# 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

Victor Mauri, MD; Won K. Kim, MD; Mohammad Abumayyaleh; Thomas Walther, MD; Helge Moellmann, MD; Ulrich Schaefer, MD; Lenard Conradi, MD; Christian Hengstenberg, MD; Michael Hilker, MD; Thorsten Wahlers, MD; Stephan Baldus, MD; Volker Rudolph, MD; Navid Madershahian, MD; Tanja K. Rudolph, MD

***Background***—Surgical aortic valve replacement in patients with small annular dimensions is challenging because they are at increased risk for prosthesis–patient mismatch and impaired outcomes. Transcatheter aortic valve replacement might be a good alternative; however, comparative data on different transcatheter heart valves are missing.

***Methods and Results***—This multicenter, propensity score–matched study compared hemodynamics and early clinical outcomes in 246 patients with an aortic annulus area <400 $mm^2$ undergoing transcatheter aortic valve replacement with either a self-expanding transcatheter heart valve (Boston Scientific ACURATE *neo*, n=129) or a balloon-expandable transcatheter heart valve (Edwards SAPIEN 3, n=117). The 1:1 propensity score matching resulted in 92 matched pairs. For ACURATE *neo* versus SAPIEN 3-treated patients, 30-day mortality (0.0% versus 1.0%), 1-year mortality (8.3% versus 13.3%), incidence of stroke (3.3% versus 2.2%), life-threatening bleeding (1.1% versus 1.1%), and major vascular complications (2.2% versus 6.5%), as well as pacemaker implantation rate (12.0% versus 15.2%), were similar. Paravalvular regurgitation ≥moderate was rare in both groups (4.5% versus 3.6%). The ACURATE *neo* presented lower mean transvalvular gradients (9.3 versus 14.5 mm Hg; $P<0.001$), larger indexed effective orifice areas (0.96 versus 0.80 $cm^2/m^2$; $P=0.003$), and lower rates of severe prosthesis–patient mismatch (3% versus 22%; $P=0.004$). Hemodynamics were sustained at 1-year follow-up.

***Conclusions***—Albeit a similar safety profile with low clinical event rates, transcatheter aortic valve replacement with the ACURATE *neo* valve resulted in lower transvalvular gradients and consequently less prosthesis–patient mismatch compared with the SAPIEN 3 in patients with small annulus. These results emphasize the need of careful prosthesis selection in each individual patient. **(*Circ Cardiovasc Interv*. 2017;10:e005013. DOI: 10.1161/CIRCINTERVENTIONS.117.005013.)**

**Key Words:** follow-up studies ■ heart valve prosthesis ■ pacemaker, artificial ■ propensity score ■ transcatheter aortic valve replacement

Surgical aortic valve replacement (sAVR) in patients with small aortic annulus has been associated with a high incidence of prosthesis–patient mismatch (PPM),[1] a condition defined by a relatively too small effective orifice area (EOA) which negatively impacts short- and long-term outcomes, as well as durability of bioprostheses.[2–4] Aortic root enlargement strategies or implantation of stentless bioprostheses have been proposed to reduce the risk of PPM after sAVR in this patient group.[5,6] Treatment with transcatheter aortic valve replacement (TAVR) might be another treatment option because TAVR results in superior hemodynamics with a significantly lower incidence of PPM.[7,8] The impact of PPM on outcome after TAVR is of current debate. Although PPM was not associated with worse outcome after TAVR as opposed to sAVR

Received January 16, 2017; accepted August 22, 2017.

From the Departments of Cardiology (V.M., M.A., S.B., V.R., T.K.R.) and Cardiothoracic Surgery (T.W., N.M.), Heart Center, University of Cologne, Germany; Departments of Cardiology (W.K.K.) and Cardiac Surgery (T.W.), Kerckhoff Clinic, Bad Nauheim, Germany; Department of Internal Medicine, St. Johannes-Hospital, Dortmund, Germany (H.M.); Departments of General and Interventional Cardiology (U.S.) and Cardiovascular Surgery (L.C.), University Heart Center, University Hospital Hamburg-Eppendorf (UKE), Germany; Klinik für Herz-und Kreislauferkrankungen, Deutsches Herzzentrum München, Technische Universität München, Germany (C.H.); DZHK (German Centre for Cardiovascular Research), partner site Munich Heart Alliance, Germany (C.H.); and Department of Cardiothoracic Surgery, University Medical Center, Regensburg, Germany (M.H.).

**The Data Supplement is available at http://circinterventions.ahajournals.org/lookup/suppl/doi:10.1161/CIRCINTERVENTIONS.117.005013/-/DC1.**

Correspondence to Tanja K. Rudolph, MD, Department of Cardiology, Heart Center, University of Cologne, Kerpener St. 62, 50937 Cologne, Germany. E-mail tanja.rudolph@uk-koeln.de

## WHAT IS KNOWN

- Patients with small annular dimensions are at high risk for prosthesis–patient mismatch resulting in impaired long-term outcome and decreased durability of bioprostheses.

## WHAT THE STUDY ADDS

- Transcatheter aortic valve replacement with balloon-expandable and self-expanding devices in patients with small annulus has a low clinical event rate.
- Transcatheter aortic valve replacement with the self-expanding ACURATE *neo* valve resulted in superior hemodynamics regarding transvalvular gradients, indexed effective orifice area, and frequency of prosthesis–patient mismatch compared with transcatheter aortic valve replacement with the balloon-expandable SAPIEN 3 in patients with small annulus.
- These results emphasize the need of careful prosthesis selection in each individual patient.

in the PARTNER A trial (Placement of Aortic Transcatheter Valves A trial), PPM was a clear predictor of 1-year mortality in the subgroup of patients without relevant paravalvular regurgitation (PVR).[7] Moreover, severe PPM was associated with increased 1-year mortality in the CoreValve Pivotal trial.[8]

Several transcatheter heart valve (THV) systems are currently commercially available, both balloon-expandable with intra-annular and self-expanding (SE) THV with supra-annular location of leaflets which might affect hemodynamic performance and EOA and thus the incidence of PPM. However, there are no comparative data available on this specific topic.

The ACURATE *neo* aortic bioprosthesis (Symetis SA; a Boston Scientific company, Ecublens, Switzerland) is a next-generation SE THV with an X-shaped stent design featuring porcine pericardial leaflets located in a supra-annular position. The delivery system is inserted via an 18F sheath, and the THV can be implanted without rapid ventricular pacing.[9] Prior balloon valvuloplasty is recommended.

The widely used balloon-expandable SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA) has bovine pericardial leaflets in an annular position and a low delivery profile (14F expandable sheath). The device is implanted with or without prior valvuloplasty with mandatory rapid ventricular pacing during implantation.[10]

The present study sought to compare hemodynamics and early to 1-year clinical outcomes after TAVR with a small sized SE THV or current generation 23-mm balloon-expandable THV in patients with small aortic annuli.

## Methods

A total of 246 patients undergoing transfemoral TAVR between February 2014 and August 2016 at 5 high-volume centers in Germany with established multidisciplinary TAVR programs were included into the analysis. Inclusion criteria were small annular dimension defined as an annulus area <400 $mm^2$ and transfemoral TAVR with either a Boston Scientific ACURATE *neo* THV size S (Symetis SA; a Boston Scientific company, Ecublens, Switzerland) or an Edwards SAPIEN 3 THV size 23 mm (Edwards Lifesciences, Irvine, CA). One hundred and twenty-nine patients received an ACURATE *neo* THV while 117 patients received a SAPIEN 3 THV (Figure I in the Data Supplement). All patients provided written informed consent. Eligibility of the individual candidate for TAVR had been decided within the local institutional heart team. All patients underwent a preinterventional screening process, including echocardiography to confirm diagnosis of severe aortic stenosis and contrast-enhanced multislice computed tomography for evaluation of the device landing zone and vascular access site. Because of the absence of established guidelines, prosthesis selection was at the discretion of the operating physicians at each center. Implantation technique for both valves has been described previously.[9,10] Standard balloon filling was used for SAPIEN 3 implantation. Procedural outcomes were reported according to the Valve Academic Research Consortium (VARC)-2 consensus.[11] Accordingly, early safety was defined as composite end point of all-cause mortality, all stroke, life-threatening bleeding, stage 2 or 3 acute kidney injury, coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeat procedure. Residual PVR, mean transvalvular gradient, and indexed EOA (iEOA) were evaluated by transthoracic echocardiography pre-discharge. PVR severity was evaluated using a multiparametric approach and classified as follows: none/trace, mild, moderate, and severe.[11] Left ventricular outflow tract area was calculated from its diameter at baseline, and EOA was assessed with the continuity equation. EOA was indexed to body surface area as calculated with the DuBois formula. PPM was defined as an iEOA ≤0.85 $cm^2/m^2$ and classified moderate (0.65 $cm^2/m^2$ < iEOA ≤ 0.85 $cm^2$ /$m^2$) or severe (iEOA ≤0.65 $cm^2/m^2$) in accordance to the VARC-2 recommendations.[11]

### Statistical Analysis

Continuous variables are presented as mean±SD while categorical variables are reported as frequencies and percentages. Kolmogorov–Smirnov test was used to test for normal distribution. Student *t* test, Mann–Whitney *U* test, or the Wilcoxon signed-rank test was used accordingly. The exact Fisher test or the McNemar test was used for distribution analysis of categorical variables. Because of the nonrandomized nature of the study and the different participating centers, we applied a propensity score (PS)–based matching method to control for confounding baseline variables. PS was modeled with a multivariate logistic regression model based on the following baseline characteristics: sex, age, left ventricular ejection fraction, annulus diameter, body surface area, and logistic EuroSCORE. A rigorous 1:1 nearest neighbor matching algorithm without replacement was used with a 0.2 caliper setting. Standardized mean differences (d values) were calculated, and absolute standardized mean differences <0.2 were considered as indicator of adequate balance and thus sufficient bias reduction. Paired statistical tests were used to compare the matched populations. Two-sided $P<0.05$ was considered statistically significant. PS matching and all statistical analyses were performed with IBM SPSS Statistics, version 22, including the PS-matching extension bundle based on the R MatchIt package.

## Results

### Patient Populations and PS Matching

A total of 246 patients with symptomatic severe aortic stenosis and small annular dimension underwent transfemoral TAVR at 5 centers in Germany. An ACURATE *neo* device size S was implanted in 129 patients, whereas 117 patients received a SAPIEN 3 size 23 mm prosthesis (Figure I in the Data Supplement). Baseline characteristics of ACURATE *neo* and SAPIEN 3 patients were similar regarding age, sex, body surface area, and aortic root calcification. Before matching,

versus 366.4 mm$^2$; *P*=0.004). Baseline characteristics of all patients are presented in Table 1.

ACURATE *neo* patients were matched to SAPIEN 3 patients by the means of PS matching to control for confounders. PS matching resulted in 92 matched pairs. Baseline characteristics of the matched patient population are shown in Table 1. After matching, absolute standardized mean differences (d values) of all matched covariates were <0.2, indicating adequate balance of baseline characteristics and thus sufficient bias reduction (Figure II in the Data Supplement). Especially, annular dimensions were well balanced after PS matching.

## Procedural Characteristics

Procedural characteristics are listed in Table 2. The rates of balloon pre- and post-dilation were significantly higher in the ACURATE *neo* group (pre-dilation: 94.6% versus 31.5%; odds ratio, 37.8; confidence interval, 13.9–103.1; *P*<0.001; post-dilation: 44.6% versus 6.5%; odds ratio, 11.5; confidence interval, 4.6–29.0; *P*<0.001). Pre-dilation rate in SAPIEN 3 patients decreased over time (70.0%, 19.4%, and 6.5% in the first, second, and last third of patients, respectively; *P*<0.001). Valve implantation was performed under rapid ventricular pacing in 100% of SAPIEN 3 patients but only in 34.8% of patients in the ACURATE *neo* group (*P*<0.001). The average number of rapid ventricular pacing episodes in ACURATE *neo* and SAPIEN 3 patients was 1.7±0.8 and 1.3±0.6, respectively (*P*=0.001). Mean area oversizing (15.6±8.2% versus 15.1±9.9%; *P*=0.705) and mean perimeter oversizing (4.9±3.5% versus 5.3±4.6%; *P*=0.633) were similar in both groups. According to the manufacturers' sizing recommendations, prosthesis size was within sizing range in 86% and 77%, undersized in 6% and 0%, and oversized in 8% and 23% of ACURATE *neo* and SAPIEN 3 patients, respectively (*P*<0.001).

## Clinical Outcome

Periprocedural VARC-2 events of the 2 THV systems were comparable (Table 2). There was 1 death within 30 days in the ACURATE *neo* group and 2 deaths in the SAPIEN 3 group (*P*=1.000). Stroke occurred in 3 and 2 patients, respectively. The rate of vascular complications was 12.0% (major: 2.2%) in the ACURATE *neo* group and 20.7% (major: 6.5%) in the SAPIEN 3 group (*P*=0.152). Also, bleeding was similar in both groups (14.1% versus 12.0%; *P*=0.832). Life-threatening bleeding was identical in both groups (1.1% versus 1.1%; *P*=1.000). Accordingly, the VARC-2 early safety composite end point was similar in both groups (ACURATE *neo*: 93.5%; SAPIEN 3: 90.2%; *P*=0.607). One patient treated with an ACURATE *neo* valve required conversion to open surgery because of ventricular perforation. The permanent pacemaker implantation (PI) rate post-TAVR was similar in both groups, with 12.0% in the ACURATE *neo* group and 15.2% in the SAPIEN 3 group (*P*=0.678).

Median follow-up time was 367 days (interquartile range, 334–438 days; total follow-up time, 206.8 patient years). One-year mortality was numerically lower in the ACURATE *neo* group; however, this difference was statistically not significant (8.3% versus 13.3%; log-rank *P*=0.233; Figure III in the Data

**Table 1. Baseline Patient Parameter Before and After Propensity Score Matching**

| | Unmatched (n=246) | | | | Matched (n=184) | | | |
|---|---|---|---|---|---|---|---|---|
| | ACURATE *neo* | SAPIEN 3 | | | ACURATE *neo* | SAPIEN 3 | | |
| | n=129 | n=117 | d | *P* Value | n=92 | n=92 | d | *P* Value |
| Age, y | 81.8±5.0 | 82.8±6.3 | 0.176 | 0.057 | 82.8±6.5 | 81.9±5.3 | 0.157 | 0.151 |
| Female sex | 120 (93.0) | 106 (90.6) | 0.089 | 0.496 | 85 (92.4) | 85 (92.4) | 0.000 | 1.000 |
| Weight, kg | 70.4±13.9 | 66.9±14.0 | 0.247 | 0.024 | 69.5±14.3 | 67.8±14.5 | 0.116 | 0.351 |
| Height, cm | 160±6 | 161±7 | 0.168 | 0.228 | 160±6 | 161±7 | 0.223 | 0.184 |
| BSA, m$^2$ | 1.73±0.2 | 1.70±0.2 | 0.155 | 0.079 | 1.72±0.2 | 1.71±0.2 | 0.029 | 0.593 |
| BMI, kg/m$^2$ | 27.5±5.6 | 25.7±4.6 | 0.365 | 0.006 | 27.3±5.5 | 26.0±4.7 | 0.242 | 0.174 |
| Logistic EuroSCORE I (%) | 15.8±9.1 | 18.7±11.9 | 0.268 | 0.056 | 16.2±8.8 | 16.6±8.8 | 0.050 | 0.570 |
| Mean gradient, mm Hg | 46±16 | 47±17 | 0.090 | 0.656 | 46±16 | 47±16 | 0.057 | 0.734 |
| AVA, cm$^2$ | 0.69±0.20 | 0.64±0.18 | 0.265 | 0.059 | 0.68±0.19 | 0.65±0.17 | 0.179 | 0.283 |
| LVEF (%) | 58±9 | 59±11 | 0.099 | 0.105 | 59±8 | 59±10 | 0.018 | 0.554 |
| Annulus perimeter, mm | 68.6±2.3 | 69.0±3.0 | 0.115 | 0.058 | 68.9±2.2 | 68.7±2.9 | 0.089 | 0.797 |
| Annulus area, mm$^2$ | 359±25 | 366±29 | 0.291 | 0.004 | 361±24 | 364±29 | 0.098 | 0.207 |
| Aortic root calcification | | | 0.138 | 0.641 | | | 0.059 | 0.599 |
| Mild | 40 (31.0) | 28 (23.9) | | | 27 (29.3) | 23 (25) | | |
| Moderate | 63 (48.8) | 61 (52.1) | | | 46 (50.0) | 48 (52.2) | | |
| Severe | 23 (17.8) | 26 (22.2) | | | 16 (17.4) | 20 (21.7) | | |
| Very severe | 3 (2.3) | 2 (1.7) | | | 3 (3.3) | 1 (1.1) | | |
| Propensity score | 0.45 ±0.09 | 0.50 ±0.12 | 0.437 | 0.001 | 0.47±0.09 | 0.48±0.10 | 0.090 | 0.523 |

Values are mean±SD or n (%). AVA indicates aortic valve area; BMI, body mass index; BSA, body surface area; and LVEF, left ventricular ejection fraction.

**Table 2. Procedural Characteristics and Clinical Outcome**

| | ACURATE neo n=92 | SAPIEN 3 n=92 | *P* Value |
|---|---|---|---|
| Procedural characteristics | | | |
| Pre-dilation | 87 (94.6) | 29 (31.5) | <0.001 |
| Post-dilation | 41 (44.6) | 6 (6.5) | <0.001 |
| Rapid ventricular pacing during deployment | 32 (34.8) | 92 (100.0) | <0.001 |
| No. of rapid ventricular pacing episodes | 1.7±0.8 | 1.3±0.6 | 0.001 |
| Sizing* | | | <0.001 |
| Undersized | 5 (5.9) | 0 (0) | |
| Within sizing range | 73 (85.9) | 71 (77.2) | |
| Oversized | 7 (8.2) | 21 (22.8) | |
| Oversizing (area %) | 15.6±8.2 | 15.1±9.9 | 0.705 |
| Oversizing (perimeter %) | 4.9±3.5 | 5.3±4.6 | 0.633 |
| Clinical outcome | | | |
| 30-d mortality | 1 (1.1) | 2 (2.2) | 1.000 |
| 1-y mortality | 6 (8.3) | 10 (13.3) | 0.233 |
| All stroke | 3 (3.3) | 2 (2.2) | 1.000 |
| Vascular complications | 11 (12.0) | 19 (20.7) | 0.152 |
| Major | 2 (2.2) | 6 (6.5) | |
| Minor | 9 (9.8) | 13 (14.1) | |
| Bleeding | 13 (14.1) | 11 (12.0) | 0.832 |
| Life-threatening | 1 (1.1) | 1 (1.1) | |
| Major | 3 (3.3) | 1 (1.1) | |
| Minor | 9 (9.8) | 9 (9.8) | |
| Permanent pacemaker implantation | 11 (12.0) | 14 (15.2) | 0.678 |
| Conversion to open surgery | 1 (1.1) | 0 (0.0) | 1.000 |
| Cardiac tamponade | 1 (1.1) | 1 (1.1) | 1.000 |
| Unplanned use of cardiopulmonary bypass | 1 (1.0) | 1 (1.0) | 1.000 |
| Ventricular perforation | 1 (1.1) | 0 (0.0) | 1.000 |
| Early safety | 86 (93.5) | 83 (90.2) | 0.607 |

Values are mean±SD or n (%).

*Sizing category was based on perimeter for ACURATE *neo* and area for SAPIEN 3.

Supplement). New York Heart Association functional class at 1-year did not differ significantly between groups (*P*=0.303; Figure 1). There was no reintervention in either group.

## Hemodynamics and PPM

Transthoracic echocardiography before discharge revealed a comparable amount of PVR in both groups (*P*=0.208; Figure 2). Moderate PVR was similar (ACURATE *neo*: 4.5% versus SAPIEN 3: 3.6%), whereas there were numerically more patients with no/trace PVR in the SAPIEN 3 group (40.9% versus 52.4%). There was no patient with severe PVR in either group. At 1-year follow-up, moderate PVR was

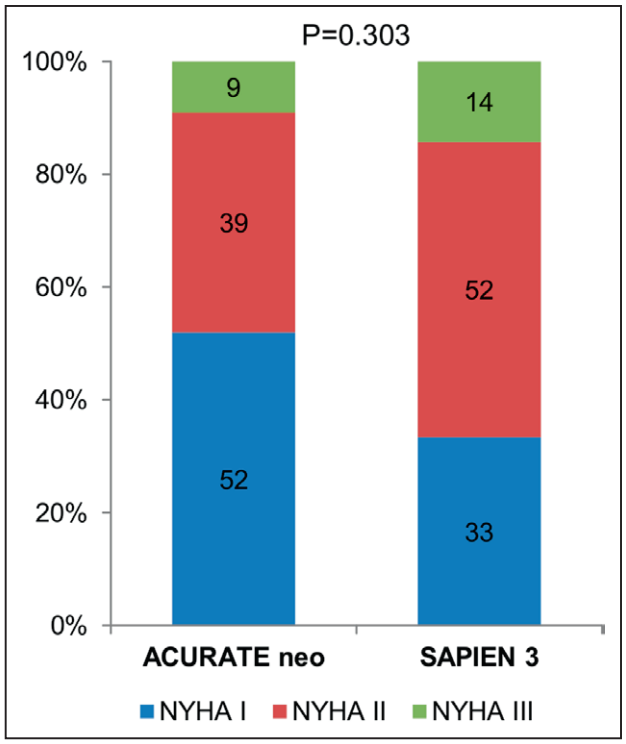


**Figure 1.** New York Heart Association (NYHA) class at 1-year follow-up.

3.9% in the ACURATE *neo* group and 3.6% in the SAPIEN 3 group (Figure 2B). Mean transvalvular gradients were 9.3±3.9 mm Hg in the ACURATE *neo* group and 14.5±5.5 mm Hg in the SAPIEN 3 group, and thus, significantly lower in ACURATE *neo* patients (*P*<0.001; Figure 3). Also, iEOA was significantly larger in ACURATE *neo* patients (0.96±0.3 versus SAPIEN 3: 0.80±0.2 $cm^2/m^2$; *P*=0.003). Consequently, PPM occurred significantly more often in the SAPIEN 3 group (ACURATE: 41% versus SAPIEN 3: 67%; *P*=0.002) and was classified as severe PPM in 3% of ACURATE patients and 22% of SAPIEN 3 patients (*P*=0.004). The observations were sustained at 1-year follow-up with mean transvalvular gradients of 6.6±2.7 versus 17.5±6.5 mm Hg (*P*<0.008) and iEOA of 1.01±0.3 versus 0.74±0.2 $cm^2/m^2$ (*P*=0.031) in ACURATE *neo* and SAPIEN 3 patients, respectively.

## Discussion

The present study comprises a multicenter PS-matched comparison of hemodynamic performance and clinical outcome up to 1 year of the SE supra-annular Boston Scientific ACURATE *neo* valve and the balloon-expandable intra-annular Edwards SAPIEN 3 valve in patients with small aortic annulus. The main findings of the study are (1) low all-cause mortality and early safety event rates showed feasibility and safety of both valve systems with no significant differences; (2) the incidence of new onset conduction disturbances requiring permanent PI was comparable in both groups; (3) the ACURATE *neo* valve presented significantly lower transvalvular mean gradients and larger iEOA at discharge and 1-year follow-up and consequently, lower rates of PPM.

As expected, pre- and post-dilation rates were significantly higher in the ACURATE *neo* group. Because

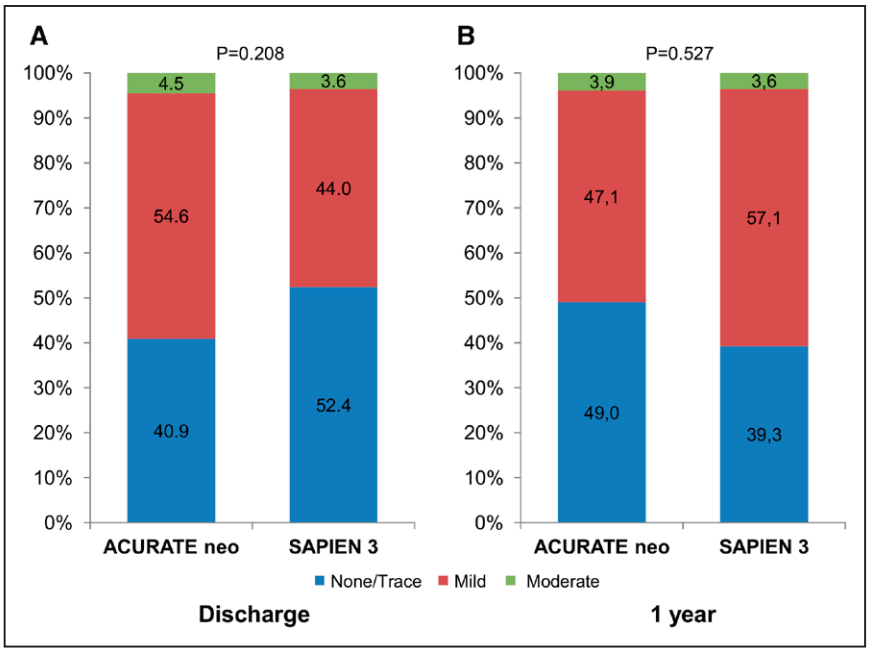


**Figure 2.** Paravalvular regurgitation (PVR). The incidence of moderate PVR was comparable with both valves at discharge (**A**) and at 1-year follow-up (**B**).

of the SE nature with less radial force of the stent frame, the ACURATE *neo* implantation is performed without pre-dilation only in selected cases. Conversely, currently pre-dilation is rarely used for SAPIEN 3 implantation and decreased over time in our cohort. However, the different dilation strategies did not impact the overall safety. Clinical event rates were low in both groups with regard to death, stroke, life-threatening bleeding, and major vascular complications, consistent with contemporary TAVR outcome data.[12] Although post-dilation has been associated with higher rates of cerebrovascular events in some studies,[13] incidence of stroke was similar in both groups. Moreover, the incidence of stroke in the ACURATE *neo* group did not differ from the much larger SAVI-TF registry (Boston Scientific ACURATE *neo*™ Valve Implantation SAVI TF Registry) (1[4].9%).

The PI rate was 12.0% in the ACURATE *neo* group and thus remarkably low for a SE THV system. In comparison, PI rates from 22% to 38% have been reported for the first-generation SE CoreValve THV (Medtronic Inc).[15,16] Also for its successor, the Evolut R THV, PI rates up to 26.7% have been reported in the recent SURTAVI trial (Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients).[17–19] The PI rate of 15.2% after SAPIEN 3 implantation is in line with numerous recent reports.[20,21] The respective design of the stent frames may contribute to the observed differences in PI rate: while the new sealing skirt of the SAPIEN 3 creates higher local pressure on the atrioventricular conduction system in the left ventricular outflow tract, the ACURATE *neo* applies only moderate pressure on the conduction system because of the X-shaped stent design and compared with the SAPIEN 3 only intermediate radial force. Although the impact

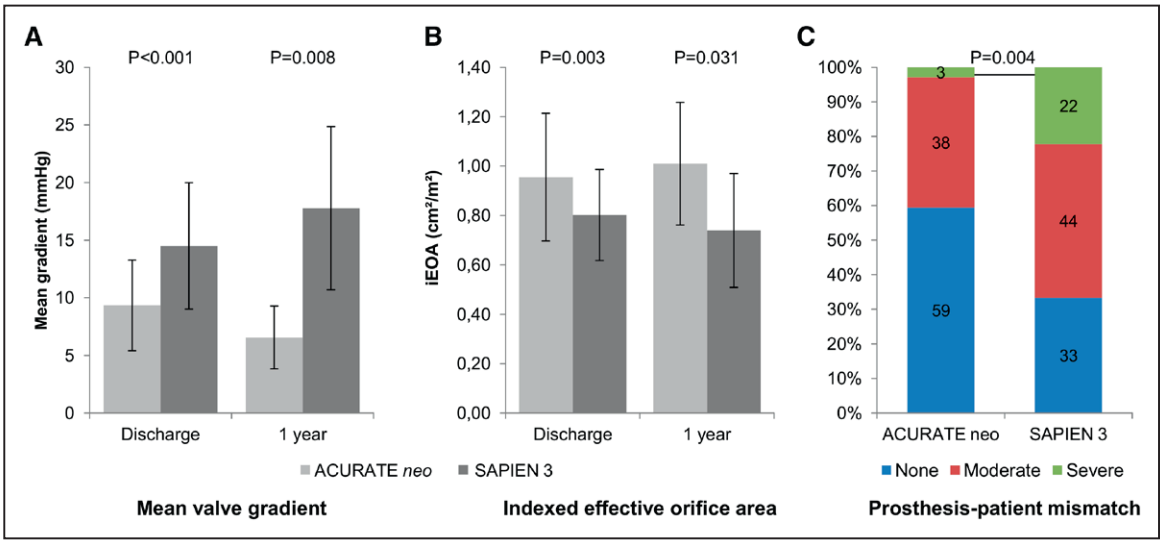


**Figure 3.** Echocardiographic outcome of ACURATE *neo* and SAPIEN 3 at discharge and 1-year follow-up. ACURATE *neo* implanted patients presented with significantly lower transvalvular gradients (**A**); larger indexed effective orifice areas (iEOA; **B**); and lower rates of moderate and severe prosthesis–patient mismatch (**C**).

of PI after TAVR on long-term outcome is of current debate, deleterious effects of long-term right ventricular pacing are well studied, and it is debatable whether PI rates >10% are acceptable in lower risk populations.[22–24]

Both prostheses provided efficient protection against PVR. Clinically relevant PVR ≥moderate, a major predictor of adverse outcome in numerous studies,[25] was low in both groups. However, SAPIEN 3 implantation resulted numerically more often in no or only trace PVR compared with ACURATE *neo* implantation, and even mild PVR has been associated with increased mortality in some studies of first-generation THV.[26] Of interest, hemodynamic parameters of the 2 valve systems differed substantially with significantly lower transvalvular gradients and larger iEOA at discharge and at 1-year follow-up and consequently lower rates of PPM in ACURATE *neo* patients. The observed mean aortic valve gradients in SAPIEN 3 patients were higher than those reported for earlier generations of balloon-expandable valves, which is in line with recent reports.[21,27,28] In a recent study, Theron et al[28] found a 15.2-fold increase of PPM risk of the SAPIEN 3 valve compared with its predecessor, the SAPIEN XT in small 23 mm prostheses. It may be speculated that the additional material of the sealing skirt in the left ventricular outflow tract is responsible for the increase in transvalvular gradient. However, the supra-annular location of the ACURATE *neo* valve leaflets seems to be beneficial to achieve lower gradients and higher iEOA. After sAVR, elevated transvalvular gradients have been identified as an important risk factor for decreased prostheses durability because of structural valve deterioration which occurs significantly more often in small bioprostheses.[29] Moreover, PPM is a well-known predictor of unfavorable short- and long-term outcomes after sAVR and predicts structural valve deterioration.[2–4] The clinical relevance of elevated transvalvular gradients and PPM after TAVR is not yet defined. PPM occurs less frequently after TAVR but was a relevant predictor of 1-year mortality in the subgroup of patients without PVR in the PARTNER A trial.[7] Because PVR almost disappeared with the introduction of next-generation THV, it may be speculated that PPM may become an issue of primary clinical attention after TAVR with those devices.

Of interest, data from the VIVID registry (Valve-in-Valve International Data) showed that severe PPM after valve-in-valve implantation for failing bioprosthesis results in decreased 1-year survival. This observation confirms that initial implantation of the prosthesis with the best hemodynamic performance and without PPM is crucial for an optimal outcome after subsequent valve-in-valve treatments.[30]

In the present study, the higher rate of PPM in the SAPIEN 3 group had no significant impact on 1-year mortality or New York Heart Association functional class. Long-term follow-up of next-generation THV in large patient cohorts is necessary to elucidate the impact of elevated gradients on prosthesis lifetime after TAVR. However, the reported pressure gradients for the SAPIEN 3 are still lower than those of widely used surgical valves, for which excellent long-term durability has been shown in numerous studies.[29,31,32]

Summarized, both THV systems demonstrated similar safety profiles. However, the ACURATE *neo* presented superior hemodynamics regarding transvalvular gradients, iEOA, and frequency of PPM. This may be particularly beneficial in patients with small aortic annulus, who are at risk for PPM, which in turn might be a risk factor for structural valve deterioration and impaired outcome. Interestingly, despite inclusion criteria focusing only on annuli with an area <400 $mm^2$, in the unmatched population, annular dimensions of ACURATE *neo* patients were smaller than those of SAPIEN 3 patients. This may indicate that the participating centers already tend to select the ACURATE *neo* prosthesis over the SAPIEN 3 in small annuli. Whether PPM after TAVR translates into decreased prosthesis durability and impaired long-term outcome remains to be elucidated. However, the results emphasize the need of careful prosthesis selection in each individual patient.

### Study Limitations

This is a retrospective multicenter analysis and typical limitations apply. A PS-based matching process was used to control for confounding baseline variables. Although PS matching resulted in sufficient balance of baseline characteristics, bias because of unknown or unmeasured confounders cannot be excluded because patients were not randomized to the respective treatment group. Regarding mean transvalvular gradient and subsequently calculated parameters, like iEOA and PPM, there was no center effect in ACURATE *neo* patients. In SAPIEN 3 patients, there was an effect in the matched population with significantly higher mean transvalvular gradients in one of the participating centers, which might be partially explained by a slightly but significantly higher ejection fraction. Because the effect is not opposing the results of the overall analysis, a significant bias seems to be unlikely. Finally, longer follow-up in larger patient cohorts is necessary to evaluate the impact of hemodynamics on valve degeneration and mortality.

## Disclosures

Drs Kim, Moellmann, and Walther are proctors for Symetis and received speaker honoraria from Symetis. Dr Schaefer is proctor for Symetis and Edwards and received research grants and travel honoraria from Symetis and Edwards. Dr Conradi is proctor for Edwards. Dr Hengstenberg is proctor for Symetis and Edwards. Dr Hilker is proctor for Symetis and received research grants and travel honoraria from Symetis. Drs Wahlers and Madershahian are proctors for Edwards. Dr Baldus is proctor for Edwards and received a research grant from Edwards. Dr Rudolph is proctor for Symetis and Edwards and received speaker honoraria from Symetis and Edwards. The other authors report no conflicts.

## References

1. Pibarot P, Dumesnil JG. Prosthetic heart valves: selection of the optimal prosthesis and long-term management. *Circulation*. 2009;119:1034–1048. doi: 10.1161/CIRCULATIONAHA.108.778886.
2. Head SJ, Mokhles MM, Osnabrugge RL, Pibarot P, Mack MJ, Takkenberg JJ, Bogers AJ, Kappetein AP. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27 186 patients with 133 141 patient-years. *Eur Heart J*. 2012;33:1518–1529. doi: 10.1093/eurheartj/ehs003.
3. Dayan V, Vignolo G, Soca G, Paganini JJ, Brusich D, Pibarot P. Predictors and outcomes of prosthesis-patient mismatch after aortic valve replacement. *JACC Cardiovasc Imaging*. 2016;9:924–933. doi: 10.1016/j.jcmg.2015.10.026.
4. Flameng W, Herregods MC, Vercalsteren M, Herijgers P, Bogaerts K, Meuris B. Prosthesis-patient mismatch predicts structural valve degeneration in bioprosthetic heart valves. *Circulation*. 2010;121:2123–2129. doi: 10.1161/CIRCULATIONAHA.109.901272.

5. Ghoneim A, Bouhout I, Demers P, Mazine A, Francispillai M, El-Hamamsy I, Carrier M, Lamarche Y, Bouchard D. Management of small aortic annulus in the era of sutureless valves: a comparative study among different biological options. *J Thorac Cardiovasc Surg*. 2016;152:1019–1028. doi: 10.1016/j.jtcvs.2016.06.058.
6. Peterson MD, Borger MA, Feindel CM, David TE. Aortic annular enlargement during aortic valve replacement: improving results with time. *Ann Thorac Surg*. 2007;83:2044–2049. doi: 10.1016/j.athoracsur.2007.01.059.
7. Pibarot P, Weissman NJ, Stewart WJ, Hahn RT, Lindman BR, McAndrew T, Kodali SK, Mack MJ, Thourani VH, Miller DC, Svensson LG, Herrmann HC, Smith CR, Rodés-Cabau J, Webb J, Lim S, Xu K, Hueter I, Douglas PS, Leon MB. Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis: a PARTNER trial cohort–a analysis. *J Am Coll Cardiol*. 2014;64:1323–1334. doi: 10.1016/j.jacc.2014.06.1195.
8. Zorn GL, 3rd, Little SH, Tadros P, Deeb GM, Gleason TG, Heiser J, Kleiman NS, Oh JK, Popma JJ, Adams D, Huang J, Reardon MJ. Prosthesis-patient mismatch in high-risk patients with severe aortic stenosis: a randomized trial of a self-expanding prosthesis. *J Thorac Cardiovasc Surg*. 2016;151:1014–1022, 1023.e1. doi: 10.1016/j.jtcvs.2015.10.070.
9. Möllmann H, Diemert P, Grube E, Baldus S, Kempfert J, Abizaid A. Symetis ACURATE TF™ aortic bioprosthesis. *EuroIntervention*. 2013;9(suppl):S107–S110. doi: 10.4244/EIJV9SSA22.
10. Binder RK, Rodés-Cabau J, Wood DA, Mok M, Leipsic J, De Larochellière R, Toggweiler S, Dumont E, Freeman M, Willson AB, Webb JG. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. *JACC Cardiovasc Interv*. 2013;6:293–300. doi: 10.1016/j.jcin.2012.09.019.
11. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB; Valve Academic Research Consortium-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Thorac Cardiovasc Surg*. 2013;145:6–23. doi: 10.1016/j.jtcvs.2012.09.002.
12. Athappan G, Gajulapalli RD, Tuzcu ME, Svensson LG, Kapadia SR. A systematic review on the safety of second-generation transcatheter aortic valves. *EuroIntervention*. 2016;11:1034–1043. doi: 10.4244/EIJV11I9A211.
13. Auffret V, Regueiro A, Del Trigo M, Abdul-Jawad Altisent O, Campelo-Parada F, Chiche O, Puri R, Rodés-Cabau J. Predictors of early cerebrovascular events in patients with aortic stenosis undergoing transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2016;68:673–684. doi: 10.1016/j.jacc.2016.05.065.
14. Moellmann H. Results from the global registry SAVI TF. Abstract presented at EuroPCR 2016. May 17, 2016.
15. Abdel-Wahab M, Mehilli J, Frerker C, Neumann FJ, Kurz T, Tölg R, Zachow D, Guerra E, Massberg S, Schäfer U, El-Mawardy M, Richardt G; CHOICE Investigators. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA*. 2014;311:1503–1514. doi: 10.1001/jama.2014.3316.
16. Chieffo A, Buchanan GL, Van Mieghem NM, Tchetche D, Dumonteil N, Latib A, van der Boon RM, Vahdat O, Marcheix B, Farah B, Serruys PW, Fajadet J, Carrié D, de Jaegere PP, Colombo A. Transcatheter aortic valve implantation with the Edwards SAPIEN versus the Medtronic CoreValve Revalving system devices: a multicenter collaborative study: the PRAGMATIC Plus Initiative (Pooled-RotterdAm-Milano-Toulouse In Collaboration). *J Am Coll Cardiol*. 2013;61:830–836. doi: 10.1016/j.jacc.2012.11.050.
17. Noble S, Stortecky S, Heg D, Tueller D, Jeger R, Toggweiler S, Ferrari E, Nietlispach F, Taramasso M, Maisano F, Grünenfelder J, Jüni P, Huber C, Carrel T, Windecker S, Wenaweser P, Roffi M. Comparison of procedural and clinical outcomes with Evolut R versus Medtronic CoreValve: a Swiss TAVI registry analysis. *EuroIntervention*. 2017;12:e2170–e2176. doi: 10.4244/EIJ-D-16-00677.
18. Manoharan G, Walton AS, Brecker SJ, Pasupati S, Blackman DJ, Qiao H, Meredith IT. Treatment of symptomatic severe aortic stenosis with a novel resheathable supra-annular self-expanding transcatheter aortic valve system. *JACC Cardiovasc Interv*. 2015;8:1359–1367. doi: 10.1016/j.jcin.2015.05.015.
19. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP; SURTAVI Investigators. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2017;376:1321–1331. doi: 10.1056/NEJMoa1700456.
20. De Torres-Alba F, Kaleschke G, Diller GP, Vormbrock J, Orwat S, Radke R, Reinke F, Fischer D, Reinecke H, Baumgartner H. Changes in the pacemaker rate after transition from Edwards SAPIEN XT to SAPIEN 3 transcatheter aortic valve implantation: the critical role of valve implantation height. *JACC Cardiovasc Interv*. 2016;9:805–813. doi: 10.1016/j.jcin.2015.12.023.
21. Binder RK, Stortecky S, Heg D, Tueller D, Jeger R, Toggweiler S, Pedrazzini G, Amann FW, Ferrari E, Noble S, Nietlispach F, Maisano F, Raber L, Roffi M, Grunenfelder J, Juni P, Huber C, Windecker S, Wenaweser P. Procedural results and clinical outcomes of transcatheter aortic valve implantation in Switzerland: an observational cohort study of SAPIEN 3 versus SAPIEN XT transcatheter heart valves. *Circ Cardiovasc Interv*. 2015;8:e002653. doi: 10.1161/CIRCINTERVENTIONS.115.002653.
22. Dizon JM, Nazif TM, Hess PL, Biviano A, Garan H, Douglas PS, Kapadia S, Babaliaros V, Herrmann HC, Szeto WY, Jilaihawi H, Fearon WF, Tuzcu EM, Pichard AD, Makkar R, Williams M, Hahn RT, Xu K, Smith CR, Leon MB, Kodali SK; PARTNER Publications Office. Chronic pacing and adverse outcomes after transcatheter aortic valve implantation. *Heart*. 2015;101:1665–1671. doi: 10.1136/heartjnl-2015-307666.
23. Tops LF, Schalij MJ, Bax JJ. The effects of right ventricular apical pacing on ventricular function and dyssynchrony implications for therapy. *J Am Coll Cardiol*. 2009;54:764–776. doi: 10.1016/j.jacc.2009.06.006.
24. Elder DH, Lang CC, Choy AM. Pacing-induced heart disease: understanding the pathophysiology and improving outcomes. *Expert Rev Cardiovasc Ther*. 2011;9:877–886. doi: 10.1586/erc.11.82.
25. Athappan G, Patvardhan E, Tuzcu EM, Svensson LG, Lemos PA, Fraccaro C, Tarantini G, Sinning JM, Nickenig G, Capodanno D, Tamburino C, Latib A, Colombo A, Kapadia SR. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. *J Am Coll Cardiol*. 2013;61:1585–1595. doi: 10.1016/j.jacc.2013.01.047.
26. Kodali S, Pibarot P, Douglas PS, Williams M, Xu K, Thourani V, Rihal CS, Zajarias A, Doshi D, Davidson M, Tuzcu EM, Stewart W, Weissman NJ, Svensson L, Greason K, Maniar H, Mack M, Anwaruddin S, Leon MB, Hahn RT. Paravalvular regurgitation after transcatheter aortic valve replacement with the Edwards sapien valve in the PARTNER trial: characterizing patients and impact on outcomes. *Eur Heart J*. 2015;36:449–456. doi: 10.1093/eurheartj/ehu384.
27. Bocksch W, Grossmann B, Geisler T, Steeg M, Droppa M, Jorbenadze R, Haap M, Gawaz M, Fateh-Moghadam S. Clinical outcome and paravalvular leakage of the new balloon-expandable Edwards Sapien 3 valve in comparison to its predecessor model (Edwards Sapien XT) in patients undergoing transfemoral aortic valve replacement. *Catheter Cardiovasc Interv*. 2016;88:466–475. doi: 10.1002/ccd.26562.
28. Theron A, Pinto J, Grisoli D, Griffiths K, Salaun E, Jaussaud N, Ravis E, Lambert M, Messous L, Amanatiou C, Cuisset T, Gariboldi V, Giorgi R, Habib G, Collart F. Patient-prosthesis mismatch in new generation transcatheter heart valves: a propensity score analysis. *Eur Heart J Cardiovasc Imaging*. 2017. doi: 10.1093/ehjci/jex019.
29. Johnston DR, Soltesz EG, Vakil N, Rajeswaran J, Roselli EE, Sabik JF, 3rd, Smedira NG, Svensson LG, Lytle BW, Blackstone EH. Long-term durability of bioprosthetic aortic valves: implications from 12,569 implants. *Ann Thorac Surg*. 2015;99:1239–1247. doi: 10.1016/j.athoracsur.2014.10.070.
30. Pibarot P, Barbanti M, Rudolph T, Spence M, Simonato M, Moat N, Mennuni M, Iadanza A, Amrane H, Kim W-K, Brecker S, Linke A, Finkelstein A, Spargias K, Hernandez J-M, Latib A, Dvir D. Prosthesis-patient mismatch of surgical valves significantly impacts survival following aortic valve-in-valve implantation. Abstract presented at EuroPCR 2017. May 2017.
31. Matsumoto Y, Fujita T, Hata H, Shimahara Y, Sato S, Kobayashi J. Hemodynamic performance and durability of mosaic bioprostheses for aortic valve replacement, up to 13 years. *Circ J*. 2015;79:1044–1051. doi: 10.1253/circj.CJ-14-0990.
32. Yankah CA, Pasic M, Musci M, Stein J, Detschades C, Siniawski H, Hetzer R. Aortic valve replacement with the Mitroflow pericardial bioprosthesis: durability results up to 21 years. *J Thorac Cardiovasc Surg*. 2008;136:688–696. doi: 10.1016/j.jtcvs.2008.05.022.