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Comparison of the Sapien 3 versus the ACURATE neo valve system: A propensity score analysis

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Abstract

Objectives: To compare the outcomes of transfemoral ACURATE neo (NEO) and Sapien 3 (S3) patients in terms of device success and clinical safety outcomes using a propensity score analysis.

Background: Differences in clinical outcomes between the latest-generation balloon-expandable S3 and self-expanding NEO in a "real-world transfemoral TAVI population" are still unclear.

Methods: We compared up to 6 months clinical outcomes using a propensity score analysis (inverse probability of treatment weighting [IPTW]) to account for differences in baseline characteristics.

Results: A total of 345 patients underwent transfemoral transcatheter aortic valve implantation (TAVI) with either NEO or S3 at two centers in the Netherlands. Composite device success and early safety endpoints were comparable between NEO and S3 (Device success: IPTW-adjusted OR: 0.35 [95% CI: 0.12–1.18], and early safety: IPTW-adjusted OR: 0.51 [95% CI: 0.19–1.38]). Six-months mortality was 5.3 versus 3.6%, stroke was 2.8 versus 3.3%, and pacemaker rate was 6.1 versus 8.6%, respectively with p = NS. Mean aortic gradient was lower in the NEO group (5.72 ± 2.47 vs. 9.05 ± 3.48; p = <.001), with a comparable rate of moderate or severe paravalvular leak (0 versus 2.1%; p = NS).

Conclusions: Device success and clinical safety outcomes were comparable for both valves. Up to 6-months follow-up clinical outcomes and mortality rate remained excellent. Mean aortic gradient was lower after ACURATE neo implantation.

Abbreviations: AS, aortic stenosis; NEO, ACURATE neo; NYHA, New York Heart Association; PPI, permanent pacemaker implantation; PVL, paravalvular leak; S3, Sapien 3; TAVI, transcatheter aortic valve implantation; THVs, transcatheter heart valves; TIA, transient ischemic attack; VARC-2, Valve Academic Research Consortium-2.

Nynke H. Kooistra and Valent M. P. Intan-Goey contributed equally to this study.

KEYWORDS
aortic valve stenosis, balloon-expandable, femoral, self-expanding, transcatheter aortic valve implantation

1 | INTRODUCTION

The transcatheter heart valves (THVs) used in transcatheter aortic valve implantation (TAVI) are rapidly evolving and leading to an improved safety profile and higher rates of clinical success in low to high risk and inoperable patients with severe aortic stenosis.[1] Over the last decade, the deployment of THVs in TAVI is based mainly on two technical concepts: the balloon-expandable and the self- expanding approach. Both technologies have shown excellent clinical results.[2] In earlier-generation THVs, comparison of both techniques showed superiority of balloon-expandable over self-expanding THVs.[2] The rate of device success of the self-expanding THVs was lower due to more residual moderate or severe aortic regurgitation. Moreover, placement of a new permanent pacemaker was more frequent in self-expanding THVs. The development of new generation balloon-expandable (Sapien 3 [S3], Edwards Lifesciences, Irvine, CA) and self-expanding (e.g., ACURATE neo [NEO], Boston Scientific, Ecublens, Switzerland; CoreValve Evolut R, Medtronic, Dublin, Ireland) THVs has taken place to address limitations of earlier-generation devices and to improve safety and clinical outcomes. With the increasing number of procedures and expansion of TAVI into low risk and younger patients, improving safety and clinical outcomes gain increasing relevance. For these clinical improvements, strengths and limitations of different valves need to be studied to enable a patient-tailored device selection.

Current results of single-arms registries of the S3 and NEO THV suggest important advances for both valves with high rates of device success, low rates of pacemaker implantation and low mortality.[3-10] Several retrospective and prospective observational studies comparing both valves have been published recently.[11-16] However, these studies reported inconsistent results, only short term outcomes up to 1 month, or only a subgroup of TAVI patients were included. In the most recent randomized SCOPE I trial, the NEO valve did not meet non-inferiority compared to S3 device in terms of early safety and clinical efficacy outcomes at 30 days.[17]

Currently, no data are available comparing the latest-generation balloon-expandable S3 and self-expanding NEO in a "real-world transfemoral TAVI population". The present study aims to elucidate causal treatment effects and differences in clinical outcome of both devices in terms of device success, 30-days and 6-months clinical outcome after transfemoral TAVI using real-world observational TAVI data.

2 | METHODS

2.1 | Study design and patient population

Between March 2016 and November 2018, all consecutive patients with symptomatic, severe aortic stenosis who underwent transfemoral TAVI using S3 or NEO at two Dutch centers were included in this retrospective study. Patients with pre-existing aortic bioprostheses or bicuspid valve were excluded due to no occurrence in one of the groups. Patients with missing baseline data necessary for the propensity score were excluded. All TAVI candidates were discussed by the Heart Team and consensus was achieved regarding the optimal therapeutic strategy. The final decision on prosthesis type and size was left at the discretion of the treating interventional cardiologist. This was mainly based on the proper sizing between the available valve size of each valve type, the aortic annulus size of the patient, local experience, and the extent of aortic valve calcification. Table S1 provides a general overview of determinant features for device selection. Statistical analysis using IPTW was performed on this retrospective data to compensate for the lack of random assignment of the valves and to be able to estimate the causal treatment effects of both valves. The study complies with the Declaration of Helsinki and was approved by the local ethics committee.

2.2 | Study devices and procedure

The balloon-expandable S3 is a trileaflet valve made of bovine pericardial tissue, which is incorporated into a cobalt-chromium frame. An external polyethylene terephthalate sealing cuff was complemented to the inflow of the frame to reduce paravalvular leak (PVL). The S3 is delivered with the Commander delivery system, 14 or 16 French e-sheath and mandatory rapid ventricular pacing during implantation and is available in the sizes 23-, 26-, and 29-mm.[18]

The self-expanding NEO is a supra-annular positioned tri-leaflet valve made of a porcine pericardial tissue, which is incorporated into an X-shaped nitinol frame. The inner and outer surface of the stent body is covered by a pericardial sealing skirt. The NEO is delivered with the NEO delivery system, 14 French iSleeve which can be implanted without rapid ventricular pacing and is available in the sizes 23-, 25- and 27- mm.[19]

The transfemoral TAVI procedures were mainly performed under conscious sedation or local anesthesia with fluoroscopic guidance for prosthesis positioning and deployment. Accurate positioning and function of the prosthesis and the patency of the coronary ostia were ascertained by angiographic guidance. Finally, in case of significant aortic regurgitation post-dilation or second valve implantation was performed, at discretion of the operator.

2.3 | Echocardiographic and multislice computed tomography evaluation

All patients underwent transthoracic echocardiogram and multislice computed tomography. Transthoracic echocardiogram was performed

before the procedure, at discharge, and at 6 months to evaluate valve's function and degree of aortic regurgitation. Multislice computed tomography was performed pre-procedural to evaluate the aortic annulus measurements and aortic root dimensions and to determine the eligibility of access site for the TAVI procedure.

2.4 | Study endpoints and follow-up definitions

The endpoints of this study were set according to the VARC-2 criteria.[20] Outcomes were device success, early safety composite endpoint at 30 days and clinical complications at 6 months. Device success is a composite endpoint of absence of peri-procedural mortality, correct positioning of a single valve, mean aortic valve gradient <20 mmHg and absence of moderate or severe PVL. Early safety composite endpoint at 30 days includes mortality, any stroke, life-threatening bleeding, acute kidney injury (stage 2 or higher), major vascular complication, coronary artery obstruction requiring intervention, and all valve-related dysfunction requiring repeat procedure. Follow-up data were obtained using documentation of standard care of outpatient visits. Information regarding survival status was obtained by interrogation of the Dutch national institute of statistics.

2.5 | Statistical analysis

Continuous variables are expressed as means with the standard deviation or as the median with the interquartile range depending on the distribution, and categorical variables as counts and percentages. Continuous variables were compared using two-sample *t*-tests, when data was normally distributed, or Mann–Whitney *U* test, when data was not normally distributed. Categorical variables were compared using Chi-square, for large-sized sample, or Fisher's Exact test, for small-sized samples, as appropriate.

Because of the nonrandomized nature of this study, the inverse probability of treatment weighting (IPTW) method using propensity score was performed to reduce the imbalance in patient baseline characteristics with the aim of minimizing the potential effect of selection bias on the outcomes for comparing NEO and S3.[21] The baseline features used for the propensity score were: age, sex, body mass index, logistic EuroSCORE I, New York Heart Association (NYHA) functional class III/IV, diabetes mellitus, hypertension, hypercholesterolemia, glomerular filtration rate, peripheral artery disease (PAD), prior myocardial infarction, coronary artery bypass grafting, left ventricular ejection fraction <30%, prior stroke, prior transient ischemic attack (TIA), prior coronary artery disease, chronic obstructive pulmonary disease, porcelain aorta, atrial fibrillation/flutter, prior permanent pacemaker, and moderate/severe mitral regurgitation. Standardized mean differences (SMD) were calculated, and absolute SMD <0.1 were considered as a negligible difference between the means of the two cohorts and thus sufficient bias reduction.[22]

IPTW uses the whole dataset but reweights individuals to increase the weights of those who received unexpected exposures. IPTW weights were stabilized and the weights under first and above 99th percentile were respectively set to the value of the first and 99th percentile to address extreme weights.[23] The confidence interval of IPTW was computed with robust standard errors.[24] To estimate the overall treatment effect and confidence limits, the odds ratio's for clinical outcome, the mean aortic gradient, PVL, and NYHA class, and time-to-event Kaplan–Meier for mortality were adjusted for IPTW. Two-tailed *p* values <.05 were considered statistically significant. Data were analyzed using the R Statistics software version 3.5.1 and the packages "MatchIt" and "Survey."

3 | RESULTS

3.1 | Baseline characteristics

Overall, 345 patients were treated with transfemoral TAVI with either S3 or NEO. In total, 37 patients were excluded due to valve-in-valve procedures (*n* = 8), bicuspid aortic valve (*n* = 18) and due to missing data in variables required for the propensity score (*n* = 11). Of the remaining 308 patients, 230 received the balloon-expandable valve S3 and 78 patients the self-expanding valve NEO (Figure 1).

The IPTW-adjusted groups were well balanced in terms of baseline characteristics (Table 1), except for gender, PAD and left ventricle ejection fraction (LVEF) <30%. Patients treated with NEO were more frequently female compared to patients treated with S3 (59.6 vs. 53.0%; SMD = 0.133). In the NEO group the incidence of patients with PAD and LVEF <30% was significantly lower compared with the S3 group (9.7 vs. 14.5%; SMD = 0.148, and 5.2 vs. 0%; SMD = 0.331, respectively). Approximately half of the patients in both groups were severely symptomatic (NYHA class III/IV). Most of the patients had an intermediate surgical risk as predicted by the Logistic EuroSCORE I (14.6 ± 10.1 in the S3 group and 14.9 ± 9.4 in the NEO group).

3.2 | Procedural features

An overview of the procedural features is shown in Table 2. Pre- and post-dilation were performed significantly more frequent in NEO; for pre-dilation (NEO 97.4% vs. S3 65.2%; IPTW-adjusted OR: 14.6 [95% CI: 2.9–73.7]; p = .001), for post-dilation (NEO 35.9% vs. S3 13.5%; IPTW-adjusted OR: 5.25 [95% CI: 2.69–10.24]; p = <.001). There were no significant differences in fluoroscopy time, contrast volume used and intervention time between both valves. Rates of conversion to cardiac surgery during the procedure were low and similar for both valves.

3.3 | Device success

Table 2 shows the rate of device success for both THVs (Table 2). There was no significant difference in device success between both groups (NEO 89.3% vs. S3 94.6%; IPTW-adjusted OR: 0.35 [95% CI: 0.12–1.18]; p = .061), with NEO's higher rate of second valve

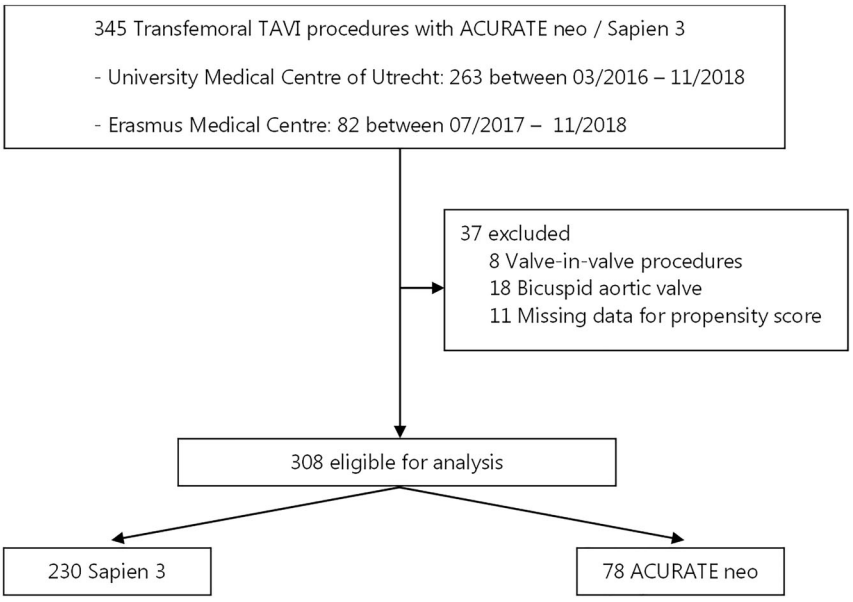

FIGURE 1 Study flowchart

TABLE 1 Baseline patient characteristics of the unmatched and IPTW-adjusted cohort

Variable	Unmatched			IPTW-adjusted		
	NEO (*n* = 78)	S3 (*n* = 230)	SMD	NEO (*n* = 69.89)	S3 (*n* = 229.74)	SMD
Age (years)	81.2 ± 5.6	80.2 ± 7.2	0.150	80.8 ± 5.8	80.4 ± 7.1	0.055
Female (%)	58 (74.4)	104 (45.2)	0.622	41.6 (59.6)	121.7 (53.0)	0.133
BMI (kg/m^2)	26.3 ± 4.8	26.5 ± 5.2	0.020	26.7 ± 5.2	26.3 ± 5.3	0.064
Logistic EuroSCORE I (%)	13.4 ± 7.6	14.8 ± 10.6	0.151	14.9 ± 9.4	14.6 ± 10.1	0.026
NYHA class III/IV (%)	43 (55.1)	100 (43.5)	0.235	34.4 (49.2)	106.4 (46.3)	0.057
Diabetes mellitus (%)	24 (30.8)	60 (26.1)	0.104	22.1 (31.6)	63.2 (27.5)	0.089
Hypertension (%)	52 (66.7)	151 (65.7)	0.021	44.3 (63.4)	150.3 (65.4)	0.042
Hypercholesterolemia (%)	44 (56.4)	127 (55.2)	0.024	41.1 (58.8)	129.1 (56.2)	0.053
eGFR ml/min/1.73 m^2	61 ± 19	61 ± 20)	0.020	61 ± 19	61 ± 20	0.010
Stroke (%)	8 (10.3)	18 (7.8)	0.085	6.8 (9.7)	19.7 (8.6)	0.041
TIA (%)	6 (7.7)	36 (15.7)	0.250	9.7 (13.9)	31.6 (13.8)	0.005
Peripheral artery disease (%)	5 (6.4)	40 (17.4)	0.344	6.8 (9.7)	33.3 (14.5)	0.148
Prior myocardial infarction (%)	10 (12.8)	42 (18.3)	0.151	11.2 (16.0)	39.2 (17.1)	0.030
Coronary artery disease (%)	39 (50.0)	95 (41.3)	0.175	30.8 (44.1)	99.7 (43.4)	0.014
Chronic pulmonary disease (%)	12 (15.4)	44 (19.1)	0.099	13.4 (19.2)	42.7 (18.6)	0.015
Porcelain aorta (%)	7 (9.0)	10 (4.3)	0.186	4.0 (5.7)	12.1 (5.3)	0.018
Atrial fibrillation (%)	20 (25.6)	83 (36.1)	0.228	23.4 (33.5)	77.4 (33.7)	0.005
Permanent pacemaker (%)	5 (6.4)	25 (10.9)	0.159	7.7 (11.0)	22.9 (10.0)	0.032
LVEF<30% (%)	0 (0.0)	16 (7.0)	0.387	0.0 (0.0)	11.9 (5.2)	0.331
Moderate or severe MR (%)	10 (12.8)	42 (18.3)	0.151	10.5 (15.1)	38.7 (16.9)	0.049

Note: Values are expressed as *n* (%) or mean ± *SD*.

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; IPTW, inverse probability of treatment weighting; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association; SMD, standardized mean differences; TIA, transient ischemic attack.

implantation as main difference between both valves. Peri-procedural mortality rate was 2.6% for NEO and 1.3% for S3 (IPTW-adjusted OR: 3.34 [95% CI: 0.42–26.46]; p = .255). There was no significant difference in rate of post-procedural mean gradient ≥20 mmHg and rate of moderate or severe PVL between both valves.

TABLE 2 Periprocedural and 30-days outcome

Periprocedural	Crude (unadjusted)			IPTW-adjusted		
	NEO (*n* = 78)	S3 (*n* = 230)	*p*-value	NEO (*n* = 69.89)	S3 (*n* = 229.74)	*p*-value
Fluoroscopy time (min)	17 (13–20)	15 (12–19)	.204	16 (12–20)	15 (12–19)	.626
Contrast volume (ml)	134 ± 32	118 ± 29	<.001	131 ± 32	119 ± 29	.007
Intervention time (min)	79 (68–97)	76 (66–92)	.248	79 (67–101)	76 (66–93)	.336
Valvesize						
20	0 (0)	1 (0.4)				
23 (small)	7 (9.0)	37 (16.1)				
25 (medium)	38 (48.7)	0 (0)				
26	0 (0)	115 (50)				
27 (large)	33 (42.3)	0 (0)				
29	0 (0)	77 (33.5)				
				IPTW-adjusted OR		
General anesthesia (%)	0/78 (0.0)	8/230 (3.5)	.209	0.99 (0.74–1.33)		.957
Pre-dilation (%)	76/78 (97.4)	150/230 (65.2)	<.001	14.6 (2.89–73.68)		.001
Post-dilation (%)	28/78 (35.9)	31/230 (13.5)	<.001	5.25 (2.69–10.24)		<.001
Conversion to cardiac surgery (%)	2/78 (2.6)	1/230 (0.4)	.159	4.32 (0.38–48.72)		.238
Device success[a] (%)						
Device success[a]	67/75 (89.3)	212/224 (94.6)		0.35 (0.12–1.05)		.061
Periprocedural mortality (%)	2/78 (2.6)	3/230 (1.3)		3.34 (0.42–26.46)		.255
Valve malpositioning (%)	2/78 (2.6)	0/230 (0.0)		—		—
Single valve implantation (%)	73/78 (93.6)	227/230 (98.7)		0.17(0.03–0.84)		.031
Prosthetic valve mean gradient <20 mmHg (%)	72/73 (98.6)	221/224 (98.7)		1.33 (0.13–13.10)		.807
Moderate or severe prosthetic valve regurgitation (%)	1/73 (1.4)	3/225 (1.3)		2.84 (0.29–28.04)		.371
30-days outcome						
Early safety at 30 days (%)	66/76 (86.8)	209/226 (92.5)		0.53 (0.20–1.43)		.214
Mortality (%)	3/78 (3.8)	4/230 (1.7)		3.54 (0.63–19.84)		.152
Stroke (%)	1/73 (1.4)	5/224 (2.2)		0.40 (0.04–3.50)		.406
Life-threatening bleeding (%)	5/76 (6.6)	10/225 (4.4)		1.48 (0.39–5.53)		.563
Acute kidney injury stage 2 or 3 (%)	0/77 (0)	0/229 (0)		—		
Major vascular complication (%)	7/74 (9.5)	14/226 (6.2)		1.32 (0.42–4.17)		.640
Coronary artery obstruction requiring intervention	3/78 (3.8)	0/230 (0)		—		
Valve-related dysfunction requiring repeat procedure	0/72 (0)	0/222 (0)		—		
Pacemaker implantation[b]	3/68 (4.4)	14/197 (7.1)		0.55 (0.14–2.09)		.380

Note: Values are expressed as *n* (%), mean ± *SD* or median (IQR).

Abbreviation: IPTW, inverse probability of treatment weighting.

[a]Device success is a composite of absence of periprocedural mortality, correct positioning of a single valve, mean aortic valve gradient <20 mmHg and absence of moderate or severe prosthetic valve regurgitation.

[b]Patients with pacemaker at baseline were excluded.

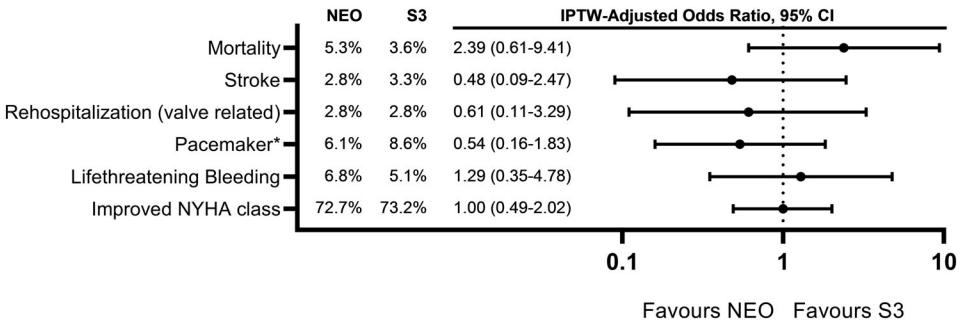

FIGURE 2 Clinical outcomes at 6 months. *Patients with pacemaker at baseline were excluded

3.4 | Thirty-days outcome

The early safety composite endpoint at 30 days was comparable in both groups (NEO 86.5% vs. S3 92.5%; IPTW-adjusted OR: 0.51 [95% CI: 0.19–1.38]; p = .189) (Table 2). Comparing the individual contributors to the composite endpoint showed no statistically significant differences. There were no cases of acute kidney injury stage 2 or 3 in both groups. Rate of new permanent pacemaker implantation (PPI) was comparable in both groups (NEO 4.4% vs. S3 7.1%; IPTW-adjusted OR: 0.55 [95% CI: 0.14–2.09]; p = .380).

3.5 | 6 months outcome

At 6 months, there were no significant differences in clinical outcomes (Figures 2 and 3). Six-months mortality was 5.3 vs. 3.6%, stroke was 2.8 vs. 3.3%, and pacemaker rate was 6.1 vs. 8.6% for NEO vs. S3 respectively with p = NS). Cardiovascular related deaths were also comparable between both valves (NEO 3.9% vs. S3 2.3%, p = NS) with annulus rupture being the most important reason of death periprocedural (1 case in NEO versus 2 cases in S3). Generally, symptomatic improvement after TAVI was similar in both valve types (Figure 4).

Echocardiographic data regarding the valve function up to 6 months is shown in Figure 5. The mean aortic gradient remained significantly lower in the NEO compared to S3 at 6 months of follow-up (5.72 ± 2.47 vs. 9.05 ± 3.48; p = <.001; Figure 5a).

At discharge there were significantly more patients with mild PVL in the NEO group (51.6 vs. 22%; p = <.001) (Figure 5b). However, at 6 months the rate of mild PVL in the NEO group was reduced from 51.6 to 33%, which was not different from the patients receiving a S3 valve (29.9%; p = .887). There were no cases of central regurgitation.

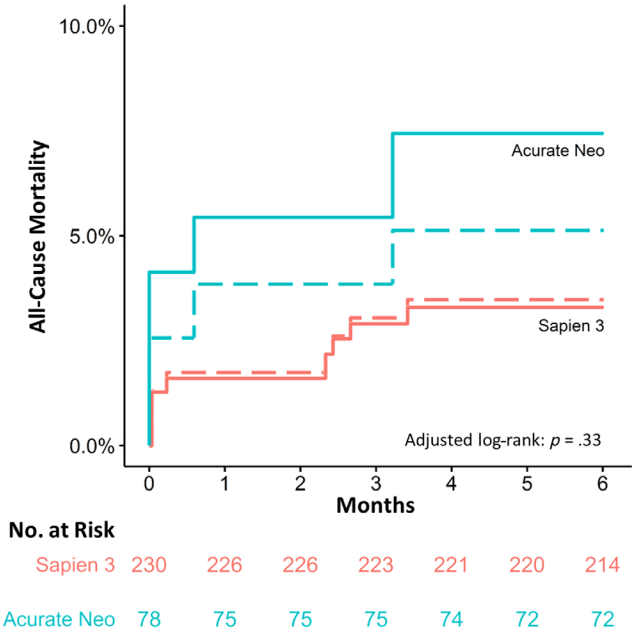

FIGURE 3 Adjusted Kaplan–Meier survival analysis, compared between both devices. Dashed line is unadjusted Kaplan–Meier [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

To our knowledge, this is the first propensity score adjusted comparison of clinical outcomes up to 6-months in a real-world population of patients that underwent a transfemoral TAVI with either a NEO or S3 valve. Main findings of this study were as follows: (a) PPI rate was low for both NEO and S3, (b) device success and outcomes regarding the early safety composite endpoint within 30 days were comparable between both valve types, (c) the post-procedural mean aortic valve gradient is significantly lower within the NEO group, (d) and overall clinical outcomes at 6 months were comparable between both valve types.

4.1 | New permanent pacemaker implantation

The rate of new PPI in our study was similar for both valves, nevertheless impressively low, especially for the self-expanding NEO. In earlier-generation self-expanding THVs, new PPI rates ranged between 21–45%.[2,25,26] Although the trend of lower PPI rates are observed in several newer generation self-expanding THVs (e.g., Evolut R/PRO 17–18%),[16,26,27] the study of Toggweiler et al has reported in a large series of patients with the NEO valve the lowest pacemaker rate that has ever been published after TAVI, that is, 2.5%.[7] In that study, pre-dilation and post-dilation were performed with a smaller balloon than the perimeter-derived annular diameter to

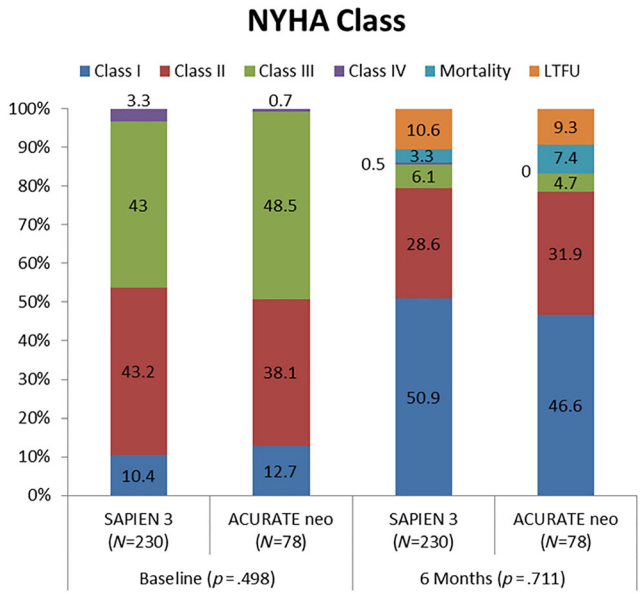

FIGURE 4 Improvement of the New York Heart Association (NYHA) functional class after transcatheter aortic valve implantation (TAVI) [Color figure can be viewed at wileyonlinelibrary.com]

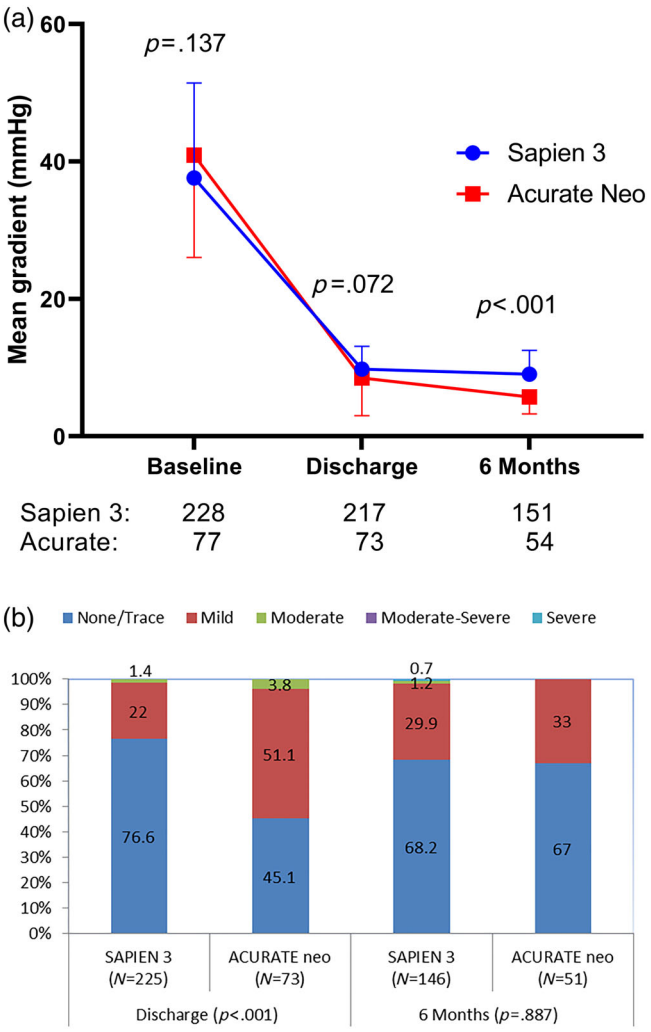

FIGURE 5 Mean aortic gradient (a) and aortic regurgitation (b) after transcatheter aortic valve implantation (TAVI) [Color figure can be viewed at wileyonlinelibrary.com]

minimize trauma. Furthermore, the low PPI rate of this NEO valve might be explained by the top-down implantation with less LVOT interaction and the lower radial force on the conduction system. Other studies of the NEO valve have reported slightly higher PPI rates ranging between 8 and 13%, however, these percentages are still very encouraging and lowest compared to all other TAVI valves.[5-17]

4.2 | Device success

Our study showed a comparable device success rate for both studied valves, which was similar to previous reports (82.4–95.6%).[10-14,25,28] These results might argue against the "traditional" perception of the lower device success rate of the earlier-generation self-expanding (77.5%) compared to the balloon-expandable (95.9%) THVs.[2] The lower device success in the past was mainly caused by the higher incidence of residual moderate or severe aortic regurgitation after procedure. In our study, we found a low rate of moderate or severe PVL of 1.3%, which was similar between both valve types, and which is in line with most studies.[5-15] Remarkably, the only randomized trial performed, that is, SCOPE I, reported a significantly higher rate of moderate or severe PVL for the NEO valve compared to the S3 (9 vs. 3%).[17] Since device success is related to anatomical characteristics of the aortic complex (degree and pattern of annulus calcification) which were not taken into account in the IPTW adjustment, the device success rate might have been influenced by selection bias (based on operators experience in device choice) in the present retrospective study. Nevertheless, the low moderate or severe PVL rates of NEO in most of the studies are encouraging, since residual moderate/severe PVL after TAVI has been associated with higher rate of mortality and therefore motivated the development of internal skirts and external cuffs to reduce PVL by sealing the prosthesis to the aortic annulus.[29]

4.3 | Thirty-days outcome

In the present study, the rates of freedom from the early safety composite endpoint were comparable for both valves, without any differences in the individual contributors to the early safety composite endpoint. This finding is in line with the results that were reported recently by other retrospective studies, which reported an early safety rate between 86 and 94%.[11-13,15] The similar stroke rate between both valves is noteworthy, since post-dilation rate is higher in the NEO group which has been previously associated with higher incidence of stroke after TAVI.[30] This increased rate of post-dilation is consistent with previous studies[11-15,17] and might be explained by the higher incidence of significant residual aortic regurgitation after initial valve implantation. Therefore, we assume that higher rate post-

dilatation with NEO did not affect the clinical outcome negatively compared to S3.

4.4 | Six-months outcome

We found comparable clinical event rates at 6 months in both THVs. Even NYHA improvement was similar between both valves. However, intuitive to the lower radial strength of the NEO,[15] a relatively higher rate of mild PVL with NEO was observed in our study shortly after TAVI. This finding was also reported by Mauri et al and Barth et al.[13,15] In the SCOPE I study, a similar rate of mild PVL was reported, with a higher rate of moderate or severe PVL of 9%.[17] At 6 months, the rate of mild PVL was in our study almost reduced with 50% between discharge and 6 months post-TAVI in the NEO group resulting in a comparable rate of PVL in both THVs. The mechanism of the reduction of PVL might be explained by the possibility of the self-expanding valve to further expand after initial implant in combination with occupation of residual interstices by fibrous tissue.[31]

Furthermore, with both THVs a normal mean aortic gradient is obtained after TAVI. However, this gradient was significantly lower in the NEO group compared to S3 up to 6 months of follow-up. These findings are in line with previous comparative studies.[11-15] Mean gradients might influence long-term durability and clinical performance, however data are limited.[32] Thus, the impact of the lower mean gradient of NEO has yet to be determined by longer-term of follow-up.

4.5 | Clinical implication

This study included all patients with a native tricuspid aortic stenosis that received a S3 or NEO via transfemoral approach based on the local experience and preference of the local heart team. Unfortunately, because of the retrospective nature of the study design, the findings are subject to certain selection bias by the heart team based on patient and valve specific features and we could not adjust for all unknown or known selection bias, such as extent of valve calcification. For example, the specific technological features of the NEO may be preferable to S3 in specific patients and vice versa; patients with a higher risk for annulus rupture due to a small aortic annulus or patients with an increased risk of PPI might have advantage of the reduced radial force at the level of LVOT of the NEO valve.[10,15]

On the other hand, patients with extensive valve calcification might preferably receive a S3 valve to reduce the risk for incomplete stent expansion for which post-dilatation is required. Previous studies have been reporting comparisons between the NEO and S3 as well. However, these studies consisted of different study populations (e.g., both transfemoral and transapical approach) or a specific patient group such as only small annulus. Therefore, the results of these studies might be biased by for example approach type or not applicable to all patients. Observational registries are the only way to capture all-comers data. By using the IPTW method instead of for example, propensity score matching, no patients had to be excluded, resulting in a comparison between NEO and S3 reflecting "real-world" clinical outcomes. The NEO valve might be especially of interest in low risk and younger patients in which due to the consequences of long-term right ventricular pacing a PPI is preferably avoided.[33] However, recent results of the SCOPE I trial reported that NEO did not meet non-inferiority compared with S3 with respect to a composite safety and efficacy endpoint at 30 days, driven primarily by lower rates of AKI, and moderate or severe aortic PVL in TAVI patients treated with S3.[17] The disparate findings between SCOPE I and our study might be caused by the fact that none of our patients developed AKI stage 2 or 3 compared to 3.0% in the NEO group of the SCOPE I study. The authors of SCOPE I reported the following possible explanations for this increased rate of AKI; the longer mean procedure time, the higher frequencies of pre- and post-dilation and the higher mean contrast volume used with NEO valve implantation. Similar trends of these factors were observed In the present study, however, did not result in an increase of AKI in the NEO group despite a significant higher mean contrast volume used. Therefore, other factors contributing to the rate of AKI should be investigated as well. For example, the differences in AKI rate between our studies could be due to the different protocols between centers used for the prevention of contrast-induced AKI.

A potential factor contributing to the greater PVL rate in the NEO group in the SCOPE I trial (9.4%) compared to our study (1.4%) include the difference in pre-dilation rate of these NEO patients. Pre-dilation ensures optimal valve expansion (by reducing radial counterforces) and thereby reducing paravalvular regurgitation. In our study pre-dilation (with balloon size based on minimum annulus diameter) was performed in almost all NEO patients (97.4%) compared to 88% in SCOPE I.

The disparate findings underline the need for future comparison studies including other new-generation devices, to demonstrate strengths and limitations of available valve devices and to enable an optimized patient-tailored device selection.

To note, a novel next-generation ACURATE neo2 valve has been designed, which will receive CE approval shortly. A new feature of this new device is the annular sealing technology, which was designed to further reduce occurrences of PVL. Results demonstrated a high procedural success rate (97.5%) and a low rate of PVL (3% had moderate PVL and no cases of more than moderate PVL) at 30-days and one-year follow-up.[34,35] Since most of the features of the first ACURATE neo valve have been maintained in this new device, we would expect that the results of the present study would be broadly the same if the study was performed with the novel ACURATE neo2 system. In terms of PVL, this novel device might even give a superior outcome compared to the first-generation NEO valve.

4.6 | Limitations

Main limitation of this study is the nonrandomized retrospective design with the lack of an independent core-laboratory analysis of the echocardiographic results. In nonrandomized retrospective studies

propensity score analysis is a well-accepted approach in addressing imbalance in baseline characteristics after the lack of random allocation. However, when not all influential baseline characteristics are taken into account in this analysis, for example, the extent of valve calcification, correction cannot be made for all selection bias and the results might have been biased by these (hidden) confounders.

5 | CONCLUSION

In this IPTW, two-center, retrospective study, we found a comparable result with NEO and S3 regarding device success and early safety composite endpoint at 30 days according to VARC-2 criteria. Use of NEO might be associated with a higher incidence of mild PVL compared with S3. However, at medium-term follow up the prevalence of PVL became similar in both THVs in the presence of a lower mean aortic gradient in NEO. Up to 6-months follow-up clinical outcomes remained excellent and comparable.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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