Original Article

Trends and effect of atrial fibrillation on inpatient outcomes after transcatheter aortic valve replacement

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Background: Atrial fibrillation (AF) is common in patients undergoing transcatheter aortic valve replacement (TAVR) but there is conflicting evidence on whether AF impacts outcomes after TAVR.

Methods: Hospitalizations of adults ≥50 years old who had undergone elective TAVR from 2012 to 2015 were included. Poisson regression was used to assess changes in in-hospital complications, average length of stay (LOS) after TAVR, and discharge disposition over time. Multivariable logistic, linear, and generalized logistic regression models, adjusting for patient and hospital characteristics, were used to estimate the effect of AF on inpatient outcomes.

Results: A total of 7,266 TAVR hospitalizations were included; AF was present in 44% of patients. Between 2012 and 2015, there was a significant decrease in the incidence of acute kidney injury, blood transfusion, average LOS, and inpatient mortality both for AF and non-AF patients. However, the incidences of vascular complications and major bleeding decreased only among non-AF patients. After adjustment, AF was associated with increased incidences of TIA/stroke (OR 1.36, 95% CI: 1.01, 1.85), acute kidney injury (OR 1.54, 95% CI: 1.33, 1.78), blood transfusion (OR 1.14, 95% CI: 1.00, 1.30), transfer to a skilled nursing facility (OR 1.38, 95% CI: 1.23, 1.55), and longer average LOS (CIE 1.30, 95% CI: 1.06, 1.54). AF was not associated with inpatient mortality (OR 1.09, 95% CI: 0.81, 1.48).

Conclusions: AF is prevalent among patients undergoing TAVR, and is associated with higher incidences of inpatient complications, discharge to a skilled nursing facility, and longer average LOS. While the incidence of many complications has declined in the past few years, continued efforts to further reduce complications in patients with AF is urgently required for expansion of TAVR to broader populations.

Keywords: Transcatheter aortic valve replacement (TAVR); transcatheter; atrial fibrillation (AF); hospitalization; inpatient outcomes

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Introduction

Transcatheter aortic valve replacement (TAVR) has emerged as a less invasive treatment for patients with aortic stenosis at prohibitive, high and intermediate surgical risk (1). Since its inception, better patient selection, better techniques and expertise in TAVR have led to improving patient outcomes (2). As we expand the benefit of TAVR to patients at a lower surgical risk, it is more important than ever to explore the prognostic indicators of patient

outcomes after TAVR.

Atrial fibrillation (AF) is common in patients undergoing TAVR (3). AF is also a well-known risk factor for stroke (4), is common in patients with heart failure of valvular origin (5), and is associated with worse outcomes after cardiac procedures such as percutaneous coronary intervention (6) and aortic valve replacement (7). There is conflicting evidence on whether AF impacts various outcomes after TAVR (8,9). It is also unknown if patients undergoing TAVR with AF have seen similar improvements in outcomes over years, as compared to those without AF. Thus, the purpose of this analysis was to assess the effect of AF on inpatient complications, the average length of stay (LOS), and discharge disposition (including inpatient mortality) after TAVR, and to investigate whether improvements in patient outcomes over the years are spread similarly across populations depending on the presence or absence of AF.

Methods

Study design and population

The National Inpatient Sample (NIS) is the largest all-payer database of inpatient hospital stays in the United States and is sponsored by the Agency on Healthcare Research and Quality. It includes data from over 7 million hospitalizations at over 1,000 hospitals each year and represents a 20% stratified random sample of all hospital discharges nationwide (10). The International Classification of Disease, 9th revision, Clinical Modification (ICD-9-CM) diagnostic and procedural codes were used to identify patients.

Hospitalizations of adults ≥50 years old with aortic stenosis (ICD-9-CM 424.1) who had undergone elective TAVR (35.05 and 35.06) from January 1, 2012, to September 30, 2015 (when ICD-10 codes were implemented) were eligible for inclusion. Patients with a history of congenital aortic valve disorders (746.3), rheumatic aortic stenosis (395.0–395.9), or hypertrophic obstructive cardiomyopathy (425.11), who had undergone concomitant procedures involving the coronary vessels (0.61–0.69 and 36.00–36.99), such as percutaneous coronary intervention or coronary artery bypass grafting, who had surgery >2 days after admission (to further limit to elective surgeries), were discharged against medical advice, or had an unknown discharge status were excluded. AF was identified using ICD-9-CM codes 427.31 and 427.32.

The outcomes were inpatient complications, LOS after TAVR, and discharge disposition (including inpatient mortality). Complications of interest included permanent pacemaker placement (PPM) implantation (0.50, and 37.8–37.83), acute kidney injury (584–584.9), transient ischemic attack (TIA)/stroke (344.6–344.61, 431, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 435–435.9, and 997.02), acute myocardial infarction (410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.71, 410.81, 410.91, and 411.1), cardiogenic shock (785.51), cardiac arrest (427.5), bleeding (430, 431, 432–432.9), blood transfusion (99.00–99.09), and vascular complications (39.31, 39.41, 39.49, 39.52, 39.56, 39.57, 39.59, 39.79, 441.0–441.03, 441.1, 441.3, 441.5, 441.6, 414.1–414.19, 443.22, 444–444.9, 447.0, 868.04, 900–904.9, 997.7, 998.2, and 999.2). A composite 'any complication' variable was also created. Disposition was categorized as: (I) routine/home health care; (II) transfer to short-term hospital; (III) transfer to skilled nursing facility, intermediate care facility, or other care facility; and (IV) died.

Statistical analysis

Differences in patient and hospital characteristics between hospitalizations of patients with and without AF were compared using Student's *t*-tests and Chi-square tests as appropriate. A P value <0.05 was considered statistically significant. Charlson comorbidity index (CCI) was calculated using the Deyo *et al.* coding scheme (11). Quarterly rates of AF, per 100 TAVR procedures, were estimated using Poisson regression, and changes over time were evaluated using likelihood ratio tests. Additional trend tests were performed to assess changes in in-hospital complications, average LOS after surgery, and discharge disposition over time, stratified by AF. NIS sampling weights were not applied since obtaining national estimates was not a goal of this study.

Multivariable logistic, linear, and generalized logistic regression models were used to estimate the effect of AF on inpatient complications, average LOS after TAVR and discharge disposition, respectively. All models were adjusted for year of TAVR, age, sex, race/ethnicity, CCI, primary insurance, median household income in each patient's ZIP code, hospital region, hospital type, and hospital size. Both age and CCI were modeled as restricted cubic splines. Because of the low incidence of acute myocardial infarction and cardiogenic shock, adjusted estimates could not be obtained.

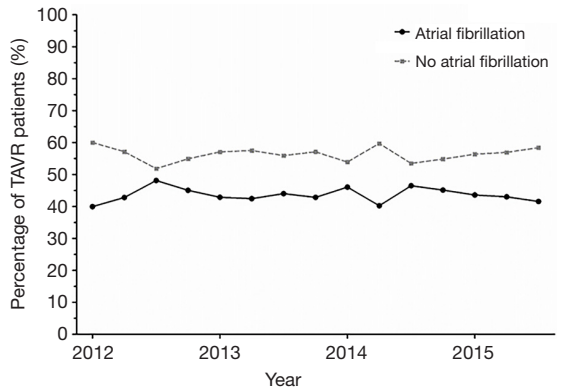

Figure 1 Trends in the prevalence of atrial fibrillation, in hospitalizations of adults ≥50 years old and undergoing transcatheter aortic valve replacement.

All analyses were performed using SAS 9.4 (SAS Inc., Cary, NC, USA).

Results

Overall, 7,266 TAVR hospitalizations were included, and 44% had a diagnosis of AF. The proportion of patients with AF undergoing TAVR has remained relatively stable between 2012 and 2015 (P=0.62, *Figure 1*). CCI also remained stable over this time in both patients with and without AF (P=0.38 and P=0.34, respectively) (data not shown). Patients with AF were more likely to be non-Hispanic white (92% *vs.* 87%, P<0.0001, *Table 1*). The vast majority of hospitalizations occurred at urban teaching hospitals (89%), and at large hospitals (77%).

Patients with AF were more likely to have at least one inpatient complication (57% *vs.* 53%, P<0.0001). Specifically, AF was associated with increased incidences of TIA/stroke (3% versus 2%, P=0.02), cardiogenic shock (2% versus 1%, P=0.0006), acute kidney injury (17% versus 11%, P<0.0001), major bleeding (34% versus 32%, P=0.02), and require a blood transfusion (20% versus 17%, P=0.01) during their hospitalization (*Table 2*). No significant difference in the incidences of permanent pacemaker implantation, acute myocardial infarction, cardiac arrest, or vascular complications was seen. While the majority of AF and non-AF patients had a routine/home health discharge, patients with AF were more likely to be transferred to a skilled nursing facility (29% versus 22%, P<0.0001). There was no significant difference in inpatient mortality (3% in both groups). Patients with AF also had, on average, longer

Table 1 Baseline characteristics in hospitalizations of adults ≥50 years old who underwent transcatheter aortic valve replacement (TAVR) between 2012 and 2015, stratified by atrial fibrillation status

Characteristics	AF, N=3,171 (44%)	No AF, N=4,095 (56%)
Age, years, mean (SD)	82 (6.9)	81 (8.3)
Male, n [%]	1,745 [55]	2,192 [54]
Race/ethnicity, n [%]		
Non-Hispanic White	2,722 [92]	3,322 [87]
Non-Hispanic Black	56 [2]	174 [5]
Hispanic	82 [3]	165 [4]
Other	100 [3]	164 [4]
Missing	211	270
Charlson comorbidity score, mean (SD)	2.8 (1.7)	2.6 (1.7)
Primary insurance, n [%]		
Medicaid/Medicare	2,934 [93]	3,693 [90]
Private	177 [6]	329 [8]
Other/Self-pay	58 [2]	63 [2]
Median household income[a], n [%]		
Low	643 [21]	860 [21]
Medium	792 [25]	1,048 [26]
High	820 [26]	1,037 [26]
Highest	856 [27]	1,087 [27]
Hospital region, n [%]		
Northeast	701 [22]	941 [23]
Midwest	774 [24]	957 [23]
South	1,043 [33]	1,389 [34]
West	653 [21]	808 [20]
Hospital location, n [%]		
Rural, non-teaching	31 [1]	28 [1]
Urban, non-teaching	312 [10]	431 [11]
Urban, teaching	2,828 [89]	3,636 [89]
Hospital size[b], n [%]		
Small	164 [5]	202 [5]
Medium	560 [18]	742 [18]
Large	2,447 [77]	3,151 [77]

[a], income was characterized into quartiles within each ZIP code; [b], hospital size is based on the number of short-term acute care hospital beds; cut points were chosen for each region and location combination so that approximately 1/3 of hospitals would appear in each category. AF, atrial fibrillation; SD, standard deviation.

Table 2 Incidence of inpatient complications, length of stay (LOS) after discharge, and discharge disposition in hospitalizations of adults ≥50 years old who underwent transcatheter aortic valve replacement, stratified by atrial fibrillation status

Variable	AF, N=3,171 (44%)	No AF, N=4,095 (56%)	P value
Inpatient complications, n [%]			
Permanent pacemaker implantation	344 [11]	412 [10]	0.28
TIA/stroke	99 [3]	92 [2]	0.02
Acute myocardial infarction	11 [0]	20 [0]	0.36
Cardiogenic shock	74 [2]	52 [1]	0.0006
Cardiac arrest	99 [3]	101 [2]	0.10
Acute kidney injury	528 [17]	461 [11]	<0.0001
Major bleeding	1,087 [34]	1,299 [32]	0.02
Blood transfusion	619 [20]	705 [17]	0.01
Vascular complications	167 [5]	215 [5]	0.98
Any complication	1,816 [57]	2,153 [53]	<0.0001
Discharge disposition, n [%]			
Routine/home health	2,153 [68]	3,069 [75]	<0.0001
Transfer, short term hospital	18 [1]	25 [1]	0.81
Transfer, skilled nursing facility	912 [29]	893 [22]	<0.0001
Death	88 [3]	108 [3]	0.72
LOS after TAVR, days, mean (SD)	6.2 (5.5)	4.9 (4.3)	<0.0001

AF, atrial fibrillation; TIA, transient ischemic attack; LOS, length of stay; TAVR, transcatheter aortic valve replacement; SD, standard deviation.

lengths of stay (6.2 versus 4.9 days, P<0.0001).

The yearly incidence of PPM implantation, TIA/stroke, cardiac arrest, acute kidney injury, major bleeding, requiring a blood transfusion, vascular complications, transfer to a skilled nursing facility, and inpatient mortality between 2012 and 2015 are depicted in *Figure 2*. Among AF patients, there was a significant decrease in the incidence of acute kidney injury (20% in 2012, 13% in 2015, P=0.002), requiring a blood transfusion (31% in 2012 versus 14% in 2015, P<0.0001), inpatient mortality (4% in 2012 versus 2% in 2015, P=0.001) and transfer to a skilled nursing facility (28% in 2012 versus 25% in 2015, P=0.009), and the incidence of routine discharge increased significantly (67% in 2012 versus 73% in 2015, P=0.01, *Figure 2A*,*C*). The incidence of PPM implantation (P=0.17), TIA/stroke (P=0.98), cardiac arrest (P=0.74), major bleeding (P=0.07), and vascular complications (P=0.64) did not change. In patients without AF, there was also significant decrease in the incidence of acute kidney injury (11% in 2012 versus 8% in 2015, P=0.0002), requiring a blood transfusion (27% in 2012 versus 11% in 2015, P<0.0001), inpatient mortality (4% in 2012 versus 2% in 2015, P=0.003), and transfer to a skilled nursing facility (27% in 2012 versus 18% in 2015, P<0.0001), and an increase in routine discharge (68% in 2012 versus 80% in 2015, P=0.0001), between 2012 and 2015 (*Figure 2B*,*D*). However non-AF patients also had a significant decrease in the incidences of major bleeding (37% in 2012 versus 28% in 2015, P<0.0001) and vascular complications (11% in 2012 versus 4% in 2015, P<0.0001). There was also a significant increase in PPM implantation in non-AF patients (7% in 2012 versus 11% in 2015, P=0.01). No changes were seen in the incidence of TIA/stroke (P=0.32) or cardiac arrest (P=0.40).

The average LOS decreased, on average, by around 2 days in both patients with and without AF between 2012 and 2015 (7.1 versus 5.3 days and 5.7 versus 4.0 days, respectively, P<0.0001 for both; *Figure 3*).

After adjusting for year of TAVR, patient demographics,

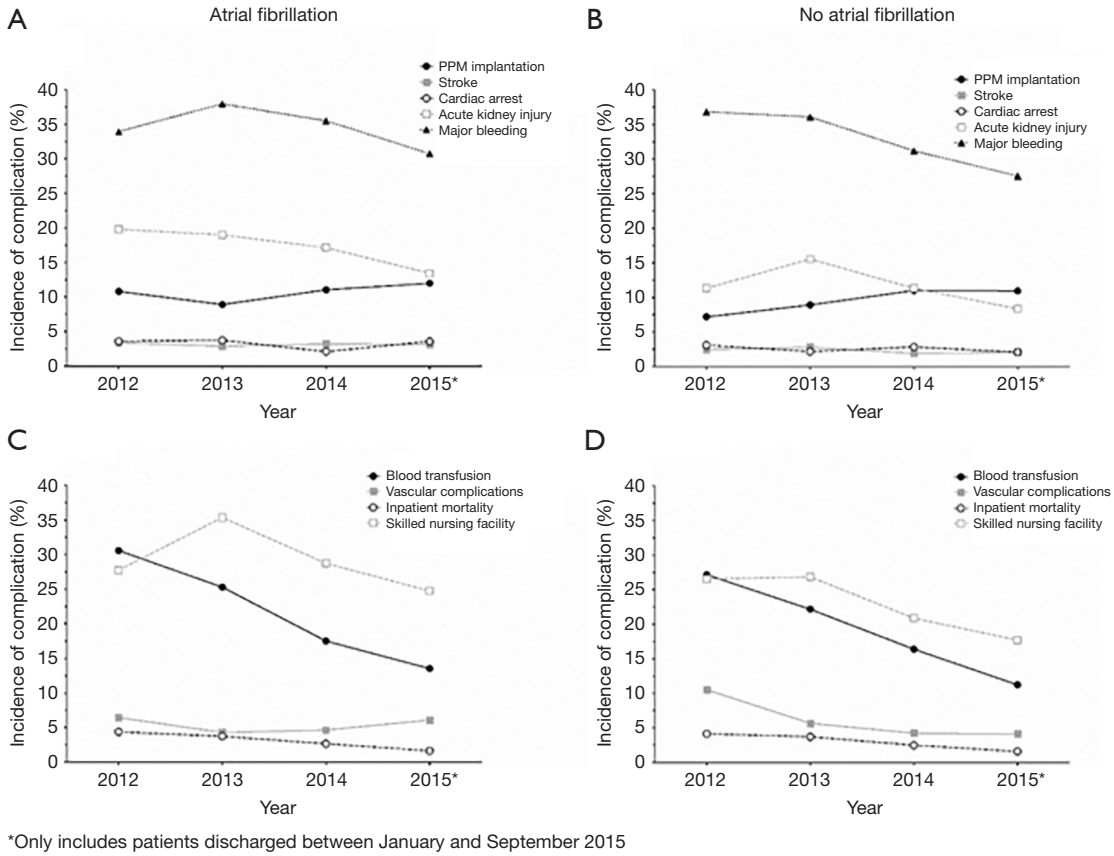

Figure 2 Trends in inpatient complications in hospitalizations of patients (A and C) with and (B and D) without atrial fibrillation. PPM, pacemaker.

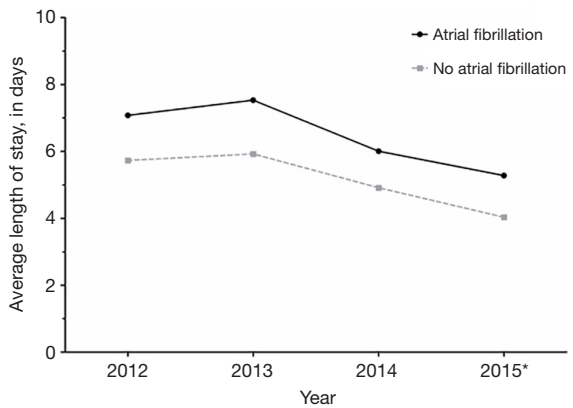

Figure 3 Trends in average length of stay, in days, after transcatheter aortic valve replacement, stratified by atrial fibrillation status. *Only includes patients discharged between January and September 2015.

comorbidities, and hospital characteristics AF was still associated with increased odds of TIA/stroke (OR 1.36, 95% CI: 1.01, 1.85), acute kidney injury (OR 1.54, 95% CI: 1.33, 1.78), and requiring a blood transfusion (OR 1.14, 95% CI: 1.00, 1.30; *Table 3*). AF was not associated with permanent pacemaker implantation, cardiac arrest, major bleeding or vascular complications. AF was also associated with increased transfer to a skilled nursing facility (OR 1.38, 95% CI: 1.23, 1.55), and an increased LOS [change in estimate (CIE) 1.30, 95% CI: 1.06, 1.54]. AF was not associated with inpatient mortality (OR 1.09, 95% CI: 0.81, 1.48).

Discussion

Our study found that AF is prevalent among patients undergoing TAVR, and that these patients have increased

Table 3 Crude and adjusted association of atrial fibrillation on inpatient complications, discharge disposition, and length of stay after surgery, among adults ≥50 years old who underwent TAVR

Variable	Crude		Adjusted[a]	
	OR (95% CI)	P value	OR (95% CI)	P value
Inpatient complications				
Permanent pacemaker implantation	1.09 (0.94, 1.27)	0.28	1.03 (0.88, 1.21)	0.69
TIA/stroke	1.40 (1.05, 1.87)	0.02	1.36 (1.01, 1.85)	0.05
Acute myocardial infarction	0.70 (0.34, 1.48)	0.36	NA	–
Cardiogenic shock	1.86 (1.30, 2.66)	0.0007	NA	–
Cardiac arrest	1.27 (0.96, 1.69)	0.09	1.24 (0.92, 1.67)	0.16
Acute kidney injury	1.58 (1.38, 1.80)	<0.0001	1.54 (1.33, 1.78)	<0.0001
Major bleeding	1.12 (1.02, 1.24)	0.02	1.10 (0.99, 1.23)	0.06
Blood transfusion	1.17 (1.04, 1.31)	0.01	1.14 (1.00, 1.30)	0.05
Vascular complications	1.00 (0.82, 1.24)	0.98	1.04 (0.83, 1.29)	0.75
Any complication	1.21 (1.10, 1.33)	<0.0001	1.19 (1.06, 1.30)	0.002
Discharge disposition[b]				
Transfer, short term hospital	1.03 (0.56, 1.89)	0.93	1.05 (0.56, 1.97)	0.87
Transfer, skilled nursing facility	1.46 (1.31, 1.62)	<0.0001	1.38 (1.23, 1.55)	<0.0001
Died	1.16 (0.87, 1.55)	0.31	1.09 (0.81, 1.48)	0.57
LOS after TAVR, days	1.30 (1.07, 1.53)*	<0.0001	1.30 (1.06, 1.54)*	<0.0001

*, CIE (95% CI); [a], adjusted for year of TAVR, age, sex, race/ethnicity, Charlson score, primary insurance, median household income, hospital region, hospital type, and hospital size; both age and Charlson score were modeled as restricted cubic splines; [b], compared to routine/home health care discharge. OR, odds ratio; CI, confidence interval; TIA, transient ischemic attack; NA, not analyzable; CIE, change in estimate; LOS, length of stay; TAVR, transcatheter aortic valve replacement.

odds of TIA/stroke, acute kidney injury, requiring a blood transfusion, being transferred to a skilled nursing facility, and increased average LOS. However, there was no difference in inpatient mortality between patients with and without AF. Between 2012 and 2015, the incidence of acute kidney injury, requiring a blood transfusion, inpatient mortality, and average LOS decreased among both patients with and without AF. While major bleeding and vascular complications was consistent in AF patients, the incidence of both of these complications significantly declined in non-AF patients. Similarly, the increase in PPM implantation was only seen in non-AF patients.

We found AF to be prevalent in 44% of patients undergoing TAVR. This is similar to the findings of a previous study among patients with heart failure of valvular origin (5). Additionally, we found that AF patients were more likely to be non-Hispanic white, which has also been previously described (12). Interestingly, while older age is known to be associated with AF, we did not find that in our cohort; however, this may be explained by the fact that TAVR patients were older and sicker during the years we studied here.

As compared to patients without AF, we found that patients with AF were at higher odds of having TIA/stroke, requiring a blood transfusion and acute kidney injury. The association between AF and a higher risk of stroke/TIA is well known (4). Patients with AF were also at higher odds of requiring a blood transfusion. This effect could at least be partly explained by the fact that those with AF are more likely to be on anticoagulants (13). The association of AF with a higher incidence of AKI is also consistent with a previous study (14). Additionally, the association between higher rates of blood transfusion requirement with acute kidney injury post-TAVR has also been noted in previous studies (14,15). Between the study years 2012 to 2015, we found that the incidence of acute kidney injury

and requiring a blood transfusion steadily declined, both in those with AF and those without suggesting that the decline in rates of these complications was not dependent on presence or absence of AF.

Patients with AF were also more likely to have an increased LOS after TAVR and be discharged to a skilled nursing facility. The association between pre-existing AF with a longer LOS has been previously investigated (16). In another study of 663 patients undergoing elective TAVR, the absence of AF was predictive of next-day discharge after TAVR (17). There are several possible mechanisms contributing to the increased LOS in patients with AF, including the increased incidence of several complications. Prior research has found that acute kidney injury and postoperative delirium (not studied here) can contribute to longer hospitalizations (15,18). Moreover, longer hospitalizations were previously shown to be associated with functional dependence, which in turn was associated with transfers to a nursing home (19). Although the LOS decreased from 2012 to 2015, it remained higher in patients with AF.

Furthermore, while the odds of having major bleeding or vascular complications were similar in patients with or without AF, there was a decrease in the incidence of major bleeding and vascular complications in the group without AF between 2012 and 2015 but not in the AF group. It is possible that the improving trend in the rates of vascular complications and bleeding was blunted in the AF group due to the effect of anticoagulants. We also found that AF was not associated with PPM implantation, cardiac arrest, or mortality. There is conflicting evidence on the impact of AF on mortality after TAVR. While one study found that AF was not associated with 30-day mortality but was associated with long-term mortality, another analysis found that AF was associated with increased 1-year mortality (9,20). Thus, it is possible that AF only impacts longer-term mortality, which may explain our findings.

Finally, while a similar study utilizing the NIS databases was recently published, our study has several notable differences (21). First, our study spanned across longer study years which may have contributed to the fact that we found a significantly higher rate of TIA/stroke and acute kidney injury in patients with AF. Additionally, as hinted above, we assessed the trends in these complications. Since TAVR has disseminated quickly throughout the US and clinicians have gained expertise in the procedure, as well as the numerous changes to the hardware and procedure itself have been implemented, assessing both the overall effect and trends is of critical importance.

This study has several limitations. The NIS is deidentified database, so we were unable to capture outcomes outside of the index hospitalizations, which only represent a portion of all complications. We are also unable to determine if this study includes repeated observations of patients who underwent more than one TAVR during the study period; however, results were interpreted at the hospitalization-level, not patient-level to account for this. There was also a potential for coding errors and differences in coding practices across the hospitals included in the database. Coding errors could have caused us to underestimate the prevalence of AF, comorbidities, and in-hospital complications. AF misclassification (i.e., labeling a patient as not having AF when they do) would, in expectation, bias results towards the null. Additionally, we suspect that differences in comorbidity and in-hospital complication reporting are random and would not be expected to differ across AF status. This study cannot assess the causal relationship between AF and these outcomes but only an association. While we adjusted for the CCI, we did not have the information needed to calculate surgical risk scores, frailty scores or echocardiographic characteristics, which may have influenced the differences in patient outcomes. Additionally, ICD-9-CM coding prevents us from being able to differentiate between paroxysmal and persistent AF.

Finally, because dates are not attached to diagnosis codes, we had to assume that all patients with AF were diagnosed before they underwent TAVR. While there are wide variations in the reported incidence of new-onset AF in patients undergoing TAVR, an analysis from the SOURCE XT prospective multicenter registry found the prevalence of pre-existing AF was 36% and new-onset AF was only 7%, suggesting that misclassification of pre-existing AF is limited (20). Moreover, in another study, 24-hour ECG monitoring the day before TAVR diagnosed paroxysmal atrial flutter/atrial tachycardia (similar to AF) in 30% of patients who were diagnosed with new-onset atrial flutter/atrial tachycardia after TAVR, suggesting it may have been present before the procedure (22).

Conclusions

After initial concerns about the high incidences of inpatient complications after TAVR, these rates have declined with improvement in TAVR technology, both in those with and without AF. However, AF continues to be associated with higher incidences of inpatient complications, discharge

to a skilled nursing facility, and longer average LOS as compared to those without AF. With prevalence in almost half of the patients undergoing TAVR, recognition of the association of AF with adverse outcomes and protocols for closer monitoring of AF patients undergoing TAVR are suggested as we expand TAVR to broader populations.

Acknowledgments

None.

Footnote

Conflicts of Interest: Ms. PD Strassle has received salary support from researchEZ LLC and Dr. S Arora's spouse has proprietary role in researchEZ LLC. The other authors have no conflicts of interest to declare.

Ethical Statement: Study was reviewed by IRB and rendered exempt.

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