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# Impact of Predilatation Prior to Transcatheter Aortic Valve Implantation with the Self-Expanding Acurate neo Device (From the Multicenter NEOPRO Registry)

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# Impact of Predilatation Prior to Transcatheter Aortic Valve Implantation with the Self-Expanding Acurate *neo* Device (From the Multicenter NEOPRO Registry)

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## Abstract

Safety and feasibility of transfemoral Acurate *neo* implantation without systematic predilatation are not fully investigated. Our aim was to evaluate the use and impact of pre-implantation balloon aortic valvuloplasty (pre-BAV) before transcatheter aortic valve implantation (TAVI) with Acurate *neo*. The NEOPRO Registry retrospectively included 1,263 patients who underwent transfemoral TAVI with Acurate *neo* at 18 centers between January 2012 and March 2018. Information on pre-BAV was available for 1,262 patients (99.9%). Primary endpoints were pre-discharge moderate-to-severe paravalvular aortic regurgitation (PAR II+), 30-day new permanent pacemaker implantation (PPI), and 30-day all-cause mortality or stroke. A total of 1,262 patients who underwent TAVI with (n=1,051) or without predilatation (n=211) were included. A reduction in the pre-BAV rate was observed during the study period (from 95.7% in the first date quintile to 78.4% in the last date quintile). Patients who underwent pre-BAV had higher degrees of aortic valve (AV) and left ventricular outflow tract (LVOT) calcification. Primary endpoints were similar between pre-BAV and no pre-BAV groups (PAR II+ 5.5% vs. 3.4%, p=0.214; 30-day PPI 9.0% vs. 8.0%, p=0.660; 30-day death or stroke 4.9% vs. 4.4%, p=0.743). The need for postdilatation and other procedural outcomes were comparable between groups. Predilatation did not have a significant impact on primary endpoints across AV and LVOT calcification subgroups (subgroup analyses) and was not independently associated with primary endpoints (multivariate analyses). In conclusion, transfemoral Acurate *neo* implantation without predilatation appears to be feasible and safe, especially in patients with milder degrees of AV and LVOT calcification.

**Keywords:** TAVI; predilatation; predilation; Acurate *neo*.

## Introduction

Transcatheter aortic valve implantation (TAVI) has become a first-line therapeutic option in patients with severe, symptomatic aortic stenosis at increased surgical risk.[1,2] TAVI technology has been strategically developed over years, leading to a progressive development of several next-generation transcatheter heart valves (THVs) and improvement in clinical outcomes.[3] The self-expanding Acurate *neo* bioprosthesis (Boston Scientific, Marlborough, Massachusetts) is a next-generation THV that has been associated with promising results in the Conformité Européene mark trial and the large SAVI-TF (Symetis ACURATE neo Valve Implantation Using Transfemoral Access) registry.[4–6] Furthermore, the NEOPRO (A Multicenter Comparison of Acurate NEO versus Evolut PRO Transcatheter Heart Valves) registry has recently shown similar outcomes after transfemoral TAVI with Acurate *neo* and the third-generation self-expanding Evolut PRO (Medtronic, Minneapolis, Minnesota) devices.[7] Considering the lower radial force of the Acurate *neo* THV, predilatation before valve implantation was recommended and almost always performed in early experience with this device.[4] However, omitting predilatation could be appealing to simplify the procedure and reduce the risk of potential balloon aortic valvuloplasty (BAV)-related complications. A small single-center study has recently reported the safety and feasibility of Acurate *neo* THV implantation without pre-implantation BAV (pre-BAV).[8] Therefore, our aim was to evaluate the use and impact of predilatation before transfemoral TAVI with the Acurate *neo* bioprosthesis in the large, multicenter NEOPRO Registry.

## Methods

The study design of the multicenter, observational, retrospective NEOPRO Registry has been previously described.[7] In brief, our registry included a total of 1,551 consecutive patients undergoing transfemoral TAVI with the Acurate *neo* (n=1,263) or Evolut PRO (n=288) devices for symptomatic, severe aortic stenosis of the native aortic valve (AV). For the purpose of this study, only patients who underwent TAVI with the Acurate *neo* THV were considered. Acurate *neo* TAVI procedures were performed between January 2012 and March 2018 at 18 centers; information on predilatation was available for 1,262 out of 1,263 patients undergoing Acurate *neo* implantation (99.9%). The number of patients included from each participating center is detailed in **Supplemental Table S1**. Patients were divided in two groups depending on whether pre-BAV was performed (n=1,051) or not (n=211). The decision to perform predilatation was left to operator's discretion at each participating center. As previously described, Acurate *neo* THV is implanted transfemorally using a dedicated delivery system and is available in three sizes (S, M, and L).[9] All

patients provided written informed consent for the procedure and subsequent data collection as per local practice for retrospective data.

Pre-procedural screening was performed by means of clinical assessment, echocardiography, and multidetector computed tomography (MDCT). Calcifications of native AV and left ventricular outflow tract (LVOT) were classified and graded using a semi-quantitative scoring system, as previously described.[10] In addition to standard measurements (annular area, annular perimeter, minimum and maximum annular diameter, area-derived annular diameter, perimeter-derived annular diameter), annular eccentricity (maximum/minimum annular diameter) and cover index for area- and perimeter-derived annular diameter (100 x [prosthesis diameter – MDCT annular size]/prosthesis diameter) were calculated.[11]

The primary objective of the study was to evaluate post-procedural (pre-discharge) moderate-to-severe paravalvular aortic regurgitation (PAR), permanent pacemaker implantation (PPI) at 30-days, and the composite of all-cause mortality or stroke at 30-days in patients who underwent TAVI with or without predilatation. Primary endpoints were assessed according to Valve Academic Research Consortium - 2 (VARC-2) criteria.[12] Secondary endpoints of interest were VARC-2-defined procedural complications, 30-day clinical outcomes, and 1-year all-cause mortality and stroke. Echocardiographic outcomes were evaluated pre-discharge; PAR severity was assessed according to VARC-2 criteria (graded as none or trace, mild, moderate, or severe).[12] Predictors of moderate-to-severe PAR, 30-day PPI, and 30-day all-cause mortality or stroke were also evaluated.

Continuous variables are presented as mean ± standard deviation and compared with the unpaired Student's *t* test. Categorical variables are presented as numbers and percentages and compared with the chi-square test. Primary and secondary endpoints were compared between patients who underwent TAVI with or without pre-BAV. The primary endpoints were also evaluated in AV and LVOT calcification subgroups by means of formal interaction testing analysis (subgroup analysis). Multivariate binary logistic regression was performed to identify independent predictors of the primary endpoints. All variables with a univariate p-value < 0.10 or variables judged to be of clinical relevance (including predilatation) were included into the final multivariate model. Results of the binary logistic regression are presented as odds ratio (OR) with 95% confidence interval (CI). All-cause mortality and stroke at 1-year (either the composite endpoint and the two individual endpoints) were calculated and compared between groups using the Kaplan-Meier method.

All reported p-values are 2-sided, and a p-value < 0.05 was considered statistically significant. All statistical analyses were performed using STATA version 13.0 (STATA Corp., College Station, Texas).

**Results**

A total of 1,262 patients who underwent transfemoral Acurate *neo* implantation with (n=1,051; 83.3%) or without pre-BAV (n=211; 16.7%) were included in the present analysis. As shown in **Figure 1**, a reduction in the use of predilatation was observed during the study period (between January 2012 and March 2018), from 95.7% to 78.4% of TAVI performed in the first and fifth date quintiles, respectively. Mean age of included patients was 81.8 ± 5.8 years and 35.1% of patients were male; mean Society of Thoracic Surgeons Predicted Risk of Mortality (STS-M) score was 5.0 ± 3.2%. Patients who underwent direct TAVI (without pre-BAV) had more frequently a history of prior stroke and atrial fibrillation or flutter, whereas patients who underwent predilatation had higher mean AV gradient and smaller aortic valve area at baseline echocardiography (**Table 1**). MDCT data was available for 982/1262 patients (77.8%); in particular, information on MDCT-derived AV and LVOT calcification were available in 977 and 975 patients, respectively. Significant differences in MDCT characteristics were observed between the two groups: patients who underwent pre-BAV had higher annular dimensions (in terms of maximum and minimum annular diameter, annular area, annular perimeter, area-derived and perimeter-derived annular diameter) and higher degrees of AV and LVOT calcification; furthermore, cover index for perimeter-derived annular diameter (a measure of degree of prosthesis oversizing) was significantly lower in the predilatation group (**Table 2**).

Procedural characteristics and in-hospital outcomes are depicted in **Table 3**. TAVI was performed under conscious sedation more frequently in the no pre-BAV group. Valve size was significantly higher in the predilatation group (p=0.036), driven by a higher percentage of M size in this group. As shown in **Figure 2**, the need for postdilatation was numerically but not statistically different after valve implantation with or without predilatation (42.9% vs. 36.0%; p=0.066). VARC-2 peri-procedural complications were similar among both groups, including second THV implantation, annular rupture, pericardial tamponade, and conversion to surgery (**Table 3**). The incidence of post-procedural moderate-to-severe PAR was similar between pre-BAV and no pre-BAV groups. Similarly, there were no significant differences in post-procedural mean AV gradient among both groups. VARC-2 device success was high and similar after TAVI with or without predilatation (91.4% vs. 94.5%; p=0.140).

Clinical outcomes at 30-days are reported in **Table 4**. The composite of all-cause mortality or any stroke at 30-days was similar in patients who underwent TAVI with or without predilatation (4.9% vs. 4.4%; p=0.743). No significant differences between both groups were observed in several 30-day clinical outcomes, including all-cause mortality, cardiovascular mortality, any stroke,

disabling stroke, hospitalization for valve-related symptoms or worsening congestive heart failure, any vascular complication, valve dysfunction requiring repeat procedure, and VARC-2 early safety composite endpoint. The rate of 30-day new PPI was similar after TAVI with or without pre-BAV (9.0% vs. 8.0%; p=0.660). The incidence of any bleeding at 30-days was significantly higher in the predilatation group (15.8% vs. 10.3%; p=0.045), driven by a higher rate of minor bleeding in this group (**Table 4**).

At subgroup analyses, no significant interactions between AV and LVOT calcification subgroups and predilatation with respect to the primary endpoints were observed (**Supplemental Figure S1**). At multivariate analyses performed to identify predictors of the primary endpoints, predilatation was not independently associated with the risk of 30-day all-cause death or stroke, post-procedural moderate-to-severe PAR, and 30-day new PPI. The following variables were identified as independent predictors of the primary endpoints: New York Heart Association functional class III-IV for the composite of all-cause death or stroke at 30-days (**Supplemental Table S2**); heavy AV calcification and postdilatation for post-procedural moderate-to-severe PAR (**Supplemental Table S3**); STS-M score and cover index for area-derived diameter for new PPI at 30-days (**Supplemental Table S4**).

Kaplan-Meier curves for 1-year all-cause mortality and stroke in patients who underwent Acurate *neo* implantation with or without pre-BAV are shown in **Figure 3**. No significant differences were observed between predilatation and no predilatation groups in the composite of all-cause mortality or stroke at 1-year (16.9% vs. 12.8%; log-rank p=0.658) and in the individual endpoints of 1-year all-cause mortality (13.3% vs. 12.2%; log-rank p=0.644) and 1-year stroke (4.5% vs. 1.3%; log-rank p=0.133).

## Discussion

The main findings of our study are as follows:

1) In our large, real-world, multicenter NEOPRO Registry, predilatation before transfemoral Acurate *neo* implantation was performed in the majority of cases (overall rate 83.3%), with a slight reduction in its use during the study period (from 95.7% in the first date quintile to 78.4% in the last date quintile).
2) Transfemoral Acurate *neo* implantation without predilatation was performed more frequently in patients with milder degrees of AV and LVOT calcification and was not associated with an increased need for postdilatation.
3) Direct TAVI with Acurate *neo* (avoiding predilatation) seems to be feasible and safe, with similar rates of 30-day all-cause mortality or stroke, post-procedural moderate-to-severe

PAR, and 30-day new PPI compared to THV implantation performed with predilatation; these findings were confirmed across AV and LVOT calcification subgroups (subgroup analyses) and after adjustment for clinical and MDCT variables including AV and LVOT calcification (multivariate analyses).

Direct TAVI (without predilatation) has emerged as an appealing option during the last few years in an effort to simplify the procedure and to avoid potential BAV-related complications [13]. This simplified approach has been increasingly studied and the feasibility of direct TAVI with the balloon-expandable Sapien THVs (Edwards Lifesciencesc, Irvine, California) and the self-expanding CoreValve THVs (Medtronic, Minneapolis, Minnesota) has been demonstrated by several studies.[14–22] The Acurate *neo* THV is a next-generation self-expanding device that has been associated with good clinical outcomes in recent studies.[4–7] A specific feature of the Acurate *neo* device is its relatively low radial force, that is probably implicated in the particularly low PPI rate observed after its implantation;[4–7] however, predilatation before THV implantation was recommended and almost always performed in early experience with Acurate *neo*.[4] In our large, real-world, multicenter NEOPRO Registry reporting data on 1,262 transfemoral Acurate *neo* implantation performed at 18 high-volume TAVI centers in the last 6 years (between January 2012 and March 2018), we observed that predilatation was performed in almost all cases during early experience (pre-BAV rate of 95.7% in the first date quintile). However, during the study period there was a slight reduction in the use of predilatation (pre-BAV rate 78.4% in the last date quintile), probably reflecting the increased confidence of some experienced TAVI operators in performing direct THV implantation also with the Acurate *neo* device.

Despite the low radial force of Acurate *neo* THV, direct valve implantation without pre-BAV was not associated with a higher rate of postdilatation, moderate-to-severe PAR, and 30-day death or stroke in our study. Furthermore, a low rate of 30-day new PPI (8.0%) was observed after direct TAVI, not significantly different compared to the rate observed after TAVI with pre-BAV. Importantly, degrees of AV and LVOT calcification were milder in the no predilatation group, potentially reflecting a selection bias on the part of the operators that preferred to avoid predilatation in less challenging anatomies. The omission of pre-BAV did not have a significant impact on primary endpoints across AV and LVOT calcification subgroups (subgroup analyses); however, considering the low number of patients with heavy AV calcification or moderate-to-severe LVOT calcification undergoing direct TAVI in our registry, this subanalysis could have been underpowered to detect a significant impact of pre-BAV across AV and LVOT subgroups. Interestingly, predilatation was not independently associated with primary endpoints also after

adjustment for several variables including AV and LVOT calcification (multivariate analyses). Independent predictors of post-procedural moderate-to-severe PAR were heavy AV calcification (as previously reported[11]) and postdilatation (which may be explained by the higher need for postdilatation in more calcified valves and challenging anatomies, eventually not avoiding residual significant PAR), whereas cover index for area-derived diameter was independently associated with new PPI at 30-days (reflecting the impact of higher degree on oversizing on PPI[11]). Of note, mean AV gradient was higher and aortic valve area was smaller in the pre-BAV group, potentially reflecting a tendency of operators to perform predilatation in cases with more severe aortic stenosis; however, these parameters of aortic stenosis severity were accounted for in multivariate analyses.

A recent small, single-center study reported the feasibility of direct TAVI with Acurate *neo* in selected patients with mild-to-moderate AV calcification, reporting similar in-hospital outcomes after TAVI with or without pre-BAV.[8] Our multicenter registry confirms the safety and feasibility of this approach in a larger, unselected population, demonstrating the lack of impact of the omission of predilatation on clinical outcomes after Acurate *neo* implantation, in line with findings observed with the Sapien and CoreValve THVs.[14–22] However, our findings should be considered as hypothesis-generating, and future prospective studies with centralized analysis are needed to definitively confirm the safety and feasibility of this straightforward, simplified Acurate *neo* implantation technique.

Our study had a retrospective observational design and, therefore, had all the usual limitations associated with this design. Furthermore, no core-laboratory analysis of MDCT data, echocardiographic outcomes, and procedural results, or independent adjudication of clinical events were performed. Of note, the semi-quantitative scoring system used for AV and LVOT calcifications was derived from a study employing a centralized MDCT data assessment,[10] hence the reproducibility in a large number of MDCT readers could be dissimilar and this could impact the study findings. Similarly, the lack of a centralized echocardiography evaluation could impact the assessment of procedural results. MDCT data was not available for all patients included in the registry, and this could have had an impact on subgroup and multivariate analyses. Moreover, the operator's decision regarding predilation was based on personal evaluation rather than on a set of prespecified guidelines.

In conclusion, transfemoral Acurate *neo* implantation without predilatation appears to be feasible and safe, especially in patients with milder degrees of AV and LVOT calcification. This simplified, direct TAVI approach is increasingly performed across high-volume TAVI centers and is associated with similar clinical outcomes compared to standard Acurate *neo* implantation (with predilatation).

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**Disclosures**

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**Figure Legends**

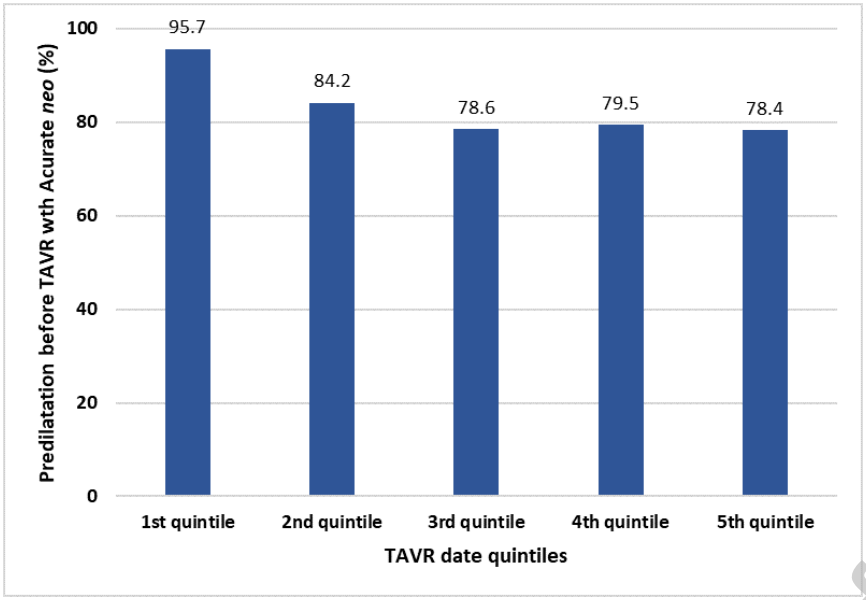


**Figure 1: Rate of predilatation across TAVI date quintiles.**

The rate of predilatation before transcatheter aortic valve implantation (TAVI) is reported across TAVI date quintiles, showing a significant reduction during the study period (p <0.001).

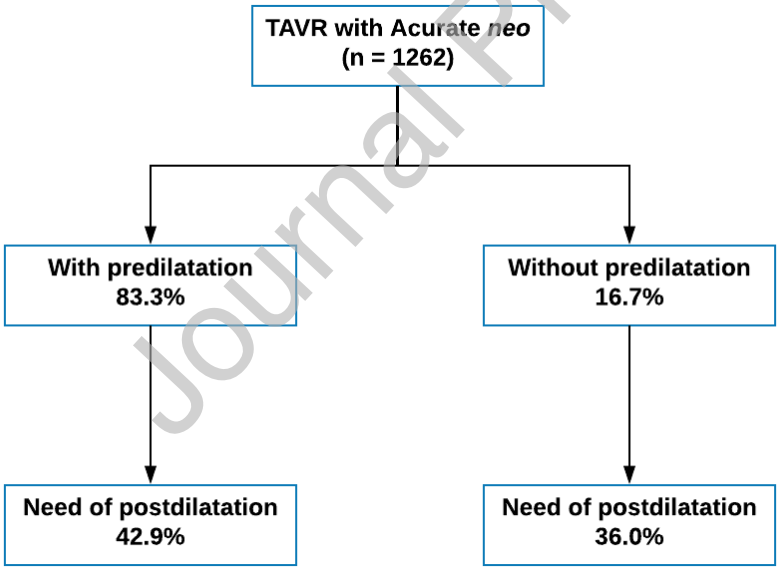


**Figure 2: Need for postdilatation after Acurate *neo* implantation with or without predilatation**.

The rate of postdilatation after valve implantation is not significantly different in the predilatation vs. no predilatation groups (42.9% vs. 36.0%; p=0.066).

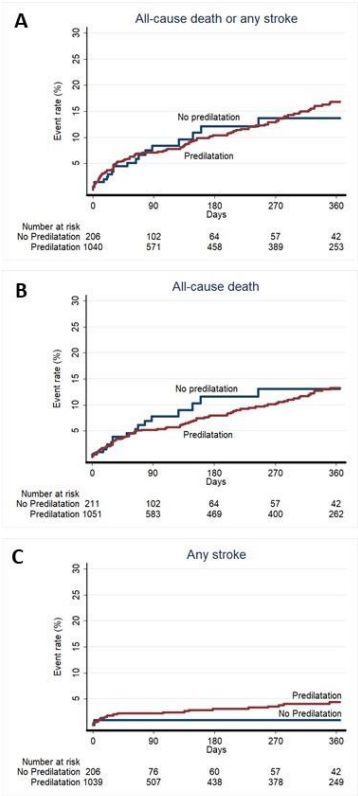


**Figure 3: 1-year mortality and stroke after Acurate *neo* implantation with or without predilatation.**

The figure shows Kaplan-Meier curves for 1-year all-cause mortality and stroke (either the composite endpoint and the two individual endpoints) in patients who have undergone transfemoral Acurate *neo* implantation with or without predilatation.

**Table 1: Baseline patients characteristics.**

| Variable | Predilatation | | p-value |
|---|---|---|---|
| | Yes (n=1051) | No (n=211) | |
| Age (years) | 81.9 ± 5.8 | 81.1 ± 5.8 | 0.074 |
| Men | 374 (35.6%) | 69 (32.7%) | 0.423 |
| Body mass index (kg/m$^2$) | 27.5 ± 5.1 | 27.2 ± 4.7 | 0.519 |
| Chronic obstructive pulmonary disease | 194 (18.5%) | 50 (23.7%) | 0.079 |
| Hypertension | 890 (87.4%) | 189 (90.9%) | 0.164 |
| Estimated glomerular filtration rate (mL/min/1.73/m$^2$) | 58.5 ± 21.2 | 57.8 ± 23.8 | 0.519 |
| Estimated glomerular filtration rate <30 mL/min/1.73/m$^2$ | 90 (8.6%) | 23 (11.0%) | 0.263 |
| Prior percutaneous coronary intervention | 306 (29.1%) | 64 (30.3%) | 0.729 |
| Prior coronary artery bypass graft | 124 (11.8%) | 23 (10.9%) | 0.711 |
| Prior balloon aortic valvuloplasty | 22 (2.4%) | 4 (2.1%) | 0.800 |
| Peripheral vascular disease | 135 (12.8%) | 21 (10.0%) | 0.244 |
| Prior stroke | 94 (9.2%) | 32 (15.4%) | **0.008** |

| | | | |
|---|---|---|---|
| Atrial fibrillation / flutter | 327 (31.4%) | 81 (38.6%) | **0.042** |
| Pacemaker or implantable cardioverter defibrillator | 127 (12.1%) | 31 (14.5%) | 0.296 |
| New York Heart Association class III-IV | 809 (77.1%) | 172 (81.5%) | 0.154 |
| Society of Thoracic Surgeons Predicted Risk of Mortality (%) | 5.0 ± 3.1 | 5.2 ± 3.7 | 0.486 |
| ***Echocardiographic data*** | | | |
| Mean aortic valve gradient (mmHg) | 45.4 ± 16.6 | 34.0 ± 13.6 | **<0.001** |
| Aortic valve area ($cm^2$) | 0.69 ± 0.19 | 0.76 ± 0.17 | **<0.001** |
| Moderate-to-severe AR | 150 (14.7%) | 27 (13.0%) | 0.515 |
| Left ventricular ejection fraction (%) | 57.0 ± 11.4 | 55.8 ± 13.7 | 0.188 |
| Severe pulmonary hypertension* | 140 (17.3%) | 29 (17.3%) | 0.984 |
| Moderate-to-severe mitral regurgitation | 234 (22.9%) | 48 (23.3%) | 0.911 |

Values are mean ± standard deviation or n/N (%). *Systolic pulmonary artery pressure on echocardiography >55 mmHg.

## Table 2: Multidetector computed tomography data.

| Variable | Predilatation | | p-value |
|---|---|---|---|
| | Yes (n=804) | No (n=182) | |
| Min annular diameter (mm) | 21.0 ± 2.0 | 20.4 ± 2.0 | **<0.001** |
| Max annular diameter (mm) | 26.3 ± 2.1 | 25.7 ± 2.4 | **<0.001** |
| Annular eccentricity | 1.26 ± 0.11 | 1.26 ± 0.12 | 0.535 |
| Annulus area ($mm^2$) | 435.5 ± 67.4 | 416.6 ± 64.5 | **0.001** |
| Annulus perimeter ($mm^2$) | 75.0 ± 5.9 | 73.4 ± 5.8 | **<0.001** |
| Area-derived annular diameter (mm) | 23.5 ± 1.8 | 23.0 ± 1.8 | **0.001** |
| Perimeter-derived annular diameter (mm) | 23.9 ± 1.9 | 23.4 ± 1.9 | **<0.001** |
| Cover index for area-derived annular diameter (%) | 6.7 ± 4.2 | 7.4 ± 4.1 | 0.058 |
| Cover index for perimeter-derived annular diameter (%) | 5.0 ± 4.6 | 6.1 ± 4.5 | **0.008** |
| Aortic valve calcification | | | **<0.001** |
| None | 1 (0.1%) | 3 (1.7%) | |
| Mild | 168 (21.1%) | 114 (63.3%) | |
| Moderate | 387 (48.6%) | 41 (22.8%) | |
| Heavy | 241 (30.2%) | 22 (12.2%) | |
| Left ventricular outflow tract calcification | | | **<0.001** |
| None | 418 (52.6%) | 123 (68.3%) | |
| Mild | 223 (28.1%) | 42 (23.3%) | |
| Moderate | 99 (12.5%) | 8 (4.4%) | |
| Severe | 55 (6.9%) | 7 (3.9%) | |

Values are mean ± standard deviation or n/N (%).

## Table 3: Procedural characteristics and early (pre-discharge) echocardiographic outcomes.

| Variable | Predilatation | | p-value |
|---|---|---|---|
| | Yes (n=1051) | No (n=211) | |
| Conscious sedation | 892 (84.5%) | 202 (95.7%) | **<0.001** |
| Valve size | | | 0.036 |
| S | 276 (26.3%) | 72 (34.1%) | |
| M | 447 (42.5%) | 73 (34.6%) | |
| L | 328 (31.2%) | 66 (31.3%) | |
| Predilatation | - | - | - |
| Postdilatation | 450 (42.9%) | 76 (36.0%) | 0.066 |

| | | | |
|---|---|---|---|
| Second transcatheter heart valve implanted | 12 (1.1%) | 2 (1.0%) | 0.806 |
| Valve embolization | 11 (1.1%) | 2 (1.0%) | 0.897 |
| Annular rupture | 2 (0.2%) | 2 (1.0%) | 0.074 |
| Pericardial tamponade | 15 (1.4%) | 5 (2.4%) | 0.317 |
| Aortic dissection | 1 (0.1%) | 0 (0.0%) | 0.654 |
| Coronary occlusion | 1 (0.1%) | 1 (0.5%) | 0.207 |
| Conversion to surgery | 12 (1.1%) | 1 (0.5%) | 0.381 |
| Mean aortic valve gradient (mmHg) | 8.5 ± 4.1 | 8.2 ± 3.8 | 0.230 |
| Mean aortic valve gradient ≥20 mmHg | 13 (1.4%) | 1 (0.5%) | 0.300 |
| Moderate-to-severe paravalvular aortic regurgitation | 55 (5.5%) | 7 (3.4%) | 0.214 |
| Left ventricular ejection fraction (%) | 58.9 ± 9.5 | 57.7 ± 12.6 | 0.158 |
| Valve Academic Research Consortium – 2 device success | 862 (91.4%) | 190 (94.5%) | 0.140 |

Values are mean ± standard deviation or n/N (%).

**Table 4: Clinical outcomes at 30 days.**

| Variable | Predilatation | | p-value |
|---|---|---|---|
| | Yes (n=1051) | No (n=211) | |
| All-cause mortality or any stroke | 51 (4.9%) | 9 (4.4%) | 0.743 |
| All-cause mortality | 30 (2.9%) | 8 (3.8%) | 0.475 |
| Cardiovascular mortality | 24 (2.3%) | 5 (2.4%) | 0.947 |
| Any stroke | 23 (2.2%) | 2 (1.0%) | 0.245 |
| Disabling stroke | 18 (1.7%) | 2 (1.0%) | 0.427 |
| Non-disabling stroke | 5 (0.5%) | 0 (0.0%) | 0.318 |
| Transient ischemic attack | 3 (0.3%) | 0 (0.0%) | 0.432 |
| Hospitalization for valve-related symptoms or worsening congestive heart failure | 10 (1.2%) | 2 (1.1%) | 0.945 |
| Myocardial infarction | 5 (0.5%) | 2 (1.0%) | 0.428 |
| Any bleeding | 156 (15.8%) | 21 (10.3%) | **0.045** |
| Life-threatening | 22 (2.2%) | 3 (1.5%) | 0.495 |
| Major | 47 (4.8%) | 9 (4.4%) | 0.836 |
| Minor | 87 (8.8%) | 9 (4.4%) | **0.036** |
| Any vascular complication | 182 (17.5%) | 31 (15.1%) | 0.390 |
| Major | 59 (5.7%) | 16 (7.8%) | 0.250 |
| Minor | 123 (11.8%) | 15 (7.3%) | 0.057 |
| Acute kidney injury stage 2-3 | 35 (3.6%) | 2 (1.0%) | 0.057 |
| Valve embolization or migration | 11 (1.1%) | 2 (1.0%) | 0.911 |
| Valve dysfunction requiring repeat procedure* | 3 (0.3%) | 0 (0.0%) | 0.432 |
| New permanent pacemaker implantation** | 82 (9.0%) | 14 (8.0%) | 0.660 |
| Valve Academic Research Consortium – 2 early safety composite endpoint | 146 (16.7%) | 27 (14.8%) | 0.521 |

Values are n/N (%). * Balloon aortic valvuloplasty, transcatheter or surgical aortic valve replacement. **Excluding patients with pacemaker at baseline.