	0.592	–	–	–

Values are mean ± SD or n (%).

AVBI° = first degree atrioventricular block with PQ duration >200 ms in patients with sinus rhythm; CA = conduction abnormalities; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; GFR = glomerular filtration rate; IVCA = intraventricular conduction abnormalities; LAHB = left anterior hemiblock; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; RBBB = right bundle branch block.

The independent predictors for new or worsened CA or PPI were implantation depth at the septal side (OR: 1.063 [95% CI: 1.017 to 1.110]; p = 0.006 per each % of frame below the aortic annulus), out-of-range prosthesis oversizing (OR: 3.489 [95% CI: 1.236 to 9.848]; p = 0.018), and QRS duration on admission (OR: 1.033 [95% CI: 1.011 to 1.056]; p = 0.003 per ms). However, there was no difference in incidence of new or worsened CA or PPI across the tertiles of consecutive cases (p for the trend = 0.962) (Online Figure 1).

DISCUSSION

In the present study, we report the rate of PPI and new or worsened CA with the SAPIEN 3 device. Although yielding excellent clinical results in terms of device success and in-hospital mortality, we found a relatively high rate of PPI and new or worsened CA. In a comprehensive analysis, we identified a strong influence of implantation depth and extreme prosthesis oversizing on the occurrence of new or worsened CA.

PPIS AND NEW OR WORSENED CA AFTER TAVR—INCIDENCE AND CLINICAL EFFECT. The incidence of PPI after TAVR with balloon-expandable valves, especially with the Edwards SAPIEN XT, ranges between 5% to 12% (6-8), and the effect on clinical outcome remains controversial. Although no negative effect on survival has been observed (9,10), PPI may limit clinical benefit from TAVR due to lack of AV-synchrony and right ventricular pacing (12). Additionally, PPI after TAVR has been identified as an important cause of prolonged hospital stay, thereby increasing procedural costs (11).

There are still limited available data on the incidence of PPI after TAVR with the SAPIEN 3 valve,

TABLE 3 Procedural Characteristics and Outcome

	All Patients (N = 208)	New Permanent Pacemaker			PPI and New or Worsened CA		
		Yes (n = 34)	No (n = 174)	p Value	Yes (n = 57)	No (n = 127)	p Value
Device dimension				0.173			0.576
23 mm	91 (44)	12 (35)	79 (45)		24 (42)	60 (47)	
26 mm	79 (38)	12 (35)	67 (39)		21 (37)	48 (38)	
29 mm	38 (18)	10 (29)	28 (16)		12 (21)	19 (15)	
Conscious sedation	81 (39)	17 (50)	64 (37)	0.148	29 (51)	44 (35)	0.037
Procedural time, min	61 ± 24	61 ± 21	61 ± 24	0.929	61 ± 27	61 ± 23	0.967
Fluoroscopy time, min	16 ± 16	13 ± 5	16 ± 17	0.353	13 ± 4	16 ± 15	0.186
Contrast, ml	116 ± 67	92 ± 27	120 ± 71	0.027	109 ± 63	123 ± 71	0.205
Post-dilation	72 (35)	11 (32)	61 (35)	0.762	19 (33)	48 (38)	0.561
Multiple valves	1 (1)	0 (0)	1 (1)	0.999	0 (0)	1 (1)	0.999
Paravalvular leakage II+	4 (2)	1 (3)	3 (2)	0.513	1 (2)	3 (2)	0.999
Device success	203 (98)	33 (97)	170 (98)	0.999	56 (98)	123 (97)	0.999
Days in hospital	6 ± 4	7 ± 3	6 ± 4	0.118	7 ± 3	6 ± 4	0.313
Intrahospital death	0 (0)	0 (0)	0 (0)	–	0 (0)	0 (0)	–
30-day mortality	1 (0.5)	1 (3)	0 (0)	0.163	0 (0)	0 (0)	–
Depth of implantation, % of frame height below aortic annulus at:							
Septal side, NCC	26 ± 8	27 ± 9	26 ± 8	0.265	29 ± 8	25 ± 7	0.003
Nonseptal side, LCC	26 ± 7	28 ± 9	25 ± 7	0.081	27 ± 8	25 ± 7	0.035
Mean	26 ± 7	28 ± 9	25 ± 7	0.145	28 ± 8	25 ± 7	0.010

Values are n (%) or mean ± SD.
CA = conduction abnormalities; LCC = left coronary cusp; NCC = noncoronary cusp; PPI = permanent pacemaker implantation.

although emerging figures indicate a rate of PPI between 13% and 25.5% (16-18). In a preliminary series analyzing the SAPIEN 3 prosthesis, our group found a PPI rate of 12.5% (24). With increasing experience, this rate was not reduced and was 16% in this extended patient cohort, which is in line with the mentioned reports from the published data.

There are other reasons for an elevated PPI rate apart from device- or technical-related causes. One reason may be a substantial percentage of pre-existent RBBB. As reported in previous studies (25) and in a recent meta-analysis (8), pre-existing RBBB is a strong predictor for PPI after TAVR. This was also observed in our study, where baseline ECG parameters were most important for the prediction of PPI.

The incidence of new or worsened CA after TAVR with balloon-expandable valves ranges between 8% and 30% (1-5). Although no effect on mortality could be demonstrated (2), new or worsened CA are

TABLE 4 MSCT Measurements of the Aortic Annulus

	All Patients (N = 206)	New Permanent Pacemaker			PPI and New or Worsened CA		
		Yes (n = 34)	No (n = 172)	p Value	Yes (n = 57)	No (n = 126)	p Value
Minimal diameter, mm	21.03 ± 2.35	21.61 ± 2.33	20.91 ± 2.34	0.116	20.98 ± 2.52	20.99 ± 2.25	0.983
Maximal diameter, mm	26.94 ± 2.70	27.78 ± 2.90	26.77 ± 2.64	0.046	26.89 ± 2.69	26.84 ± 2.68	0.906
Eccentricity index	0.22 ± 0.06	0.22 ± 0.07	0.22 ± 0.06	0.799	0.22 ± 0.06	0.22 ± 0.06	0.727
Perimeter, mm	77.06 ± 7.43	79.10 ± 7.51	76.66 ± 7.37	0.080	76.97 ± 7.68	76.85 ± 7.34	0.920
% oversizing	2 [−1 to 5]	1 [0 to 3]	2 [−2 to 5]	0.495	2 [0 to 6]	2 [−2 to 5]	0.209
Area, cm^2	4.62 ± 0.91	4.87 ± 0.91	4.57 ± 0.91	0.083	4.61 ± 0.95	4.60 ± 0.90	0.932
% oversizing	7 [0 to 14]	6 [2 to 11]	8 [−1 to 15]	0.566	6 [2 to 15]	7 [−1 to 19]	0.177
Degree of calcification							
Cusps, moderate/severe	148 (72)	24 (71)	124 (72)	0.859	30 (68)	93 (74)	0.452
Annulus, moderate/severe	21 (10)	3 (9)	18 (11)	0.999	9 (16)	12 (10)	0.218
LVOT, moderate/severe	12 (6)	2 (6)	10 (6)	0.999	5 (9)	7 (6)	0.521

Values are mean ± SD or n (%) or median [interquartile range].
LVOT = left ventricular outflow tract; MSCT = multislice computed tomography; other abbreviations as in Table 3.

TABLE 5 Prosthesis Sizing According to Sizing Recommendation by MSCT-Derived Area

	All Patients (N = 206)	New Permanent Pacemaker			PPI and New or Worsened CA		
		Yes (n = 34)	No (n = 172)	p Value	Yes (n = 57)	No (n = 126)	p Value
Undersized	24 (12)	2 (6)	22 (13)	0.097	3 (5)	20 (16)	0.007
Within sizing range	159 (77)	31 (91)	128 (74)		43 (75)	98 (78)	
Oversized	23 (11)	1 (3)	22 (13)		11 (19)	8 (6)	
23-mm SAPIEN 3 prosthesis	91 (44)	12 (35)	79 (46)	–	24 (42)	60 (48)	–
Undersized	13 (14)	1 (8)	12 (15)	0.269	1 (4)	11 (18)	0.166
Within sizing range	67 (74)	11 (92)	56 (71)		19 (79)	44 (73)	
Oversized	11 (12)	0 (0)	11 (14)		4 (17)	5 (8)	
26-mm SAPIEN 3 prosthesis	77 (37)	12 (35)	65 (38)	–	21 (37)	48 (38)	–
Undersized,	8 (10)	1 (8)	7 (11)	0.404	2 (10)	6 (13)	0.049
Within sizing range	61 (79)	11 (92)	50 (78)		14 (67)	39 (83)	
Oversized	8 (10)	0 (0)	8 (12)		5 (24)	2 (4)	
29-mm SAPIEN 3 prosthesis	38 (18)	10 (29)	28 (16)	–	12 (21)	19 (15)	–
Undersized	3 (8)	0 (0)	3 (11)	0.551	0 (0)	3 (16)	0.235
Within sizing range	31 (82)	9 (90)	22 (79)		10 (83)	15 (79)	
Oversized	4 (11)	1 (10)	3 (11)		2 (17)	1 (5)	

Values are n (%).
MSCT = multislice computed tomography; other abbreviations as in Table 3.

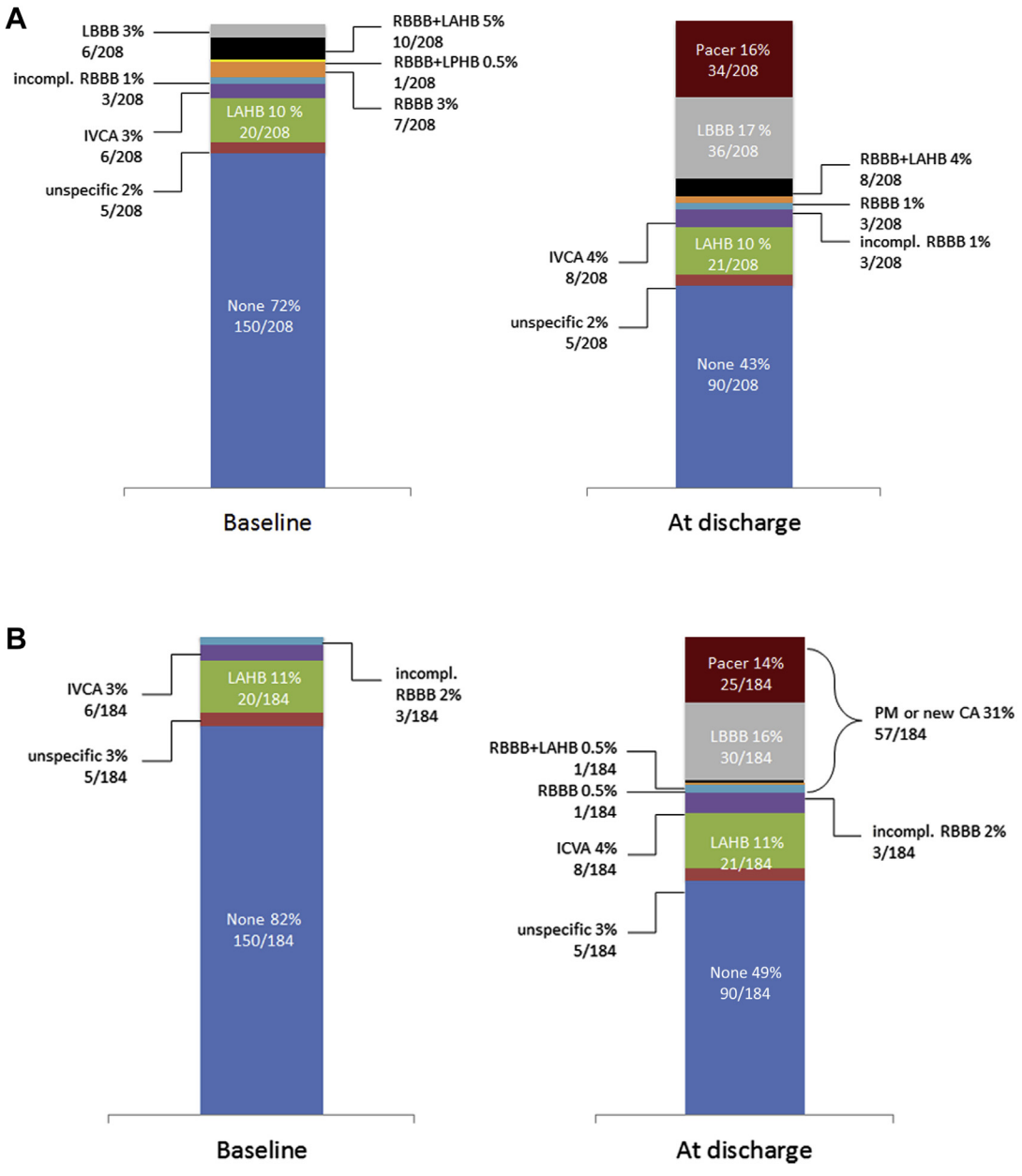
associated with impaired recovery of left ventricular function (13,14). Also, a higher risk of late PPI due to new or worsened CA (4,5) may prompt prophylactic PPI in these patients.

Data on the incidence of new or worsened CA after TAVR with the SAPIEN 3 as well as the potential determinants are scarce. Recent data from 150 patients treated with this device indicated an incidence of LBBB of 21%; however, the underlying mechanisms were not addressed (16). In the present study, we found new LBBB in 16% of patients not undergoing TAVR-related PPI and a strong relationship to implantation depth and prosthesis oversizing. Previous studies have shown that new-onset CA after TAVR with balloon-expandable valves may be dynamic, and a certain percentage resolves after implantation to hospital discharge and during follow-up (2). In the present study, we have focused on the pre-discharge ECG. The degree of resolution of new-onset CA with the SAPIEN 3 during follow-up still needs to be investigated.

ROLE OF IMPLANTATION DEPTH AND PROSTHESIS OVERSIZING. A deeper positioning of the prosthesis below the aortic annulus might cause CA via mechanical stress and direct damage of the conduction system. Accordingly, depth of implantation has been identified as a predictor of new or worsened CA, mainly with self-expandable but also balloon-expandable valves (2,26,27). The present study extends these findings to the SAPIEN 3 valve, showing depth of implantation as an independent predictor of new or worsened CA or PPI. The SAPIEN 3 valve possesses a higher frame and extends deep into the left ventricular outflow tract (15). However, in case of PPI, results were not univocal. Recently, in a very small sample size of 29 patients, Tarantini et al. (17) found a relation between implantation depth and PPI (17), whereas the present study found only a trend toward deeper implantations in case of PPI.

The role of MSCT-guided prosthesis sizing and oversizing has been investigated primarily to address paravalvular leakage (28). Recently, Yang et al. (29) have demonstrated that the SAPIEN 3 valve requires less annular oversizing to prevent paravalvular leakage. However, data on the influence of MSCT-derived measures of oversizing with PPI and new or worsened CA are scarce, as this issue has mainly been addressed using echocardiography (30,31). We found a strong relationship of out-of-range oversizing with the incidence of new CA or PPI. Indeed, extreme out-of-range oversizing resulted in a 3- to 4-fold increase in new or worsened CA or PPI. Of note, the sizing range assessed in this study includes the recommended sealing zones for prostheses deployed with nominal volumes and not the areas in which prosthesis size may still be considered adequate when underfilled. The observation that oversizing was associated with new or worsened CA but not with PPI has been observed before using post-procedural MSCT data (32). For prevention of paravalvular leakage, a modest degree of oversizing of the SAPIEN 3 valve seems sufficient (29), whereas excessive oversizing increases the risk of new CA and

FIGURE 4 Intraventricular Conduction at Baseline and Before Discharge



Intraventricular conduction at baseline and before discharge in the population for PPI analysis **(A)** and for new or worsened CA or PPI **(B)**. Abbreviations as in Figure 1.

PPI. This should be considered in future sizing recommendations.

A somewhat counterintuitive finding in this study is the weak relationship between PPI and both oversizing and depth of implantation. PPI after TAVR is a more multifactorial phenomenon than the rather objective ECG endpoint "new or worsened CA." There are several clinical scenarios, unrelated to the procedure itself, that may lead to PPI after TAVR, including a pre-existing indication for pacing (e.g., pre-existent sick sinus syndrome and pauses) or a prophylactic indication (e.g., tri-fascicular block or bradycardia). Therefore, PPI may be a somewhat subjective endpoint to analyze, and the effect of

implantation depth and oversizing may thus become more difficult to evaluate. Moreover, it is possible that in the absence of pre-existent CA, direct trauma to the left bundle branch during deployment of the prosthesis may cause new CA but not necessarily complete heart block requiring PPI. However, given that patients with new onset of CA had a 2-fold elevated rate of PPI compared with patients without CA (30% [14 of 46] vs. 12% [20 of 162]; p = 0.003), and the fact that other studies have also been able to demonstrate a direct relationship of implantation depth with PPI after TAVR with the SAPIEN 3 (17), there is a clear suggestion of the importance of both appropriate valve sizing and implantation depth to achieve better outcomes.

STUDY LIMITATIONS. Using fluoroscopic images offers an approximation of implantation depth, which in certain cases may be subject to underestimation due to discrepancies between the annulus plane and prosthesis plane.

CONCLUSIONS

In a large population of patients undergoing TAVR with the SAPIEN 3 valve, we found an overall incidence of new or worsened CA or PPI in 1 of 3 patients and a clear relationship to implantation depth and out-of-range extreme oversizing. An adjustment of implantation height and careful adherence to the sizing algorithms may result in a reduction of new or worsened CA or PPI.

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PERSPECTIVES

WHAT IS KNOWN? Post-procedural new or worsened CA and PPI after TAVR with the SAPIEN 3 remain of concern, and their incidence and predictors are unclear.

WHAT IS NEW? Using the SAPIEN 3 in 208 patients, the incidence of new PPI and new or worsened CA or PPI was 16.4% and 31%, respectively. Implantation depth and extreme prosthesis oversizing were predictors of new CA or PPI using the SAPIEN 3.

WHAT IS NEXT? Future studies should assess if higher implantation and avoidance of extreme oversizing lead to a decrease in PPI and new or worsened CA using the SAPIEN 3 device.

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KEY WORDS conduction abnormalities, permanent pacemaker implantation, predictors, transcatheter aortic valve replacement

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