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Incidence and predictors of readmissions to non-index hospitals after transcatheter aortic valve replacement and the impact on in-hospital outcomes: From the nationwide readmission database

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ABSTRACT

Introduction: Whether readmission to non-index hospitals (where the initial procedure was not performed) could result in adverse outcomes and increased utilization of healthcare resources compared with readmission to index hospitals after transcatheter aortic valve replacement (TAVR) remains unclear.
Methods: From January 2012 to September 2015, a nationwide readmission database was queried to identify those who were older than 50 years and had endovascular TAVR, using the International Classification of Disease, 9th Revision, Clinical Modification code 35.05. Elective readmissions were excluded. In-hospital outcomes were compared between the index and non-index hospital readmissions. A multivariable logistic regression analysis was performed to identify predictors of non-index hospital readmissions.
Results: A total of 6808 readmissions were identified of which 2564 (37.7%) were readmitted to non-index hospitals. Residents at smaller counties, metropolitan non-teaching hospitals, or hospitals at large metropolitan areas were predictors of non-index readmissions. In-hospital mortality (adjusted odds ratio [aOR] 1.27, $p = 0.20$), acute myocardial infarction (aOR 0.83, $p = 0.53$), pacemaker placement (aOR 0.97, $p = 0.90$), acute kidney injury (aOR 0.98, $p = 0.84$), and stroke (aOR 1.03, $p = 0.90$) were similar between index and non-index readmissions but bleeding events requiring transfusions were more frequently observed in readmissions at non-index hospitals (aOR 1.32, $p = 0.025$). Hospital cost (15,410 dollars vs. 16,390 dollars, $p = 0.25$) and length of stay (5.70 days vs. 5.65 days, $p = 0.85$) were comparable between groups.
Conclusions: Non-index readmissions post-TAVR was relatively common but did not result in increased hospital mortality or healthcare utilization. Our results are reassuring for TAVR recipients with limited access to index hospitals.

1. Introduction

Candidates for transcatheter aortic valve replacement (TAVR) are usually older, frail, and have multiple comorbid conditions resulting in relatively high readmission rate, ranging from 15 to 18% within 30-days [1,2]. Early readmission has a negative impact on clinical and financial outcomes and could potentially be considered as a performance metric of TAVR [3,4].

Readmission to non-index hospitals could result in fragmentation of care. Worse outcomes have been reported with the fragmentation of care or when readmissions occurred at non-index hospitals [5–7]. However, the rate and impact of readmission to non-index hospitals are scarce post-TAVR. To avoid readmission to non-index hospitals and fragmentation of care, patients should ideally be readmitted to index hospitals but geographical access and socioeconomic factors may limit readmission to index hospitals given that TAVR is often performed at large centers. The incidence and predictors of non-index hospitalization, as well as its impact on clinical and financial outcomes, are limited in TAVR population.

The aim of this study was to clarify these clinically important issues from the Nationwide Readmission Database (NRD).

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2. Methods

2.1. Patient selection

The NRD, released by the Healthcare Cost and Utilization project (HCUP) of the Agency for Healthcare Research and Quality, is an all-payer, publicly available database of hospital inpatient stays that can be used to generate national estimates of readmissions. The NRD data are collected from 22 separate and individual state inpatient databases, which represent approximately 50% of all hospitalizations nationwide. It contains verified patient linkage variables that allow for the following of patients through separate hospitalizations within a state for that year. Readmission to a facility other than the index facility is accounted for within a given state. In addition, transfers between facilities are accounted for by representing the transfer within a single record between transferring and referring facility, to avoid counting the transfer facility as readmission. The NRD includes all discharges from all hospitals (each only known by de-identified number) in the participating states. Each entry has a unique verified patient linkage number that is used to track patients across hospitals and therefore can be used to analyze readmissions. Variables in the data set include patient demographics, disease-specific diagnostic codes for each admission, outcomes, and hospital-level characteristics. The represented states in the sample are geographically dispersed in order to account for variation in populations [8].

2.2. Patient population

Data from January 2012 to September 2015 were utilized for this analysis. We selected all adult patients (aged ≥50 years) from the NRD who were undergoing endovascular TAVR within the first 11 months of the year. For 2015 dataset, we included patients within the first 8 months. By doing so, all patients had at least 30 days of follow-up time. *International Classification of Disease*, *Ninth Edition*, *Clinical Modifications* (*ICD-9-CM*) procedure codes were used to identify patients who underwent endovascular TAVR (Supplemental Table 1) and Fig. 1 illustrates the selection process. Comorbidities included the Agency for HealthCare Research and Quality–generated Elixhauser comorbidity variables. These variables were used to generate a comorbidity score for each patient and grouped patients into 3 categories (1, 2 to 3 or ≥4 comorbidities).

For each index hospitalization, the NRD includes information regarding patient and hospital factors that were utilized in univariate and multivariable analysis. Patient factors included: payer information (Medicare, Medicaid, private insurance, no charge, other, self-pay), age, patient location (central counties and fringe counties of metro areas >1 million, counties in metro areas of >250,000, counties in metro areas of 50,000–250,000, micropolitan counties, and not metropolitan or micropolitan), and median household income quartile (quartiles 1–4). Patient age was included in NRD as a continuous variable and categorized for analysis (50–74, 75–84 ≥ 85 years old). Hospital factors in NRD included: bed size (small, medium, large), teaching status (metropolitan non-teaching, metropolitan teaching, nonmetropolitan). In addition, *ICD-9-CM* diagnosis codes were generated for variables such as dyslipidemia, prior myocardial infarction, atrial fibrillation, prior cerebrovascular disease, prior percutaneous coronary intervention, prior coronary artery bypass graft and major complications such as acute renal failure, acute stroke, acute myocardial infarction, pacemaker placement, and bleeding requiring transfusions (Supplemental Table 1). Hospital costs were generated by merging hospital charges with the cost-to-charge ratio files provided with the data set. Costs were inflation adjusted using the US Bureau of Labor Statistics Consumer Price Index, with 2017 as the reference year [9]. The time-to-readmission variable and the primary admission date and length of stay were used to calculate the number of days to readmission. All 30-day non-elective readmissions were categorized as index vs. non-index. Index hospitals were those at which the patient had the initial TAVR performed; all other hospitals were non-index hospitals. Patients who were transferred to an index hospital during initial non-index readmission are categorized as index. We performed a comparative analysis between the index and non-index hospital readmissions. Our primary outcome was in-hospital mortality. Other secondary outcome variables were discharge disposition, length of hospital stay, cost and complications.

2.3. Statistical analysis

Discharge-level weights provided with the data set provided for national estimates. All data extraction and analyses were done with Statistical Analysis System (SAS V.9.4, SAS Institute Inc., Cary, NC, US). We reported the effect sizes, 95% confidence intervals (CI), and p-values. All non-elective readmissions that occurred within 30 days of discharge were included in this analysis. Descriptive analyses were performed for the readmission by index vs. non-index hospital status. We reported the mean and standard deviation (SD) for continuous variables, and percentages for categorical variables. Paired *t*-test was used for comparisons of continuous variables with normal distribution and Rao-Scott chi-square for categorical variables. Generalized estimating equations multivariable logistic regression with an exchangeable working correlation matrix was used to identify factors present on the primary admission (the admission during which TAVR was performed) that were associated with readmission to a non-index vs. an index hospital. Cardiogenic shock, acute kidney injury, discharge disposition status, gender, age category at admission, Elixhauser comorbidity burden, resident of state vs. nonresident of state, insurance, income, hospital location, teaching hospital status, hospital urban-rural designation, hospital bed size and days to readmission were included in the model. Choice of covariates for the multivariate analyses was based on the clinical plausibility that they could be associated with non-index readmission. Bonferroni corrected p-values were computed given multiple comparisons. The trends of readmission rates were computed by fitting a Poisson regression model with a robust error variance to evaluate for changes in the number of readmissions bimonthly and keeping the "year" as a continuous variable in the model.

We performed a multivariable regression model that accounted for clustering of observations as above to compute the comparative outcome differences between the 2

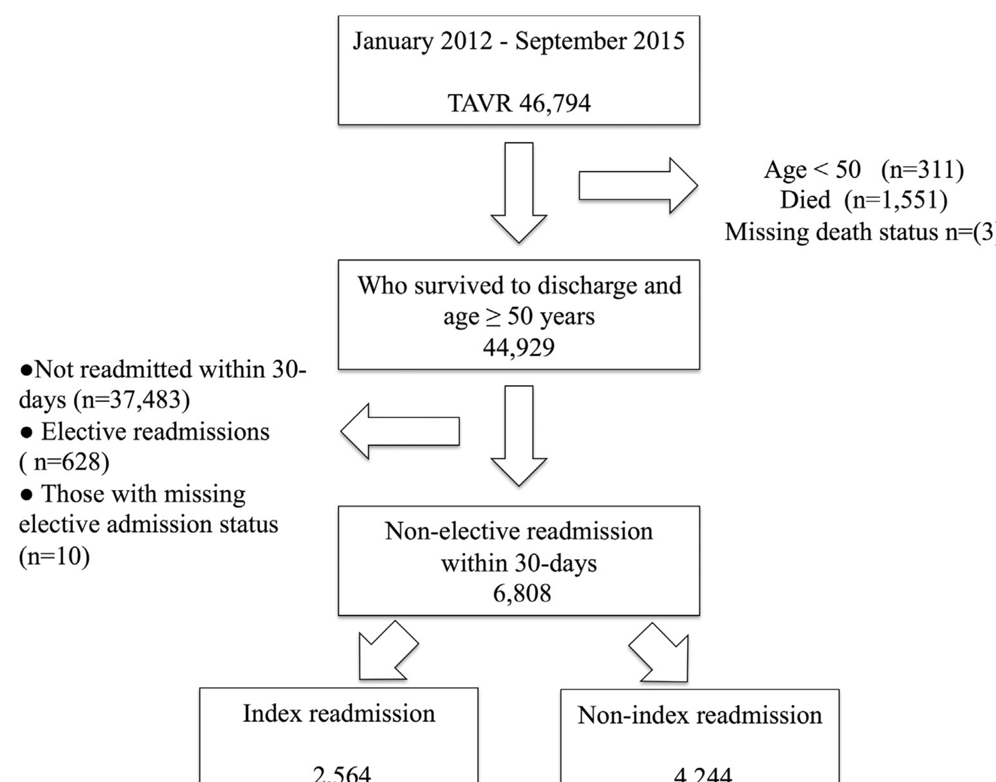

Fig. 1. Patient selection flow chart.

hospital categories. In-hospital mortality, major complications, and discharge disposition were compared using logistic regression. Differences in length of stay and hospital cost were computed using generalized linear modeling, with log link-poisson and gamma distributions- for hospital length of stay and cost respectively. As recommended by HCUP, survey-specific techniques accounting for clustered sampling methodology of the data were used for weighting in order to obtain national estimates [10].

3. Results

3.1. Patient, geographical, and hospital demographics

From a total of 46,794 TAVR performed during the study period, a total of 6808 readmissions (14.5%) after endovascular TAVR (age ≥ 85 46.7% and 47.8% female) were identified and 2564 (37.7%) were admitted to non-index hospitals. Flow chart of patient selection is summarized in Fig. 1. Days to readmission from discharge were significantly longer in those readmitted to non-index hospitals (10 vs. 9 days, $p < 0.001$). There was no difference in age categories and Elixhauser score but female sex was more frequently observed in index hospital readmissions compared with non-index readmissions. Non-index readmissions had higher rates of peripheral vascular disease while index hospital readmissions had higher rates of dyslipidemia, congestive heart failure, and chronic renal failure. Those readmitted to non-index hospitals were more residents within the same state with the index hospitals ($p < 0.001$) and had higher median household income ($p = 0.003$) but similar insurance type ($p = 0.45$). Hospital bed size was significantly larger in index compared with non-index hospital readmissions ($p < 0.001$). Patient characteristics are summarized in Table 1. Characteristics of patients readmitted and not readmitted are summarized in Supplement Table 2.

3.2. Predictors of readmission to non-index hospitals

Residents in the same state as index hospital (aOR [adjusted odds ratio] 6.7, 95%CI 4.1–10.8), in smaller size counties in metro areas with 50,000–249,999 population (aOR 3.1, 95%CI 1.8–5.3), counties with 250,000–999,999 populations (aOR 2.3, 95%CI 1.4–3.9), and micropolitan counties (aOR 3.0, 95%CI 1.7–5.4) were more likely to be readmitted to non-index hospitals. Regarding the teaching status of the hospitals, metropolitan non-teaching hospitals (aOR 2.7, 95%CI 1.9–4.0) were associated with higher non-index readmissions. As for hospital locations and size, hospitals located in small metropolitan areas with less than one million residents (aOR 0.29, 95%CI 0.20–0.40), micropolitan areas (aOR 0.08, 95%CI 0.04–0.16), and medium (aOR 0.49, 95%CI 0.27–0.89) or large hospital size bed (aOR 0.43, 95%CI 0.26–0.71) were associated with lower rates of non-index readmission. The results of regression analysis are presented in Table 2.

3.3. Reasons for readmissions

In both groups, the most common reasons for readmissions were congestive heart failure. Cardiac conditions included congestive heart failure, conduction abnormalities, and atrial fibrillation. Septicemia, pneumonia, gastrointestinal bleeding, and acute respiratory failure were more readmitted to non-index hospitals whereas post-operative infection was more often readmitted to index hospitals. The top 10 reasons for readmissions are summarized in Fig. 2 and differences in incidence between index and non-index hospitals are summarized in Supplement Table 3.

3.4. In-hospital outcomes in index vs. non-index hospital readmissions

There was no difference in in-hospital mortality between non-index and index readmission (6.0% vs. 5.1%, aOR 1.27, 95%CI 0.88–1.82). Other in-hospital outcomes such as acute myocardial infarction (2.1% vs. 2.6%, aOR 0.83, 95%CI 0.46–1.49), pacemaker placement (3.5% vs. 4.4%, aOR 0.97, 95%CI 0.46–1.49), stroke (2.8% vs. 2.7%, aOR 1.03, 95%CI 0.60–

Table 1
Baseline characteristics of participants undergoing transcatheter aortic valve replacement between 2012 and 2015 by index vs. non-index readmission.

	Total	Index	Non-index	p value
No. of observation, weighted	6808	4244	2564	
Day to readmission, median, (IQR)	9 (14)	9 (13)	10 (14)	0.0001
Age category				0.494
50–74	16.15	16.78	15.14	
75–84	37.18	36.82	37.78	
≥85	46.66	46.40	47.09	
Female	47.81	49.36	45.28	0.038
Dyslipidemia	55.50	57.15	52.83	0.030
Prior myocardial infarction	9.47	9.98	8.64	0.222
Prior percutaneous coronary intervention	19.78	20.41	18.77	0.294
Prior coronary bypass graft	19.76	20.65	18.32	0.128
Prior pacemaker	19.64	19.29	20.19	0.586
Atrial fibrillation	51.38	49.94	46.47	0.066
Chronic obstructive pulmonary disease	31.61	31.30	32.12	0.629
Carotid artery disease	3.17	3.41	2.78	0.349
Prior cerebrovascular disease	13.34	13.87	13.00	0.523
Hypertension	71.93	72.64	70.77	0.326
Peripheral vascular diseases	28.87	27.32	31.43	0.019
Hypothyroidism	21.70	21.51	22.01	0.749
Diabetes	36.70	36.35	37.27	0.635
Obese	12.06	12.06	10.04	0.112
Anemia	37.60	37.19	38.27	0.611
Congestive heart failure	65.88	68.42	61.76	0.0004
Chronic renal failure	39.24	40.80	36.71	0.031
Chronic liver disease	2.65	2.90	2.26	0.299
Maintenance dialysis	4.79	4.60	5.11	0.538
Smoker	24.42	25.49	22.70	0.132
Weekend admission	23.61	23.28	24.14	0.364
Resident within same state with the hospital	92.72	89.75	97.54	<0.0001
Elixhauser score				0.770
1	4.79	4.59	5.12	
2–3	28.45	28.72	28.02	
≥4	66.75	66.69	66.85	
Hospital bed size				<0.0001
Small	8.90	2.96	18.54	
Medium	20.64	13.92	31.55	
Large	70.47	83.12	49.91	
Expected primary payer				0.451
Medicare	93.64	94.03	93.01	
Medicaid	0.87	0.83	0.95	
Private	4.43	4.31	4.62	
Others	1.06	0.84	1.43	
Median household income in quartile				0.003
1st	19.58	21.83	15.91	
2nd	23.87	23.83	23.92	
3nd	26.87	25.65	28.86	
4th	29.68	28.69	31.31	
Teaching status of hospital				<0.0001
Metropolitan non-teaching	20.95	7.87	42.18	
Metropolitan teaching	73.60	91.12	45.18	
Non-metropolitan hospital	5.45	1.01	12.65	
Hospital urban-rural designation				<0.0001
Large metropolitan areas with at least 1 million residents	63.59	66.33	59.16	
Small metropolitan areas with <1 million residents	30.96	32.66	28.19	
Micropolitan areas	4.16	1.01	9.28	
Not metropolitan or micropolitan (non-urban residual)	1.28	0.00	3.37	
Patient location: NCHS urban-rural				0.030
"Central" counties of metro areas of ≥1 million population	25.05	25.53	24.27	
"Fringe" counties of metro areas of ≥1 million population	30.82	29.39	33.16	
Counties in metro areas of 250,000–999,999 population	18.95	20.91	15.76	
Counties in metro areas of 50,000–249,999 population	8.39	7.62	9.65	
Micropolitan counties	9.11	8.43	10.23	
Not metropolitan or micropolitan counties	7.67	8.13	6.92	

Table 2
Predictors of non-index readmission.

Odds ratio estimates				
Effect	Point estimate	95% confidence limits		P value
Cardiogenic shock	1.098	0.748	1.612	0.633
Acute kidney injury	1.047	0.869	1.262	0.630
Elixhauser score				
1 (ref.)				
2–3	0.85	0.64	1.11	0.685
≥4	1.06	0.81	1.37	1.000
Routine home discharge	0.937	0.791	1.110	0.453
Weekend admission	0.960	0.736	1.250	0.760
Days to readmission	1.019	1.011	1.028	<0.0001
Admission year				
2012 (ref.)				
2013	0.971	0.549	1.719	1.000
2014	1.020	0.619	1.681	1.000
2015	0.900	0.563	1.439	1.000
Age category				
50–74 (ref.)				
75–84	1.200	0.925	1.556	0.280
≥85	1.239	0.933	1.645	0.212
Female	0.925	0.797	1.075	0.311
Expected primary payer				
Medicare (ref.)				
Medicaid	0.455	0.129	1.492	0.481
Private	1.255	0.743	2.122	1.000
Others	1.115	0.472	2.635	1.000
Median household income in quartile				
1st (ref.)				
2nd	1.303	0.959	1.770	0.136
3rd	1.446	1.058	1.977	0.011
4th	1.323	0.958	1.826	0.134
Hospital bed size				
Small (ref.)				
Medium	0.489	0.269	0.887	0.012
Large	0.427	0.256	0.714	0.0002
Resident in same state as hospital	6.672	4.124	10.795	<0.0001
Patient location: National Center for Health Statistics Urban-rural				
"Central" counties of metro areas of ≥1 million population (ref.)				
"Fringe" counties of metro areas of ≥1 million population	1.155	0.788	1.692	0.269
Counties in metro areas of 250,000–999,999 population	2.313	1.362	3.930	<0.0001
Counties in metro areas of 50,000–249,999 population	3.107	1.819	5.306	<0.0001
Micropolitan counties	3.046	1.732	5.357	<0.0001
Not metropolitan or micropolitan counties	2.379	1.238	4.574	0.0015
Teaching status of hospital				
Metropolitan teaching (ref.)				
Metropolitan non-teaching	2.740	1.884	3.986	0.0002
Non-metropolitan hospital	2.384	1.774	3.204	0.0017
Hospital urban-rural designation				
Large metropolitan areas with at least 1 million residents (ref.)				
Small metropolitan areas with <1 million residents	0.285	0.203	0.402	<0.0001
Micropolitan areas	0.081	0.041	0.162	<0.0001

1.79), and acute kidney injury (23.9% vs. 25.9%, aOR 0.98, 95%CI 0.81–1.19) were similar in both groups. Bleeding requiring transfusion was higher in non-index readmissions compared with index readmissions (23.8% vs. 17.1%, aOR 1.32, 95%CI 1.03–1.69). Length of stay (5.70 days vs. 5.65 days, $p = 0.85$) and cost (16,390 dollars vs. 15,410 dollars, $p = 0.25$) was also comparable between the two groups. The results are shown in Supplement 4. Rate of readmission trends were similar during the in 2012 for both index ($p = 0.82$) and non-index ($p = 0.39$). However, during 2013–2015, the readmission rate to index hospitals significantly decreased while it remained the same for non-index hospitals (Supplement 5).

4. Discussion

To our knowledge, this is the first to assess the details and compare outcomes of readmissions after TAVR between index and non-index hospitals from a nationally representative database. Our salient findings could be summarized as follows:

1: Among those readmitted within 30-days post TAVR, approximately one third (37.7%) were readmitted to non-index hospitals.
2: Residents at smaller counties, small bed size hospitals, metropolitan non-teaching hospitals, and hospitals at large metropolitan areas predicted increased incidence of non-index readmissions.
3: In-hospital outcomes (mortality, myocardial infarction, acute kidney injury, and stroke) were comparable between the index and non-index readmissions except that bleeding event requiring transfusions were more frequently observed during readmissions to non-index hospitals. The cost and length of stay were also similar between both groups.

In a previous study that included adults from the NRD year 2013, among those re-admitted, more than one fifth were readmitted to non-index hospitals and had a 21% increased risk of mortality [6]. In other medical conditions, the rate of readmission to non-index hospitals ranged from 17 to 31% [6,11–14]. According to our study, the readmission rate to non-index hospitals was 37.7% post-TAVR and was numerically higher compared with previous studies, suggesting that many TAVR recipients did not have access to index hospitals. However, the number of centers performing TAVRs has been steadily increasing [15] and given that our analysis was limited to the use of data until 2015, readdressing this topic in the future may show lower readmission rates to non-index hospitals. Another explanation of this phenomenon is that because the reason of readmission was mainly heart failure, a condition requiring prompt diagnosis and treatment, the emergency medical services could have preferred to choose hospitals geographically closest to the patients' residence rather than the index hospitals. Unlike previous analyses of re-admissions in other conditions, our study showed similar in-hospital mortality between the index and non-index admissions [6,11–14]. Several factors could account for similar outcomes between readmission to index and non-index hospitals. First, the reasons for readmission were mostly common medical conditions that can be appropriately managed with similar outcomes between the index and non-index hospitals. Secondary, with better patient selection, preoperative planning, device improvements, and learning curve, the perioperative complications of TAVR have decreased significantly [16,17]. Lastly, adherence to guideline-directed medical therapies and chronic disease management program development have decreased heart failure re-admission rates [18,19]. Standardization of heart failure management and post-discharge follow-up may have contributed to similar outcomes between the two groups. Of note, bleeding events were more common when readmitted to non-index hospitals. This finding could be explained by deficit or delay in obtaining information on antiplatelet or anticoagulation therapy and previous bleeding events at non-index hospitals. However, it did not impact the hospital cost and the length of stay.

We identified several hospitals and regional related characteristics as predictors of non-index hospital readmissions. After major procedures, patients prefer the continuity of care within the same healthcare system where index hospitals are affiliated and could become anxious when access to these hospitals is restricted. Previous studies suggested that better continuity of care was associated with reduced non-elective readmission after hospital discharge and support such patients' perception [20,21]. Multivariable regression analysis showed that residents at smaller counties were more likely to be readmitted to non-index hospitals, suggesting that residents in these areas had restricted access to index hospitals for non-elective medical visits. This finding is likely due to geographic distance and limited accessibility to the index

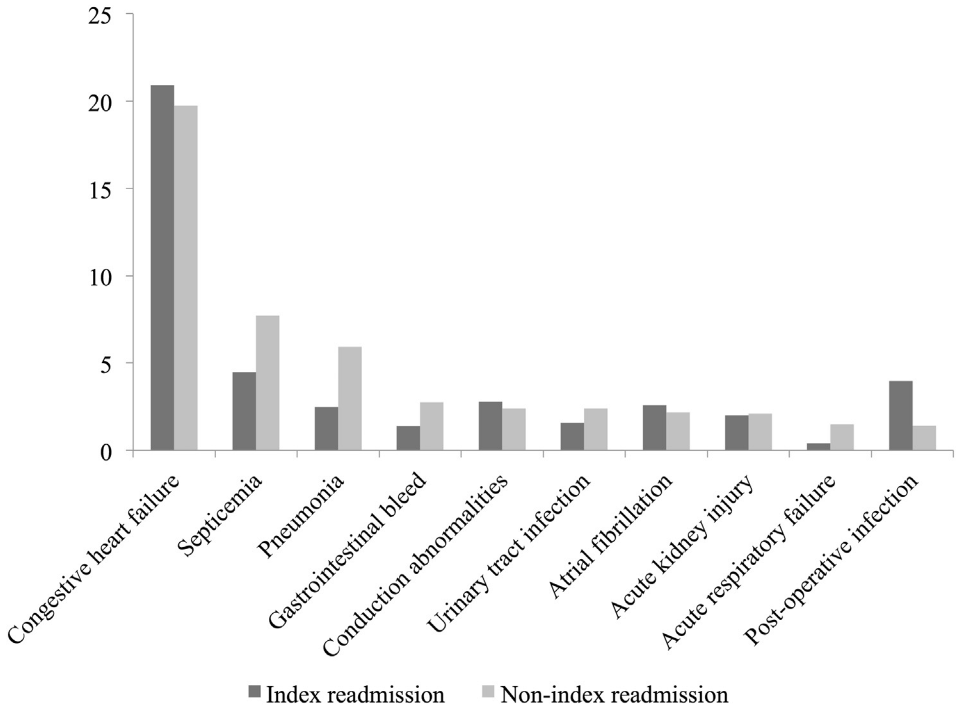

Fig. 2. Causes of readmission between index and non-index readmissions.

hospitals [22,23]. Our results are reassuring for index hospital providers and post-TAVR patients who encounter difficulties accessing index hospitals for non-elective medical visits. Although our results suggest that clinical outcomes were similar between those readmitted to index and non-index hospitals, when patients require additional intervention to rhe aortic valve such as valve-in-valve or surgical valve replacement, readmission to index hospitals may result in better outcomes. Additionally, when readmission for heart failure is related to valve dysfunction including valve thrombosis, endocarditis, worsening aortic regurgitation, or patient-prosthesis mismatch, the baseline gradient, paravalvular aortic regurgitation and antiplatelet/anticoagulation regimen at discharge would be key information for prompt decision-making which may not be possible if readmitted to non-index hospitals [24].

Antithrombotic regimen post-discharge could affect reasons for readmission post-TAVR. Patients are usually discharged on aspirin and clopidogrel for 6 months followed by single anti-platelet or with single antiplatelet and oral anticoagulant when anticoagulants are indicated [25]. A previous study showed higher bleeding rate with dual antiplatelet therapy compared with single-antiplatelet therapy while the rate of ischemic events did not differ [26]. Thus, the difference in antithrombotic regimen could have impacted our results.

There are several limitations that need to be acknowledged. NRD is an administrative database capturing conditions and clinical events through ICD-9 codes. The coding is subject to errors, which could lead to inaccurate results. Second, this was a retrospective analysis subject to several biases and only able to demonstrate association and not causation. Third, there are several important variables missing in the NRD that could have influenced our results such as Society of Thoracic Surgeons score, access site, antithrombotic therapy, valve types, distance from home to the hospitals, and frailty. Lastly, TAVR is currently a rapidly evolving field and current clinical patterns and outcomes are different from this study period.

In conclusion, approximately one-third of TAVR recipients were readmitted to hospitals other than where the initial procedures were performed. Several geographical and hospital characteristics were associated with increased risk of non-index hospital readmission but the major clinical outcomes and healthcare resource utilization were comparable between the index and non-index hospital readmission following TAVR. Our results suggest that non-index hospitals are safe alternatives to index-hospitals for non-elective medical visits or readmissions following TAVR.

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Appendix A. Supplementary data

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