Transcatheter Aortic Valve Replacement With Next-Generation Self-Expanding Devices

A Multicenter, Retrospective, Propensity-Matched Comparison of Evolut PRO Versus Acurate *neo* Transcatheter Heart Valves

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ABSTRACT

OBJECTIVES The aim of this study was to compare transcatheter aortic valve replacement (TAVR) with the Acurate *neo* (NEO) and Evolut PRO (PRO) devices.

BACKGROUND The NEO and PRO bioprostheses are 2 next-generation self-expanding devices developed for TAVR.

METHODS The NEOPRO (A Multicenter Comparison of Acurate NEO Versus Evolut PRO Transcatheter Heart Valves) registry retrospectively included patients who underwent transfemoral TAVR with either NEO or PRO valves at 24 centers between January 2012 and March 2018. One-to-one propensity score matching resulted in 251 pairs. Pre-discharge and 30-day Valve Academic Research Consortium (VARC)-2 defined outcomes were evaluated. Binary logistic regression was performed to adjust the treatment effect for propensity score quintiles.

RESULTS A total of 1,551 patients (n = 1,263 NEO; n = 288 PRO) were included. The mean age was 82 years, and the mean Society of Thoracic Surgeons score was 5.1%. After propensity score matching (n = 502), VARC-2 device success (90.6% vs. 91.6%; p = 0.751) and pre-discharge moderate to severe (II+) paravalvular aortic regurgitation (7.3% vs. 5.7%; p = 0.584) were comparable between the NEO and PRO groups. Furthermore, there were no significant differences in any 30-day clinical outcome between matched NEO and PRO pairs, including all-cause mortality (3.2% vs. 1.2%; p = 0.221), stroke (2.4% vs. 2.8%; p = 1.000), new permanent pacemaker implantation (11.0% vs. 12.8%; p = 0.565), and VARC-2 early safety endpoint (10.6% vs. 10.4%; p = 1.000). Logistic regression on the unmatched cohort confirmed a similar risk of VARC-2 device success, paravalvular aortic regurgitation II+, and 30-day clinical outcomes after NEO and PRO implantation.

CONCLUSIONS In this multicenter registry, transfemoral TAVR with the NEO and PRO bioprostheses was associated with high device success, acceptable rates of paravalvular aortic regurgitation II+, and good 30-day clinical outcomes. After adjusting for potential confounders, short-term outcomes were similar between the devices. (J Am Coll Cardiol Intv 2019;12:433–43) © 2019 Published by Elsevier on behalf of the American College of Cardiology Foundation.

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of patients with severe, symptomatic aortic stenosis, becoming a first-line therapeutic option among patients at increased surgical risk (1,2). As a result of continuous TAVR evolution, several next-generation transcatheter heart valves (THVs) have been developed to minimize procedural complications and improve patients' outcomes (3).

The Acurate *neo* (NEO) bioprosthesis (developed by Symetis, Ecublens, Switzerland; now Boston Scientific, Marlborough, Massachusetts) is a next-generation self-expanding THV commercially available for TAVR in several countries. Interesting clinical and echocardiographic results have been recently reported after transfemoral TAVR with the NEO valve (4,5), and 2 randomized controlled trials are currently ongoing to compare such device with the SAPIEN 3 and the Evolut R THVs (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], respectively). Recently, the self-expanding Evolut PRO (PRO) system, the latest generation device in the CoreValve family (Medtronic, Minneapolis, Minnesota), has shown excellent outcomes in the prospective Medtronic Evolut PRO US Clinical Study and has been introduced into clinical practice (6).

To date, no study exists comparing the NEO and latest generation PRO devices; furthermore, the ongoing SCOPE II trial was designed to compare

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the NEO valve with the second-generation Evolut R device. Therefore, our aim was to perform a multicenter observational study to compare clinical and echocardiographic outcomes after transfemoral TAVR with the next-generation self-expanding NEO and PRO THVs.

METHODS

STUDY POPULATION. Our multicenter, observational, retrospective NEOPRO (A Multicenter Comparison of Acurate NEO Versus Evolut PRO Transcatheter Heart Valves) registry included a total of 1,551 patients who underwent transfemoral TAVR with either NEO (n = 1,263) or PRO (n = 288) devices between January 2012 and March 2018 at 24 centers. The number of patients included from each participating center is detailed in Online Table 1. All consecutive patients treated with transfemoral TAVR for symptomatic, severe aortic stenosis of the native aortic valve (AV) with either NEO or PRO implantation were included in the registry. The treatment period was January 2012 to March 2018 for the NEO device and August 2017 to March 2018 for the PRO device. Local multidisciplinary heart teams evaluated all cases and confirmed eligibility for transfemoral TAVR. All patients provided written informed consent for the procedure and subsequent data collection per local practice for retrospective data.

Pre-procedural screening was performed by means of clinical assessment (patient demographics, symptoms, comorbidities, laboratory examinations, and risk evaluation), echocardiography, and multidetector computed tomography. Native AV and left ventricular outflow tract (LVOT) calcifications were classified and graded using a semiquantitative scoring system, as previously described (7). The selection of prosthesis type and size was at the discretion of the treating physician at each center.

DEVICE DESCRIPTION. The NEO bioprosthesis is implanted using a dedicated transfemoral delivery system inserted through a 20-F sheath, as previously described (8). The device is available in sizes small, medium, and large, which correspond to annular diameters of 23, 25, and 27 mm, respectively. The self-expanding nitinol frame has porcine pericardial valve leaflets in a supra-annular position, with a pericardial sealing skirt on the outer and inner surface of the stent body.

The PRO bioprosthesis is delivered transfemorally using a dedicated sheathless delivery system with an outer diameter similar to a 16-F sheath. The device has similar properties to the second-generation Evolut R THV (9); the principal design modification is the presence of an external pericardial wrap to enhance annular sealing. The PRO valve is currently available in 23-, 26-, and 29-mm sizes.

STUDY ENDPOINTS. The primary endpoint of the study was post-procedural device success, defined according to Valve Academic Research Consortium–2 (VARC-2) criteria (10). Secondary endpoints of interest were procedural complications and VARC-2-defined clinical outcomes at 30 days (including the early safety composite endpoint). Echocardiographic outcomes were evaluated pre-discharge; paravalvular aortic regurgitation (PAR) severity was assessed according to VARC-2 criteria and classified as follows: none or trace, mild, moderate, and severe (10).

STATISTICAL ANALYSIS. Continuous variables are presented as mean ± SD and were compared using the unpaired Student's *t*-test. Categorical variables are presented as numbers and percentages and were compared using the Fisher exact test (given the high frequency of low proportions).

Propensity score (PS) matching was used to adjust for differences in baseline characteristics and potential confounders that may lead to biased estimates of treatment outcomes (11,12). A PS was calculated for each patient to estimate the propensity toward belonging to a specific treatment group (NEO vs. PRO). This was done by means of a nonparsimonious multivariate logistic regression including the following covariates: age, sex, body mass index, diabetes mellitus, chronic obstructive pulmonary disease, estimated glomerular filtration rate, prior myocardial infarction, peripheral vascular disease, prior cardiac surgery, prior balloon aortic valvuloplasty, previous pacemaker or implantable cardioverter-defibrillator, New York Heart Association functional class III or IV, left ventricular ejection fraction, Society of Thoracic Surgeons Predicted Risk of Mortality score, moderate to heavy AV calcification, and moderate to severe LVOT calcification. The *C* statistic for the PS model was 0.78, indicating good discrimination. The Hosmer-Lemeshow goodness-of-fit test p value was 0.35, confirming good calibration and fit of the multivariate model. A 1-to-1 nearest neighbor matching algorithm without replacement (caliper 0.20) was performed to identify PS-matched pairs. The pseudo-R^2 value was 0.08 (p < 0.0001) before matching and very low (0.007; p = 0.995) after matching, thus confirming the good quality of the match and the adequate balancing of covariate distribution between the matched groups (13).

Pre-specified primary and secondary endpoints were compared between the NEO and PRO groups in both the overall and PS-matched cohorts. In the

overall cohort, binary logistic regression was also performed to adjust the treatment effect for the PS quintiles. Results of the binary logistic regression are presented as adjusted odds ratio (OR_{adj}) with 95% confidence interval (CI). The primary endpoint was evaluated in clinically relevant subgroups of the entire population with a post hoc formal interaction testing analysis.

All reported p values are 2 sided, and a p value <0.05 was considered to indicate statistical significance. All statistical analyses were performed using Stata version 13.0 (STATACorp, College Station, Texas).

RESULTS

BASELINE PATIENT CHARACTERISTICS.
A total of 1,551 patients who underwent transfemoral TAVR with the NEO (n = 1,263) or PRO (n = 288) THV were included. Baseline characteristics of the entire study population are shown in Table 1. The mean age was 81.8 ± 5.8 years, and 35.3% of patients were men; the mean Society of Thoracic Surgeons Predicted Risk of Mortality score was 5.1 ± 3.4%. Patients treated with the NEO were more frequently in New York Heart Association functional class III or IV (77.8% vs. 66.9%; p < 0.001). Patients treated with the PRO more frequently had peripheral vascular disease (24.3% vs. 12.4%; p < 0.001), history of myocardial infarction (22.7% vs. 11.5%; p < 0.001), and history of previous balloon aortic valvuloplasty (5.3% vs. 2.4%; p = 0.017). Severity of AV calcification was higher in the PRO group, while degrees of LVOT calcification were similar among the NEO and PRO groups (Table 1).

A 1-to-1 PS matching analysis (for variables summarized in "Methods") resulted in a total of 251 matched pairs. As shown in Table 1, there was no significant difference in any baseline characteristic among the PS-matched NEO and PRO groups, including the degrees of AV and LVOT calcification.

PROCEDURAL CHARACTERISTICS.
Procedural characteristics of the entire population are depicted in Table 2. Most patients underwent TAVR under conscious sedation (87.7%), with a significantly higher rate in the PRO group (92.3% vs. 86.7%; p = 0.007). Pre-dilatation and post-dilatation were more frequent in the NEO group (pre-dilatation, 83.3% vs. 37.1%; post-dilatation, 41.7% vs. 23.7%; p < 0.001 for both). The type of vascular closure technique was different between groups, with ProGlide and Manta used more frequently in the PRO group and Prostar used more frequently in the NEO group (p < 0.001). VARC-2 periprocedural complications were similar between the groups,

except for pericardial tamponade that was higher in the NEO group (1.6% vs. 0.0%; p = 0.036). Overall, 4 patients had coronary obstruction: 2 patients had coronary obstruction after THV embolization and subsequent valve-in-valve implantation (1 in the NEO group and 1 in the PRO group); 1 patient had annular rupture after NEO implantation as a result of post-dilatation, eventually leading to an aorto-right ventricular fistula and right coronary artery obstruction; and 1 patient had cardiac arrest 1 day after NEO implantation with evidence on coronary angiography of left circumflex artery thrombosis.

After PS matching, conscious sedation was similar between the NEO and PRO groups (96.4% vs. 92.8%; p = 0.112), while the use of pre-dilatation and post-dilatation remained significantly higher in the NEO group (pre-dilatation, 86.5% vs. 37.9%; post-dilatation, 41.4% vs. 25.0%; p < 0.001 for both). There was no significant difference in any peri-procedural complication after PS matching, including pericardial tamponade, second THV implantation, valve embolization, annular rupture, aortic dissection, coronary occlusion, and conversion to open surgery (Table 2). Length of hospital stay was similar between matched NEO and PRO groups (p = 0.129).

EARLY ECHOCARDIOGRAPHIC OUTCOMES.
Early echocardiographic data after TAVR (before discharge) are shown in Table 2. The mean AV gradient was significantly higher after NEO implantation (8.5 ± 4.0 mm Hg vs. 7.2 ± 3.5 mm Hg; p < 0.001), although the proportion of patients with mean AV gradients ≥20 mm Hg was similar between groups (1.2% vs. 1.1%; p = 1.000). As depicted in Figure 1, the overall amount of PAR was higher after NEO implantation (p < 0.001), driven by a higher rate of none or trace PAR in the PRO group (52.1% vs. 37.9%). The incidence of moderate-to-severe PAR was similar between the PRO and NEO groups (5.7% vs. 5.2%; p = 0.659). After adjustment for PS quintiles, the risk for moderate-to-severe PAR remained similar with the PRO and NEO devices (OR_{adj}: 0.85; 95% CI: 0.46 to 1.60; p = 0.625).

In the PS-matched population (Table 2), the mean AV gradient remained higher after NEO implantation (8.3 ± 4.0 mm Hg vs. 7.3 ± 3.6 mm Hg; p = 0.003), with no significant difference in mean AV gradient ≥20 mm Hg between matched NEO and PRO pairs (1.2% vs. 1.3%; p = 1.000). The overall amount of PAR was not different between the matched groups (p = 0.055) (Figure 1), with a similar rate of moderate-to-severe PAR after NEO and PRO implantation (7.3% vs. 5.7%; p = 0.584).

TABLE 1 Baseline Patients Characteristics Before and After Propensity Score Matching

	Entire Population				PS-Matched Population			
	Overall (N = 1,551)	Acurate *neo* (n = 1,263)	Evolut PRO (n = 288)	p Value	Overall (N = 502)	Acurate *neo* (n = 251)	Evolut PRO (n = 251)	p Value
Clinical characteristics								
Age (yrs)	81.8 ± 5.8 (N = 1,551)	81.8 ± 5.8 (n = 1,263)	81.7 ± 5.9 (n = 288)	0.911	81.5 ± 6.3 (n = 502)	81.4 ± 6.5 (n = 251)	81.6 ± 6.1 (n = 251)	0.742
Male	548/1,551 (35.3)	444/1,263 (35.2)	104/288 (36.1)	0.785	172/502 (34.3)	86/251 (34.3)	86/251 (34.3)	1.000
BMI (kg/m^2)	27.4 ± 5.1 (N = 1,479)	27.4 ± 5.1 (n = 1,195)	27.1 ± 5.2 (n = 284)	0.316	27.4 ± 5.3 (n = 502)	27.7 ± 5.2 (n = 251)	27.2 ± 5.3 (n = 251)	0.369
COPD	294/1,548 (19.0)	244/1,262 (19.3)	50/286 (17.5)	0.505	92/502 (18.3)	46/251 (18.3)	46/251 (18.3)	1.000
Diabetes mellitus	455/1,546 (29.4)	379/1,262 (30.0)	76/284 (26.8)	0.281	140/502 (27.9)	72/251 (28.7)	68/251 (27.1)	0.765
Hypertension	1,312/1,489 (88.1)	1,079/1,226 (88.0)	233/263 (88.6)	0.834	428/424 (88.4)	224/251 (89.2)	204/233 (87.6)	0.573
Serum creatinine (mg/dl)	1.18 ± 0.85 (N = 1,546)	1.18 ± 0.86 (n = 1,258)	1.21 ± 0.81 (n = 288)	0.499	1.18 ± 0.72 (n = 502)	1.17 ± 0.63 (n = 251)	1.19 ± 0.80 (n = 251)	0.699
eGFR (ml/min/1.73 m^2)	57.9 ± 21.4 (N = 1,546)	58.4 ± 21.7 (n = 1,258)	55.7 ± 20.2 (n = 288)	0.052	56.6 ± 20.7 (n = 502)	57.2 ± 21.4 (n = 251)	56.2 ± 20.1 (n = 251)	0.609
eGFR <30 ml/min/1.73 m^2	141/1,546 (9.1)	113/1,258 (9.0)	28/288 (9.7)	0.733	46/502 (9.2)	23/251 (9.2)	23/251 (9.2)	1.000
Dialysis	30/1,548 (1.9)	22/1,262 (1.7)	8/286 (2.8)	0.238	11/502 (2.2)	4/251 (1.6)	7/251 (2.8)	0.544
Prior MI	203/1,491 (13.6)	138/1,205 (11.5)	65/286 (22.7)	<0.001	109/502 (21.7)	52/251 (20.7)	57/251 (22.7)	0.665
Prior cardiac surgery (CABG or MV intervention)	178/1,549 (11.5)	154/1,263 (12.2)	24/286 (8.4)	0.080	41/502 (8.2)	21/251 (8.4)	20/251 (8.0)	1.000
Prior CABG	169/1,549 (10.9)	147/1,263 (11.6)	22/286 (7.7)	0.058	39/502 (7.8)	20/251 (8.0)	19/251 (7.6)	0.868
Prior MV surgery	9/1,549 (0.6)	7/1,263 (0.6)	2/286 (0.7)	0.675	2/502 (0.4)	1/251 (0.4)	1/251 (0.4)	1.000
Prior BAV	41/1,387 (3.0)	26/1,102 (2.4)	15/285 (5.3)	0.017	17/502 (3.4)	6/251 (2.4)	11/251 (4.4)	0.324
Peripheral vascular disease	225/1,546 (14.6)	156/1,262 (12.4)	69/284 (24.3)	<0.001	124/502 (24.7)	62/251 (24.7)	62/251 (24.7)	1.000
Prior stroke	148/1,512 (9.8)	126/1,226 (10.3)	22/286 (7.7)	0.224	44/502 (8.8)	25/251 (10.0)	19/251 (7.6)	0.430
Atrial fibrillation/flutter	506/1,539 (32.9)	408/1,253 (32.6)	98/286 (34.3)	0.578	184/502 (36.7)	93/251 (37.1)	91/251 (36.3)	0.926
PM or ICD	184/1,550 (11.9)	158/1,262 (12.5)	26/288 (9.0)	0.106	44/502 (8.8)	21/251 (8.4)	23/251 (9.2)	0.875
NYHA functional class III or IV	1,173/1,548 (75.8)	981/1,261 (77.8)	192/287 (66.9)	<0.001	344/502 (68.5)	175/251 (69.7)	169/251 (67.3)	0.631
STS-M (%)	5.08 ± 3.37 (N = 1,446)	5.02 ± 3.23 (n = 1,160)	5.35 ± 3.87 (n = 286)	0.137	5.17 ± 3.40 (n = 502)	5.08 ± 3.05 (n = 251)	5.25 ± 3.72 (n = 251)	0.577
EuroSCORE II (%)	6.17 ± 6.03 (N = 1,383)	6.23 ± 5.99 (n = 1,109)	5.96 ± 6.22 (n = 274)	0.510	6.05 ± 5.62 (n = 473)	6.34 ± 5.21 (n = 228)	5.78 ± 5.97 (n = 245)	0.279
Echocardiographic data								
Mean AV gradient (mm Hg)	43.4 ± 16.6 (N = 1,501)	43.5 ± 16.7 (n = 1,221)	43.2 ± 16.5 (n = 280)	0.833	44.5 ± 16.4 (n = 493)	45.7 ± 16.1 (n = 247)	43.2 ± 16.6 (n = 246)	0.084
Maximum AV gradient (mm Hg)	69.9 ± 24.9 (N = 1,474)	69.8 ± 25.0 (n = 1,201)	70.3 ± 24.5 (n = 273)	0.758	71.7 ± 24.5 (n = 482)	73.1 ± 24.5 (n = 243)	70.1 ± 24.5 (n = 239)	0.181
AVA (cm^2)	0.71 ± 0.19 (N = 1,450)	0.71 ± 0.19 (n = 1,172)	0.71 ± 0.20 (n = 278)	0.834	0.70 ± 0.20 (n = 480)	0.68 ± 0.17 (n = 234)	0.71 ± 0.20 (n = 246)	0.083
Moderate to severe AR	213/1,507 (14.1)	177/1,227 (14.4)	36/280 (12.9)	0.568	71/495 (14.3)	41/249 (16.5)	30/246 (12.2)	0.200
LVEF (%)	56.7 ± 11.7 (N = 1,526)	56.8 ± 11.8 (n = 1,245)	56.3 ± 11.6 (n = 281)	0.549	56.5 ± 11.7 (n = 502)	56.5 ± 11.6 (n = 251)	56.5 ± 11.7 (n = 251)	0.957
Severe pulmonary hypertension*	214/1,261 (17.0)	169/976 (17.3)	45/285 (15.8)	0.591	77/463 (16.6)	36/214 (16.8)	41/249 (16.5)	1.000
Moderate to severe MR	357/1,504 (23.7)	282/1,226 (23.0)	75/278 (27.0)	0.161	132/492 (26.8)	72/247 (29.2)	60/245 (24.5)	0.264
Moderate to severe TR	263/1,489 (17.7)	209/1,215 (17.2)	54/274 (19.7)	0.335	93/489 (19.0)	45/247 (18.2)	48/242 (19.8)	0.730
MDCT								
AV calcification				<0.001				0.313
None	5/1,243 (0.4)	4/977 (0.4)	1/266 (0.4)		2/502 (0.4)	1/251 (0.4)	1/251 (0.4)	
Mild	323/1,243 (26.0)	282/977 (28.9)	41/266 (15.4)		76/502 (15.1)	37/251 (14.7)	39/251 (15.5)	
Moderate	545/1,243 (43.9)	428/977 (43.8)	117/266 (44.0)		241/502 (48.0)	130/251 (51.8)	111/251 (44.2)	
Heavy	370/1,243 (29.8)	263/977 (26.9)	107/266 (40.2)		183/502 (36.5)	83/251 (33.1)	100/251 (39.8)	
LVOT calcification				0.229				0.206
None	682/1,246 (54.7)	541/975 (55.5)	141/271 (52.0)		243/502 (48.4)	113/251 (45.0)	130/251 (51.8)	
Mild	337/1,246 (27.0)	265/975 (27.2)	72/271 (26.6)		139/502 (27.7)	72/251 (28.7)	67/251 (26.7)	
Moderate	138/1,246 (11.1)	107/975 (11.0)	31/271 (11.4)		75/502 (14.9)	45/251 (17.9)	30/251 (12.0)	
Severe	89/1,246 (7.1)	62/975 (6.4)	27/271 (10.0)		45/502 (9.0)	21/251 (8.4)	24/251 (9.6)	

Values are mean ± SD or n/N (%). *Systolic pulmonary artery pressure on echocardiography >55 mm Hg.

AR = aortic regurgitation; AV = aortic valve; AVA = aortic valve area; BAV = balloon aortic valvuloplasty; BMI = body mass index; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; MDCT = multidetector computed tomography; MI = myocardial infarction; MR = mitral regurgitation; MV = mitral valve; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PM = pacemaker; PS = propensity score; STS-M = Society of Thoracic Surgeons Predicted Risk of Mortality; TR = tricuspid regurgitation.

TABLE 2   Procedural Characteristics and Early Echocardiographic Outcomes Before and After Propensity Score Matching
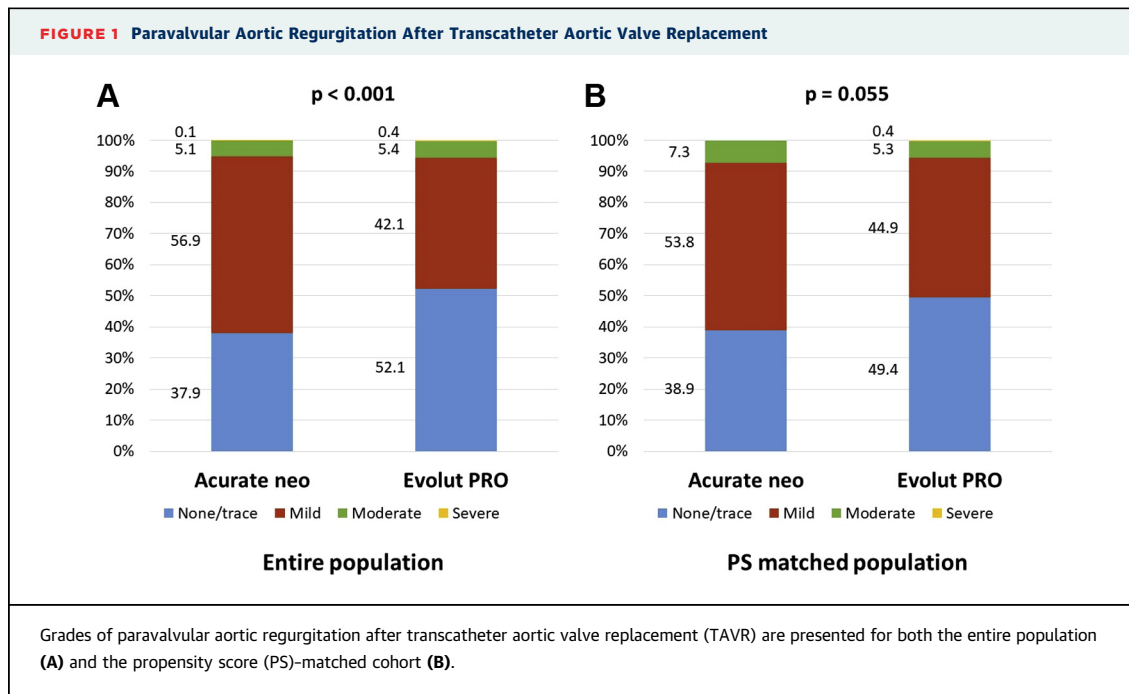
	Entire Population				PS-Matched Population			
	Overall (N = 1,551)	Acurate *neo* (n = 1,263)	Evolut PRO (n = 288)	p Value	Overall (N = 502)	Acurate *neo* (n = 251)	Evolut PRO (n = 251)	p Value
Procedural characteristics								
Conscious sedation	1,359/1,549 (87.7)	1,094/1,262 (86.7)	265/287 (92.3)	0.007	475/502 (94.6)	242/251 (96.4)	233/251 (92.8)	0.112
Valve size								
Small	–	348/1,262 (27.6)	–		–	60/251 (23.9)	–	
Medium	–	520/1,262 (41.2)	–		–	105/251 (41.8)	–	
Large	–	394/1,262 (31.2)	–		–	86/251 (34.3)	–	
23 mm	–	–	7/288 (2.4)		–	–	5/251 (2.0)	
26 mm	–	–	108/288 (37.5)		–	–	96/251 (38.3)	
29 mm	–	–	173/288 (60.1)		–	–	150/251 (59.8)	
Pre-dilatation	1,156/1,545 (74.8)	1,051/1,262 (83.3)	105/283 (37.1)	<0.001	311/499 (62.3)	217/251 (86.5)	94/248 (37.9)	<0.001
Post-dilatation	593/1,544 (38.4)	526/1,261 (41.7)	67/283 (23.7)	<0.001	166/499 (33.3)	104/251 (41.4)	62/248 (25.0)	<0.001
Vascular closure technique				<0.001				<0.001
ProGlide	946/1,550 (61.0)	717/1,262 (56.8)	229/288 (79.5)		344/502 (68.5)	138/251 (54.5)	206/251 (82.1)	
Prostar	555/1,550 (35.8)	525/1,262 (41.6)	30/288 (10.4)		129/502 (25.7)	108/251 (43.0)	21/251 (8.4)	
Manta	47/1,550 (3.0)	19/1,262 (1.5)	28/288 (9.7)		28/502 (5.6)	5/251 (2.0)	23/251 (9.2)	
Surgical closure	2/1,550 (0.1)	1/1,262 (0.1)	1/288 (0.4)		1/502 (0.2)	0/251 (0.0)	1/251 (0.4)	
Valve repositioning	–	–	21/264 (8.0)	–	–	–	20/233 (8.6)	–
Second THV implanted	20/1,551 (1.3)	14/1,263 (1.1)	6/288 (2.1)	0.240	5/502 (1.0)	2/251 (0.8)	3/251 (1.2)	1.000
Valve embolization	16/1,551 (1.0)	13/1,263 (1.0)	3/288 (1.0)	1.000	3/502 (0.6)	1/251 (0.4)	2/251 (0.8)	1.000
Annular rupture	4/1,551 (0.3)	4/1,263 (0.3)	0/288 (0.0)	1.000	0/502 (0.0)	0/251 (0.0)	0/251 (0.0)	–
Pericardial tamponade	20/1,551 (1.3)	20/1,263 (1.6)	0/288 (0.0)	0.036	5/502 (1.0)	5/251 (2.0)	0/251 (0.0)	0.061
Aortic dissection	1/1,551 (0.1)	1/1,263 (0.1)	0/288 (0.0)	1.000	0/502 (0.0)	0/251 (0.0)	0/251 (0.0)	–
Coronary occlusion	3/1,551 (0.2)	2/1,263 (0.2)	1/288 (0.4)	0.460	0/502 (0.0)	0/251 (0.0)	0/251 (0.0)	–
Conversion to surgery	13/1,551 (0.8)	13/1,263 (1.0)	0/288 (0.0)	0.144	2/502 (0.4)	2/251 (0.8)	0/251 (0.0)	0.499
Length of hospital stay (days)	8.1 ± 6.2 (N = 1,453)	8.3 ± 5.9 (n = 1,168)	7.5 ± 7.2 (n = 285)	0.050	8.1 ± 6.8 (n = 494)	8.5 ± 5.9 (n = 245)	7.6 ± 7.5 (n = 249)	0.129
Pre-discharge echocardiographic outcomes								
Mean AV gradient (mm Hg)	8.3 ± 4.0 (N = 1,416)	8.5 ± 4.0 (n = 1,145)	7.2 ± 3.5 (n = 271)	<0.001	7.8 ± 3.8 (n = 483)	8.3 ± 4.0 (n = 245)	7.3 ± 3.6 (n = 238)	0.003
Mean AV gradient ≥20 mm Hg	17/1,416 (1.2)	14/1,145 (1.2)	3/271 (1.1)	1.000	6/483 (1.2)	3/245 (1.2)	3/238 (1.3)	1.000
Moderate to severe total AR	84/1,481 (5.7)	68/1,201 (5.7)	16/280 (5.7)	1.000	32/492 (6.5)	18/247 (7.3)	14/245 (5.7)	0.584
Moderate to severe paravalvular AR	78/1,481 (5.3)	62/1,201 (5.2)	16/280 (5.7)	0.659	32/492 (6.5)	18/247 (7.3)	14/245 (5.7)	0.584
LVEF (%)	58.6 ± 10.2 (N = 1,196)	58.7 ± 10.2 (n = 940)	58.1 ± 10.2 (n = 256)	0.439	58.5 ± 9.7 (n = 454)	58.6 ± 9.1 (n = 224)	58.4 ± 10.4 (n = 230)	0.826
VARC-2 device success	1,297/1,414 (91.7)	1,052/1,144 (92.0)	245/270 (90.7)	0.539	439/482 (91.1)	222/245 (90.6)	217/237 (91.6)	0.751

Values are n/N (%) or mean ± SD.

THV = transcatheter heart valve; VARC-2 = Valve Academic Research Consortium–2; other abbreviations as in Table 1.

VARC-2 DEVICE SUCCESS AND 30-DAY CLINICAL OUTCOMES. Device success was 91.7%, with a similar rate between the NEO and PRO groups (92.0% vs. 90.7%; p = 0.539). Information on 30-day survival status was available for 1,544 of 1,551 patients (99.5%), with 43 deaths in the 30-day period after TAVR (all-cause mortality rate 2.8%); the remaining 7 patients were lost to follow-up. As shown in Table 3, in the entire population there were no significant differences in all-cause mortality (3.0% vs. 1.8%; p = 0.319) and cardiovascular mortality (2.3% vs. 1.1%; p = 0.249) at 30 days. Rates of hospitalization for valve-related symptoms or worsening congestive heart failure, any stroke, disabling stroke, myocardial infarction, acute kidney injury stage 2 or 3, coronary obstruction, valve embolization or migration, endocarditis, THV thrombosis, and valve dysfunction requiring repeat procedure did not differ between the NEO and PRO groups (Table 3). TAVR with NEO was associated with a higher rate of any bleeding (14.9% vs. 8.5%; p = 0.004) and any vascular complication (8.1% vs. 4.6%; p = 0.025), with no significant differences in life-threatening bleeding, major bleeding, and major vascular complications between the NEO and PRO groups. The unadjusted rate of new permanent pacemaker implantation (PPI) was higher with

FIGURE 1 Paravalvular Aortic Regurgitation After Transcatheter Aortic Valve Replacement

Grades of paravalvular aortic regurgitation after transcatheter aortic valve replacement (TAVR) are presented for both the entire population **(A)** and the propensity score (PS)–matched cohort **(B)**.

the PRO compared with the NEO (13.2% vs. 8.8%; p = 0.045). The VARC-2 safety composite endpoint at 30 days (all-cause mortality, any stroke, life-threatening bleeding, acute kidney injury stage 2 or 3, coronary obstruction, major vascular complications, or valve dysfunction requiring repeat procedure) was higher in the NEO group (16.4% vs. 10.9%; p = 0.025).

After adjustment for PS quintiles, VARC-2 device success was similar with the PRO and NEO devices (OR$_{adj}$: 1.15; 95% CI: 0.68 to 1.96; p = 0.598). Similarly, the implanted valve did not have a significant impact on all-cause mortality (OR$_{adj}$: 0.42; 95% CI: 0.12 to 1.43; p = 0.166), cardiovascular mortality (OR$_{adj}$: 0.19; 95% CI: 0.02 to 1.42; p = 0.104), hospitalization for valve-related symptoms or worsening congestive heart failure (OR$_{adj}$: 2.21; 95% CI: 0.80 to 6.11; p = 0.126), any stroke (OR$_{adj}$: 1.15; 95% CI: 0.47 to 2.82; p = 0.758), any bleeding (OR$_{adj}$: 0.63; 95% CI: 0.38 to 1.03; p = 0.067), any vascular complication (OR$_{adj}$: 0.75; 95% CI: 0.48 to 1.16; p = 0.196), new PPI (OR$_{adj}$: 1.49; 95% CI: 0.93 to 2.39; p = 0.100), and VARC-2 early safety composite endpoint (OR$_{adj}$: 0.76; 95% CI: 0.48 to 1.20; p = 0.234) at 30 days.

No significant interactions between implanted valve and relevant subgroups with respect to VARC-2 device success were observed in the overall population (Online Figure 1).

In the PS-matched population, VARC-2 device success was similar between the NEO and PRO groups (90.6% vs. 91.6%; p = 0.751). There were no

significant differences in any other 30-day clinical outcome between matched NEO and PRO pairs (Table 3), including all-cause mortality (3.2% vs. 1.2%; p = 0.221), cardiovascular mortality (2.4% vs. 0.4%; p = 0.122), any stroke (2.4% vs. 2.8%; p = 1.000), any bleeding (13.0% vs. 8.4%; p = 0.112), any vascular complication (14.2% vs. 11.7%; p = 0.424), new PPI (11.0% vs. 12.8%; p = 0.565), and VARC-2 early safety composite endpoint (10.6% vs. 10.4%; p = 1.000).

DISCUSSION

Our multicenter study represents the first comparison of transfemoral TAVR with the next-generation self-expanding NEO and PRO devices in a total of 1,551 patients. The main findings of our registry are as follows. 1) VARC-2 device success was obtained in 91.7% of patients, with similar rates after NEO and PRO implantation in the entire population, after adjustment for PS quintiles, and in the PS-matched cohort. 2) The rate of moderate to severe PAR after TAVR was acceptable (5.3%), with no difference between the NEO and PRO groups in the entire population, after adjustment for PS quintiles, and in the PS-matched cohort. 3) In the overall population, the rate of new PPI was higher after PRO implantation (13.2% vs. 8.8%), and the VARC-2 early safety composite endpoint was higher after NEO implantation (16.4% vs. 10.9%); however, there was no difference in any 30-day clinical endpoint after adjustment for PS quintiles and in the PS-matched groups.

TABLE 3   Clinical Outcomes at 30 Days Before and After Propensity Score Matching

	Entire Population				PS-Matched Population			
	Overall (N = 1,551)	Acurate *neo* (n = 1,263)	Evolut PRO (n = 288)	p Value	Overall (N = 502)	Acurate *neo* (n = 251)	Evolut PRO (n = 251)	p Value
All-cause mortality	43/1,544 (2.8)	38/1,258 (3.0)	5/286 (1.8)	0.319	11/501 (2.2)	8/251 (3.2)	3/250 (1.2)	0.221
Cardiovascular mortality	32/1,544 (2.1)	29/1,258 (2.3)	3/286 (1.1)	0.249	7/501 (1.4)	6/251 (2.4)	1/250 (0.4)	0.122
Hospitalization for valve-related symptoms or worsening CHF	19/1,300 (1.5)	12/1,016 (1.2)	7/284 (2.5)	0.156	10/494 (2.0)	3/245 (1.2)	7/249 (2.8)	0.339
Any stroke	39/1,529 (2.1)	25/1,245 (2.0)	7/284 (2.5)	0.645	13/496 (2.6)	6/247 (2.4)	7/249 (2.8)	1.000
Disabling stroke	24/1,529 (1.6)	20/1,245 (1.6)	4/284 (1.4)	1.000	9/496 (1.8)	5/247 (2.0)	4/249 (1.6)	0.751
MI	8/1,476 (0.5)	7/1,192 (0.6)	1/284 (0.4)	1.000	2/499 (0.4)	1/250 (0.4)	1/249 (0.4)	1.000
Any bleeding	201/1,472 (13.7)	177/1,188 (14.9)	24/284 (8.5)	0.004	53/496 (10.7)	32/247 (13.0)	21/249 (8.4)	0.112
Life-threatening	28/1,472 (1.9)	25/1,188 (2.1)	3/284 (1.1)	0.335	8/496 (1.6)	6/247 (2.4)	2/249 (0.8)	0.175
Major	64/1,472 (4.4)	56/1,188 (4.7)	8/284 (2.8)	0.195	16/496 (3.2)	10/247 (4.1)	6/249 (2.4)	0.323
Minor	109/1,472 (7.4)	96/1,188 (8.1)	13/284 (4.6)	0.044	29/496 (5.9)	16/247 (6.5)	13/249 (5.2)	0.572
Any vascular complication	246/1,529 (16.1)	213/1,245 (17.1)	33/284 (11.6)	0.025	64/496 (12.9)	35/247 (14.2)	29/249 (11.7)	0.424
Major	85/1,529 (5.6)	75/1,245 (6.0)	10/284 (3.5)	0.114	20/496 (4.0)	12/247 (4.9)	8/249 (3.2)	0.372
Minor	161/1,529 (10.5)	138/1,245 (11.1)	23/284 (8.1)	0.163	44/496 (8.9)	23/247 (9.3)	21/249 (8.4)	0.754
AKI stage 2 or 3	43/1,469 (2.9)	37/1,185 (3.1)	6/284 (2.1)	0.438	10/495 (2.0)	6/246 (2.4)	4/249 (1.6)	0.543
Coronary obstruction	4/1,530 (0.3)	3/1,245 (0.2)	1/285 (0.4)	0.562	0/496 (0.0)	0/247 (0.0)	0/249 (0.0)	-
Valve embolization or migration	17/1,532 (1.1)	14/1,247 (1.1)	3/285 (1.1)	1.000	3/497 (0.6)	1/247 (0.4)	2/250 (0.8)	1.000
Endocarditis	1/1,370 (0.1)	1/1,086 (0.1)	0/284 (0.0)	1.000	0/496 (0.0)	0/247 (0.0)	0/249 (0.0)	-
THV thrombosis	0/1,300 (0.0)	0/1,016 (0.0)	0/284 (0.0)	-	0/480 (0.0)	0/231 (0.0)	0/249 (0.0)	-
Valve dysfunction requiring repeat procedure (BAV, TAVR, or SAVR)	5/1,370 (0.4)	3/1,086 (0.3)	2/284 (0.7)	0.278	2/496 (0.4)	0/247 (0.0)	2/249 (0.8)	0.499
New permanent pacemaker implantation*	130/1,347 (9.7)	96/1,089 (8.8)	34/258 (13.2)	0.045	54/453 (11.9)	25/227 (11.0)	29/226 (12.8)	0.565
VARC-2 early safety composite endpoint	204/1,342 (15.2)	173/1,058 (16.4)	31/284 (10.9)	0.025	52/495 (10.5)	26/246 (10.6)	26/249 (10.4)	1.000

Values are n/N (%). *Excluding patients with pacemaker at baseline.

AKI = acute kidney injury; BAV = balloon aortic valvuloplasty; CHF = congestive heart failure; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; TIA = transient ischemic attack; other abbreviations as in **Tables 1 and 2**.

VARC-2 DEVICE SUCCESS. A high rate of VARC-2 device success (91.7%) was obtained in our real-world TAVR population treated with the latest generation NEO and PRO THVs, with a similar rate between both treatment groups (NEO 92.0%, PRO 90.7%). This finding was confirmed also after adjustment for PS quintiles and in the PS-matched groups (251 pairs). Furthermore, the rates of moderate-to-severe PAR and elevated gradients (mean AV gradient ≥20 mm Hg) were comparable between the NEO and PRO groups.

Recently, the prospective Evolut PRO US Clinical Study reported a high rate of device success with the PRO device (84.0%) (6). Regarding the NEO valve, a very high device success rate (98.7%) was reported in the largest available prospective registry (5), whereas 2 recent studies reported similar rates (89.0% and 89.6%) compared with our NEOPRO registry (14,15). Pending the results of the SCOPE II trial, there is a lack of randomized data comparing the safety and performance of self-expanding THVs. In this context,

our study reports a similar rate of VARC-2 device success between the next-generation NEO and PRO valves, also after adjustment for a range of baseline clinical and anatomic variables that may affect procedural outcome.

PARAVALVULAR LEAK. In our study, the incidence of moderate-to-severe PAR prior to discharge was 5.3%, with a similar rate after NEO and PRO implantation (5.2% vs. 5.7%); this finding was confirmed also after adjustment for PS quintiles and in the PS-matched cohort. The PRO device was specifically designed to enhance annular sealing compared with the earlier generation Evolut R (by means of an external pericardial wrap), thus aiming to reduce PAR. As a result of progressive device evolution, the rate of moderate-to-severe PAR after TAVR has been progressively reduced with iterations of CoreValve THVs: 8% to 10% with the first-generation CoreValve (10.5% in the CoreValve US Pivotal Extreme Risk Trial [16], 7.8% in the CoreValve US

Pivotal High Risk Trial [17], and 8.6% in the CHOICE [Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis] trial [18]), 2% to 3% with the second-generation Evolut R (3.1% in the CoreValve Evolut R US Study [19], 2.0% in the CoreValve Evolut R FORWARD Study [20]), and 0% with the latest generation PRO in the recent Evolut PRO US Clinical Study [6]. In our registry, we observed a higher rate of moderate-to-severe PAR after PRO implantation (5.7%) compared with the Evolut PRO US Clinical Study (0%) [6]. This finding may be partially explained by the high percentage of patients with moderate to heavy AV calcification (84.2%) and any LVOT calcification (48.0%) treated with PRO THV in our registry. This may reflect a selection bias on the part of the operators who choose the PRO in more challenging anatomies. The degrees of AV and LVOT calcification were not reported in the Evolut PRO US Clinical Study, thus preventing a comparison of anatomic characteristics between the 2 patient populations. The NEO device features a pericardial sealing skirt to minimize PAR and was associated with a moderate-to-severe PAR rate of 4% to 5% in previous studies [4,5,14]. In our study, the incidence of significant PAR after NEO implantation was similar to that in previous NEO studies (5.2%), with no differences compared with the latest generation PRO valve. Not surprisingly, we observed a higher rate of both pre-dilatation and post-dilatation in the NEO group, which may be related to the lower radial force of this prosthesis and could have had an impact on mitigating pre-discharge PAR rate. Although there was no difference in significant PAR at discharge, the lower rates of PAR may have been obtained at the price of a higher need for pre-dilatation and post-dilatation with NEO implantation, procedural steps that could potentially be linked to a higher risk for adverse events such as annular rupture, conduction disturbances requiring PPI [15], or cerebrovascular events [21,22].

Despite a similar rate of moderate-to-severe PAR between the NEO and PRO groups, the overall amount of PAR was higher after NEO implantation in the entire population, driven by a higher rate of mild PAR in this group (56.9% vs. 42.1%). Because residual mild PAR has been associated with worse prognosis [23,24] and TAVR is expanding toward lower risk, younger, and asymptomatic patients with expected longer survival [3], we hope that future studies will further evaluate the impact of mild PAR after TAVR.

NEW PERMANENT PACEMAKER. New conduction disturbances requiring PPI still represent a major concern of TAVR procedures, with highly variable rates reported for both early- and next-generation devices [25]. In our registry, the incidence of new PPI at 30 days was significantly higher after PRO implantation in the entire population (13.2% vs. 8.8%), but this difference was not maintained after adjustment for PS quintiles (OR_{adj}: 1.49; 95% CI: 0.93 to 2.39; p = 0.100) and in the PS-matched cohort (12.8% vs. 11.0%). The rate of new PPI after NEO implantation observed in our study (8.8% in the overall cohort, 11.0% in the PS-matched cohort) is consistent with rates reported in previous studies evaluating this device (8% to 12%) [4,5,14,15,26]. Regarding CoreValve THVs, a progressive reduction in the incidence of 30-day new PPI has been observed with device iterations: 20% to 38% with the first-generation CoreValve (21.6% in the CoreValve US Pivotal Extreme Risk Trial [16], 19.8% in the CoreValve US Pivotal High Risk Trial [17], 37.6% in the CHOICE Trial [18]), 16% to 20% with the second-generation Evolut R (16.4% in the CoreValve Evolut R US Study [19], 19.7% in the CoreValve Evolut R FORWARD Study [20]), and 11.8% with the latest generation PRO in the Evolut PRO US Clinical Study [6]. This improvement may be determined by several reasons, including device evolution, technical refinement, careful patient selection, and increased operator experience with new Evolut THV delivery features (such as resheathing and recapturing). The rate of new PPI after PRO observed in our registry (13.2% in the overall cohort, 12.8% in the PS-matched cohort) is consistent with that reported in the Evolut PRO US Clinical Study (11.8%) [6]. Our findings confirm an acceptable incidence of new PPI with both next-generation self-expanding devices, with no significant differences between the NEO and PRO THVs after adjustment for potential clinical and anatomic confounders.

VARC-2 EARLY SAFETY COMPOSITE ENDPOINT AND CLINICAL OUTCOMES AT 30 DAYS. The patient population of the NEOPRO registry represents a real-world TAVR population with mean age of 82 years and increased surgical risk, thus reflecting current clinical practice. The VARC-2 early safety composite endpoint occurred in 15.2% of patients in the entire population, significantly more common after NEO implantation (16.4% vs. 10.9%), but this difference was not maintained after adjustment for PS quintiles (OR_{adj}: 0.76; 95% CI: 0.48 to 1.20; p = 0.234) and in the PS-matched cohort (10.6% vs. 10.4%). Overall rates of all-cause mortality (2.8%), cardiovascular mortality (2.1%), any stroke (2.1%), and disabling

stroke (1.6%) at 30 days were very low in our study, consistent with previous studies evaluating NEO and PRO devices (4-6,14). Importantly, there were no significant differences in these major clinical outcomes between the 2 treatment groups. Four cases of coronary obstruction were observed in our registry, which seemed to be related to periprocedural complications (annular rupture, valve embolization, and emergent valve-in-valve implantation) or unexplained coronary thrombosis and not to specific device-related features. In the entire population, rates of any vascular complication and any bleeding were significantly higher after NEO implantation, with no significant difference in major vascular complications, life-threatening bleeding, and major bleeding between the groups. Although these differences may be related to the use of different vascular closure techniques between groups or to the lower profile of the transfemoral delivery system of the PRO THV (16-F sheath) compared with the NEO device (20-F sheath), it is worth mentioning that such differences were not maintained after adjustment for PS quintiles and in the PS-matched cohort. Overall, good clinical outcomes at 30 days were observed with both devices in our registry, reflecting current TAVR standards with next-generation THVs (3,27,28).

STUDY LIMITATIONS. Our study had a retrospective observational design, with no core laboratory analysis of procedural results and independent adjudication of clinical events. We performed PS adjustment and PS-matched comparison to overcome differences in baseline characteristics and potential confounders; however, a potential impact of unknown or unmeasured confounding factors on study outcomes cannot be excluded. Furthermore, the different sample sizes between the NEO and PRO groups in the overall cohort and the relatively small numbers of patients and events in the PS-matched groups may have influenced study results.

CONCLUSIONS

In this multicenter registry, transfemoral TAVR with the NEO and PRO bioprostheses was associated with high device success, acceptable rates of moderate-to-severe PAR, and good 30-day clinical outcomes. After adjustment for potential confounders by means of PS-matched analysis, short-term outcomes were similar between the 2 next-generation self-expanding devices.

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PERSPECTIVES

WHAT IS KNOWN? To date, no study exists comparing TAVR with the next-generation self-expanding NEO and PRO THVs.

WHAT IS NEW? In the multicenter NEOPRO registry, transfemoral TAVR with the NEO and PRO was associated with high device success, acceptable rates of moderate-to-severe PAR, and good 30-day clinical outcomes. After adjustment for potential confounders, short-term outcomes were similar between the 2 next-generation self-expanding devices.

WHAT IS NEXT? Future randomized trials and observational studies are needed to further explore procedural success and short-term outcomes after TAVR with self-expanding devices, provide insight into long-term outcomes and device durability, and identify the subsets of patients gaining the most benefit from implantation of a specific self-expanding THV.

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KEY WORDS Acurate *neo*, Evolut PRO, self-expanding, TAVR, VARC-2

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