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Predictors and incidence of access site complications in transcatheter aortic valve implantation with the use of new delivery systems

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Abstract

Objectives: The aim of this single-center study was to assess the incidence and predictors of in-hospital access site complications related to transcatheter aortic valve implantation (TAVI) performed with new delivery systems in our hospital which has the largest case series in Turkey.

Materials and method: We performed successful TAVI with the Edwards Sapien XT valve to 127 (46 male) patients via a transfemoral (121), trans-subclavian (5) and transapical (1) approach. Access site complications were defined according to the Valve Academic Research Consortium (VARC) end-point definitions.

Results: Vascular complications occurred in 10.1% of patients. There was negative correlation between vascular complications and diameter of the common femoral artery (r = – 0.301, p=0.004), external iliac artery (r = – 0.327, p=0.004) and common iliac artery (r = – 0.324, p=0.004), but positive correlation between diabetes (r =0.240, p=0.008), sheath to femoral artery ratio (SFAR), sheath to external iliac artery ratio (SEIAR), procedure time, discharge time and the Society of Thoracic Surgeons (STS) score (respectively; r=0.339, 0.001, 0.527, 0.361, 0.289, p=0.003, 0.001, 0.001, 0.001, 0.002). The incidence of vascular complications was significantly higher in patients with diabetes and a high STS score. VARC bleeding complications occurred in 11.7 % of patients. The learning curve pointing out the importance of experience was significantly important in decreasing both bleeding and vascular complications.

Conclusions: In this study, we demonstrated that major vascular complications related to TAVI decrease with the use of smaller delivery systems and experience and increase with high-risk scores (STS) and the presence of diabetes. In addition, VARC major vascular complications, observed mostly in patients with diabete mellitus (DM) and high STS scores, were associated with vascular diameters. These results further underline the importance of experience and a multidisciplinary team in patient selection and management for TAVI.

Keywords

transcatheter aortic valve implantation; vascular complication; bleeding complication

Introduction

Transcatheter aortic valve implantation (TAVI) has emerged as a promising therapeutic option for patients with severe aortic stenosis (AS) who are ineligible for conventional surgical aortic valve replacement.[1,2] In the case of favorable anatomy, the transfemoral route is usually the preferred access site of first choice. Bleeding and vascular complications have been identified as a major concern in catheter-based interventions, in general, and TAVI, in particular.[3–5] Vascular complications are among the most frequent and serious complications of transfemoral TAVI

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Table 1. VARC end-point definitions.

Major vascular complications

1- Any aortic dissection, aortic rupture, annulus rupture, left ventricle perforation or new apical aneurysm/pseudo-aneurysm OR
2- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia or neurological impairment OR
3- Distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage
4- The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment
5- Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam and/or decreased or absent blood flow on lower extremity angiogram OR
6- Surgery for access site-related nerve injury OR
7- Permanent access site-related nerve injury

Minor vascular complications

1- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneuysms, hematomas, percutaneous closure device failure) not leading to death, life-threatening or major bleeding, visceral ischemia or neurological impairment OR
2- Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage OR
3- Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication OR
4- Vascular repair or the need for vascular repair (via surgery, ultrasound-guided compression, transcatheter embolization or stent-graft)
5- Percutaneous closure device failure

Life-threatening or disabling bleeding

1- Fatal bleeding (BARC type 5) OR
2- Bleeding in a critical organ, such as intracranial, intraspinal, intraocular or pericardial necessitating pericardiocentesis or intramuscular with compartment syndrome (BARC type 3b and 3c) OR
3- Bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery (BARC type 3b)
4- Overt source of bleeding with drop in hemoglobin >5 g/dL or whole blood or packed red blood cells (RBCs) transfusion >4 units (BARC type 3b)

Major bleeding (BARC type 3a)

1- Overt bleeding either associated with a drop in the hemoglobin level of at least 3.0 g/dl or requiring transfusion of two or three units of whole blood/RBC or causing hospitalization or permanent injury or requiring surgery AND
2- Does not meet criteria of life-threatening or disabling bleeding

Minor bleeding (BARC type 2 or 3a, depending on the severity)

Any bleeding worthy of clinical mention (e.g. access site hematoma) that does not qualify as life-threatening, disabling or major

The degree of vessel tortuosity was evaluated as follows: 0 = no tortuosity; 1 = mild tortuosity (30° to 60°); 2 = moderate tortuosity (60° to 90°); and 3 = marked tortuosity (>90°). The calcification was evaluated by multislice computed tomography and defined as follows: 0 = no calcification; 1 = mild calcification; 2 = moderate calcification; and 3 = marked calcification.

and have been associated with significantly increased patient morbidity and mortality.[6–8] Despite improved patient selection and down-sizing of the delivery system, these complications remain the vulnerable points of this novel procedure. Previous studies have reported on vascular complications in transfemoral TAVI.[2–5] However, due to the lack of a concensus in end-point definitions, the interpretation and comparison of outcome data from these studies are diffucult. To overcome this problem, the Valve Academic Research Consortium (VARC) has recently come up with a consensus on these TAVI-related end-point definitions.[9]

The aim of this study was to determine the incidence and influence of vascular and bleeding complications in a large cohort of TAVI patients, based on VARC criteria, and to identify predictors of these events.

Methods

Study population and design

Between June 2011 and March 2014, 127 consecutive high-risk patients with symptomatic severe AS treated with TAVI by using an Edwards Sapien XT valve at our institution were enrolled into this study. After the VARC consensus document was published, the proposed end-point definitions were adopted and the respective local databases were modified accordingly (Table 1).[9] Patients

with sypmtomatic severe AS (valve area<0.8 cm^2) were considered for TAVI if they had a logistic European System for Cardiac Operative Risk Evaluation score (EuroSCORE) >20% or if surgery was deemed to be prohibitive due to significant comorbidities (e.g.malignancy, cirrhosis, bleeding diathesis) or if other risk factors not included in these risk scoring systems (e.i., porcelain aorta) were present. The decision to proceed with TAVI was discussed by a dedicated heart team, which included cardiologists, cardiac surgeons, anesthesiologists and specialists in cardiac imaging. All patients selected for TAVI underwent physical examination, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE), baseline laboratory assays and coronary and peripheral angiography to assess anatomic suitability for TAVI and to determine the optimal access strategy. Peripheral arteries and the relation of the femoral artery bifurcation level to the femoral head and neck were assessed by selective iliofemoral angiography and multislice computed tomography (MSCT). Peripheral angiography of the femoral, external iliac, common iliac and subclavian arteries and the aorta was performed to measure the vessel lumen diameter, the degree of tortuosity and calcification and to identify the relationship of the common femoral artery bifurcation to the femoral head (under femoral neck, femoral neck-middle border of femoral head, middle-superior border of the femoral head, above the femoral head). The minimal lumen diameter of these arteries was also measured by MSCT, if needed. Measurement and qualitative assessment were performed by two independent operators.

The transfemoral route was the access site of first choice in our patients, as in other studies. When the transfemoral access site was decided to be inappropriate according to the consensus of the local heart team, a trans-subclavian or transapical approach was considered. After all evaluations, the suitable patients were taken to the catheterization laboratory and underwent TAVI with the smallest delivery system possible, including sheath size (16 and 18 Fr sheath in 92.1 % of patients) and valve size (23 mm valve in 55.9 % of patients).

Percutaneous access and closure were applied in 107 patients (84.3%) and a surgical strategy in 20 patients (15.7%). Fourteen of the femoral cases, all of the subclavian and the single apical case were performed by the surgical cut-down technique. Briefly, direct puncture of the common femoral artery was provided by iliofemoral angiography from the contralateral side. A single Prostar® XL (ProStar™ XL10Fr, Abbott Vascular, Abbott Park, IL, USA) device was used in 85.1% of the patients and two Proglide (Abbott Vascular Inc., Redwood City, CA, USA) devices in 14.9% of the patients for percutaneous closure. After Prostar® deployment, the femoral artery introducer sheath was carefully inserted over a stiff guidewire. Following aortic valve implantation, the introducer sheath was retracted to the external iliac artery and angiography was performed to evaluate any complications (e.g., dissections, rupture). The femoral artery was subsequently closed by tying the sutures before a final iliofemoral angiogram was performed from the contralateral side. For a surgical access strategy, standard vascular techniques were performed.

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

All TAVI procedures were performed using a flat-panel digital detector X-ray system (Siemens Axiom Artis Zee, Siemens Medical Solutions, Erlangen, Germany). Unlike the first 30 TAVI procedures performed under general anesthesia, all other patients received local anesthesia with mild sedation only. The VISIPAQUE™ Injection (GE Healthcare, Waukesha, WI, USA) was the contrast media delivered during all procedures. The total dose of radiation parameters and contrast were recorded for each patient.

All patients were pretreated with aspirin 100 mg and clopidogrel 75 mg daily. If the patients were not on dual antiplatelet therapy, a loading dose of clopidogrel (300 mg) was administered. During the procedure, a bolus of intravenous heparin (60 IU/kg) was administered to achieve a target activated clotting time (ACT) of 250 to 300 s and the ACT was measured every 30 min thereafter. If the target ACT was not achieved, an additional bolus dose, according to the ACT level, was added.

Age, gender, body mass index (BMI), logistic EuroSCORE score, STS score, ejection fraction, glomerular filtratation rate, presence of diabetes mellitus and peripheral artery disease, arterial vessel size, sheath to vessel size ratio, the degree of tortuosity and calcification and procedure time were the variables selected to assess potential predictors for vascular and bleeding complications.

To evaluate the association between the complications and the accumulating experience and learning curve of the operating team, we divided our cohort into two subgroups: a group with early experience, consisting of the first 30 TAVI cases, and a group with late experience, consisting of the latter 97 patients. Process measures (procedure times, contrast volume), length of stay and presence of vascular-bleeding complications were chosen as markers for increased procedural proficiency.

Statistical analysis

Statistical analyses were performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov test was used to control the data distribution. Student's t test was used for the analysis of parametric, continuous parameters. The Pearson test was used for analysis of non-parametric and discontinuous parameters. Pearson's and Spearman's correlation analyses were

used to assess the correlation. P-values <0.05 were considered as statistically significant.

Results

A total of 127 patients underwent TAVI using commercially available Edwards Sapien XT valves (Edwards Lifesciences, Irvine, California). Of these patients, 121 were treated by transfemoral TAVI, 5 by transsubclavian TAVI and 1 by transapical TAVI.

Patient demographics are presented in Table 2. The mean age was 78.1 ± 7.13 years with a mean STS of 7.53± 5.0% and a mean logistic EuroSCORE of 23.0±15.5%. Of the patients, 36.2% were men. The incidence of renal dysfunction (estimated glomerular filtration rate (eGFR) <60 ml/dL), peripheral artery disease, diabetes and smoking was 29.9%, 33.8%, 25.1% and 18%, respectively. The procedural characteristics are shown in Table 3. The femoral artery minimal lumen diameter (MLD) was 7.82 ± 0.84 mm, the mean external iliac artery MLD 8.4 ± 0.98 and the mean sheath outer diameter 6.97 ± 0.28 mm, giving a sheath to femoral artery ratio (SFAR) of 0.89 (0.72–1.2) and a sheath to external iliac artery ratio (SEIAR) of 0.82 (0.65–1.07). The relationship of the femoral access site was inferior to the femoral head in 37.9%, inferomedial to in 37.9%, superomedial to in 15.5% and superior to in 8.6% of patients. The right femoral artery was preferred in 53.2% of patients undergoing TAVI via the femoral artery. The degree of tortuosity and calcification in peripheral arteries was assessed by computed tomography angiography. Accordingly, severe tortuosity and calcification were observed in 13.0% and 14.3% of patients, respectively.

The rates of vascular and bleeding complications are presented in Table 4. Vascular complications occurred in 13 patients (10.1%) and included 5 (3.9%) VARC major complications and 8 (6.2%) VARC minor complications. All vascular complications were observed in patients undergoing transfemoral TAVI. Major femoral complications (n = 5) included 3 dissections, 1 vessel rupture and 1 hematoma. These complications were treated with balloon angioplasty (1 of 3 dissection cases), iliac stenting (vessel rupture case) and emergency surgical repair (hematoma case and 2 of 3 dissection cases). All these patients recovered. When baseline characteristics of the patients with and without vascular complications were analyzed (Table 5), it was observed that the incidence of diabetes mellitus and STS score, procedure time and length of stay were higher in the complication positive group than the negative group. In addition, the diameters of the superficial femoral artery, the external iliac artery and the common iliac artery were larger and the SFAR and SEIAR were found to be higher in patients with, rather than without, vascular complications. There was a negative correlation between vascular complications and the diameter of the superficial femoral artery (r : –0.301, p=0.008), the external iliac artery (r : –0.327, p=0.004) and the common iliac artery (r : –0.324, p=0.004) whereas there was positive correlation between diabetes (r : 0.240, p=0.008), STS score (r : 0.289, p=0.002), SFAR (r : 0.339 p=0.003) and SEIAR (r : 0.387, p=0.001) (Table 6). In addition, it was detected that procedure time and the length of hospital stay for patients with vascular complications were significantly longer compared to patients without vascular complications (respectively; r: 0.527, 0.361 p=0.001, 0.001).

Bleeding complications were observed in 15 patients (11.7%) and included 7 (5.5%) VARC life-threatening bleeding, 5 (3.9%) VARC major bleeding and 3 (2.3%) VARC minor bleeding. When baseline characteristics of patients with and without bleeding complications were analyzed (Table 7), no differences were detected between the groups.

Table 2. Baseline characteristics of the patients (n = 127).

Age, years	78.1 ± 7.13
Men, n (%)	46 (36.2 %)
BMI, kg/m²	28.4 ± 7.9
NYHA functional class III or IV, n (%)	118 (92 %)
Logistic EuroSCORE, %	23.0 ± 15.5
STS score, %	7.53 ± 5.0
SURTAVI, %	
Low risk	10.1
Moderate risk	31.2
High risk	58.7
Hemoglobin level at baseline (g/dL)	11.5 ± 1.9
Previous PCI, n (%)	24 (19.0%)
Previous CABG, n (%)	28 (22.2 %)
Previous MI, n (%)	29 (22.8 %)
Previous cerebrovascular disease	7 (5.5 %)
Previous cardiac surgery, n (%)	33 (25.9 %)
Peripheral vascular disease, n (%)	43 (33.8%)
Coronary artery disease, n (%)	94 (74%)
COPD, n (%)	69 (54.3%)
eGFR, ml/min/1.73 m²	57.6 ± 19.6
eGFR <60 ml/min/1.73 m², n(%)	30 (29.9 %)
Diabetes mellitus, n (%)	32 (25.1 %)
Current smoking, n (%)	23 (18 %)
Malignancy, n (%)	9 (7.0 %)
Pulmonary hypertension, n (%)	74 (58.2 %)
Permanent pacemaker, n (%)	4 (3.1%)
Echocardiography	
Aortic valve annulus, mm	21.3 ± 2.5
LVEF, %	52.8 ± 15.0
LVEF ⩽35 %, n (%)	22 (17.3 %)
Aortic valve area, cm²	0.61 ± 0.16
Mean aortic gradient, mmHg	52.2 ± 13.7

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 3. Procedural characteristics of the study population (n = 127).

Edwards SAPIEN XT valve	127 (100%)
Prosthesis size, mm	
23, n (%)	71 (55.9 %)
26, n (%)	52 (40.9 %)
29, n (%)	4 (3.1 %)
General anesthesia, n (%)	30 (23.6 %)
Local anesthesia -deep sedation, n (%)	97 (76.3)
Access and closure strategy	
Percutaneous, n (%)	107 (84.3 %)
Prostar XL, n (%)	91 (85.1 %)
Proglide, n (%)	16 (14.9 %)
Surgical, n (%)	20 (15.7 %)
Sheath size, Fr	
16, n (%)	61 (48 %)
18, n (%)	56 (44 %)
19, n (%)	6 (4.8 %)
20, n (%)	4 (3.2 %)
Relationship of access site to femoral head	
Under femoral neck, (%)	37.9 %
Neck-middle border, (%)	37.9 %
Middle-superior, (%)	15.5 %
Above the femoral head, (%)	8.6 %
Femoral artery MLD, mm	7.82 ± 0.84
SFAR	0.89 (0.72–1.2)
Common iliac artery MLD, mm	10.1 ± 1.73
External iliac artery MLD, mm	8.4 ± 0.98
SEIAR	0.82 (0.65–1.07)
Calcification score (0–3)	1.7 ±0.7
Tortuisity score (0–3)	1.67 ± 0.7

MLD: mean lumen diameter; SFAR: sheath to femoral artery ratio; SEIAR: sheath to external iliac artery ratio.

Table 4. Vascular access site and bleeding complications according to VARC classification (n = 127).

Vascular complications	
Major, n (%)	5 (3.9 %)
Minor, n (%)	8 (6.2%)
Bleeding complications	
Life-threatening/disabling, n (%)	7 (5.5 %)
Major, n (%)	5 (3.9 %)
Minor, n (%)	3 (2.3 %)

There was no significant relationship between vascular and bleeding complications and the degree of vascular calcification and tortuosity, the presence of peripheral artery disease, sex, smoking status and peripheral artery closure strategy (percutaneous or surgical). The first 30 patients (Group 1) were compared with the second 97 patients (Group 2) to evaluate the influence of a learning curve on vascular and bleeding complications (Table 8). Bleeding and vascular complication were detected to be significantly lower in Group 2 compared to Group 1 (p=0.003, p=0.012). There were significant differences between the two groups in terms of procedure time, contrast volume and length of stay. (p=0.001, p=0.007, p=0.001) (Table 9).

Discussion

The importance of vascular and bleeding complications in transfemoral TAVI patients remains unclear.[4,5,10] The two small series of Edwards valve (n = 54)[5] and mixed Edwards and CoreValve patients (n = 45)[4] and a large international registry (n = 463) of Edwards valve patients[10] found no association between vascular and bleeding 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%.[6] In our study, VARC vascular and bleeding complications were not associated with in-hospital mortality.

In this single-center, retrospective study, we found major vascular, major bleeding and life-threatening bleeding complications occurred in 3.9%, 3.9% and 5.5% of patients, respectively. Studies that also used the VARC definitions have reported a frequency of major vascular complications from 6% to 17%, of major bleeding 7% to 36% and of life-threatening bleeding from 7% to 14%.[11–15] In the Partner study, the only randomized controlled study regarding TAVI, the incidence of major vascular complications was 14% in inoperable patients at high operative risk undergoing TAVI (cohort A) and 16.2% in the inoperable cohort B.[1,16] To date, vascular complications have been described in 8% to 30.7% of Edwards valve recipients.[1–4,10] As you extrapolate, our complication rates are by far lower than the previous studies. This can be explained by some factors. First, all of the complications defined in the previous studies didn't have standardized end-point definitions for vascular and bleeding complications. For this reason, the true frequency of these complications in transfemoral TAVI may have been overestimated. To overcome this and to standardize the reporting of TAVI data, the VARC have recently developed a consensus on TAVI-related endpoints.[9] In our study, we defined vascular and bleeding complications based on VARC criteria and observed vascular and bleeding complication rates lower than previously described.

The sheath-to-femoral artery ratio (SFAR) has previously been identified as a significant predictor of vascular complications.[13] In the Milan experience, the incidence of major vascular complications was threefold lower in the 18Fr or 19Fr Sapien XT cohort versus the >19Fr Edwards Sapien cohort (11.1% vs 33.3%, relative risk 0.40, 95% confidence interval 0.28 to 0.57,

Table 5. Baseline and procedural characteristics according to the presence of vascular complications.

Variables	Vascular Complication (+)	Vascular Complication (-)	p-value
	n=13	n=114	
Age, years	80.6 ± 7.9	77.85 ± 7.0	0.184
Female, %	69.2	63.2	0.667
BMI, kg/cm²	28.21 ± 6.02	28.43 ± 8.14	0.939
NYHA functional class	3.16 ± 0.71	3.25 ± 0.56	0.73
STS score, %	11.6 ± 7.0	7.03 ± 4.48	0.002
Logistic Euroscore, %	28.56 ± 19.6	22.41 ± 15.0	0.213
PAD, %	38.5	35.8	0.854
DM, %	58.3	22.9	0.009
HT, %	58.3	81.3	0.065
Sigara, %	25	18.7	0.601
EF, %	55.0 ± 16.37	52.71 ± 14.86	0.617
CIA diameter, cm	8.76 ± 0.5	10.35 ± 1.76	0.004
EIA diameter, cm	7.69 ± 0.53	8.60 ± 0.99	0.004
SFA diameter, cm	7.2 ± 0.6	7.92 ± 0.84	0.008
SFAR	0.98 (0.84–1.2)	0.88 (0.72–1.12)	0.004
SEIAR	0.92 (0.82–1.07)	0.81 (0.65–1.03)	0.001
Tortuosity	1.72 ± 0.64	1.69 ± 0.2	0.799
Calcification	1.63 ± 0.67	1.68 ± 0.70	0.886
Procedure time, min	105.3 ± 21.1	60.2 ± 12.5	0.001
Discharge time, days	8.16 ± 3.63	4.68 ± 2.59	0.001

STS: Society of Thoracic Surgeons; PAD: peripheral artery disease; DM: diabetes mellitus; HT: hypertension; CIA: common iliac artery; EIA: external iliac artery; SFA: superficial femoral artery; SFAR: sheath to femoral artery ratio; SEIAR: sheath to external iliac artery ratio.

Table 6. Correlations between vascular complications and procedural and clinical characteristics.

Variables	Cor. Coeff.	p-value
SFAR	0.339	0.003
SEIAR	0.387	0.001
DM	0.240	0.008
STS score	0.289	0.002
CIA diameter	− 0.324	0.004
EIA diameter	− 0.327	0.004
SFA diameter	− 0.301	0.008
Procedure time	0.527	0.001
Discharge time	0.361	0.001

PAD: peripheral artery disease; CIA: common iliac artery; EIA: external iliac artery; SFA: superficial femoral artery; SFAR: sheath to femoral artery ratio; SEIAR: sheath to external iliac artery ratio; STS: Society of Thoracic Surgeons.

p = 0.004).[17] A beneficial effect of smaller sheaths has been shown with transfemoral coronary procedures.[18]

The second reason for our lower complication rate could be explained by the use of smaller sheath sizes in patients undergoing TAVI. We used 16Fr and 18Fr sheaths in 92.1% (n=117) of our patients. Because most of the the patients with degenerative AS are older in age and their vessels are tortuous, calcific and rigid, the smaller the sheath size the smaller the driving force of it on the vessel. Therefore, we assumed less vascular complications, as in our study. The third reason is the comprehensive evaluation of patients with multimodal imaging devices, such as TTE, TEE, MSCT, peripheral angiography and, if needed, magnetic resonance angiography before the procedure. With the help of TTE and TEE, the anulus size was measured and the most convenient valve size to be implanted during TAVI was established. Thus, we prevented improper over- or undersized valve and sheath usage. Moreover, we evaluated the peripheral vasculature with both multislice computed tomography angiography and invasive coronary angiography and, when needed, magnetic resonance angiography. Thus, our study reflects real world practice where peripheral

Table 7. Baseline and procedural characteristics according to presence of bleeding complication.

Variables	Bleeding Complication(+)	Bleeding Complication(-)	p-value
	n=15	n=112	
Age, years	78.7 ± 8.74	78.06 ± 7	0.75
Female, %	71.4	62.8	0.529
BMI, kg/cm²	27.3 ± 5.64	28.5 ± 8.1	0.665
NYHA functional class	3.28 ± 0.61	3.23 ± 0.57	0.751
STS score, %	7.31 ± 4.37	7.56 ± 5.09	0.867
Logistic Euroscore, %	26.04 ± 21.6	22.6 ± 14.8	0.497
PAD, %	46.2	34.9	0.428
DM, %	25	26.6	0.905
HT, %	75	79.4	0.722
Smoking, %	8.3	20.6	0.311
EF, %	55.5 ± 13.4	52.6 ± 15.1	0.617
CIA diameter, cm	10.95 ± 1.64	9.96 ± 1.71	0.069
EIA diameter, cm	8.85 ± 1.09	8.4 ± 0.96	0.142
SFA diameter, cm	7.85 ± 0.96	7.82 ± 0.83	0.912
SFAR	0.90 (0.76–1.03)	0.89 (0.72–1.2)	0.727
SEIAR	0.80 (0.65–0.90)	0.83 (0.65–1.07)	0.294
Tortuosity	1.45 ± 0.52	1.74 ± 0.72	0.256
Calcification	1.45 ± 0.52	1.71 ± 0.71	0.311
Procedure time, min	68.1 ± 15.7	77.2 ± 24.4	0.266
Discharge time, days	6.58 ± 3.36	4.86 ± 2.8	0.051

BMI: body mass index; NYHA: New York Heart Association; PAD: peripheral artery disease; DM: diabetes mellitus; HT: hypertension; CIA: common iliac artery; EIA: external iliac artery; SFA: superficial femoral artery; SFAR: sheath to femoral artery ratio; SEIAR: sheath to external iliac artery ratio.

Table 8. Vascular and bleeding complications.

All patients (n=127)	Major	Minor
Patients with vascular complications, n (%)	5 (3.9%)	8 (6.3%)
Femoral artery		
Rupture, n (%)	1 (0.8)	0
Dissection, n (%)	3 (2.4)	1 (0.8)
Stenosis/occlusion, n (%)	0	1 (0.8)
Pseudoaneurysm, n (%)	0	2 (1.6)
Hematoma, n (%)	1 (0.8)	1 (0.8)
Prostar failure, n (%)	0	3 (2.4)
Local infection, n (%)	0	0
Vascular intervention		
Balloon angioplasty, n (%)	1 (0.8)	1 (0.8)
Femoral stenting, n (%)	0	0
Iliac stenting, n (%)	1 (0.8)	0
Aortic stenting, n (%)	0	0
Vascular surgery, n (%)	3 (2.4)	4 (3.2)
Conservative therapy, n (%)	0	3 (2.4)
In-hospital mortality, n (%)	0	0

vessels are mostly assessed by conventional angiography. In that way, we determined the technique (transfemoral, transsubclavian or transaortic), the site (whether left or right) and the closure method (surgical or percutaneous) of the procedure.

To assess the learning curve, the 127 patients were divided into two groups. The first 30 patients were classified as first experience, the latter 97 patients as a late experience group. The reason why we used the first 30 patients as a first experience group is based on a study

Table 9. Effect of learning curve on procedural changes and complications.

Variables	Patients 1–30	Patients 31–127	p-value
Vascular complication, n (%)	7 (21.2%)	6 (6.4%)	0.012
Bleeding complication, n (%)	8 (25.0%)	6 (6.3%)	0.003
Procedure time, min	82.3 ± 25.1	60.1 ± 14.5	0.001
Length of stay, days	6.45 ± 3.93	4.54 ± 2.26	0.001
Contrast volume	201.9 ± 49.5	176 ± 60.7	0.007

published by Alli and colleagues which reported that TAVI learning curves plateau after about the 30th procedure.[19] In their study, although they found significant decreases in median contrast volume, valvuloplasty to valve deployment time and fluoroscopy times, vascular complication rates, length of hospital stay and mortality did not significantly change across the groups. However, in our study, we found bleeding and vascular complications significantly lower, procedure time shorter and lesser contrast volume in the latter 97 patient. These results support our idea about the importance of the learning curve on the rates of vascular complications during TAVI.

Another confounding factor to analyse the true effect of the learning curve on vascular and bleeding complication is TAVI training programs. Currently, most new centers will begin with proctored cases. Gurvitch and colleagues[20] reported significant improvement in in-hospital and 30-day mortality with increasing experience, but there was no difference in procedural complications between the first and second halves of their series. As with our study, STS scores were lower in the second half of their series than in the first, which likely reflects better patient selection based on experience.

In another study, Lange et al. reported their experience regarding patient selection for TAVI.[21] They divided all the patients into four quartiles (each quartile included 105 patients, 420 in total) and compared their basal characteristic features. As a result, compared with the fourth-quartile (Q4), patients in first quartile (Q1) had higher logistic EuroSCOREs (25.4 vs 17.8, $p<0.001$) and STS scores (7.1 vs 4.8, $p<0.001$), indicating their having a higher risk of complications from surgery than those in Q4. In addition, Lange et al. observed a decrease in the rate of femoral complications over time, which they ascribed to the learning curve for preclosure devices. In this study, we also compared the basal characteristics of our patients after dividing them into two groups. Eventually, all baseline demographic variables, including vessel diameter, calcification and tortuosity degree, were similar between the groups, apart from the significantly higher STS scores (10.14 ± 5.35, 6.55 ± 4.51, $p=0.002$) in the first group. This difference seems to undermine the effect of experience.

The fourth reason is the experience. As the experience increases, the success of the procedure and percutaneous closure of the access site increases as well. Because the failure of the Prostar® or the Proglide® devices is one reason for the increase in vascular and bleeding complications, with experience, this failure will decrease and, accordingly, these complications will decrease as well.

Although we clearly observed improvements in the process measures, such as procedural time, contrast volume and complication rates, our series was not powered to detect differences in hard end-points, such as morbidity and mortality, due to the small sample size.

Conclusion

Bleeding and vascular complications are still the Achilles' heel of transfemoral TAVI. However, with improved experience, the use of multimodal imaging devices and the development of smaller delivery systems (means smaller SFAR and SEIAR) as in our TAVI series, VARC vascular complications and clinically significant bleeding complications were observed only in a small number (10.1% and 11.7%, respectively) of patients. VARC major vascular complications, observed mostly in patient with DM and high STS scores, were associated with vascular diameters. Therefore, multimodal imaging of peripheral arteries and determining the most suitable approach and access site before TAVI and, in addition, the use of smaller delivery systems, are the vital precautions to reduce access site complications together with the length of hospital stay and procedure time in these patients.

Limitations of the study

This study is a single-center cohort of TAVI and reports our initial experience with the Edwards Sapien XT valve. Our sample size is relatively limited, but comparable to previous reports.[3,4] This study was not powered to examine outcome variables as a reflection of procedural proficiency and learning. Further studies with larger sample size and smaller delivery systems are required to confirm our results.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

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References

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who can't undergo surgery. *N Engl J Med* 2010; 363: 1597–1607.
2. Lefevre T, Kappetein AP, Wolner E, et al. One year follow-up of the multi-centre European PARTNER transcatheter heart valve study. *Eur Heart J* 2010; 32: 148–157.
3. Ducrocq G, Francis F, Serfaty JM, et al. Vascular complications of transfemoral aortic valve implantation with the Edwards SAPIEN prosthesis: incidence and impact on outcome. *Eurointervention* 2010; 5: 666–672.
4. Tchetche D, Dumonteil N, Sauguet A, et al. Thirty-day outcome and vascular complications after transarterial aortic valve implantation using both Edwards Sapien and Medtronic CoreValve bioprosthesis in a mixed population. *Eurointervention* 2010; 5: 659–665.
5. Van Mieghem NM, Nuis RJ, Piazza N, et al. Vascular complications with transcatheter aortic valve implantation using the 18 Fr Medtronic CoreValve System(R): the Rotterdam experience. *Eurointervention* 2010; 5: 673–679.
6. Rodes-Cabau J, Webb JG, Cheung A, et al. Transcatheter aortic valve implantation for the treatment of severe aortic stenosis in patients at very high or prohibitive surgical risk: acute and late outcomes of the multicenter Canadian experience. *J Am Coll Cardiol* 2010; 55: 1080–1090.
7. Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation* 2006; 113: 842–850.
8. Piazza N, Grube E, Gerckens U, et al. Procedural and 30-day outcomes following transcatheter aortic valve implantation using third generation (18 Fr) CoreValve revalving system: results from the multicenter, expanded evaluation registry 1-year following CE mark approval. *EuroIntervention* 2008; 4: 242–249.
9. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2) *Eur J Cardiothorac Surg* 2012; 42: S45–60.
10. Thomas M, Schymik G, Walther T, et al. Third-day results of the SAPIEN Aortic Bioprosthesis Europian Outcome (SOURCE) Registry: a European registry of transcatheter aortic valve implantation using Edwards SAPIEN valve. *Circulation* 2010; 122: 62–69.
11. Stahli BE, Bunzli R, Grunenfelder J, et al. Transcatheter aortic valve implantation (TAVI) outcome according to standardized end-point definitions by the Valve Academic Research Consortium (VARC). *J Invasive Cardiol* 2011; 23: 307–312.
12. Wenaweser P, Pilgrim T, Roth N, et al. Clinical outcome and predictors for adverse events after transcatheter aortic valve implantation with the use of different devices and access routes. *Am Heart J* 2011; 161: 1114–1124.
13. Hayashida K, Lefevre T, Chevalier B, et al. Transfemoral aortic valve implantation new criteria to predict vascular complications. *JACC Cardiovasc Interv* 2011; 4: 851–858.
14. Gurvitch R, Toggweiler S, Willson AB, et al. Outcomes and complications of transcatheter aortic valve replacement using a balloon expandable valve according to the Valve Academic Research Consortium (VARC) guidelines. *Eurointervention* 2011; 7: 41–48.
15. Nuis RJ, Piazza N, Van Mieghem NM, et al. In-hospital complications after transcatheter aortic valve implantation revisited according to the Valve Academic Research Consortium definitions. *Catheter Cardiovasc Interv* 2011; 78: 457–467.
16. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011; 364: 2187–2198.
17. Mussardo M, Latib A, Chieffo A, et al. Periprocedural and short-term outcomes of transfemoral transcatheter aortic valve implantation with the Sapien XT as compared with the Edwards Sapien valve. *JACC Cardiovasc Interv* 2011; 4: 743–750.
18. Dauerman HL, Rao SV, Resnic FS, Applegate RJ. Bleeding avoidance strategies. consensus and controversy. *J Am Coll Cardiol* 2011; 58: 1–10.
19. Alli OO, Booker JD, Lennon RJ, Greason KL, Rihal CS, Holmes DR Jr. Transcatheter aortic valve implantation: assessing the learning curve. *JACC Cardiovasc Interv* 2012; 5: 72–79.
20. Gurvitch R, Tay EL, Wijesinghe N, et al. Transcatheter aortic valve implantation: lessons from the learning curve of the first 270 high-risk patients. *Catheter Cardiovasc Interv* 2011; 78: 977– 984.
21. Lange R, Bleiziffer S, Mazzitelli D, et al. Improvements in transcatheter aortic valve implantation outcomes in lower surgical risk patients. A glimpse into the future. *J Am Coll Cardiol* 2011; 59: 280–287.