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CVN Interview

Transfemoral Aortic Valve Implantation

New Criteria to Predict Vascular Complications

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Objectives This study sought to evaluate the incidence, impact, and predictors of vascular complications in transcatheter aortic valve implantation (TAVI).

Background Vascular complications increase morbidity and mortality in transfemoral TAVI; however, there remains a paucity of data describing these serious events.

Methods We performed a prospective cohort study of 130 consecutive transfemoral TAVI recipients. Vascular complications were defined by the Valve Academic Research Consortium (VARC) criteria. The ratio of the sheath outer diameter (in millimeters) to the minimal femoral artery diameter (in millimeters) defined the sheath to femoral artery ratio (SFAR).

Results In our cohort of elderly patients (83.3 ± 5.9 years), the logistic EuroScore was 25.8% ± 11.9%. The Edwards valve was used in 102 cases (18- to 24-F) and the CoreValve in 27 (18-F). The minimal femoral artery diameter was 8.17 ± 1.14 mm, and the calcification (0 to 3) and tortuosity scores (0 to 3) were 0.58 ± 0.72 and 0.28 ± 0.53, respectively. The mean sheath diameter was 8.10 ± 0.82 mm, and the mean SFAR was 0.99 ± 0.16. Vascular complications occurred in 27.6% (VARC major: 17.3%, minor: 10.2%), and major vascular complications predicted 30-day mortality (22.7% vs. 7.6%, p = 0.049). The SFAR (hazard ratio [HR]: 186.20, 95% confidence interval [CI]: 4.41 to 7,855.11), center experience (HR: 3.66, 95% CI: 1.17 to 11.49), and femoral calcification (HR: 3.44, 95% CI: 1.16 to 10.17) predicted major complications by multivariate analysis. An SFAR threshold of 1.05 (area under the curve = 0.727) predicted a higher rate of VARC major complications (30.9% vs. 6.9%, p = 0.001) and 30-day mortality (18.2% vs. 4.2%, p = 0.016).

Conclusions Vascular complications in transfemoral TAVI are relatively frequent. VARC major vascular complications increase 30-day mortality and are predicted by experience, femoral calcification, and SFAR. Routine application of SFAR will improve patient selection for transfemoral TAVI and may improve outcome. (J Am Coll Cardiol Intv 2011;4:851–8) © 2011 by the American College of Cardiology Foundation

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Transcatheter aortic valve implantation (TAVI) has emerged as a promising therapeutic option for patients with severe symptomatic aortic stenosis (AS), who are ineligible for conventional surgical aortic valve replacement (1,2). Two transcatheter heart valves, the Edwards SAPIEN valve (Edwards Lifesciences, Irvine, California) and the Medtronic CoreValve (Medtronic, Minneapolis, Minnesota), are commercially available in Europe. The Edwards valve can be implanted via a transfemoral or transapical approach, and the CoreValve using a transfemoral or trans-subclavian approach. Since 2002, more than 30,000 procedures have been performed worldwide, and the technique is now reaching relative maturity.

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Abbreviations and Acronyms

AS = aortic stenosis
CI = confidence interval
eGFR = estimated glomerular filtration rate
HR = hazard ratio
MLD = minimal lumen diameter
MSCT = multislice computed tomography
SEIAR = sheath to external iliac artery ratio
SFAR = sheath to femoral artery ratio
TAVI = transcatheter aortic valve implantation
VARC = Valve Academic Research Consortium

Vascular complications are among the most frequent and serious complications of transfemoral TAVI, and have been associated with significantly increased patient morbidity and mortality (3–5). Despite improved patient selection and down-sizing of the delivery system, these complications remain the Achilles' heel of this novel procedure. Previous studies have reported on vascular complications in transfemoral TAVI (2,6–8); however, the absence of a uniform definition of what constitutes a major vascular complication has made it difficult to obtain a comprehensive picture of these significant events. To address this problem, the Valve Academic Research Consortium (VARC) have recently developed a consensus on TAVI-related endpoints (9), including a uniform definition of vascular complications.

The aim of this study was to describe the incidence and clinical impact of vascular complications in a large cohort of transfemoral TAVI patients, based on the VARC criteria, and to identify predictors of these serious events.

Methods

Study population and design. Between October 2006 and June 2010, consecutive high-risk patients with symptomatic severe AS treated with TAVI at our institution were prospectively included in our TAVI database. Patients with symptomatic severe AS (valve area ≤ 0.8 cm^2) were considered candidates for TAVI if they had a logistic European System for Cardiac Operative Risk Evaluation score (EuroSCORE) >20%, or if surgery was deemed to be of excessive risk due to significant comorbidities, or if other risk factors not captured by these scoring systems (e.g., porcelain aorta) were present. The decision to proceed with TAVI was discussed by a dedicated heart team, which included cardiologists, interventional cardiologists, anesthesiologists, cardiac surgeons, and specialists in cardiac imaging. All patients selected for TAVI underwent screening physical examination, transthoracic echocardiogram, baseline laboratory indexes, and coronary angiography. The assessment of the iliofemoral vessels was performed by selective iliofemoral angiography from 2 orthogonal planes. In addition, screening multislice computed tomography (MSCT) of the iliofemoral vasculature was performed in patients without significant renal dysfunction.

All patients agreed to participate in the study, and written informed consent was obtained in all cases.

Procedures. The technical aspects of the transfemoral TAVI procedures using the Edwards valve and CoreValve systems have been previously described in detail (10–12). Most patients were pretreated with aspirin 160 mg and clopidogrel 75 mg daily. If patients were not on dual antiplatelet therapy, a loading dose of clopidogrel (300 to 600 mg) was administered. A bolus of intravenous heparin (80 IU/kg) was administered at the beginning of the procedure to achieve a target activated clotting time of 250 to 300 s, and the activated clotting time was measured every 30 min thereafter.

Between October 2006 and March 2008, closure of the femoral artery access site was performed surgically (n = 28). Afterwards (n = 99), we applied a "true percutaneous approach" using a "pre-closing technique" with the Prostar XL 10-F vascular closure system (Abbott Vascular, Abbott Park, Illinois), which has been previously described (13,14). In brief, direct puncture of the common femoral artery was ensured by iliofemoral angiography from the contralateral side. A single Prostar device was used for 18- to 19-F sheaths and 2 devices used for 22- and 24-F sheaths. The second Prostar device was placed at 45° to the first one. After Prostar deployment, the femoral artery introducer sheath was carefully inserted over a stiff guidewire. Following aortic valve deployment, the introducer sheath was retracted to the external iliac artery, and angiography was performed to assess for iliac artery complications. The femoral artery was subsequently closed by tying the Prostar sutures before a final iliofemoral angiogram was performed from the contralateral side.

Iliofemoral vascular assessment. Quantitative angiography of the femoral, external iliac, and common iliac arteries was performed offline after calibration with a contrast-filled catheter. The minimal lumen diameter (MLD) of the iliofemoral access was also measured by MSCT where possible. Measurements and qualitative assessment were performed by 2 independent operators. Vessel tortuosity and calcification were evaluated as previously described (15).

The tortuosity score was defined as follows: 0 = no tortuosity; 1 = mild tortuosity (30° to 60°); 2 = moderate tortuosity (60° to 90°); and 3 = marked tortuosity (>90°). The calcification score was evaluated under fluoroscopy before contrast injection or by MSCT, and defined as follows: 0 = no calcification; 1 = mild calcification; 2 = moderate calcification; and 3 = marked calcification. The Edwards system introducer sheath outer diameters for the 24-, 22-, 19-, and 18-F sheaths are 9.2, 8.4, 7.5, and 7.2 mm, respectively. The 18-F Large Check-Flo Introducer system (Cook Medical, Bloomington, Indiana) used with the CoreValve is 7.3 mm in diameter.

Treatment of vascular complications. Treatment of vascular complications was left to the operators' discretion. However, significant iliofemoral dissections and stenoses were treated with conventional balloon angioplasty, or balloon-expandable stents in cases where balloon angioplasty yielded suboptimal results. Femoral perforations, insufficiently managed with manual compression or balloon angioplasty, were treated with covered stents. Vessel ruptures associated with hemodynamic instability were temporarily managed with contralateral balloon occlusion while covered stents were prepared.

Post-procedural care. All patients were observed in the intensive care unit for at least 24 h, with 4 hourly vascular assessments to detect complications. Dual antiplatelet therapy (aspirin 160 mg, clopidogrel 75 mg) was administered for 3 to 6 months, and thereafter, aspirin was continued indefinitely. When patients required chronic anticoagulation, the dose of warfarin was reduced to obtain an international normalized ratio between 2.5 and 3.

Endpoint definitions. The primary endpoints of this study were vascular complications as defined by the VARC criteria (9), and all-cause mortality (in-hospital and 30-day mortality).

The VARC major vascular complications are defined as: 1) any thoracic aortic dissection; 2) access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arteriovenous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, or compartment syndrome) leading to either death, significant blood transfusion (≥4 U), unplanned percutaneous or surgical intervention, or irreversible end organ damage; or 3) distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end organ damage.

The VARC minor vascular complications are defined as: 1) access site or access-related vascular injury not requiring unplanned percutaneous or surgical intervention and not resulting in irreversible end organ damage; 2) distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end organ damage; and 3) failure of percutaneous access site closure resulting in interventional or surgical correction and not associated with death, significant blood transfusions, or irreversible end organ damage.

The sheath to femoral artery ratio (SFAR) was defined as the ratio between the sheath outer diameter (in millimeters) and the femoral artery MLD (in millimeters). The sheath to external iliac artery ratio (SEIAR) was defined as the ratio between sheath outer diameter (in millimeters) and external iliac MLD (in millimeters). To evaluate the impact of the learning curve, the first 50% of transfemoral TAVI procedures (63 cases of 127) were defined as the "early center experience" group.

Statistical analysis. Quantitative variables are expressed as mean ± SD, and qualitative variables as number and percentage. Comparison of quantitative variables was performed with an unpaired Student *t* test or Wilcoxon rank sum test, depending on variable distribution. The chi-square test or Fisher exact test was used to compare qualitative variables. A stepwise logistic regression analysis, including all variables with a p value ≤0.1 in the univariate analysis, was performed to determine the predictors of VARC major vascular complications. The SFAR threshold that best predicted vascular complications was determined by the intersection of the sensitivity and specificity curves. Statistical significance was defined as $p < 0.05$. The data were analyzed with PASW statistics 17.0 (SPSS Inc., Chicago, Illinois).

Results

During the enrollment period, a total of 285 patients were deemed eligible for TAVI by the heart team after appropriate screening. Of these patients, 195 (68.4%) were identified as transfemoral TAVI candidates, and 130 underwent valve implantation. A further 90 patients were selected for nontransfemoral TAVI, due to nonfavorable aortic or iliofemoral anatomy (aortic debris; excessively small, tortuous, or calcified iliofemoral vessels). Of these patients, 66 were treated by transapical TAVI and 5 by trans-subclavian TAVI.

Thus, 130 patients underwent transfemoral TAVI using both of the commercially available percutaneous bioprostheses: the Edwards valve (n = 102) (Cribier-Edwards, Edwards-SAPIEN or SAPIEN XT, Edwards Lifesciences), and the CoreValve Revalving system (n = 28) (Medtronic). In 3 patients, valve implantation was not achieved: 1 case of recurrent ventricular fibrillation and 1 case of aortic annulus rupture after balloon valvuloplasty, and 1 failed femoral artery access. These patients were not included in the statistical analysis.

Patient and procedural characteristics. Patient demographics and procedural characteristics are presented in Tables 1 and 2. The mean age was 83.3 ± 5.9 years, with a logistic EuroScore of 25.8 ± 11.9%, and 63% had renal dysfunction (estimated glomerular filtration rate [eGFR] <60 ml/min/

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Table 1. Baseline Characteristics of the Study Population (N = 127)

Age, yrs	83.3 ± 5.9
Female	65 (51.2%)
BMI, kg/m^2	25.3 ± 4.1
Diabetes	29 (22.8%)
Hyperlipidemia	54 (42.5%)
Hypertension	92 (72.4%)
Current smoker	5 (3.9%)
NYHA functional class III or IV	113 (89.0%)
Coronary artery disease	80 (63.0%)
Previous MI	13 (10.2%)
Previous PCI	45 (35.4%)
Previous CABG	20 (15.7%)
Cerebrovascular disease	19 (15.0%)
COPD	43 (33.9%)
eGFR, ml/min/1.73 m^2	50.4 ± 23.6
eGFR <60 ml/min/1.73 m^2	80 (63.0%)
Logistic EuroScore, %	25.8 ± 11.9
Pulmonary hypertension	42 (33.1%)
LVEF, %	48.1 ± 14.1
LVEF <40%	45 (35.4%)

Values are mean ± SD or n (%).
BMI = body mass index; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

Table 2. Procedural Characteristics of the Study Population (N = 127)

Edwards SAPIEN valve	100 (78.7%)
CoreValve	27 (21.3%)
General anesthesia	66 (52.0%)
Percutaneous femoral artery closure	99 (78.0%)
Sheath size, F	20.8 ± 2.5
18	42 (33.1%)
19	16 (12.6%)
22	37 (29.1%)
24	32 (25.2%)
Introducer sheath diameter, mm	8.10 ± 0.82
Femoral artery MLD, mm	8.17 ± 1.14
SFAR	0.99 ± 0.16
Femoral artery calcification score (0–3)	0.58 ± 0.72
Femoral artery tortuosity score (0–3)	0.28 ± 0.53
Common iliac artery MLD, mm	10.3 ± 2.43
External iliac artery MLD, mm	8.73 ± 1.60
SEIAR	0.98 ± 0.33
Iliac artery calcification score (0–3)	0.96 ± 0.83
Iliac artery tortuosity score (0–3)	0.84 ± 0.75

Values are n (%) or mean ± SD.
MLD = minimal lumen diameter; SEIAR = sheath to external iliac artery ratio; SFAR = sheath to femoral artery ratio.

1.73 m^2). The femoral artery MLD was 8.17 ± 1.14 mm, and the mean sheath outer diameter was 8.10 ± 0.82 mm, giving an SFAR of 0.994 ± 0.155 (Fig. 1). The distributions of femoral artery calcification and tortuosity scores are shown in Online Figure 1.

Vascular complications. Vascular complications were observed in 35 patients (27.6%), and included 22 (17.3%) VARC major complications and 13 (10.2%) VARC minor complications (Table 3).

Major femoral complications (n = 11 [8.7%]) included 1 vessel rupture, 6 dissections, and 3 stenosis/occlusions, and major iliac complications (n = 13 [10.3%]) consisted of 6 ruptures and 7 dissections. These serious complications were treated with balloon angioplasty alone (n = 2 [1.5%]), femoral stenting (n = 3 [2.4%]), iliac stenting (n = 5 [3.9%]), thoracic aortic stenting (n = 1 [0.8%]), and emergent surgical repair (n = 8 [6.3%]). Blood transfusion (≥4 U) was required in 5 cases, including 1 aortic and 4 iliac artery ruptures. Femoral access site infections occurred in 3 patients who underwent surgical femoral artery closure. These 3 patients were diabetic, had impaired renal function, and were treated early in our center's experience in a cardiac catheterization suite.

VARC minor complications (n = 13) included 1 access site hematoma, 1 femoral artery pseudoaneurysm, and 11 Prostar failures that resulted in bleeding (n = 8) or femoral artery occlusion (n = 3). These complications were treated with balloon angioplasty (n = 3) or femoral artery stenting (n = 5). In contrast to the femoral artery, all iliac artery complications are classified as VARC major complications.

Vascular complications and death. Death at 30 days occurred in 13 of 127 (10.2%) patients. Five died due to vascular complications (Table 4). Aortic rupture (n = 1), iliac rupture (n = 2), iliac dissection (n = 1), and femoral

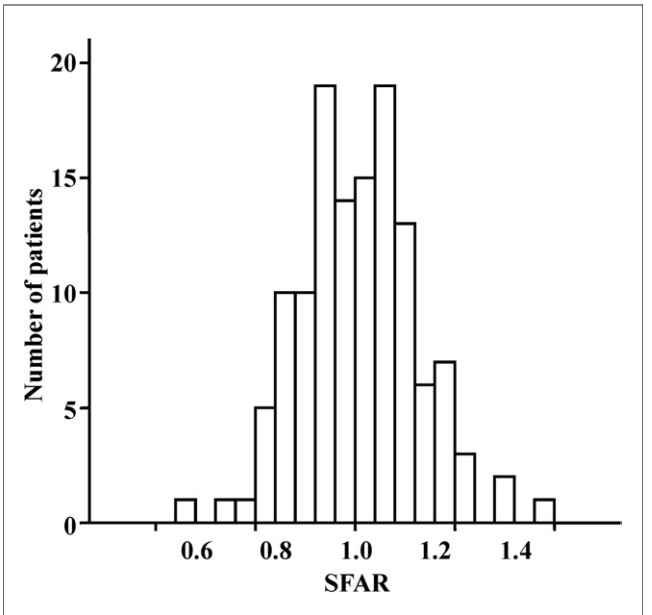

Figure 1. The Distribution of SFAR

The histogram of the sheath to femoral artery ratio (SFAR) showed a normal distribution.

Table 3. Vascular Complications

	All Patients (N = 127)	VARC Major Complications	VARC Minor Complications
Patients with vascular complications	35 (27.6%)	22 (17.3%)	13 (10.2%)
Femoral artery	24 (18.9%)	11 (8.7%)	13 (10.2%)
Rupture	1 (0.8%)	1 (0.8%)	0
Dissection	6 (4.7%)	6 (4.7%)	0
Stenosis/occlusion	3 (2.4%)	3 (2.4%)	0
Pseudoaneurysm	2 (1.6%)	1 (0.8%)	1 (0.8%)
Hematoma	1 (0.8%)	0	1 (0.8%)
Prostar failure	11 (8.7%)	0	11 (8.7%)
Death	1 (0.8%)	1 (0.8%)	0
Iliac artery	13 (10.2%)	13 (10.2%)	0
Rupture	6 (4.7%)	6 (4.7%)	0
Dissection	7 (5.5%)	7 (5.5%)	0
Death	3 (2.4%)	3 (2.4%)	0
Aorta	1 (0.8%)	1 (0.8%)	0
Rupture	1 (0.8%)	1 (0.8%)	0
Death	1 (0.8%)	1 (0.8%)	0
Blood transfusion	8 (6.2%)	7 (7.9%)	1 (0.8%)
Local infection	3 (2.4%)	3 (2.4%)	0
Vascular intervention	27 (21.3%)	19 (15.0%)	8 (6.3%)
Balloon angioplasty	5 (3.9%)	2 (1.5%)	3 (2.4%)
Femoral stenting	8 (6.3%)	3 (2.4%)	5 (3.9%)
Iliac stenting	5 (3.9%)	5 (3.9%)	0
Aortic stenting	1 (0.8%)	1 (0.8%)	0
Emergent vascular surgery	8 (6.3%)	8 (6.3%)	0
Hospital stay (days)	11.0 ± 7.9	16.5 ± 11.6	9.83 ± 4.04
In-hospital mortality	16 (12.6%)	6 (4.7%)	10 (7.9%)
30-day mortality	13 (10.2%)	5 (3.9%)	6 (4.7%)

Values are n (%) or mean ± SD.
VARC = Valve Academic Research Consortium.

artery access site infection (n = 1) were directly responsible for these deaths.

Predictors of VARC major vascular complications and outcomes. The SFAR (hazard ratio [HR]: 186.20, 95% confidence interval [CI]: 4.41 to 7,855.11, p = 0.006), early center experience (HR: 3.66, 95% CI: 1.17 to 11.49, p = 0.023), and femoral artery calcium score (HR: 3.44, 95% CI: 1.16 to 10.17, p = 0.026) were identified as independent predictors of VARC major vascular complications by multivariate analysis (Table 5). The SEIAR did not predict vascular complications, and although the diameter of the introducer sheath predicted major vascular complications in the univariate analysis (8.7 ± 0.5 mm vs. 8.0 ± 0.9 mm, p = 0.010), it was no longer significant after adjustment for other variables (p = 0.157). The type of TAVI was significantly associated with vascular complications in univariate analysis, with significantly fewer complications in the CoreValve cohort compared with the Edwards valve cohort (p = 0.004). However, the type of device was

Table 5. Univariate and Multivariate Analysis of the Clinical and Procedural Characteristics According to the Incidence of VARC Major Vascular Complications

		Multivariate		
Variable	Univariate p Value	p Value	Odds Ratio	95% CI
Age, yrs	0.069	0.860		
Female	0.937			
BMI, kg/m^2	0.850			
Diabetes	0.575			
eGFR <60 ml/min/1.73 m^2	0.222			
Logistic EuroScore, %	0.228			
LVEF <40%	0.212			
Chronic anticoagulation	0.870			
Activated clotting time, s	0.710			
TAVI type	0.004	0.057		
Early center experience	0.007	0.023	3.66	1.17–11.49
Sheath outer diameter, mm	0.010	0.157		
Femoral artery MLD, mm	0.797			
SFAR	0.001	0.006	186.20	4.41–7,855.11
Femoral artery calcification (0–3)	0.023	0.026	3.44	1.16–10.17
Femoral artery tortuosity (0–3)	0.709			
Common iliac MLD, mm	0.419			
External iliac MLD, mm	0.264			
SEIAR	0.577			
Iliac artery calcification (0–3)	0.077			
Iliac artery tortuosity (0–3)	0.459			

Three cases were excluded because of death before valve deployment and access closure.
TAVI = transcatheter aortic valve implantation; other abbreviation as in Tables 1, 2, and 3.

Table 4. Description of Death Due to Vascular Complications

Patient #	No. in Cohort	Age, yrs	Sex	Vascular Access	Sheath Size, F	SFAR	Complication	Treatment	Survival, Days	Cause of Death
1	17	84	M	Surgical	24	1.18	Iliac occlusion	Surgery	6	Multiple organ failure
2	24	89	M	Surgical	24	1.21	Femoral access site infection	Surgery	27	Sepsis, multiple organ failure
3	30	70	F	Surgical	24	1.03	Iliac rupture	Surgery	3	Multiple organ failure
4	109	84	M	Percutaneous	24	1.10	Iliac rupture	Surgery	0	Hemorrhagic shock
5	166	86	M	Percutaneous	18	0.74	Thoracic aorta rupture	Covered stent	0	Hemorrhagic shock

F = female; M = male; SFAR = sheath to femoral artery ratio.

no longer predictive of vascular complications when adjusted for other variables in the multivariate model ($p = 0.057$). It is likely that the strong association between the type of TAVI with both SFAR ($p < 0.001$) and center experience ($p = 0.001$) are responsible for this result.

Increased rates of in-hospital mortality (27.3% vs. 9.5%, $p = 0.023$), 30-day mortality (22.7% vs. 7.6%, $p = 0.049$), and longer hospital stay (16.5 ± 11.6 days vs. 9.7 ± 6.2 days, $p = 0.016$) were observed in patients with VARC major complications. VARC minor complications were not associated with increased 30-day mortality (7.7% vs. 13.2%, $p = 0.574$) or increased duration of hospital stay (9.8 ± 4.0 days vs. 11.0 ± 8.3 days, $p = 0.636$).

SFAR threshold predicts VARC major vascular complications. The sensitivity–specificity curves identified a threshold SFAR of 1.05, which predicted VARC major vascular complications (Fig. 2). With this cut point, the sensitivity, specificity, and positive and negative predictive values were 66.7%, 65.6%, 40.7%, and 84.7%, respectively, and the area under the receiver-operator characteristic curve was 0.727. Using this SFAR threshold, the minimal femoral artery diameter necessary for the 19- and 18-F introducer sheaths was calculated as 7.1 and 6.9 mm, respectively.

In noncalcified iliofemoral vessels (calcium score = 0), the SFAR increased to 1.10 and, conversely, decreased to 1.00 in calcified arteries (calcium score 1 to 3). Using this SFAR threshold, the minimal femoral artery diameter necessary for the 19- and 18-F introducer sheaths was calculated as 6.8 and 6.5 mm, respectively, in noncalcified iliofemoral vessels, and 7.5 and 7.2 mm, respectively, in calcified iliofemoral vessels.

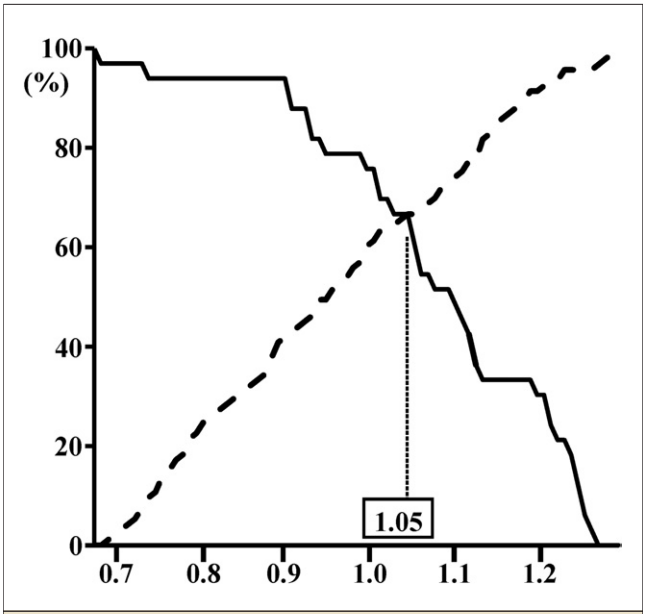

Figure 2. SFAR Threshold Predicts VARC Major Vascular Complications

The sensitivity and specificity curve identified the threshold sheath femoral artery ratio (SFAR) of 1.05 as predictive of VARC major vascular complications. **Solid line** = sensitivity; **broken line** = specificity. VARC = Valve Academic Research Consortium.

Table 6. Comparison of the Clinical Outcomes According to SFAR Threshold

Variables	SFAR ≥1.05 (n = 55)	SFAR <1.05 (n = 72)	p Value
Any vascular complication	23 (41.8%)	12 (16.7%)	**<0.001**
VARC Major	17 (30.9%)	5 (6.9%)	**0.001**
VARC Minor	6 (10.9%)	7 (9.7%)	0.827
Femoral artery complication	15 (27.3%)	9 (12.5%)	**0.035**
Iliac artery complication	11 (20.0%)	2 (2.8%)	**0.002**
In-hospital mortality	11 (20.0%)	5 (6.9%)	**0.033**
30-day mortality	10 (18.2%)	3 (4.2%)	**0.016**

Values are n (%). p Values in **bold** are statistically significant.
Abbreviations as in Tables 2 and 3.

Clinical outcomes according to SFAR. Clinical outcomes were compared according to the SFAR cut point of ≥1.05 (Table 6). This cut point predicted higher rates of VARC major complications (30.9% vs. 5.6%, $p < 0.001$). An SFAR ≥1.05 was also associated with an increased incidence of 30-day mortality (18.2% vs. 2.8%, $p = 0.004$).

Discussion

This study provides the first detailed description of vascular complications, as defined by the VARC criteria (10), in a large cohort of patients treated by transfemoral TAVI. Our results demonstrate that VARC major vascular complications predict both 30-day and in-hospital mortality. In contrast, VARC minor complications are not associated with increased mortality. Furthermore, we have described the SFAR, a novel tool which predicts VARC major vascular complications, and is strongly associated with clinical outcomes, including mortality.

Uniform definition of vascular complications with TAVI. To date, vascular complications have been described in 8% to 30.7% of Edwards valve recipients (1–3,6,8,16,17), and 1.9% to 16% of CoreValve patients (5–7,18). The considerable variation in the reported incidence of these complications arises, in part, from the absence of a standardized definition for vascular complications in TAVI (1–3,5–8,16–18). Most studies on TAVI have only reported complications that required further percutaneous or surgical intervention (6,16), and thus, the true frequency of vascular complications in transfemoral TAVI may have been underestimated. In an effort to standardize the reporting of TAVI data, the VARC have recently developed a consensus on TAVI-related endpoints (9), including a uniform definition of vascular complications. In our series of mixed implant transfemoral TAVI patients, we defined vascular complica-

tions according to the VARC criteria, and observed a complication rate of 27.6%, higher than previously described. The rate of major complications in our study was 17.3%, and is comparable to other published series (1,3,8,18); however, the overall rate of complications was amplified by the addition of VARC minor complications (10.2%). Although the routine application of the VARC criteria for vascular complications will provide reliable, standardized information for TAVI-related research, it is likely to increase the reported rates of complications despite ever-improving operator expertise and device safety.

Impact of vascular complications on mortality. The importance of vascular complications in transfemoral TAVI patients remains unclear (6,8,17). Two small series of Edwards valve (n = 54) (8) and mixed Edwards and CoreValve patients (n = 45) (6), and a large international registry (n = 463) of Edwards valve patients (17), found no association between vascular complications and mortality. In contrast, in a multicenter cohort of 168 Edwards valve recipients, major vascular complications occurred in 13% of cases and were associated with a mortality rate of 25% (3). In our study, VARC major vascular complications were associated with both in-hospital (27.3% vs. 9.5%, p = 0.023) and 30-day mortality (22.7% vs. 7.6%, p = 0.049). Consistent with previous reports (3), VARC major vascular complications were associated with a 3-fold increase in the relative risk of death. VARC minor complications were not associated with mortality. The reason for the contrasting reports on the association vascular complications with patient mortality is not known, but may be related to the definition of vascular complications used. The VARC criteria includes factors such as blood transfusion (≥4 U) and ischemia-related end organ damage, which may not have been considered vascular complications in previous reports, but nonetheless portend a poor prognosis and thus enhance the association of vascular complications and mortality. For example, the patient in our cohort who developed a wound infection with subsequent septicemia, multiorgan failure, and ultimately death would not have been classified as a major vascular complication in previous studies. The VARC criteria may therefore represent a more inclusive, representative definition of vascular complications; however, further studies are required to investigate the relationship between VARC major complications and mortality.

SFAR predicts vascular complications and mortality. There is a need to identify predictors of vascular complications, though to our knowledge, we are the first to report predictors of vascular complications in transfemoral TAVI. Femoral artery calcification and increasing diameter of the introducer sheath have been previously identified as independent predictors of major vascular complications in endovascular aortic aneurysm repair (13,19,20); however, there is a paucity of data on the predictors of these complications in TAVI patients. Our study identified femoral artery calcification and center experience to be predictive of vascular complications in transfemoral TAVI. Indeed, the SOURCE registry observed that the incidence of vascular complications decreased with improved center experience (17). In our study, the introducer sheath outer diameter predicted vascular complications in the univariate analysis; however, it was not predictive of vascular complications following adjustment for other variables. In contrast, the strongest predictor of major vascular complications was the SFAR. This novel index reflects both femoral artery diameter and size of the introducer sheath, and was a more powerful predictor of vascular events than either of these criteria taken in isolation. When the femoral artery calcium score and SFAR were combined, the minimal femoral artery diameter required for the 19- and 18-F introducer sheaths was calculated as 6.8 and 6.5 mm, respectively, in noncalcified iliofemoral vessels, and 7.5 and 7.2 mm, respectively, in calcified iliofemoral vessels. Although these measurements represent more restrictive criteria than previously recommended (6,8,15,17), we believe that they offer the best chance of avoiding serious iliofemoral complications, particularly during the initial learning curve. Alternative approaches (transapical, transaortic, trans-subclavian, or retroperitoneal) should be considered in patients with borderline femoral artery diameters (6.0 to 6.5 mm) following careful vascular screening with selective iliofemoral angiography, or if possible, MSCT. We believe that the routine application of SFAR will improve patient selection for transfemoral TAVI, reduce vascular complications, and ultimately, improve patient outcome.

Study limitations. Our study reports on a single-center, transfemoral TAVI cohort of limited size, recruited during our initial experience with this new technology. Nevertheless, our sample size is comparable to previous reports (6,8), and we believe it is important to describe the serious complications that may arise during the learning curve in a real-world experience. We opted to include patients who received the 22- and 24-F Edwards sheaths, which are no longer commercially available in Europe, as they were part of our initial experience and because the SFAR takes into account the size of the introducer sheath. Assessment of the iliofemoral vasculature with MSCT was not performed in all patients (n = 58), due to the high prevalence of renal dysfunction in our cohort; however, our study reflects real-world practice where the iliofemoral vessels are frequently assessed by conventional angiography. In the current paper, we report only in-hospital and 30-day outcomes. Longer-term follow-up, particularly in patients with vascular complications, is of significant interest and will be reported in due course.

Further studies of larger patient populations are required to confirm our results.

Conclusions

Vascular complications in transfemoral TAVI remain a significant issue despite improving center experience and smaller delivery systems. VARC major vascular complications occurred in 17.3% of patients in this series and were associated with increased 30-day mortality. VARC major complications are predicted by the SFAR, femoral artery calcification, and center experience. Routine application of the SFAR, with a cutoff value of 1.05, may improve TAVI-related outcomes.

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Key Words: aortic stenosis ■ balloon valvuloplasty ■ risk factors ■ transcatheter aortic valve implantation ■ vascular complications.

APPENDIX

For a supplementary figure, please see the online version of this article.