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Evaluation of the Incidence of New-Onset Atrial Fibrillation After Aortic Valve Replacement

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IMPORTANCE Data on the burden of new-onset atrial fibrillation after transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (AVR) is limited mostly to small series or post hoc analyses of clinical trials.

OBJECTIVES To evaluate the incidence of new-onset atrial fibrillation and assess the incidence of in-hospital mortality associated with new-onset atrial fibrillation after TAVI and AVR.

DESIGN, SETTING, AND PARTICIPANTS In this population-based observational study using the National Inpatient Sample and a validation cohort from the New York state inpatient database, the National Inpatient Sample was queried from January 1, 2012, to September 30, 2015, and the New York state inpatient database was queried from January 1, 2012, to December 31, 2014. Hospitalizations of adults undergoing TAVI or isolated AVR were examined. The incidence of in-hospital mortality across groups with new-onset atrial fibrillation was assessed in the National Inpatient Sample cohort using multivariable logistic regression modeling. Statistical analysis was conducted from August 20, 2018, to March 19, 2019.

MAIN OUTCOMES AND MEASURES The primary outcome was the occurrence of new-onset atrial fibrillation, which was identified by excluding hospitalizations in which atrial fibrillation was present on admission. The secondary outcome was in-hospital mortality in TAVI and AVR hospitalizations with and without new-onset atrial fibrillation.

RESULTS A total of 48 715 TAVI hospitalizations (47.4% women and 52.6% men; mean [SD] age, 81.3 [8.1] years; 82.3% white) and 122 765 AVR hospitalizations (39.0% women and 61.0% men; mean [SD] age, 67.8 [12.0] years; 78.0% white) were identified. New-onset atrial fibrillation occurred in 50.4% of TAVI hospitalizations and 50.1% of AVR hospitalizations. In the multivariable-adjusted model, TAVI and AVR hospitalizations with new-onset atrial fibrillation had higher odds of in-hospital mortality compared with hospitalizations without new-onset atrial fibrillation (TAVI: odds ratio, 1.57; 95% CI, 1.21-2.04; and AVR: odds ratio, 1.36; 95% CI, 1.08-1.70). The results were then confirmed with the New York state inpatient database, which contains a present on arrival indicator. The incidence of new-onset atrial fibrillation was 14.1% (244 of 1736 hospitalizations) after TAVI and 30.6% (1573 of 5141 hospitalizations) after AVR in the New York state inpatient database.

CONCLUSIONS AND RELEVANCE In this large nationwide study, a substantial burden of new-onset atrial fibrillation was observed after TAVI and AVR. The incidence of new-onset atrial fibrillation was higher after AVR than after TAVI in a patient-level state inpatient database.

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Supplemental content

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Atrial fibrillation is a common arrhythmia with a lifetime risk of 37% in individuals older than 55 years.[1] Atrial fibrillation is also associated with significant cardiovascular morbidity and mortality.[2] New-onset atrial fibrillation has been recognized as a common occurrence after noncardiac and cardiac surgery, such as aortic valve replacement (AVR).[3-5]

Several investigations have attempted to elucidate the incidence of atrial fibrillation after AVR. The incidence estimates of atrial fibrillation after transcatheter aortic valve implantation (TAVI) and surgical AVR have varied widely, ranging from 8% to 100%.[6-9] New-onset atrial fibrillation after TAVI and AVR has also been associated with increased morbidity and mortality.[10] Most investigations detailing new-onset atrial fibrillation after TAVI and AVR, however, are single-center series or post hoc analyses of clinical trials.

We conducted this investigation to evaluate the incidence of new-onset atrial fibrillation after TAVI and AVR in a large cohort of hospitalizations from the National Inpatient Sample (NIS) by excluding hospitalizations in which atrial fibrillation was present on admission. We hypothesized that atrial fibrillation is a common occurrence after both TAVI and AVR and that the incidence of atrial fibrillation was adversely associated with in-hospital stroke and mortality.

Key Points

Question What is the incidence and prognostic implication of new-onset atrial fibrillation after transcatheter aortic valve implantation and surgical aortic valve replacement?

Findings In this population-based study, new-onset atrial fibrillation was present in roughly 50% of hospitalizations for transcatheter aortic valve implantation and aortic valve replacement. Hospitalizations with new-onset atrial fibrillation were associated with higher in-hospital mortality compared with transcatheter aortic valve implantation and aortic valve replacement hospitalizations without new-onset atrial fibrillation.

Meaning The high incidence of atrial fibrillation after transcatheter aortic valve implantation and aortic valve replacement should be discussed during the consent process and prompt shared patient-physician decision making regarding the potential need for anticoagulation after aortic valve procedures.

Methods

Data Source and Study Population

The study cohort was derived from the NIS (eAppendix 1 in the Supplement).[11] *International Classification of Disease, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis codes 395.0, 395.2, 396.2, and 424.1 were used to identify hospitalizations with aortic stenosis that occurred from January 1, 2012, to September 30, 2015.[12] We identified all hospitalized patients undergoing TAVI or AVR using appropriate *ICD-9-CM* procedure codes (TAVI, 35.05 and 35.06; and AVR, 35.21 and 35.22).[13,14] We excluded hospitalizations if there was a prior diagnosis of atrial fibrillation or other arrhythmias, if TAVI and AVR occurred during the same admission, and if there was also percutaneous coronary intervention or coronary artery bypass grafting during the same hospitalization (eAppendix 2 in the Supplement).

The NIS variables were used to identify the baseline characteristics in hospitalizations for TAVI and AVR. Race/ethnicity was categorized in 2 groups: white and nonwhite individuals. Socioeconomic status was categorized using the median household income provided by the NIS. The individual comorbidities in hospitalizations for TAVI and AVR were derived from the Elixhauser comorbidity software[15] (provided by the NIS) and previously published *ICD-9-CM* codes (eTable 1 in the Supplement).

Outcomes

The primary outcome was the incidence of new-onset atrial fibrillation after TAVI and AVR, which was identified using the *ICD-9-CM* diagnosis code 427.3 if it occurred in any of the secondary discharge fields. This was under the assumption that all secondary discharge field diagnoses of atrial fibrillation were for new diagnoses of atrial fibrillation. The approach of identifying cases (ie, new-onset atrial fibrillation) that develop during hospitalization by excluding *ICD-9-CM* codes from the primary discharge field has been previously published.[16,17] We further examined the factors associated with new-onset atrial fibrillation in hospitalizations for TAVI and AVR. In-hospital outcomes, including in-hospital stroke,[18] mortality, and length of stay in hospitalizations for TAVI and AVR with and without new-onset atrial fibrillation, were also assessed. The incidence of in-hospital stroke was identified using the previously published *ICD-9-CM* codes.[18]

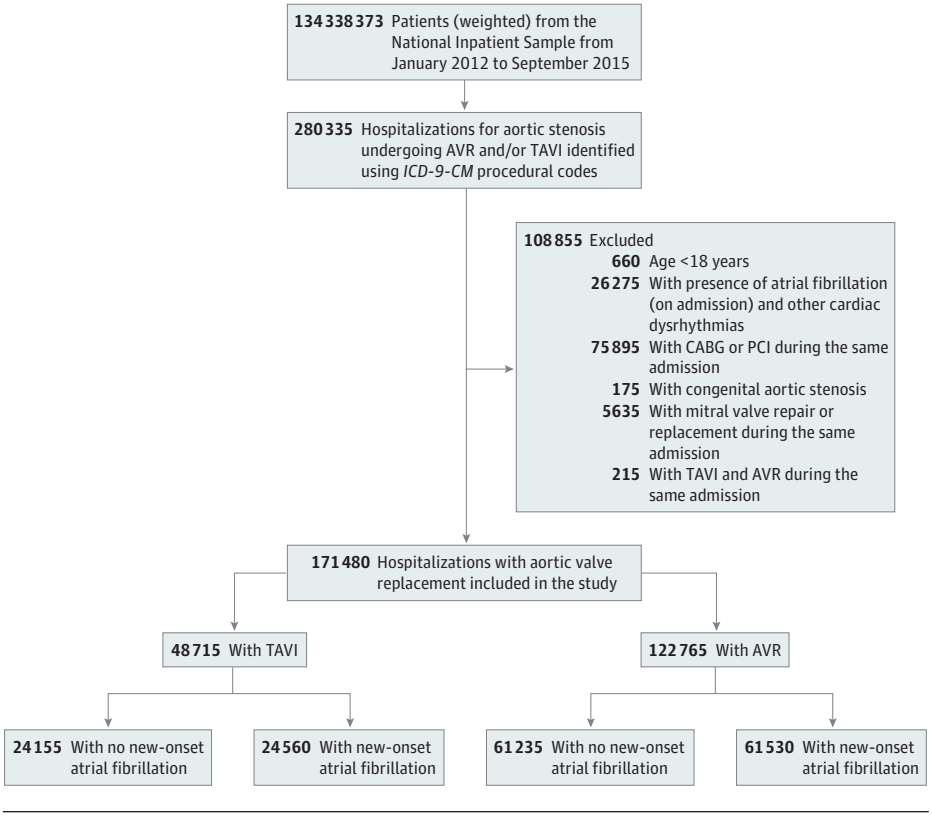
Study Population for Analysis in the Validation Cohort

To address our study approach that all secondary diagnosis of atrial fibrillation represents new-onset atrial fibrillation using the NIS database, we examined patient-linked hospitalizations (ie, VisitLink data, which is an encrypted person identifier) from the New York state inpatient database (validation cohort) between January 1, 2012, and December 31, 2014.[19] The New York state inpatient database shares similar data elements and data structure with the NIS. Furthermore, the New York state inpatient database has a unique present-on-admission identifier indicating whether each diagnosis is present at the time of admission or not.[20] This identifier allows users to specifically discriminate between preexisting conditions and diseases that occur during the hospitalization. Moreover, the approach of identifying new-onset atrial fibrillation by using the present-on-admission identifier has been previously validated against blinded medical record review, with an overall agreement of 90% and κ statistic of 0.74.[18]

Statistical Analysis

Statistical analysis was conducted from August 20, 2018, to March 19, 2019. All analyses were performed in SAS, version 9.4 (SAS Institute Inc). All statistical analyses were performed to strictly comply with Agency for Healthcare Research and Quality and expert consensus recommendations.[21,22] All analyses accounted for NIS survey nature (SURVEYMEANS,

Figure 1. Flowchart for Cohort Selection



AVR indicates surgical aortic valve replacement; CABG, coronary artery bypass grafting; *ICD-9-CM*, *International Classification of Disease, Ninth Revision, Clinical Modification*; PCI, percutaneous coronary intervention; and TAVI, transcatheter aortic valve implantation.

SURVEYLOGISTIC, and SURVEYFREQ), clustering (HOSP_NIS), stratification (NIS_STRATUM), and weights (DISCWT).[21,23]

We used a survey-specific, hierarchical, multivariate logistic regression model for the analysis of factors associated with new-onset atrial fibrillation among hospitalizations for TAVI and AVR. Similarly, to compare the in-hospital outcomes between hospitalized patients undergoing TAVI with and without new-onset atrial fibrillation, multivariable logistic and linear (for length of stay) regression modeling were used. The description of statistical analysis is outlined in eAppendix 3 in the Supplement.

In the analysis to validate the primary outcome, we used the New York state inpatient database (validation cohort) to examine the incident rates of new-onset atrial fibrillation among hospitalized patients undergoing TAVI and AVR. The same inclusion and exclusion criteria were used for this analysis.

Results

A total of 171 480 index hospitalizations for TAVI or AVR were identified using *ICD-9-CM* procedural codes (**Figure 1**). Of these, 48 715 hospitalizations were for TAVI and 122 765 hospitalizations were for AVR. There were 24 560 hospitalizations for TAVI with new-onset atrial fibrillation and 61 530 hospitalizations for AVR with new-onset atrial fibrillation. There were 24 155 hospitalizations for TAVI without new-onset atrial fibrillation and 61 235 hospitalizations for AVR without new-onset atrial fibrillation (Figure 1). Baseline characteristics for TAVI and AVR hospitalizations with new-onset atrial fibrillation are described in **Table 1**. In hospitalizations for TAVI and AVR with new-onset atrial fibrillation, compared with those without new-onset atrial fibrillation, there was a greater prevalence of blood transfusions (TAVI, 19.9% vs 17.4%; and AVR, 28.7% vs 23.9%), chronic kidney disease (TAVI, 37.8% vs 33.5%; and AVR, 16.6% vs 11.5%), chronic pulmonary disease (TAVI, 34.2% vs 32.8%; and AVR, 22.2% vs 20.0%), congestive heart failure (TAVI, 8.9% vs 7.5%; and AVR, 1.4% vs 1.0%), coronary artery disease (TAVI, 68.8% vs 67.6%; and AVR, 40.3% vs 32.3%), history of valve surgery (TAVI, 2.5% vs 1.4%; and AVR, 2.3% vs 1.7%), and peripheral vascular disease (TAVI, 29.5% vs 28.0%; and AVR, 20.8% vs 19.5%). Higher use of the transapical approach for TAVI was seen in TAVI hospitalizations with new-onset atrial fibrillation compared with those without new-onset atrial fibrillation (17.5% vs 14.2%). In AVR hospitalizations with new-onset atrial fibrillation, there was a greater prevalence of bioprosthetic valve placement compared with those without new-onset atrial fibrillation (69.1% vs 61.0%).

Factors Associated With New-Onset Atrial Fibrillation After TAVI and AVR

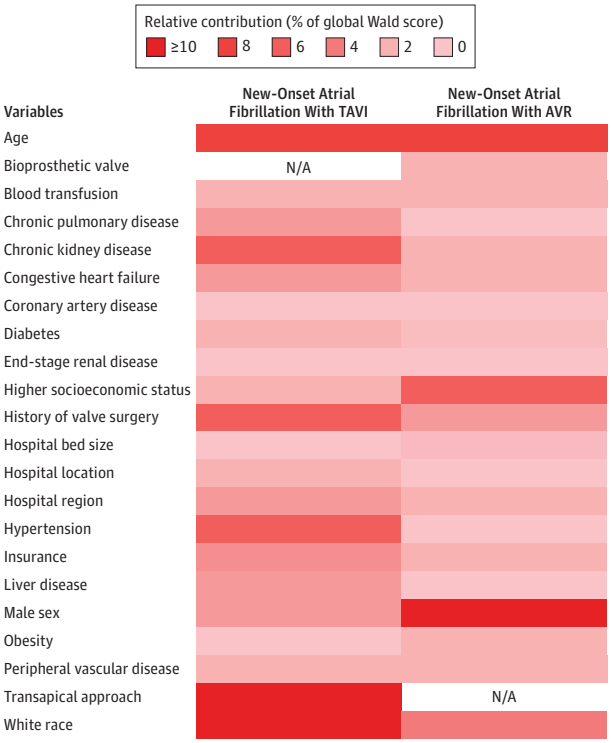
There was a statistically significant association between the occurrence of new-onset atrial fibrillation in TAVI and AVR hospitalizations with increasing age (per 10 years), white race, chronic kidney disease at baseline, chronic pulmonary disease at baseline,

Table 1. Baseline Characteristics and In-Hospital Outcomes for AVR Hospitalizations Stratified by Status of New-Onset Atrial Fibrillation

Variable	TAVI (n = 48 715), No. (%)		AVR (n = 122 765), No. (%)	
	No New-Onset Atrial Fibrillation With TAVI (n = 24 155)	New-Onset Atrial Fibrillation With TAVI (n = 24 560)	No New-Onset Atrial Fibrillation With AVR (n = 61 235)	New-Onset Atrial Fibrillation With AVR (n = 61 530)
Age, mean (SD), y	80.2 (9.1)	82.2 (7.1)	64.1 (13.5)	71.5 (10.6)
Male sex	12 470 (51.6)	13 165 (53.6)	36 770 (60.0)	38 100 (61.9)
Race/ethnicity				
White	19 310 (79.9)	20 760 (84.5)	45 520 (74.3)	50 205 (81.6)
Nonwhite	4845 (20.1)	3800 (15.5)	15 715 (25.7)	11 325 (18.4)
Socioeconomic status				
0-50th Percentile	11 340/23 805 (47.6)	10 905/24 125 (45.2)	29 575/59 880 (49.4)	27 245/60 275 (45.2)
51-100th Percentile	12 465/23 805 (52.4)	13 220/24 125 (54.8)	30 305/59 880 (50.6)	33 030/60 275 (54.8)
Comorbidities				
Chronic kidney disease	8085 (33.5)	9290 (37.8)	7030 (11.5)	10 235 (16.6)
Chronic pulmonary disease	7925 (32.8)	8405 (34.2)	12 230 (20.0)	13 630 (22.2)
Congestive heart failure	1810 (7.5)	2195 (8.9)	605 (1.0)	860 (1.4)
Coronary artery disease	16 335 (67.6)	16 895 (68.8)	19 755 (32.3)	24 800 (40.3)
Diabetes	7110 (29.4)	7185 (29.3)	14 710 (24.0)	15 225 (24.7)
End-stage renal disease	595 (2.5)	470 (1.9)	550 (0.9)	470 (0.8)
History of valve surgery	350 (1.4)	615 (2.5)	1025 (1.7)	1385 (2.3)
Hypertension	19 860 (82.2)	19 645 (80.0)	43 840 (71.6)	47 180 (76.7)
Liver disease	805 (3.3)	460 (1.9)	1175 (1.9)	1025 (1.7)
Obesity	3900 (16.1)	3375 (13.7)	13 610 (22.2)	13 735 (22.3)
Peripheral vascular disease	6765 (28.0)	7250 (29.5)	11 940 (19.5)	12 805 (20.8)
Procedure-related characteristics				
Blood transfusion	4215 (17.4)	4880 (19.9)	14 620 (23.9)	17 650 (28.7)
Bioprosthetic valve	NA	NA	37 375 (61.0)	42 535 (69.1)
Mechanical valve	NA	NA	23 860 (39.0)	18 995 (30.9)
Transapical approach	3440 (14.2)	4300 (17.5)	NA	NA
Transfemoral approach	20 715 (85.8)	20 260 (82.5)	NA	NA
Primary payment method				
Medicaid	340 (1.4)	145 (0.6)	3750 (6.1)	2000 (3.3)
Medicare	21 450 (88.8)	22 655 (92.2)	32 350 (52.8)	44 470 (72.3)
Private insurance	1920 (7.9)	1310 (5.3)	21 940 (35.8)	13 220 (21.5)
Other	445 (1.8)	450 (1.8)	3295 (5.4)	1840 (3.0)
Hospital region				
Midwest	5200 (21.5)	5590 (22.8)	14 120 (23.1)	15 560 (25.3)
Northeast	6050 (25.0)	6205 (25.3)	13 170 (21.5)	14 090 (22.9)
South	8470 (35.1)	8160 (33.2)	21 455 (35.0)	19 040 (30.9)
West	4435 (18.4)	4605 (18.8)	12 490 (20.4)	12 840 (20.9)
Hospital bed size				
Small	1140 (4.7)	1165 (4.7)	4535 (7.4)	4270 (6.9)
Medium	4380 (18.1)	4410 (18.0)	13 070 (21.3)	12 935 (21.0)
Large	18 635 (77.1)	18 985 (77.3)	43 630 (71.3)	44 325 (72.0)
Hospital location				
Rural	185 (0.8)	225 (0.9)	1465 (2.4)	1370 (2.2)
Urban, nonteaching	2425 (10.0)	2295 (9.3)	13 935 (22.8)	13 070 (21.2)
Urban, teaching	21 545 (89.2)	22 040 (89.7)	45 835 (74.9)	47 090 (76.5)
In-hospital outcomes				
In-hospital mortality	475 (2.0)	850 (3.5)	690 (1.1)	1195 (1.9)

Abbreviations: AVR, aortic valve replacement; NA, not applicable; TAVI, transcatheter aortic valve implantation.

Figure 2. Heat Map for Factors Associated With New-Onset Atrial Fibrillation



The shade of red demonstrates the strength of association of the risk factor with new-onset atrial fibrillation. Darker shades of red represent a larger contribution to the global Wald score and therefore a stronger association with the risk factor for new-onset atrial fibrillation. AVR indicates aortic valve replacement; N/A, not applicable; and TAVI, transcatheter aortic valve implantation.

congestive heart failure at baseline, and a prior history of valve surgery (eFigures 1 and 2 in the Supplement). The relative contribution of these factors to the global Wald score for the development of new-onset atrial fibrillation was demonstrated as a heat map (**Figure 2**).

Outcomes for TAVI Hospitalizations

The incidence of new-onset atrial fibrillation was 50.4% (24 560 of 48 715 hospitalizations; 95% CI, 49.4%-51.4%) among TAVI hospitalizations. There was a higher incidence of in-hospital all-cause mortality for TAVI hospitalizations with new-onset atrial fibrillation compared with those without new-onset atrial fibrillation in the unadjusted analyses (3.5% vs 2.0%) (Table 1). In the multivariable adjusted analyses, TAVI hospitalizations with new-onset atrial fibrillation had 57% higher odds of in-hospital mortality compared with those without new-onset atrial fibrillation (odds ratio, 1.57; 95% CI, 1.21-2.04; $P < .001$) (**Table 2**). Unadjusted and multivariable adjusted in-hospital outcomes of TAVI hospitalizations with new-onset atrial fibrillation were also compared with TAVI hospitalizations without new-onset atrial fibrillation. TAVI hospitalizations with new-onset atrial fibrillation had higher odds of in-hospital stroke and had a longer median length of stay compared with those without new-onset atrial fibrillation (eAppendix 4 and eTable 2 in the Supplement).

Table 2. In-Hospital Mortality Among Hospitalizations With New-Onset Atrial Fibrillation After TAVI and AVR

Model	Odds Ratio (95% CI)	*P* Value
In-hospital mortality (TAVI group)		
Model 1[a]	1.70 (1.31-2.20)	<.001
Model 2[b]	1.56 (1.20-2.02)	<.001
Model 3[c]	1.57 (1.21-2.04)	<.001
In-hospital mortality (AVR group)		
Model 1[a]	1.52 (1.22-1.90)	<.001
Model 2[b]	1.34 (1.08-1.70)	.008
Model 3[c]	1.36 (1.08-1.70)	.008

Abbreviations: AVR, aortic valve replacement; TAVI, transcatheter aortic valve implantation.

[a] Adjusted for age, sex, and race/ethnicity.

[b] Adjusted for age, sex, race/ethnicity, individual Elixhauser comorbidities, blood transfusion, history of coronary artery disease, history of valve surgery, and transapical and transfemoral approach.

[c] Adjusted for age, sex, race/ethnicity, individual Elixhauser comorbidities, blood transfusion, transapical and transfemoral approach, socioeconomic status, insurance status, and hospital-level characteristics.

Outcomes for AVR Hospitalizations

The incidence of new-onset atrial fibrillation among AVR hospitalizations was 50.1% (61 530 of 122 765 hospitalizations; 95% CI, 49.5%-50.7%). As was seen in the TAVI hospitalizations, there was a higher incidence of in-hospital all-cause mortality in the AVR hospitalizations with new-onset atrial fibrillation compared with those without new-onset atrial fibrillation (1.9% vs 1.1%) (Table 1). In the multivariable adjusted analyses, AVR hospitalizations with new-onset atrial fibrillation had 36% higher odds of in-hospital mortality compared with those without new-onset atrial fibrillation (odds ratio, 1.36; 95% CI 1.08-1.70; $P = .008$) (Table 2). In the unadjusted and multivariable adjusted in-hospital outcomes associated with AVR stratified by new-onset atrial fibrillation, we found that AVR hospitalizations with new-onset atrial fibrillation had a longer median length of stay than those without new-onset atrial fibrillation but similar odds of new-onset in-hospital stroke (eAppendix 5 and eTable 2 in the Supplement).

Analysis in the Validation Cohort

A total of 6877 index hospitalizations for TAVI and AVR that met the study inclusion criteria were identified between January 1, 2012, and December 31, 2014, from the New York state inpatient database validation cohort (**Table 3**). Among these hospitalizations, 1736 were for TAVI and 5141 were for AVR. We observed that incident new-onset atrial fibrillation was frequent in hospitalized patients undergoing TAVI and AVR (14.1% [244 of 1736 hospitalizations] after TAVI, and 30.6% [1573 of 5141 hospitalizations] after AVR). These rates add to the validity of our findings for the primary outcome, as the rates of new-onset atrial fibrillation from the NIS database were also high. We found that the odds of in-hospital mortality were higher and length of stay was longer across both TAVI and AVR arms in patients developing new-onset

Table 3. Baseline Characteristics for Hospitalized Patients Undergoing AVR Stratified by the Status of New-Onset Atrial Fibrillation From the New York State Inpatient Database

Variable	TAVI (n = 1736), No. (%)		AVR (n = 5141), No. (%)	
	No New-Onset Atrial Fibrillation With TAVI (n = 1492)	New-Onset Atrial Fibrillation With TAVI (n = 244)	No New-Onset Atrial Fibrillation With AVR (n = 3568)	New-Onset Atrial Fibrillation With AVR (n = 1573)
Age, mean (SD), y	82.2 (8.7)	83.4 (8.1)	65.3 (13.7)	71.8 (10.4)
Male sex	678 (45.4)	96 (39.3)	2096 (58.7)	922 (58.6)
Race/ethnicity				
White	1138 (76.3)	195 (79.2)	2427 (68.0)	1150 (73.1)
Nonwhite	354 (23.7)	49 (20.1)	1141 (32.0)	423 (26.9)
Socioeconomic status				
0-50th Percentile	336 (22.7)	54 (22.3)	1117 (32.0)	438 (28.3)
51-100th Percentile	1143 (77.3)	188 (77.7)	2371 (68.0)	1112 (71.7)
Comorbidities				
Blood transfusion	456 (30.6)	97 (39.8)	1170 (32.8)	569 (36.2)
Bioprosthetic valve	NA	NA	2715 (76.1)	1308 (83.1)
Chronic kidney disease	535 (35.9)	84 (34.4)	404 (11.3)	201 (12.8)
Chronic pulmonary disease	500 (33.5)	94 (38.5)	696 (19.5)	331 (21.0)
Congestive heart failure	164 (11.0)	32 (13.1)	39 (1.1)	14 (0.9)
Coronary artery disease	1005 (67.4)	159 (65.2)	1316 (36.9)	654 (41.6)
Diabetes	435 (29.2)	59 (24.2)	831 (23.3)	388 (24.7)
End-stage renal disease	62 (4.2)	13 (5.3)	68 (1.9)	32 (2.0)
History of valve surgery	30 (2.0)	3 (1.2)	60 (1.7)	11 (0.7)
Hypertension	1253 (84.0)	197 (80.7)	2595 (72.7)	1236 (78.6)
Liver disease	54 (3.6)	6 (2.5)	70 (2.0)	24 (1.5)
Mechanical valve	NA	NA	853 (23.9)	265 (16.9)
Obesity	195 (13.1)	35 (14.3)	638 (17.9)	296 (18.8)
Peripheral vascular disease	398 (26.7)	75 (30.7)	665 (18.6)	304 (19.3)
Transapical approach	241 (16.2)	80 (32.8)	NA	NA
Transfemoral approach	1251 (83.8)	164 (67.2)	NA	NA
Primary payment method				
Medicaid	20 (1.3)	3 (1.2)	315 (8.8)	71 (4.5)
Medicare	1369 (91.8)	225 (92.2)	1953 (54.7)	1123 (71.4)
Private insurance	92 (6.2)	12 (4.9)	1190 (33.3)	352 (22.4)
Other	11 (0.7)	4 (1.6)	110 (3.1)	27 (1.7)

Abbreviations: AVR, aortic valve replacement; NA, not applicable; TAVI, transcatheter aortic valve implantation.

atrial fibrillation in the New York state inpatient database (eTable 3 in the Supplement).

Discussion

We found an approximately 50% incidence of atrial fibrillation during hospitalizations for both TAVI and AVR in a large national cohort. In the New York state inpatient database validation cohort, the incidence of atrial fibrillation was 14.1% in patients undergoing TAVI and 30.6% in patients undergoing AVR. The occurrence of new-onset atrial fibrillation was associated with a poor prognosis in both TAVI and AVR hospitalizations, with increased length of stay and higher odds of in-hospital mortality in both the unadjusted and adjusted analyses. In addition, in the TAVI population, the occurrence of new-onset atrial fibrillation was also associated with higher odds of in-hospital stroke in the unadjusted and adjusted analyses.

There are multiple possible mechanistic explanations for the frequent occurrence of new-onset atrial fibrillation after TAVI and AVR. New-onset atrial fibrillation is likely due to a combination of patient substrate and context-specific precipitating factors.[24,25] The patient substrate is reflected in our investigation through the higher odds of new-onset atrial fibrillation with increasing age and greater comorbidity. There are probably many identifiable precipitating triggers in the periprocedural period. Atrial fibrillation has been previously linked to the hyperadrenergic state in the perioperative period surrounding TAVI and AVR.[26] This state is likely driven by the combination of pain and myocardial trauma, among other factors. The onset of local inflammation after aortic valve surgery

has also been previously posited to be a specific driver of new-onset atrial fibrillation after AVR.[27] The myocardial trauma and the sympathovagal fibers may be the drivers of this inflammation.[26] This finding suggests that the inflammatory threshold needed to cause atrial fibrillation is likely relatively low if new-onset atrial fibrillation is occurring with such a high frequency after a percutaneous procedure such as TAVI. However, the amount of inflammation is still likely higher in AVR than TAVI, as the incidence of atrial fibrillation after AVR was higher than in the patients undergoing TAVI in our validation cohort. Increased intra-atrial pressure and left atrial stretch due to paravalvular leak after TAVI or postoperative volume overload may also precipitate new-onset periprocedural atrial fibrillation.[6,24] Electrolyte derangement, particularly hypokalemia, from use of high-dose diuretics after surgical procedures has also been implicated in the occurrence of atrial fibrillation after AVR.[28] Finally, patients who have undergone TAVI or AVR spend more time on a monitor, which makes it more likely to have the atrial fibrillation detected.[25]

There are multiple proposed mechanistic explanations for the links between new-onset atrial fibrillation, stroke, and increased mortality. Biviano et al[10] previously showed in their PARTNER (Placement of Aortic Transcatheter Valve) post hoc analysis that the group of patients with new-onset atrial fibrillation had a higher incidence of pacemaker implantation after TAVI and more end-organ dysfunction after TAVI. Barbash et al[6] also found that patients with new-onset atrial fibrillation had higher rates of acute kidney injury and heart failure and greater need for mechanical ventilation and hemodynamic support prior to the development of atrial fibrillation. Taken together, patients may have new-onset atrial fibrillation after AVR as they are more physiologically frail and/or the onset of atrial fibrillation may also represent a patient group that has had greater systemic insult and complication from the index procedure. The combination of these insults may lead to greater stroke and mortality.

Our investigation also adds to the existing literature base regarding new-onset atrial fibrillation and AVR. First, we estimate that the incidence of new-onset atrial fibrillation after AVR is approximately 50% in a large nationwide cohort. Although the estimates were different, the incidence of new-onset atrial fibrillation after TAVI and AVR was also high in the validation cohort. The finding in our validation cohort that the incidence of new-onset atrial fibrillation is 2 times higher in patients undergoing AVR compared with patients undergoing TAVI is consistent with prior estimates from randomized controlled trials.[29-34] Vora et al[9] recently published an analysis from the National Cardiovascular Data Registry Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry that describes the incidence of atrial fibrillation to be approximately 8.4% in a patient population with a mean age of 84 years that is receiving TAVI. However, we believe that this number is low, given the recent findings from a human genetics study in which the lifetime risk of atrial fibrillation is 37% among individuals older than 55 years.[1] Moreover, the incidence rate of atrial fibrillation in a population-based cohort of patients age 80 years or older from a population-based Dutch cohort was 20.7 per 1000 person-years, without the added acute triggers of an invasive procedure or hospitalization.[35] Our investigation suggests that the incidence of new-onset atrial fibrillation is high among hospitalized patients undergoing both TAVI and AVR. With more than 171 000 hospitalizations, our investigation is, to our knowledge, larger than the previously published series that outline the clinical characteristics of patients who develop new-onset atrial fibrillation after TAVI[36-38] and AVR.[8,37] Our investigation also has a greater number of index hospitalizations compared with a previously published meta-analysis.[39] Multiple prior investigations are limited by the inclusion of patients with chronic atrial fibrillation at baseline.[6,10,40-43] We also estimate that baseline congestive heart failure, chronic pulmonary disease, and chronic kidney disease are associated with the development of new-onset atrial fibrillation after both TAVI and AVR.

Our findings are consistent with those of previous reports that suggest that the development of new-onset atrial fibrillation after TAVI increases length of stay,[6,26] incidence of new-onset stroke,[36,44,45] and mortality.[10,26,38,43] Our investigation is also consistent with previous reports that suggest that the development of new-onset atrial fibrillation after AVR is associated with increased in-hospital mortality.[8,9] Finally, our investigation reiterates previously published data suggesting that the transapical approach[36,38] and advancing age[37,38] are associated with new-onset atrial fibrillation after TAVI.

Our findings have significant public health implications given the medical and socioeconomic burdens that atrial fibrillation and aortic valve disease carry on a population level. Our investigation raises the question of how perioperative anticoagulation strategies must be altered for TAVI and AVR with such a high incidence of postprocedural atrial fibrillation. This issue is underscored by the relatively high odds of incident in-hospital stroke (especially after TAVI) that we observed in the multivariable adjusted analyses. The subclinical thrombosis of TAVI valves has also garnered significant attention recently and reiterates the need to consider chronic anticoagulation after TAVI.[46,47] Finally, given the significant morbidity and mortality effects conferred on patients with new-onset atrial fibrillation after TAVI and AVR, we agree with Yankelson et al[41] that there may be a rationale for the inclusion of atrial fibrillation at baseline and/or new-onset atrial fibrillation in the risk stratification scoring schemes for patients undergoing TAVI. This may inform shared patient-physician decision making, especially in an era in which proposed federal cuts may affect the sustainability of TAVIs.[14]

Limitations

Our investigation has some limitations. The limitations of large inpatient cohorts, such as the NIS, are well known. Coding errors are also a noted issue; we acknowledge that coding errors could blur the distinction between new-onset atrial fibrillation and prevalent or preprocedural atrial fibrillation. This is most evident in the marked differences in the rates of incident atrial fibrillation (particularly after TAVI) between the NIS cohort and the New York state database. The difference in incidence estimates may be explained by the high burden of prevalent atrial fibrillation in the New York state database co-

hort. However, the similar effect estimates for length of stay, stroke, and in-hospital mortality for both cohorts imply that both prevalent and incident atrial fibrillation carry significant prognostic implications. However, as we have outlined above, the accuracy of *ICD-9-CM* diagnostic codes for new-onset atrial fibrillation using the secondary diagnosis field in the NIS[16,17] and the present-on-admission status approach in the New York state database has been published and also validated.[18] This suggests that patients with atrial fibrillation prior to the index hospitalization were likely to be adequately excluded using our data retrieval strategies. Atrial fibrillation could also have been a concealed diagnosis at the time of hospitalization. The heterogeneity of atrial fibrillation definitions (ie, based on results of 12-lead electrocardiogram, treated or simply coded) is also a limitation and we were unable to distinguish atrial fibrillation duration and subtypes, such as paroxysmal or persistent. There is a possibility that new-onset atrial fibrillation that occurred after TAVI and AVR may also be limited to the duration of the hospitalization. We were only able to capture the in-hospital disease course.

Not all new-onset atrial fibrillation may be clinically relevant or associated with poor clinical outcomes. In particular, the temporality of stroke is difficult to distinguish from our observational study; therefore, the occurrence of new-onset atrial fibrillation could also have been due to the occurrence of stroke. Our investigation is limited in its value in determining causality of stroke from new-onset atrial fibrillation. There may be inherent biases in the inpatient management of individuals who underwent percutaneous procedures compared with those who underwent surgical procedures that may alter the incidence of stroke, such as the prescription of new anticoagulants.

The administrative database lacks clinical details for each individual. Our investigation is therefore limited by the lack of some baseline data and long-term follow-up data, owing to the nature of the NIS data sampling. This limitation precluded the inclusion of baseline use of antiarrhythmic and anticoagulant medication in the study cohort and identification of whether treatment of the new-onset atrial fibrillation with rate control, rhythm control, and/or anticoagulation strategies altered the prognosis for patients with new-onset atrial fibrillation. We were also unable to identify differences based on the use of different percutaneous and surgical prostheses, including the performance of minimally invasive surgical ablation procedures and other surgical left atrial appendage strategies aimed at prevention of atrial fibrillation.

Finally, the study period in this investigation was prior to the publication of the randomized controlled trials comparing TAVI and AVR in patients with medium and low surgical risk.[29,32] Hence, the TAVI procedures were most likely largely limited to patients deemed to have high surgical risk. We also acknowledge that the transapical approach is used less frequently in contemporary practice than it was during the study period. However, by this logic, the patients who underwent AVR were likely those with low or intermediate surgical risk. It is then of great interest to us that there was still a significant incidence of new-onset atrial fibrillation and adverse outcomes among these patients who underwent AVR and the patients at high surgical risk who underwent TAVI.

Conclusions

This study found that new-onset atrial fibrillation is a common occurrence among hospitalizations for TAVI and AVR. New-onset atrial fibrillation is associated with a marked increase in incident length of stay, stroke, and in-hospital mortality.

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