Incidence, Predictors, and In-Hospital Outcomes of Transcatheter Aortic Valve Implantation After Nonelective Admission in Comparison With Elective Admission: From the Nationwide Inpatient Sample Database

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Candidates for transcatheter aortic valve implantation (TAVI) are generally older with multiple co-morbidities and are therefore susceptible to nonelective admissions before scheduled TAVI. Frequency, predictors, and outcomes of TAVI after nonelective admission are under-explored. We queried the Nationwide Inpatient Sample database, an administrative database, from January 2012 to September 2015 to identify hospitalization in those age ≥50 who had transarterial TAVI. A propensity-matched cohort was created to compare the outcomes between nonelective and elective admission who had TAVI. The primary outcome was in-hospital mortality. A total of 9,521 TAVI admissions were identified during the study period. Of these admissions, 22.3% were nonelective admissions. Pulmonary circulation disorders (adjusted odds ratio [aOR] 1.38), anemia (aOR 1.54), congestive heart failure (aOR 1.37), chronic kidney disease (aOR 1.28; all $p < 0.001$), and atrial fibrillation (aOR 1.17, $p = 0.006$) were independent risk factors for nonelective admission. In a propensity-matched cohort (1,683 admissions in each cohort), in-hospital mortality was similar (4.0% vs 2.8%, $p = 0.052$). Nonelective admissions had higher rates of acute myocardial infarction (5.2% vs 0.7%), fatal arrhythmia (9.4% vs 6.0%), acute kidney injury (25.9% vs 17.1%), respiratory failure requiring intubation (0.26% vs 0.19%), cardiogenic shock (5.1% vs 2.1%; all $p < 0.001$), and bleeding requiring transfusion (13.1% vs 10.1%, $p = 0.006$) during the index-hospitalization. Hospital length of stay (11.4 days vs 6.5 days, $p < 0.001$) and hospital cost ($68,669 vs $57,442, $p < 0.001$) were both increased in nonelective admissions. Nonelective admission accounted for approximately one-fifth of total TAVI with significantly different cohort profiles. Our results suggest that nonelective TAVI has higher adverse outcomes and increased health resource utilization. Expedition in TAVI process in high-risk cohorts may result in better outcomes. **(Am J Cardiol 2019;123:100−107)**

Candidates of transcatheter aortic valve implantation (TAVI) often have atherosclerosis-related and non-related co-morbidities (i.e., lung disease, malignancy) and are thus vulnerable to clinical events requiring emergency department visit before undergoing scheduled TAVI.[1] Even after TAVI, 30 days readmissions rate remains relatively as high as 18%.[2] Patient awaiting TAVI could be even at higher risk of nonelective medical visit and admission. Kolte et al have reported the outcomes of TAVI as a rescue therapy for decompensated severe aortic stenosis.[3] However, it remains under-explored how often TAVI candidates are admitted in a nonelective manner (i.e., through the emergency department), its predictors, and the outcomes compared with those who had TAVI after elective admission. We used the Nationwide Inpatient Sample (NIS) database to explore outcomes of TAVI between elective and nonelective admission.

Methods

Our study was performed using data from Healthcare Cost and Utilization Project (HCUP)—NIS from January 2012 to September 2015. NIS is the largest publically accessible database of all-payer inpatient care in the United

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States, and it includes unique identifiers and clinical information for each hospital admission. It surveys 20% of every admission from over 4,000 hospitals across 30 States. NIS has been validated in numerous studies to provide reliable estimates of admissions in the United States.[4] NIS is validated in many studies to provide a reliable estimate of admissions within the United States.[5,6] Data collection methods and administration of NIS are detailed further detailed.[7] We identified all patients who were hospitalized with aortic stenosis and underwent transarterial TAVI during the study period using the International Classification of Disease, Ninth Revision, Clinical Modification. Patients aged 50 years and older were included. They were identified based on elective and nonelective hospitalization for TAVI as specified in the NIS dataset. Those patients who had a diagnosis of aortic insufficiency without a diagnosis of aortic stenosis and transapical TAVI were excluded from the study. In order to minimize categorizing bias, we also excluded hospitalizations who had listed secondary outcomes as their initial diagnosis. We compared outcomes between elective and nonelective TAVI hospitalization and our primary outcome was in-hospital mortality. Secondary outcome variables were identified using International Classification of Disease, Ninth Revision, Clinical Modification codes (Supplement Table 1), these included length of stay (LOS), hospitalization cost, acute myocardial infarction, fatal arrhythmias (ventricular fibrillation, ventricular tachycardia, or cardiac arrest), conversion to open surgical aortic valve replacement, percutaneous coronary intervention, pacemaker placement, bleeding requiring transfusion, vascular complications, acute kidney injury, acute kidney injury requiring hemodialysis, in-hospital stroke, acute respiratory failure requiring intubation, use of mechanical circulatory support, and cardiogenic shock.

The following baseline characteristics were used: age, gender, race, insurance status, and hospital outcomes such as cardiogenic shock, length of stay and cost. To calculate the estimated cost of hospitalization, the NIS data were merged with cost to charge ratios available from HCUP.[7] We estimated the cost of each inpatient stay by multiplying total hospital charge with cost-to-charge ratios. Costs were adjusted for inflation using U.S. Bureau of Labor Statistics Consumer Price Index with 2017 as the reference year.[8] We used the Elixhauser co-morbidity index to quantify the severity of co-morbidities.

To balance differences in patient and hospital-related characteristics, propensity score matching was performed. We used a multivariate logistic regression model with elective hospitalization as the dependent variable and all others listed in Table 1 including weekend and year of admission as covariates. As described in previous studies,[9–11] we performed a 1-to-1 greedy matching protocol with a caliper width of 0.1× the standard deviation of the logit of the propensity score to match 1,683 (weighted 8,415) elective admissions with 1,683 (weighted 8,415) nonelective admissions. We verified the balance of baseline characteristics using McNemar's test for categorical variables and paired *t* test for normally distributed continuous variables.

The statistical analysis was completed using the Statistical Analysis System (SAS V.9.4, SAS Institute Inc., Cary, North Carolina). P values are 2-sided with a significant threshold of < 0.05. Chi-square tests were used for categorical variables and Wilcoxon-Mann-Whitney test was used for non-normal distributed continuous variables such as length of stay. Stepwise backward logistic regression models with a p value of 0.3 for entry into the model were built to determine the independent predictors of mortality in elective versus nonelective admissions. The model included patient-level variables such as gender, co-morbidities and hospital-level variables such as hospital size (number of beds), hospital region, and teaching status.

The baseline characteristics of matched cohorts were computed with a paired *t* test for continuous variables with normal distribution and McNemar's test for categorical variables. Because observations are missing at random, we excluded all missing variables from analysis and did a complete case analysis. Binary outcomes like in-patient mortality were modeled with binomial logistic regressions. Due to the skewed distribution, log-transformed length of stay and total hospital costs were computed using Generalized Linear Model procedure with appropriate response probability distribution-Poisson and Gamma distributions, respectively. We also reported odds ratio (OR) for binary outcome and mean ratio (MR) for LOS and cost of hospitalization. For trend analyses, survey logistic regression was used to assess the changes in the proportion of nonelective admission performed per yearly quarter. The yearly quarter was modeled as the continuous independent variable. The statistical analysis was performed on weighted numbers and we accounted for the complex sampling of the NIS dataset as, recommended.[7,12]

Results

A total of unweighted 9,521 (weighted 36,990) TAVI (nonelective 2,123, elective 7,398) admissions were identified during the study period. The overall TAVI admission characteristics showed a mean age of 81.5 ± 7.8 years old, 46.3% were women, 87.8% were Caucasian, and approximately half had high (≥ 4) Elixhauser score. Mean age was similar between nonelective and elective admissions (81.3 ± 8.3 vs 81.5 ± 7.7 years old) but nonelective admissions were more likely to be women (49.1% vs 45.6%, $p = 0.003$) as compared with elective admissions (Table 1). Multivariate regression analysis identified pulmonary circulation disorders (OR 1.38, 95% confidence intervals [CI] 1.22 to 1.57, $p < 0.001$), anemia (OR 1.54, 95% CI 1.37 to 1.75, $p < 0.001$), congestive heart failure (OR 1.37, 95% CI 1.20 to 1.57, $p < 0.001$), chronic kidney disease (1.28, 95% CI 1.13 to 1.44, $p < 0.001$), and atrial fibrillation (OR 1.17, 95% CI 1.05 to 1.31, $p = 0.006$) to be the associated risk factors for nonelective admission (Table 2). TAVI was performed on a median of day 0 (interquartile range 1) and day 2 (interquartile range 6) for elective and nonelective admissions, respectively. Nonelective admission was more frequent on weekend compared to elective admissions (14.1% vs 3.5%, $p < 0.001$). Balloon aortic valvuloplasty was performed in 2.9% in nonelective admissions whereas it was 1.1% ($p < 0.001$) in elective admissions. These results are summarized in Table 1. There was no significant trend in

Table 1
Baseline characteristics of participants who underwent transcatheter aortic valve implantation between 2012 and 2015 by elective hospitalization status in the United States—Unmatched

Variables	Total	Elective	Nonelective	p value
Number of observation, unweighted	9,521	7,398	2,123	
Number of observation, weighted	47,605	36,990	10,615	
Age, mean (SD) (Years)	81.50 (7.80)	81.54 (7.65)	81.33 (8.31)	0.271
Transcatheter aortic valve implantation day, median (IQR)	0 (1.0)	0 (1.0)	2.0 (6.0)	< .0001
Women	46.34%	45.55%	49.08%	0.003
White	87.76%	89.07%	83.23%	< .0001
Black	4.04%	3.58%	5.64%	
Hispanic	3.62%	3.42%	4.34%	
Asia	1.05%	1.07%	0.95%	
Dyslipidemia	65.83%	67.41%	60.34%	< .0001
Prior myocardial infarction	13.31%	13.66%	12.06%	0.050
Prior percutaneous coronary intervention	20.62%	21.37%	17.99%	0.0013
Prior coronary bypass	21.55%	22.71%	17.52%	< .0001
Prior pacemaker	10.76%	11.19%	9.23%	0.010
Atrial fibrillation	43.17%	42.34%	46.07%	0.003
Chronic obstructive pulmonary disease	32.29%	31.86%	33.77%	0.088
Carotid artery disease	6.87%	7.15%	5.89%	0.039
Prior cerebrovascular disease	13.66%	13.84%	13.05%	0.361
Hypertension	80.96%	81.31%	79.75%	0.123
Peripheral vascular diseases	27.84%	27.59%	28.73%	0.326
Pulmonary circulation disorders	22.28%	20.72%	27.70%	< .0001
Balloon valvuloplasty	1.51%	1.12%	2.87%	< .0001
Diabetes mellitus with complications	6.10%	5.65%	7.68%	0.001
Diabetes mellitus	35.92%	35.42%	37.88%	0.043
Obesity	15.25%	15.57%	14.13%	0.108
Anemia deficiency	24.78%	22.45%	32.88%	< .0001
Congestive heart failure	73.95%	72.05%	80.59%	< .0001
Renal failure	35.84%	33.87%	42.68%	< .0001
Liver disease	2.67%	2.70%	2.54%	0.694
Oxygen dependent	6.35%	6.37%	6.31%	0.929
Maintenance dialysis	2.89%	2.37%	4.71%	< .0001
Smoker	29.60%	30.58%	26.19%	0.0002
Weekend admission	5.83%	3.45%	14.13%	< .0001
Elixhauser score				< .0001
0	1.55%	1.66%	1.18%	
1 - 3	47.96%	50.03%	40.74%	
≥ 4	50.49%	48.31%	58.08%	
Hospital bed size				0.0002
Small	0.81%	0.80%	0.85%	
Medium	9.11%	10.08%	5.70%	
Large	90.09%	89.12%	93.45%	
Expected primary payer				< .0001
Medicare	90.91%	90.88	91.00%	
Medicaid	0.97%	0.70%	1.89%	
Private	6.49%	6.74%	5.61%	
Others	1.64%	1.68%	1.51%	
Median household income in quartile				< .0001
1st	21.00%	21.01%	20.95%	
2nd	24.95%	25.86%	21.81%	
3nd	25.70%	26.10%	24.29%	
4th	28.35%	27.02%	32.95%	
Hospital region				< .0001
Northeast	25.80%	23.53%	33.67%	
Midwest	22.13%	23.66%	16.83%	
South	33.74%	32.78%	37.07%	
West	18.33%	20.03%	12.43%	

Deficiency anemia- ICD-9-CM codes: 280.1-281.9, 285.21-285.29, 285.9.
Obesity- ICD-9-CM codes: 278.0, 278.00, 278.01.
Dyslipidemia: Clinical classification code 53.

Table 2
Risk factors for nonelective admission

	Point Estimate	95% CI		p value
Pulmonary circulation disorders	1.383	1.218	1.569	< .0001
Diabetes with chronic complication	1.228	0.970	1.554	0.0872
Race/Ethnicity				
White (ref.)	-	-	-	
Black	1.362	1.047	1.772	0.3633
Hispanic	1.433	1.075	1.909	0.2153
Asia	0.811	0.447	1.472	0.1017
Age, every 5 years increase	0.993	0.985	1.001	0.0674
Deficiency anemia	1.544	1.365	1.748	< .0001
Congestive heart failure	1.371	1.197	1.571	< .0001
Diabetes mellitus	1.073	0.946	1.217	0.2736
Chronic liver disease	0.822	0.579	1.167	0.2734
Obesity	0.836	0.708	0.986	0.0337
Chronic renal failure	1.276	1.133	1.437	< .0001
Smoker	0.835	0.737	0.946	0.0045
Prior percutaneous coronary intervention	0.915	0.794	1.054	0.2179
Prior coronary bypass	0.774	0.669	0.895	0.0006
Prior pacemaker	0.805	0.667	0.972	0.0238
Atrial fibrillation	1.170	1.045	1.310	0.0064
Dyslipidemia	0.787	0.701	0.885	< .0001
Maintenance dialysis	1.320	0.975	1.787	0.0724
Carotid artery disease	0.875	0.696	1.100	0.2534
Hospital region				
Northeast (ref.)	-	-	-	-
Midwest	0.584	0.491	0.695	0.0050
South	0.882	0.765	1.016	< .0001
West	0.439	0.366	0.527	< .0001
Median Household income in quartile				
1st	0.765	0.648	0.904	0.2777
2nd	0.700	0.597	0.820	0.0039
3nd	0.811	0.698	0.942	0.9804
4^{th} (ref.)	-	-	-	

Variables used in the model: All baseline variables in Table 1 were used in the model except hospital teaching status; hospital bed size; weekend admission and primary payment status.

This analysis uses a significance level of 0.32 (SLSTAY = 0.32) to retain variables in the model. Multivariate analysis without the stay selection criteria; women versus men (OR 1.06, 95% CI: 0.94 to 1.19 p = 0.332).

the percentage of nonelective admission during the study period (p = 0.12; Figure 1).

After propensity score matching, well-matched 1,683 (weighted 8,415) TAVI admissions in each group were identified for comparison of clinical events during index hospitalizations. The details of matched cohort are summarized in Table 3. In-patient mortality tended to be higher in nonelective admissions (4.0% vs 2.8%, p = 0.052) but was statistically insignificant. Acute myocardial infarction (5.23% vs 0.65%, p < 0.001), fatal arrhythmia (9.4% vs 6.0%, p < 0.001), percutaneous coronary intervention (5.8% vs 2.6%, p < 0.001), acute kidney injury (25.9% vs 17.1%, p < 0.001), bleeding requiring transfusion (13.1% vs 10.1%, p = 0.006), acute respiratory failure requiring intubation (0.26% vs 0.19%, p < 0.001), and cardiogenic shock (5.1% vs 2.1%, p < 0.001) were more frequent in nonelective admissions group during the index hospitalization. Vascular complications (5.6% vs 5.3%, p = 0.71), pacemaker implantation (12.1% vs 10.9%, p = 0.29), acute kidney injury requiring dialysis (2.3% vs 1.5%, p = 0.11), stroke (2.2% vs 2.6%, p = 0.43), use of mechanical circulatory support (2.1% vs 1.7%, p = 0.34), and conversion to surgical aortic valve replacement (0.12% vs 0.18%, p = 0.61) were similar between the 2 groups. The results are summarized in Figures 2 and 3. Independent variables associated with in-hospital mortality for elective and nonelective admission are summarized in Supplement 2 and 3. Hospital stay length (11.4 days vs 6.5 days, MR 1.75 95% CI 1.65 to 1.85 p < 0.001) and hospitalization cost ($68,669 vs $57,442, MR 1.20 95% CI 1.15 to 1.24, p < 0.001) were longer and more expensive in nonelective admissions, respectively. In addition, nonroutine discharge was significantly more frequently observed in nonelective TAVI admissions (69.8% vs 64.7%, p = 0.002).

Discussion

The percentage of nonelective TAVI admission was 22.3%. Recently, a population-based study from Canada reported mortality and heart failure hospitalization rate (2% and 12%, respectively) during a median of 80 days wait-time for TAVI. In addition, longer wait-time was associated with an increase in event number.[13] Bainey et al reported that 10% (17 of 170) of patients (mean Society of Thoracic

Table 3
Baseline characteristics of participants who underwent transcatheter aortic valve implantation between 2012 and 2015 by elective hospitalization status in the United States—Matched 1:1

Variables	Elective	Nonelective	p value
Number of observation, unweighted	1,683	1,683	
Number of observation, weighted	8,415	8,415	
Age, mean (SD), years	81.37 (7.79)	81.33 (8.20)	0.878
Women	48.90%	49.61%	0.667
White	85.38%	84.19%	0.842
Black	5.11%	5.41%	
Hispanic	3.86%	4.10%	
Asia	0.48%	0.77%	
Dyslipidemia	62.57%	61.50%	0.534
Prior myocardial infarction	11.88%	11.82%	0.955
Prior percutaneous coronary intervention	19.25%	18.36%	0.535
Prior coronary bypass	16.52%	17.41%	0.516
Prior pacemaker	9.69%	9.15%	0.599
Atrial fibrillation	46.64%	45.93%	0.686
Chronic obstructive pulmonary disease	32.92%	33.16%	0.884
Carotid artery disease	5.53%	6.00%	0.331
Prior cerebrovascular disease	14.74%	13.13%	0.177
Hypertension	80.99%	79.98%	0.484
Peripheral vascular diseases	28.10%	28.05%	0.971
Pulmonary circulation disorders	27.68%	27.99%	0.849
Balloon valvuloplasty	2.67%	2.50%	0.725
Diabetes mellitus with complications	7.61%	7.31%	0.749
Diabetes	38.50%	37.55%	0.553
Obese	14.14%	13.78%	0.769
Anemia deficiency	30.66%	31.13%	0.766
Congestive heart failure	79.38%	79.92%	0.746
Renal failure	42.96%	41.71%	0.518
Liver disease	2.73%	2.67%	0.916
Oxygen dependent	6.18%	5.76%	0.618
Maintenance dialysis	4.75%	4.34%	0.579
Smoker	26.38%	26.26%	0.939
Weekend admission	10.81%	11.71%	0.394
Elixhauser score			0.603
0	1.43%	1.31%	
1 - 3	39.81%	41.47%	
≥4	58.76%	57.22%	
Hospital bed size			0.919
Small	0.71%	0.77%	
Medium	5.82%	5.41%	
Large	93.46%	93.82%	
Expected primary payer			0.580
Medicare	92.34%	91.62%	
Medicaid	1.54%	1.54%	
Private	5.29%	5.53%	
Others	0.83%	1.31%	
Median household income in quartile			0.798
1st	20.26%	20.92%	
2nd	20.08%	20.80%	
3nd	23.53%	24.00%	
4th	36.13%	34.28%	
Hospital region			0.987
Northeast	35.65%	34.82%	
Midwest	14.97%	15.03%	
South	37.20%	37.85%	
West	12.18%	12.30%	

Surgeons surgical risk score 12.8 ± 8.0) died while waiting for TAVI procedure during wait-time of 4 to 6 weeks [14]. Although the NIS does not provide data on waiting time for TAVI, the percentage of 22.3% of nonelective admission appears to be high compared with 12% of heart failure admission from a previous report.[13] Nonelective admission in TAVI from NIS included all causes and not limited to cardiac etiologies and could partially explain the discrepancy. Because our analysis showed increased clinical events and healthcare resource utilization in nonelective

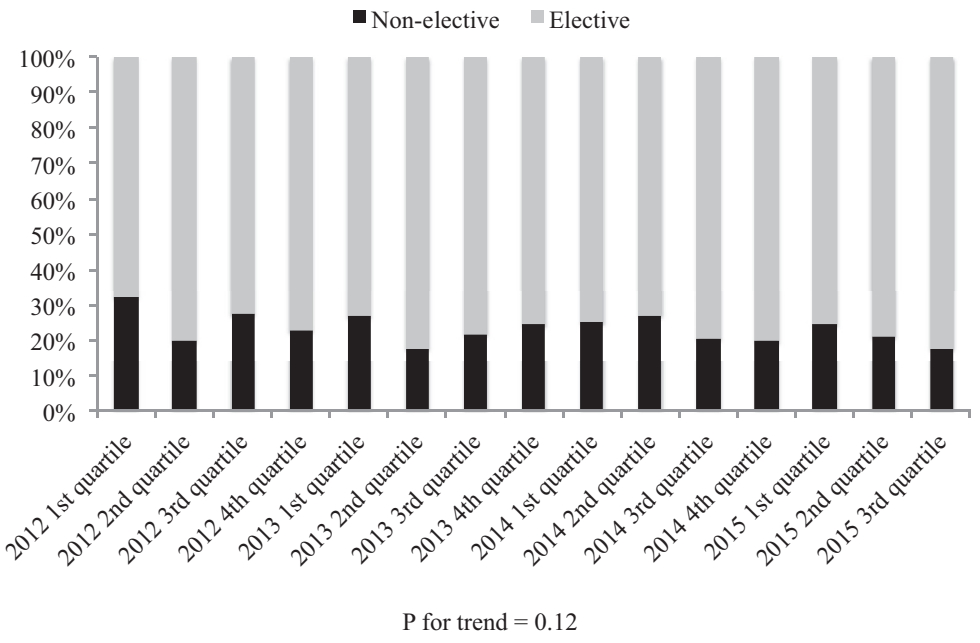

Figure 1. National trends in elective and nonelective admissions.

admission, our study adds to the current body of literature that an effort to shorten the waiting time of TAVI is warranted from a clinical standpoint. The previous study that examined the outcomes in acute refractory and persistent heart failure showed similar 30 days mortality compared with elective TAVI whereas the mortality was elevated in acutely decompensated aortic stenosis or those in cardiogenic shock.[3,15,16] The difference in underlying acuity and severity of the decompensation is likely the main cause of discrepancies in these studies.

Multivariate regression analysis identified that pulmonary circulation disorders, anemia, congestive heart failure, chronic kidney disease, and atrial fibrillation were independent predictors of nonelective admission. These co-

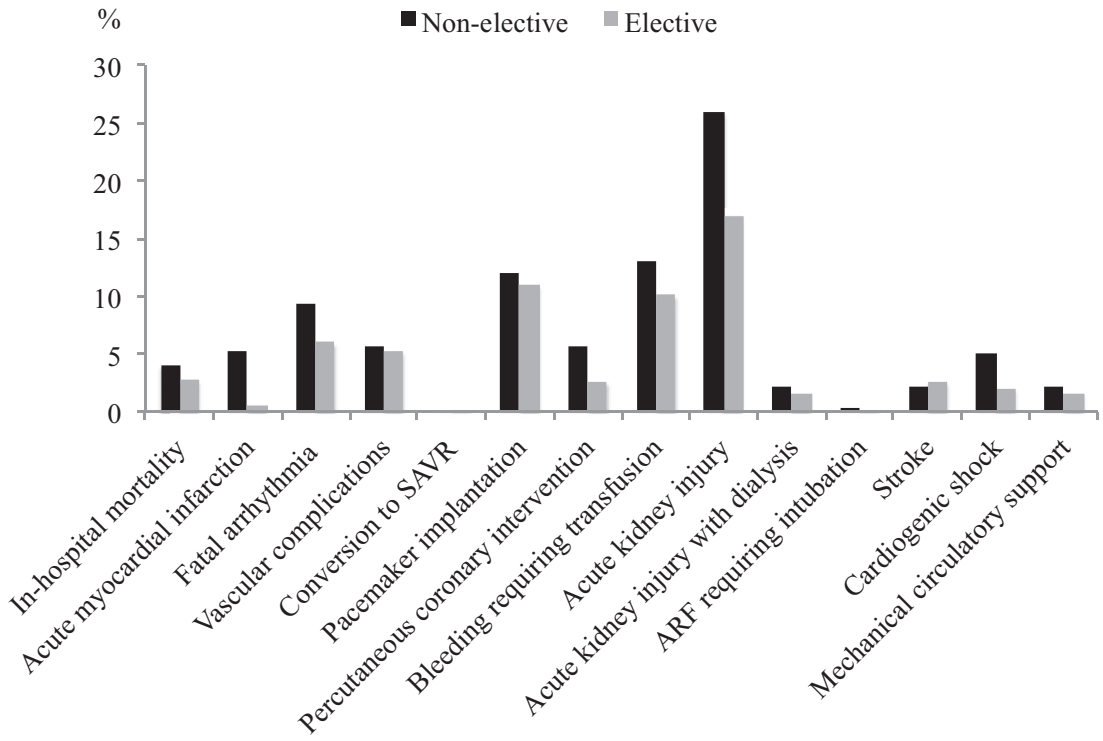

Figure 2. Incidence of in-hospital clinical events. ARF = acute respiratory failure, SAVR = surgical aortic valve replacement.

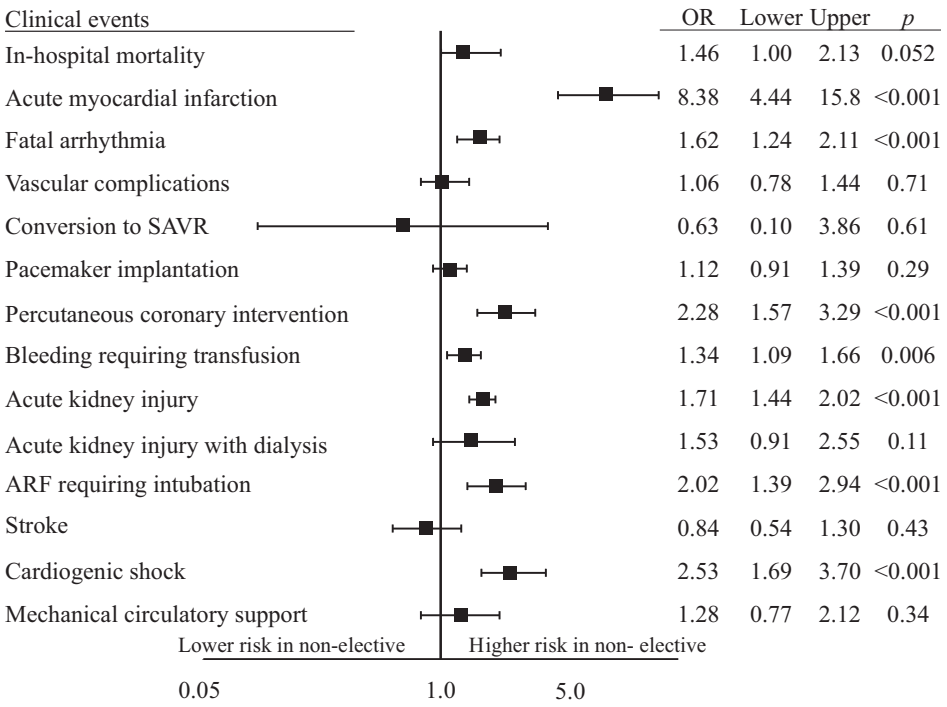

Figure 3. Forest plot of clinical events between elective and nonelective admission in TAVI. AKI = acute kidney injury, ARF = acute respiratory failure, SAVR = surgical aortic valve replacement, TAVI = transcatheter aortic valve implantation.

morbidities are well known to be associated with heart failure exacerbation and therefore those with severe aortic stenosis, these co-morbidities may easily make the severe aortic stenosis patients in heart failure exacerbation.[17–19] Because it may be difficult and not cost-effective to expedite TAVI in all candidates, selective expedition of TAVI with these risk factors may be more appropriate and cost-efficient.

The in-hospital cost was significantly higher in the nonelective admission compared with elective admission, likely as a cause of increased hospital events. Ribera et al reported the waiting-time for TAVI from prospective registries and demonstrated that shorter waiting time (<3 months) was more cost-effective compared with longer (≥ 3 months) waiting period.[20] Our study adds that TAVI after nonelective admission ended up having much higher in-hospital cost. Our study also demonstrated that lower nonroutine discharges in elective admission TAVI, which would likely further decrease healthcare-related cost even after discharge. Considering these data, developing a system for faster implementation of TAVI may be beneficial throughout the TAVI process from not only clinical but also from an economic perspective as well.

There are several limitations that need to be noticed. First, the NIS is an administrative database and therefore subject to biases such as coding error. However, the NIS database has been used in a wide variety of medical research and has proved its benefit when analyzed properly.[12] Second, we were unable to match between the group for other commonly reported variables such as Society of Thoracic Surgeon's score, frailty, and other nonreported confounders.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.amjcard.2018.09.023.

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