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Multicentre propensity-matched comparison of transcatheter aortic valve implantation using the ACURATE TA/neo self-expanding versus the SAPIEN 3 balloon-expandable prosthesis

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KEYWORDS

- clinical research
- death
- myocardial infarction
- stroke
- TAVI

Abstract

Aims: In the absence of randomised data, we aimed to compare the transapical ACURATE and transfemoral ACURATE *neo* with the SAPIEN 3 prosthesis using propensity matching.

Methods and results: From 2012 to 2016, 1,306 patients at three German centres received either the ACURATE/ACURATE *neo* prosthesis (n=591) or the SAPIEN 3 prosthesis (n=715). Through nearest neighbour matching with exact allocation for access route and centre, pairs of 329 patients (250 transfemoral, 79 transapical) per group were determined. Patients were 81 years old on average and had a logistic EuroSCORE I of 19%. Predilatation and post-dilatation were more frequent in the ACURATE group (97.6% versus 52.1%, p<0.001 for predilatation and 40.4% versus 11.6%, p<0.001 for post-dilatation), but rapid pacing for implantation was used less frequently (37.1% versus 98.2%, p<0.001). More-than-mild aortic regurgitation at postoperative echocardiography was 12.0% for the ACURATE group and 3.1% for the SAPIEN group, p≤0.001). More-than-mild aortic regurgitation in the ACURATE group differed amongst the centres with 6.0% (3/50) in centre A, 34.1% (29/85) in centre B and 3.4% (6/181) in centre C. Patients in the ACURATE group less frequently had pacemaker implantation compared to the SAPIEN 3 group (11.9% versus 18.5%, p=0.020), 30-day mortality was 4.6% versus 2.1%, respectively, p=0.134, and one-year survival was 83.1% (95% CI: 77.6-87.4) versus 88.8% (95% CI: 84.0-92.2).

Conclusions: In this propensity score analysis, patients treated with the transapical ACURATE or transfemoral ACURATE *neo* prosthesis less frequently had pacemakers at 30 days but had more aortic regurgitation and lower one-year survival.

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Abbreviations

AR aortic regurgitation
PVL paravalvular leakage
TAVI transcatheter aortic valve implantation

Introduction

Numerous randomised controlled trials have been conducted to compare outcomes between surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI)[1]. With increasing use of TAVI[1-3], refined techniques and devices, it is now paramount to compare devices in randomised controlled trials to identify the best device for the individual patient.

To date, only a few randomised controlled trials are available. The CHOICE study randomised patients to the self-expanding CoreValve® prosthesis (Medtronic, Minneapolis, MN, USA) versus the SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) and found statistically lower device success and higher pacemaker rates in the self-expanding group[4]. The recently published REPRISE III study randomised patients to the mechanically expandable Lotus™ prosthesis (Boston Scientific, Marlborough, MA, USA) and to a self-expanding prosthesis and found non-inferiority to the CoreValve® and CoreValve® Evolut™ R (Medtronic) prostheses for the primary safety endpoint and superiority for the primary efficacy endpoint[5].

To the best of our knowledge, no randomised data are available comparing the transapical ACURATE TA, the transfemoral ACURATE *neo*™ (Symetis, a Boston Scientific company, Ecublens, Switzerland), and the SAPIEN 3 (Edwards Lifesciences) prostheses. In the absence of randomised data, we aimed to provide further clinical evidence using a propensity-matched comparison of the transapical ACURATE TA and the transfemoral ACURATE *neo* with the SAPIEN 3 prosthesis.

Methods

STUDY DESIGN AND PATIENT SELECTION

Retrospective data collection of patients treated for aortic stenosis was conducted at three centres in Germany from 2012 to 2016. Treatment and patient follow-up were according to the standard of care at the respective hospitals. No core laboratory or clinical events committee was used; however, all clinical events were categorised by one study physician and the degree of calcification was assessed by two study physicians.

The self-expanding transapical ACURATE TA and transfemoral ACURATE *neo* systems, as well as the transfemoral and transapical balloon-expandable SAPIEN 3 system, have been described previously[6-8]. Endpoints including mortality are classified according to VARC-2 criteria.

STATISTICAL ANALYSIS

The unpaired patient population included all patients in whom an implant was attempted. **Figure 1** shows the variables used for the propensity-score analysis. The estimation was performed with logistic regression analysis. The variables centre and access route were exactly matched. Calculated score estimates with callipers of 0.2 (x standard deviation of the logit of the estimated propensity score) were used for matching. The algorithm was the greedy nearest neighbour matching method.

The follow-up time was calculated from procedure date to the last available subject information. Categorical variables are expressed as numbers and percentages of the total and continuous variables as mean±SD. Confidence intervals were calculated when appropriate. The unmatched groups were compared using Pearson's chi-square and one-way ANOVA. Matched groups were compared using the Wilcoxon and McNemar tests and Kaplan-Meier survival analysis using the log-rank test. The hazard ratio was calculated with Cox logistic regression. All statistical analyses were performed using SPSS, Version 23 (IBM Corp., Armonk, NY, USA).

Results

We retrospectively collected data at three German centres from the date of the first use of the transapical ACURATE and transfemoral ACURATE *neo* prostheses at the respective centres until 2016. Centre and access route details of the unmatched population are provided in **Table 1**, which also includes other transcatheter heart valves implanted during the same time period. Of the 1,306 patients in the unmatched cohort, 658 patients remained after propensity matching **(Figure 1)**. There was an exact match for centre (57 patients in each group in centre A, 90 in centre B, and 182 in centre C) and access route (250 transfemoral and 79 transapical patients in each group).

In the unmatched cohort, the ACURATE/ACURATE *neo* group had more females, smaller annuli, lower gradients, less cusp and annular calcification, more left ventricular outflow tract (LVOT)

Table 1. Distribution of the unmatched patient cohort.

	Enrolment period	ACURATE *neo*		SAPIEN 3		TF	TA	Total	Other THVs
Centre A	2014-2016	142		82		174	50	224	28 CoreValve 20 CoreValve Evolut R
		TF 108	TA 34	TF 66	TA 16				
Centre B	2012-2016	186		277		361	102	463	66 CoreValve
		TF 102	TA 84	TF 259	TA 18				
Centre C	2012-2016	263		356		374	245	619	62 CoreValve
		TF 154	TA 109	TF 220	TA 136				
Total		591		715		909	397	1,306	176
		TF 364	TA 227	TF 545	TA 170				

TA: transapical; TF: transfemoral; THV: transcatheter heart valve

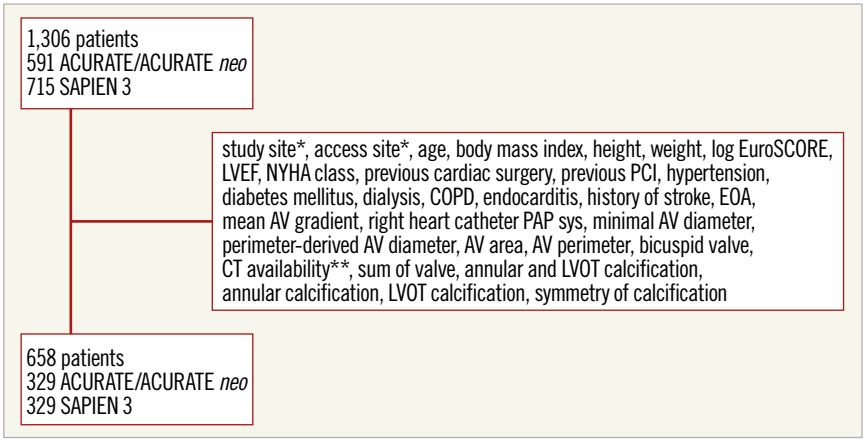

Figure 1. *Propensity matching. *exact match. ** only patients with available CT scans were included in the analysis. AV: aortic valve; COPD: chronic obstructive pulmonary disease; CT: computed tomography; EOA: effective orifice area; LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow tract; PAP sys: systolic pulmonary artery pressure; PCI: percutaneous coronary intervention*

calcification and more symmetric calcification compared to the SAPIEN 3 group **(Supplementary Table 1, Supplementary Table 2)**. In the matched cohort, baseline characteristics were similar between the groups. Mean patient age was 81 years and the logistic EuroSCORE I was 19%. More than three quarters of the patients had moderate to severe cusp calcification respective to none to mild LVOT calcification **(Table 2, Table 3)**. The baseline and valve characteristics per centre are provided in **Supplementary Table 3** and **Supplementary Table 4**.

Nearly all patients (96%) received general anaesthesia. Patients treated with the ACURATE *neo* had significantly more predilatation performed (97.6% versus 52.1%, p<0.0001), less rapid pacing for implantation (37.1% versus 98.2%, p<0.001) and more post-dilatation (40.4% versus 11.6%, p<0.001). There was a significant difference in the rate of post-dilatation amongst the three centres (7.0%, 18.3% and 35.7%, p<0.001). There were no differences in technical success and procedural complications between the groups except for TAVI-in-TAVI, which was more frequent in the ACURATE group (n=6, 1.8% versus 0%, p=0.031) **(Table 4, Supplementary Table 5)**.

All six TAVI-in-TAVI patients were treated via transfemoral access. Cusp calcification was mild in one patient, moderate in three, and severe in two; annulus calcification was absent in one patient, mild in four and severe in one. Calcification of the LVOT was absent in all cases. Rapid pacing for implantation was used in three cases and post-dilatation in two. Device malpositioning occurred in two, one of which resulted in a device embolisation. All TAVI-in-TAVI patients were alive at follow-up. Postoperative echocardiographic data are available for four patients; in all, aortic regurgitation was absent.

The average hospital stay was 18±12 days (range 2-94) for the ACURATE group and 17±10 days for the SAPIEN 3 group (range 4-71 days), p=0.831.

For 20 patients in centre A (8.9%), 23 patients in centre B (5.0%) and 27 patients in centre C (4.4%) no post-procedural gradients were documented. Postoperative echocardiography revealed a lower mean gradient in the ACURATE group (8.6±4.6 mmHg versus 10.9±4.2 mmHg, p<0.001) and a higher

Table 2. Baseline characteristics of the matched study cohort.

	ACURATE/ ACURATE *neo*	SAPIEN 3
Age, years	81±5	81±6
Male, n, (%)	145 (44.1%)	146 (44.4%)
Body mass index	28.7±5.5	28.4±5.8
Log. EuroSCORE I, %	18.8±14.7	19.1±13.6
LVEF, %	53±13	54±15
LVEF		
≤35%	31 (9.4)	34 (10.3)
36-45%	77 (23.4)	72 (21.9)
>45%	221 (67.2)	223 (67.8)
NYHA		
Class I	13 (4.0)	12 (3.6)
Class II	56 (17.0)	60 (18.2)
Class III	218 (66.3)	216 (65.7)
Class IV	42 (12.8)	41 (12.5)
Hypertension	307 (93.3)	306 (93.0)
Previous cardiac surgery	49 (14.9)	48 (14.6)
Previous PCI	108 (32.8)	111 (33.7)
Diabetes mellitus	121 (36.8)	115 (35.0)
Previous stroke	46 (14.0)	48 (14.6)
COPD	52 (15.8)	49 (14.9)
Preop dialysis	9 (2.7)	9 (2.7)
Endocarditis	0	1 (0.3)
Atrial fibrillation	125 (38.0)	127 (38.7)

Data are displayed as mean±SD or n (%). COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention

Table 3. Baseline valve characteristics of the matched study cohort.

	ACURATE/ ACURATE *neo*	SAPIEN 3
Echocardiographic assessments		
EOA	0.68±0.18	0.67±0.17
Mean gradient, mmHg	44±15	45±14
CT assessments		
Diameter min, mm	21±2	21±3
Area, mm²	458±68	459±93
Perimeter, mm	77.3±5.9	77.3±7.9
Bicuspid	2 (0.6)	2 (0.6)
Cusp calcification		
None	4 (1.2)	5 (1.5)
Mild	68 (20.7)	70 (21.3)
Moderate	125 (38.0)	116 (35.3)
Severe	132 (40.1)	138 (41.9)
Annular calcification		
None	37 (11.2)	49 (14.9)
Mild	125 (38.0)	123 (37.4)
Moderate	105 (31.9)	97 (29.5)
Severe	62 (18.8)	60 (18.2)
LVOT calcification		
None	222 (67.5)	231 (70.2)
Mild	29 (8.8)	32 (9.7)
Moderate	30 (9.1)	25 (7.6)
Severe	48 (14.6)	41 (12.5)
Symmetric calcification	218 (66.3)	213 (64.7)

Data are displayed as mean±SD or n (%). EOA: effective orifice area; LVOT: left ventricular outflow tract

Table 4. Procedural data of the matched study cohort.

	ACURATE/ ACURATE *neo*	SAPIEN 3	*p*-value
Access route			
Transfemoral	249 (75.7)	245 (74.5)	0.219
Transapical	80 (24.3)	84 (25.5)	
Prosthesis diameter, mm	25±2	25±2	0.915
General anaesthesia	316 (96.0)	317 (96.4)	1.000
Predilatation	321 (97.6)	171 (52.1)	<0.001
Rapid pacing for implantation	122 (37.1)	322 (98.2)	<0.001
Post-dilatation	133 (40.4)	38 (11.6)	<0.001
Technical success*	324 (98.5)	323 (98.2)	1.000
Procedure time, min	62±24	59±26	0.002
Fluoroscopy time, min	9.2±4.4	8.5±4.9	0.049
Amount of contrast, ml	128±54	106±43	0.001
Procedural complications			
Conversion to HLM	3 (0.9)	5 (1.5)	0.727
Conversion to surgery	3 (0.9)	3 (0.9)	1.000
TAVI-in-TAVI	6 (1.8)	0	0.031
Device embolisation	3 (0.9)	1 (0.3)	0.625
Rhythm disturbances			
Atrial fibrillation	5 (1.5)	9 (2.7)	0.219
Others	1 (0.3)	5 (1.5)	
Device malpositioning	3 (0.9)	1 (0.3)	0.625
Coronary occlusion	1 (0.3)	0	1.000
Aortic dissection	2 (0.6)	0	0.500
Annular rupture	1 (0.3)	3 (0.9)	0.625
Ventricular perforation	4 (1.2)	1 (0.3)	0.375
Pericardial tamponade	8 (2.4)	5 (1.5)	0.581

Data are displayed as mean±SD or n (%). * Valve implanted via the planned route and in the intended position. HLM: heart-lung machine

aortic regurgitation rate (more-than-mild aortic regurgitation in 12.0% versus 3.1%, p<0.001). Therefore, more-than-mild aortic regurgitation differed significantly (p<0.001) amongst the centres with 6.0% (3/50) in centre A, 34.1% (29/85) in centre B and 3.4% (6/181) in centre C **(Supplementary Table 6)**.

The ACURATE group had a numerically higher early safety composite outcome (14.0% versus 9.1%, p=0.073) and significantly fewer pacemaker implants at 30 days (11.9% versus 18.5%, p=0.018) compared to the SAPIEN 3 group. Device success (82.4% versus 91.5%, p=0.001) and clinical efficacy endpoints (80.9% versus 91.2%, p<0.001) favoured the SAPIEN 3 group significantly. Stroke rate (2.4% versus 0.9%, p=0.13) and 30-day mortality (4.6% versus 2.1%, p=0.08) did not differ between the groups. Furthermore, there was a large variation in 30-day mortality, ranging from 2.2% to 8.8%, p=0.06, per centre in the ACURATE/ACURATE *neo* group **(Table 5)**. Patients with more-than-mild aortic regurgitation had a similar 30-day mortality as compared to patients without (4.8% versus 3.1%, p=0.44). VARC-2 criteria per centre are shown in **Supplementary Table 7**.

Mean follow-up was 319±291 days for the ACURATE group and 367±296 days for the SAPIEN 3 group; the median follow-up time was 364 versus 390 days, respectively. At one year (365 days), survival was 83.1% (95% CI: 77.6-87.4) and 88.8% (95% CI: 84.0-92.2), respectively **(Figure 2)**. Considering the full follow-up time, Cox regression analysis revealed a hazard ratio of 1.89 (95% CI: 1.25-2.86) for the estimated linear mortality rate in the ACURATE group (p=0.02). There was no overlap of confidence intervals for the estimated linear mortality rate of the matched SAPIEN 3 group of 11.34% (95% CI: 8.18-15.71) and ACURATE group of 20.59% (95% CI: 15.88-26.69). There was a variation amongst the centres with a hazard ratio of 4.5 (95% CI: 1.24-16.34) for centre A, a hazard ratio of 3.0 (95% CI: 1.22-7.35) for centre B, and a hazard ratio of 1.15 (95% CI: 0.68-1.95) for centre C, where the acceptable severity of relevant aortic regurgitation appears to be less than in the other two centres.

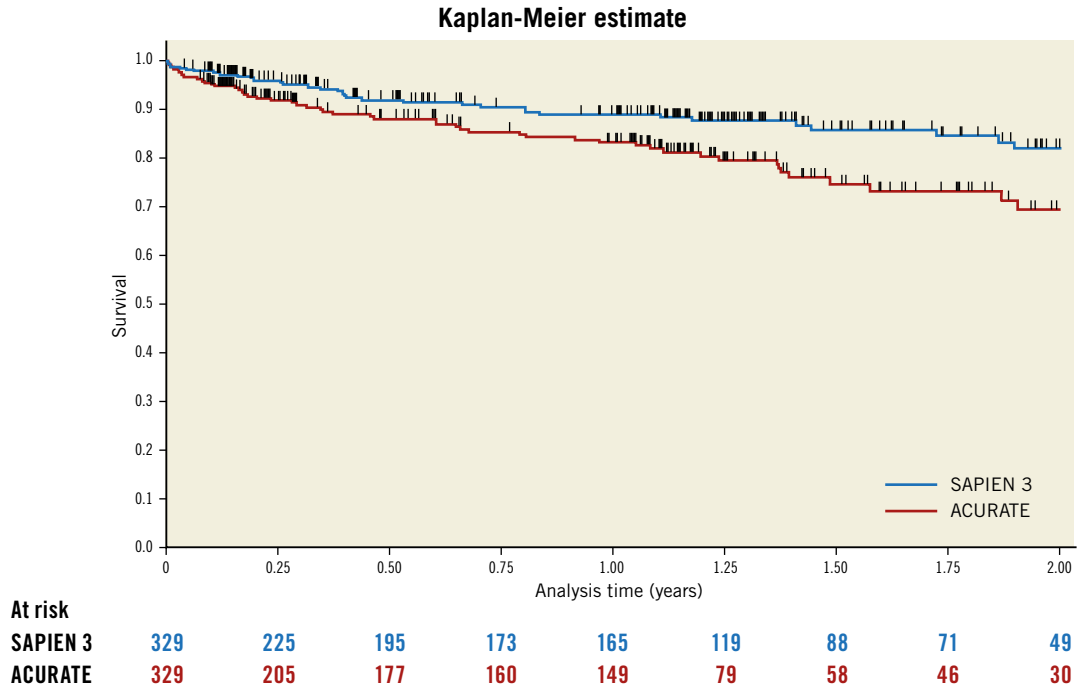

Figure 2. *Survival of SAPIEN 3 versus ACURATE patients. Mean follow-up was 330 days.*

Table 5. Clinical outcomes at 30 days post procedure of the matched study cohort.

		ACURATE/ ACURATE *neo*	SAPIEN 3	*p*-value
Early safety composite*		46 (14.0)	30 (9.1)	0.073
Failed clinical efficacy**		63 (19.1)	29 (8.8)	<0.001
Device success#		271 (82.4)	329 (91.5)	0.001
Prosthesis dysfunction¶		40 (12.2)	19 (5.8)	0.005
Mortality		15 (4.6)	7 (2.1)	0.134
Centre 1		5 (8.8)	1 (1.8)	0.093
Centre 2		6 (6.7)	1 (1.1)	0.054
Centre 3		4 (2.2)	5 (2.7)	0.736
Transfemoral		12 (4.8)	6 (2.4)	0.160
Transapical		3 (3.8)	1 (1.3)	0.288
Cardiovascular mortality		11 (3.3)	4 (1.2)	0.118
Periprocedural MI <72 hrs		1 (0.3)	0	
New AV block III		28 (8.5)	42 (12.8)	0.104
New pacemaker§		39 (11.9)	61 (18.5)	0.020
New dialysis at discharge		0	2 (0.6)	0.500
Stroke		6 (2.4)	3 (0.9)	0.314
Bleeding	Life-threatening	19 (5.8)	10 (3.0)	0.137
	Major	10 (3.0)	8 (2.4)	0.815

Data are displayed as n (%). * Early safety is a composite of all-cause mortality, all stroke, life-threatening bleeding, acute kidney injury stage 2 or 3, coronary artery obstruction requiring intervention, major vascular complication, valve-related dysfunction requiring repeat procedure. ** Clinical efficacy is a composite of 30-day mortality, stroke, hospitalisation for valve-related symptoms or congestive heart failure, mean aortic valve gradient ≥20 mmHg, prosthetic valve regurgitation >2. # Device success is a composite of absence of procedural mortality, correct positioning of a single valve, mean aortic valve gradient <20 mmHg and prosthetic valve regurgitation <2. ¶ Prosthesis dysfunction is a composite of mean gradient >20 mmHg and prosthetic regurgitation ≥2. § In-hospital.

Survival curves per centre and per access route are provided in **Supplementary Figure 1** and **Supplementary Figure 2**. If only patients without post-interventional aortic regurgitation are analysed (n=166), the hazard ratio of one-year mortality is 1.6. The survival rate was 88.8% (95% CI: 83.96-92.24) for the SAPIEN group and 83.14% (95% CI: 77.60-87.42) for the ACURATE group. For transfemoral access, the estimated linear mortality rate was 10.39% (95% CI: 7.08-15.26) in the SAPIEN group and 18.80% (95% CI: 13.30-26.59) in the ACURATE group. For transapical access, the rates were 14.84% (95% CI: 7.98-27.58) in the SAPIEN group and 23.43% (95% CI: 15.83-34.67) in the ACURATE group.

Discussion

The unmatched population showed the typical distribution amongst ACURATE and SAPIEN 3 prostheses, with the ACURATE more frequently used in smaller annuli and hence in more females. This is attributed to the differences in valve size with the SAPIEN 3 offering larger prostheses; however, it may also be attributed to the supra-annular design of the ACURATE *neo* prosthesis making this valve particularly attractive in small annuli to avoid patient-prosthesis mismatch[9]. Furthermore, the tendency rather to use self-expanding prostheses in patients with less cusp and annular calcification or in patients with more LVOT calcification[6] is reflected in the unmatched cohort.

Nearly all procedures were performed under general anaesthesia, according to the standard of care at the respective centres. We believe that there is no harm in conducting the procedure under general anaesthesia, even though a recent state-of-the-art paper

states that – amongst other parameters – transfemoral implants under local anaesthesia may reduce invasiveness and costs[2]. Due to the lower radial strength of the ACURATE prostheses, more predilatation and post-dilatation were performed. In the SAVI-TF registry, post-dilatation after ACURATE *neo* implantation did not negatively affect clinical outcomes[10].

The low pacemaker rate of the ACURATE prostheses, which is even lower than for the balloon-expandable SAPIEN 3 prosthesis, is not surprising and has already been reported in other propensity-matched comparisons[7,9]. However, what is striking in our series is the high rate of more-than-mild aortic regurgitation in the ACURATE group. It is intuitive that the lower radial strength of the ACURATE prosthesis may lead to a higher risk of regurgitation and multicentre propensity-matched comparisons have reported higher paravalvular leakage (PVL) rates for the ACURATE *neo* as compared to the SAPIEN 3 (4.8% versus 1.8%, p=0.01; in small annuli 4.5% versus 3.6%, p=ns)[7,9]. However, the more-than-mild PVL rates reported there and those observed in the 2,000 patients of the SAVI TA and TF registries (1.9% and 4.1%)[11,12] were substantially lower than the 12% observed in our series; a recent state-of-the-art paper even reported a cumulative rate of only 1.7% for the ACURATE prosthesis[2].

When interpreting the outcomes, the following points have to be considered. a) The ACURATE/ACURATE *neo* group includes the first patient implanted with this device and hence includes not only the operator learning curve but also the learning curve on how best to use the device[10]. In contrast, users of the SAPIEN 3 were able to implement the knowledge already gained with the precursor device, the SAPIEN XT. b) No core laboratory was used. Sizing issues did in fact lead to a wrong prosthesis selection. In another propensity-matched comparison, there was a significant difference in sizing between the ACURATE *neo* and the SAPIEN 3. Undersizing was observed in 5.9% of ACURATE *neo* versus 0% of SAPIEN 3 procedures, accurate sizing (within the size range) was observed in 85.9% versus 77.2%, and oversizing was observed in 8.2% versus 22.8%, p<0.001[9]. A similar trend was observed in our series. c) Assessing PVL in supra-annular prostheses is not easy; there might have been an overinterpretation of outcomes in the absence of an experienced core laboratory[13,14].

There was a non-significant trend towards higher one-year mortality in the ACURATE/ACURATE *neo* group compared to the SAPIEN 3 group (16.8% versus 11.2%) and a higher estimated linear mortality rate. When excluding patients with post-interventional aortic regurgitation ≥1, an elevated hazard ratio for one-year mortality persists irrespective of access route for the ACURATE group, suggesting a harmful effect on survival exceeding the effect of valve type-related aortic regurgitation. In contrast, a propensity-matched comparison comparing the ACURATE *neo* with the SAPIEN 3 in patients with small annuli showed a non-significant trend towards lower mortality in the ACURATE *neo* group (8.3% versus 13.3%, p=0.233)[9]. Particularly in the transfemoral arm of this analysis, the one-year mortality for the ACURATE *neo* (16.9%) was higher than that observed in the propensity matching described above, higher than for the 1,000 patients of the SAVI-TF registry[10] and higher than in a single-centre analysis[6], all with single-digit one-year mortality. In contrast, the one-year mortality of the SAPIEN 3 (11.2%) was similar to other reports, e.g., 12.6% in the SOURCE 3 registry (including 87.1% transfemoral patients) and 14.4% in high-risk patients of the PARTNER trial (including 84% transfemoral patients)[8,15]. This negative trend was visible irrespective of access route, although smaller sample sizes prevented statistical significance.

These outcomes might in part be explained by the substantial differences amongst the centres. In relation to procedural techniques, centre C post-dilated more frequently than centres A and B due to a policy of "zero tolerance of more-than-mild paravalvular leak". This "zero tolerance policy" is probably one of the reasons for the better survival in the ACURATE group in this centre as compared to the other centres.

Furthermore, in centre C, the regurgitation rate was in the expected range and no difference between the prostheses was observed (3.4% for ACURATE vs 1.1% for SAPIEN 3), whereas it was exorbitantly higher in centre B. Specifically, more-than-mild regurgitation rates in ACURATE patients were 6.0%, 34.1%, and 3.4% in centres A, B and C, respectively.

Centre C, with the lowest moderate or severe AR rate and best one-year survival (87.4% [95% CI: 79.6-92.3] compared to 75.4% [95% CI: 60.4-85.3] and 81.3% [95% CI: 70.1-88.6]) is also the centre with the largest series of implants. In contrast, the other two centres had either small patient numbers (centre A) or several different operators (centre B, which has operators from six different hospitals). Similarly, and in alignment with other studies, a recent publication of the compulsory German Quality Assurance Registry on Aortic Valve Replacement[3] of more than 10,000 transfemoral implants conducted in 2014 in Germany showed that there is a continuous association of lower in-hospital mortality (and risk-adjusted mortality) with increasing TAVI volumes (p<0.001). Furthermore, procedure times and hospital stays were lower in more experienced centres[3].

Limitations

Common in propensity-matched analysis is the possibility of unknown confounders. However, a strength of this study is the thorough propensity score matching, taking all known confounders into consideration. On the other hand, that also restricts the interpretation of results to this specific patient population. Echocardiographic and computed tomography core laboratory data would have been paramount for adequate comparison of aortic regurgitation amongst centres and to identify the root cause(s) of the unexpectedly high aortic regurgitation rate at one centre, e.g., sizing issues. Additionally, the ACURATE TA is outdated as the ACURATE *neo* TA system gained CE certification in June 2017[16]. Data from the SCOPE I trial (NCT03011346), randomising patients to the ACURATE *neo* versus the SAPIEN 3 are expected to provide further clarity.

Conclusions

Treatment with the ACURATE or ACURATE *neo* resulted in fewer pacemaker implants and lower mean gradients compared to the SAPIEN 3 but comes with the price of more aortic regurgitation and possibly lower one-year survival. Large centre differences suggest that it is paramount to conduct post-dilatation for residual more-than-mild aortic regurgitation and to conduct TAVI in high-volume centres with experienced operators.

Impact on daily practice

TAVI has become an established practice but should still be used only in experienced hands. The ACURATE *neo* appears to be particularly vulnerable to paravalvular leakage. Therefore, undersizing should be avoided. Furthermore, meticulous post-dilatation in case of residual paravalvular regurgitation appears to be mandatory to achieve survival rates comparable to usage of the SAPIEN 3 prosthesis.

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Conflict of interest statement

K. Hamm reports non-financial support from Boston Scientific, from null, during the conduct of the study. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Figure 1. One-year survival per centre.

Supplementary Figure 2. Two-year survival per access route.

Supplementary Table 1. Baseline patient characteristics of the unmatched cohort.

Supplementary Table 2. Baseline valve characteristics of the unmatched cohort.

Supplementary Table 3. Baseline patient characteristics of the matched cohort per centre.

Supplementary Table 4. Baseline valve characteristics of the matched cohort per centre.

Supplementary Table 5. Procedural data of the matched cohort per centre.

Supplementary Table 6. Postoperative echocardiographic assessment of the matched cohort per centre.

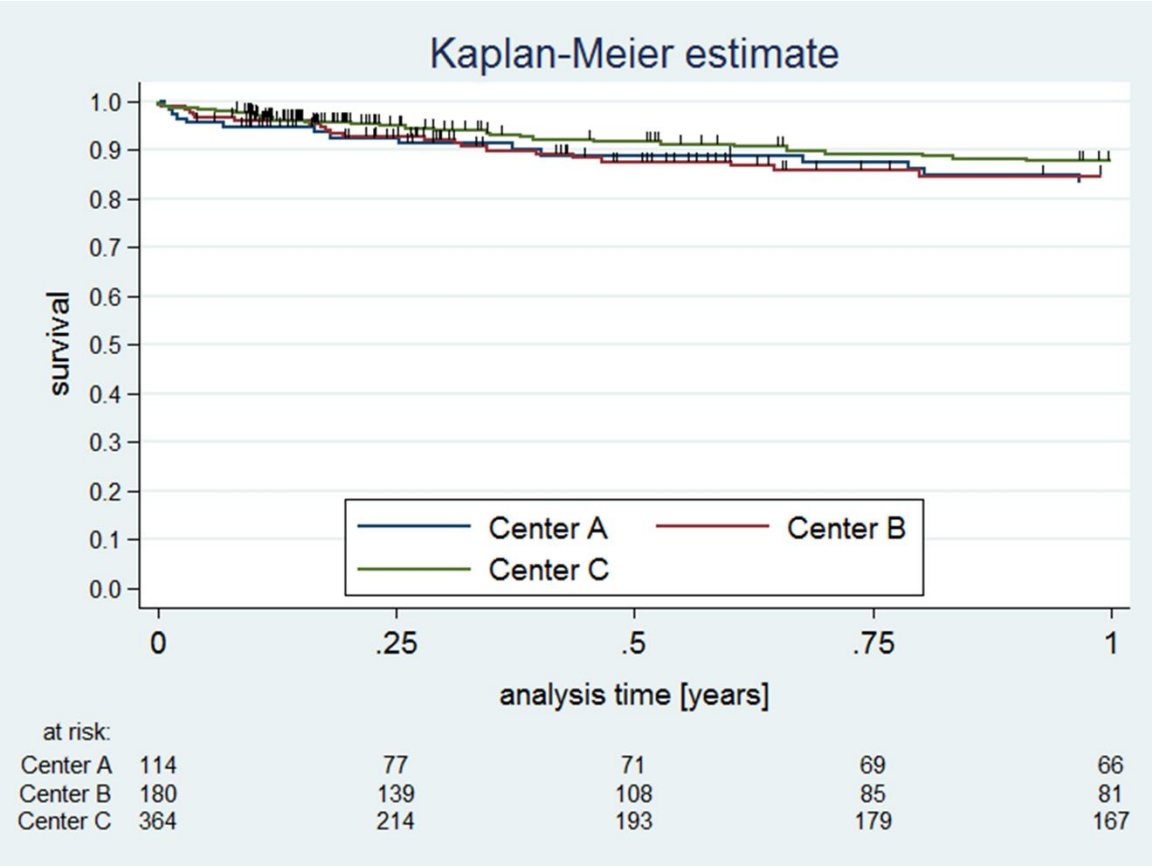
Supplementary Table 7. VARC-2 criteria of the matched cohort per centre.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-18-01120

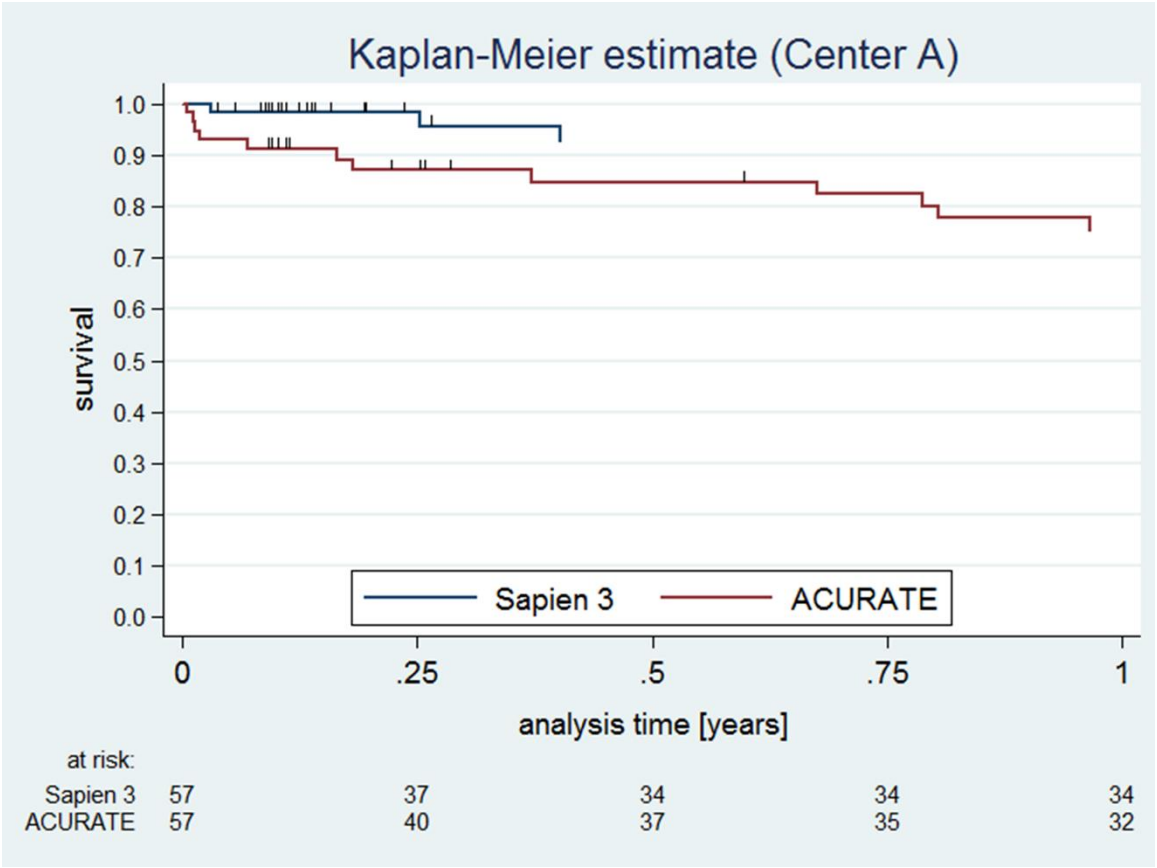
Supplementary data

Supplementary Figure 1. One-year survival per centre.

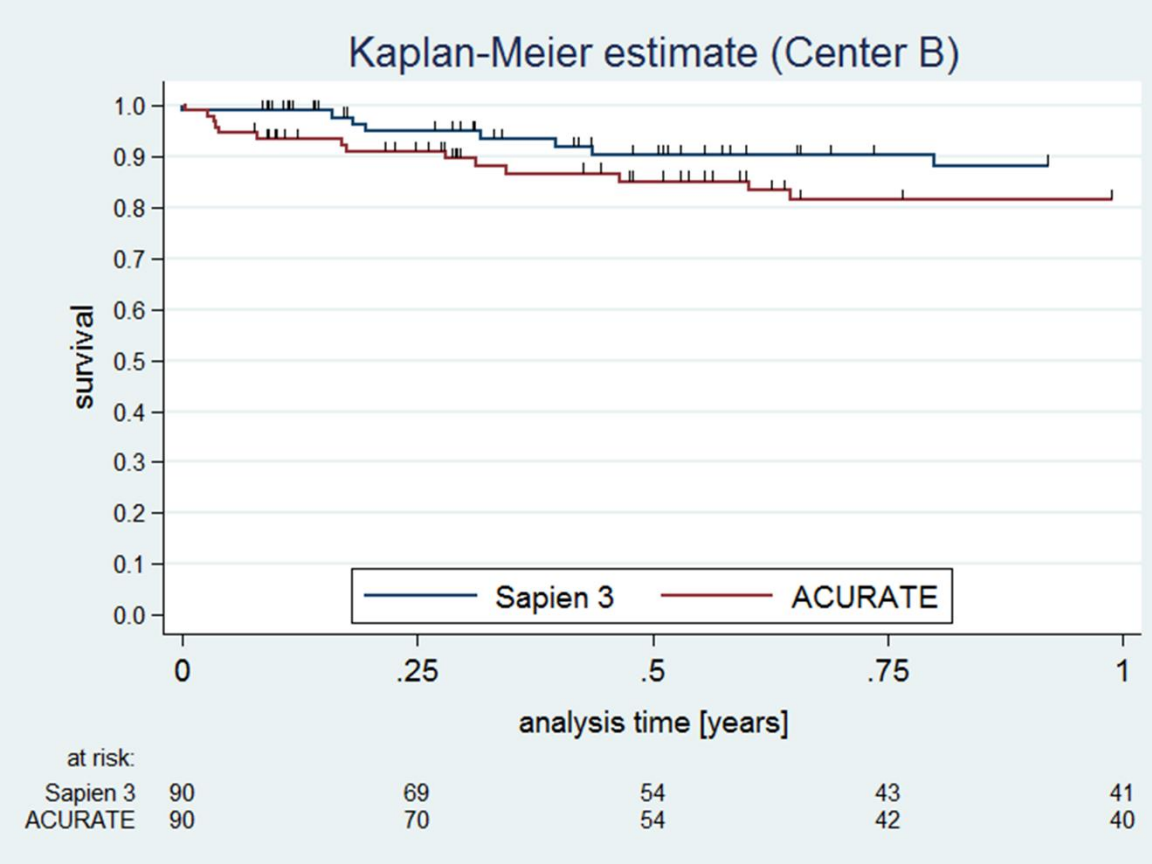
A. Mean follow-up was 319±291 days for ACURATE and 367±296 days for SAPIEN 3.



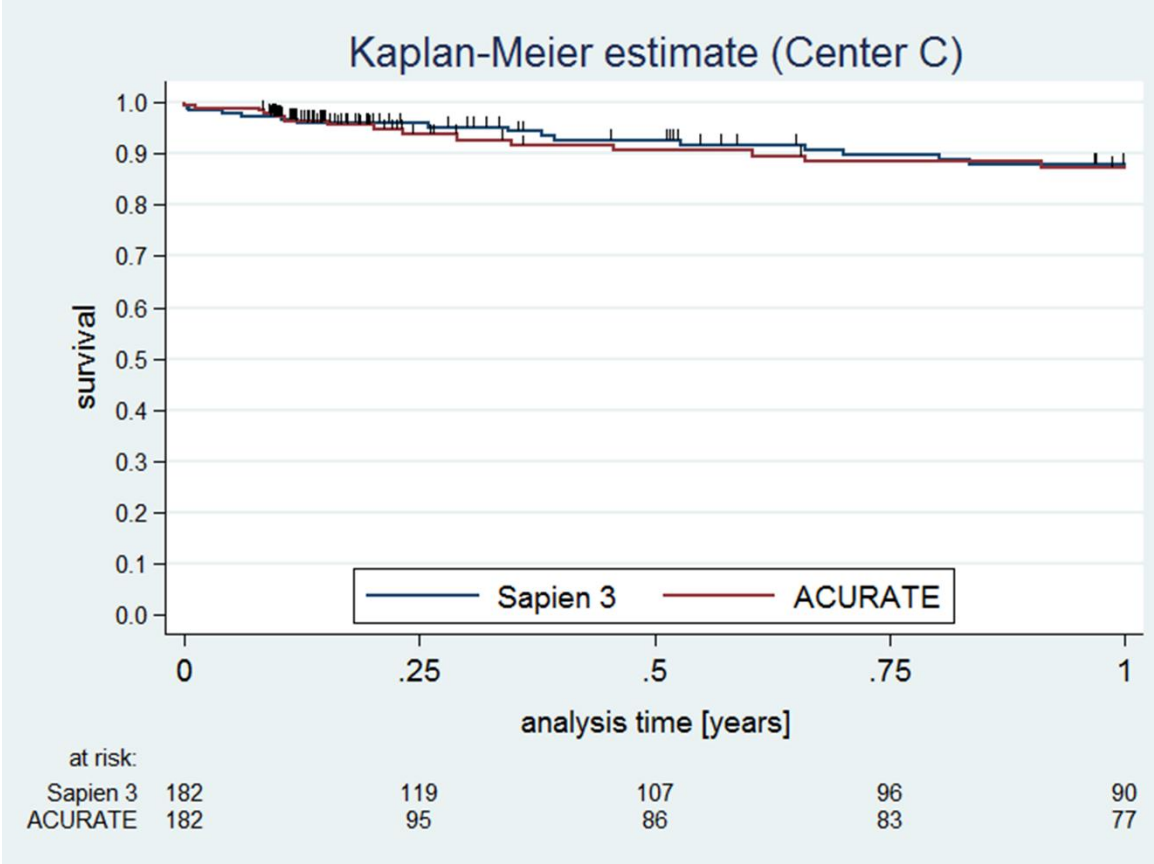
B. One-year survival was 75.4% (95% CI: 60.4-85.3) for ACURATE and 92.9% (95% CI: 79.1-97.7) for SAPIEN 3.



C. One-year survival was 81.3% (95% CI: 70.1-88.6) for ACURATE and 88.1% (95% CI: 77.3-94.0) for SAPIEN 3.



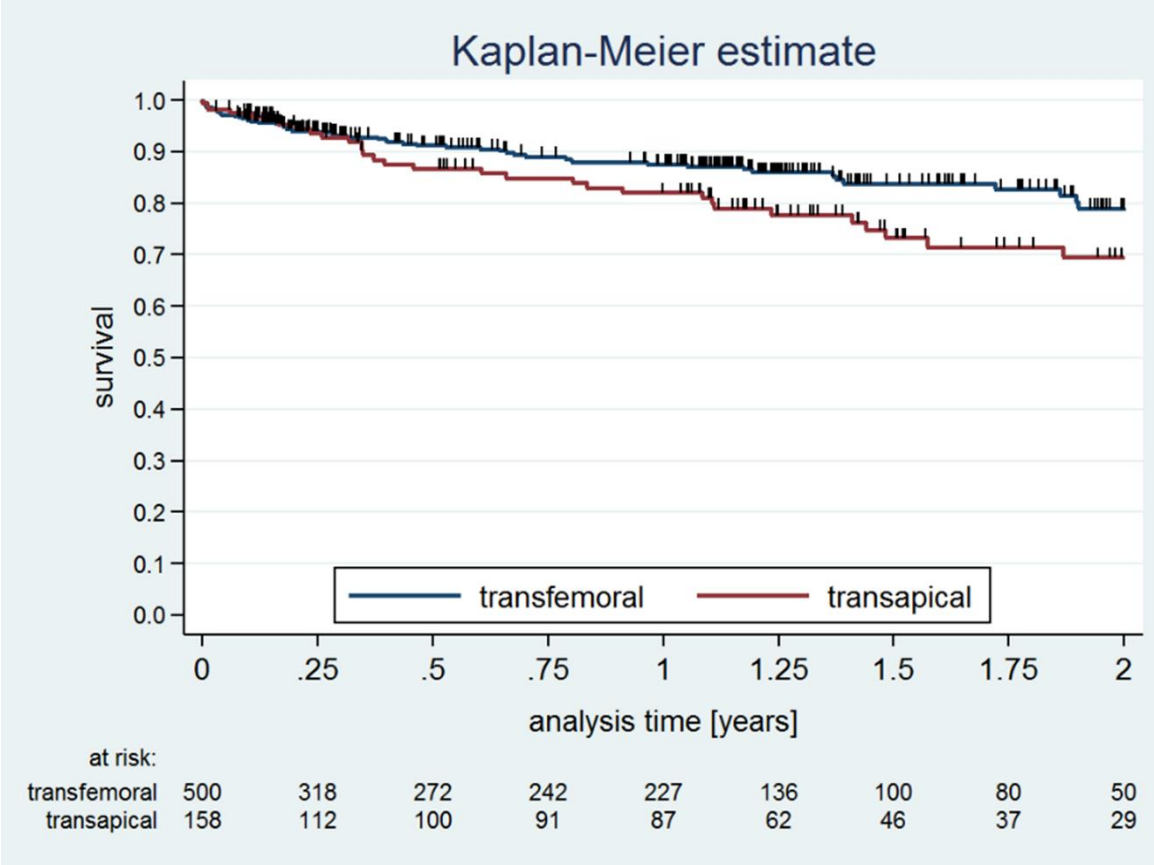
D. One-year survival was 87.4% (95% CI: 79.6-92.3) for ACURATE and 88.0% (95% CI: 80.8-92.5) for SAPIEN 3.



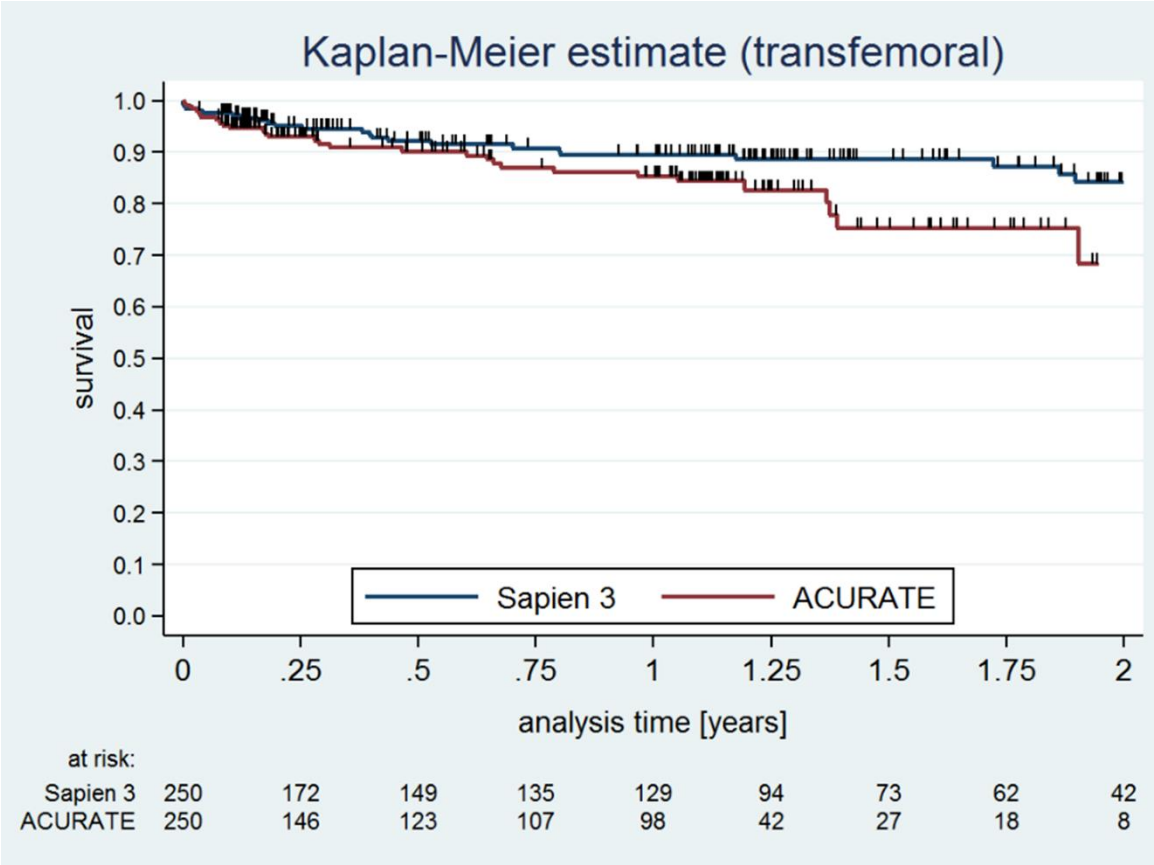
Supplementary Figure 2. Two-year survival per access route.

Overall survival per access route (A) and for transfemoral (B) and transapical (C) access. Mean follow-up was 319±291 days for ACURATE and 367±296 days for SAPIEN 3.

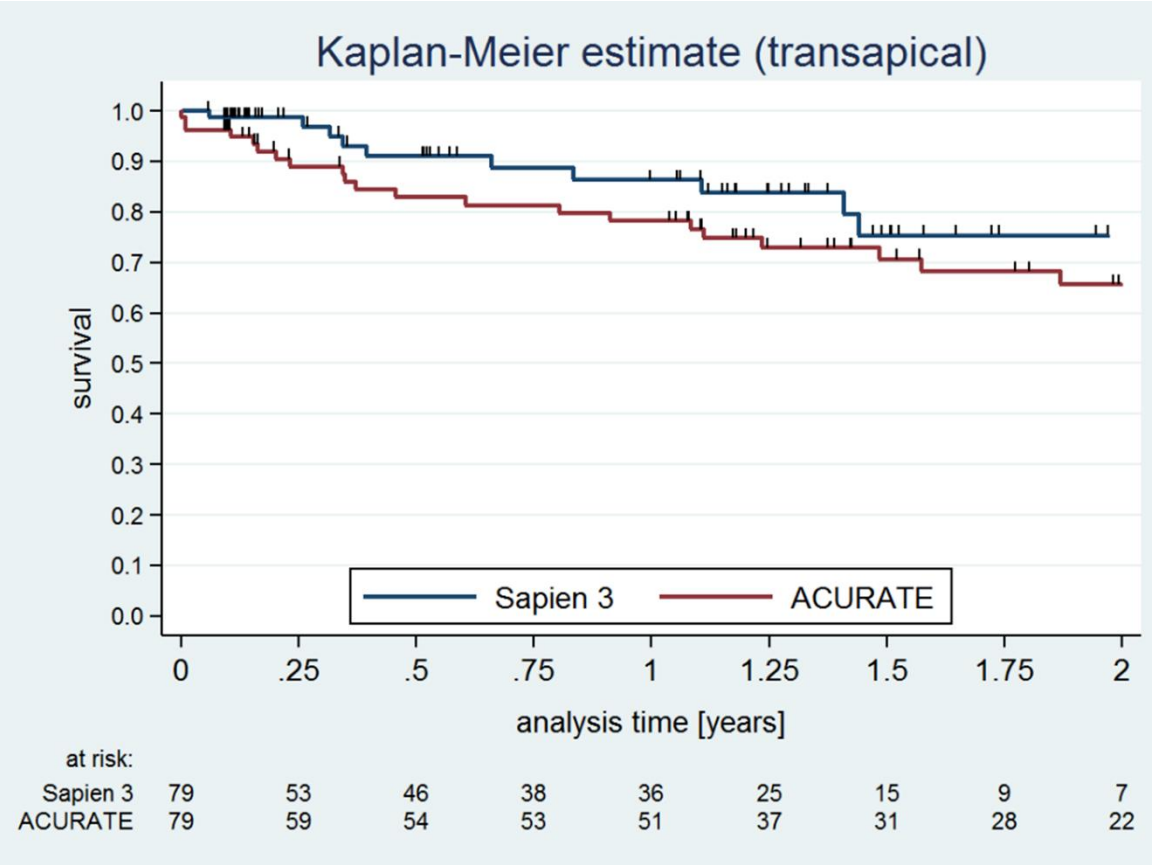
A)



B)


Kaplan-Meier estimate (transfemoral)
survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Sapien 3
ACURATE
0
.25
.5
.75
1
1.25
1.5
1.75
2
analysis time [years]
at risk:
Sapien 3 250 172 149 135 129 94 73 62 42
ACURATE 250 146 123 107 98 42 27 18 8

C)


Kaplan-Meier estimate (transapical)
survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Sapien 3
ACURATE
0
.25
.5
.75
1
1.25
1.5
1.75
2
analysis time [years]
at risk:
Sapien 3 79 53 46 38 36 25 15 9 7
ACURATE 79 59 54 53 51 37 31 28 22

Supplementary Table 1. Baseline patient characteristics of the unmatched cohort.

	ACURATE/ACURATE *neo* N=591	SAPIEN 3 N=715	*p*-value
Age, years	81.0±4.8	80.4±5.7	**0.045**
Male	243 (41.1%)	398 (55.7%)	**<0.001**
Body mass index	28.4±5.3	28.7±5.7	0.356
Log EuroSCORE I, %	18.5±14.8	20.3±14.0	**0.025**
LVEF, %	53.0±13.4	51.3±15.3	**0.035**
LVEF ≤35%	66 (11.2)	105 (14.7)	0.111
36-45%	135 (22.8)	172 (24.1)	
>45%	390 (66.0)	438 (61.3)	
NYHA Class I	16 (2.7)	25 (3.5)	0.740
Class II	97 (16.4)	126 (17.6)	
Class III	407 (68.9)	475 (66.4)	
Class IV	71 (12.0)	89 (12.4)	
Hypertension	554 (93.7)	663 (92.7)	0.470
Previous cardiac surgery	86 (14.6)	99 (13.8)	0.621
Previous PCI	200 (33.8)	275 (38.5)	0.084
Diabetes mellitus	236 (39.9)	271 (37.9)	0.454
Previous stroke	92 (15.6)	102 (14.3)	0.510
COPD	94 (15.9)	138 (19.3)	0.110
Pre-op dialysis	25 (4.2)	15 (2.1)	**0.026**
Endocarditis	1 (0.2)	1 (0.1)	0.893
Atrial fibrillation	250 (42.3)	278 (38.9)	0.218

Data are displayed as mean±SD or n (%).

COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention

Supplementary Table 2. Baseline valve characteristics of the unmatched cohort.

	ACURATE/ ACURATE *neo*	SAPIEN 3	*p*-value
Echocardiographic assessments			
EOA	0.70±0.18	0.70±0.30	0.796
Mean gradient, mmHg	40.9±14.6	44.3±14.5	**<0.001**
CT assessments			
Diameter min, mm	21.2±2.0	22.2±2.6	**<0.001**
Area, mm²	452.7±76.4	485.5±99.5	**<0.001**
Perimeter in mm	76.6±6.1	79.3±8.2	**<0.001**
Bicuspid	2 (0.4)	6 (0.9)	0.386
Cusp calcification*			**<0.001**
None	17 (3.1)	12 (1.8)	
Mild	142 (26.0)	105 (15.7)	
Moderate	194 (35.5)	234 (35.0)	
Severe	193 (35.3)	317 (47.5)	
Annular calcification			**0.003**
None	84 (15.4)	102 (15.3)	
Mild	187 (34.2)	214 (32.0)	
Moderate	187 (34.2)	189 (28.3)	
Severe	88 (16.1)	163 (24.4)	
LVOT calcification			**<0.001**
None	374 (68.5)	474 (71.0)	
Mild	39 (7.1)	83 (12.4)	
Moderate	46 (8.4)	51 (7.6)	
Severe	87 (15.9)	60 (9.0)	
Symmetric calcification	387 (71.0)	364 (54.5)	**<0.001**

Data are displayed as mean±SD or n (%).

EOA: effective orifice area; LVOT: left ventricular outflow tract

Supplementary Table 3. Baseline patient characteristics of the matched cohort per centre.

	Centre A	Centre B	Centre C
Age, years	80±6	81±6	81±5
Body mass index	27.7±5.2	28.2±5.1	29.0±6.0
Log EuroSCORE I, %	15.6±12.9	21.5±17.0	18.8±12.7
LVEF, %	56±11	53±14	53±15
LVEF ≤35%	8 (7.0)	25 (13.9)	32 (8.8)
36-45%	17 (14.9)	30 (16.7)	102 (28.0)
>45%	89 (78.1)	125 (69.4)	230 (63.2)
NYHA Class I	0	3 (1.7)	22 (6.0)
Class II	9 (7.9)	24 (13.3)	83 (22.8)
Class III	81 (71.1)	130 (72.2)	223 (61.3)
Class IV	24 (21.1)	23 (12.8)	36 (9.9)
Hypertension	105 (92.1)	172 (95.6)	336 (92.3)
Previous cardiac surgery	25 (21.9)	22 (12.2)	50 (13.7)
Previous PCI	57 (50.0)	59 (32.8)	103 (28.3)
Diabetes mellitus	40 (35.1)	71 (39.4)	125 (34.3)
Previous stroke	18 (15.8)	27 (15.0)	49 (13.5)
COPD	36 (31.6)	32 (17.8)	33 (9.1)
Pre-op dialysis	6 (5.3)	3 (1.7)	9 (2.5)
Endocarditis	1 (0.9)	0	0
Atrial fibrillation	63 (55.8)	79 (43.9)	110 (30.2)

Data are displayed as mean±SD or n (%).

COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention

Supplementary Table 4. Baseline valve characteristics of the matched cohort per centre.

	Centre A	Centre B	Centre C
Echocardiographic assessments			
EOA	0.73±0.18	0.73±0.21	0.64±0.16
Mean gradient, mmHg	40.5±15.5	43.8±15.0	44.0±13.6
CT assessments			
Diameter min, mm	20.7±1.9	21.4±2.03	21.4±2.4
Area, mm^2	462±80	475±91	451±78
Perimeter in mm	77.6±6.6	78.9±7.7	76.6±6.6
Bicuspid	2 (1.8)	1 (0.6)	1 (0.3)
Cusp calcification			
None	1 (0.9)	0	8 (2.2)
Mild	18 (15.8)	25 (13.9)	95 (26.1)
Moderate	39 (34.2)	68 (37.8)	134 (36.8)
Severe	56 (49.1)	87 (48.3)	127 (34.9)
Annular calcification			
None	17 (14.9)	15 (8.3)	54 (14.8)
Mild	49 (43.0)	41 (22.8)	158 (43.4)
Moderate	35 (30.7)	62 (34.4)	105 (28.8)
Severe	13 (11.4)	62 (34.4)	47 (12.9)
LVOT calcification			
None	86 (75.4)	102 (56.7)	265 (72.8)
Mild	8 (7.0)	18 (10.0)	35 (9.6)
Moderate	11 (9.6)	16 (8.9)	28 (7.7)
Severe	9 (7.9)	44 (24.4)	36 (9.9)
Symmetric calcification	74 (64.9)	142 (78.9)	215 (59.1)

Data are displayed as mean±SD or n (%).

EOA: effective orifice area; LVOT: left ventricular outflow tract

Supplementary Table 5. Procedural data of the matched cohort per centre.

	Centre A		Centre B		Centre C	
	ACURATE/ ACURATE *neo*	**SAPIEN 3**	**ACURATE/ ACURATE *neo***	**SAPIEN 3**	**ACURATE/ ACURATE *neo***	**SAPIEN 3**
Access route						
Transfemoral	48 (84.2)	48 (84.2)	80 (88.9)	80 (88.9)	121 (66.5)	117 (64.3)
Transapical	9 (15.8)	9 (15.8)	10 (11.1)	10 (11.1)	61 (33.5)	65 (35.7)
Prosthesis diameter, mm	26±1	26±2	25±2	25±2	25±1	25±2
General anaesthesia	48 (84.2)	50 (87.7)	90 (100.0)	90 (100.0)	178 (97.8)	177 (97.3)
Predilatation	57 (100.0)	54 (94.7)	90 (100.0)	90 (100.0)	174 (95.6)	27 (14.9)
Rapid pacing for implantation	3 (5.3)	52 (91.2)	90 (100.0)	90 (100.0)	29 (15.9)	180 (99.4)
Post-dilatation	7 (12.3)	1 (1.8)	30 (33.3)	3 (3.3)	96 (52.7)	34 (18.7)
Technical success*	55 (96.5)	57 (100.0)	88 (97.8)	88 (97.8)	181 (99.5)	178 (97.8)
Procedure time, min	62±26	72±29	63±25	55±19	62±23	56±27
Fluoroscopy time, min	10.8±4.1	12.5±4.7	10.4±5.6	9.4±4.2	6.9±4.4	8.1±3.7
Amount of contrast, ml	129±61	124±48	153±57	112±37	116±45	97±42
Procedural complications						
Conversion to HLM	1 (1.8)	1 (1.8)	1 (1.1)	1 (1.1)	1 (0.5)	3 (1.6)
Conversion to surgery	1 (1.8)	0	2 (2.2)	2 (2.2)	1 (0.5)	3 (1.6)
TAVI-in-TAVI	1 (1.8)	0	1 (1.1)	0	4 (2.2)	0
Device embolisation	2 (3.5)	0	0	0	1 (0.5)	1 (0.5)
Rhythm disturbances						
Atrial fibrillation	0	3 (5.3)	3 (3.3)	1 (1.1)	2 (1.1)	5 (2.7)
Others	0	2 (3.5)	0	2 (2.2)	1 (0.5)	1 (0.5)
Device malpositioning	0	0	1 (1.1)	0	2 (1.1)	1 (0.5)
Coronary occlusion	0	0	1 (1.1)	0	0	0
Aortic dissection	1 (1.8)	0	0	0	1 (0.5)	0
Annular rupture	0	0	0	0	0	1 (0.5)
Pericardial tamponade	0	1 (1.8)	4 (4.4)	3 (3.3)	4 (2.2)	1 (0.5)
LV decompensation	4 (7.0)	2 (3.5)	9 (10.0)	5 (5.6)	1 (0.5)	2 (1.1)

Data are displayed as mean±SD or n (%). * Valve implanted via the planned route and in the intended position.

HLM: heart-lung machine; LV: left ventricle

Supplementary Table 6. Postoperative echocardiographic assessment of the matched cohort per centre.

	Centre A		Centre B		Centre C	
	ACURATE/ ACURATE *neo*	**SAPIEN 3**	**ACURATE/ ACURATE *neo***	**SAPIEN 3**	**ACURATE/ ACURATE *neo***	**SAPIEN 3**
Aortic regurgitation						
None	19 (38.0)	32 (58.2)	10 (11.8)	43 (49.4)	131 (72.4)	170 (93.9)
Mild	28 (56.0)	22 (40.0)	46 (54.1)	37 (42.5)	44 (24.3)	9 (5.0)
Moderate	3 (6.0)	1 (1.8)	29 (34.1)	7 (8.0)	5 (2.8)	2 (1.1)
Severe	0	0	0	0	1 (0.6)	0
Aortic mean gradient (mmHg)	7.1±3.8	8.8±3.1	8.5±4.1	11.6±4.5	9.1±5.0	11.1±4.2

Data are displayed as mean±SD or n (%).

Supplementary Table 7. VARC-2 criteria of the matched cohort per centre.

	Centre A		Centre B		Centre C	
	ACURATE/ ACURATE *neo*	**SAPIEN 3**	**ACURATE/ ACURATE *neo***	**SAPIEN 3**	**ACURATE/ ACURATE *neo***	**SAPIEN 3**
Pacemaker (30 days)	5 (8.8)	15 (26.3)	16 (17.8)	19 (21.1)	18 (9.9)	27 (14.8)
Stroke (30 days)	1 (1.8)	0 (0)	2 (2.2)	2 (2.2)	5 (2.7)	1 (0.5)
Life-threatening bleeding	2 (3.5)	1 (1.8)	7 (7.8)	5 (5.6)	10 (5.5)	4 (2.2)
Major bleeding	3 (5.3)	2 (3.5)	2 (2.2)	1 (1.1)	5 (2.7)	5 (2.7)
Minor bleeding	10 (17.5)	8 (14.0)	1 (1.1)	1 (1.1)	17 (9.3)	18 (9.9)
Major vascular complication	6 (10.5)	3 (5.3)	5 (5.6)	2 (2.2)	8 (4.4)	7 (3.8)
Minor vascular complication	5 (8.8)	5 (8.8)	6 (6.7)	3 (3.3)	7 (3.8)	7 (3.8)
Prosthesis dysfunction	4 (7.0)	1 (1.8)	30 (33.3)	13 (14.4)	6 (3.3)	5 (2.7)
Early safety (30 days)	12 (21.1)	5 (8.8)	13 (14.4)	10 (11.1)	21 (11.5)	15 (8.2)
Clinical efficacy (30 days)	10 (17.5)	2 (3.5)	36 (40.0)	16 (17.8)	17 (9.3)	11 (6.0)
Device success	47 (82.5)	55 (96.5)	54 (60.0)	76 (84.4)	170 (93.4)	170 (93.4)
Complete heart block	5 (8.8)	11 (19.3)	9 (10.0)	13 (14.4)	14 (7.7)	18 (9.9)
Perioperative sepsis	5 (8.8)	3 (5.3)	4 (4.4)	2 (2.2)	2 (1.1)	3 (1.6)
Hospital mortality	6 (10.5)	1 (1.8)	5 (5.6)	1 (1.1)	3 (1.6)	4 (2.2)
Cardiovascular mortality (30 days)	4 (7.0)	0 (0)	4 (4.4)	1 (1.1)	3 (1.6)	3 (1.6)
Mortality (30 days)	5 (8.8)	1 (1.8)	6 (6.7)	1 (1.1)	4 (2.2)	5 (2.7)

Data are displayed as n (%).