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ORIGINAL RESEARCH

Comparative Outcomes of Transapical Versus Transfemoral Access for Transcatheter Aortic Valve Replacement in Diabetics

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ABSTRACT

Introduction: The outcomes of transfemoral (TF) compared with transapical (TA) access for transcatheter aortic valve replacement (TAVR) in diabetics are unknown.

Methods: We queried the NIS database (2011–2014) to identify diabetics who underwent TAVR. We performed a propensity matching analysis comparing TF-TAVR versus TA-TAVR.

Results: The analysis included 14.555 diabetics who underwent TAVR. After matching, in-hospital mortality was not different between TF-TAVR and TA-TAVR. (3.5 vs. 4.4%, $p = 0.11$). TF-TAVR was associated with lower rates of cardiogenic shock (2.7 vs. 4.7%, $p = 0.02$), use of mechanical circulatory support (2.0 vs. 2.9%, $p = 0.03$), acute renal failure (17.8 vs. 26.5%, $p < 0.001$), major bleeding (35.8 vs. 40.7%, $p < 0.001$) and respiratory complications (1.1 vs. 4.4%, $p < 0.001$) compared with TA-TAVR. However, TF-TAVR was associated with a higher rate of vascular complications (2.9 vs. 0.9%, $p < 0.001$), cardiac tamponade (0.5 vs. 0.0%, $p < 0.001$), complete heart block (10.8 vs. 7.7%, $p < 0.001$) and pacemaker insertion (11.8 vs. 8.3%, $p < 0.001$). There was no difference between both groups in acute stroke (1.8 vs. 2.2%, $p = 0.39$), hemodialysis (2.0 vs. 2.2%, $p = 0.71$), and ventricular arrhythmias (4.9 vs. 4.2%, $p = 0.19$). Notably,

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TF-TAVR was associated with higher mortality, acute stroke, AKI, hemodialysis, PCI, and respiratory complications in complicated diabetics compared with non-complicated diabetics.
Conclusions: This observational analysis showed no difference in-hospital mortality between TF-TAVR and TA-TAVR among diabetic patients. Studies exploring the optimal access for TAVR among diabetics are recommended.

Keywords: Diabetics; Transapical access; Transcatheter aortic valve replacement; Transfemoral access

Key Summary Points

There is a paucity of data on the comparative outcomes between trans-femoral and trans-apical accesses in diabetics undergoing TAVR.

We found no overall difference among diabetics between TF-TAVR and TA-TAVR as regards to in-hospital mortality.

Compared with TA-TAVR, TF-TAVR was associated with lower rates of cardiogenic shock, major bleeding, respiratory complications, and shorter length of stay, at the expense of higher incidence of vascular complications, cardiac tamponade, and permanent pacemaker requirements with TF-TAVR.

Subgroup analysis demonstrated that TF-TAVR was associated with higher mortality among complicated diabetics, and lower mortality among non-complicated diabetics, compared with TA-TAVR.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has become a viable alternative compared with surgical aortic valve replacement (SAVR) in patients with aortic stenosis irrespective of the surgical risk [1–3]. Diabetic patients with aortic stenosis have a different disease profile compared to the general population, with more rapid disease progression and tendency toward left ventricular remodeling and dysfunction [4, 5]. Studies have proposed TAVR as an appealing option for diabetics, compared with SAVR [6], yet its outcomes remain affected by the burden of diabetes mellitus (DM) [5]. Among TAVR patients, DM was demonstrated as an independent predictor of short- and long-term mortality in patients undergoing TAVR [7–9]. DM is a known risk factor for microvascular and macrovascular angiopathies [5]. Also, diabetics were found to have higher rates of vascular complications post-TAVR [10]. In this study, we hypothesized that there is an interaction between the access site of TAVR procedures and the outcomes among diabetics undergoing TAVR. To evaluate this hypothesis, we conducted an observational analysis using real-world data to compare outcomes of transapical (TA) versus transfemoral (TF) TAVR procedures among diabetic patients.

METHODS

The data source for this study was the National Inpatient Sample (NIS) database. The NIS is the largest inpatient all-payer healthcare database. Unweighted, the NIS contains data from more than 7 million hospital stays each year, while after appropriate weighting, it estimates more than 35 million hospital stays nationally. The NIS was developed for the Health Care Cost and Utilization Project (HCUP) [11]. The NIS has been validated internally and externally [12, 13]. It has been used previously for describing trends and outcomes of various diseases [14, 15]. This study was exempt from local institutional review board approval, since the NIS contains de-identified data that are publicly available.

We queried the NIS years 2011–2014 to identify hospitalizations that have the International Classification of Diseases, Ninth Edition (ICD-9) procedure codes for TAVR procedures (trans-femoral 35.05 and trans-apical 35.06). We then selected records that carried ICD-9

clinical modification codes for DM (ICD-9-CM codes: 250.00 to 250.33 and 250.40 to 250.93). We excluded cases with missing data on comorbidities, in-hospital mortality, or other study outcomes.

We conducted a propensity-score matched analysis to compare hospitalizations with DM who underwent TF-TAVR to those who underwent TA-TAVR. We reported the trends of TA-TAVR and TF-TAVR in diabetic patients during the study years. The main outcome was all-cause in-hospital mortality. Other outcomes included: cardiogenic shock, acute myocardial infarction (MI), cardiac tamponade, acute stroke, acute kidney injury (AKI), hemodialysis for AKI, major bleeding, requirements of blood transfusion, vascular complications, ventricular arrhythmias, complete heart block, use of mechanical circulatory support devices (MCS), permanent pacemaker insertions, length of hospital stay, and discharges to skilled nursing facilities. Baseline characteristics and clinical outcomes were reported using relevant ICD-9 codes, CCS, and Elixhauser comorbidities as reported by HCUP (Supplemental Table 1).

We conducted a 1:1 propensity score analysis to match TF-TAVR with TA-TAVR, using MatchIt R package. X [16]. Nearest-neighbor technique was adopted to match each case to a control that is closest in terms of calculated propensity score. The propensity score was calculated from the following clinical variables: age, sex, race, hypothyroidism, fluid/electrolytes abnormalities, hypertension, liver disease, heart failure, history of smoking, chronic kidney disease (CKD), chronic lung disease, peripheral arterial disease (PAD), anemia, pulmonary circulatory disorders, obesity, history of percutaneous coronary intervention (PCI), previous coronary artery bypass grafting (CABG), and prior MI. Prespecified subgroup analyses were conducted for all study outcomes in TF-TAVR versus TA-TAVR in patients with complicated DM compared with those with uncomplicated DM. Complicated DM was defined per DM-related complications including neuropathy, nephropathy, ophthalmopathy, and angiopathies. In the subgroup analysis, to maintain the baseline balance between the TF-TAVR and TA-TAVR groups, only the corresponding matched pairs in a subgroup were selected.

We used the updated weighting samples for national estimates in accordance with HCUP regulations [17]. We compared categorical values using Chi-square test and continuous variables using Student's t test. We reported categorical variables as numbers and percentages, while continuous variables were reported as mean ± standard deviation or median and interquartile range, depending on the skewness of distribution. Breslow–Day test was used to test the homogeneity of the odds ratio. Linear regression analysis was used to evaluate time trend analyses. Effect sizes were expressed using odds ratios (OR) and 95% confidence interval (CI). Associations were considered significant if the p value was < 0.05. We used SPSS software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY, USA: IBM Corp Released 2016) and R software for all statistical analysis [18].

RESULTS

The study flow sheet is outlined in Fig. 1. From 2011 to 2014, our search yielded 14,555 diabetics who underwent TAVR. After excluding 12 cases with missing baseline characteristics, a total of 14,543 hospitalizations were included. TF-TAVR was performed in 11,769 (80.9%) of those hospitalizations, while TA-TAVR was performed in 2774 (19.1%) hospitalizations. There was no change in the trend of TF-TAVR or TA-TAVR procedures in diabetics from 2011 to 2014 ($P_{\text{trend}} = 0.60$ and 0.41, respectively) (Fig. 2). Propensity score analysis, the matched cohort included a total of 5437 hospitalizations; 2718 in the TF-TAVR and 2719 in the TA-TAVR groups.

The baseline characteristics of the study population are outlined in Table 1. Before matching, the TF-TAVR group were more likely to be older, females, whites, African Americans, and to have a history of heart failure, prior PCI, CKD, pulmonary circulation disorders, obesity, and anemia. The TA-TAVR group had higher prevalence of Hispanics, Asians, prior CABG, chronic lung disease, and PAD. After matching, the standardized mean differences between

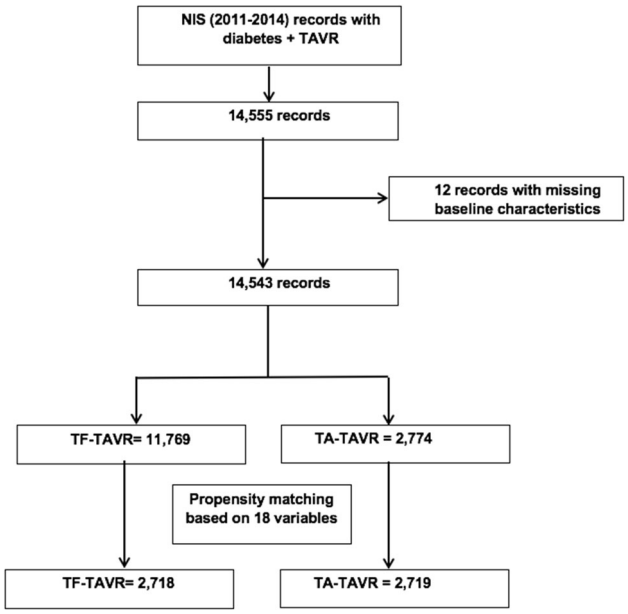

Fig. 1 Study flow sheet

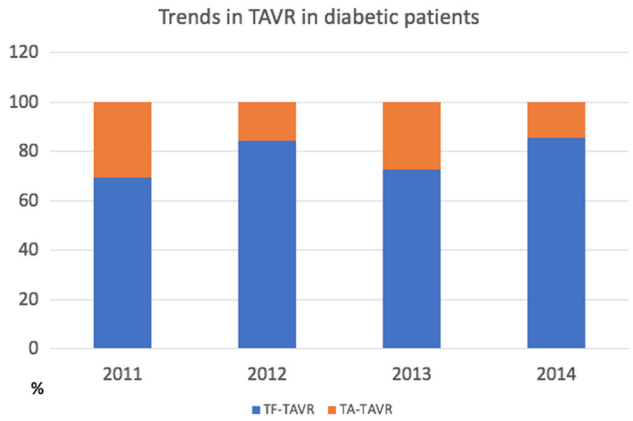

Fig. 2 Trend of TF-TAVR and TA-TAVR procedures among diabetics

both groups in the baseline characteristics were all less than 10% suggesting minimal differences (Supplemental Fig. 1).

After matching, in-hospital mortality was not different between TF-TAVR and TA-TAVR (3.5 vs. 4.4%, OR 0.79; 95% CI 0.60–1.04, $p = 0.11$). TF-TAVR was associated with lower rates of cardiogenic shock (2.7 vs. 4.7%, OR 0.61; 95% CI 0.46–0.82, $p = 0.02$), utilization of MCS (2.0 vs. 2.9%, OR 0.67; 95% CI 0.47–0.95, $p = 0.03$), AKI (17.8 vs. 26.5%, OR 0.60; 95% CI 0.53–0.68, $p < 0.001$), major bleeding (35.8 vs. 40.7%, OR 0.82; 95% CI 0.73–0.91, $p < 0.001$), blood transfusions (21.4 vs. 31.3%, OR 0.60; 95% CI 0.53–0.68, $p < 0.001$), respiratory complications (1.1 vs. 4.4%, OR 0.24; 95% CI 0.16–0.36, $p < 0.001$), discharge to skilled facilities (26.1 vs. 39.3%, OR 0.55; 95% CI 0.49–0.61, $p < 0.001$), and shorter mean length of stay (7.8 ± 6.8 vs. 9.9 ± 7.4 days, $p < 0.001$) compared with TA-TAVR. However, TF-TAVR was associated with a higher rate of vascular complications (2.9 vs. 0.9%, OR 3.4; 95% CI 2.1–5.3, $p < 0.001$), cardiac tamponade (0.5 vs. 0.0%, OR 0.1.005; 95% CI 1.002–1.008, $p < 0.001$), complete heart block (10.8 vs. 7.7%,

Table 1 Baseline characteristics of unmatched and matched cohorts

	Unmatched cohort					Matched cohort[a]			
	TF-TAVR (n = 11,769) N %		TA-TAVR (n = 2774) N %		p value	TF-TAVR (n = 2718) N %		TA-TAVR (n = 2719) N %	
Age	79.5 ± 8.1		78.2 ± 8.6		< 0.001	78.61 ± 8.48		78.31 ± 8.6	
Female sex	5268	44.7%	1370	49.4%	< 0.001	1288	47.4%	1330	48.9%
Fluid and electrolyte disorders	2713	23.0%	1074	38.7%	< 0.001	908	33.4%	1034	38.0%
Hypothyroidism	2331	19.8%	568	20.5%	0.428	579	21.3%	563	20.7%
Liver disease	453	3.8%	84	3.0%	0.040	70	2.6%	84	3.1%
Race									
White	9344	79.4%	2097	75.6%	< 0.001	2164	79.6%	2082	76.6%
Black	569	4.8%	95	3.4%	0.001	90	3.3%	95	3.5%
Hispanic	495	4.2%	184	6.6%	< 0.001	120	4.4%	179	6.6%
Asian Pacific Islander	140	1.2%	55	2.0%	0.001	35	1.3%	55	2.0%
Native American	NR	NR	35	1.3%	< 0.001	NR	NR	NR	NR
Other races	397	3.4%	89	3.2%	0.721	74	2.7%	84	3.1%
Hypertension	9865	83.8%	2336	84.2%	0.605	2212	81.4%	2281	83.9%
Complicated diabetes	1977	16.8%	518	18.7%	0.018	453	16.7%	503	18.5%
History of heart failure	1430	12.1%	175	6.3%	< 0.001	150	5.5%	175	6.4%
History of smoking	3214	27.3%	802	28.9%	0.089	769	28.3%	782	28.7%
History of PCI	2547	21.6%	507	18.3%	< 0.001	508	18.7%	502	18.5%
History of CABG	3116	26.5%	792	28.6%	0.027	746	27.5%	762	28.0%
Prior MI	1872	15.9%	404	14.6%	0.082	390	14.3%	399	14.7%
Chronic kidney disease	5037	42.8%	118	40.3%	0.017	1129	41.5%	1098	40.4%
Chronic lung disease	4183	35.5%	1044	37.6%	0.039	1103	40.6%	1019	37.5%
Pulmonary circulation disorder	500	4.2%	45	1.6%	< 0.001	45	1.7%	45	1.7%
Peripheral artery disease	3300	28.0%	1091	39.3%	< 0.001	997	36.7%	1051	38.6%
Obesity	2718	23.1%	560	20.2%	0.001	522	19.2%	555	20.4%
Anemia	3409	29.0%	738	26.6%	0.013	766	28.2%	723	26.6%

SD standard deviation, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass grafting, *MI* myocardial infarction, *NR* not reportable; Per HCUP regulations, frequencies fewer than 11 should not be reported

[a] After matching, the standardized differences between both groups in all matched variables were less than 10%, suggesting minimal differences

OR 1.45; 95% CI 1.20–1.75, $p < 0.001$) and permanent pacemaker insertion (11.8 vs. 8.3%, OR 1.49; 95% CI 1.25–1.78, $p < 0.001$). There was no difference between both groups in acute stroke (1.8 vs. 2.2%, OR 0.83; 95% CI 0.57–1.2, $p = 0.39$), acute MI (2.6 vs. 2.8%, OR 0.93; 95% CI 0.67–1.30, $p = 0.74$) hemodialysis (2.0 vs. 2.2%, OR 0.92; 95% CI 0.63–1.33, $p = 0.71$) and ventricular arrhythmias (4.9 vs. 4.2%, OR 1.19; 95% CI 0.92–1.53, $p = 0.19$) (Fig. 3) (Table 2).

On subgroup analysis, TF-TAVR in patients with complicated diabetes was associated with higher rate of in-hospital mortality compared with TA-TAVR (7.7 vs. 2.0%, OR 4.13; 95% CI 2.02–8.44, $p < 0.001$), while in non-complicated diabetics TF-TAVR was associated with lower in-hospital mortality compared with TA-TAVR (2.7 vs. 4.9%, OR 0.53; 95% CI 0.38–0.73, $p < 0.001$); $P_{\text{interaction}} < 0.001$. Results of subgroup analysis for the other study outcomes are presented in Table 3. Compared with non-complicated diabetics, TF-TAVR among complicated diabetics was associated with higher rate of acute stroke ($P_{\text{interaction}} = 0.05$), AKI ($P_{\text{interaction}} = 0.05$), hemodialysis ($P_{\text{interaction}} = 0.05$), blood transfusions ($P_{\text{interaction}} = 0.03$), percutaneous coronary intervention ($P_{\text{interaction}} = 0.02$), and respiratory complications ($P_{\text{interaction}} < 0.001$).

DISCUSSION

In this observational analysis including 14,543 hospitalizations, we sought to evaluate the comparative outcomes between trans-femoral and trans-apical accesses in diabetics undergoing TAVR. After propensity matching, we found no overall difference among diabetics between TF-TAVR and TA-TAVR as regards to in-hospital mortality. After matching, TF-TAVR was associated with lower rates of cardiogenic shock, utilization of MCS, AKI, major bleeding, blood transfusions, respiratory complications, and shorter length of stay compared with TA-TAVR. On the other side, TF-TAVR was associated with higher incidence of vascular complications, cardiac tamponade, complete heart block, and permanent pacemaker requirements. No difference was observed between both groups in the rates of acute stroke, acute MI, hemodialysis, and ventricular arrhythmias. Subgroup analysis showed that among complicated diabetics, TF-TAVR was associated with higher rates of in-hospital mortality, acute stroke, AKI,

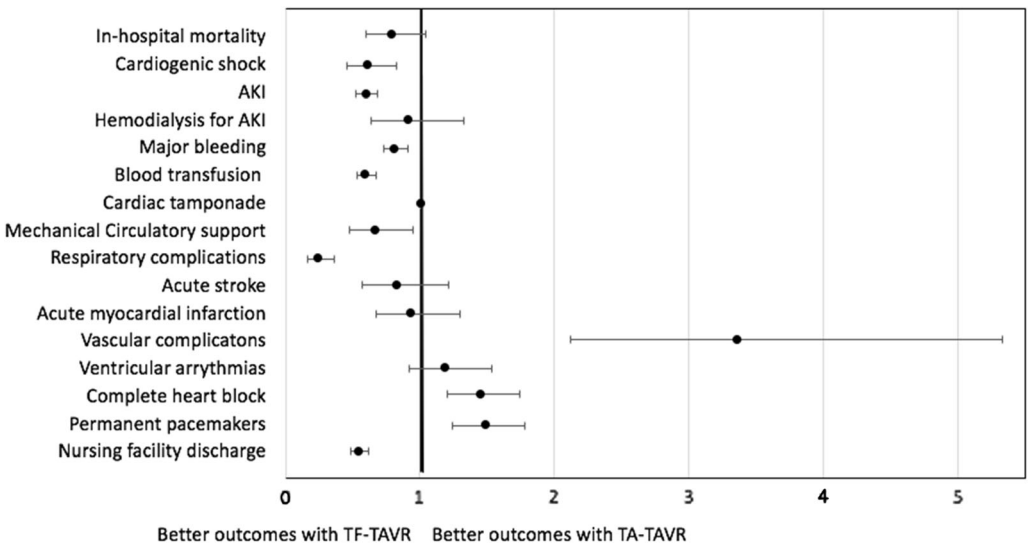

Fig. 3 Comparative outcomes between TF-TAVR and TA-TAVR in the matched cohort. *AKI* acute kidney injury

Table 2 In-hospital outcomes for TF-TAVR compared with TA-TAVR in the matched cohort

Outcome	TF-TAVR (n = 2718) N %		TA-TAVR (n = 2719) N %		p value	OR	95% confidence interval
Mortality	95	3.5%	119	4.4%	0.108	0.791	0.601–1.042
Cardiogenic shock	74	2.7%	119	4.4%	0.001	0.612	0.455–0.822
Vascular complications	79	2.9%	24	0.9%	0.000	3.363	2.123–5.327
Acute stroke	50	1.8%	60	2.2%	0.386	0.831	0.569–1.214
TIA/Stroke	65	2.4%	70	2.6%	0.728	0.928	0.659–1.306
Acute kidney injury	483	17.8%	720	26.5%	< 0.001	0.600	0.527–0.683
Acute myocardial infarction	70	2.6%	75	2.8%	0.736	0.932	0.670–1.297
Cardiac tamponade	14	0.5%	NR	NR	< 0.001	1.005	1.002–1.008
MCS	54	2.0%	80	2.9%	0.028	0.669	0.472–0.949
Major bleeding	974	35.8%	1106	40.7%	< 0.001	0.815	0.730–0.909
Blood transfusion	581	21.4%	850	31.3%	< 0.001	0.598	0.529–0.676
Hemodialysis	55	2.0%	60	2.2%	0.706	0.916	0.633–1.325
Complete heart block	294	10.8%	210	7.7%	< 0.001	1.450	1.204–1.745
Ventricular arrhythmias	134	4.9%	114	4.2%	0.194	1.185	0.918–1.531
PPM	322	11.8%	225	8.3%	< 0.001	1.490	1.245–1.782
Respiratory complications	30	1.1%	120	4.4%	< 0.001	0.242	0.161–0.362
PCI	80	2.9%	80	2.9%	1.000	1.001	0.731–1.371
Discharge to SNF	710	26.1%	1068	39.3%	< 0.001	0.547	0.487–0.614
Length of stay (mean ± SD)	7.78 ± 6.77		9.87 ± 7.43		< 0.001		

TIA transient ischemic attack, *MCS* mechanical circulatory support device, *PPM* permanent pacemaker insertion, *PCI* percutaneous coronary intervention, *SNF* skilled nursing facility, *NR* not reportable; Per HCUP regulations, frequencies fewer than 11 should not be reported

hemodialysis, PCI, and respiratory complications, compared with non-complicated diabetics.

Diabetes is a traditional risk factor that has been established to confer additional morbidity and mortality to various surgical and transcatheter procedures [19, 20]. DM is included as a risk factor in the Society of Thoracic Surgeons Risk Score and EuroSCORE II, both of which are validated tools in predicting 30-day mortality after cardiac surgery [19, 20]. Specifically, studies have suggested an interaction for diabetes with clinical outcomes after TAVR, with reports of unfavorable outcomes associating diabetics undergoing TAVR at short and long term [7–9]. Abramowitz et al. conducted an analysis using the Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/TVT) Registry, including 47,643 patients. Their analysis showed that diabetes was a significant predictor of 1-year mortality [5]. Also, in the Ibero-American registry including 1220 TAVRs, diabetes was found to be an independent predictor of long-term mortality [7]. However, the

Table 3 Subgroup analysis according to the status of diabetes for in-hospital complications for TF-TAVR versus TA-TAVR

Outcome	Uncomplicated diabetes							Complicated diabetes							$P_{interaction}$
	TF-TAVR (n = 1268) N %		TA-TAVR (n = 1189) N %		OR	95% CI		TF-TAVR (n = 254) N %		TA-TAVR (n = 281) N %		OR	95% CI		
Cardiac arrest	39	3.1%	55	4.6%	0.654	0.431	0.994	18	7.1%	16	5.7%	1.263	0.630	2.533	0.110
Cardiogenic shock	34	34	48	4.0%	0.655	0.419	1.024	NR	NR	13	4.6%	0.757	0.318	1.803	0.770
Vascular complications	39	3.1%	14	1.2%	2.663	1.439	4.930	NR	NR	NR	NR	1.024	1.005	1.044	0.208
Acute stroke	21	1.7%	29	2.4%	0.674	0.382	1.188	NR	NR	NR	NR	3.375	0.675	16.875	0.048
TIA/Stroke	29	2.3%	35	2.9%	0.772	0.469	1.271	NR	NR	NR	NR	3.375	0.675	16.875	0.068
AKI	193	15.2%	293	24.6%	0.549	0.449	0.672	78	30.7%	98	34.9%	0.828	0.576	1.189	0.052
AMI	26	2.1%	25	2.1%	0.975	0.560	1.698	15	5.9%	16	5.7%	1.039	0.503	2.148	0.890
Cardiac tamponade	NR	NR	NR	NR	1.007	1.002	1.012	NR	NR	NR	NR	NA			0.325
MCS	28	2.2%	41	3.4%	0.632	0.388	1.029	NR	NR	NR	NR	1.667	0.276	10.060	0.325
Major bleeding	447	35.3%	484	40.7%	0.793	0.674	0.934	100	39.4%	109	38.8%	1.025	0.724	1.451	0.191
Blood transfusion	254	20.0%	374	31.5%	0.546	0.454	0.656	73	28.7%	89	31.7%	0.870	0.601	1.260	0.027
Hemodialysis	20	1.6%	26	2.2%	0.717	0.398	1.291	12	4.7%	NR	NR	2.273	0.840	6.148	0.046
Complete heart block	142	11.2%	99	8.3%	1.388	1.060	1.818	30	11.8%	19	6.8%	1.847	1.012	3.371	0.395
PPM	150	11.8%	97	8.2%	1.510	1.155	1.976	35	13.8%	28	10.0%	1.444	0.851	2.451	0.882
Ventricular arrhythmias	63	5.0%	45	3.8%	1.329	0.899	1.965	12	4.7%	14	5.0%	0.946	0.429	2.085	0.448
Respiratory complications	NR	NR	59	5.0%	0.168	0.088	0.321	NR	NR	NR	NR	2.242	0.555	9.059	< 0.001
PCI	24	1.9%	33	2.8%	0.676	0.397	1.150	16	6.3%	NR	NR	2.294	0.965	5.456	0.016
Discharges to facilities	325	25.6%	481	40.5%	0.507	0.427	0.602	75	29.5%	106	37.7%	0.692	0.482	0.993	0.126

TIA transient ischemic attack, *AKI* acute kidney injury, *AMI* acute myocardial infarction, *PPM* permanent pacemaker insertion, *PCI* percutaneous coronary intervention, *NR* not reportable; Per HCUP regulations, frequencies fewer than 11 should not be reported

impact of access site on the interaction between diabetes and TAVR procedures has not been adequately characterized.

Multiple studies have compared TF-TAVR and TA-TAVR in all comers with results suggesting favorable short- and long-term mortality with TF-TAVR. Kumar et al. conducted an analysis using the NIS database to compare TF-TAVR and TA-TAVR in all comers. Their results showed that TF-TAVR was associated with lower rates of in-hospital mortality compared with TA-TAVR [21]. Results from other registries showed similar survival benefit with TF-TAVR [22, 23].

Unlike the studies on all-comers, our analysis showed no significant difference between trans-femoral and trans-apical accesses in diabetics undergoing TAVR. This lack of difference might be attributed to higher incidences of vascular complications and bradyarrhythmia complications, which might have neutralized the overall benefits observed with TF-TAVR in studies on all-comers. In our analysis, we found a threefold higher rates of vascular complications among diabetics who underwent TF-TAVR compared with TA-TAVR. Prior studies have demonstrated that diabetes is associated with higher vascular complications among patients undergoing TF-TAVR [10, 24]. In a pooled analysis from the Placement of Aortic Transcatheter Valve (PARTNER) Trial, major vascular complications were evaluated in 419 patients [10]. Insulin-dependent diabetics had more than threefold higher rates of vascular complications compared with non-diabetics [10].

Consistent with other studies, TF-TAVR had more favorable hemodynamic outcomes; with less rates of cardiogenic shock, use of MCS, AKI, as well as less respiratory complications [25, 26]. We found no difference between TF-TAVR and TA-TAVR in acute stroke. The theoretical benefit for TA-TAVR by avoiding manipulation of the aorta and direct valve implantation, did not translate to lower stroke risk in many clinical studies, similar to our results [25, 27].

In our study, subgroup analysis identified significant interaction between the status of diabetes (i.e., complicated or not) with mortality outcomes in TF-TAVR compared with TA-TAVR. Such interaction seemed to be driven by higher rates of acute stroke, AKI, hemodialysis, and PCI for TF-TAVR among complicated diabetics. Patients with complicated diabetes are mostly insulin-dependent and are likely to have diabetes-related complications. Other reports have suggested an interaction between the status of diabetes and outcomes after TAVR. In the analysis by Abramowitz et al., insulin-treated diabetes was a stronger predictor of 1-year mortality compared with non-insulin-treated diabetes among TAVR patients [5], driven by higher requirements of hemodialysis, MI, and heart failure readmissions [5]. Data from an Italian registry showed that being insulin-treated DM, but not orally treated DM, was an independent predictor of mortality and MI at 1-year follow-up [9]. Data from a single-center study also showed the same results with worse mid-term mortality after TAVR in insulin-treated diabetics [28].

Compared to all-comers undergoing TAVR, the relatively worse outcomes with DM, in particularly complicated DM, could be related to the pathophysiological changes associating DM. Diabetic patients with severe aortic stenosis have a different profile compared with the general population. They have more accelerated progression of AS, left ventricular remodeling, and reduced systolic function compared with non-diabetic AS patients [4, 5]. The worse outcomes with advanced DM are attributed to diabetes-related complications including renal disease and vasculopathies at multiple vascular beds with more propensity for cardiac, cerebrovascular, and peripheral vascular complications. Increased post-operative inflammation and oxidative stress among diabetics is also a contributing factor to worse post-procedural outcomes [29].

This current analysis is the first analysis to date exploring the impact of DM on access site for TAVRs. The lack of mortality benefit with TF-TAVR versus TA-TAVR in diabetics compared with studies on all-comers is an important finding. Patients with complicated DM might have higher in-hospital mortality with TF-TAVR compared with TA-TAVR. The results of our subgroup analysis highlight the importance of

careful patient selection and individualized decisions on access sites for TAVR in diabetic patients. Further studies are warranted to explore the outcomes of alternative access sites for TAVR in diabetics, in particular complicated diabetes.

This analysis has several limitations. The NIS is an administrative database, which is liable to coding and documentation errors. It is also a time-discrete database, with no available data on long-term outcomes. Given the timeframe of our study, the evaluated TAVR procedures were mostly using first-generation TAVR valves. Newer generations of TAVR valves have smaller vascular profiles and might carry less vascular complications. Also, the use of TA-TAVR has decreased and has lower incidence than that reported in our study. Other relevant information could not be retrievable from this dataset including data on imaging tests, types of TAVR valves utilized, or laboratory results. Being an observational analysis, there is potential for selection bias. However, we conducted a propensity match analysis to reduce allocation biases. Nevertheless, the possibility of unmeasured confounders exists. Despite the aforementioned limitations, the current study contributes to the literature regarding the impact of diabetes on outcomes of TAVR procedures.

CONCLUSIONS

This observational analysis of a large national database showed no difference in in-hospital mortality between TF-TAVR and TA-TAVR among diabetic patients. Among complicated diabetics, TF-TAVR might be associated with unfavorable outcomes compared with TA-TAVR. Studies exploring the optimal access for TAVR among diabetics are still required.

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Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

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