Undescribed Anatomical Predictors of Vascular Injury after Fully-Percutaneous Trans Femoral Trans Catheter Aortic Valve Implantation

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Abstract

Background: Vascular injury (VI) remains frequent after trans catheter aortic valve implantation (TAVI). We aimed to assess the incidence, predictive factors, and the impact of early VI after fully-percutaneous (FP) TAVI.

Method: We included a total of 139 consecutive patients who underwent FP transfemoral TAVI in our institution with 14 to 18Fr sheath systems, through right (119, 85.6%) or left (20, 14.4%) femoral arteries. VI was classified as mayor or minor according to VARC-2 definitions. In hospital data were prospectively collected. Follow-up was available for all patients. Reassessment of femoral artery anatomy as determined by computed tomography was performed including lumen diameters, calcification, tortuosity, height of femoral bifurcation and marked collateral circulation around common femoral artery.

Results: Mean age was 81 ± 6.5, 54% were men, logEuroSCORE were 13.9 ± 7.9 and STS-score was 6.3 ± 4.9. Balloon-expandable and self-expandable devices were used in 14 (10.1%) and 125 patients (89.9%), respectively. Mayor and minor VI were observed in 25 (18%) and in 20 patients (14.3%) respectively, 20 of them due to suboptimal femoral closure (80% of major VI occurring in the first half of the learning curve). Lower platelet count (p=0.043), higher calcification of aortic valve (p=0.049), presence of femoral collaterals (OR=4.5, [95% CI: 1.6-12.9], p=0.005), height of femoral bifurcation (OR=14.5, [95% CI: 5.0-42.1], p<0.001), and failed femoral closure (OR=21.3, [95% CI: 4.5-101.4], p<0.001) were associated to higher rate of VI. The median length of hospitalization was 11.6 days [IQR: 7-14], (15.7 days [IQR: 8-19] in the VI cohort, p<0.001). VI was associated to higher in hospital mortality (13.3 *vs.* 2.1%, p=0.014).

Conclusion: In patients who underwent FP TAVI, the rate of VI is still high and associated to worse outcomes. A high common femoral artery bifurcation and the presence of collaterals, especially if associated to other concomitant predisposing factors for VI, should be handled with special care and surgical access may be considered.

Keywords: Vascular injury; TAVI; Percutaneous vascular closure; Vascular repair

Introduction

Trans catheter aortic valve implantation (TAVI) is an alternative to surgical aortic valve replacement (AVR) in high-risk patients [1, 2]. Over the past years, this procedure has proved to be safe; however there are still related complications that need to be addressed. Probably, the most frequent complication is peripheral vascular injury (VI) and bleeding events involving the access site. According to previous research, major vascular complications during TAVI may range between 5% and 25% of patients [3]. Early VI is often associated to serious bleeding requiring urgent surgical or invasive treatment and, therefore, VI is one of the most frequent causes of in-hospital mortality and, probably, the most worrisome safety issue during fully percutaneous procedures. Moreover, late survival rate seems to be also conditioned by early VI according to the long-term published results of the PARTNER trial [4, 5]. Complications in the vascular access site are probably influenced by several factors, including technical issues as the size of the devices (progressively improving due to lower profile of newer generation devices), the learning curve of fully-percutaneous procedures, and also, factors related to patient´s anatomy [6]. Our aims were: 1) To evaluate the incidence of early VI and to define the clinical and anatomical predictors through computed tomography (CT) analysis including a detailed description of femoral-iliac axis particularities, and 2) To assess the impact of early VI on post-TAVI prognosis.

Methods

Study population

Single-center, observational study of early VI related to TAVI. We collected the data of 139 consecutive patients who underwent TAVI in our center between April, 2009 and October, 2015. TAVI was decided by the local Heart Team following the recommendations of the European Society of Cardiology (in high risk patients) or when there were other criteria that precluded from conventional surgery despite lower risk score (including porcelain aorta and liver disease).

Procedural methods

The procedures were performed through 14Fr to 18Fr sheath systems, using right (119, 85.6%) or left (20, 14.4%) femoral arteries on the basis of CT angiography parameters that included, minimal lumen diameter, degree of calcification,

and severity of tortuosity. The vascular access was achieved in all cases percutaneously with pre-closure technique based on the puncture of the common femoral artery defined by contralateral ilio-femoral angiography. A single Prostar® or ProGlide® (Abbott Vascular, Santa Clara, CA, USA) device was placed in femoral artery before the aortic valve deployment. After tightening the sutures, a final angiogram was performed from contralateral side. The puncture was not ultrasound-guided.

Data gathering

All in hospital data were prospectively collected. Follow-up was available for all patients through clinical visit at 1 month, 6 month and 1 year after discharge.

Re-assessment of the femoral arteries' anatomy was determined by re-evaluation of the computed tomography images by 2 independent operators (J. T. and I. J. A. S) that determined: 1) minimal diameter of the access site. Vessel diameter was defined as the distance between the internal vessel walls. The diameters of the common femoral arteries were measured below the inguinal ligament. 2) Femoral artery severe wall calcification, defined as the presence of calcium >50% of the arterial perimeter ("C" shape) or bulky calcification protruding to the lumen of the vessel. 3) Presence of marked collateral circulation (defined as 3 or more collateral vessels around common femoral artery visualized with angiography). 4) Height of the bifurcation of common femoral artery, determined as schematically depicted in **Figure 1**.

The assessment of vascular injury was determined by 2 independent operators (J.T. and I.J.A.S); in case of discrepancy a third observer (J.C.) contributed to the final decision. Vascular injury major or minor was defined according to the consensus from the Valve Academic Research Consortium (version 2) [7]. The study group was divided into two

subgroups to assess the influence of a learning curve on early vascular injury. Subgroups presented consecutive patients that underwent TAVI earlier and later during the follow-up period.
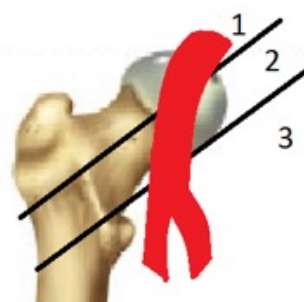

Figure 1 Type 1- upper half of femoral head, type 2- lower half of femoral head and type 3 below femoral head. *According to a coaxial line though femoral neck.

Statistical methods

The data are expressed as absolute rate and percentage in case of qualitative variables. Quantitative variables are described as mean (SD) or median (25th-75th) interquartile range [IQR]) depending on variable distribution. Group comparisons were analyzed using Student's t-test or its non-parametric equivalent, Mann-Whitney U-test for continuous variables, and Chi-square test or Fisher's exact test for categorical variables. Statistical significance was defined as p-value <0.05. The univariate normality assumptions were verified with the Kolmogorov-Smirnov tests. A cox multivariable analysis including all variables with P value <0, 10 in the univariable analysis was used to determinate the predictive factors of vascular injury. All analyses were conducted using the statistical package SPSS, version 18.0 (SPSS, Inc.; Chicago, Illinois, USA).

Table 1 Description of the different types of vascular injury and their treatment.

Type of CV event	All VI events n=45	Mayor VI n=25	Minor VI n=20	Intervention
Retroperitoneal bleeding	5	5	0	Vascular surgery - 3 Death - 2 Transfusion - 1
Aorta rupture	2	2	0	Death - 2
Femoral artery rupture	1	1	0	Femoral stenting
Femoral artery dissection	4	1	3	Surgery - 1 Femoral stenting - 1 No intervention - 2
Femoral stenosis/occlusion	4	3	1	Vascular surgery - 3 No intervention
Closure failure	12	7	5	Vascular surgery - 8 Balloon stenting - 4
Femoral distal embolization	2	2	0	Vascular surgery - 2
Hematoma	5	0	5	Blood transfusion - 5
Femoral pseudo aneurysm	8	4	4	Surgery - 4 Compression - 4
Femoral arterio-venous fistulae	2	1	1	Surgery - 1 Compression - 1
CV: Cardiovascular; VI: Vascular Injury				

Table 2 Baseline and procedural characteristics of the patients. Main predictors of vascular injury in our study population.

	Total of patients n=139	Without VI (%) n=94 patients	With VI (%) n=45 patients	P value
Age (years)	81.01 +/- 6.5	81.48 +/- 6.1	80 +/- 7.1	P=0.216
Female	64 (46%)	40 (42.6%)	24 (53.3%)	P=0.233
Diabetes mellitus	49 (35.3%)	31 (33%)	18 (40%)	P=0.418
Hypertension	45 (32.4%)	29 (30.9%)	16 (35.6%)	P=0.579
Dyslipidemia	53 (38.1%)	36 (38.3%)	17 (37.8%)	P=0.953
Peripheral vascular disease	8 (5.8%)	5 (5.3%)	3 (6.7%)	P=0.71
Stroke/TIA	13 (9.4%)	9 (9.6%)	4 (8.9%)	P=0.99
AR (3 and 4 degree)	16 (11.6%)	9 (9.6%)	7 (15.9%)	P=0.279
Body mass index (kg/m2)	26.87 +/- 4.6	27.2 +/- 4.6	26 +/- 4.6	P=0.164
Hemoglobin (g/dL)	11.9 +/- 1.9	11.84 +/- 5.6	12 +/- 5.9	P=0.614
Platelets (mil/mm3)	179 +/-53 X 10³	192 +/- 48 X 10³	172 +/- 59 X 10³	P=0.043
Serum creatinine (mg/dL)	1.11 +/- 0.4	1.15 +/- 0.43	1.04 +/- 0.31	P=0.104
Coronary artery disease	62 (44.7%)	42 (44.7%)	20 (44.4%)	P=0.979
Porcelain aorta	9 (6.5%)	4 (4.3%)	5 (11.1%)	P=0.149
Right femoral approach	119 (85.6%)	82 (87.2%)	37 (82.2%)	P=0.431
Collateral circulation	46 (33.1%)	25 (27.2%)	21 (46.7%)	P=0.023
STS score (%)	6.34 +/- 4.9	6.59 +/- 4.7	5.82 +/- 5.3	P=0.07
Log Euro SCORE	13.89 +/- 7.9	13.15 +/- 8.9	15.44 +/- 8.6	P=0.292
Bifurcation femoral				
Type 1	9 (6.5%)	1 (1.1%)	8 (17.8%)	P=0.001
Type 2	53 (38.1%)	24 (25.5%)	29 (64.4%)	
Type 3	77 (55.4%)	69 (73.3%)	8 (17.8%)	
Prostar® closure device	114 (83.8%)	78 (83.9%)	36 (83.7%)	P=0.982
Severe femoral wall calcification	31 (22.5%)	19 (20.2%)	12 (27.3%)	P=0.354
Self-expandable Valve	125 (89.9%)	85 (90.4%)	40 (88.9%)	P=0.946
Minor femoral diameter*	7.42 +/-1.31	7.57 +/- 1.28	7.07 +/- 1.32	P=0.069

AR: Aortic Regurgitation; TIA: Transient Ischemic Accident *(mm)

Results

A total of 139 consecutive patients (pts) were included. Mean age was 81 ± 6.5, 54% were men, logistic Euroscore was 13.9 ± 7.9 and STS-score was 6.3 ± 4.9. The balloon-expandable SAPIEN XT/SAPIEN-3 and the self-expandable Medtronic Core Valve were used in 14 (10,1%) and 125 patients (89,9%), respectively. Mayor and minor VI were observed in 25 (18%) and in 20 patients (14.3%) respectively, 20 of them due to suboptimal femoral closure. The different types of VI, the severity, and their treatment are briefly described in the **Table 1**. The learning curve had impact on early VI rate after TAVI, with 80% of the episodes of major VI occurring in the first half of our population.

Main predictors of VI are summarized in **Table 2**. To remark lower platelet count (173 *vs.* 192 × 10³, p=0.043), higher calcification of aortic valve (3692 UA *vs.* 2486 UA, p=0.049), the presence of collateral circulation (P=0.023), and height of femoral bifurcation (type 1 *vs.* types 2 and 3 according to **Figure 1**) (p<0.001) were related to higher rate of VI. The 62 patients (44.6%) who presented a height of the common femoral artery bifurcation at the level of the femoral head or above (types 1 and 2 in **Figure 1**) suffered VI in up to 82,2% of the cases, as opposed to 17.8% (8 patients) among those with bifurcation type 3 (77 patients, 55.4%), p<0.001.

Concerning the procedure, the use of Prostar® device (n=114, 83.8%) for access site closure or ProGlide® system (n=22, 16.2%) (Abbott Vascular Inc., Santa Clara, CA, USA) was not associated to differences in outcomes in terms of VI. Neither was the type of prosthesis implanted as shown in **Table 2**.

The median length of hospitalization was 11.6 days [IQR: 7-14], being longer for patients who complicated with VI (15.7 days [IQR: 8-19], p<0.001). The in-hospital rates of acute kidney injury, heart failure, and need for oro-tracheal intubation were higher in patients who suffered major vascular injury (p<0.001).

Multivariate analyses helped to determine that height of bifurcation (OR=14.5, [95% CI: 5.0-42.1], p<0.001), presence of collateral circulation (OR=4.5, [95% CI: 1.6-12.9], p<0.001), and failed femoral closure (OR=21.3, [95% CI: 4.5-101.4], p<0.001) were independent predictors of VI. Patients who presented in hospital death (8 patients, 5.8%), also had a higher rate of VI (75% *vs.* 25%, p=0.014). Post-procedural VI was the main reason for 4 early deaths (within the first 24 h after the implantation), 2 of them due to retroperitoneal bleeding and 2 due to aortic rupture. The other 4 patients died due to septic shock by nosocomial pneumonia in 2 cases and heart failure in the remaining 2 cases.

The impact of VI during the hospitalization did no significantly impact the outcomes at 1 year of follow up.

Discussion

According to previous data, vascular injury after transfemoral TAVI has raised as the most common peri-procedural complication and with the worst effect on outcomes [8]. Our results highlight the impact of this problem in the in-hospital mortality rate despite a significant decrease of this complication together with the progression of the learning curve and the better profile of newer devices. However, the impact of large semi-rigid introducers in severely atherosclerotic peripheral vessels is still a challenge that requires exquisite evaluation of the anatomy. To this end, the lessons learnt with the experience of CT analysis should not be denied. Beyond vessels diameter and calcification, several factors including tortuosity, presence of a prominent collateral circulation around common femoral artery, and a bifurcation of the access site in the upper segment of the femoral head have demonstrated in this study to act as predictors of vascular complications. Importantly, the development of VI was associated to higher in-hospital mortality, suggesting that the presence of adverse femoral anatomy (even if diameters are adequate) should lead to switch to surgical cut-down or, at least, promote the presence of the surgeon during the procedure in order to promptly correct eventual vascular damage by the TAVI system. The higher rate of VI reported in series with fully percutaneous approach as compared to those with surgical cut-down [5-8] has been a source of conflict. Although surgical cut-down can be performed with local anesthesia, in many centers general anesthesia is still used for such intervention. The current tendency to minimize the complexity of the procedures includes the avoidance of oro-tracheal intubation and favors the use of fully percutaneous approach due to the general belief that this strategy may improve outcomes in frail patients. However, as lower risk patients undergo this procedure more and more often, competitive results to those of open heart surgery can only be obtained through optimization of outcomes with reduction of main complications as VI [8, 9]. In addition, the impact of the learning curve is probably more relevant in fully percutaneous procedures as highlights the fact that 80% of the major vascular complications in our population occurred in the first half of the treated patients.

With regard to arterial morphology, we demonstrated that a greater arterial wall calcification, height of bifurcation, and presence of collateral circulation significantly increased the risk for early VI. Moreover, collateral circulation and especially height of bifurcation were independent predictors of early VI. Collaterals may reflect a worse vascular disease, with stenotic peripheral vessels that promote the development of such collaterals. But also, it may be the source of unnoticed punction of these vessels that may bleed in the peri-procedural period. The impact of the height of the bifurcation can probably be explained by the fact that, this height also reflects the need for a deeper femoral punction. Even when this maneuver is normally angiographically guided, as the tip of the needle is deeper, control of its trajectory is worse. Also,

the knots of the percutaneous closure devices had higher risk of tighten too far from the vessels' wall, not achieving a correct hemostasis.

Previous research had tried to address the worrisome issue of VI through real-time ultrasound guidance. Compared with standard fluoroscopic guidance, they achieved to improve common femoral artery cannulation only in the subgroup of patients with higher bifurcations [10]. Although surgical cut-down has been supported by some groups, as experience with percutaneous approach increases, this less invasive percutaneous method seems associated with similar rates of major and minor vascular complications, with lower access site infection and bleeding, and shorter hospital stay compared to the surgical approach [11]. Nevertheless, a role to surgical vascular approach may continue to be necessary in patients that present a combination of anatomical predisposing factors for VI, as previously described.

The main limitation of our study was its retrospective nature and single-center registry of data. However, report of this real-world experience is of utmost importance in order to draw a picture of outcomes and main complications in moderate-volume centers so that the best strategies to improve the results can be implemented, mainly, as lower risk patients are the new target for this technology.

Conclusion

In conclusion, in spite of the careful patient-level selection in order to avoid vascular access complications, vessels' injury can still occur, being likely related to a higher rate of in-hospital mortality. More detailed anatomical description of vascular access will be required in the future in order to improve outcomes. Also, surgical cut-down, should not be excluded in case of extremely challenging anatomies.

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