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Validation of the VARC 3 Technical Success Definition in Patients undergoing Transcatheter Aortic Valve Replacement

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ABSTRACT

Background: The Valve Academic Research Consortium (VARC-3) has introduced a composite endpoint to assess the immediate technical success of transcatheter aortic valve replacement (TAVR).

Objectives: The authors aimed to investigate the rates, predictors, and prognostic impact of technical success in patients undergoing TAVR.

Methods: In the prospective Bern TAVR registry, patients were stratified according to VARC-3 technical success. Technical failure differentiated between vascular and cardiac complications.

Results: In a total of 1,624 patients undergoing TAVR between March 2012 and December 2019, 1,435 (88.4%) patients had technical success. Among 189 patients with technical failure, 140 (8.6%) had vascular and 49 (3.0%) had cardiac technical failure. Female sex, larger device landing zone calcium volume, and the early term of the study period were associated with an increased risk for cardiac technical failure, while higher body mass index and the use of the Prostar/MANTA compared with the ProGlide were predictors of vascular technical failure. In multivariable analysis, technical failure conferred an increased risk for cardiovascular death or stroke (HR: 2.01; 95% CI: 1.37-2.95). The adverse effect remained when stratified to cardiac (HR: 2.62; 95% CI: 1.38-4.97) or vascular technical failure (HR: 1.95; 95% CI: 1.28-2.95) and limited to the periprocedural period (0-

30 days: HR 3.42; 95% CI 2.05-5.69; 30-360 days: HR 1.36; 95% CI 0.79-2.35, p for interaction = 0.002).

Conclusions: Technical failure according to VARC-3 was observed in one out of ten patients undergoing TAVR and was associated with a 2-fold increased risk of the composite outcome at 1 year after TAVR.

Clinical Trial Registration: https://www.clinicaltrials.gov. NCT01368250.

Keywords: aortic stenosis; transcatheter aortic valve replacement; technical success; valve academic research consortium

ABBREVIATIONS

AS = aortic stenosis

TAVR = transcatheter aortic valve replacement

VARC = Valve Academic Research Consortium

CONDENSED ABSTRACT

In a prospective TAVR registry, 1,624 patients with aortic stenosis were retrospectively stratified according to the Valve Academic Research Consortium 3 (VARC-3) technical success definition. Technical success according to VARC-3 was observed in nine out of ten patients undergoing TAVR. In multivariable analysis, technical failure conferred an increased risk for cardiovascular death or stroke (HR: 2.01; 95% CI: 1.37-2.95). The adverse effect remained when stratified to cardiac (HR: 2.62; 95% CI: 1.38-4.97) or vascular technical failure (HR: 1.95; 95% CI: 1.28-2.95) and limited to the periprocedural period.

Introduction

The Valve Academic Research Consortium (VARC) definitions, providing guidance for uniform and standardized reporting of clinical outcomes, are widely accepted and updated in response to accumulating evidence, technological advancements, and increasing operator experience. The VARC has recently updated the standardized definitions of clinical endpoints for future transcatheter aortic valve replacement (TAVR) trials(1). In the updated document (VARC-3), technical success has been introduced as a new composite endpoint to replace VARC-2 device success. While the latter required echocardiographic evaluation in a resting state, technical success represents an accurate indicator of immediate success of a procedure at the time when the patients leaves the operating room(2). The effect of technical failure on clinical endpoints has not been assessed so far, but the clinical relevance of technical failure in terms of cardiovascular death or stroke is critical. In the present study, we sought to investigate the rate, predictors, and prognostic impact of the newly defined VARC-3 technical success endpoint in a contemporary TAVR population from a large prospective registry.

Methods

Study design and population

All patients undergoing TAVR at Bern University Hospital, Bern, Switzerland, are consecutively recorded in a prospective institutional database as part of the SwissTAVI registry which is mandated by the Swiss health authorities (registered at clinicaltrials.gov with NCT01368250)(3). The present analysis included patients that underwent TAVR with contemporary balloon-expandable (SAPIEN 3, SAPIEN 3 Ultra [Edwards Lifesciences, Irvine, California]) or self-expanding devices (Evolut R/PRO [Medtronic, Minneapolis, Minnesota]), Portico [Abbott, Chicago, Illinois], Symetis ACURATE/ACURATE neo [Boston Scientific, Marlborough, Massachusetts]) between August 2007 and December 2019. Patients that underwent TAVR with old devices (SAPIEN THV/XT [Edwards Lifesciences, Irvine, California], Medtronic CoreValve [Medtronic, Minneapolis, Minnesota], and Lotus/Lotus Edge [Boston Scientific, Marlborough, Massachusetts]) (n = 1,001) were excluded. The registry is approved by the Bern cantonal ethics committee, and patients provided written informed consent to participate.

TAVR procedure

TAVR was performed by transfemoral approach by default. Alternative access was reserved for patients with unfavourable peripheral anatomy and included transapical, trans-subclavian/axillary, transcarotid, and transcaval access. Device selection was performed according to

anatomical and clinical criteria during a heart team discussion. In case of transfemoral TAVR, the puncture site was closed using suture-based devices (ProGlide or Prostar, both from Abbott Vascular Inc., Santa Clara, CA, USA) by default. In case of incomplete vascular closure, a plug-based device (Angio-seal, Shibuya, Tokyo, Japan or MANTA, Teleflex, Wayne, Pennsylvania, USA), was used to achieve complete hemostasis. In case of closure failure, vessel rupture, and flow-limiting dissection or stenosis, percutaneous treatment with a balloon or a self-expanding/balloon-expandable covered/uncovered stent was performed if feasible. A catheter from the contra-lateral femoral access site was placed in the primary access as a routine practice and was used for bailout angioplasty. Surgical bailout was reserved for patients in whom a percutaneous approach was unsuccessful or not feasible. In a small number of cases, MANTA was used as the initial closure system instead of a suture-based device; catheter-based or surgical bailout was performed in case of incomplete vascular closure. Surgical cut-down was only performed in case of heavily diseased femoral access where the hemostatic devices were deemed unfeasible or for alternative access sites including transapical, trans-subclavian/axillary, and transcarotid access.

Data collection and clinical endpoints

Baseline clinical, procedural, and follow-up data were prospectively recorded in a web-based database, held at the Clinical Trials Unit of the University of Bern, Switzerland. Echocardiographic

and CT measurements were re-evaluated by dedicated imaging specialists and integrated into the database. Device landing zone calcium volume was quantified in the contrast images by using a predefined Hounsfield unit threshold of 850, as previously validated(4,5). Low coronary height was defined as either left or right coronary height ≤10 mm(6,7). Transcatheter heart valve (THV) sizing was retrospectively evaluated as previously described: the sizing was considered suboptimal if the implanted THV size was outside the recommended annular size range by manufacturers(8). Clinical follow-up data at 30 days and at 1 year were obtained by standardized interviews, documentation from referring physicians, and hospital discharge summaries. All adverse events were systematically collected and adjudicated by a dedicated clinical event committee based on the VARC definitions applicable at the time of the procedure(1,2,9). Technical success or failure according to the recently released VARC-3 definition was retrospectively adjudicated based on detailed documentation of adjudicated endpoints that form the individual components of this composite endpoint. Technical success included (1) freedom from death; (2) successful access, delivery of the device, and retrieval of the delivery system; (3) correct positioning of a single prosthetic heart valve into the proper anatomical location; and (4) freedom from surgery or intervention related to the device or to a major vascular or access-related, or cardiac structural complication. For the purpose of the present analysis,

technical failure was categorized into vascular technical failure limited to vascular complications and cardiac technical failure including all others.

Statistical analysis

Categorical variables are represented as frequencies and percentages, and the differences between groups were evaluated with the chi-square test or Fisher's exact test. Continuous variables are presented as mean values ± standard deviation (SD) and were compared between groups using Student's t-test. Cumulative incidence curves were constructed using the Kaplan-Meier method. Univariable and multivariable Cox proportional hazards models were used to calculate crude or adjusted hazard ratios (HR) and 95% confidence intervals (95% CI). In addition, landmark analyses were performed with the landmark set at 30 days after the procedure. Patients with procedural death were excluded from the outcome analyses. All variables potentially related to outcomes of interest were entered into the multivariable model and variables with a p-value <0.2 were subsequently entered in the final model. All statistical tests were two-sided and p-value of <0.05 were considered significant. Statistical analyses were performed using Stata 15.1 (StataCorp, College Station, TX, USA).

Results

Study population and baseline characteristics

A total of 1,624 patients underwent TAVR with contemporary devices between March 2012 and December 2019. All of these patients had adequate data for the evaluation of technical success/failure according to the VARC-3 definitions and were eligible for the present study (**Supplementary Figure**). Of these, 1,435 (88.4%) patients had technical success according to VARC-3. Among 189 patients (11.6%) with technical failure, 140 cases (8.6%) were related to vascular complications (vascular technical failure) and 49 (3.0%) were related to procedural death or cardiac complications (cardiac technical failure). The reasons for technical failure are shown in **Central Illustration**. In contrast, VARC-2 device success, a former technical composite endpoint, was observed in only 66.1% of patients. The high rate of device failure was largely attributable to the high incidence of prosthesis-patient mismatch (28.0%) (**Table 1** and **Supplementary Table 1**). In a cohort exclusively including transfemoral TAVR (n=1,502), technical failure occurred in 180 patients (12.0%) including 137 cases of vascular technical failure (9.1%) and 43 cases of cardiac technical failure (2.9%). When the study period was divided into tertiles (- July 22, 2016; July 22, 2016 - June 18, 2018; June 18, 2018 -), both cardiac (4.8% vs. 2.8% vs. 1.5%; P = 0.006) and vascular (12.7% vs. 7.2% vs. 5.9%; P < 0.001) technical failure tended to decrease as the period progressed.

Baseline characteristics according to technical success/failure are shown in **Table 1**. Patients with technical failure were older (age: 82.7 ± 5.6 vs. 81.7 ± 6.5; P = 0.049), had a higher body mass index (BMI) (27.8 ± 6.1 kg/m^2 vs. 26.7 ± 5.3 kg/m^2; P = 0.011) and more advanced heart failure symptoms (NYHA class III or IV: 76.2% vs. 67.3%; P = 0.016) than those with technical success. There were no significant differences in echocardiographic or CT data between the two groups.

Procedural characteristics are summarized in **Table 1**. TAVI was performed by transfemoral access in 92.5% of patients without differences among the groups. There was a difference in the type of vascular closure device used between groups (ProGlide; 41.4% vs, 78.9%; P <0.001, Prostar; 54.5% vs. 19.2%; P <0.001; MANTA; 4.1% vs. 1.9%; P = 0.117). There were no significant differences in the anesthetic strategy, valve type, valve size, and pre- or post- dilatation.

Predictors of technical failure

Variables associated with technical failure are reported in **Table 2** and **Supplementary Table 2**. In the multivariable analyses, female sex, device landing zone calcium volume (per 100 mm^3), and the first tertile of the study period were significantly associated with an increased risk for cardiac technical failure, while a higher BMI and the use of the Prostar/MANTA (compared with the ProGlide) were predictors of vascular technical failure.

Impact of technical success on cardiovascular mortality and stroke

Clinical follow-up at 1 year was complete in 1,621 patients (98.6%). Clinical outcomes at 30 days and 1 year after technical success and failure are shown in **Table 3**. At 30 days, patients with technical failure had a higher incidence of the composite endpoint of cardiovascular death or stroke (11.5% vs. 3.5%, P <0.001), cardiovascular death (6.0% vs. 1.0%, P <0.001), and stroke (7.2% vs. 2.9%, P = 0.003) compared with those with technical success.

At 1 year, the composite endpoint of cardiovascular death or stroke occurred in 20.0% of patients with technical failure and in 10.3% of patients with technical success (HR: 2.09; 95% CI: 1.45-3.02; P <0.001) (**Central Illustration**). Compared with patients with technical success, those with technical failure had higher rates of both cardiovascular death (HR: 2.09; 95% CI: 1.31-3.33; P = 0.002) and stroke (HR: 2.01; 95% CI: 1.18-3.41; P = 0.010) (**Figure 1**). The results were consistent in the cohort of transfemoral TAVR (**Supplementary Table 3**). In a landmark analysis with the landmark set at 30 days, the effect of technical failure on adverse clinical outcome was limited to the first 30 days after intervention (composite endpoint 0-30 days: HR 3.42; 95% CI 2.05-5.69; P <0.001; 30-360 days: HR 1.36; 95% CI 0.79-2.35; P = 0.266, p for interaction = 0.002) (**Figure 2**).

In a multivariable analysis, technical failure was independently associated with an increased risk of the composite of cardiovascular death or stroke at 1 year (HR: 2.01; 95% CI: 1.37-2.95; P

<0.001) (**Table 4** and **Supplementary Table 4**). The other associated factors included a history of peripheral artery disease (HR: 1.97; 95% CI: 1.35-2.89; P <0.001), NYHA III or IV (HR 1.86; 95% CI 1.23-2.82; P = 0.003), baseline moderate or greater mitral regurgitation (HR: 1.48; 95% CI: 1.05-2.10; P = 0.025), atrial fibrillation (HR: 1.40; 95% CI: 1.02-1.92; P = 0.038), and Society of Thoracic Surgeons Predicted Risk of Mortality (HR: 1.04; 95% CI: 1.0-1.08; P = 0.043).

At 1 year, the composite endpoint of cardiovascular death or stroke occurred in 24.1% of patients with cardiac technical failure (HR: 2.62; 95% CI: 1.38-4.97; P = 0.003), in 18.8% of patients with vascular technical failure (HR: 1.95; 95% CI: 1.28-2.95; P = 0.002), and in 10.3% of patients with technical success (**Supplementary Table 5**, **Central Illustration**, and **Figure 1**). In multivariable analyses, both cardiac and vascular technical failure were independently associated with an increased risk of the composite of cardiovascular death or stroke at 30 days (**Supplementary Table 6**) and 1 year (**Table 4** and **Supplementary Table 7**).

Discussion

The key findings of this study can be summarized as follows: 1) VARC-3 technical success was documented in 88.4% of patients undergoing TAVR with contemporary devices and techniques; 2) Furthermore, there was an increase in the rate of technical success (both cardiac and vascular) in

the most recent study period; 3) Female sex, larger device landing zone calcium volume, and earlier cases were independently associated with an increased risk of cardiac technical failure, while higher BMI and use of the Prostar/MANTA (compared with ProGlide) were associated with an increased risk of vascular technical failure; 4) Technical failure was associated with a 2-fold increased risk of the composite of cardiovascular death or stroke at 1 year.

VARC endpoint definitions currently serve as a reproducible and standardized tool to compare clinical results in studies in the field of transcatheter and surgical aortic valve replacement. The updated VARC-3 definitions will be instrumental in the design of future studies. VARC-3 technical success reflects successful transcatheter heart valve replacement and complete retrieval of the delivery system without procedural mortality or need for emergent surgery or intervention. In conjunction with improvements in TAVR technology and techniques, the number of procedural complications, including annular rupture, acute coronary obstruction, valve dislocation/embolization and vascular complications, decreased over recent years(3,10,11). In our prospective registry, nine out of ten patients had technical success after TAVR with contemporary devices and techniques. Technical failure was related to vascular access complications in three quarters of cases, while technical failure owing to cardiac complications occurred in 3.0% of all patients.

Prediction of technical failure is of key importance in the selection of the appropriate treatment strategy. In our study, female sex, larger device landing zone calcium volume, and the early term of the study period were associated with an increased risk of cardiac technical failure. Female patients are more likely to have unfavorable aortic root anatomies, such as greater degree of aortic valve calcification or smaller valve anatomies, which may explain at least in part a higher incidence of cardiac complications compared with male patients(12-14). Device landing zone calcification is a risk factor for paravalvular regurgitation, annular rupture, and device embolization(5,15). Anatomical characteristics of the aorto-valvular complex become increasingly important with the expansion of TAVR to low risk patients. A gradual decrease in cardiac technical failure over time may be explained by both accumulating center experience(16,17) as well as technical refinements of contemporary devices(18,19).

The use of the Prostar/MANTA (compared with ProGlide) and higher BMI were identified as an independent predictor of vascular technical failure, which is in consistent with previous studies(20-23). The enhanced efficacy of ProGlide as compared with Prostar has been previously reported(20,21). In a randomized controlled trial comparing MANTA versus ProGlide, there was no significant difference in the primary endpoint of access site-related vascular complications. However, patients treated with MANTA required numerically more covered stents and surgical

bailouts, which are considered as vascular technical failure in the present study(23). Excessive subcutaneous tissue at the site of femoral access complicates percutaneous suture-mediated vascular closure due to the long distance between the presutured knots and the arterial wall, thus explaining the increased risk of vascular complications(24). Therefore, particular caution is warranted in the selection of the puncture site and the preparation of the femoral access in obese patients, and a bailout strategy for vascular complications by use of plug-based devices or covered stent implantation from a cross-over approach should be at hand. It should also be noted that despite the higher incidence of major vascular complications an inverse relationship between obesity and mortality in TAVR populations has been suggested in previous studies(22,25). Excessive abdominal fat requires particular caution in gaining femoral access, but does not lessen the effectiveness of TAVR overall and should not deter from a transcatheter treatment strategy.

Technical failure importantly affects clinical outcomes. Of note, both cardiac and vascular technical failures were independently associated with a 2.6-fold and 1.9-fold increased risk of cardiovascular death and stroke at 1 year following TAVR. This finding underscores the need for further improvements in TAVR devices, techniques, and patient selection(15,26-28).

Even after more than 15 years of evolution, TAVR remains a rapidly evolving field with iterative refinements in both devices and techniques(18,19,29-31). Our findings underscore that

technical success, the newly defined endpoint in the updated VARC-3 document, is highly clinically relevant and may serve as one of the pivotal endpoints to evaluate the improvement of TAVR or for head-to-head comparisons of new devices in future clinical trials.

Study Limitations

The findings of our study should be interpreted in light of several limitations. First, this was a single-center observational study based on a prospective registry. Thus, the findings may have been confounded by unmeasured or unrecognized variables. In turn, we provide comprehensive data on more than 1,600 patients evaluated for technical success from a large prospective registry adhering to high standards of data quality with rigorous data collection, standardized follow-up, independent analysis of echocardiographic and CT data by dedicated imaging specialists, and independent event adjudication. Second, the results of the present study reflect the experience of a single high-volume center with high-experience operators and may not be generalizable to other heart centers. Third, vascular anatomy (diameter, tortuosity, distribution and extent of calcification) was not systematically assessed in the present study. Future studies with detailed vascular assessment may further improve the risk stratification for vascular complications. Finally, although we included only patients treated with contemporary devices, minor refinements have been made to some of the

devices as well as to the implantation techniques during the study period. Thus, the study cohort may not represent the population treated with the most updated TAVR devices and techniques.

Conclusion

One out of ten patients undergoing TAVR with a contemporary device experiences technical failure, according to the newly defined endpoint in the updated VARC-3 document. Technical failure was associated with a 2-fold increased risk of cardiovascular death and stroke at 1 year after TAVR. VARC-3 technical success may represent a useful endpoint to assess iterations of future TAVR devices in clinical trials.

Perspective

What Is Known?

Valve Academic Research Consortium endpoint definitions provide as a reproducible and standardized tool to compare clinical results in studies related to transcatheter and surgical aortic valve replacement. In the updated document, a new composite endpoint, technical success, has been introduced to capture the immediate success of a procedure, but it has not been validated.

What Is New?

In the prospective TAVR registry, VARC-3 technical success was documented in approximately 90% of patients undergoing TAVR with contemporary devices and techniques. Technical failure was associated with a 2-fold increased risk of the composite of cardiovascular death or stroke at 1 year.

What Is Next?

Our findings underscores the need for further improvements in TAVR devices, techniques, and patient selection.

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Figure Legends

Central Illustration. Prevalence, Reasons, and Prognostic Impact of Technical Success.

Pie chart illustrating the proportions of technical success, cardiac technical failure, and vascular technical failure (upper left). Table showing reasons for technical failure (upper right). Kaplan-Meier curve for the composite of cardiovascular death or stroke comparing technical failure (lower left) or cardiac and vascular technical failure (lower right) vs. technical success. Hazard ratios and p-values were calculated with the use of Cox proportional hazards models. CI = confidence interval; HR = hazard ratio; TAVR = transcatheter aortic valve replacement.

Figure 1. Kaplan-Meier curves according to technical success.

Kaplan-Meier curves for clinical outcomes comparing technical failure (left) or cardiac and vascular technical failure (right) vs. technical success. Hazard ratios and p-values were calculated with the use of Cox proportional hazards models. Abbreviations as in **Central Illustration**.

Figure 2. Landmark analysis of the cumulative incidence of clinical outcomes between 30 days and 1 year.

Abbreviations as in **Central Illustration**.

Central Illustration.

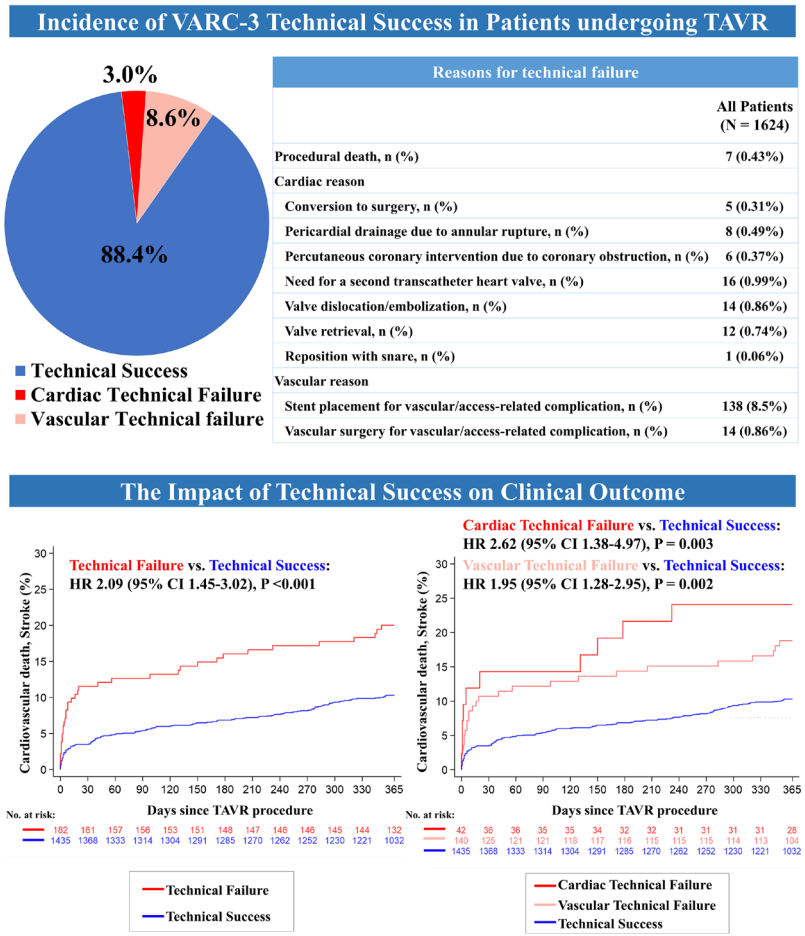


Figure 1.

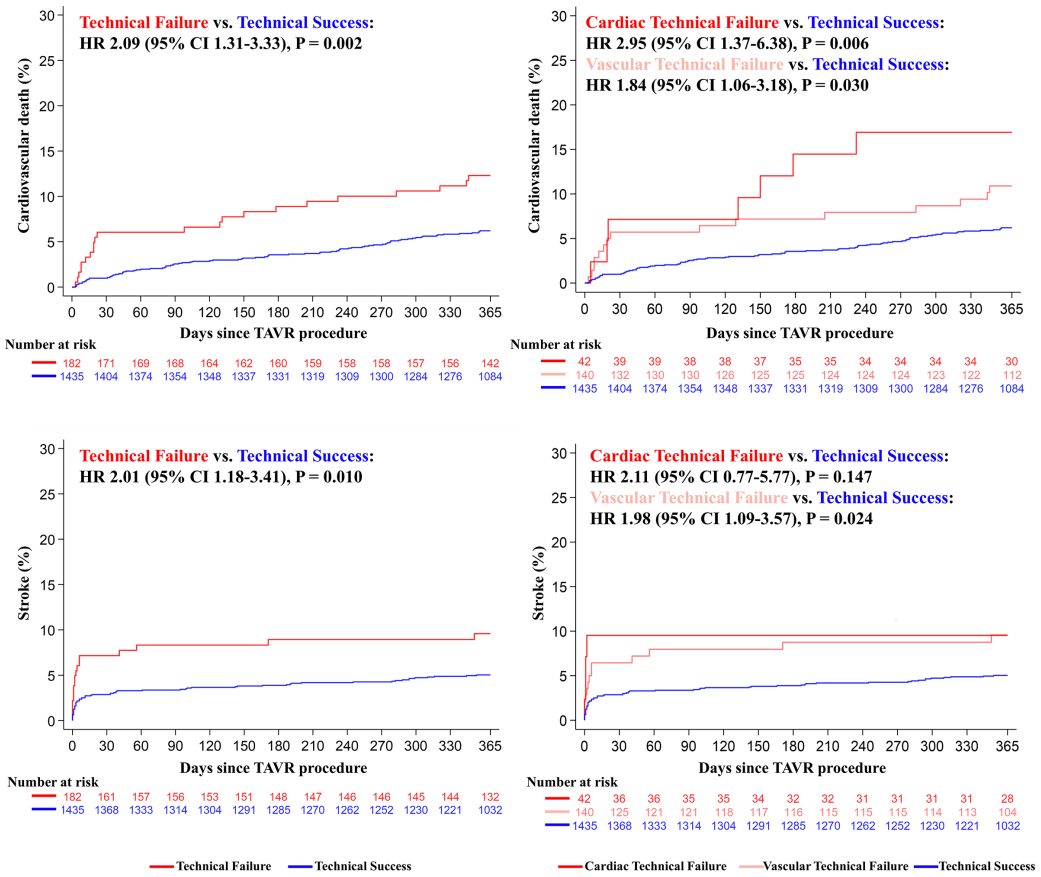
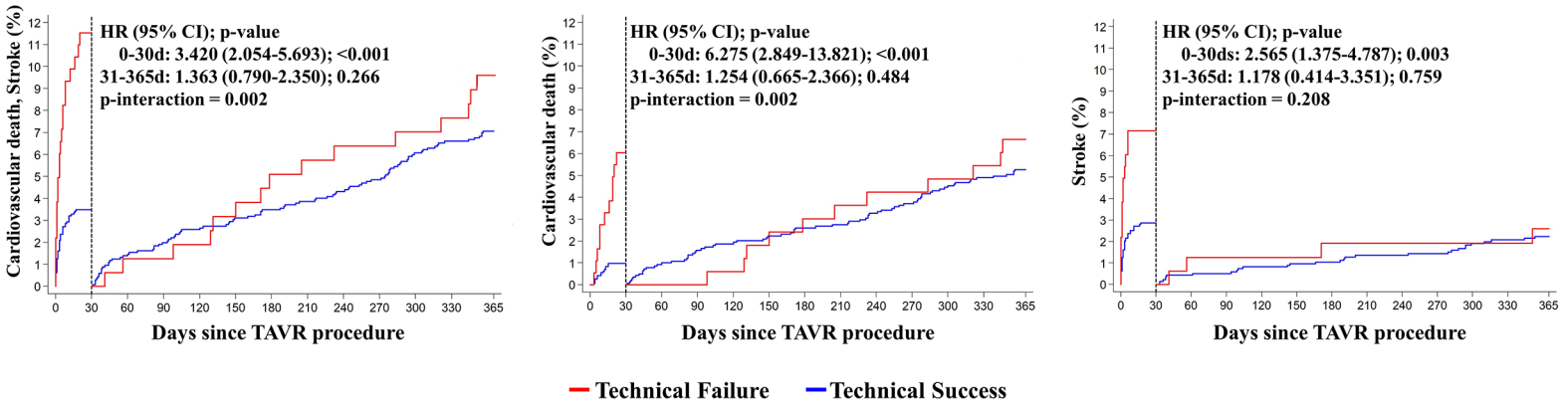

Technical Failure vs. Technical Success:
HR 2.09 (95% CI 1.31-3.33), P = 0.002
Cardiovascular death (%)
Days since TAVR procedure
Number at risk
182 171 169 168 164 162 160 159 158 158 157 156 142
1435 1404 1374 1354 1348 1337 1331 1319 1309 1300 1284 1276 1084
Cardiac Technical Failure vs. Technical Success:
HR 2.95 (95% CI 1.37-6.38), P = 0.006
Vascular Technical Failure vs. Technical Success:
HR 1.84 (95% CI 1.06-3.18), P = 0.030
Cardiovascular death (%)
Days since TAVR procedure
Number at risk
42 39 39 38 38 37 35 35 34 34 34 34 30
140 132 130 130 126 125 125 124 124 124 123 122 112
1435 1404 1374 1354 1348 1337 1331 1319 1309 1300 1284 1276 1084
Technical Failure vs. Technical Success:
HR 2.01 (95% CI 1.18-3.41), P = 0.010
Stroke (%)
Days since TAVR procedure
Number at risk
182 161 157 156 153 151 148 147 146 146 145 144 132
1435 1368 1333 1314 1304 1291 1285 1270 1262 1252 1230 1221 1032
Technical Failure
Technical Success
Cardiac Technical Failure vs. Technical Success:
HR 2.11 (95% CI 0.77-5.77), P = 0.147
Vascular Technical Failure vs. Technical Success:
HR 1.98 (95% CI 1.09-3.57), P = 0.024
Stroke (%)
Days since TAVR procedure
Number at risk
42 36 36 35 35 34 32 32 31 31 31 31 28
140 125 121 121 118 117 116 115 115 115 114 113 104
1435 1368 1333 1314 1304 1291 1285 1270 1262 1252 1230 1221 1032
Cardiac Technical Failure
Vascular Technical Failure
Technical Success

Figure 2.


Cardiovascular death, Stroke (%)
HR (95% CI); p-value
0-30d: 3.420 (2.054-5.693); <0.001
31-365d: 1.363 (0.790-2.350); 0.266
p-interaction = 0.002
Days since TAVR procedure
Cardiovascular death (%)
HR (95% CI); p-value
0-30d: 6.275 (2.849-13.821); <0.001
31-365d: 1.254 (0.665-2.366); 0.484
p-interaction = 0.002
Days since TAVR procedure
Stroke (%)
HR (95% CI); p-value
0-30ds: 2.565 (1.375-4.787); 0.003
31-365d: 1.178 (0.414-3.351); 0.759
p-interaction = 0.208
Days since TAVR procedure
Technical Failure
Technical Success

Tables

Table 1. Baseline and procedural characteristics according to technical success

	All patients (N = 1624)	**Technical failure (N = 189)**	**Technical Success (N = 1435)**	**P value**
Age, years	81.8 ± 6.4	82.7 ± 5.6	81.7 ± 6.5	0.049
Female, n (%)	834 (51.4%)	106 (56.1%)	728 (50.7%)	0.188
Body mass index, kg/m^2	26.8 ± 5.4	27.8 ± 6.1	26.7 ± 5.3	0.011
STS-PROM, %	4.9 ± 3.9	5.2 ± 3.9	4.8 ± 3.9	0.226
NYHA III or IV, n (%)	1109 (68.4%)	144 (76.2%)	965 (67.3%)	0.016
Urgent case, n (%)	31 (1.9%)	4 (2.1%)	27 (1.9%)	0.777
TAVR for degenerative prosthesis, n (%)	53 (3.3%)	11 (5.8%)	42 (2.9%)	0.047
Comorbidities				
Hypertension, n (%)	1425 (87.7%)	172 (91.0%)	1253 (87.3%)	0.158
Diabetes mellitus, n (%)	430 (26.5%)	49 (25.9%)	381 (26.6%)	0.930

Renal failure (eGFR <60 ml/min/1.73 m^2), n (%)	1097 (67.7%)	132 (69.8%)	965 (67.4%)	0.563
Coronary artery disease, n (%)	969 (59.7%)	108 (57.1%)	861 (60.0%)	0.478
Peripheral artery disease, n (%)	193 (11.9%)	20 (10.6%)	173 (12.1%)	0.633
Echocardiography				
Indexed aortic valve area, cm^2/m^2	0.25 ± 0.09	0.24 ± 0.09	0.25 ± 0.09	0.136
Mean aortic valve gradient, mmHg	38.1 ± 16.9	39.3 ± 18.8	37.9 ± 16.6	0.289
LVEF, %	55.1 ± 14.5	56.1± 13.4	55.0 ± 14.7	0.308
Moderate/severe aortic regurgitation, n (%)	133 (9.2%)	21 (11.9%)	112 (8.8%)	0.209
Moderate/severe mitral regurgitation, n (%)	305 (20.5%)	35 (19.9%)	270 (20.6%)	0.921
Moderate/severe tricuspid regurgitation, n (%)	186 (12.7%)	16 (9.2%)	170 (13.2%)	0.180
Computed tomography				
Bicuspid valve, n (%)	77 (5.4%)	11 (6.7%)	66 (5.3%)	0.461
Annulus area, mm^2	451.6 ± 88.2	447.1 ± 88.6	452.2 ± 88.1	0.490
Left coronary height, mm	14.5 ± 3.5	14.7 ± 3.3	14.5 ± 3.5	0.560
Right coronary height, mm	17.4 ± 3.2	17.0 ± 3.4	17.4 ± 3.2	0.118
Low coronary height, n (%)	124 (8.8%)	12 (7.5%)	112 (9.0%)	0.656

Aortic angulation degree, °	49.9 ± 9.5	50.6 ± 10.8	49.8 ± 9.3	0.307
Annulus eccentricity	0.77 ± 0.06	0.77 ± 0.07	0.78 ± 0.06	0.906
Device landing zone calcium, mm^3	301.6 ± 308.9	311.0 ± 329.5	300.4 ± 306.3	0.691
Porcelain aorta, n (%)	53 (3.8%)	5 (3.1%)	48 (3.8%)	0.827
Procedure				
General anesthesia, n (%)	288 (17.7%)	31 (16.4%)	257 (17.9%)	0.686
Femoral main access site, n (%)	1502 (92.5%)	180 (95.2%)	1322 (92.1%)	0.143
Type of valve, n (%)				0.420
Balloon-expandable	892 (54.9%)	109 (57.7%)	783 (54.6%)	0.438
Self-expandable	732 (45.1%)	80 (42.3%)	652 (45.4%)	0.438
Valve size, mm	26.4 ± 2.3	26.4 ± 2.1	26.4 ± 2.3	0.999
Suboptimal sizing, n (%)	251 (18.1%)	30 (19.2%)	221 (18.0%)	0.661
Pre-dilation, n (%)	970 (59.8%)	109 (58.0%)	861 (60.0%)	0.635
Post-dilation, n (%)	462 (28.5%)	49 (26.1%)	413 (28.8%)	0.492
Vascular closure device use, n (%)	1510 (93.0%)	180 (95.2%)	1330 (92.7%)	0.227
Type of device				<0.001

ProGlide, n (%)	991 (74.5%)	65 (42.5%)	926 (78.7%)	<0.001
Prostar, n (%)	310 (23.3%)	82 (53.6%)	228 (19.4%)	<0.001
MANTA, n (%)	29 (2.2%)	6 (3.9%)	23 (2.0%)	0.134
Device success according to VARC-2, n (%)	1073 (66.1%)	105 (55.6%)	968 (67.5%)	0.001

Values are mean ± SD or n (%).

Device success according VARC-2 defined as absence of procedural death and correct positioning of a single prosthetic heart valve into the proper anatomical location and intended performance of the prosthetic heart valve (no prosthesis-patient mismatch and mean aortic valve gradient <20 mmHg, and no moderate or severe prosthetic valve).

Low coronary height was defined as either left or right coronary height ≤10 mm.

eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement; VARC = Valve Academic Research Consortium.

31 **Table 2.** Predictors of technical failure

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Cardiac Technical Failure			**Vascular Technical Failure**		
Final model			**Final model**		
Variables	**Odds ratio (95% CI)**	**P value**	**Variables**	**Odds ratio (95% CI)**	**P value**
Female sex	2.20 (1.09-4.43)	0.028	Age (per 10 years)	1.33 (0.90-1.98)	0.155
Device landing zone calcium total (per 100mm^3)	1.12 (1.03-1.21)	0.007	Body mass index (per 10 kg/m^2)	1.84 (1.29-2.64)	<0.001
Tertiles of the study periods			STS-PROM	1.05 (0.99-1.12)	0.125
1st	[Ref.]		Closure device used*		

2nd	0.56 (0.28-1.12)	0.102	ProGlide	[Ref.]	
3rd	0.28 (0.11-0.70)	0.006	ProStar	5.76 (2.63-12.62)	<0.001
			MANTA	5.81 (1.89-17.85)	0.002
			Tertiles of the study periods		
			1st	[Ref.]	
			2nd	0.93 (0.45-1.91)	0.839

			3rd	1.26 (0.50-3.21)	0.627

Variables with a p-value <0.2 were entered in the final mode. Full models were shown in **Supplemental Table 2**.

+ Tertiles of the study period (1st: - July 22, 2016; 2nd: July 22, 2016 - June 18, 2018; 3rd: June 18, 2018 -).

* Closure device was not entered for all patients before 2016 and asssumed Prostar used in n=168 patients.

CI = confidence interval; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve ireplacement.

Table 3. Clinical outcomes comparing technical success and technical failure

	Technical Success	Technical Failure	Technical Failure vs. Technical Success	
	(N = 1435)	**(N = 182)***	**HR (95% CI)**	**P value**
At 30 days+				
Composite of cardiovascular death or stroke, n (%)	50 (3.5%)	21 (11.5%)	3.42 (2.05-5.69)	<0.001
Cardiovascular death, n (%)	14 (1.0%)	11 (6.0%)	6.27 (2.85-13.82)	<0.001
Stroke, n (%)	41 (2.9%)	13 (7.2%)	2.57 (1.37-4.79)	0.003
At 1 year‖				
Composite of cardiovascular death or stroke, n (%)	144 (10.3%)	36 (20.0%)	2.09 (1.45-3.02)	<0.001
Cardiovascular death, n (%)	86 (6.2%)	22 (12.3%)	2.09 (1.31-3.33)	0.002
Stroke, n (%)	70 (5.0%)	17 (9.6%)	2.01 (1.18-3.41)	0.010

Number of first events (% from Kaplan-Meier estimates) and HR (95% CI) from Cox's regression (Wald p-value).

* Excluded 7 patients who died during the procedure. + Censored at 30 days. ‖ Censored at 365 days.

CI = confidence interval; HR = hazard ratio.

41 **Table 4.** Predictive factors for the composite of cardiovascular death or stroke at 1 year after TAVR.

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Technical Failure			**Stratified Cardiac or Vascular Technical Failure**		
Final model			**Final model**		
Variables	**HR (95% CI)**	**P value**	**Variables**	**HR (95% CI)**	**P value**
Technical success	[Ref.]		Technical success	[Ref.]	
Technical failure	2.01 (1.37-2.95)	<0.001	Cardiac Technical failure	1.85 (1.19-2.86)	0.006
Urgent case	1.97 (0.84-4.60)	0.118	Vascular Technical failure	2.59 (1.31-5.10)	0.006
NYHA III or IV	1.86 (1.23-2.82)	0.003	Age (per 10 years)	1.99 (0.85-4.63)	0.112
STS-PROM	1.04 (1.00-1.08)	0.043	Female sex	1.86 (1.23-2.82)	0.003
Atrial fibrillation	1.40 (1.02-1.92)	0.038	Body mass index (per 10 kg/m^2)	1.04 (1.00-1.08)	0.039
Peripheral artery disease	1.97 (1.35-2.89)	<0.001	Urgent case	1.39 (1.02-1.91)	0.040
Baseline MR ≥moderate	1.48 (1.05-2.10)	0.025	NYHA III or IV	1.96 (1.34-2.86)	<0.001

			STS-PROM	1.48 (1.04-2.09)	0.028

Variables with a p-value <0.2 were entered in the final mode. Full models were shown in **Supplemental Tables 2** and **4**.

Excluded are the n=7 patients who died during the procedure.

CI = confidence interval; HR = hazard ratio; MR = mitral regurgitation; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

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