EuroIntervention 2023;18:987-995 published online ahead of print October 2022

ACURATE *neo*2 versus SAPIEN 3 Ultra for transcatheter aortic valve implantation

Costanza Pellegrini[1], MD; Tobias Rheude[1], MD; Matthias Renker[2], MD; Alexander Wolf[3], MD; Jan Martin Wambach[3], MD; Hector A. Alvarez-Covarrubias[1,4], MD; Oliver Dörr[5], MD; Parminder Singh[5], MD; Efstratios I. Charitos[2,6], MD; Erion Xhepa[1], MD, PhD; Michael Joner[1,7], MD; Won-Keun Kim[2,6,8]*, MD

1. Klinik für Herz- und Kreislauferkrankungen, Deutsches Herzzentrum München, Technical University Munich, Munich, Germany; 2. Department of Cardiology, Kerckhoff Heart and Lung Center, Bad Nauheim, Germany; 3. Department of Cardiology, Elisabeth Hospital Essen, Essen, Germany; 4. Hospital de Cardiología, Centro Médico Nacional Siglo XXI, IMSS, Cd. de México, México; 5. Department of Cardiology and Angiology, Justus-Liebig University of Giessen and Marburg, Giessen, Germany; 6. Department of Cardiac Surgery, Kerckhoff Heart and Lung Center, Bad Nauheim, Germany; 7. Deutsches Zentrum für Herz- und Kreislauf-Forschung (DZHK) e.V. (German Centre for Cardiovascular Research), Partner Site Munich Heart Alliance, Munich, Germany; 8. DZHK e.V. (German Centre for Cardiovascular Research), Partner Site Rhine-Main, Frankfurt, Germany

C. Pellegrini and T. Rheude contributed equally to this manuscript.

This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-22-00164

KEYWORDS

- aortic stenosis
- femoral
- TAVI

Abstract

Background: No comparative data exist with the latest generation self-expanding ACURATE *neo*2 (Neo2) and the balloon-expandable SAPIEN 3 Ultra (Ultra) transcatheter heart valves (THV).

Aims: We aimed to compare the outcomes after transcatheter aortic valve implantation (TAVI) using the Neo2 and the Ultra THV.

Methods: A total of 1,356 patients at 4 centres were treated either with the Neo2 (n=608) or the Ultra (n=748). The primary endpoint was device success according to the latest Valve Academic Research Consortium definitions. The association of the THV used and the primary endpoint was assessed using inverse probability treatment weighting (IPTW) and 1:1 propensity score matching (PSM), which identified 472 matched pairs.

Results: After PSM, there were no relevant differences between the groups. While rates of moderate to severe paravalvular leakage (PVL) were overall low (0.6% vs 1.1%; p=0.725), elevated transvalvular gradients (≥20 mmHg) were less frequent with the Neo2 (2.4% vs 7.7%; p<0.001), which translated into a significantly higher rate of device success with the Neo2 compared with the Ultra (91.9% vs 85.0%; p<0.001). Consistently, the Neo2 was associated with higher rates of device success in the IPTW analysis (odds ratio [OR] 1.961, 95% confidence interval [CI]: 1.269-3.031; p=0.002). Rates of mild PVL were significantly lower with the Ultra compared with the Neo2 (20.0% vs 32.8%; p<0.001). Clinical events at 30 days were comparable between the 2 groups.

Conclusions: Short-term outcomes after TAVI using the Neo2 or Ultra THV were excellent and, overall, comparable. However, transvalvular gradients were lower with the Neo2, which translated into higher rates of device success. Rates of mild PVL were significantly lower with the Ultra THV.

**Corresponding author: Kerckhoff Heart Center, Benekestr. 2-8, 61231 Bad Nauheim, Germany. E-mail: w.kim@kerckhoff-klinik.de*

SUBMITTED ON 21/02/2022 - REVISION RECEIVED ON 02/07/2022 - ACCEPTED ON 14/08/2022

DOI: 10.4244/EIJ-D-22-00164

Abbreviations

BE balloon-expandable
PPI permanent pacemaker implantation
PVL paravalvular leakage
SE self-expanding
TAVI transcatheter aortic valve implantation
THV transcatheter heart valve

Introduction

Since the beginning of interventional therapy of severe aortic valve stenosis, transcatheter aortic valve implantation (TAVI) has become a standard therapeutic treatment[1,2]. A continuous development of transcatheter heart valve (THV) technology has led to considerable improvement in procedural and clinical outcomes. To date, both self-expanding (SE) and balloon-expandable (BE) THV are being implanted. For both platforms, scientific evidence exists from several randomised and registry-based trials over the years, supporting their broad application. However, there are few data available from randomised clinical trials with direct comparisons of specific THV. Among them, the SCOPE I trial randomised the SE ACURATE *neo* THV (Neo; Boston Scientific) and the BE SAPIEN 3 THV (S3; Edwards Lifesciences). The Neo system did not meet the prespecified non-inferiority criteria as compared to the S3 THV[3] with regard to the primary composite endpoint; this was mainly driven by valve-related dysfunction due to relevant paravalvular leakage (PVL).

For both THV, new iterations have become available recently: the SE ACURATE *neo*2 (Neo2; Boston Scientific) and the BE SAPIEN 3 Ultra THV (Ultra; Edwards Lifesciences). Both THV showed very promising early results compared to their predecessors[4-6]. To date, no direct comparison exists between the 2 latest-generation THV.

Hence, the purpose of this study was to compare the Neo2 and the Ultra THV with regard to 30-day outcomes in a propensity score-matched population.

Editorial, see page 949

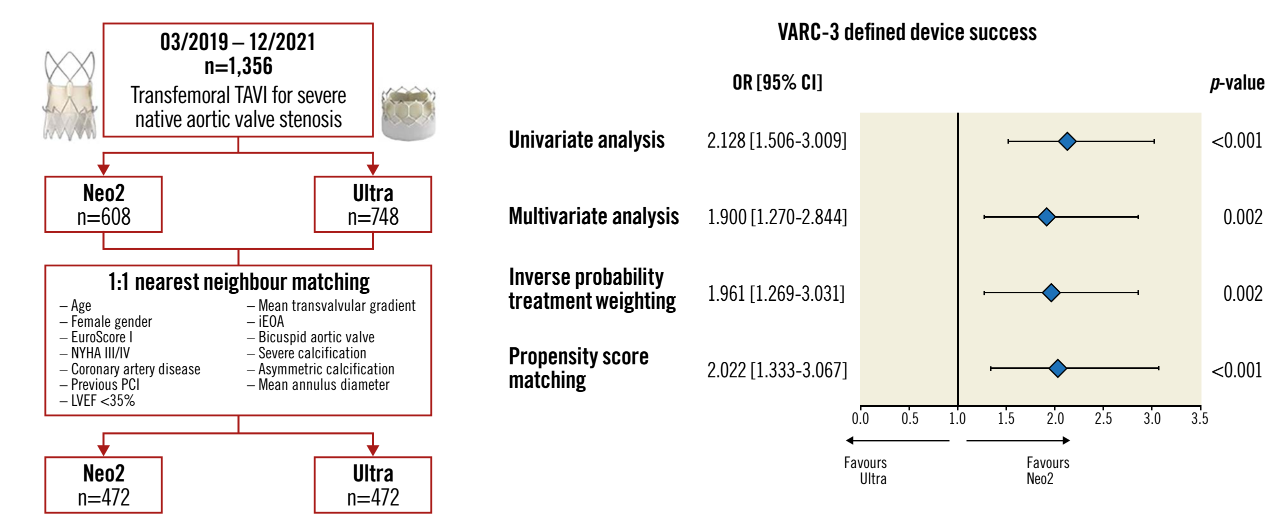
Methods

PATIENT POPULATION AND PROCEDURE

A total of 1,356 patients undergoing transfemoral TAVI for severe, native aortic valve stenosis between March 2019 and December 2021 at 4 centres in Germany (Deutsches Herzzentrum München, Munich; Kerckhoff Heart and Lung Center, Bad Nauheim; Elisabeth Hospital Essen, Essen; and Justus-Liebig University of Giessen and Marburg, Giessen) were considered for this retrospective analysis. Of these, 608 patients were treated with the Neo2 from September 2020, while 748 patients were treated with the Ultra THV over the whole inclusion period **(Central illustration)**. The number of patients included from each participating centre is depicted in detail in **Supplementary Figure 1**. Procedures were performed according to local standards. However, at 1 centre, a minimalistic approach, the "SLIM" (single arterial access and low contrast agent volume) approach was implemented during the inclusion time[7]. Valve selection was based on the patients' anatomies, the manufacturers' recommendations and was left to the discretion of the responsible operator performing the procedure. The study was approved by each local ethics committee and complied with the Declaration of Helsinki.

EuroIntervention

CENTRAL **ILLUSTRATION** **Study flow and variables used for propensity matching and risk of the primary composite endpoint device success according to THV.**



Device illustrations reproduced with permission from Boston Scientific and Edwards Lifesciences. CI: confidence interval; iEOA: indexed effective orifice area; LVEF: left ventricular ejection fraction; Neo2: ACURATE neo2; NYHA: New York Heart Association Functional Class; OR: odds ratio; PCI: percutaneous coronary intervention; TAVI: transcatheter aortic valve implantation; THV: transcatheter heart valve; Ultra: SAPIEN 3 Ultra: VARC-3: Valve Academic Research Consortium 3

DEVICE DESCRIPTION

The SE Neo2 THV was granted the Conformité Européenne (CE) mark in April 2020 based on the results of the Neo2 CE-mark study[5]. This new iteration was designed to address the major drawback seen with the former Neo THV, i.e., to reduce PVL rates. This has been achieved through a new annular sealing technology designed to conform to irregular, calcified anatomies, which extends to cover the full waist of the stent. Further, the implementation of new radiopaque markers aids reference during positioning. The Neo2 is available in 3 sizes (small, medium and large), covering an annulus range from 21 to 27 mm. Currently, the Neo2 is being investigated in the ACURATE IDE clinical trial (ClinicalTrials.gov: NCT03735667).

The balloon-expandable Ultra THV received the CE mark in November 2018. The new features of the Ultra THV have already been described elsewhere[4]. The main difference, compared to its predecessor, is a revised outer skirt, allowing up to 50% more surface contact area with the native valve anatomy. In contrast to the S3, the Ultra THV is available in 3 sizes (20 mm, 23 mm and 26 mm) covering an annulus range from 18.6 to 26.4 mm.

DEFINITION OF ENDPOINTS AND FOLLOW-UP

Data were acquired during hospital stay and follow-up through routine visits at the outpatient clinic, review of hospital records, contact with primary care physicians or with the patients and collected in individual institutional databases. Data were then collected in a joint database for statistical analysis. Data collection involved demographic information, procedural data, and clinical and echocardiographic assessment prior to TAVI and before discharge. Adverse events were recorded up to 30 days after TAVI and were categorised according to the novel Valve Academic Research Consortium 3 (VARC-3) criteria[8]. The primary endpoints were the composite endpoint of technical success and device success. Technical success was achieved at exit from the procedure room if the following criteria were met: freedom from mortality; successful access, delivery of the device and retrieval of the delivery system; correct positioning of a single prosthetic heart valve into the proper anatomical location; and freedom from surgery or intervention related to the device or to a major vascular, access-related or cardiac structural complication. Device success was defined as technical success, freedom from mortality, freedom from surgery or intervention related to the device or to a major vascular, access-related or cardiac structural complication, and performance of the valve as intended (mean gradient <20 mmHg, peak velocity <3 m/s, Doppler velocity index ≥0.25 and less than moderate aortic regurgitation) at 30 days. Secondary endpoints comprised VARC-3 clinical endpoints at 30 days.

Haemodynamic valve performance in terms of transvalvular gradients, PVL, indexed effective orifice area (iEOA) and patient-prosthesis mismatch (PPM) was obtained from discharge echocardiography. Severe PPM was defined if the iEOA was <0.65 cm^2/m^2 for a body mass index <30kg/m^2 and <0.60 cm^2/m^2 for a body mass index ≥30 kg/m^2. Calcium volume of the valvular apparatus was measured as previously described in non-contrast and contrast-enhanced multislice computed tomography (MSCT) scans, as per the availability at each centre[9]. Patients with a calcium volume beyond the 75th percentile were categorised as severely calcified. For patients without an available calcium volume measurement (n=30/1,356), visual grading was used. Asymmetric calcification was considered if its distribution varied significantly between the leaflets as previously described[10]. The cover index was derived from MSCT measurements in relation to the prosthesis area or perimeter, as appropriate.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean with standard deviation (SD) or median with interquartile range (IQR) and were compared using the Student's t-test or the Mann-Whitney U test, respectively. The influence of the THV on the primary outcome of device success was tested using several approaches: first, the univariate association was analysed; and, second, a multivariable model adjusted for covariates yielding a p-value <0.1 in the univariate analysis was performed. To adjust for a potential centre-specific influence, the variable "participating centre" was entered into the model, independent from its p-value. The variables included were age, diabetes mellitus, chronic obstructive pulmonary disease, previous dialysis, coronary artery disease, peripheral artery disease, mean transvalvular gradients, bicuspid valve, asymmetric calcification, mean annular diameter, use of the Neo2 THV and participating centre. Further, to reduce the imbalance in baseline characteristics and the effect of a potential selection bias, including potential centre-specific influence, an inverse probability treatment weighting (IPTW) analysis was performed, adjusted for variables selected based on their p-value in the univariate analysis and on their potential influence on outcome. The selected variables were age, diabetes mellitus, chronic obstructive pulmonary disease, previous dialysis, coronary artery disease, peripheral artery disease, mean transvalvular gradients, bicuspid valve, asymmetric calcification, mean annular diameter, use of the Neo2 THV and participating centre.

Lastly, nearest neighbour propensity score matching (PSM) was performed as previously described (calliper width 0.1)[11]. Baseline demographic, clinical and echocardiographic characteristics as well as MSCT measurements showing significant differences between both treatment groups or with a known influence on outcome were included in the matching algorithm. Missing data were imputed using the R package "mice" (R Foundation for Statistical Computing) before matching and weighting. The **Central illustration** summarises the study flow and variables used for PSM.

A 2-sided p-value of <0.05 was considered statistically significant for all analyses. SPSS Statistics, version 27.0.1.0 (IBM) and RStudio, version 1.4.1103 (R Foundation for Statistical Computing) including the package "MatchIt" were used for all analyses.

Results

PATIENT POPULATION

A total of 1,356 patients (Neo2: n=608; Ultra: n=748) were included in the present analysis. The median age was 81.7 years (IQR 77.9, 85.0), 50.7% were female, and the median logistic

EuroSCORE was 13.29% (IQR 7.81, 22.65). As displayed in **Table 1**, patients treated with the Neo2 THV had a higher logistic EuroSCORE compared to patients treated with the Ultra THV (14.37% [IQR 8.05, 23.42] vs 12.34% [IQR 7.63, 21.31]; p=0.008) and presented more frequently with New York Heart Association (NYHA) Class III/IV symptoms (420 [69.1%] vs 429 [57.4%]; p<0.001), while patients treated with the Ultra THV were more often female (398 [53.2%] vs 289 [47.5%]; p=0.038) and more frequently had coronary artery disease (558 [74.6%] vs 376 [61.8%]; p<0.001), including prior percutaneous coronary interventions (310 [41.4%] vs 216 [35.5%]; p=0.029). Aortic valve stenosis was more severe in patients treated with the Ultra THV, in terms of higher mean transvalvular gradients (44.00 mmHg [IQR 37.00, 54.00] vs 42.00 mmHg [IQR 31.30, 50.00]; p<0.001) and smaller iEOA (0.36 cm^2 [IQR 0.30, 0.42] vs 0.38 cm^2 [IQR 0.32, 0.44]; p<0.001). Furthermore, significant anatomical differences were found between the treatment groups, with higher rates of bicuspid valves (97 [13.0%] vs 20 [3.3%]; p<0.001), severe calcification (206/747 [27.6%] vs 126/606 [20.8%]; p=0.004), asymmetric calcification (336 [44.9%] vs 123 [20.2%]; p<0.001) and larger aortic annuli (24.85 mm [IQR 23.35, 26.20] vs 23.65 mm [IQR 22.39, 25.05; p<0.001]) in the Ultra THV treatment group.

PSM yielded 472 well-balanced pairs of patients treated either with the Neo2 or the Ultra THV with a standardised mean difference of 0.0573. After matching, no further statistically significant differences regarding baseline characteristics or anatomical variables persisted, particularly in terms of bicuspid aortic valve, severe aortic valve calcification and asymmetric calcification, with the

Table 1. Baseline characteristics of patients for the entire population and matched population according to implanted THV.

	Entire population			Matched population		
	Neo2 n=608	Ultra n=748	*p*-value	Neo2 n=472	Ultra n=472	*p*-value
Age, years	82.00 [78.72, 85.00]	81.37 [77.05, 85.00]	0.032	82.00 [78.65, 85.00]	81.60 [77.61, 85.07]	0.584
Female gender	289 (47.5)	398 (53.2)	0.038	239 (50.6)	246 (52.1)	0.696
BMI, kg/m^2	26.30 [23.67, 29.95]	26.42 [24.15, 29.38]	0.896	26.30 [23.74, 29.90]	26.36 [24.09, 29.62]	0.943
Logistic EuroSCORE, %	14.37 [8.05, 23.42]	12.34 [7.63, 21.31]	0.008	13.84 [7.94, 22.97]	12.49 [7.85, 21.84]	0.184
EuroSCORE II, %	3.02 [2.11, 5.01]	3.01 [1.90, 5.18]	0.508	2.96 [2.04, 4.99]	3.11 [2.00, 5.18]	0.827
NYHA III/IV	420 (69.1)	429 (57.4)	<0.001	305 (64.6)	297 (62.9)	0.636
Arterial hypertension	530 (87.2)	659 (88.1)	0.619	412 (87.3)	428 (90.7)	0.119
Hypercholesterolaemia	368 (60.5)	476 (63.6)	0.260	295 (62.5)	305 (64.6)	0.543
Diabetes mellitus	207 (34.0)	234 (31.3)	0.294	154 (32.6)	155 (32.8)	0.999
Coronary artery disease	376 (61.8)	558 (74.6)	<0.001	340 (72.0)	336 (71.2)	0.829
Previous PCI	216 (35.5)	310 (41.4)	0.029	193 (40.9)	190 (40.3)	0.895
Previous CABG	55 (9.0)	53 (7.1)	0.191	49 (10.4)	37 (7.8)	0.213
Previous myocardial infarction	58 (9.5)	87 (11.6)	0.251	50 (10.6)	54 (11.4)	0.755
Previous stroke	77 (12.7)	94 (12.6)	0.999	57 (12.1)	55 (11.7)	0.920
COPD	74 (12.2)	86 (11.5)	0.735	57 (12.1)	56 (11.9)	0.999
Peripheral artery disease	84 (13.8)	130 (17.4)	0.085	61 (12.9)	81 (17.2)	0.083
On dialysis	13 (2.1)	6 (0.8)	0.060	10 (2.1)	5 (1.1)	0.298
eGFR, mL/min/1.73m^2	65.00 [47.00, 83.00]	64.00 [48.50, 79.50]	0.684	65.00 [47.00, 84.25]	62.00 [47.70, 79.00]	0.198
Previous pacemaker	75 (12.3)	71 (9.5)	0.095	57 (12.1)	46 (9.7)	0.296
Atrial fibrillation	256 (42.1)	291 (38.9)	0.243	190 (40.3)	191 (40.5)	0.999
Right bundle-branch block	56 (9.2)	85 (11.4)	0.211	50 (10.6)	60 (12.7)	0.361
Left bundle-branch block	61 (10.0)	57 (7.6)	0.122	48 (10.2)	36 (7.6)	0.208
LVEF <35%	17 (2.8)	42 (5.6)	0.011	17 (3.6)	13 (2.8)	0.579
Mean transvalvular gradient, mmHg	42.00 [31.30, 50.00]	44.00 [37.00, 54.00]	<0.001	43.00 [34.00, 52.00]	42.50 [34.75, 51.00]	0.940
Indexed effective orifice area, cm^2	0.38 [0.32, 0.44] (n=601)	0.36 [0.30, 0.42] (n=721)	<0.001	0.37 [0.31, 0.43]	0.36 [0.31, 0.43]	0.518
Bicuspid aortic valve	20 (3.3)	97 (13.0)	<0.001	20 (4.2)	25 (5.3)	0.542
Severe aortic valve calcification	126/606 (20.8)	206/747 (27.6)	0.004	114 (24.3)	115 (24.4)	0.954
Asymmetric calcification	123 (20.2)	336 (44.9)	<0.001	120 (25.4)	135 (28.6)	0.305
Mean annulus diameter, mm	23.65 [22.39, 25.05]	24.85 [23.35, 26.20]	<0.001	23.80 [22.35, 25.21]	24.85 [23.35, 26.16]	<0.001

Data are median [interquartile range] or n (%). In case of missing data, numbers of available measurements are given. BMI: body mass index; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; LV: left ventricular; NYHA: New York Heart Association Functional Class; PCI: percutaneous coronary intervention; THV: transcatheter heart valve

EuroIntervention 2023;18:987-995

exception of patients treated with the Ultra THV who presented with larger mean annulus diameters by 1 mm (24.85 mm [IQR 23.35, 26.16] vs 23.80 mm [IQR 22.35, 25.21]; p<0.001). Detailed information on the distribution and balance of the propensity score across treatment and control cases is depicted in **Supplementary Table 1** and **Supplementary Figure 2**.

PROCEDURAL OUTCOME AND DEVICE SUCCESS

Procedural characteristics of the entire and matched population are displayed in **Table 2**. Most (>99%) procedures were performed under conscious sedation. The small, medium and large sizes of the Neo2 THV were implanted in 21.9%, 43.4% and 34.7% of patients, respectively, with an overall cover index calculated by perimeter of 6.04% (IQR 3.91, 8.15). The Ultra THV sizes 20 mm, 23 mm and 26 mm were deployed in 1.5%, 28.7% and 69.8% of cases, respectively, with a median cover index calculated by area of 2.65% (IQR -0.23, 6.10). Patients treated with the Neo2 presented higher rates of pre- and post-dilatation compared with the Ultra THV in the entire population (predilatation: 534 [87.8%] vs 268 [35.8%]; p<0.001; post-dilatation: 250 [41.1%] vs 111 [14.8%]; p<0.001) as well as in the matched cohort (predilatation: 434 [91.9%] vs 148 [31.4%]; p<0.001; post-dilatation: 211 [44.7%] vs 69 [14.6%]; p<0.001). Furthermore, a significantly lower amount of contrast agent was used with the Neo2 compared with the Ultra THV in the entire population (40.00 ml [IQR 20.00, 116.00] vs 115.00 ml [IQR 36.00, 160.00]; p<0.001) as well as in the matched population (40.00 ml [IQR 22.00, 130.00] vs 117.50 ml [IQR 37.75, 160.00]; p<0.001), while the fluoroscopy time differed only in the entire population (9.40 min [IQR 7.01, 13.29] vs 10.21 min [IQR 7.10, 14.62]; p=0.033).

Technical success was comparable between both groups in the entire and matched populations. On the contrary, the crude rate of the composite endpoint device success was 91.6% with the Neo2 THV, which was significantly higher than with the Ultra THV (83.7%, OR 2.128, 95% CI: 1.506-3.009; p<0.001) **(Table 2, Central illustration)**. The significant risk reduction persisted after multivariate adjustment (OR 1.900, 95% CI: 1.270-2.844; p=0.002) **(Central illustration, Supplementary Table 2)**, as well as after IPTW analysis (OR 1.961, 95% CI: 1.269-3.031; p=0.002) **(Central illustration)**. Consistently, after PSM, device success rates were higher with the Neo2 compared to the Ultra (434 [91.9%] vs 401 [85.0%]; OR 2.022, 95% CI: 1.333-3.067; p<0.001) **(Table 2, Central illustration)**. This finding was mainly driven by elevated mean transvalvular gradients (≥20 mmHg), which were higher

Table 2. Procedural and post-procedural characteristics for the entire population and matched population according to implanted THV.

	Entire population			Matched population		
	Neo2 n=608	Ultra n=748	*p*-value	Neo2 n=472	Ultra n=472	*p*-value
Procedural characteristics						
Conscious sedation	606 (99.7)	742 (99.2)	0.308	471 (99.8)	467 (98.9)	0.217
Predilatation	534 (87.8)	268 (35.8)	<0.001	434 (91.9)	148 (31.4)	<0.001
Post-dilatation	250 (41.1)	111 (14.8)	<0.001	211 (44.7)	69 (14.6)	<0.001
Procedural time, min	44.00 [35.00, 59.00]	46.00 [35.00, 58.00]	0.867	45.00 [36.00, 59.00]	46.00 [35.00, 57.00]	0.472
Contrast agent, ml	40.00 [20.00, 116.00]	115.00 [36.00, 160.00]	<0.001	40.00 [22.00, 130.00]	117.50 [37.75, 160.00]	<0.001
Fluoroscopy time, min	9.40 [7.01, 13.29]	10.21 [7.10, 14.62]	0.033	9.82 [7.30, 13.81]	10.20 [6.90, 14.11]	0.974
Cover index by area	8.00 [5.61, 10.00]	2.65 [-0.23, 6.10]	<0.001	7.83 [5.60, 9.67]	2.42 [-0.38, 6.04]	<0.001
Cover index by perimeter	6.04 [3.91, 8.15]	0.71 [-2.35, 4.12]	<0.001	6.00 [3.90, 7.93]	0.59 [-2.69, 4.19]	<0.001
Technical success (VARC-3)	575 (94.6)	714 (95.5)	0.529	448 (94.9)	450 (95.3)	0.880
Device success (VARC-3)	557 (91.6)	626 (83.7)	<0.001	434 (91.9)	401 (85.0)	0.001
Procedural mortality	0 (0.0)	4 (0.5)	0.132	0 (0.0)	2 (0.4)	0.499
Correct implant position	602 (99.0)	747 (99.9)	0.050	467 (98.9)	472 (100.0)	0.062
Multiple valves	3 (0.5)	1 (0.1)	0.331	3 (0.6)	1 (0.2)	0.624
Conversion to surgery	1 (0.2)	6 (0.8)	0.138	1 (0.2)	3 (0.6)	0.624
Post-procedural characteristics						
Moderate to severe PVL*	4 (0.7)	6 (0.8)	1.000	3 (0.6)	5 (1.1)	0.723
Mean gradient ≥20 mmHg	11 (1.8)	69 (9.3)	<0.001	11 (2.4)	36 (7.7)	<0.001
Indexed effective orifice area, cm²**	0.92 [0.79, 1.05] (n=453)	0.78 [0.68, 0.90] (n=261)	<0.001	0.92 [0.79, 1.05] (n=342)	0.78 [0.67, 0.91] (n=167)	<0.001
Severe PPM**	10 (2.2) (n=453)	39 (14.9) (n=261)	<0.001	10 (2.9) (n=342)	25 (15.0) (n=167)	<0.001
Annular rupture	1 (0.2)	2 (0.3)	1.000	1 (0.2)	0 (0.0)	0.999

Data are median [interquartile range] or n (%). *As assessed by echocardiography at discharge, for missing data aortic regurgitation was assessed by angiography (n=10/1,356). **Available for 714/1,356 in the entire population and for 509/944 in the matched population. PPM: patient-prosthesis mismatch; PVL: paravalvular leakage; THV: transcatheter heart valve; VARC-3: updated Valve Academic Research Consortium 3 in patients treated with the Ultra compared with the Neo2 THV, both in the entire and matched populations (entire population: 69 [9.3%] vs 11 [1.8%]; p<0.001; matched population: 36 [7.7%] vs 11 [2.4%]; p<0.001). Further, the Ultra cohort presented smaller iEOA in the entire (0.78 cm^2 [0.68, 0.90] vs 0.92 cm^2 [0.79, 1.05]; p<0.001) and matched populations (0.78 cm^2 [0.67, 0.91] vs 0.92 cm^2 [0.79, 1.05]; p<0.001) compared to the Neo2 cohort, resulting in higher rates of severe PPM (entire population: 39 [14.9%] vs 10 [2.2%]; p<0.001 and matched population: 25 [15.0%] vs 10 [2.9%]; p<0.001).

IN-HOSPITAL AND 30-DAY OUTCOMES

Table 3 displays clinical outcomes during hospital stay and at 30 days for the entire and the matched populations. There were no significant differences with respect to in-hospital events between the treatment groups. Notably, despite differences in the use of contrast agent, rates of acute kidney injury stage 2-4 were low and comparable in both groups. Haemodynamic performance as measured by echocardiography improved substantially after TAVI as shown in **Figure 1** with a reduction in mean transvalvular gradients for both platforms. However, transprosthetic gradients were significantly lower with the Neo2 THV compared with the Ultra THV after TAVI in the entire (9±4 mmHg vs 13±5 mmHg; p<0.001) and matched populations (9±4 mmHg vs 13±4 mmHg; p<0.001) **(Figure 1A, Figure 1B)**. Rates of moderate PVL were overall low and similar for both THV before and after matching, with no case of severe PVL in either group **(Figure 1C, Figure 1D)**. Conversely, rates of mild PVL were lower in Ultra compared with Neo2 recipients in the entire (19.2% vs 32.6%; p<0.001) and matched populations (20.0% vs 32.8%; p<0.001).

Follow-up at 30 days was complete for 95.0% of the entire population, specifically for matched patients in 98.3% (464 of 472) of patients treated with the Neo2 THV and for 98.5% (465 of 472) of patients treated with the Ultra THV. As shown in **Table 3**, clinical event rates at 30 days were low and did not differ between Neo2 and Ultra recipients.

Discussion

The main results can be summarised as follows: 1) VARC-3 technical success was comparable in both THV, while device success was higher with the Neo2 THV than with the Ultra THV due to significantly lower transvalvular gradients after TAVI. 2) Rates of moderate or severe PVL were overall low and comparable with both THV, whereas mild PVL was significantly lower in Ultra THV compared to Neo2 THV recipients. 3) Event rates were overall low with both THV up to 30 days.

Growing evidence from randomised clinical trials and large registry studies with different TAVI platforms corroborate excellent results, promoting their fast expansion. Still, some procedural shortcomings including PVL and permanent pacemaker implantation (PPI) need to be addressed to safely move to a routine treatment of low-risk and younger patients. With this in mind, new iterations of THV need to overcome these drawbacks, focusing on novel designs and modified implantation techniques. In particular, for the

Table 3. In-hospital and 30-day clinical outcomes for the entire population and matched population according to implanted THV.

	Entire population			Matched population		
	Neo2 n=608	Ultra n=748	*p*-value	Neo2 n=348	Ultra n=348	*p*-value
In-hospital clinical outcomes						
All-stroke	17 (2.8)	24 (3.2)	0.778	16 (3.4)	11 (2.3)	0.435
New permanent pacemaker implantation*	40/553 (7.5)	66/677 (9.7)	0.170	33/415 (8.0)	42/426 (9.9)	0.332
Major vascular complication (VARC-3)	39 (6.4)	66 (8.8)	0.122	29 (6.1)	45 (9.5)	0.069
Bleeding type 3 and 4 (VARC-3)	26 (4.3)	33 (4.4)	0.999	18 (3.8)	17 (3.6)	0.999
Cardiac structural complication (VARC-3)	5 (0.8)	12 (1.6)	0.298	4 (0.8)	5 (1.1)	0.999
Myocardial infarction	0 (0.0)	3 (0.4)	0.326	0 (0.0)	2 (0.4)	0.479
Coronary obstruction requiring PCI	1 (0.2)	3 (0.4)	0.768	1 (0.2)	2 (0.4)	0.999
AKIN 2/3/4	18 (3.0)	23 (3.1)	0.999	15 (3.2)	15 (3.2)	0.999
In-hospital mortality	7 (1.2)	7 (0.9)	0.904	5 (1.1)	4 (0.8)	0.999
30-day clinical outcomes	**Neo2 n=598****	**Ultra n=734****	***p*-value**	**Neo2 n=464****	**Ultra n=465****	***p*-value**
All-cause mortality	11 (1.8)	18 (2.5)	0.566	8 (1.7)	11 (2.4)	0.646
All-stroke	18 (3.0)	23 (3.1)	0.999	16 (3.4)	11 (2.4)	0.435
Cardiovascular rehospitalisation	5 (0.8)	7 (1.0)	0.999	5 (1.1)	3 (0.6)	0.723
New pacemaker implantation*	40/522 (7.7)	70/664 (10.5)	0.090	33/406 (8.1)	43/419 (10.3)	0.289
Repeat procedure	0 (0.0)	1 (0.1)	0.999	0 (0.0)	0 (0.0)	–

Data are median [interquartile range] or n (%). *Excluding patients with pacemaker at baseline. **Patients with available follow-up at 30 days in the entire population 1,332/1,356 and in the matched population 929/944. AKIN: Acute Kidney Injury Network classifcation; CHF: congestive heart failure; PCI: percutaneous coronary intervention; THV: transcatheter heart valve

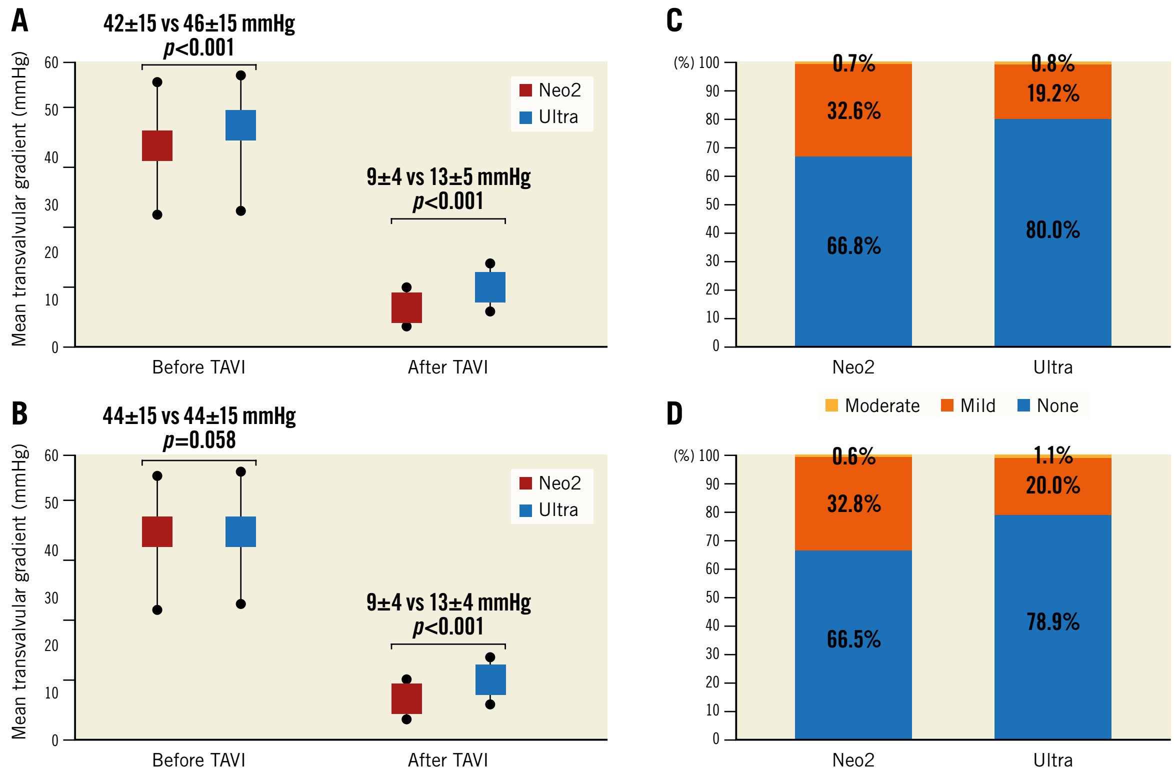


Figure 1. *Mean transvalvular gradients before and after TAVI and rates of paravalvular leakage after transcatheter aortic valve implantation according to implanted THV for the entire (A, C) and the matched populations (B, D). Neo2: ACURATE neo2; TAVI: transcatheter aortic valve implantation; THV: transcatheter heart valve; Ultra: SAPIEN 3 Ultra*

SE Neo THV the previous clinical experience showed consistently higher rates of PVL compared to other available THV platforms, not least in the randomised SCOPE I and II trials[3,12]. To cope with this Achilles´ heel, the revised Neo2 THV exhibits a 60% larger sealing skirt. So far, promising early results were yielded in recent multicentric registries showing significantly lower rates of moderate to severe PVL with the Neo2 THV compared to its predecessor[6,13]. At the same time, the latest-generation Ultra THV with its adapted sealing properties, showed a further improvement in PVL rates, with already low rates of moderate to severe PVL ranging from 0.1% to 2.7%, and a further significant reduction of mild PVL rates[4,14]. In the current study, we present exceedingly low moderate to severe PVL rates for both platforms, reinforcing the positive evidence for these new THV. Compared with the Neo2, the Ultra THV further showed lower rates of mild PVL. While the presence of moderate to severe PVL is largely considered to negatively influence outcome[15], the impact of mild PVL on outcome is still controversial. A recent meta-analysis suggested an association with increased mortality, especially in selected subsets of patients, which needs to be further investigated in larger analyses[16].

The main driver leading to the marked difference found in device success rates was the presence of elevated transvalvular gradients ≥20 mmHg after TAVI, which were significantly higher in Ultra recipients. These findings are in line with previous data[3,17-19] and may likely be explained by the supra-annular design of the Neo2 THV. The clinical relevance of higher transvalvular gradients and PPM with potential less symptomatic benefit and faster THV deterioration is still a matter of debate. Yet, a recent analysis from the FRANCE-2 Registry showed an increased mortality among patients with persistently elevated gradients at 1 year[20]. Thus, further knowledge and evidence are needed to fully comprehend this subject.

The need for PPI remains a considerable downside even in contemporary TAVI practice with rates ranging from 6.7% to 39.2%[21]. The lowest pacemaker rates were found with the Neo THV, with rates ranging from 2%-10%[22-24]. Of note, pacemaker rates with the SAPIEN 3 valve showed a decrease after the initial experience from 16% to 5.5% due to a higher device positioning approach[25,26]. While no difference in pacemaker rates was found in the SCOPE I trial, registry data showed consistently lower rates when using the Neo THV[17,27]. Recent analyses of the Neo2 THV showed similarly low PPI rates ranging from 8% to 11%, despite its revised annular sealing properties[6,13]. Similarly, recent experience with the Ultra THV showed excellent pacemaker rates of 4.5% to 6.4%[4,14]. Consistently, in this direct comparison we found overall low and comparable rates of PPI for both valves. Addressing the issue of pacemaker implantation is of the utmost importance to reduce potential adverse long-term effects, especially when moving towards the treatment of younger patients.

Despite the significantly higher use of pre- and post-dilatation in Neo2 recipients, this did not translate into longer procedural times or alleged higher complication rates, such as stroke, annulus rupture or the need for PPI. Evidence from randomised clinical trials comparing the BE SAPIEN 3 THV (DIRECT TAVI trial; ClinicalTrials.gov: NCT02729519) and the SE CoreValve Evolut R/PRO THV (Medtronic) (DIRECT trial; ClinicalTrials.gov: NCT02448927), with or without predilatation, showed no difference in clinical outcome[28,29], suggesting the feasibility of both implantation techniques and thereby leaving the decision to the discretion of the operators, who should then take into consideration important anatomical characteristics, particularly valvular calcification. For the Neo/Neo2 THV, which exhibit less radial force compared to BE and other SE THV, predilatation is mandatory. A recent analysis focusing on dilatation strategy from the NEOPRO registry showed a comparable outcome when predilatation was omitted[30]. However, randomised data with the novel Neo2 THV are warranted to fully assess the optimal implantation technique for this THV.

The significant difference concerning the amount of contrast agent used for TAVI found in this analysis can be attributed to a minimalistic approach used in 1 participating centre and should be interpreted with care[7].

Limitations

Besides the inherent limitations of a retrospective, non-randomised study setting, we would like to address some limitations. Firstly, the sample size is rather modest. However, this is the first ever comparative analysis of the 2 valve platforms. PSM may not rule out immeasurable confounders. After PSM, severely calcified anatomies were excluded; thus, these findings are limited to mildly and moderately calcified aortic valves. Although clinical events were categorised according to standardised definitions, there was no adjudication by an independent committee. Echocardiography was performed according to current recommendations; however, there was no core laboratory for echocardiographic analyses[8,31].

Conclusions

In this multicentre registry, outcomes after TAVI using the Neo2 and the Ultra THV were excellent and, overall, comparable. However, transvalvular gradients were lower for the Neo2 platform and translated into a higher rate of device success. Rates of moderate to severe PVL were low with both THV; however, the Ultra THV showed significantly lower rates of mild PVL.

Impact on daily practice

No direct comparisons between latest-generation self-expanding and balloon-expandable transcatheter prostheses are available so far. In this multicentre, propensity-matched comparison of the self-expanding ACURATE *neo*2 and the balloon-expandable SAPIEN 3 Ultra prostheses, we found comparable short-term outcomes with both valves. However, transprosthetic gradients were lower with the ACURATE *neo*2 platform, which translated into a higher rate of device success. Rates of mild PVL were significantly lower with the SAPIEN 3 Ultra prosthesis.

Conflict of interest statement

A. Wolf received proctor fees from Edwards Lifesciences and Boston Scientific. E.I. Charitos has received proctor fees from Boston Scientific and holds stock or stock options in Edwards Lifesciences. M. Joner reports lecture fees and research grants from Edwards Lifesciences, Cardiac Dimensions, Infraredx, and Boston Scientific; is a consultant for Biotronik, Boston Scientific, Cardiac Dimensions, and Shockwave Medical; has received honoraria from Abbott, AstraZeneca, Biotronik, Boston Scientific, Edwards Lifesciences, ReCor, Shockwave Medical, and Orbus Neich; and is a Member of the Board of Biotronik and Shockwave Medical. W-K. Kim received proctor and/or speaker and/or advisory honoraria from Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, Meril Life Sciences, and Shockwave Medical. C. Pellegrini received a personal research grant from Else Kröner Fresenius Stiftung. T. Rheude received lecture fees from SIS Medical AG, and Astra Zeneca; and travel support from SIS Medical AG. O. Dörr received honoraria for lectures from Edwards Lifesciences. E. Xhepa reports lecture fees and honoraria from AstraZeneca, Boston Scientific, and SIS Medical, not related to the current work; he reports proctor fees from Abbott Vascular, and financial support for attending meetings and/or travel expenses from Abbott Vascular. The other authors have no conflicts of interest to declare.

References

1. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A, Toly C. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation.* 2021;143:e35-71.

2. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sádaba JR, Tribouilloy C, Wojakowski W. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention.* 2022;17:e1126-96.

3. Lanz J, Kim WK, Walther T, Burgdorf C, Möllmann H, Linke A, Redwood S, Thilo C, Hilker M, Joner M, Thiele H, Conzelmann L, Conradi L, Kerber S, Schymik G, Prendergast B, Husser O, Stortecky S, Heg D, Jüni P, Windecker S, Pilgrim T; SCOPE I investigators. Safety and efficacy of a self-expanding versus a balloon-expandable bioprosthesis for transcatheter aortic valve replacement in patients with symptomatic severe aortic stenosis: a randomised non-inferiority trial. *Lancet.* 2019;394:1619-28.

4. Rheude T, Pellegrini C, Lutz J, Alvarez-Covarrubias HA, Lahmann AL, Mayr NP, Michel J, Kasel MA, Joner M, Xhepa E. Transcatheter Aortic Valve Replacement With Balloon-Expandable Valves: Comparison of SAPIEN 3 Ultra Versus SAPIEN 3. *JACC Cardiovasc Interv.* 2020;13:2631-8.

5. Möllmann H, Holzhey DM, Hilker M, Toggweiler S, Schäfer U, Treede H, Joner M, Søndergaard L, Christen T, Allocco DJ, Kim WK. The ACURATE *neo*2 valve system for transcatheter aortic valve implantation: 30-day and 1-year outcomes. *Clin Res Cardiol.* 2021;110:1912-20.

6. Scotti A, Pagnesi M, Kim W, Schäfer U, Barbanti M, Costa G, Baggio S, Casenghi M, De Marco F, Vanhaverbeke M, Søndergaard L, Wolf A, Schofer J, Ancona MB, Montorfano M, Kornowski R, Assa HV, Toggweiler S, Ielasi A, Hildick-Smith D, Windecker S, Schmidt A, Buono A, Maffeo D, Siqueira D, Giannini F, Adamo M, Massussi M, Wood DA, Sinning JM, Van der Heyden J, van Ginkel DJ, Van Mieghem N, Veulemans V, Mylotte D, Tzalamouras V, Taramasso M, Estévez-Loureiro R, Colombo A, Mangieri A, Latib A. Haemodynamic performance and clinical outcomes of transcatheter aortic valve replacement with the self-expanding ACURATE *neo*2. *EuroIntervention.* 2022;18:804-11.

7. Kim WK, Doerr O, Renker M, Choi YH, Liakopoulos O, Hamm CW, Nef H. Initial experience with a novel, modular, minimalistic approach for transfemoral aortic valve implantation. *Int J Cardiol.* 2021;332:54-9.

8. VARC-3 Writing Committee, Généreux P, Piazza N, Alu MC, Nazif T, Hahn RT, Pibarot P, Bax JJ, Leipsic JA, Blanke P, Blackstone EH, Finn MT, Kapadia S, Linke A,

Mack MJ, Makkar R, Mehran R, Popma JJ, Reardon M, Rodes-Cabau J, Van Mieghem NM, Webb JG, Cohen DJ, Leon MB. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *Eur Heart J.* 2021;42:1825-57.

9. Alqahtani AM, Boczar KE, Kansal V, Chan K, Dwivedi G, Chow BJ. Quantifying Aortic Valve Calcification using Coronary Computed Tomography Angiography. *J Cardiovasc Comput Tomogr.* 2017;11:99-104.

10. Kim WK, Bhumimuang K, Renker M, Fischer-Rasokat U, Möllmann H, Walther T, Choi YH, Nef H, Hamm CW. Kim WK, Bhumimuang K, Renker M, Fischer-Rasokat U, Möllmann H, Walther T, Choi YH, Nef H, Hamm CW. Determinants of paravalvular leakage following transcatheter aortic valve replacement in patients with bicuspid and tricuspid aortic stenosis. *Eur Heart J Cardiovasc Imaging.* 2021 Feb 14. [Epub ahead of print].

11. Ho D, Imai K, King G, Stuart E. MatchIt: Nonparametric Preprocessing for Parametric Causal Inference. *Journal of Statistical Software*. 2011;42:1-28.

12. Tamburino C, Bleiziffer S, Thiele H, Scholtz S, Hildick-Smith D, Cunnington M, Wolf A, Barbanti M, Tchetchè D, Garot P, Pagnotta P, Gilard M, Bedogni F, Van Belle E, Vasa-Nicotera M, Chieffo A, Deutsch O, Kempfert J, Sondergaard L, Butter C, Trillo-Nouche R, Lotfi S, Möllmann H, Joner M, Abdel-Wahab M, Bogaerts K, Hengstenberg C, Capodanno D. Comparison of Self-Expanding Bioprostheses for Transcatheter Aortic Valve Replacement in Patients With Symptomatic Severe Aortic Stenosis: SCOPE 2 Randomized Clinical Trial. *Circulation.* 2020;142:2431-42.

13. Buono A, Gorla R, Ielasi A, Costa G, Cozzi O, Ancona M, Soriano F, De Carlo M, Ferrara E, Giannini F, Massussi M, Fovino LN, Pero G, Bettari L, Acerbi E, Messina A, Sgroi C, Pellicano M, Sun J, Gallo F, Franchina AG, Bruno F, Nerla R, Saccocci M, Villa E, D'Ascenzo F, Conrotto F, Cuccia C, Tarantini G, Fiorina C, Castriota F, Poli A, Petronio AS, Oreglia J, Montorfano M, Regazzoli D, Reimers B, Tamburino C, Tespili M, Bedogni F, Barbanti M, Maffeo D; ITAL-neo Investigators. Transcatheter Aortic Valve Replacement With Self-Expanding ACURATE *neo*2: Postprocedural Hemodynamic and Short-Term Clinical Outcomes. *JACC Cardiovasc Interv.* 2022;15:1101-10.

14. Nazif TM, Cahill TJ, Daniels D, McCabe JM, Reisman M, Chakravarty T, Makkar R, Krishnaswamy A, Kapadia S, Chehab BM, Wang J, Spies C, Rodriguez E, Kaneko T, Hahn RT, Leon MB, George I. Real-World Experience With the SAPIEN 3 Ultra Transcatheter Heart Valve: A Propensity-Matched Analysis From the United States. *Circ Cardiovasc Interv.* 2021;14:e010543.

15. Takagi H, Umemoto T; ALICE (All-Literature Investigation of Cardiovascular Evidence) Group. Impact of paravalvular aortic regurgitation after transcatheter aortic valve implantation on survival. *Int J Cardiol.* 2016;221:46-51.

16. Ando T, Briasoulis A, Telila T, Afonso L, Grines CL, Takagi H. Does mild paravalvular regurgitation post transcatheter aortic valve implantation affect survival? A meta-analysis. *Catheter Cardiovasc Interv.* 2018;91:135-47.

17. Husser O, Kim WK, Pellegrini C, Holzamer A, Walther T, Mayr PN, Joner M, Kasel AM, Trenkwalder T, Michel J, Rheude T, Kastrati A, Schunkert H, Burgdorf C, Hilker M, Möllmann H, Hengstenberg C. Multicenter Comparison of Novel Self-Expanding Versus Balloon-Expandable Transcatheter Heart Valves. *JACC Cardiovasc Interv.* 2017;10:2078-87.

18. Mauri V, Kim WK, Abumayyaleh M, Walther T, Moellmann H, Schaefer U, Conradi L, Hengstenberg C, Hilker M, Wahlers T, Baldus S, Rudolph V, Madershahian N, Rudolph TK. Short-Term Outcome and Hemodynamic Performance of Next-Generation Self-Expanding Versus Balloon-Expandable Transcatheter Aortic Valves in Patients with Small Aortic Annulus: A Multicenter Propensity-Matched Comparison. *Circ Cardiovasc Interv.* 2017;10:e005013.

19. Wilde N, Rogmann M, Mauri V, Piayda K, Schmitz MT, Al-Kassou B, Shamekhi J, Maier O, Sugiura A, Weber M, Zimmer S, Zeus T, Kelm M, Adam M, Baldus S, Nickenig G, Veulemans V, Sedaghat A. Haemodynamic differences between two generations of a balloon-expandable transcatheter heart valve. *Heart.* 2022;108:1479-85.

20. Didier R, Benic C, Nasr B, Le Ven F, Hannachi S, Eltchaninoff H, Koifman E, Donzeau-Gouge P, Fajadet J, Leprince P, Leguerrier A, Lièvre M, Prat A, Teiger E, Lefevre T, Cuisset T, Le Breton H, Auffret V, Iung B, Gilard M. High Post-Procedural Transvalvular Gradient or Delayed Mean Gradient Increase after Transcatheter Aortic Valve Implantation: Incidence, Prognosis and Associated Variables. The FRANCE-2 Registry. *J Clin Med*. 2021;10:3221.

21. Bruno F, D'Ascenzo F, Vaira MP, Elia E, Omedè P, Kodali S, Barbanti M, Rodès-Cabau J, Husser O, Sossalla S, Van Mieghem NM, Bax J, Hildick-Smith D, Munoz-Garcia A, Pollari F, Fischlein T, Budano C, Montefusco A, Gallone G, De Filippo O, Rinaldi M, la Torre M, Salizzoni S, Atzeni F, Pocar M, Conrotto F, De Ferrari GM. Predictors of pacemaker implantation after transcatheter aortic valve implantation according to kind of prosthesis and risk profile: a systematic review and contemporary meta-analysis. *Eur Heart J Qual Care Clin Outcomes*. 2021;7:143-53.

22. Toggweiler S, Nissen H, Mogensen B, Cuculi F, Fallesen C, Veien KT, Brinkert M, Kobza R, Rück A. Very low pacemaker rate following ACURATE neo transcatheter heart valve implantation. *EuroIntervention.* 2017;13:1273-80.

23. Pellegrini C, Husser O, Kim WK, Holzamer A, Walther T, Rheude T, Mayr NP, Trenkwalder T, Joner M, Michel J, Chaustre F, Kastrati A, Schunkert H, Burgdorf C, Hilker M, Möllmann H, Hengstenberg C. Predictors of Need for Permanent Pacemaker Implantation and Conduction Abnormalities With a Novel Self-expanding Transcatheter Heart Valve. *Rev Esp Cardiol.* 2019;72:145-53.

24. Kim WK, Möllmann H, Walther T, Hamm CW. Predictors of permanent pacemaker implantation after ACURATE neo transcatheter heart valve implantation. *Pacing Clin Electrophysiol.* 2021;44:410-5.

25. Wendler O, Schymik G, Treede H, Baumgartner H, Dumonteil N, Ihlberg L, Neumann FJ, Tarantini G, Zamarano JL, Vahanian A. SOURCE 3 Registry: Design and 30-Day Results of the European Postapproval Registry of the Latest Generation of the SAPIEN 3 Transcatheter Heart Valve. *Circulation.* 2017;135:1123-32.

26. Pellegrini C, Kim WK, Holzamer A, Walther T, Mayr NP, Michel J, Rheude T, Nuñez J, Kasel AM, Trenkwalder T, Kaess BM, Joner M, Kastrati A, Schunkert H, Hilker M, Möllmann H, Hengstenberg C, Husser O. Multicenter Evaluation of Prosthesis Oversizing of the SAPIEN 3 Transcatheter Heart Valve. Impact on Device Failure and New Pacemaker Implantations. *Rev Esp Cardiol.* 2019;72:641-8.

27. Barth S, Reents W, Zacher M, Kerber S, Diegeler A, Schieffer B, Schreiber M, Lauer B, Kuntze T, Dahmer M, Hamm C, Hamm K. Multicentre propensity-matched comparison of transcatheter aortic valve implantation using the ACURATE TA/neo self-expanding versus the SAPIEN 3 balloon-expandable prosthesis. *EuroIntervention.* 2019;15:884-91.

28. Leclercq F, Robert P, Akodad M, Macia JC, Gandet T, Delseny D, Chettouh M, Schmutz L, Robert G, Levy G, Targosz F, Maupas E, Roubille F, Marin G, Nagot N, Albat B, Lattuca B, Cayla G. Prior Balloon Valvuloplasty Versus Direct Transcatheter Aortic Valve Replacement: Results From the DIRECTAVI Trial. *JACC Cardiovasc Interv.* 2020;13:594-602.

29. Toutouzas K, Benetos G, Voudris V, Drakopoulou M, Stathogiannis K, Latsios G, Synetos A, Antonopoulos A, Kosmas E, Iakovou I, Katsimagklis G, Mastrokostopoulos A, Moraitis S, Zeniou V, Danenberg H, Vavuranakis M, Tousoulis D. Pre-Dilatation Versus No Pre-Dilatation for Implantation of a Self-Expanding Valve in All Comers Undergoing TAVR: The DIRECT Trial. *JACC Cardiovasc Interv.* 2019;12:767-77.

30. Pagnesi M, Kim WK, Conradi L, Barbanti M, Stefanini GG, Schofer J, Hildick-Smith D, Pilgrim T, Abizaid A, Zweiker D, Testa L, Taramasso M, Wolf A, Webb JG, Sedaghat A, Van der Heyden JAS, Ziviello F, MacCarthy P, Hamm CW, Bhadra OD, Schäfer U, Costa G, Tamburino C, Cannata F, Reimers B, Eitan A, Alsanjari O, Asami M, Windecker S, Siqueira D, Schmidt A, Bianchi G, Bedogni F, Saccocci M, Maisano F, Jensen CJ, Naber CK, Alenezi A, Wood DA, Sinning JM, Brouwer J, Tzalamouras V, Van Mieghem NM, Colombo A, Latib A. Impact of Predilatation Prior to Transcatheter Aortic Valve Implantation With the Self-Expanding Acurate neo Device (from the Multicenter NEOPRO Registry). *Am J Cardiol.* 2020;125:1369-77.

31. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging.* 2015;16:233-70.

Supplementary data

Supplementary Table 1. Standardised mean difference for baseline characteristics used for propensity score matching before and after matching.

Supplementary Table 2. Uni- and multivariate analysis for the primary endpoint device success, only variables with p<0.100 shown.

Supplementary Figure 1. Flow chart showing overview of treated patients according to participating centre.

Supplementary Figure 2. Distribution of propensity score in treated and control patients (A), density of propensity score in treated and control patients (B) and Love plot (C).

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-22-00164

Supplementary data

Supplementary Table 1. Standardised mean difference for baseline characteristics used for propensity score matching before and after matching.

	Before matching SMD	After matching SMD
Age, years	0.118	0.025
Female gender	0.114	0.030
Logistic EuroScore, %	0.112	0.083
NYHA III/IV	0.245	0.035
Coronary artery disease	0.277	0.019
Previous PCI	0.122	0.013
LVEF <35%	0.141	0.045
Mean transvalvular gradient, mmHg	0.261	0.012
Indexed effective orifice area (cm^2)	0.251	0.052
Bicuspid aortic valve	0.360	0.050
Severe aortic valve calcification	0.198	0.069
Asymmetric calcification	0.546	0.072
Mean annulus diameter, mm	0.044	0.036

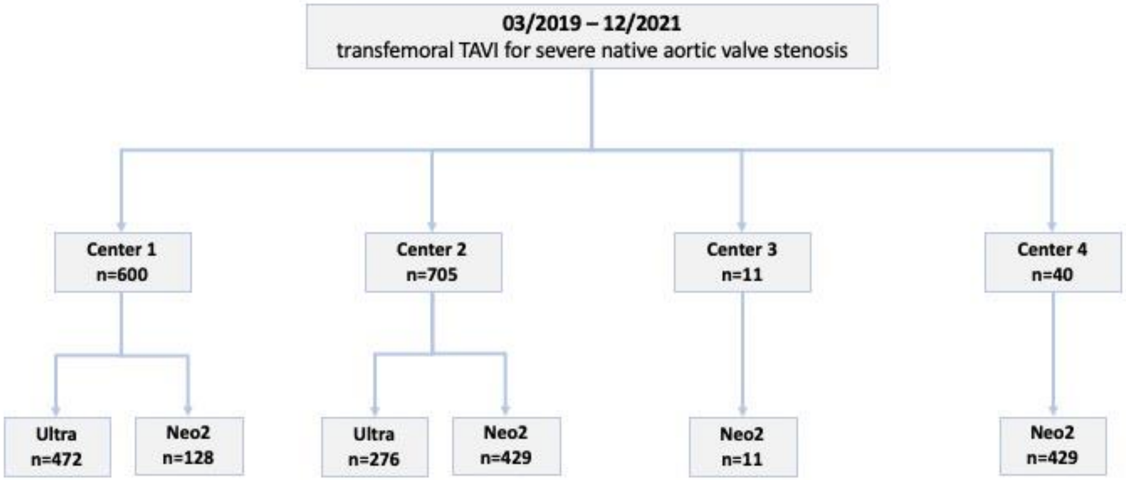
Abbreviations: LV, left ventricular; NYHA, New York Heart Association functional class; PCI, percutaneous coronary intervention.

Supplementary Table 2. Uni -and multivariate analysis for the primary endpoint device success, only variables with p<0.100 shown.

	Device success – n=173	**Device success + n=1183**	**p-value**	**OR**	**95% CI**	**p-value**
Age, years	80.41 [76.83, 83.88]	81.85 [78.00, 85.00]	0.004	1.022	[0.997 – 1.048]	0.084
Diabetes mellitus	44 (25.4)	397 (33.6)	0.037	1.511	[1.035 – 2.206]	**0.033**
COPD	34 (19.7)	126 (10.7)	0.001	0.466	[0.302 – 0.719]	**<0.001**
On dialysis	5 (2.9)	14 (1.2)	0.083	0.400	[0.134 – 1.196]	0.101
Coronary artery disease	108 (62.4)	826 (69.8)	0.053	1.566	[1.090 – 2.251]	0.015
Peripheral artery disease	37 (21.4)	177 (15.0)	0.034	0.652	[0.430 – 0.991]	0.045
Mean transvalvular gradient, mmHg	44.00 [36.50, 56.00]	43.00 [34.00, 52.00]	0.041	0.992	[0.982 – 1.003]	0.176
Bicuspid valve	21 (12.1)	96 (8.1)	0.083	1.083	[0.624 – 1.883]	0.776
Asymmetric calcification	76 (43.9)	383 (32.4)	0.003	0.740	[0.519 – 1.056]	0.097
Mean annular diameter, mm	23.85 [22.30-25.45]	24.35 [22.9, 25.8]	0.010	1.001	[0.999 – 1.002]	0.383
Use of Neo2 THV	51 (29.5)	557 (47.1)	<0.001	1.900	[1.270 – 2.844]	**0.002**
Center				1.175	[0.846 – 1.631]	0.335
1	84 (48.6)	516 (43.6)	0.025			
2	88 (50.9)	617 (52.2)				
3	1 (0.6)	10 (0.8)				
4	0 (0)	40 (3.4)				

Abbreviations: CI, Confidence Interval; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; OR, Odds Ratio; THV, transcatheter heart valve

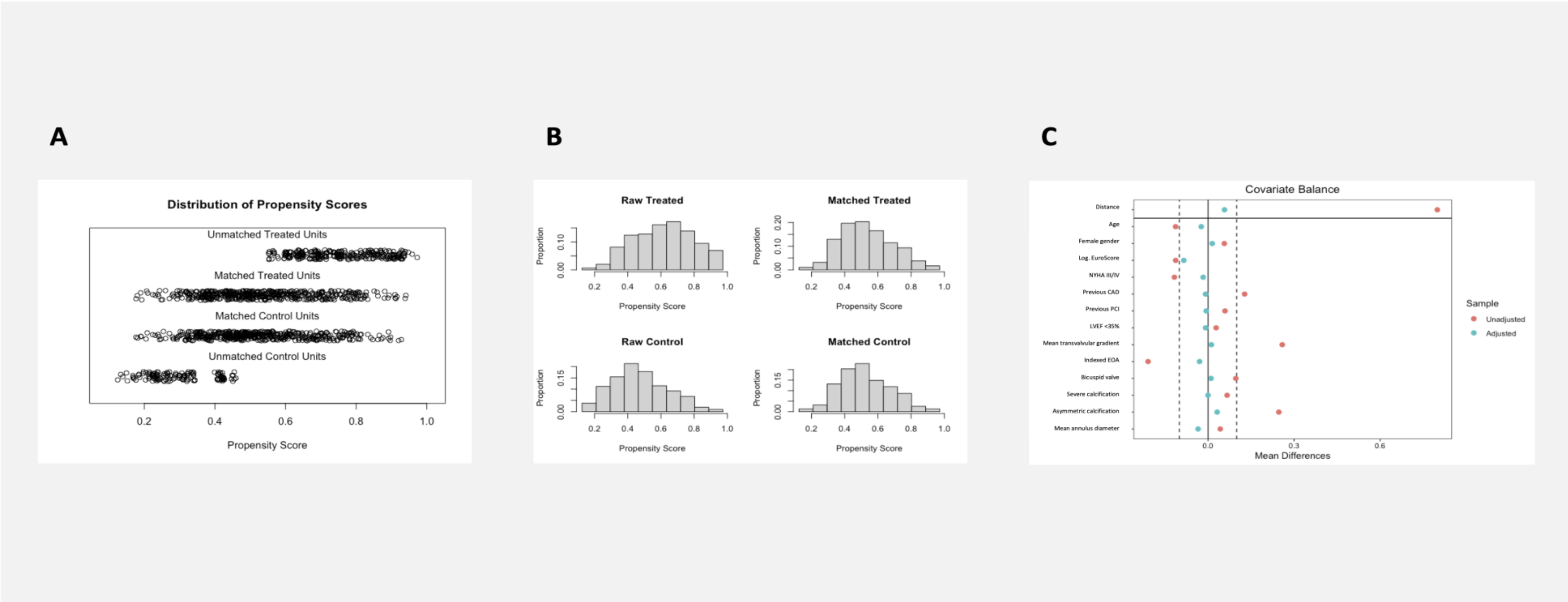
Supplemental Figure 1



Supplementary Figure 1. Flow chart showing overview of treated patients according to participating centre.

Abbreviations: Neo2, ACURATE neo2; Ultra; SAPIEN 3 Ultra

Supplemental Figure 2



Supplementary Figure 2. Distribution of propensity score in treated and control patients (A), density of propensity score in treated and control patients (B) and Love plot (C).

Abbreviations: CAD, coronary artery disease; iEOA, indexed effective orifice area; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class; PCI, percutaneous coronary intervention.