

## ORIGINAL ARTICLE

# How accurate are manufacturers' recommendations in determining ineligibility for transfemoral transcatheter aortic valve implantation?



Beytullah Çakal<sup>a,\*</sup>, Sinem Çakal<sup>a,b</sup>, Oguz Karaca<sup>a</sup>, Filiz Kizilirmak Yilmaz<sup>a</sup>,  
 Hacı Murat Gunes<sup>a</sup>, Arzu Yıldırım<sup>a</sup>, Yeliz Guler<sup>a</sup>, Özgür Ulaş Ozcan<sup>a</sup>, Bilal Boztosun<sup>a</sup>

<sup>a</sup> Istanbul Medipol University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey

<sup>b</sup> Haseki Training and Research Hospital, Cardiology Clinic, Istanbul, Turkey

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## KEYWORDS

Transcatheter aortic valve implantation;  
 Aortic valve disease;  
 Complications;  
 Vascular access

## Abstract

**Introduction:** Up to one-third of patients indicated for transcatheter aortic valve implantation (TAVI) may be unsuitable for transfemoral TAVI (TF-TAVI) according to manufacturers' recommendations and numerous professional societies.

**Objective:** This study aimed to investigate the predictive value of manufacturers' guidelines for major vascular access site complications using the Perclose ProGlide device.

**Methods:** Among 208 patients undergoing TF-TAVI, 144 patients (69.2%) were deemed eligible for TF-TAVI according to the manufacturer's instructions. A minimal lumen diameter (MLD) of the femoral artery below the manufacturer's specified limits and/or the presence of circumferential calcification were the reasons for ineligibility. Calcium score (CS), sheath-to-femoral artery ratio (SFAR) and MLD were estimated from computed tomography imaging. Vascular complications (VCs) (defined according to VARC-2 criteria) were retrospectively compared.

**Results:** Patients in the ineligible group had higher SFAR ( $1.13 \pm 0.15$  vs.  $0.88 \pm 0.107$ ,  $p < 0.001$ ) and CS ( $1.66 \pm 0.99$  vs.  $1.24 \pm 0.73$ ;  $p = 0.003$ ), and significantly lower MLD ( $7.72 \pm 1.03$  vs.  $6.31 \pm 0.96$  mm;  $p < 0.001$ ) compared to the eligible group. Major (6.3% vs. 12.3%,  $p = 0.13$ ) and minor VCs (10.4% vs. 15.6%,  $p = 0.29$ ) were similar in the eligible and ineligible groups. The ineligible group had higher rates of rupture (0.7% vs. 6.3%;  $p = 0.03$ ). SFAR was the only independent predictor of major VCs (OR 469.1, 95% CI 4.95–44466.57,  $p = 0.008$ ).

**Conclusion:** The TAVI team should not decide whether the patient is suitable for a femoral approach based solely on the manufacturer's criteria, and should incorporate additional factors that could be predictive of major VCs.

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\* Corresponding author.

E-mail address: [bcakal@hotmail.com](mailto:bcakal@hotmail.com) (B. Çakal).

**PALAVRAS-CHAVE**

Implantação valvular aórtica percutânea;  
Doença valvular aórtica;  
Complicações;  
Acesso vascular

## Qual a importância das recomendações do fabricante para determinar a não elegibilidade para TAVI transfemoral?

**Resumo**

**Introdução:** Até um terço dos doentes pode não ser elegível para implantação de válvula aórtica percutânea transfemoral (TAVI-TF) devido a recomendações do fabricante e de múltiplas sociedades profissionais.

**Objetivo:** Investigar o valor preditivo das recomendações do fabricante nas complicações *major* no local de acesso vascular utilizando o dispositivo Perclose ProGlide.

**Métodos:** De 208 doentes submetidos a TAVI-TF, 144 (69,2%) foram considerados elegíveis para TAVI-TF de acordo com as instruções do fabricante. Um diâmetro mínimo do lúmen iliofemoral (DMLI) abaixo dos limites especificados pelos fabricantes e/ou a presença de calcificação concêntrica constituíram as razões de não indicação/elegibilidade. O *score* de calcificação (SC), a relação bainha-artéria femoral (RBAF) e o DMLI foram avaliados através de tomografia computadorizada. As complicações vasculares (CV) (definidas segundo os critérios VARC-II) foram comparadas retrospectivamente.

**Resultados:** Os doentes do grupo não elegível apresentaram valores mais elevados de RBAF ( $1,13 \pm 0,15$  versus  $0,88 \pm 0,107$ ,  $p < 0,001$ ), SC ( $1,66 \pm 0,99$  versus  $1,24 \pm 0,73$ ;  $p = 0,003$ ) e valores significativamente mais baixos de DMLI ( $7,72 \pm 1,03$  versus  $6,31 \pm 0,96$ ;  $p < 0,001$ ) quando comparados com o grupo elegível. As CV *major* (6,3% versus 12,3%,  $p = 0,13$ ) e minor (10,4% versus 15,6%,  $p = 0,29$ ) foram semelhantes nos dois grupos. O grupo não elegível apresentou taxa de rotura mais elevada (0,7% versus 6,3%;  $p = 0,03$ ). A RBAF foi o único fator preditivo independente de CV *major* (OR 469,1 [IC] 95% 4,95-44 466,57,  $p = 0,008$ ).

**Conclusões:** A equipa responsável pela TAVI não deve decidir a elegibilidade para a abordagem femoral com base apenas nos critérios do fabricante, devendo incorporar na avaliação fatores adicionais que possam ser preditivos de complicações vasculares *major*.

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**What's new?**

Up to one third of transcatheter aortic valve implantation (TAVI) procedures may not be suitable for a transfemoral approach. Manufacturers' size charts for determining whether transfemoral TAVI is feasible are not evidence-based. Current manufacturers' recommendations for transfemoral TAVI cannot predict the possibility of major vascular complications. The sheath-to-femoral artery ratio seems to be the only predictor of major vascular events.

vast majority of TAVI procedures, although the proportion of patients undergoing transfemoral access varies widely, and it is projected that 89% of patients will undergo transfemoral access with the use of new-generation TAVI systems.<sup>4,5</sup>

Despite advances in device technology, including contemporary lower-profile delivery systems, in conjunction with improved vascular screening and operator experience, VCs remain the most frequent adverse events associated with transfemoral (TF) TAVI (TF-TAVI) procedures.<sup>6</sup>

Risk factors such as small femoral artery diameter and arterial calcification have been defined to help identify high-risk patients particularly vulnerable to VCs.<sup>7</sup> In addition, valve manufacturers provide guidelines recommending minimal artery diameters for their device sizes, but these are not evidence-based. However, a standardized methodology to predict complications at the vascular access site is still lacking. This study sought to clarify whether manufacturers' recommendations could predict VCs in TF-TAVI.

**Introduction**

Transcatheter aortic valve implantation (TAVI) has become the generally accepted treatment option for inoperable or high- and intermediate-risk patients with severe aortic stenosis.<sup>1,2</sup> Compared to surgical aortic valve replacement, TAVI is associated with fewer major bleeding events and similar survival rates, but has a higher incidence of vascular complications (VCs) and conduction abnormalities.<sup>3</sup> Transfemoral access is the most commonly used pathway for the

**Methods**

Between April 2015 and December 2019, 208 patients undergoing TF-TAVI treated with the Perclose ProGlide suture-mediated closure system were analyzed in this single-center study. All the study procedures were approved by the local research ethics committee and patients provided written informed consent for the procedure and inclusion in the

registry. Screening included baseline characteristics, iliac and femoral artery characteristics (minimal lumen diameter [MLD], calcification and tortuosity), procedural data including sheath type and size, and VCs. Contrast-enhanced multislice computed tomography (MSCT) of the aorta including the iliofemoral vessels was performed in all patients. All cases were discussed, and the indications were confirmed, with the institutional heart team.

Only patients with a TF approach (n=208) were included in the final analysis. During the study period, TF-TAVI was performed using the following valve types: balloon-expandable Edwards SAPIEN S3™ and Edwards SAPIEN XT™ valves (Edwards Lifesciences Inc., Irvine, CA); self-expanding Medtronic CoreValve® Evolut™ R System valves (Medtronic, Minneapolis, MN); and the Portico™ valve (St. Jude Medical, Minneapolis, MN).

Patients were divided into two subgroups, classified as eligible or ineligible based on the MLD recommendations given by the valve manufacturers and presence of circumferential arterial calcification. Current recommendations require an MLD of 6.0, 6.5 and 7.0 mm for the 23, 26, and 29 mm SAPIEN XT™ (Edwards), respectively. The recommended MLD for the SAPIEN S3™ is 5.5 mm for the 14F eSheath and 6 mm for the 16F eSheath. A 14F-equivalent system with InLine™ (MLD 5.0 mm) is used with the Evolut™ R (Medtronic) TAVI system. Whereas 23- and 25-mm valves are loaded onto an 18F delivery system, 27- and 29-mm valves are loaded onto a 19F delivery system with a minimum MLD requirement of 6 mm for the Portico™ valve (St. Jude Medical, Inc.).

### Vessel access and definitions

Assessment and measurement of peripheral access before TAVI was accomplished with preprocedural MSCT. Vessel tortuosity and calcifications were also assessed by MSCT.<sup>8,9</sup> Tortuosity was graded as no tortuosity, mild (30°-60°), moderate (60°-90°), and severe (>90°). Arterial calcification was graded as no calcification, mild (90° of total circumferential arc), moderate (90°-180° of total circumferential arc), marked (180°-270° of total circumferential arc), and severe (>270° of total circumferential arc). The sheath-to-femoral artery ratio (SFAR) was defined as the ratio between the outer sheath diameter and the MLD of the femoral artery<sup>10</sup> and was calculated for all patients. Major clinical endpoints were assessed according to the updated Valve Academic Research Consortium (VARC-2) criteria.<sup>11</sup>

Close attention was paid to procedure-related VCs such as rupture, dissection, perforation, access site hematoma and pseudoaneurysm formation, as well as to management of peripheral interventions including balloon angioplasty, stenting, and need for unplanned surgical intervention.

### Statistical analysis

The statistical analysis was performed using IBM SPSS Statistics for Windows, version 25 (IBM SPSS, Armonk, NY). Continuous variables are expressed as mean (standard deviation). Categorical variables are reported as frequencies (%). Normality of distribution of continuous variables was tested by the Kolmogorov-Smirnov goodness-of-fit test. Continuous

variables were compared with the Student's t test or the Mann-Whitney U test, as appropriate. Categorical variables were compared with the chi-square test. Multivariate logistic regression was used to identify independent predictors of VCs. Receiver operating characteristic (ROC) curve analysis was used to assess the SFAR threshold with the best sum of sensitivity and specificity. Variables with a p-value ≤0.1 were entered in the regression model, and variables known to be associated with an increased risk of VCs (gender, vascular calcification, ineligibility, anticoagulation, and SFAR) were also included a priori into the analysis. The level of significance was set at p<0.05.

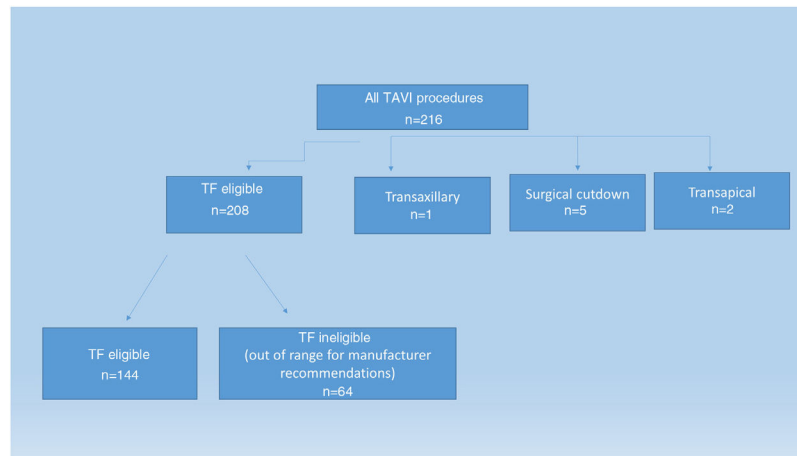
## Results

During the study period, 208 of 216 patients underwent TF-TAVI (Figure 1). Table 1 represents the baseline characteristics of the overall study population. After appropriate screening, 144 patients fulfilled the manufacturer's recommendations for a transfemoral approach (TF eligible group). In addition, 64 patients with either circumferential calcifications or less than the recommended iliofemoral MLD underwent TF-TAVI (TF ineligible group).

The groups were similar with regard to gender, age, and log EuroSCORE. The ineligible group had a slightly higher rate of peripheral artery disease (29.7% vs. 18.1%, p=0.06) and coronary artery disease (67.2% vs. 53.5%, p=0.07). Anticoagulant therapy was more frequent in eligible patients (33.3% vs. 18.8%, p=0.03). The ineligible cohort had smaller MLD (7.72±1.03 vs. 6.31±0.96 mm; p<0.001) and higher calcification scores (1.24±0.73 vs. 1.66±0.99; p=0.003), however no difference was observed in vessel tortuosity score between eligible and ineligible patients (1.44±0.96 vs. 1.39±0.98; p=0.96, respectively). Double Perclose ProGlide failure was more frequent in ineligible patients and adjunctive Angio-seal was used to achieve hemostasis in this cohort (18.1% vs. 31.3%; p=0.03).

### Vascular complications and in-hospital mortality

The characteristics and outcomes of VCs are reported in Table 2. Forty-two patients (20.2%) experienced VCs. There were no significant differences in the incidence of major vascular events (eligible group 6.3% vs. ineligible group 12.5%, p=0.13) or minor vascular events (eligible group 10.4% vs. ineligible group 15.6%, p=0.29). Overall, the in-hospital mortality rate was 7.7%, with no difference between eligible and ineligible patients (n=11, 7.6% vs. n=5, 7.8%, p=0.96). Minor bleeding tended to occur more frequently in the ineligible group (5.6% vs. 12.5%, p=0.08). MLD did not differ significantly according to complication types, although MLD was lower in the major and overall complication groups (p=0.070) (Figure 2). In terms of complication type, peripheral arterial rupture was significantly more frequent in the ineligible group (n=1, 0.7% vs. n=4 6.3%, p=0.03). A detailed list of major VCs is presented in Table 3. Most (13/17; 80%) of the complications occurred with the SAPIEN XT, suggesting that newer-generation devices with lower profiles may have reduced the incidence of VCs over time.



**Figure 1** Flow chart of the study population. TAVI: transcatheter aortic valve implantation; TF: transfemoral access.

**Table 1** Baseline patient and procedural characteristics.

	Total (n=208)	TF eligible (n=144)	TF ineligible (n=64)	p
Age, years	79.15±7.62	79.3±7.0	78.9±8.8	0.73
Male, n (%)	109 (52.4%)	79 (54.9%)	30 (46.9%)	0.28
log EuroSCORE	25.9±4	26.07±4.2	25.58±3.5	0.42
NYHA III-IV, n (%)	109 (52.4%)	78 (54.2%)	31 (48.4%)	0.44
LVEF, %	51.3±12	50.5±12.7	52.9±10.1	0.15
BMI, kg/m <sup>2</sup>	25.9±3.38	26.07±4.2	25.6±3.5	0.32
Hypertension, n (%)	187 (89.9%)	130 (90.3%)	57 (89.1%)	0.79
Diabetes, n (%)	46 (22.1%)	36 (25%)	10 (15.6%)	0.13
CAD, n (%)	120 (57.7%)	77 (53.5%)	43 (67.2%)	0.07
PAD, n (%)	45 (21.6%)	26 (18.1%)	19 (29.7%)	0.06
GFR, ml/min/1.73 m <sup>2</sup>	70.4±25.2	70.4±25.4	70.7±24.8	0.93
Previous MI, n (%)	55 (26.4%)	37 (25.7%)	18 (28.1%)	0.71
Previous CVO, n (%)	12 (5.8%)	8 (5.6%)	4 (6.3%)	0.72
Previous PCI, n (%)	56 (26.9%)	43 (29.9%)	13 (20.3%)	0.15
CABG, n (%)	39 (18.8%)	26 (18.1%)	13 (20.3%)	0.7
AF, n (%)	50 (24%)	38 (26.6%)	12 (18.8%)	0.22
Anticoagulation, n (%)	60 (28.8%)	48 (33.3%)	12 (18.8%)	0.03
Iliofemoral CS <sup>a</sup>	1.37±0.84	1.24±0.73	1.66±0.99	0.003
Tortuosity score <sup>a</sup>	1.39±0.96	1.44±0.96	1.39±0.98	0.97
IFMLD, mm	7.29±1.2	7.72±1.03	6.31±0.96	<0.001
CFMLD, mm	7.6±1.24	8.05±1.11	6.59±0.89	<0.001
SFAR	0.96±0.17	0.88±0.107	1.13±0.15	<0.001
Median SFAR (IQR)	0.94 (0.85-1.06)	0.90 (0.8-0.96)	1.08 (1.05-1.16)	<0.001
Sheath ≥18F, n (%)	108 (51.9%)	41 (38%)	67 (64%)	0.019
Sheath outer diameter, mm	6.83±0.70	6.74±0.69	7.03±0.72	0.005
Number of PP per patient	1.91±0.46	1.88±0.48	2±0.39	0.07
Adjunctive Angio-seal after ≥2 PP failures, n (%)	46 (39.1)	26 (18.1)	20 (31.3)	0.03
1 PP+1 AS, n (%)	29 (13.9)	24 (16.7)	5 (7.8)	0.09

AF: atrial fibrillation; AS: Angio-seal; BMI: body mass index; CABG: coronary artery bypass grafting; CAD: coronary artery disease; CFMLD: common femoral artery minimal lumen diameter; CS: calcium score; CVO: cerebrovascular occlusion; IFMLD: iliofemoral artery minimal lumen diameter; MI: myocardial infarction; NYHA: New York Heart Association functional class; PAD: peripheral artery disease; PP: Perclose ProGlide; SFAR: sheath-to-femoral artery ratio; TF: transfemoral approach; VC: vascular complication.

<sup>a</sup> Measured by multislice computed tomography.

### Predictors of major vascular complications

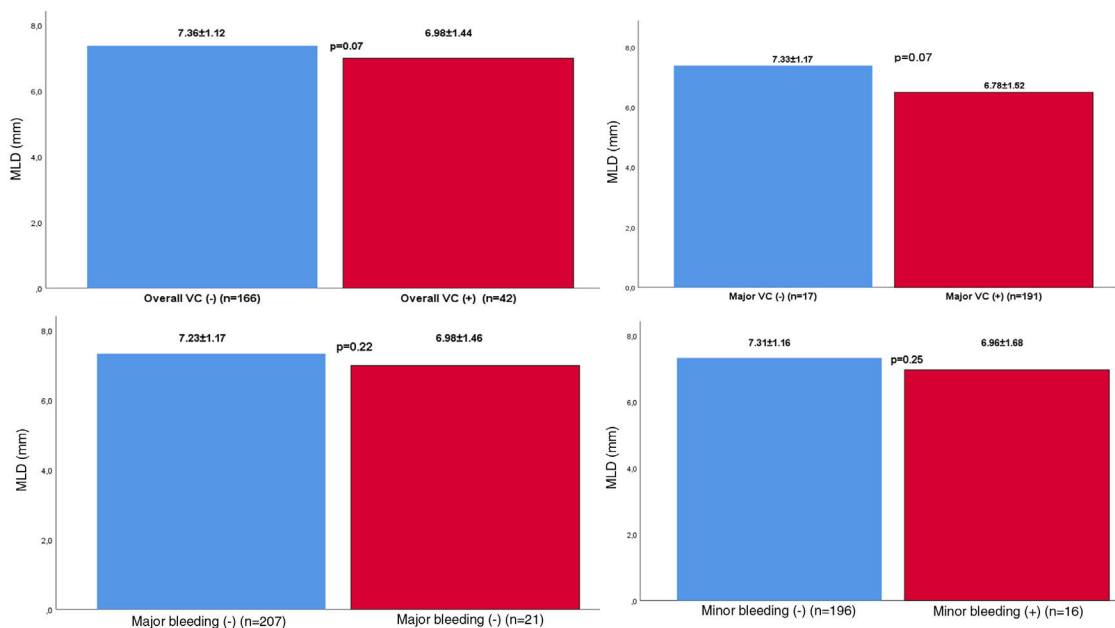
The multivariate logistic regression analysis showed that SFAR (odds ratio [OR] 469.1, 95% confidence interval [CI]

4.95-44 466.57, p=0.008), but not iliofemoral calcification (OR 0.67, 95% CI: 0.33-1.37, p=0.27) or manufacturer's recommendations (OR: 0.39, 95% CI: 0.09-1.77, p=0.22) predicted major VCs (Table 4). As shown in Figure 3, ROC

**Table 2** Vascular access site complications according to group.

	Total (n=208)	TF eligible (n=144)	TF ineligible (n=64)	p
Major VARC-2 complication, n (%)	17 (8.2%)	9 (6.3%)	8 (12.5%)	0.13
Minor VARC-2 complication, n (%)	25 (12%)	15 (10.4%)	10 (15.6%)	0.29
Overall VARC-2 complication, n (%)	42 (20.2)	24 (16.7%)	18 (28.2%)	0.057
Major bleeding, n (%)	21 (10.1%)	12 (8.3%)	9 (14.1%)	0.21
Minor bleeding, n (%)	16 (7.7%)	8 (5.6%)	8 (12.5%)	0.08
Hematoma, n (%)	12 (5.8%)	8 (5.6%)	4 (6.3%)	1
Surgical treatment, n (%)	10 (4.8%)	5 (3.5%)	5 (7.8%)	0.29
Aortic dissection, n (%)	1 (0.5%)	1 (0.7%)	-	-
Rupture, n (%)	5 (2.4%)	1 (0.7%)	4 (6.3%)	0.03
Stenosis/occlusion, n (%)	16 (7.7%)	10 (6.9%)	6 (9.4%)	0.58
Pseudoaneurysm, n (%)	2 (1%)	1 (0.7%)	1 (1.6%)	0.52
Closure device failure, n (%)	4 (1.9%)	2 (1.4%)	2 (3.1%)	0.58
Annular rupture, n (%)	1 (0.5%)	1 (0.7%)	-	-
Length of hospital stay, days (IQR)	4 (3-6)	4 (3-7)	4 (3-5)	0.9
In-hospital mortality, n (%)	16 (7.7%)	11 (7.6%)	5 (7.8%)	0.96
Stroke, n (%)	10 (4.8%)	8 (5.6%)	2 (3.1%)	0.72

IQR: interquartile range; TF: transfemoral approach; VARC-2: Valve Academic Research Consortium-2.



**Figure 2** Comparison of minimal iliofemoral luminal diameters according to types of vascular complication. (+): with; (-): without; MLD: minimal lumen diameter of the iliofemoral artery; VC: vascular complications.

analysis identified a cutoff value of SFAR=0.99 for major vascular complication after TAVR with a sensitivity of 69% and specificity of 77% (area under the curve [AUC]=0.69, 95% CI: 0.56-0.84, p=0.007).

## Discussion

Our study shows that vascular access site complications are still common among patients undergoing TF-TAVI using the ProGlide device. The major access site complication rate was 8.2%, which is comparable to that described by other centers, ranging between 5.0% and 7%.<sup>1,12</sup> Moreover, this study emphasizes another important point, that

manufacturers' guidelines do not provide an individualized risk prediction of major VCs. However, SFAR (>0.99) provided prior knowledge of which patients were most likely to have major vascular adverse events.

The incidence of major VCs in the TF-eligible and TF-ineligible groups was 6.3% and 12.5%, respectively, while minor VCs occurred in 10.4% and 15.6% of patients in the respective groups. Barbash et al. reported major and minor complication rates of 1.9% and 18%, respectively, using the Perclose ProGlide device.<sup>13</sup> Dimitridas et al.<sup>14</sup> demonstrated major and minor complication rates of 3.8% and 12.6%, respectively; however, in the present study the higher rates of major and minor access site complications in the

**Table 3** Overview of Valve Academic Research Consortium-2 major vascular complications.

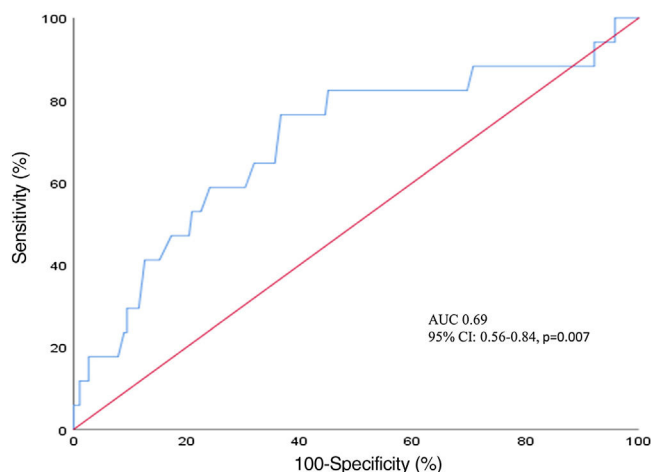
Patient	Group	Year	Sheath type	Type of vascular complication	Treatment strategy	Treatment success
1	Ineligible	2015	16F SAPIEN XT	VCD failure	Surgical repair	Yes
2	Ineligible	2016	16F SAPIEN XT	Iliac rupture	Surgery	No, death
3	Ineligible	2016	20F SAPIEN XT	Hematoma, transfusion of 2 units of RBC	Manual compression	Yes
4	Ineligible	2016	18F SAPIEN XT	CFA rupture	Stent graft	Yes
5	Eligible	2017	20F SAPIEN XT	Hematoma, transfusion of 3 units of RBC	Manual compression	Yes
6	Eligible	2017	20F SAPIEN XT	Aortic dissection	Surgery	No, death
7	Ineligible	2017	16F SAPIEN XT	VCD failure, transfusion of 3 units of RBC	Surgical repair	Yes
8	Ineligible	2017	14F SAPIEN 3	Iliac rupture	Stent graft	Yes
9	Eligible	2018	18F SAPIEN XT	Annulus rupture	Surgery	No, death
10	Eligible	2018	16F SAPIEN XT	Right CFA occlusive dissection	Failed Stenting	No, death
11	Eligible	2018	18F Sapen XT	Hematoma, transfusion of 3 units of RBC	Manuel Compression	Yes
12	Eligible	2018	18F SAPIEN XT	Right CFA nonocclusive dissection	Stenting	No, acute renal failure and death
13	Ineligible	2018	18F SAPIEN XT	Sheath fracture leading to failure of sheath removal	Surgery	Yes
14	Eligible	2019	18F SAPIEN XT	Right CFA rupture, retroperitoneal hemorrhage	Surgery	Yes
15	Eligible	2019	19F Portico	Pseudoaneurysm requiring transfusion of 3 units of RBC	Thrombin injection	Yes
16	Eligible	2019	14F Evolute R	Hematoma requiring 2 units of RBC	Manuel compression	Yes
17	Ineligible	2019	16F Evolute R	Iliac rupture	Stent graft	Yes

CFA: common femoral artery; RBCs: red blood cells; VCD: vascular closure device.

**Table 4** Predictors of major vascular complications.

	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.969 (0.91-1.03)	0.33		
Female gender	2.146 (0.76-6.03)	0.15	2.49 (0.78-7.98)	0.12
EuroSCORE	1.03 (0.92-1.16)	0.59		
BMI	1 (0.86-1.16)	0.99		
Diabetes	0.738 (0.20-2.67)	0.64		
PAD	2.82 (1.01-7.89)	0.05	2.91 (0.92-9.24)	0.07
GFR<60 ml/min/1.73 m <sup>2</sup>	1.08 (0.98-1.03)	0.47		
SFAR	54.66 (3.72-802.48)	0.004	469.1 (4.95-44466.57)	0.008
Iliofemoral CS	1.07 (0.60-1.90)	0.81	0.67 (0.33-1.37)	0.27
Tortuosity score	0.953 (0.57-1.59)	0.85		
CAD	0.95 (0.34-2.60)	0.92		
Late experience group	0.81 (0.29-2.19)	0.67		
Anticoagulation	0.31 (0.06-1.38)	0.12	3.37 (0.68-16.7)	0.14
Ineligibility	2.14 (0.78-5.84)	0.13	0.39 (0.09-1.77)	0.22
LVEF	0.99 (0.97-1.03)	0.69		
Sheath ≥18F	1.33 (0.48-3.6)	0.58		

BMI: body mass index; CAD: coronary artery disease; CI: confidence interval; CS: calcium score; GFR: glomerular filtration rate; LVEF: left ventricular ejection fraction; PAD: peripheral artery disease; SFAR: sheath-to-femoral artery ratio.



**Figure 3** Receiver operating characteristic curve analysis of sheath-to-femoral artery ratio for prediction of major vascular complications. AUC: area under the curve; CI: confidence interval.

overall cohort compared to previous studies could plausibly be explained by the presence of the ineligible TF-TAVI group.

Several variables have been described as predictive factors of access site complications, including center and surgeon experience, female gender, femoral artery calcification (especially when circumferential), MLD, and  $SFAR \geq 1.05$ .<sup>15,16</sup> Since previously defined SFAR measures were mainly based on the use of 22F and 24F delivery sheaths, lower SFAR values in our study could be due to smaller, flexible delivery systems with hydrophilic coatings. Insertion of a large-caliber delivery sheath through an extensively calcified artery causes compression and displacement of large amount of plaque burden, and can lead to dissection or rupture. Barbant et al. found that the risk of vascular trauma increases with larger sheath sizes (complication rates 0.5% vs. 10.5% in 14-18F vs. 19-24F sheaths) and showed a downward trend with the new-generation TAVR delivery systems.<sup>17</sup> However, Kodali et al. and Manoharan et al. reported the rate of major VCs as 6.1% and 8.3%, respectively, which was associated with the use of 14F and 16F sheaths.<sup>18,19</sup> These conflicting results mean that larger-scale randomized trials are needed to ascertain whether sheath diameter and/or SFAR can affect the incidence of VCs.

Access site-related VCs were mainly driven by bleeding and/or hematoma. Iliofemoral MLD and circumferential calcifications were defined as determinants of appropriateness for TF-TAVI. According to these recommendations, 30.8% (64/208) of our cohort were classified as ineligible for TF-TAVI. Although alternative pathways could be preferred for patients who had small iliofemoral vessel diameters and/or iliofemoral circumferential calcifications, major VCs did not differ between the TF-TAVI eligible and ineligible groups. However, overall VCs tended to occur more frequently in the ineligible group, as did rupture. In addition, even though not statistically significant ( $p=0.08$ ), the ineligible group had more minor bleeding events.

Similar to our study, Reinthaler et al.<sup>20</sup> showed that patients unsuitable for TF-TAVI experienced slightly more major VCs during TF-TAVI (10.7% vs. 2.6%,  $p=0.07$ ).

Circumferential calcifications and SFAR were the predictors of major vascular events. Interestingly, we did not find circumferential iliofemoral calcification as a predictor. The sheath diameters used during TF-TAVI in the present study ( $\geq 18F$ , 51.9%) were smaller than in the study by Reinthaler et al. using either ProGlide or Prostar vascular closure devices ( $\geq 18F$ , 89%). In our opinion, the impact of iliofemoral calcifications, rather than SFAR or MLD, on access site complications could have been mitigated by use of lower-profile delivery systems and the ProGlide compared to the Prostar XL.<sup>13</sup>

## Limitations

This study has some limitations. First, due to its retrospective, non-randomized nature, selection bias cannot be excluded. A randomized prospective study or propensity score matching would provide a more reliable analysis. Second, our study was performed as a single-center analysis and the size of the study population was limited. Third, the physical properties of four sheaths with different manufacturers and models could have affected outcomes in our study.

## Conclusions

Manufacturers' recommendations may not predict the incidence of major VCs during TF-TAVI. Of note, only SFAR was associated with major VCs in patients undergoing TF-TAVI in the multivariate regression analysis. Smaller peripheral anatomy and circumferential calcifications should not be the only criteria for unsuitability for TF-TAVI.

## Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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