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ORIGINAL RESEARCH

Efficacy and Safety of ProGlide Versus Prostar XL Vascular Closure Devices in Transcatheter Aortic Valve Replacement: The RISPEVA Registry

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BACKGROUND: Transcatheter aortic valve replacement (TAVR) requires large-bore access, which is associated with bleeding and vascular complications. ProGlide and Prostar XL are vascular closure devices widely used in clinical practice, but their comparative efficacy and safety in TAVR is a subject of debate, owing to conflicting results among published studies. We aimed to compare outcomes with Proglide versus Prostar XL vascular closure devices after TAVR.

METHODS AND RESULTS: This large-scale analysis was conducted using RISPEVA, a multicenter national prospective database of patients undergoing transfemoral TAVR treated with ProGlide versus Prostar XL vascular closure devices. Both multivariate and propensity score adjustments were performed. A total of 2583 patients were selected. Among them, 1361 received ProGlide and 1222 Prostar XL. The predefined primary end point was a composite of cardiovascular mortality, bleeding, and vascular complications assessed at 30 days and 1-year follow-up. At 30 days, there was a significantly greater reduction of the primary end point with ProGlide versus Prostar XL (13.8% versus 20.5%, respectively; multivariate adjusted odds ratio, 0.80 [95% CI, 0.65–0.99]; *P*=0.043), driven by a reduction of bleeding complications (9.1% versus 11.7%, respectively; multivariate adjusted odds ratio, 0.76 [95% CI, 0.58–0.98]; *P*=0.046). Propensity score analysis confirmed the significant reduction of major adverse cardiovascular events and bleeding risk with ProGlide. No significant differences in the primary end point were found between the 2 vascular closure devices at 1 year of follow-up (multivariate adjusted hazard ratio, 0.88 [95% CI, 0.72–1.10]; *P*=0.902). Comparable results were obtained by propensity score analysis. During the procedure, compared with Prostar XL, ProGlide yielded significant higher device success (99.2% versus 97.5%, respectively; *P*=0.001).

CONCLUSIONS: ProGlide has superior efficacy as compared with Prostar XL in TAVR procedures and is associated with a greater reduction of composite adverse events at short-term, driven by lower bleeding complications.

REGISTRATION INFORMATION: URL: clinicaltrials.gov; Unique identifier: NCT02713932.

Key Words: ProGlide ■ Prostar ■ transcatheter aortic valve replacement ■ vascular closure devices

Transcatheter aortic valve replacement (TAVR) has become the treatment of choice for patients with symptomatic severe aortic stenosis. TAVR is associated with vascular and bleeding complications despite the continuous technical refinements with significant downsizing of the large-bore delivery devices.[1,2]

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CLINICAL PERSPECTIVE

What Is New?

- ProGlide versus Prostar XL, 2 widely used vascular closure devices in transcatheter aortic valve replacement were compared in the RISPEVA database.
- As compared with Prostar XL, ProGlide use reduced composite adverse outcomes driven by a reduction in bleeding complications at 30-day follow-up but not afterwards.
- As compared with Prostar XL, ProGlide was associated with the highest device procedural success.

What Are the Clinical Implications?

- Despite the technology improvements of transcatheter aortic valve replacement devices, the still frequent rates of bleeding and vascular complications after transcatheter aortic valve replacement demand adequately powered randomized trials and large-scale analyses comparing the efficacy and safety profile of various vascular closure device types to optimize the access-related outcomes associated with this procedure.

Nonstandard Abbreviations and Acronyms

STS	Society of Thoracic Surgery
TAVR	transcatheter aortic valve replacement
VCD	vascular closure device

The optimal management of access site with current vascular closure devices (VCDs) is therefore pivotal to improve clinical outcomes after TAVR.[3] Prostar XL and ProGlide (Abbott) are 2 VCDs widely used in clinical practice for TAVR, but their short- and medium-term comparative efficacy and safety is currently a subject of debate, owing to substantial heterogeneity among published reports in the number of included patients, study design, and follow-up time.[4–8]

We aimed to investigate the procedural, 30-day, and 1-year comparative performance of ProGlide versus Prostar XL in a large cohort of patients undergoing transfemoral TAVR prospectively followed in a continuously updated national registry database.

METHODS

Study Population and Design

RISPEVA is a multicenter prospective study, which addressed the procedural, 30-day, and 1-year comparative performance of the ProGlide versus Prostar XL VCDs in patients undergoing transfemoral TAVR (Figure 1). The RISPEVA registry (ID: NCT02713932) has been endorsed by the Italian Society of Invasive Cardiology (GISE). Details on the registry are reported elsewhere.[9] Briefly, RISPEVA is a prospective database designed to address complications and outcomes with ProGlide or Prostar XL VCDs in TAVR involving over 20 Italian centers. Data were collected between March 2012 and July 2019. Centers contributing to this study have long-standing and high-volume experience in TAVR. Relevant baseline information, as well as procedural, 30-day, and 1-year clinical outcomes, were entered into prespecified electronic case report forms. The authors declare that all supporting data are available within the article. The study received approval by local ethics committees of all participating centers, and patients signed a written informed consent form.

Study Definitions

The primary end point was addressed at 30 days and 1 year and predefined as the composite of cardiovascular mortality, bleeding, and vascular complications. Clinical events were classified according to Valve Academic Research Consortium-2 criteria.[10] Information on follow-up events was site-reported and adjudicated by a trained physician-investigator. Secondary end points were the individual components included in the primary outcome, procedural complications, and length of hospital stay. Device success occurred if the optimal hemostasis was attained at the end of the procedure. First device failure was defined as the failure of the first closure device (ProGlide or Prostar XL) to achieve haemostasis at the arteriotomy site. In case of multiple events for any of the explored outcomes (>1 episode), the first occurring event contributed to the analyses.

Access-Site Management

The preclosure technique was performed in all procedures. We performed contralateral angiography to the access site in all patients to confirm the accuracy of the femoral puncture, the integrity of the vessel and ascertain the onset of access-site vascular complications. The optimal deployment technique of 2 ProGlide VCDs during the procedure was defined following standard recommendations[3] as the rotation of the 2 devices in opposite sides at 30° to 45°, to create an interrupted X figure, and then closure of the arteriotomy was achieved at the end of the procedure by tying down the 2 knots using the 2 node pushers sequentially.

Statistical Analysis

Categorical variables are reported as number (percentage) and continuous variables as mean (SD).

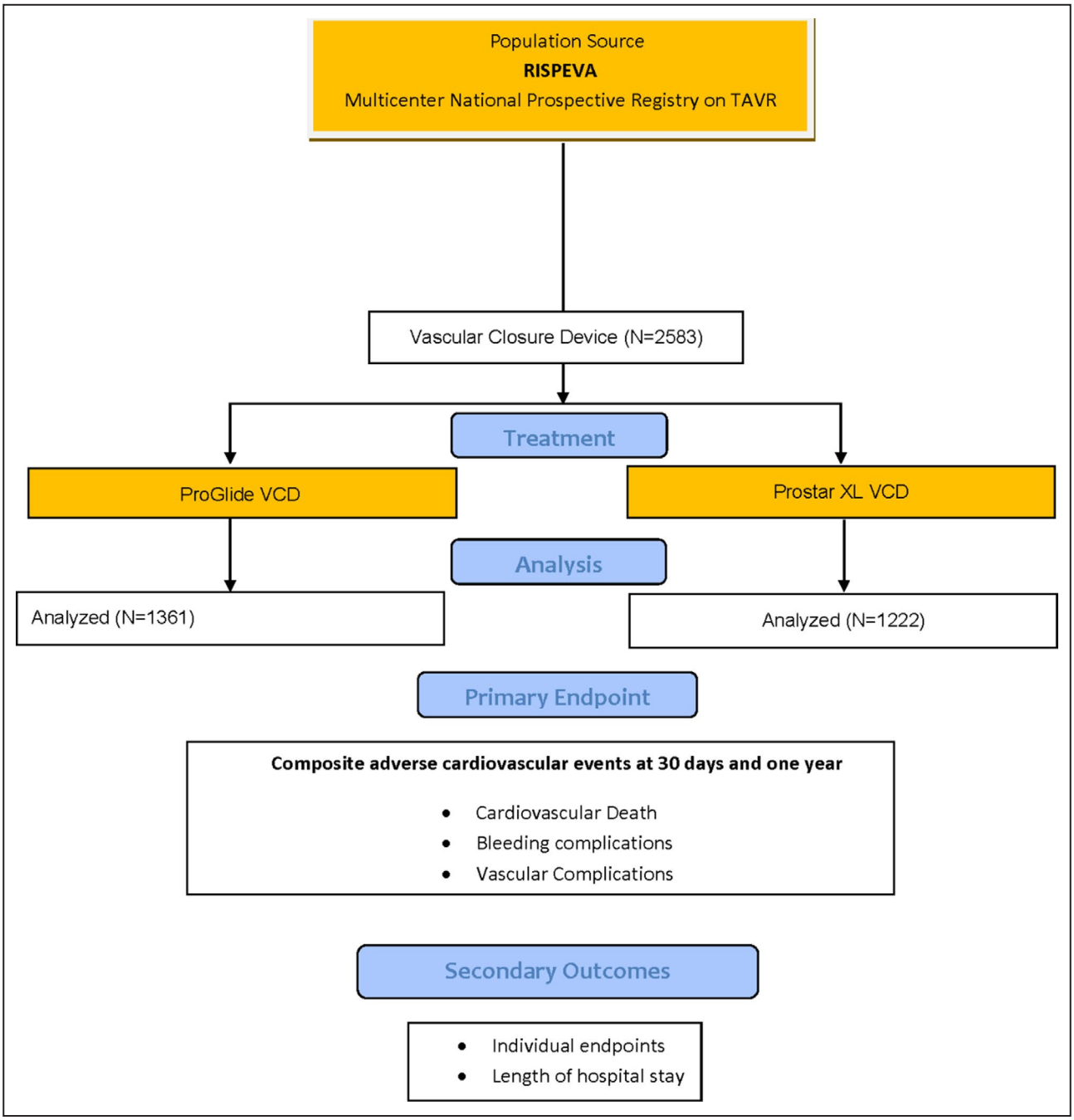

Figure 1. Flowchart of the RISPEVA study.
VCD indicates vascular closure device.

Categorical variables were compared by χ^2 or Fisher exact tests, as appropriate. Continuous data were analyzed by independent-samples *t* test. To determine independent predictors of outcomes at 30 days and 1 year after TAVR in the ProGlide versus Prostar XL, univariate and multivariate analysis on the full set of data were performed using logistic regression and Cox regression analysis. Potential confounders were entered into the logistic and Cox model on the basis of known clinical relevance or of associations (P<0.10) observed at univariate analysis; final variable selection was performed by a logistic or Cox regression model with LASSO (least absolute shrinkage and selection operator) penalty and a tuning parameter selected by cross-validation, which allows to minimize overfitting.[11] A list of covariates considered for inclusion in the multivariate model is presented in Table S1.

The final variables included in the multivariate model were age, surgical risk estimated with the Society of

Thoracic Surgery (STS) score, coronary artery disease, frailty status, anticoagulant therapy, hemoglobin level, platelet count, diabetes mellitus, chronic kidney disease, obesity, New York Heart Association class at admission, hypertension, peripheral artery disease, sheath size, TAVR device, and vascular calcifications. The results of the logistic regression analysis are presented as unadjusted and adjusted odds ratio (ORs) with 95% CIs. The results of the Cox regression at 1 year of follow-up are presented both as unadjusted and adjusted hazard ratios with 95% CIs.

Propensity score matching was used to identify a cohort of patients with similar baseline characteristics. The propensity score was estimated with the use of a nonparsimonious multivariable logistic regression model.[12] Matching was performed with the use of a 1:1 matching protocol without replacement (greedy-matching algorithm), with a caliper width equal to 0.2 of the SD of the logit of the propensity score, as this value was associated with minimized mean squared error of the estimated treatment effect.[13] The list of included variables in the propensity score is reported in Table S2. The R MatchThem package was used for the matching procedure. Logistic regression and Cox proportional hazards regression analyses were performed on the matched pairs. All analyses were performed using STATA (version 16.0; StataCorp LLC) and R Project (version 3.6.2) for statistical computing.

A $P<0.05$ was considered statistically significant for all analyses. For the subgroup analyses, P interaction was calculated and a value <0.10 was considered significant.

RESULTS

Study Population

A total of 2583 patients undergoing TAVR were included. Demographic, clinical, and outcome data of patients treated with ProGlide were compared with those of patients receiving Prostar XL. All TAVR procedures were performed via femoral access with local anesthesia. Clinical, echocardiographic, and procedural characteristics at presentation are reported in Table 1. A preprocedural screening of vascular anatomy of iliac-femoral arteries using multidetector computed tomography was performed during the TAVR planning, to assess the presence and severity of atherosclerotic disease and determine the feasibility of a femoral approach. The average age in the ProGlide cohort was 84.5±6.1 years, compared with 83.4±2 in the Prostar XL group. Patients treated with ProGlide had higher values of average STS score as compared with those receiving Prostar XL (7.20±3.7 versus 6.35±3.45, $P=0.051$) and presented with higher New York Heart Association classes ($P<0.001$) (Table 1). In terms of procedural characteristics, ProGlide deployment was associated with a significantly greater device success rate than Prostar XL (99.2% versus 97.5%, $P=0.001$) (Table 1). Both balloon expandable and self-expanding transcatheter valves were used in the 2 cohorts. Access fluoroscopy time (seconds) was longer in the Prostar XL group (29.9±83 versus 24.1±100, $P=0.013$). An optimal implantation technique of the 2 ProGlide VCDs was achieved in 98% of treated patients. The annual rates of ProGlide versus Prostar XL use in the registry are presented in Figure S1.

Primary Outcome

The incidence of the primary end point in the ProGlide versus Prostar XL is presented in Figure 2. At 30 days, compared with Prostar XL, ProGlide yielded a significantly lower risk of the composite primary end point (13.8% versus 20.5%; multivariate adjusted OR, 0.80 [95% CI, 0.65–0.99]; $P=0.043$) (Figure 2).The reduction was driven by significantly lower bleeding complications in the ProGlide cohort (9.1% versus 11.7%; multivariate adjusted OR, 0.76 [95% CI, 0.58–0.98]; $P=0.046$) (Table 2). Consistently with the multivariate adjustment, propensity score analysis confirmed the composite outcome significant reduction with ProGlide versus Prostar XL (propensity adjusted OR, 0.78 [95% CI, 0.63–0.97]; $P=0.031$) (Figure 2), owing to the significantly lower bleeding risk associated with ProGlide (propensity adjusted OR, 0.74; 95% CI, 0.57–0.98 [$P=0.032$]) (Table 2).

At 1-year follow-up there were no significant differences in the primary end point between the 2 cohorts (multivariate adjusted hazard ratio, 0.88; 95% CI, 0.72–1.10 [$P=0.90$]) (Figure 2). Similar results were achieved using propensity scores (Figure 2).

Primary Outcome in Prespecified Subgroups

The 30-day primary outcome was explored in prespecified subgroups. When compared with Prostar XL, the risk of the primary end point remained lower in the ProGlide group, regardless of sex, presence of obesity, diabetes mellitus, chronic kidney disease, sheath diameter size, vascular tortuosity, calcifications, and sheath-to-femoral artery ratio. A significantly greater event reduction was noted with ProGlide in obese patients (29.6% versus 49%; OR, 0.43 [95 CI, 0.29–0.65]; P interaction 0.04) and in procedures requiring sheath diameter >18F (9.2% versus 27.3%; OR, 0.47 [95 CI, 0.24–0.90]; P interaction 0.05) (Figure 3). No significant differences emerged at 1 year for the explored subgroups, with nonsignificant P for interactions (Table S3).

Table 1. Baseline Clinical, Echocardiographic and Procedural Characteristics of Patients Treated With ProGlide Versus PROSTAR

	ProGlide (n=1361)	Prostar XL (n=1222)	*P* Value
Clinical characteristics			
Age, mean±SD, y	84.5±6.1	83.4±5.2	0.212
Women, n (%)	787 (57.8)	704 (57.6)	0.914
Body mass index, kg/m^2	26.18±4.6	26.36±4.2	0.341
Coronary artery disease, n (%)	509 (37.4)	424 (34.7)	0.203
Diabetes mellitus, n (%)	354 (26.0)	361 (29.5)	0.472
Arterial hypertension, n (%)	694 (51.0)	588 (48.1)	0.423
STS score, mean±SD	7.20±3.7	6.35±3.45	0.051
Euroscore II	8.88±7.3	5.81±3.9	0.073
NYHA class, n (%)			<0.001
I	29 (2.1)	16 (1.3)	
II	540 (39.7)	358 (29.3)	
III	724 (53.2)	769 (62.9)	
IV	68 (5.0)	81 (6.6)	
Prior cardiac surgery, n (%)	200 (14.7)	163 (13.3)	0.201
Prior stroke, n (%)	16 (1.2)	23 (1.9)	0.144
Echocardiographic characteristics			
LVEF, mean±SD	50.2±9.8	52.03±10.2	0.652
Aortic valve area, cm^2±SD	0.43±0.14	0.42±0.38	0.711
Peak gradient, mean±SD, mm Hg	77.9±23.3	78.6±21.2	0.083
Baseline mean gradient, mean±(SD), mm Hg	49.1±18.9	49.4±14.5	0.192
Porcelain aorta, n (%)	159 (11.7)	100 (8.2)	
Bicuspidy, n (%)			<0.001
Type 0	16 (1.2)	2 (0.2)	
Type 1	18 (1.3)	10 (0.8)	
Type 2	1 (0.1)	2 (0.2)	
Procedural characteristics			
Device success, n (%)	1350 (99.2)	1191 (97.5)	0.001
Prosthesis type			<0.001
Sapien/Sapien XT, n (%)	313 (23.0)	241 (19.7)	
Sapien 3 ultra	54 (4.0)	17 (1.4)	
Corevalve/evolute R	423 (31.1)	527 (43.1)	
Evolute Pro	124 (9.1)	42 (3.4)	
Portico	250 (18.4)	37 (3)	
Other	195 (14.4)	359 (29.4)	
Contrast, mL	165.1±100	158±83	0.182
Access fluoroscopy time, s	24.1±100	29.98±83	0.013

LVEF indicates left ventricular ejection fraction; NYHA New York Heart Association; and STS score, Society of Thoracic Surgeons 30-day mortality score.

Secondary End Points

At 30-day follow-up, cardiovascular mortality risk was comparable, with no significant differences between the 2 groups both by multivariate (multivariate adjusted OR, 1.14; 95% CI, 0.61–2.11 [*P*=0.662]) and propensity score analysis (propensity adjusted OR, 1.02; 95% CI, 0.53–1.95 [*P*=0.215]). A significant reduction of any bleeding complications, was observed in patients treated with ProGlide versus Prostar XL, which was confirmed both in multivariate (9.1% versus 11.7%; multivariate adjusted OR, 0.76 [95% CI, 0.58–0.98]; *P*=0.046) and propensity score analysis (propensity adjusted OR, 0.74 [95% CI, 0.57–0.98]; *P*=0.032) (Table 2). The reduction of vascular complications with ProGlide versus Prostar XL was numerical but not significant (Table 2). At 1 year, no significant differences were found between the 2 treatments with respect to individual end points (Table 3).

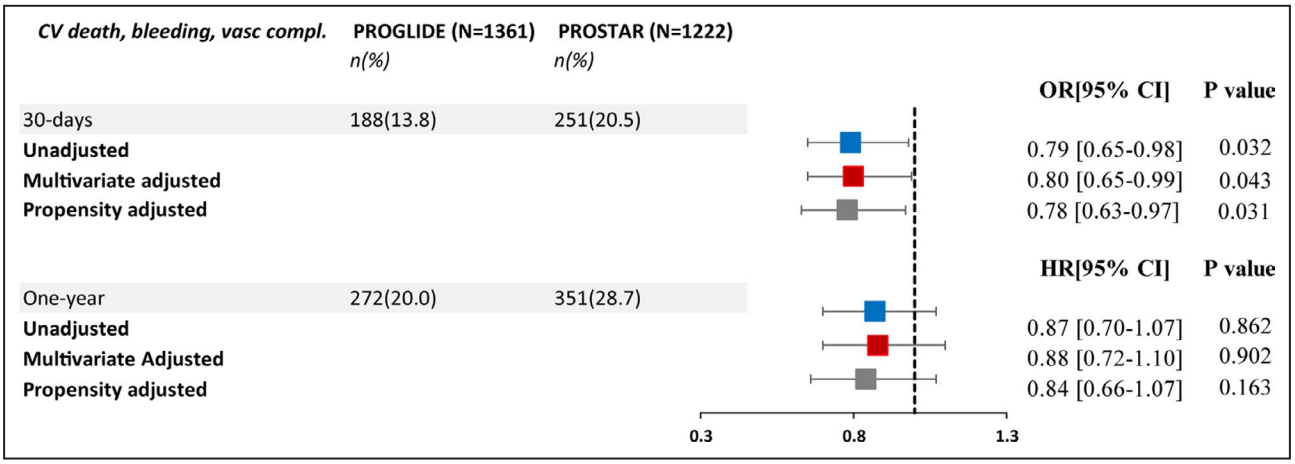

Figure 2. Primary end point (cardiovascular death, bleeding and vascular complications) risk at 30-day and 1-year follow-up unadjusted and adjusted with multivariate and propensity score methods.
Univariate, multivariate and propensity score–adjusted analyses are presented. The variables included in the multivariate model are age, surgical risk estimated with the Society of Thoracic Surgery score, coronary artery disease, frailty status, anticoagulant therapy, hemoglobin level, platelet count, diabetes mellitus, chronic kidney disease, obesity, New York Heart Association class at admission, hypertension, peripheral artery disease, sheath size, transcatheter aortic valve replacement device, and vascular calcifications. The list of covariates included in the propensity score are listed in Table S2. HR, hazard ratio; n, clinical events in the ProGlide and Prostar XL cohorts; and OR, odds ratio.

Periprocedural Complications

During the procedural phase, ProGlide, as compared with Prostar XL, yielded significantly lower rates of first device failure (1.9% versus 3.9%, respectively; *P*=0.002) and hematoma (0.7% versus 1.8%, respectively; *P*=0.012) but higher rates of vascular stenosis (0.3% versus 1.3%, respectively; *P*=0.014) (Figure 4). Hospitalization was shorter in the ProGlide versus Prostar XL groups (7.0±4.2 versus 8.3±5.3 days, respectively; *P*=0.043) (Figure S2).

DISCUSSION

TAVR is currently the treatment of choice for patients with symptomatic severe aortic stenosis. Transfemoral approach has become the standard route for TAVR procedure. Despite the TAVR device technology improvements, bleeding and vascular complications still occur. Thus, assessment of the comparative efficacy and safety profiles of VCDs has major clinical relevance in TAVR.

RISPEVA is a multicenter study designed to compare prospectively ProGlide versus Prostar XL, 2 suture-based VCDs widely used in TAVR procedures.

The main findings from this large-scale VCD-based analysis of 2583 patients with TAVR are that: (1) ProGlide, as compared with Prostar XL, was associated with a greater reduction of composite adverse cardiovascular events, driven by lower bleeding complications at 30 days but not at 1 year of follow-up; (2) the event reduction with ProGlide was more pronounced in selected

Table 2. Individual Outcomes at 30 Days With ProGlide Versus Prostar XL

	ProGlide N=1361	Prostar XL N=1222	Unadjusted OR (95% CI)	*P* Value	Multivariate Adjusted OR (95% CI)	*P* Value	Propensity Adjusted OR (95% CI)	*P* Value
	n (%)	n (%)						
Cardiovascular death	21 (1.5)	21 (1.7)	1.13 (0.60–2.15)	0.691	1.14 (0.61–2.11)	0.662	1.02 (0.53–1.95)	0.215
Any bleeding	124 (9.1)	144 (11.7)	0.76 (0.59–0.98)	0.033	0.76 (0.58–0.98)	0.046	0.74 (0.57–0.98)	0.032
Life-threatening or major bleeding	48 (3.5)	59 (4.8)	0.77 (0.51–1.15)	0.212	0.71 (0.47–1.07)	0.107	1.02 (0.73–1.41)	0.891
Minor bleeding	76 (5.5)	85 (6.9)	0.78 (0.57–1.03)	0.182	0.79 (0.57–1.09)	0.152	0.52 (0.34–0.80)	<0.001
Any vascular complications	116 (8.5)	138 (11.2)	0.82 (0.67–1.07)	0.153	0.90 (0.69–1.16)	0.434	0.86 (0.65–1.11)	0.271
Major vascular complications	36 (2.7)	40 (3.3)	0.86 (0.60–1.23)	0.424	0.74 (0.79–2.06)	0.311	0.85 (0.65–1.11)	0.253
Minor vascular complications	80 (5.9)	98 (8.0)	0.75 (0.55–1.01)	0.065	0.78 (0.75–1.06)	0.119	0.90 (0.65–1.52)	0.522

Univariate, multivariate, and propensity score–adjusted analyses are presented. The variables included in the multivariate model are age, surgical risk estimated with the Society of Thoracic Surgery score, coronary artery disease, frailty status, anticoagulant therapy, hemoglobin level, platelet count, diabetes mellitus, chronic kidney disease, obesity, New York Heart Association class at admission, hypertension, peripheral artery disease, sheath size, transcatheter aortic valve replacement device, and vascular calcifications. The list of covariates included in the propensity score are listed in Table S2. HR indicates hazard ratio; n (%), number (percentage) of clinical events in the PROGLIDE vs PROSTAR; N, total number of patients enrolled; and OR, odds ratio.

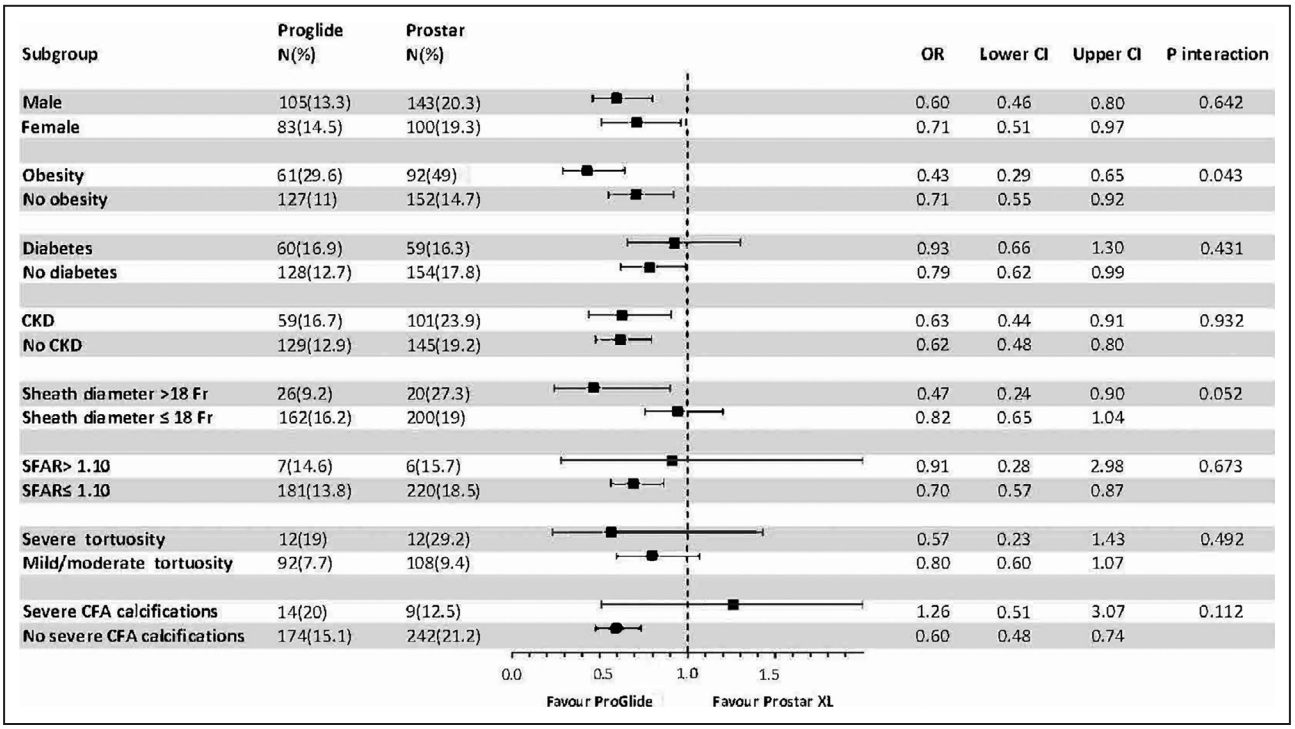

Figure 3. Primary end point (cardiovascular death, bleeding and vascular complications) risk at 30-day follow-up with ProGlide vs Prostar XL in prespecified subgroups.
CFA indicates common femoral artery; CKD, chronic kidney; N, number of events in each group; OR, odds ratio; and SFAR, sheath-to-femoral artery ratio.

populations such as obese patients and those treated with larger diameters sheaths; and (3) ProGlide conferred greater procedural efficacy than Prostar XL, carrying higher rates of device success and a lower risk of hematoma.

As compared with early TAVR studies,[14] cumulative rates of bleeding and vascular complications in TAVR have declined in more contemporary reports[15] with the availability of lower profile delivery systems, but they still remain a frequent complication of TAVR.

These complications lead to a worse prognosis and longer hospital stay, particularly in patients at higher cardiovascular risk.[14–17] Therefore, optimal access site management with a good vessel hemostasis is a cardinal step for the success of the TAVR procedure.[16] Within this framework, technical devices deployed to close vascular access play a key role in minimizing these complications.

Available studies comparing the ProGlide versus Prostar XL suture-based VCDs for TAVR were

Table 3. Individual Outcomes at 1 Year With ProGlide Versus Prostar XL

	ProGlide N=1361	Prostar XL N=1222	Unadjusted HR (95% CI)	*P* Value	Multivariate Adjusted HR (95% CI)	*P* Value	Propensity Adjusted HR (95% CI)	*P* Value
	n (%)	n (%)						
Cardiovascular death	73 (5.4)	66 (5.4)	1.21 (0.86–1.72)	0.261	1.18 (0.82–1.69)	0.368	1.23 (0.86–1.75)	0.242
Any bleeding	171 (12.5)	196 (16.0)	0.80 (0.62–1.02)	0.073	0.82 (0.61–1.09)	0.173	0.88 (0.38–1.99)	0.755
Life-threatening or major bleeding	77 (5.6)	85 (7.0)	0.83 (0.61–1.14)	0.275	1.01 (0.71–1.42)	0.951	0.89 (0.65–1.23)	0.494
Minor bleeding	94 (6.8)	111 (9.0)	0.72 (0.49–1.07)	0.574	0.89 (0.59–1.33)	0.243	0.69 (0.45–1.03)	0.072
Any vascular complications	160 (11.7)	189 (15.5)	0.82 (0.63–1.06)	0.123	0.85 (0.65–1.10)	0.235	0.83 (0.65–1.07)	0.161
Major vascular complications	79 (5.8)	81 (6.6)	0.94 (0.68–1.30)	0.772	0.82 (0.58–1.16)	0.276	0.88 (0.66–1.18)	0.413
Minor vascular complications	81 (6.0)	108 (8.8)	0.78 (057–1.04)	0.092	0.80 (0.59–1.08)	0.162	0.84 (0.65–1.09)	0.191

Univariate, multivariate and propensity score–adjusted analyses are presented. The variables included in the multivariate model are age, surgical risk estimated with the Society of Thoracic Surgery score, coronary artery disease, frailty status, anticoagulant therapy, hemoglobin level, platelet count, diabetes mellitus, chronic kidney disease, obesity, New York Heart Association class at admission, hypertension, peripheral artery disease, sheath size, transcatheter aortic valve replacement device, and vascular calcifications. The list of covariates included in the propensity score are listed in Table S2. HR indicates hazard ratio; n (%), number (percentage) of clinical events in the ProGlide vs Prostar XL; N, total number of patients enrolled; and OR, odds ratio.

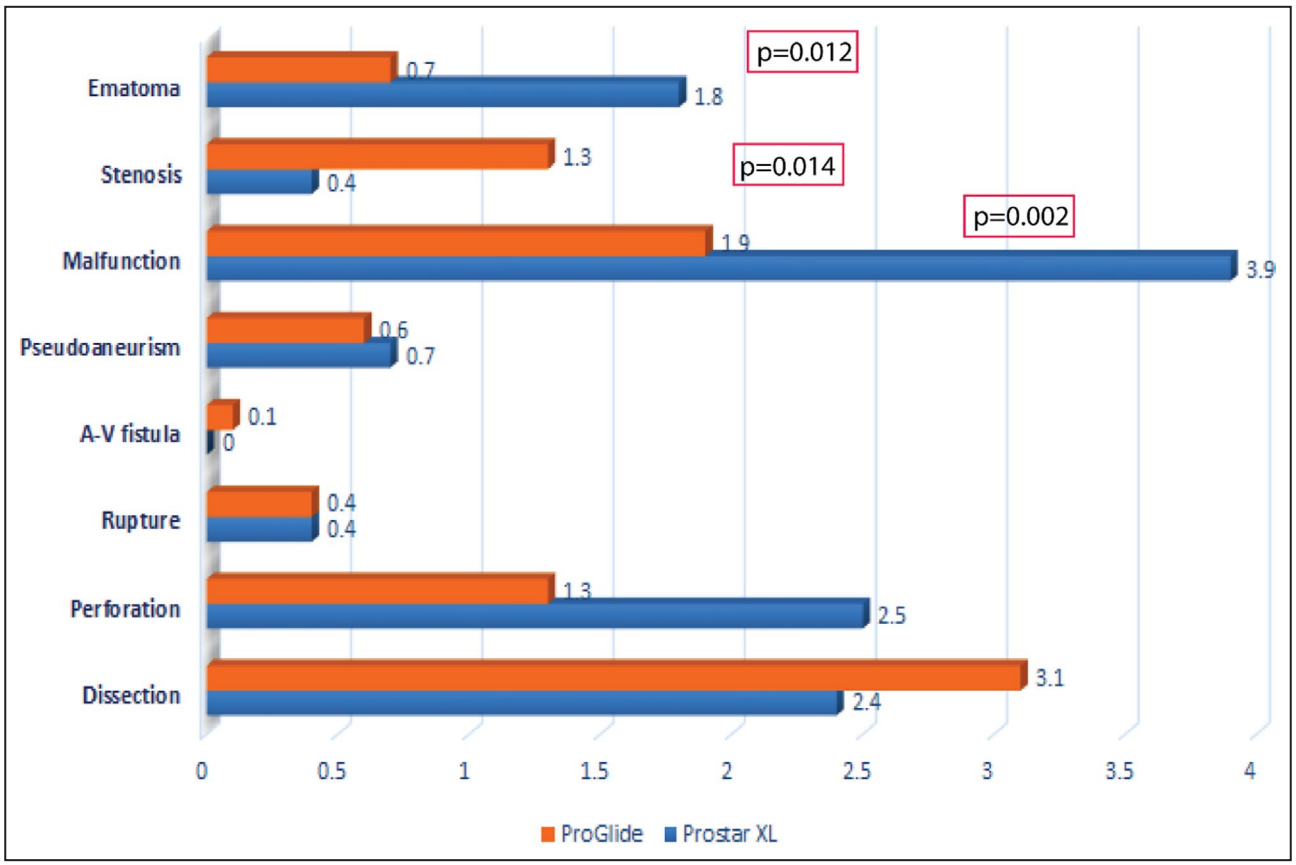

Figure 4. **Procedural vascular and bleeding complications with ProGlide vs Prostar XL.**

of great value to the interventional community since they provided first results on the comparative performance of the 2 VCDs, but they largely varied in the number of included patients and were often small in sample size, retrospective or single center by design, or without a comparator group. Thus, these figures did not allow us to reach a definitive answer regarding the clinical efficacy of ProGlide versus Prostar XL. A previous report including 558 patients treated with ProGlide versus Prostar XL in TAVR found higher rates of closure device success and lower bleeding complications in the ProGlide cohort.[8] Lower rates of bleeding and vascular complications at 30 days were also noted in a post hoc analysis in the Bivalirudin Versus Heparin Anticoagulation in Transcatheter Aortic Valve Replacement (BRAVO) study, which enrolled 756 patients.[18] These observations were not confirmed in another single-center retrospective database of 278 patients.[19] In a previous report from our group including a smaller number of patients with a shorter follow-up time, the efficacy and safety of both devices was shown, with a potential signal of bleeding reduction with ProGlide.[20] Within this framework, the current lack of head-to-head powered randomized studies prevents to estimate precisely the efficacy and safety profile of these VCDs in the TAVR setting.

The results from the RISPEVA database are in agreement with previous studies showing a bleeding reduction with ProGlide versus Prostar XL. Our report expands on previous analyses by including a larger number of patients (n=2583) enrolled prospectively and offers the distinct analysis of procedural, 30 day, and 1-year follow-up data. To our knowledge, this is the largest-scale contemporary analysis to investigate the performance at 30 days and 1 year of ProGlide and Prostar XL VCDs in TAVR. Results were confirmed using robust adjustments methods both by multivariate and propensity score models.

The findings of this large-scale study clearly indicate that ProGlide use significantly reduces the risk of the composite primary end point, driven by a risk reduction of bleeding complications >20%. The decline in bleeding risk with ProGlide use is directionally consistent with those of previous studies that included on average >300 patients,[8,18,21] allowing in aggregate to provide a more definitive estimation of the overall bleeding reduction with ProGlide versus Prostar XL in larger populations (Figure 5).

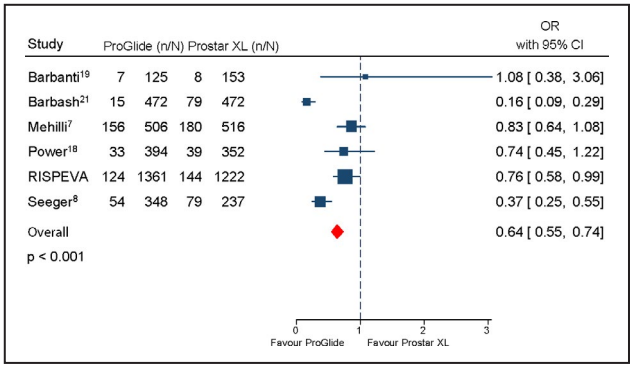

Figure 5. Bleeding outcomes at 30 days among studies with ≥100 patients comparing ProGlide vs Prostar XL.
The size of the marker is proportional to the statistical weight of the study. Individual and pooled odds ratios (ORs) are reported.

The underlying mechanism of lower bleeding complications with ProGlide versus Prostar XL should be enquired further but it may reside in the inherent differences between the 2 devices. The separation of subcutaneous tissue before needle placement as well as the mandatory use of only one bulkier device to close the access, are potential contributing factors of the higher rates of access-related complications with Prostar XL. In particular, in the event of Prostar XL malpositioning, the fact that only one device can be used might lead to higher rates of closure failure and vascular complications. On the contrary, a second ProGlide device is often used and a third device, such as a collagen-based closure device, may be employed if complete hemostasis is not achieved. Moreover, ProGlide has been demonstrated to promote primary intention healing with less scarring, ultimately reducing time to hemostasis.[22]

Of note, in the prespecified subgroup analysis, a greater primary end point reduction was observed in obese patients and procedures requiring larger femoral sheaths. This finding may reflect the relevance of the increased bleeding risk profile in these subgroups and the ensuing need for undertaking optimal measures to identify the best devices to manage the vascular access in certain higher-risk populations undergoing TAVR.

The analysis of landmark time intervals contributed to identifying the time window of the greatest event reduction associated with ProGlide versus Prostar XL, which occurred within 30 days after TAVR, but not afterward. This finding is in agreement with previous data suggesting that bleeding and vascular complications occur predominantly within 30 days after the TAVR procedure,[23] which is the most vulnerable time window.

In our analysis, the efficacy of ProGlide was already evident at the end of the TAVR procedure during the access closure, when it yielded greater device success rates with lower rates of hematoma in comparison to Prostar XL. We also noted higher rates of vascular stenosis with ProGlide versus Prostar XL. This complication was, however, observed exclusively in patients in whom the closure technique was suboptimal (<2%). This finding underlines the importance to deploy 2 ProGlide orthogonally to each other (typically at 10 o'clock and 2 o'clock) before serial dilation and insertion of the large bore sheath, to prevent vessel narrowing. Another preventive measure, particularly in small femoral arteries, may be the use of one ProGlide only, eventually associated with the deployment of a collagen-based closure device.

Currently, VCDs other than Proglide or Prostar XL have been made commercially available, which are based on collagen-based technology. A preliminary retrospective report of 222 patients pointed to the efficacy of these VCDs,[4] although a possible incomplete apposition of the collagen plug, which may have led to perivascular bleeding, was noted in other studies.[24] Future adequately powered randomized studies should compare suture-based with these other VCD types.

The findings of the current study provide a more robust estimate of the comparative efficacy and safety of 2 widely used suture-based VCDs in clinical practice and may positively influence current practice.

Limitations

The RISPEVA study is observational by design, presenting the limitations common to all nonrandomized studies, which are prone to unmeasured confounders. On the other hand, the prospective conduction and the multicenter design, as well as data collection in prespecified electronic case report forms, support our final hypothesis. Indeed, the consistency of estimates in the univariate, multivariate, propensity and sensitivity analyses performed corroborates the final assumptions.

CONCLUSIONS

Findings from the RISPEVA registry indicate that ProGlide has superior efficacy to Prostar XL at 30 days and is associated with a lower risk of adverse cardiovascular events, driven by a reduction of bleeding risk. This difference disappears at 1 year of follow-up. Based on these findings, ProGlide should be preferred to Prostar XL in TAVR procedures.

APPENDIX

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Supplementary Materials

Tables S1–S3
Figures S1–S2

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SUPPLEMENTAL MATERIAL

The RISPEVA registry

Table S1. List of covariates considered for inclusion in the multivariate model.

Age	**LVEF**	**Albuminemia**
Creatinine	Clopidogrel	LVEF
CAD	Smoke	Dyslipidemia
Prasugrel	BNP	White blood cells
Carotid stenosis	Prior PTA	Prior PCI
Syncope	Valvuloplasty	Haemoglobin
Vessel calcifications	CKD	Gender
Diabetes Mellitus	TAVR device	Frailty status
NYHA class	Vessel tortuosity	Hypertension
STS score	Haemoglobin	Sheath size
OAT	Obesity	Peripheral artery disease

CKD= chronic kidney disease; OAT=oral anticoagulant therapy; NYHA= New York Heart Association; STS= Society of Thoracic Surgery;EF=ejection fraction; PTA= percutaneous transluminal angioplasty; PCI= percutaneous coronary intervention; CAD= coronary artery disease; BNP= brain natriuretic peptide.

Table S2. List of covariates included in the propensity score.

Vessel calcifications	**CKD**	**Gender**
Diabetes Mellitus	TAVR device	Frialty score
NYHA class	Vessel tortuosity	Hypertension
STS score	Haemoglobin	Sheath size
OAT	Obesity	Peripheral artery disease

CKD= chronic kidney disease; OAT=oral anticoagulant therapy; NYHA= New York Heart Association; STS= Society of Thoracic Surgery.

Table S3. Primary endpoint (cardiovascular death, vascular and bleeding complications) risk at one-year follow-up with ProGlide vs Prostar XL in prespecified subgroups.

	HR(95%CI)	P interaction
Male	0.87(0.71-1.08)	0.192
Female	1.08(0.85-1.38)	
Obesity	0.99(0.92-1.07)	0.801
No obesity	1.01(0.63-1.65)	
Diabetes	1.0(0.74-1.36)	0.743
No diabetes	0.94(0.77-1.14)	
CKD	0.96(0.72-1.29)	1.030
No CKD	0.96(0.78-1.18)	
Sheath diameter>18 Fr	0.78(0.44-1.36)	0.542
Sheath diameter≤18 Fr	0.94(0.78-1.13)	
SFAR >1.10	0.95(0.41-2.21)	0.982
SFAR≤1.10	0.96(0.81-1.12)	
Severe Tortuosity	0.80(0.38-1.69)	0.693
Mild/Moderate tortuosity	0.94(0.74-1.20)	

HR = hazard ratio; CI =confidence interval; CKD= chronic kidney; SFAR= sheat-to-femoral artery ratio. CFA= common femoral artery. Fr=French.

Figure S1. Utilization Rates (%) of Proglide and Prostar XL across the years of enrollment.

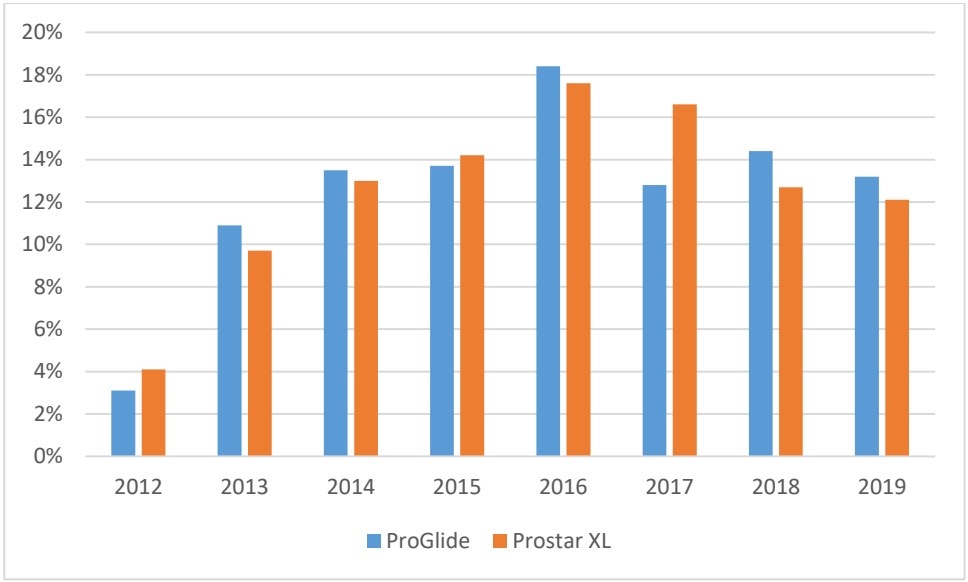

Figure S2. Average (left panel) and cumulative (right panel) hospitalization (days) in patients receiving ProGlide vs Prostar XL.