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Impact of transfemoral versus transapical access on mortality among patients with severe aortic stenosis undergoing transcatheter aortic valve replacement☆

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ABSTRACT

Objective: To compare early and late mortality of transfemoral (TF) and transapical (TA) transcatheter aortic valve replacement (TAVR) patients and assess predictors for mortality.
Background: Studies have shown conflicting results regarding impact of access on outcome in severe aortic stenosis (AS) patients undergoing TAVR.
Methods: AS patients undergoing TAVR between May 2007–December 2014 were included. Baseline demographic, clinical, and imaging parameters were compared according to access, and landmark analysis models were generated to assess outcomes and associated factors.
Results: Among 648 severe AS patients undergoing TAVR, TF was used in 516 and TA in 132. Baseline characteristics between groups demonstrated lower body mass index, higher STS score, and rate of peripheral vascular disease among TA patients. Procedural complications were more common in the TA group, especially major bleeding (15% vs. 6%, $p < 0.001$) and acute kidney injury > 1 (8% vs. 1.4%, $p < 0.001$). Landmark analysis demonstrated higher cumulative mortality rates at 30 days among TA than TF patients (log-rank $p < 0.001$), with similar mortality after 30 days and up to 1-year (13% in both log-rank $p = 0.64$). In a multivariate model, TA was an independent predictor of early mortality (HR = 4.55 95% CI [12.5–1.6], $p = 0.003$) along with pulmonary artery systolic pressure > 60 mmHg (HR = 3.08 95% CI [7.37–1.29], $p = 0.01$) and residual aortic regurgitation severity above mild (HR = 3.99 95% CI [10.2–1.56], $p = 0.004$).
Conclusions: Patients undergoing TAVR via TA have higher adjusted early mortality and similar late mortality rates compared to TF, despite higher risk profile.

1. Introduction

Transcatheter aortic valve replacement (TAVR) has been shown to improve outcome in patients with severe aortic stenosis who have been deemed inoperable [1] or high risk [2], with mortality rates similar to surgical aortic valve replacement [3]. The default access for the TAVR procedure has been the femoral arteries (TF). However, patients with small femoral and iliac arteries cannot accommodate large sheath and delivery valve systems. This led to the search for an alternative access for TAVR procedures. The transapical approach (TA) [4] has been accepted as the most common alternative access in patients who are not suitable for the TF approach. The outcome of patients who were undergoing TAVR via the TA approach was reported to be inferior to the TF approach, and it is not clear whether this is because of access selection or related to the condition of the patient [5–8]. The purpose of the present study was to compare early and late mortality rates along with other TAVR complications among patients with severe aortic stenosis undergoing TAVR and to delineate the incidence and the correlates of early and late mortality according to the different access points used for the TAVR procedure.

2. Methods

The study population consisted of patients with severe symptomatic aortic stenosis (confirmed by trans-thoracic echocardiography and hemodynamic evaluation) treated with TAVR at MedStar Washington Hospital Center between May 2007 and July 2014. Patients were categorized according to the access used for the procedure. The valves used during this period were CoreValve (Medtronic, Minneapolis, MN), Sapien and Sapien XT (Edwards Lifesciences, Irvine, California, USA), and Portico (St. Jude Medical, St. Paul, Minnesota, USA).

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Prespecified clinical, procedural, and laboratory data were prospectively collected for all patients during screening, on admission, immediately post procedure, and during follow-up. This included demographic information, medical history, New York Heart Association class, clinical data (e.g. echocardiographic indices and baseline electrocardiogram), and laboratory indices. The Society of Thoracic Surgeons score was calculated for every patient. Procedural data collected in the database included the amount of contrast injected, procedure length, devices used for valve implantation (including valve type, size, delivery system, and means of vascular access), and immediate complications. Post-procedural data used the hospital's documents as a primary source for laboratory results, length of stay, and in-hospital complications. Follow-up was based on patient visits to the outpatient clinic at 30-day, 6-months, and 1-year. Mortality data were received from family members and primary care physicians per each trial protocol or according to the Transcatheter Valve Therapy registry. An independent cardiologist adjudicated clinical events.

The primary endpoint for this study was all-cause mortality at 30-days and 1-year. Secondary endpoints consisted of peri-procedural complications according to the VARC-2 definitions.

Continuous variables were expressed as mean ± standard deviation for normally distributed variables and compared by Student's t-test. Categorical variables were expressed as numbers and percentages and were compared by chi-square or Fisher exact tests as appropriate. Time dependent analysis with a cut-off of 30 days, using Kaplan–Meier curve and log-rank, were performed to compare early and late mortality among severe aortic stenosis patients undergoing TAVR via the TA and TF approaches. Cox proportional hazard regression analysis was conducted, to assess the impact of TA on early mortality following adjustment for gender, peripheral vascular disease, body mass index below 20Kg/m^2, Society of Thoracic Surgeons score, pulmonary artery systolic hypertension above 60 mmHg, renal failure defined as glomerular filtration rate below 60 ml/min, and aortic regurgitation of more than mild severity following the procedure. Factors associated with early and late mortality in both groups were assessed by a multivariate stepwise Cox proportional hazard regression.

Statistical analysis was performed using SAS version 8.2 (SAS Institute Inc., Cary, NC), and a p-value below 0.05 was considered significant.

3. Results

Among 648 severe aortic stenosis patients undergoing TAVR at our center, 516 and 132 had the procedure performed via the TF and TA approach, respectively. Mean age was 83 ± 8, and 50% (n = 322) was male. Baseline characteristics between both groups can be found in Table 1 and shows similar characteristics with the exception of body mass index, which was significantly lower in TA patients (26 ± 6 vs. 28 ± 7, p = 0.03) with a higher Society of Thoracic Surgeons score (10.4 ± 4.6 vs. 8.7 ± 4.5, p < 0.001). In addition, cerebral and peripheral vascular disease prevalence was lower in the TF group than in TA patients (24% vs. 13%, p < 0.001, 56% vs. 30%, p < 0.001, respectively).

Procedural data show that fluoroscopy time and contrast volume used were significantly lower in the TA than the TF group (12 ± 6 vs. 24 ± 20 min, p < 0.001, and 96 ± 41 vs. 130 ± 72, p < 0.001, respectively) (Table 2) and lower rates of additional intervention, such as balloon post-dilatation and second valve deployment (Table 3), were also found in the TA group.

Complications comparison between the groups revealed higher rates of life-threatening bleeding events (15% vs. 6%, p < 0.001) and increased rates of both intra-procedural and post-procedural transfusion rates in the TA compared with the TF group (13% vs. 7%, p = 0.04, and 36% vs. 18%, p < 0.001, respectively). Acute kidney injury was also noted to occur more than 5-fold in the TA group than in the TF patients. Ventricular injury, pleural effusion, and post-procedural atrial fibrillation incidence were additional adverse events that were more prevalent among TA patients (Table 3).

Table 1
Baseline characteristics.

Variable	Transapical (n = 132)	Transfemoral (n = 516)	p-value
Age, years	84 ± 7	83 ± 8	0.14
Male	58 (44%)	264 (51%)	0.15
African American	14 (12%)	57 (12%)	0.94
Body mass index (Kg/m^2)	26 ± 6	28 ± 7	0.03
Body mass index <20Kg/m^2	13 (15%)	43 (9%)	0.12
Hypertension	122 (95%)	462 (93%)	0.45
Diabetes mellitus	38 (30%)	171 (35%)	0.28
Hyperlipidemia	101 (80%)	398 (81%)	0.7
Prior cerebrovascular accident/transient ischemic attack	29 (24%)	60 (13%)	0.003
Chronic obstructive pulmonary disease	47 (37%)	164 (33%)	0.47
Glomerular filtration rate < 60 ml/min	63 (50%)	226 (47%)	0.53
Atrial fibrillation	52 (41%)	212 (43%)	0.63
Pacemaker	26 (25%)	80 (24%)	0.75
Peripheral vascular disease	70 (56%)	143 (30%)	<0.001
Ischemic heart disease	81 (79%)	300 (74%)	0.24
Prior percutaneous coronary intervention	44 (35%)	150 (31%)	0.37
Prior bypass surgery	47 (37%)	166 (31%)	0.54
New York Heart Association III/IV	117 (94%)	423 (88%)	0.06
Society of Thoracic Surgeons score	10.4 ± 4.6	8.7 ± 4.5	<0.001
Porcelain aorta	17 (13%)	32 (7%)	0.01
Prior balloon valvuloplasty	42 (39%)	123 (28%)	0.02
Admission hemoglobin (g/dL)	11.7 ± 1.7	11.4 ± 1.6	0.13
Admission creatinine (mg/dL)	1.2 ± 0.4	1.3 ± 0.9	0.01
Ejection fraction <40%	37 (29%)	111 (23%)	0.15
Pulmonary artery systolic pressure (mmHg)	45 ± 16	46 ± 16	0.57
Pulmonary artery systolic pressure > 60 mmHg	21 (19%)	78 (20%)	0.88
Aortic valve area (cm2)	0.65 ± 0.12	0.67 ± 0.13	0.1
Indexed aortic valve area	0.37 ± 0.1	0.36 ± 0.1	0.45
Mean gradient (mmHg)	48 ± 13	47 ± 12	0.26
Mitral regurgitation >mild	14 (12%)	50 (11%)	0.87

Landmark analysis revealed significantly higher cumulative mortality rates at 30-days in TA patients than in TF patients (log-rank, p-value < 0.001). This was mainly driven by cardiac mortality that comprised 94% of early mortality in the TA group and 70% of early mortality cases in the TF group. Nonetheless, from 30 days to 1 year of follow-up, mortality rates were similar between both groups (13% in both groups, log-rank, p-value = 0.64); however, overall mortality at 1 year was higher for the TA group in comparison with the TF group (29% vs. 18%, p = 0.003) (Fig. 1).

In a multivariate analysis, the TA approach remained a significant independent predictor of early mortality among TAVR patients (hazard ratio = 4.55, 95% CI [12.5–1.67], p = 0.003), together with pulmonary artery systolic pressure (PASP) above 60 mmHg (hazard ratio = 3.08 95% CI, [7.37–1.29], p = 0.01) and aortic regurgitation severity graded more than mild following the procedure (hazard ratio = 3.99, 95% CI [10.2–1.56], p = 0.004) (Table 4).

Factors associated with early mortality among TA patients were higher Society of Thoracic Surgeons score (hazard ratio = 1.15, 95% CI [1.23–1.08], p < 0.001) and PASP > 60 mmHg (hazard ratio = 5.01,

Table 2
Procedural characteristics.

Variable	Entire cohort		p-value
	Transapical (n = 132)	Transfemoral (n = 516)	
General anesthesia	131 (100%)	67 (13%)	<0.001
Rapid pacing	128 (99%)	503 (98%)	1
Fluoroscopy time, minutes	12 ± 6	24 ± 20	<0.001
Contrast volume (ml)	96 ± 41	130 ± 72	<0.001
Balloon expandable	131 (100%)	338 (65%)	<0.001
Self expandable	0 (0%)	136 (26%)	<0.001