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Transcatheter Valve SELECTion in Patients With Right Bundle Branch Block and Impact on Pacemaker Implantations

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ABSTRACT

OBJECTIVES This study sought to evaluate the impact of the ACURATE neo (NEO) (Boston Scientific, Marlborough, Massachusetts) versus SAPIEN 3 (S3) (Edwards Lifesciences, Irvine, California) on permanent pacemaker implantation (PPI) in patients with pre-existing right bundle branch block (RBBB) after transcatheter aortic valve replacement.

BACKGROUND Pre-existing RBBB is the strongest patient-related predictor for PPI after transcatheter aortic valve replacement. No comparison of newer-generation transcatheter heart valves with regard to PPI in these patients exists.

METHODS This multicenter registry includes 4,305 patients; 296 (6.9%) had pre-existent RBBB and no pacemaker at baseline and formed the study population. The primary endpoint was new PPI at 30 days. The association of NEO versus S3 with PPI was assessed using binary logistic regression analyses and inverse probability treatment weighting in a propensity-matched population.

RESULTS The 30-day PPI rate was 39.2%. The S3 and NEO were used in 66.9% and 33.1%, respectively. The NEO was associated with lower rates of PPI compared with the S3 (29.6% vs. 43.9%; $p = 0.025$; odds ratio [OR]: 0.54; 95% confidence interval [CI]: 0.32 to 0.89; $p = 0.018$), after multivariable adjustment (OR: 0.48; 95% CI: 0.26 to 0.86; $p = 0.014$), and in the inverse probability treatment weighting analysis (OR: 0.37; 95% CI: 0.25 to 0.55; $p < 0.001$). There was no difference in device failure (8.2% vs. 6.6%; $p = 0.792$) or in-hospital course. In the propensity-matched population, PPI rate was also lower in the NEO versus S3 (23.1% vs. 44.6%; $p = 0.016$; OR: 0.37; 95% CI: 0.17 to 0.78; $p = 0.010$), with no difference in device failure (9.2% vs. 6.2%; $p = 0.742$).

CONCLUSIONS In patients with RBBB, risk of PPI was significantly lower with the NEO compared with the S3, suggesting the possibility of a patient tailored transcatheter heart valve therapy.
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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

IPTW = inverse probability treatment weighting

MSCT = multislice computed tomography

OR = odds ratio

PPI = permanent pacemaker implantations

RBBB = right bundle branch block

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

VARC-2 = Valve Academic Research Consortium-2

Transcatheter aortic valve replacement (TAVR) has become the standard of care for patients with severe symptomatic aortic stenosis at extreme or high risk for conventional surgery and is a valuable alternative for those at intermediate risk (1).

With mortality rates numerically lower than in conventional surgery (2,3), an extension of this revolutionary therapy toward lower risk patients can be expected. However, especially in these populations, it is necessary to further minimize TAVR-related complications such as need for new permanent pacemaker implantation (PPI), which may be associated with impaired survival and worse recovery of left ventricular function after the procedure (4–6).

Technical improvements of newer-generation transcatheter heart valves (THVs) have led to a reduction of PPI compared with earlier-generation devices but still considerably ranges from very low (2.3%) to high (36.1%) depending on the type of THV (7).

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Pre-existing right bundle branch block (RBBB) has consistently been shown to be the strongest patient-related predictor for PPI after TAVR, with an up to 12-fold risk increase (8–10), resulting in elevated PPI rates of up to 40% (11–13).

Currently, no direct comparison of newer-generation THVs with regard to PPI in patients with pre-existent RBBB exists. Nevertheless, the perspective to reduce PPI rates by selection of THVs with lower risk for PPI would constitute an attractive step toward patient tailored THV therapy in this high-risk subgroup for PPI.

Therefore, in the SELECT RBBB (Transcatheter heart valve SELECTion in Patients with Right Bundle Branch Block multicenter registry) registry, we compare 2 newer-generation THV in patients with pre-existing RBBB, namely the widely used, standard balloon-expandable THV SAPIEN 3 (Edwards Lifesciences, Irvine, California) and the THV with the lowest published PPI rate among newer-generation devices (14), the self-expanding ACURATE neo TF (Boston Scientific, Marlborough, Massachusetts) (**Central Illustration**).

METHODS

PATIENT POPULATION. The SELECT RBBB registry includes consecutive patients undergoing TAVR using the ACURATE neo or the SAPIEN 3 for severe symptomatic aortic stenosis in 7 centers in Germany and Switzerland between January 2014 and July 2017. Of 4,305 patients, 302 fulfilled the inclusion criteria consisting of pre-existent complete RBBB and no pacemaker at baseline. Of these, 6 patients with incomplete multislice CT data were excluded from analysis, resulting in a study population of 296 patients (ACURATE neo, n = 98; SAPIEN 3, n = 198) (for study flow, see **Figure 1** and the Online Appendix).

Data were prospectively acquired at each participating center and collected in a joint database. Procedural outcome and in-hospital complications were classified according to the updated criteria of the Valve Academic Research Consortium-2 (VARC-2) (15). Procedures were performed in a hybrid operating suite under either conscious sedation or general anesthesia. All patients provided written informed consent for the procedure.

DEVICE DESCRIPTION. The THVs used in this study were the ACURATE neo and SAPIEN 3, and both have been described in detail elsewhere (16,17). In brief, the ACURATE neo consists of a self-expanding nitinol frame with a supra-annular porcine pericardial leaflet valve and a pericardial sealing skirt and is available in a small, medium, and large sizes. The balloon-expandable SAPIEN 3 carries bovine pericardial leaflets mounted on a cobalt-chromium alloy frame with an external fabric seal and is available in sizes of 20, 23, 26, and 29 mm.

MULTISLICE COMPUTED TOMOGRAPHY DATA ANALYSIS. Aortic annulus measurements were assessed in multiple-plane reconstructions according the Society of Cardiovascular Computed Tomography

Bureau for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Medtronic, Gore, Jena Valve Technology, and New Valve Technology; and has received research support from Abbott Vascular, Boston Scientific, Jena Valve Technology, Edwards Lifesciences and New Valve Technology. Dr. Blumenstein has received proctor fees from Boston Scientific. Dr. Deuschl has received travel support from Boston Scientific, Symetis, Edwards Lifesciences, Abbott, and Neovasc; has received proctor fees from Edwards Lifesciences and Neovasc; and has served as a proctor for Edwards Lifesciences. Dr. Joner has served as a consultant for Biotronik and Orbus Neich. Dr. Hilker has received proctor fees from Boston Scientific. Dr. Hengstenberg has received speaker honoraria and proctor fees from Boston Scientific and Edwards Lifesciences. Dr. Möllmann has received speaker honoraria and proctor fees from Abbott, Biotronik, St. Jude Medical, Boston Scientific, and Edwards Lifesciences. Dr. Rheude has reported that he has no relationships relevant to the contents of this paper to disclose.

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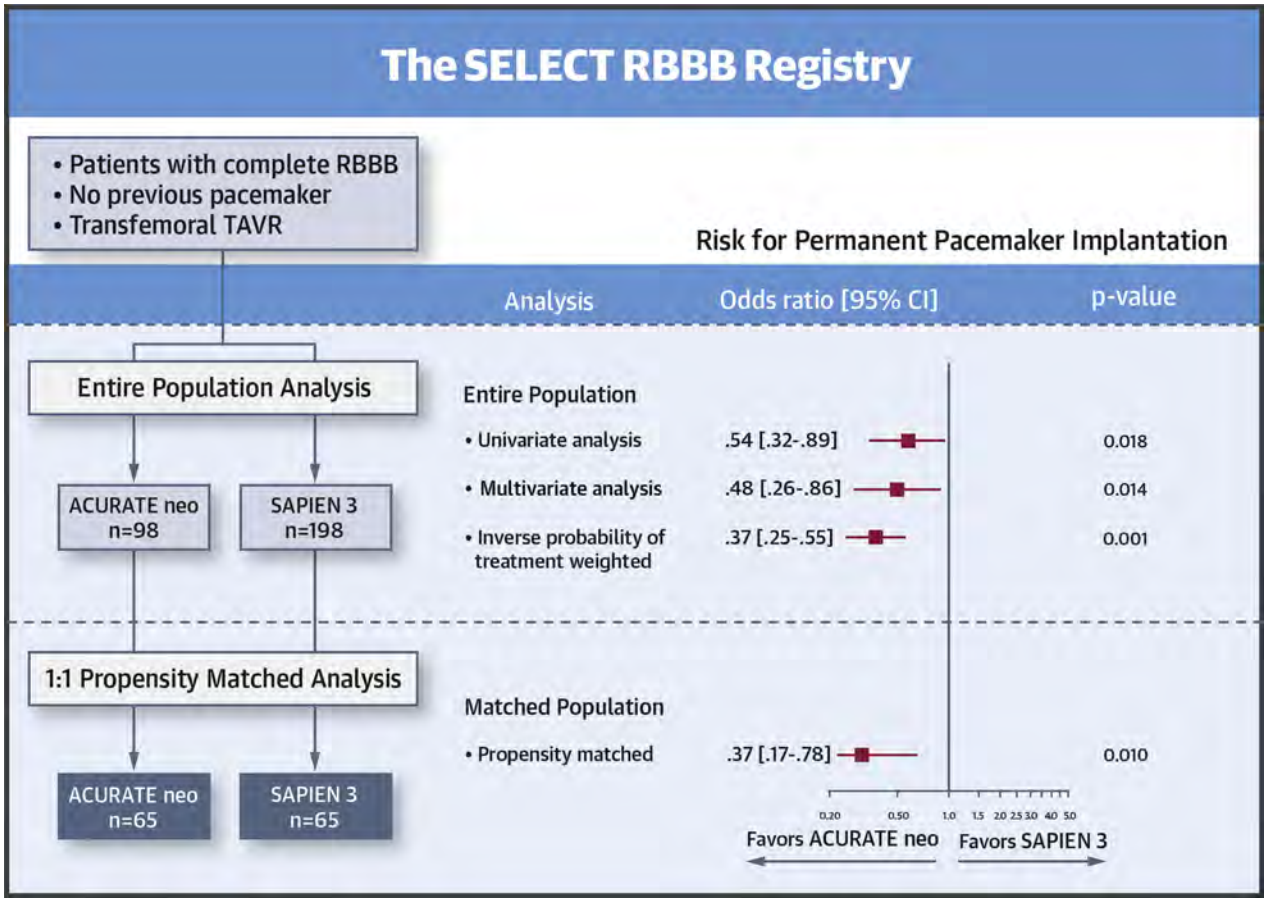
CENTRAL ILLUSTRATION **The SELECT RBBB Registry**



Husser, O. et al. J Am Coll Cardiol Intv. 2019;12(18):1781–93.

The SELECT RBBB registry recruited patients undergoing transfemoral transcatheter aortic valve implantation (TAVR) with pre-existing complete RBBB and without previous pacemaker to assess the risk for permanent pacemaker implantation according to the use of the self-expanding ACURATE neo (Boston Scientific, Marlborough, Massachusetts) and the balloon-expandable SAPIEN 3 (Edwards Lifesciences, Irvine, California) transcatheter heart valves. CI = confidence interval; RBBB = right bundle branch block.

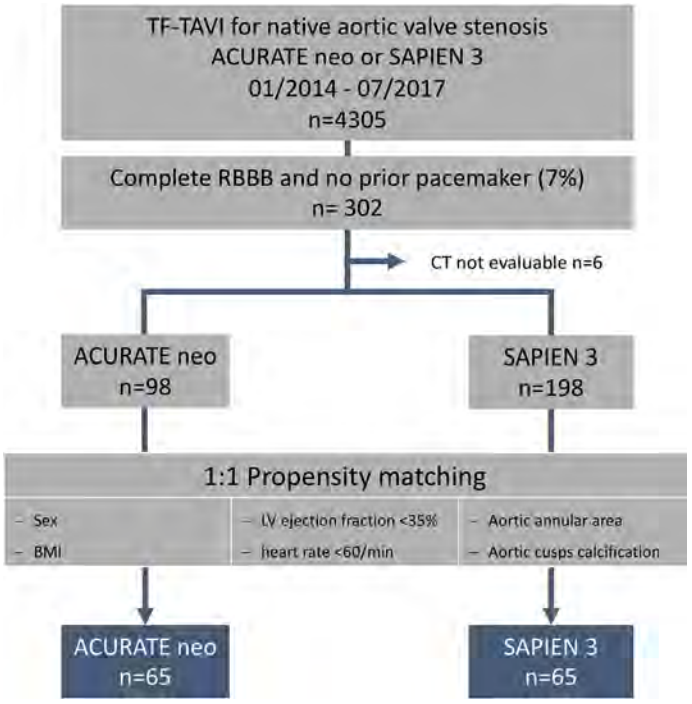
(18). In short, area and perimeter of the aortic annulus were obtained by direct planimetry, and the minimum and maximum diameters were assessed. Calcification of the valvular apparatus was visually graded and dichotomized as mild or moderate versus severe. Prosthesis oversizing was based on area and was calculated using the formula [(prosthesis nominal area / patient aortic annular area − 1)·100] as previously published (8). Final decision on the implanted prosthesis size was at the discretion of the physicians performing the procedure.

DEFINITION OF ENDPOINTS. The primary endpoint of the study was the incidence of new PPI at 30 days after TAVR. Reasons for PPI were recorded in every case, and the indication for PPI was determined by the physicians in charge of the patient according to local standard of care.

The secondary endpoint was device failure defined as absence of VARC-2-defined device success. In short, this composite endpoint includes absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomic location and intended performance (no patient-prosthesis mismatch with mean aortic valve gradient <20 mm Hg and no moderate or severe prosthetic valve regurgitation).

STATISTICAL ANALYSIS. Continuous variables are presented as the median (interquartile range) with differences analyzed using the Mann-Whitney *U* test. For comparison of group proportions, the chi-square

FIGURE 1 Study Flow and Variables Used for Propensity Matching



Study overview and variables used for propensity matching. BMI = body mass index; LV = left ventricular; RBBB = right bundle branch block; TAVR = transcatheter aortic valve replacement; TF-TAVR = transfemoral TAVR.

test or Fisher exact test were used. Missing baseline data (0.3%) were imputed using predictive mean matching (R-package mice, version 2.46). The association of THV (ACURATE neo vs. SAPIEN 3) with the primary endpoint was assessed using unadjusted and multivariate adjusted binary logistic regression analyses and by creating a propensity-matched population. The odds ratio (OR) and corresponding 95% confidence interval (CI) were computed.

The influence of THV on PPI was tested using several approaches. First, the univariate association was analyzed. Second, a multivariable model stratified by center and adjusted for covariates yielding a p value <0.10 in the univariate analysis was performed. Variables included were previous coronary artery disease, atrial fibrillation, and pulmonary artery pressure >60 mm Hg. To reduce imbalance in baseline characteristics and the effect of a potential selection bias, 2 approaches were applied. The multivariate model was repeatedly adjusted for a weighted estimation using a propensity score to undergo TAVR with the ACURATE neo. This propensity score was estimated via binary logistic regression analysis adjusted for variables selected based on their p value in univariate analysis and on their potential influence on treatment allocation. The selected variables were sex, body mass index, baseline heart rate <60 beats/min, left ventricular ejection fraction <35%, aortic annular area, and severe aortic cusps calcification. A subgroup analysis of the effect of THV on PPI was conducted according to age, sex, QRS duration, rhythm on admission, presence of atrioventricular block, and baseline heart rate.

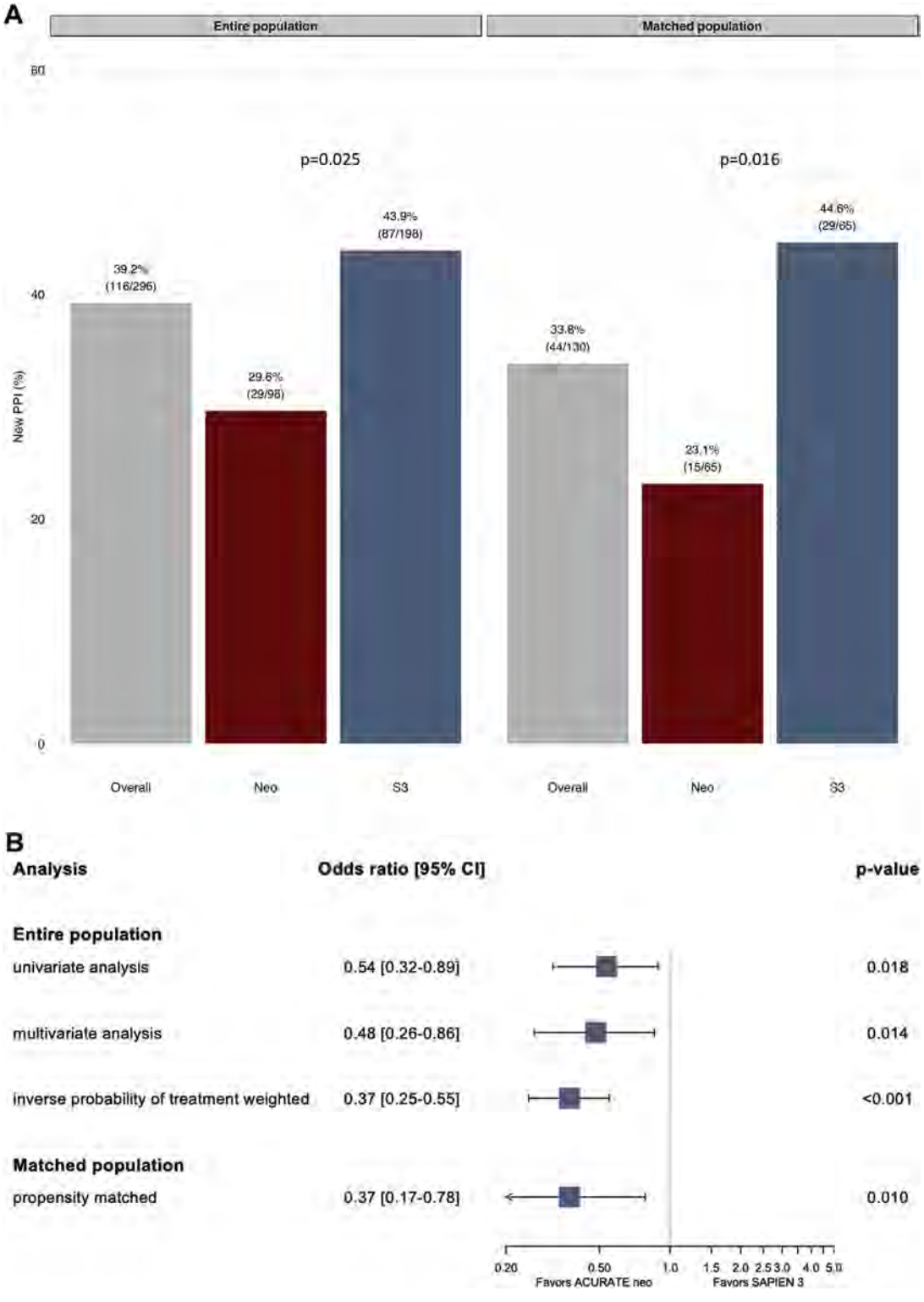
Finally, a matched population was created using propensity matching (R-package MatchIt, version 3.0.2). In short, a 1-to-1 nearest neighbor matching with a caliper of 0.1 was conducted to identify a matched population of 2 groups of 65 patients treated with each THV. A 2-sided p value <0.05 was considered statistically significant. All analyses were performed using R version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

INCIDENCE OF PERMANENT PACEMAKER IMPLANTATIONS. In total, 296 patients with preexistent RBBB, no prior pacemaker, and complete multislice computed tomography (MSCT) data were included. The primary endpoint, overall rate of new PPI at 30 days, occurred in 39.2% (n = 116 of 296) (**Figure 2A**). Comparison of patients with and without PPI showed a significantly higher prevalence of atrial fibrillation (36.2% vs. 21.7%; p = 0.009). On echocardiography, patients with PPI displayed a higher prevalence of pulmonary hypertension (25% vs. 15%; p = 0.046). There was no difference in aortic annular anatomy on MSCT (Online Table 1). Device success was comparable among patients without versus with PPI (92.9% vs. 94%; p = 0.735). Prosthesis oversizing as well as pre- and post-dilatation rates were not different between both groups. Mean implantation depth was lower in cases of PPI (6.9 mm vs. 5.8 mm; p = 0.001). Overall, median hospital stay was 7 (interquartile range: 6 to 11) days. Patients with PPI had a significantly longer ICU and hospital stay (9 days vs. 7 days; p < 0.001) and a more complicated in-hospital course (see Online Table 2).

DIFFERENCES BETWEEN PATIENTS TREATED WITH ACURATE NEO AND SAPIEN 3. The SAPIEN 3 and ACURATE neo were used in 66.9% (n = 198 of 296) and 33.1% (n = 98 of 296), respectively. Baseline characteristics according to THV are displayed in **Table 1**. There were no significant differences in clinical characteristics apart from a higher proportion of men treated with ACURATE neo (39.8% vs. 27.8%; p = 0.050). As the SAPIEN 3 covers a larger range of annular diameters, aortic annular anatomy on MSCT

FIGURE 2 Rate and Risk of PPI



(A) Overall rate of permanent pacemaker implantation (PPI) and according to the ACURATE neo (Boston Scientific, Marlborough, Massachusetts) and SAPIEN 3 (Edwards Lifesciences, Irvine, California) in the entire and matched populations. **(B)** Odds ratio for PPI according to use of ACURATE neo versus SAPIEN 3 in the entire and in the matched population. CI = confidence interval.

TABLE 1 Baseline, Electrocardiographic, Echocardiographic, and Multislice Computed Tomography Characteristics

	SAPIEN 3 (n = 198)	ACURATE neo (n = 98)	p Value	SAPIEN 3 (n = 65)	ACURATE neo (n = 65)	p Value
Age, yrs	82.0 (78.0–85.0)	81.0 (78.0–84.0)	0.509	82.0 (77.0–86.0)	81.0 (77.0–84.0)	0.638
Male	55 (27.8)	39 (39.8)	0.050	25 (38.5)	25 (38.5)	1.000
BMI, kg/m^2	26.4 (23.7–29.8)	27.9 (24.7–31.0)	0.083	25.7 (23.7–28.8)	27.2 (24.4–29.6)	0.401
Logistic EuroSCORE, %	14.8 (8.7–24.8)	14.2 (9.6–21.4)	0.921	14.9 (9.0–26.1)	14.3 (9.8–21.5)	0.926
NYHA functional class III/IV	155 (78.3)	78 (79.6)	0.914	53 (81.5)	51 (78.5)	0.826
Coronary artery disease	135 (68.2)	65 (66.3)	0.850	45 (69.2)	45 (69.2)	1.000
Previous CABG	19 (9.6)	10 (10.2)	1.000	7 (10.8)	9 (13.8)	0.789
Previous myocardial infarction	28 (14.1)	8 (8.2)	0.196	7 (10.8)	3 (4.6)	0.323
Previous PCI	84 (42.4)	42 (42.9)	1.000	24 (36.9)	26 (40.0)	0.857
Previous stroke	31 (15.7)	14 (14.3)	0.891	11 (16.9)	12 (18.5)	1.000
Diabetes	65 (32.8)	32 (32.7)	1.000	20 (30.8)	21 (32.3)	1.000
COPD	36 (18.2)	14 (14.3)	0.498	13 (20.0)	10 (15.4)	0.646
Peripheral artery disease	37 (18.7)	14 (14.3)	0.435	17 (26.2)	9 (13.8)	0.125
Hypertension	171 (86.4)	91 (92.9)	0.146	54 (83.1)	60 (92.3)	0.182
Creatinine clearance, ml/min	59.0 (43.2–75.8)	61.0 (42.0–78.8)	0.807	58.0 (43.0–81.0)	61.0 (41.0–81.0)	0.718
Atrial fibrillation	55 (27.8)	26 (26.5)	0.930	18 (27.7)	14 (21.5)	0.541
Heart rate, beats/min	70.0 (64.0–80.0)	72.0 (61.0–80.0)	0.980	70.0 (64.0–81.0)	70.0 (58.0–80.0)	0.612
Heart rate <60 beats/min	29 (14.6)	23 (23.5)	0.086	12 (18.5)	17 (26.2)	0.399
QRS duration, ms	140.0 (130.0–152.0)	140.0 (130.0–156.0)	0.698	138.0 (126.0–146.0)	144.0 (132.0–156.0)	0.043
PQ duration, ms	180.0 (160.0–201.0)	180.5 (153.5–210.0)	0.704	172.0 (151.0–192.0)	180.0 (156.0–199.0)	0.453
First-degree AV block	43 (30.1)	23 (31.9)	0.901	9 (19.1)	13 (25.5)	0.611
LVEF, %	60.0 (45.0–60.0)	60.0 (50.0–63.0)	0.017	60.0 (50.0–65.0)	60.0 (50.0–61.0)	0.378
LVEF <35%	22 (11.1)	4 (4.1)	0.073	3 (4.6)	2 (3.1)	1.000
AVA, cm^2	0.8 (0.6–0.9)	0.7 (0.6–0.9)	0.346	0.7 (0.6–0.9)	0.7 (0.6–0.9)	0.993
Mean transaortic gradient, mm Hg	43.0 (33.2–56.0)	43.0 (35.0–54.5)	0.775	46.0 (36.0–61.0)	42.0 (34.0–53.0)	0.191
Aortic regurgitation			0.258			0.437
Grade 0	93 (47.0)	40 (40.8)		34 (52.3)	28 (43.1)	
Grade 1	84 (42.4)	41 (41.8)		25 (38.5)	27 (41.5)	
Grade 2	20 (10.1)	17 (17.3)		6 (9.2)	10 (15.4)	
Grade 3	1 (0.5)	0 (0.0)				
Pulmonary hypertension (>60 mm Hg)	42 (21.2)	14 (14.3)	0.203	12 (18.5)	9 (13.8)	0.634
Maximum diameter, mm	28.6 (26.4–30.7)	26.8 (25.3–28.0)	<0.001	26.9 (25.0–29.5)	26.9 (25.4–28.1)	0.406
Minimum diameter, mm	22.8 (21.3–24.6)	21.3 (20.0–22.8)	<0.001	22.0 (20.1–23.7)	22.1 (20.7–23.0)	0.978
Effective diameter, mm	25.6 (24.0–27.6)	24.1 (23.0–25.5)	<0.001	24.6 (22.6–26.1)	24.4 (23.3–25.5)	0.782
Eccentricity index	0.2 (0.2–0.2)	0.2 (0.2–0.2)	0.703	0.2 (0.2–0.2)	0.2 (0.1–0.2)	0.173
Annular area, cm^2	5.2 (4.5–6.0)	4.6 (4.1–5.0)	<0.001	4.6 (4.0–5.3)	4.6 (4.2–5.1)	0.858
Perimeter, mm	82.2 (76.4–88.1)	77.0 (72.4–80.0)	<0.001	77.4 (72.5–83.1)	77.3 (73.8–81.2)	0.539
Severe cusps calcification	58 (29.3)	55 (56.1)	<0.001	27 (41.5)	25 (38.5)	0.858
Bicuspid valve	12 (6.1)	2 (2.0)	0.154	5 (7.7)	1 (1.5)	0.208

Values are median (interquartile range) or n (%).

AV = atrioventricular; AVA = aortic valve area; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MSCT = multislice computed tomography; NYHA = New York Heart Association; PAP = pulmonary artery pressure; PCI = percutaneous coronary intervention.

was smaller in patients treated with the ACURATE neo. The prevalence of severe aortic cusps calcification was higher in patients treated with ACURATE neo compared with SAPIEN 3 (56.1% vs. 29.3%; $p < 0.001$).

Procedural characteristic according to THV are shown in Table 2. As a consequence of the self-expanding design, median prosthesis oversizing was significantly larger with the ACURATE neo compared with SAPIEN 3 (40% vs. 6%; $p < 0.001$). Rates of pre- and post-dilatation were significantly higher with ACURATE neo, although there was no difference in implantation depth. There was no difference in complications and in-hospital course between both THV groups (Table 2).

TABLE 2 Procedural Characteristics and Clinical Outcome

	SAPIEN 3 (n = 198)	ACURATE neo (n = 98)	p Value	SAPIEN 3 (n = 65)	ACURATE neo (n = 65)	p Value
THV size			<0.001			<0.001
20	1 (0.5)	–		1 (1.5)	–	
23	40 (20.2)	–		25 (38.5)	–	
26	64 (32.3)	–		24 (36.9)	–	
29	93 (47.0)	–		15 (23.1)	–	
S	–	22 (22.4)		–	12 (18.5)	
M	–	36 (36.7)		–	22 (33.8)	
L	–	40 (40.8)		–	31 (47.7)	
Oversizing, %	6.4 (1.2–13.4)	40.0 (34.0–47.5)	<0.001	5.7 (1.5–13.7)	38.8 (33.4–46.7)	<0.001
Conscious sedation	122 (61.6)	62 (63.3)	0.882	41 (63.1)	36 (55.4)	0.475
Procedural time, min	57.5 (43.0–74.8)	60.0 (43.0–85.0)	0.461	55.0 (39.0–70.0)	58.0 (43.0–84.0)	0.320
Contrast, ml	110.0 (80.0–152.8)	100.0 (80.0–142.0)	0.378	100.0 (74.2–142.0)	112.0 (84.0–160.0)	0.146
Fluoroscopy time, min	13.0 (10.0–19.0)	14.0 (10.8–19.2)	0.672	13.5 (8.0–20.0)	14.0 (11.0–20.0)	0.539
Pre-dilatation	125 (63.1)	87 (88.8)	<0.001	35 (53.8)	60 (92.3)	<0.001
Pre-dilatation balloon size	23.0 (20.0–25.0)	23.0 (22.0–24.0)	0.195	23.0 (20.0–23.0)	23.0 (22.0–24.0)	0.005
Post-dilatation	41 (20.7)	37 (37.8)	0.003	15 (23.1)	32 (49.2)	0.003
Post-dilatation balloon size	24.0 (23.0–28.0)	24.0 (23.0–25.0)	0.179	23.0 (20.0–24.0)	24.0 (23.0–25.0)	0.071
Mean implantation depth, mm	6.2 (5.2–7.4)	6.4 (5.2–7.7)	0.559	5.7 (4.8–6.9)	6.4 (5.2–7.8)	0.036
Device success (VARC-2)	185 (93.4)	90 (91.8)	0.792	61 (93.8)	59 (90.8)	0.742
Procedural-related death	3 (1.5)	1 (1.0)	1.000	1 (1.5)	1 (1.5)	1.000
Annular rupture	2 (1.0)	0 (0.0)	1.000	0	0	-
Cardiac tamponade	4 (2.0)	2 (2.0)	1.000	0 (0.0)	2 (3.1)	0.496
Conversion to sternotomy	1 (0.5)	0 (0.0)	1.000	0	0	-
Life-threatening bleeding	11 (5.6)	6 (6.1)	1.000	4 (6.2)	4 (6.2)	1.000
Major vascular complications	23 (11.6)	16 (16.3)	0.345	10 (15.4)	11 (16.9)	1.000
Stroke (major/minor)	6 (3.0)	2 (2.0)	1.000	0 (0.0)	2 (3.1)	0.496
AKIN 2/3	8 (4.0)	2 (2.0)	0.505	5 (7.7)	1 (1.5)	0.208
Myocardial infarction	3 (1.5)	0 (0.0)	0.553	0	0	-
ICU stay, days	2.0 (1.0–3.0)	1.0 (1.0–3.0)	0.343	1.0 (1.0–3.0)	1.0 (1.0–2.0)	0.951
Hospital stay, days	7.0 (6.0–11.0)	8.0 (6.0–12.0)	0.078	8.0 (6.0–12.0)	8.0 (6.0–12.0)	0.848
In-hospital death	6 (3.0)	3 (3.1)	1.000	3 (4.6)	2 (3.1)	1.000
30-day mortality	9 (4.5)	3 (3.1)	0.757	4 (6.2)	2 (3.1)	0.680

Values are n (%) or median (interquartile range).

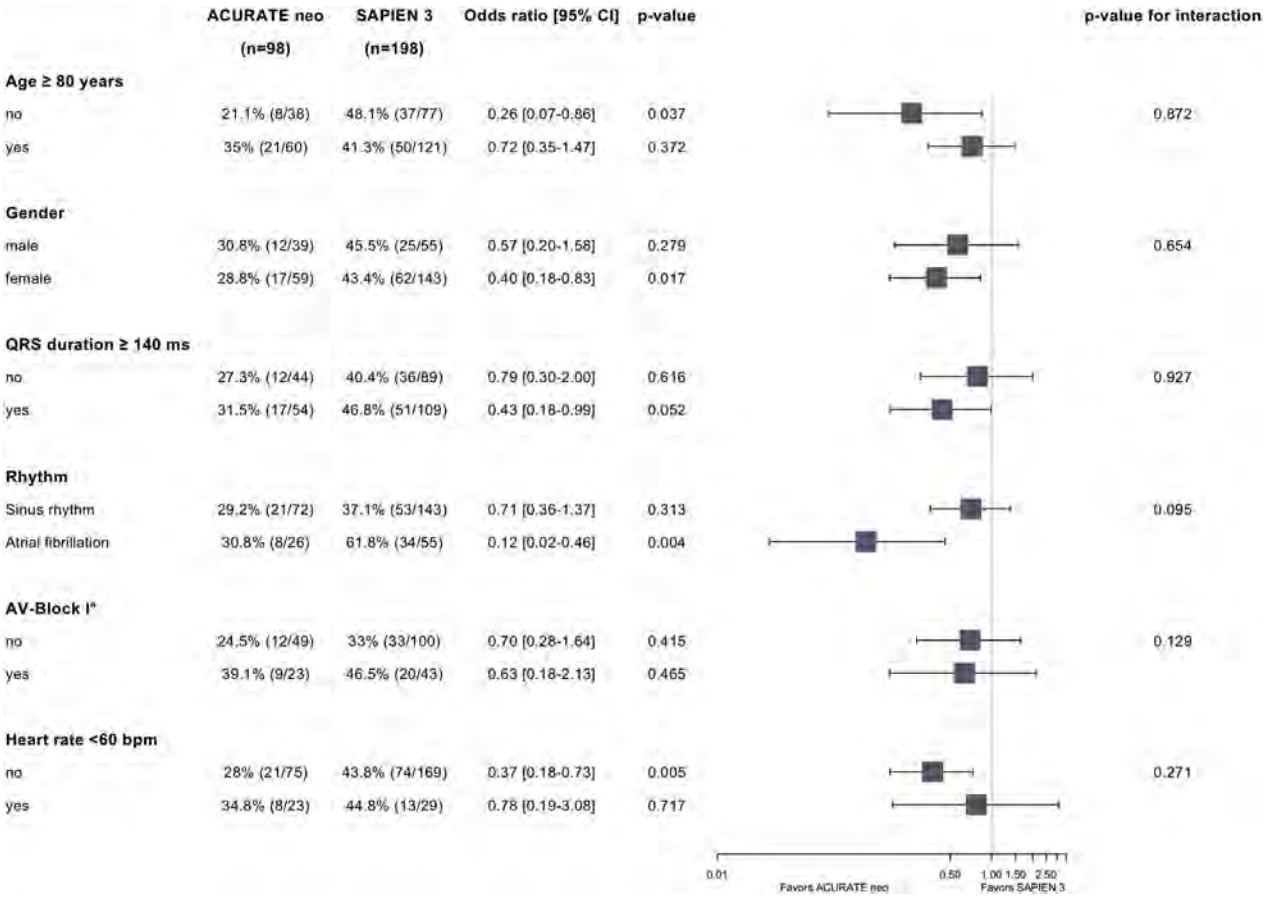
AKIN = acute kidney injury; ICU = intensive care unit; PVL = paravalvular leak; THV = transcatheter heart valve; VARC-2 = Valve Academic Research Consortium-2.

PERMANENT PACEMAKER IMPLANTATIONS. The crude rate of the primary endpoint, PPI at 30 days, was 29.6% (n = 29 of 98) with the ACURATE neo, which was significantly lower compared with the SAPIEN 3 (43.9% [n = 87 of 198], p = 0.025; OR: 0.54; 95% CI: 0.32 to 0.89; p = 0.018) (**Figures 2A and 2B**). This significant risk reduction persisted after multivariable adjustment (OR: 0.48; 95% CI: 0.26 to 0.86; p = 0.014) and was even more pronounced in the inverse probability treatment weighting (IPTW) analysis (OR: 0.37; 95% CI: 0.25 to 0.55; p < 0.001) (**Figure 2B**). Risk reduction for PPI with the ACURATE neo was consistently observed across subgroups of patients according to age, sex, QRS duration, rhythm on admission, presence of atrioventricular block, and baseline heart rate (**Figure 3**). The reason for PPI was persistent third-degree atrioventricular block in the majority of cases with both THVs (for a summary, see Online Figure 1). PPI rates according to THV at participating centers are displayed in Online Figure 2.

DEVICE FAILURE. Regarding device failure, there was no difference between the ACURATE neo and SAPIEN 3 (8.2% vs. 6.6%; p = 0.793) (**Figures 4A and 4B**). **Table 3** shows the individual contributors to device failure. Median post-procedural mean gradients were significantly lower with the ACURATE neo (8 mm Hg vs. 11 mm Hg; p < 0.001).

MATCHED POPULATION ANALYSIS. After propensity matching for variables summarized in **Figure 1**, there were 65 patients treated with the ACURATE

FIGURE 3 Risk of PPI According to THV in Subgroups



Odds ratio for permanent pacemaker implantations according to use of ACURATE neo (Boston Scientific, Marlborough, Massachusetts) versus SAPIEN 3 (Edwards Lifesciences, Irvine, California) in different subgroups of the entire population. AV = atrioventricular; THV = transcatheter heart valve; other abbreviations as in Figure 2.

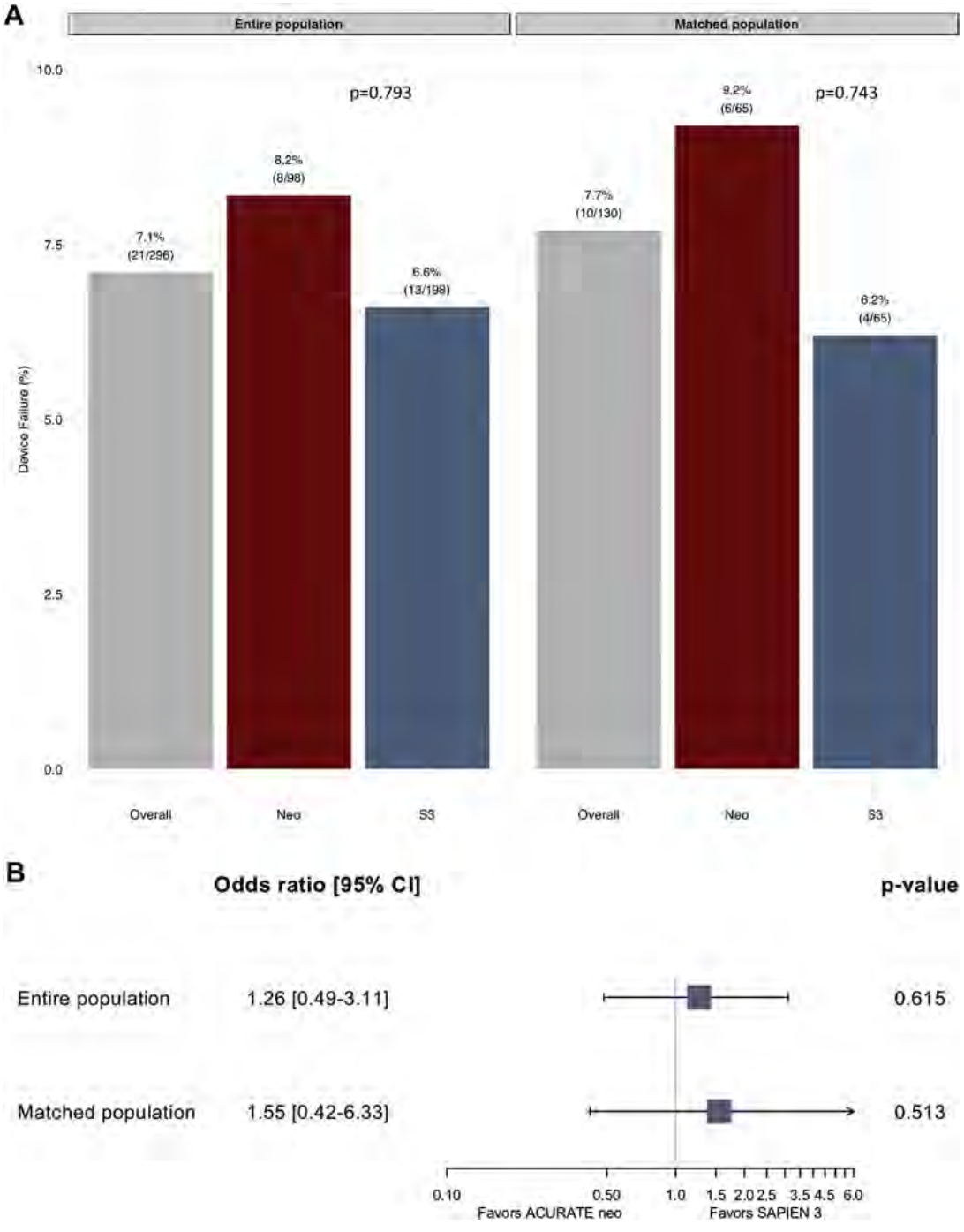
neo and 65 treated with the SAPIEN 3 available for analysis (for details on matching, see Online Figure 3). Comparison of the matched populations showed no differences in baseline characteristics between both THVs (Table 1). Procedural characteristics (Table 2) were comparable with the unmatched population with regard to the higher rate of pre- and post-dilatation and lower post-procedural mean gradients with ACURATE neo. Implantation depth was lower with ACURATE neo (6.4 mm vs. 5.7 mm; p = 0.036).

The overall PPI rate at 30 days in the matched population was 33.8% (n = 44 of 130). There was a significantly lower rate of PPI with the ACURATE neo compared with the SAPIEN 3 (23.1% [n = 15 of 65] vs. 44.6% [n = 29 of 65]; p = 0.016), with a 63% relative risk reduction (OR: 0.37; 95% CI: 0.17 to 0.78; p = 0.010) (Figures 2A and 2B), whereas there was no difference in rate and risk of device failure (9.2% vs. 6.2%; p = 0.742; OR: 1.55; 95% CI: 0.42 to 6.33; p = 0.513) (Figures 4A and 4B, Table 3).

DISCUSSION

The present study assesses the performance of 2 widely used newer-generation THVs in patients with pre-existent RBBB, a population at high risk for PPI after TAVR. First, the study shows a prevalence of RBBB and no prior pacemaker in 7% of patients undergoing TAVR. Second, it confirms previous findings of a sharply increased PPI rate in this population of 37.8%. Third, PPI rates were significantly lower with

FIGURE 4 Rate and Risk of Device Failure



(A) Overall rate of device failure and according to the ACURATE neo (Boston Scientific, Marlborough, Massachusetts) and SAPIEN 3 (Edwards Lifesciences, Irvine, California) in entire and matched populations. **(B)** Odds ratio for device failure according to use of the ACURATE neo versus SAPIEN 3 in the entire and in the matched populations. CI = confidence interval.

TABLE 3 Device Failure

	SAPIEN 3 (n = 198)	ACURATE neo (n = 98)	p Value	SAPIEN 3 (n = 65)	ACURATE neo (n = 65)	p Value
Device failure	13 (6.6)	8 (8.2)	0.792	4 (6.2)	6 (9.2)	0.742
Procedural-related death	3 (1.5)	1 (1.0)	1.000	1 (1.5)	1 (1.5)	1.000
Correct position	196 (99.0)	97 (99.0)	1.000	65 (100.0)	64 (98.5)	1.000
Intended performance	187 (94.9)	91 (92.9)	0.651	62 (95.4)	60 (92.3)	0.718
PVL II+	3 (1.5)	4 (4.1)	0.225	0 (0.0)	3 (4.6)	0.244
Elevated gradient (>20 mm Hg)	6 (3.0)	1 (1.0)	0.431	3 (4.6)	0 (0.0)	0.244
Multiple valves	1 (0.5)	2 (2.0)	0.255	0 (0.0)	2 (3.1)	0.496
Post-procedural mean gradient, mm Hg	11.0 (8.0–13.0)	8.0 (6.0–10.0)	<0.001	11.0 (9.0–13.5)	7.0 (5.0–10.0)	<0.001
Conversion to sternotomy	1 (0.5)	0 (0.0)	1.000	0 (0)	0 (0)	–

Values are n (%) or median (interquartile range).
PVL = paravalvular leak.

the self-expanding ACURATE neo compared with the balloon-expandable SAPIEN 3, with comparable device failure rates.

PROGNOSTIC IMPACT OF NEW PPI AFTER TAVR. Data on the prognostic impact of new PPI after TAVR are conflicting. Although some studies found no negative effect on outcome (5,19,20), other studies have reported a higher mortality (4) and worse recovery of left ventricular function with new PPI after TAVR (6,9). However, the majority of these data were obtained from classical high-risk cohorts. With the expected extension toward younger and lower-risk populations, a reduction in PPI rates after TAVR is of increasing interest because in these patients, the prognostic impact of PPI is not well studied and may be more relevant. Besides the crude PPI rate, pacemaker stimulation rates should be considered to fully assess the impact of new PPI after TAVR.

PRE-EXISTENT RBBB IN TAVR: INCIDENCE AND PROGNOSTIC IMPLICATIONS. The reasons for PPI after TAVR can be divided into device- or procedure-related and patient-related. RBBB is the most important patient-related factor (9,10,21,22) and is present in about 10% of patients referred for TAVR, but may be found in up to 21% (10).

In a recent multicenter pooled analysis of patients undergoing TAVR, the prevalence of pre-existent RBBB was 10% and was associated with higher rates of PPI (40.1% vs. 13.5%). Moreover, pre-existent RBBB was independently associated with all-cause and cardiovascular mortality after TAVR (11). Another study reported a prevalence of RBBB in 11% and also observed a PPI rate of 41% in these patients, confirming the highly elevated risk of PPI in this important subgroup of patients (12). Interestingly, a higher PPI rate with mechanical and self-expanding devices compared with balloon-expandable devices was observed. However, mostly earlier-generation devices were included in this study.

The present study, performing a dedicated comparison of 2 newer-generation THVs, shows a comparable prevalence of RBBB in 7% of the cases and confirms the high risk of PPI in this patient population, with a rate of 39.2%.

NEW PPI WITH NEWER-GENERATION THVs. There is a considerable variability of PPI rate among current-generation THVs (7). The highest incidence has been reported with the Lotus (Boston Scientific) in up to 32% of the cases (23–25), although the lowest rates in larger series have been reported with the ACURATE neo (10%) (26,27). Classically, PPI rate has been associated with the deployment mechanism and has been consistently higher with self-expanding devices compared with balloon-expandable THVs in earlier generations (10). With newer-generation devices, these difference according to deployment mechanism seem to vanish. Indeed, with newer-generation THVs, PPI rates for self-expanding devices such as Evolut R (Medtronic, Minneapolis, Minnesota), from 11% to 15% (28,29), and Portico (Abbott, Chicago, Illinois), from 10% to 13.5% (28,30), are comparable to the balloon-expandable SAPIEN 3 (11.6% to 16%) (8,25,31–33).

COMPARISON OF ACURATE NEO AND SAPIEN 3. When comparing PPI rates of different THVs from registry data, potential differences in baseline risk for PPI such as the prevalence of pre-existent RBBB may not allow direct comparisons. With current randomized trials of different THVs underway (SCOPE I [Safety and Efficacy of the Symetis ACURATE Neo/TF Compared to the Edwards SAPIEN 3 Bioprosthesis] [NCT03011346] and SCOPE II [Safety and Efficacy Comparison Of Two TAVI Systems in a Prospective Randomized Evaluation II] [NCT03192813] trials), comparisons of newer-generation THV are still scarce.

In the recent MoRENA (Munich Regensburg Bad Nauheim multicenter registry) multicenter registry (34), a nonrandomized, 1:2 propensity-matched comparison of ACURATE neo and SAPIEN 3, no overall difference in VARC-2-defined device failure was observed, but a significantly lower rate of PPI

with the self-expanding device (9.9% vs. 15.5%) was found. Apart from the patient-related factor of pre-existent RBBB, several procedure-related factors have also been associated with PPI.

For the ACURATE neo, need for PPI and new-onset conduction abnormalities seem to be mainly affected by patient-related factors and not by operator or device-related factors such as prosthesis oversizing or implantation depth (27). However, a recent study indicates that a strategy of cautious pre- and restrictive post-dilatation may result in an even lower PPI rate of 2.3% with this THV (14).

For the SAPIEN 3, procedural factors seem to play a more important role. Although there seems to exist an effect of prosthesis oversizing on PPI rate (8,35) implantation depth also appears to play a role (8). A modified implantation technique with a relatively high or aortic positioning of the prosthesis has been attempted and may result in lower PPI rates with the SAPIEN 3 (36,37). In the present study, implantation depth was comparable with both THV, and the THV-mediated effect of a lower PPI rate persisted even after adjustment for this variable (data not shown).

However, although potential procedure-related factors may be influenceable to a certain extent by modification of implantation techniques and sizing, patient-related factors cannot be altered and have to be considered in THV selection. In the MoRENA registry, for both the SAPIEN 3 and ACURATE neo, pre-existent RBBB was independently associated with a 6-fold (35) and an almost 4-fold (27) increase in PPI risk, respectively. Small absolute numbers of patients with pre-existent RBBB in MoRENA (only 26 patients) precluded meaningful subgroup analyses. Therefore, in the present SELECT RBBB registry, we collected significantly more cases with pre-existent RBBB to enable assessment of the performance of these 2 THVs with regard to PPI in these patients. There was a differential THV effect on PPI in this high-risk cohort. PPI rate was consistently lower with the ACURATE neo in the unadjusted, multivariate, and IPTW analysis. Of note, patients who received the ACURATE neo had lower PPI rates even despite a worse baseline risk profile, with higher rates of calcification and of pre- and post-dilatation. Using propensity matching, we aimed to further reduce this inherent selection bias of observational studies. The observed effect was even more pronounced in the matched population, with a relative risk reduction for PPI of almost 60% using the ACURATE neo. Importantly, this benefit in regard to PPI was not counterbalanced by differences in VARC-2-defined device failure. The potential mechanisms behind the lower rate of PPI with the ACURATE neo compared with the SAPIEN 3 are speculative. The top-down deployment mechanism, with little interference with the left ventricular outflow tract during implantation and a lower radial force, may account for the lower PPI rates with this THV.

Apart from PPI, several other aspects such as paravalvular leakage, durability, and future coronary access need to be taken into account in the choice of one THV over another. Especially with the expansion of TAVR toward a younger, lower-risk population, future studies are clearly warranted to further inform us on the choice of THV in these patients.

STUDY LIMITATIONS. The results of the study are limited by its observational nature and may only be applicable to patients within the sizing range of the ACURATE neo. Core laboratory analysis of procedural results and center-independent adjudication of outcomes, was not performed. PPI was performed according to local standards at each site. Although statistical methods such as IPTW and propensity matching were performed, we cannot exclude residual bias. Longer follow-up will be required to determine cumulative PPI rate, pacemaker dependency and pacing rate, and survival in patients with pre-existent RBBB treated with both THVs.

CONCLUSIONS

As the identification of patients with pre-existent RBBB is easily performed via baseline electrocardiography, the present SELECT RBBB registry suggests the possibility of a patient-tailored THV therapy to reduce PPI rate after TAVR in this subset of patients at high risk for conduction disturbances.

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PERSPECTIVES

WHAT IS NEXT? The next step is to provide a patient-tailored THV therapy for patients undergoing TAVR in order to reduce PPI.

WHAT IS NEW? In a multicenter population of 296 patients with pre-existent complete RBBB, the ACURATE neo was associated with a significantly lower rate and risk of PPI compared with the SAPIEN 3, with comparable rates of device failure.

WHAT IS KNOWN? Pre-existing RBBB is the strongest patient-related predictor for new PPI after TAVR. No direct comparison of different newer-generation THVs with regard to PPI in these patients exists.

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KEY WORDS ACURATE neo, permanent pacemaker implantations, right bundle branch block, SAPIEN 3, transcatheter aortic valve replacement

APPENDIX For supplemental tables and figures, please see the online version of this paper.