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Retrospective Cohort Study

Rates, predictors, and causes of readmission after transcatheter aortic valve replacement in patients with chronic kidney disease

Taha Teaima, Gianfranco Bittar Carlini, Rohan A Gajjar, Imran Aziz, Sami J Shoura, Abdul-Rahim Shilbayeh, Naim Battikh, Tareq Alyousef

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Abstract

BACKGROUND

Transcatheter aortic valve replacement (TAVR) is a revolutionary procedure for severe aortic stenosis. The coexistence of chronic kidney disease (CKD) and TAVR introduces a challenge that significantly impacts patient outcomes.

AIM

To define readmission rates, predictors, and causes after TAVR procedure in CKD stage 1-4 patients.

METHODS

We used the national readmission database 2018 and 2020 to look into readmission rates, causes and predictors after TAVR procedure in patients with CKD stage 1-4.

RESULTS

Out of 24758 who underwent TAVR and had CKD, 7892 (32.4%) patients were readmitted within 90 days, and had higher adjusted odds of being females (adjusted odds ratio: 1.17, 95%CI: 1.02-1.31, $P = 0.02$) with longer length of hospital stay > 6 days, and more comorbidities including but not limited to diabetes mellitus, anemia, and congestive heart failure (CHF).

CONCLUSION

Most common causes of readmission included CHF (18.0%), sepsis, and complete atrioventricular block. Controlling readmission predictors with very close follow-up is warranted to prevent such high rate of readmission.

Key Words: Chronic kidney disease; Transcatheter aortic valve replacement; Readmission;

Predictors; Rates

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Core Tip: Our analysis of national readmission database for year 2018 to 2020 for 90 days readmissions for patients with chronic kidney disease stage 1-4 undergoing transcatheter aortic valve replacement showed considerably higher readmission rate to 32.4%. Majority were females and had higher comorbidity burden. Most common cause of 90 days readmission was congestive heart failure. Hence, we recommend optimization of co-morbidities and close follow up after index admission to prevent high rate of readmissions.

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INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has emerged over the years as a revolutionary less invasive option than surgical aortic valve replacement (SAVR) for the treatment of severe aortic stenosis (AS) in patients who are either above 65 years of age or deemed intermediate to high-risk or inoperable for traditional open-heart surgery[1-3]. This groundbreaking technique offers a ray of hope for individuals with multiple medical co-morbidities who suffer from aortic valve degeneration.

However, the convergence of chronic kidney disease (CKD) and TAVR introduces a complex interplay of medical challenges that significantly impact patient outcomes. As the prevalence of both CKD and AS continue to rise[4,5], understanding the multifaceted relationship between these conditions becomes paramount in optimizing treatment strategies and improving patient care.

The prevalence of CKD is particularly high in elderly populations[6], a demographic that frequently coincides with AS. One study reported a pooled estimate of 12.4% in patients aged ≥ 75 years due to age-related valve degeneration[7,8]. As such, the encounter between CKD and AS is becoming increasingly common. Available literature indicates that presence of CKD or end-stage renal disease (ESRD) is associated with a higher risk of mortality[9,10].

To our knowledge, our study is the first to utilize a large population-based database to describe the effects of co-existence of CKD stage 1-4 on the readmission after TAVR procedure in conjunction with causes and predictors of readmission. Identifying these predictors and causes, and addressing them can establish a base-ground to limit readmission rates after TAVR in patients with CKD.

MATERIALS AND METHODS

The national readmission database (NRD) 2018 and 2020 was employed for this retrospective cohort study. NRD is one of the largest publicly available all-payer inpatient healthcare databases in the United States. The database is sustained by the Agency for Healthcare Research and Quality. It is structured as a weighted probability sample to obtain an approximate sample that statistically represents all hospitalizations in all non-federal acute care hospitals nationwide, excluding rehabilitation facilities and long-term acute care hospitals. Data was obtained from billing data submitted by hospitals to statewide data organizations, representing about 97% of the United States populace. These hospitalizations are then classified based on urban/rural divisions, hospital teaching status, geographic location, and bed size. Data from 20% of all hospitalizations in these strata are then collected, pooled, and weighted to guarantee that it is representative of the United States population.

The NRD database is entirely coded using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)/Procedure Coding System. It includes patient and hospital-level information such as primary diagnosis, secondary diagnosis, median household income, primary payer type, hospital teaching status, hospital bed size, geographic region, and urban/rural location. Diagnoses are then sorted into a single principal diagnosis, and the remaining diagnoses are considered secondary diagnoses. The principal diagnosis corresponds to the main International Classification of Diseases, Tenth Revision (ICD-10) code for hospitalization, and the secondary diagnoses are any other ICD-10 codes besides the principal diagnosis that were tied to the hospitalization.

The study population exclusively consists of adult patients over 18 years hospitalized for TAVR procedure and had co-diagnosis of CKD stage 1-4. Multiple ICD-10-CM codes for TAVR procedure (02RF37Z, 02RF38Z, 02RF3JZ, 02RF3KZ) and CKD stage 1-4 (N181, N182, N183, N184) were used to create our subpopulation. ICD-10 codes used in this study were obtained from a literature review of similar validated analyses. The population included in the analysis is outlined in

(Figure 1).

The study variables include demographic characteristics such as age, gender, mean household income, and medical insurance status. Hospital characteristics such as teaching status, and bed size are also included in the database. Comorbidity burden was assessed using the Charlson comorbidity index (CCI), adjusted for population-based research, and ICD-10-CM coding for each comorbidity to generate baseline patient characteristics.

The primary study outcome in our analysis was the readmission rates after TAVR procedure in patients with CKD stage 1-4 and most common causes of readmission. Secondary outcomes include adjusted odds of readmission predictors. Analysis STATA® (StataCorp, College Station, TX, United States) version 17 was utilized to perform the statistical analysis. Year-based discharge weights provided by the Healthcare Cost and Utilization Project (HCUP) were used to calculate weighted national estimates. Categorical variables proportions were compared using the Chi-square test. An independent sample *t*-test was used to evaluate the means of continuous data. The unadjusted odds ratio (OR) was calculated using univariate regression analysis for each outcome. Based on the significance of each univariate screen ($P < 0.2$), we selected variables to perform the multivariable logistic regression analysis to adjust for possible confounders. Other essential variables based on the literature review were included in the model. Logistic regression was used for binary or categorical outcomes, and linear regression analysis was used for continuous outcomes. All *P*-values were two-tailed, and we used a threshold of 0.05 to determine significance.

This manuscript is exempt from Institutional Review Board approval, as NRD is a de-identified national administrative database and is readily available online at <https://www.hcup-us.ahrq.gov>. Based on this exemption and according to the HCUP guidelines, our study did not require Cook County Health Institutional Review Board approval.

RESULTS

Out of 24758 adults who underwent TAVR and had co-diagnosis of CKD stage 1-4, 24375 (98.4%) discharged alive. Out of these and within 90 days of discharge, 7892 (32.4%) patients were readmitted (Figure 1). Readmitted patients were more likely to be females (42.5 % *vs* 39.3%, $P = 0.018$) with longer length of stay (LOS) > 6 days during index admission (34.8% *vs* 19.0%, $P < 0.001$), and had 3 or more comorbidities according to CCI (36.7% *vs* 26.0%, $P < 0.001$). Readmitted patients were more likely to have chronic obstructive pulmonary disease (COPD) (28.0% *vs* 23.3%, $P < 0.001$), diabetes mellitus (DM) (52.9% *vs* 46.9%, $P < 0.001$), malignancy (10.2% *vs* 6.5%, $P < 0.001$), peripheral arterial disease (PAD) (12.3% *vs* 10.6%, $P = 0.013$), atrial flutter or atrial fibrillation (33.4% *vs* 24.9%, $P < 0.001$), anemia (49.3% *vs* 37.7%, $P < 0.001$), and to be malnourished (4.5% *vs* 2.6%, $P < 0.001$) (Table 1). Most common causes of readmission were congestive heart failure (CHF) (18.0%), sepsis (4.6%), acute kidney injury (AKI) (3.4%), complete atrioventricular block (3.2%), paroxysmal atrial fibrillation (1.4%), pneumonia (1.2%), and gastrointestinal bleeding (1.2%) (Figure 2).

On multivariate regression analysis, readmitted patients had higher adjusted odds of longer hospital stay during index admission > 6 days [adjusted OR (aOR): 1.3, 95%CI: 1.15-1.40, $P < 0.001$], higher adjusted odds of being admitted to skilled nursing facility after index admission (aOR: 1.37, 95%CI: 1.22-1.52, $P < 0.001$), and females had higher adjusted odds of readmission (aOR: 1.17, 95%CI: 1.02-1.31, $P = 0.02$). Readmitted patients had also higher adjusted odds of having DM (aOR: 1.27, 95%CI: 1.17-1.39, $P < 0.001$), anemia (aOR: 1.25, 95%CI: 1.14-1.37, $P < 0.001$), CHF (aOR: 1.25, 95%CI: 1.11-1.41, $P < 0.001$), atrial flutter or atrial fibrillation (aOR: 1.32, 95%CI: 1.20-1.45, $P < 0.001$), AKI during index admission (aOR: 1.18, 95%CI: 1.05-1.34, $P = 0.006$), and cardiac complications during index admission (aOR: 1.6, 95%CI: 1.22-2.04, $P < 0.001$) (Figure 3).

Covariates of the multivariate regression analysis included age, sex, length of hospital stay, discharge destination, DM, COPD, PAD, malnutrition, anemia, CHF, coronary artery disease, atrial flutter or atrial fibrillation, AKI during index admission, cardiac, respiratory, and vascular complications during index admission.

DISCUSSION

In our study, readmission rate post TAVR in CKD stage 1-4 patients was 32.4% with the most common cause being CHF (18.0%). Readmitted patients had higher adjusted odds of longer hospital stay during index admission > 6 days, higher adjusted odds of being discharged to skilled nursing facility, and females had slightly higher adjusted odds of readmission as compared to men. Readmitted patients also had higher adjusted odds of having DM, Anemia, CHF, atrial flutter or atrial fibrillation, AKI during index admission, and cardiac complications during index admission.

Our findings suggest a substantial coexistence of CHF and CKD in patients undergoing TAVR. Given that both CHF and CKD are independently associated with increased readmission rates in various medical contexts, it is plausible to hypothesize that their confluence significantly amplifies the risk of readmissions post TAVR. The intricate interplay between cardiac and renal functions might create a synergistic effect, resulting in a higher likelihood of adverse outcomes.

Moreover, CKD may complicate the management of CHF, influencing post-TAVR readmission rates. Patients with compromised renal function may exhibit altered responses to standard CHF therapies, potentially affecting the management of their cardiac condition. This prompts consideration of tailored treatment strategies for CHF in patients with CKD, aiming to optimize cardiac health, volume status before discharge to potentially reduce readmission rates.

In the current published literature, the rates for readmissions post-TAVR after 30-days and 90-days ranged around 14.6-20.9% and 24.1%-25.1% [11,12]. If analyzed on a system-based approach, cardiovascular causes represent the most common causes of readmission, estimated to represent 38%, of which a wide range of variation, 22.8%-30.4% represent

Table 1 The baseline characteristics of the patients who were readmitted, and those who were not readmitted during index admission, *n* (%)

Patient population	Patients underwent TAVR and were discharged alive with no readmission in 90 days (<i>n</i> = 16483) (67.6)	Patients underwent TAVR and were discharged alive with readmission in 90 days (<i>n</i> = 7892) (32.4)	<i>P</i> value
18-44	0 (0)	0 (0)	0.2890
45-64	544 (3.3)	229 (2.9)	
≥ 65	15939 (96.7)	7663 (97.1)	
Female	6478 (39.3)	3354 (42.5)	0.0018
Male	10005 (60.7)	4538 (57.5)	
Insurance status			0.5559
Medicaid	15395 (93.4)	7426 (94.1)	
Medicare	164 (1.0)	71 (0.9)	
Private	890 (5.4)	379 (4.8)	
Self-pay	33 (0.2)	16 (0.2)	
Length of stay			< 0.001
Less than 3 days	10285 (62.4)	3528 (44.7)	
3 to 6 days	3065 (18.6)	1618 (20.5)	
More than 6 days	3131 (19.0)	2746 (34.8)	
Hospital bed size			0.9935
Small	807 (4.9)	379 (4.8)	
Medium	3955 (24.0)	1894 (24.0)	
Large	11719 (71.1)	5619 (71.2)	
Teaching hospital	14653 (88.9)	7000 (88.7)	0.7673
Non-teaching hospital	1830 (11.1)	892 (11.3)	
Urban hospital	16335 (99.1)	7805 (98.9)	0.3680
Rural hospital	148 (0.9)	87 (1.1)	
CCI			< 0.001
No comorbidity	1830 (11.1)	1634 (20.7)	
1 comorbidity	5011 (30.4)	1847 (23.4)	
2 comorbidities	5357 (32.5)	1515 (19.2)	
≥ 3 comorbidities	4286 (26.0)	2896 (36.7)	
Median household income			0.3420
First quartile (\$1-\$49999)	3395 (20.6)	1673 (21.2)	
Second quartile (\$50000-\$64999)	4928 (29.9)	2352 (29.8)	
Third quartile (\$65000-\$85999)	4401 (26.7)	2186 (27.7)	
Fourth quartile (\$86000+)	3758 (22.8)	1681 (21.3)	
Hypertension	181 (1.1)	79 (1.0)	0.9876
Congestive heart failure	13104 (79.5)	6740 (85.4)	< 0.001
Coronary artery disease	12329 (74.8)	5974 (75.7)	0.3283

History of cerebrovascular accidents	462 (2.8)	260 (3.3)	0.2142
Malnutrition	429 (2.6)	355 (4.5)	< 0.001
COPD	3841 (23.3)	2210 (28.0)	< 0.001
Obesity	4055 (24.6)	2036 (25.8)	0.2091
Diabetes mellitus	7731 (46.9)	4175 (52.9)	< 0.001
Dyslipidemia	12873 (78.1)	5769 (73.1)	< 0.001
Cancer	1071 (6.5)	805 (10.2)	< 0.001
Anemia	6214 (37.7)	3891 (49.3)	< 0.001
Smoking	6560 (39.8)	3038 (38.5)	0.2631
Peripheral arterial disease	1747 (10.6)	971 (12.3)	0.0133
Cirrhosis	280 (1.7)	174 (2.2)	0.0745
Alcohol abuse	165 (1.0)	95 (1.2)	0.1668
Atrial fibrillation or flutter	4104 (24.9)	2636 (33.4)	< 0.001
Vascular complications	577 (3.5)	450 (5.7)	< 0.001
Pericardial complications	82 (0.5)	110 (1.4)	< 0.001
Cardiac complications	346 (2.1)	316 (4)	< 0.001
Respiratory complications	214 (1.3)	189 (2.4)	< 0.001
Infectious complications	742 (4.5)	576 (7.3)	< 0.001
Gastrointestinal complications	143 (0.87)	77 (0.97)	0.4053
Neurological complications	59 (0.36)	36 (0.46)	0.3743
Skin related complications	138 (0.84)	118 (1.5)	0.0012
Cardiac tamponade	59 (0.36)	70 (0.89)	0.0001
Post operative bleeding	155 (0.94)	89 (1.13)	0.4053

CCI: Charlson comorbidity index; COPD: Chronic obstructive pulmonary disease; TAVR: Transcatheter aortic valve replacement.

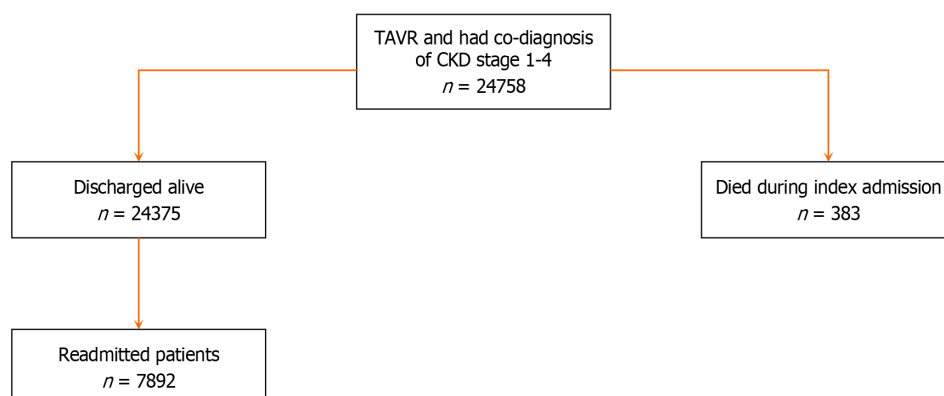


Figure 1 Flow chart of Readmission rates after transcatheter aortic valve replacement in chronic kidney disease stage 1-4 patient. TAVR: Transcatheter aortic valve replacement; CKD: Chronic kidney disease.

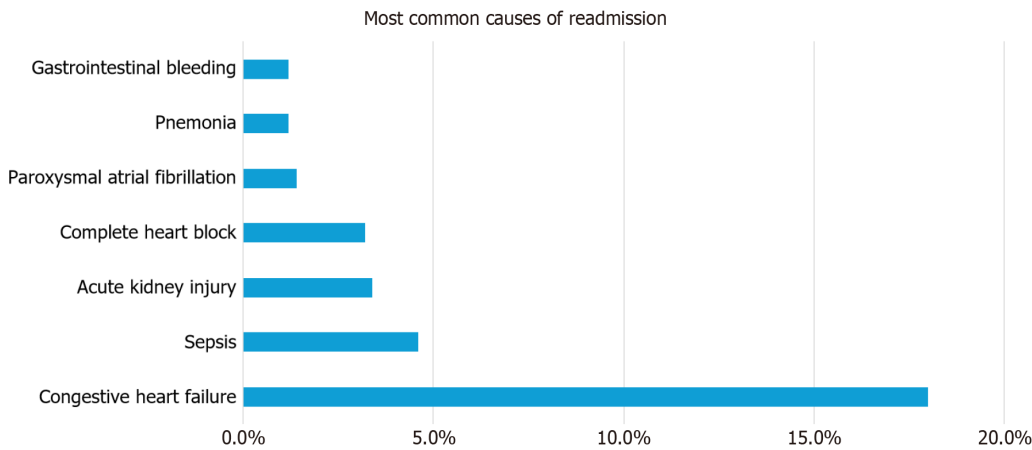


Figure 2 Most common causes of readmission.

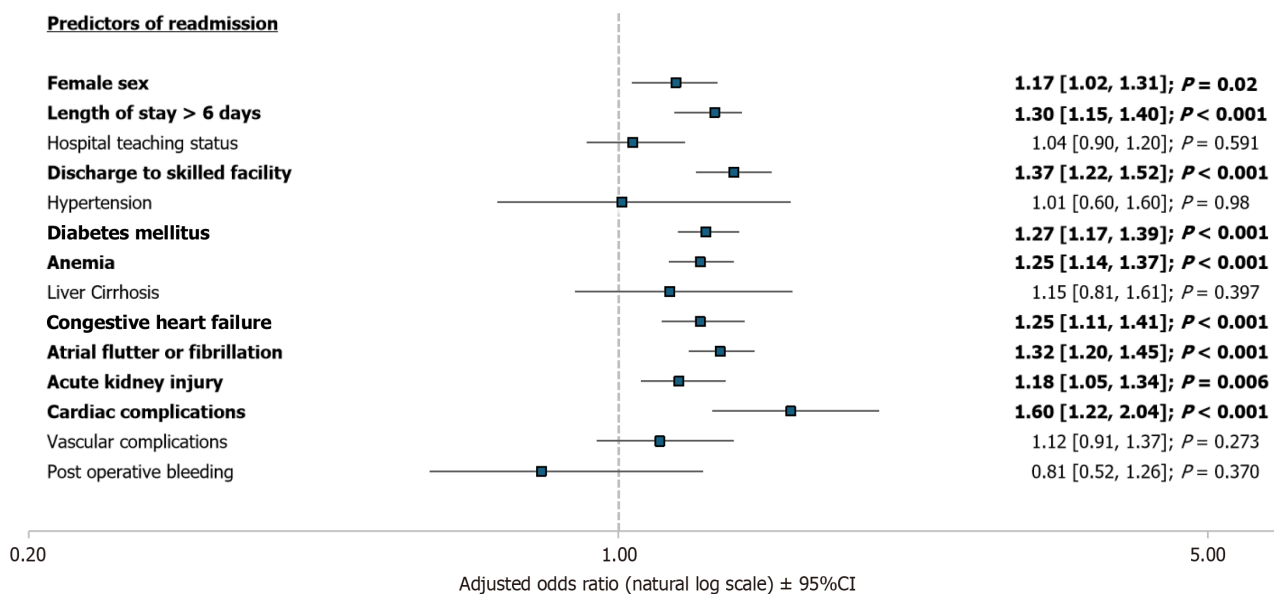


Figure 3 Forrest plot for predictors of readmission when adjusted for patient demographics, comorbidities, and hospital characteristics.

heart failure readmissions[11,12], which is similar to our findings that CHF is the most common cause of readmission post TAVR in non-ESRD CKD patients (18.0%). TAVR readmissions have decreased in the past 5-6 years. This is attributed to the advancement of imaging, provider experience, and later-generation devices for valve deployment. Other reports describe a progressive increase in readmissions due to noncardiac causes by up to 34% within a mean 1.96-year follow-up. In contrast, cardiac causes progressively decreased to 20.5%[13-15]. Our study revealed a 32.4% readmission rate for patients with CKD but not ESRD, whereas ESRD patients showed a readmission rate of 34.4% in a separate study [16]. The continuity and progression of readmission rates across the renal disease continuum favor a direct correlation between worse renal function and higher readmission rates post TAVR. A major contributor could be the difficulty in optimizing fluid status in those patients. Efficient fluid management is critical in both CHF and CKD. Based on our findings, we think that appropriate fluid balance during and after TAVR is crucial, particularly for patients with concurrent CHF and CKD. An imbalance could exacerbate cardiac and renal stress, potentially contributing to readmissions. Tailoring fluid management protocols might be beneficial in mitigating this risk.

In our study, female sex carried a higher adjusted odds of readmission. Cardiovascular disparities between males and females have been widely described in the literature. These differences include medical therapy for heart failure, interventional and surgical procedures, anticoagulation, and even preventative cardiovascular care[17-19]. Higher rates of readmissions, in-hospital mortality during index presentation, and increased LOS in 90 days post-TAVR analysis in women compared to men in this setting are well supported and attributed to complex interactions between longevity, comorbidities, and disparities in care. Common comorbidities reported among women include pulmonary hypertension, hypertension, diabetes, and anemia[17]. Proposed mechanisms in the setting of AS include a higher incidence of concentric hypertrophy than men, diastolic dysfunction, and reduced preload and stroke volume[20-22].

Trend analyses have shown progressive decrease in in-hospital mortality, overall fatality, and LOS in patients undergoing TAVR for the past years[23,24]. Previous multivariate analyses have characterized LOS greater than 5 days

and multiple comorbidities as predictors of early readmission post TAVR. The same report also found periprocedural AKI and CKD as predictors of both early readmissions and increased mortality[11]. Among readmitted patients our analysis showed a bimodal distribution where 44.7% of readmissions had index-LOS shorter than 3 days followed by 34.8% with LOS beyond 6 days. Considering that 62.4% of patients were discharged within 3 days post procedure, only patients with LOS > 6 days ties a statistically significant increase in 90-day readmission risk.

Decreased renal reserve predisposing to periprocedural AKI on CKD, decreased glomerular filtration rate, and higher diastolic dysfunction in patients with CKD have been demonstrated to play a role in longer admissions for these patients [16].

The prevalence of heart failure in patients with AS is estimated at 10% and represents the sole most common cause of readmissions post-TAVR[25,26]. Systolic dysfunction, as measured by stress-corrected midwall shortening, is an unfavorable prognostic factor in AS. An echographic study demonstrated left ventricular myocardial systolic dysfunction is common in asymptomatic AS patients with increased valvuloarterial afterload, whereas ejection fraction is generally preserved[21]. Despite known data with worse outcomes for SAVR in this population, TAVR has emerged as a reasonable alternative for afterload reduction in patients with severe AS associated with left ventricular ejection fraction < 50%, regardless of their surgical risk, and life expectancy < 20 years[27-30]. Heart failure readmissions post TAVR are associated with increased mortality and decreased quality of life compared to patients who do not require readmission. Additionally, the incidence of CHF readmissions 1 year post TAVR ranges from 9%-24%, and correlates with that of major trials for chronic systolic heart failure[31-33].

Our study showed that CKD patients with underlying CHF were more likely to experience all-cause 90-day readmissions post-TAVR (79.5% *vs* 85.4%). The proportion of patients with concomitant CHF in CKD patients occupies the higher half of the spectrum, regardless of risk for readmission. Readmitted patients significantly surpassed literature descriptions. Altogether, these findings support the coexistence of heart failure in CKD-patients as a particularly high-risk relationship for readmissions post TAVR[34]. Despite the mortality impact aortic valve replacement has brought into the natural course of disease for patients with AS, systolic dysfunction carries a baseline prognosis non-modifiable by TAVR. Ongoing clinical trials aim to determine net benefit from TAVR in patients with moderate AS and severe heart failure[35].

In our cohort, readmitted patients were more likely to have COPD. The incidence of COPD in patients undergoing aortic valve replacement is estimated to be around 22.7%-36%, with an approximate of 12%-13% with severe disease[36]. COPD significantly increases adverse outcomes in patients with TAVR, especially if associated with chronic hypoxic respiratory failure requiring home O₂ supplementation. In such patients, mortality was 2.5-fold higher compared to their non-oxygen users counterparts[37,38]. Conflicting evidence exists regarding COPD and oxygen supplementation and readmissions in TAVR-patients as an independent variable[39].

Limitations

We encountered some limitations based on the nature of the NRD database. It is a retrospective database collected based on ICD-10 codes, which may not-in some cases - be the best representative of the actual figures due to possible human errors. NRD also has limitations regarding therapeutic medications, actual investigations, and lab values, which are not accounted for in this study, with the possibility of confounding. Despite these limitations, the long study period, huge sample size, and analysis techniques empowered this study to shed light on TAVR readmissions in CKD patients stage 1-4, which is encouraging for more large prospective, multicenteric and controlled studies.

CONCLUSION

Finally, with the increased utility of TAVR for AS in an aging patient population with multiple comorbidities, physicians should consider very early and close follow up for patients with CKD post TAVR especially those with higher number of readmission predictors or with more complications during index admission. Future studies are encouraged to investigate the utility of earlier follow up, and other preventative measures that can mitigate the increased rates of readmission experienced by this patient population.

FOOTNOTES

Author contributions: Teaima T and Alyousef T conceptualized the research idea and designed the study; Teaima T curated data from database and performed statistical analysis, Gajjar RA contributed with data analysis; Teaima T, Carlini GB, Gajjar RA, Aziz I, Shoura SJ wrote the original manuscript draft; Shilbayeh AR and Battikh N contributed with manuscript review and further editing; Teaima T and Alyousef T supervised all the tasks. All authors have read and approve the final manuscript.

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