Impact of Atrial Fibrillation on Outcomes of Aortic Valve Implantation

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Abstract

New or preexisting atrial fibrillation (AF) is frequent in patients undergoing aortic valve replacement. We evaluated whether the presence of AF during transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR) impacts the length of stay, healthcare adjusted costs, and inpatient mortality. The median length of stay in the patients with AF increased by 33.3% as compared with those without AF undergoing TAVI and SAVR (5 [3 to 8] days vs 3 [2 to 6] days, $p < 0.0001$ and 8 [6 to 12] days vs 6 [5 to 10] days, $p < 0.0001$, respectively). AF increased the median value of adjusted healthcare associ- ated costs of both TAVI ($46,754 [36,613 to 59,442] vs $49,960 [38,932 to 64,201], $p < 0.0001$) and SAVR ($40,948 [31,762 to 55,854] vs $45,683 [35,154 to 63,026], $p < 0.0001$). The pres- ence of AF did not independently increase the in-hospital mortality. In conclusion, in patients undergoing SAVR or TAVI, AF significantly increased the length of stay and adjusted healthcare adjusted costs but did not independently increase the in-hospital mortality.

Severe aortic stenosis (AS), if untreated, has very high mortality: 50% in the first 2 years from symptom onset.1 Based on the symptoms at presentation, mean survival is 5 years after the onset of angina; 3 years after syncope; and 2 years after heart failure.2 Management of AS has been revolutionized with both surgical and percutaneous transcatheter valve implantation techniques.3 Surgical aortic valve replacement (SAVR)4 and transcatheter aortic valve implantation (TAVI),5 significantly improve survival and reduces the frequency of repeated hospitalizations in patients with severe AS. The prevalence of atrial fibrillation (AF) in patients undergoing TAVI is around 50% (combining preexisting and new-onset AF).6 In a recent publication, it has been shown that AF is not an independent predictor of mortality in patients with AS, after multivariable adjustment.7 Cost-benefit analysis of aortic valve interventions has been extensively studied recently, including the comparison of SAVR and TAVI.8, 9, 10, 11, 12, 13 To our knowledge, there have been no studies to evaluate the cost-benefit of AF in patients undergoing TAVI or SAVR. This study investigates the impact of new or preexisting AF in patients undergoing TAVI and SAVR in terms of length of stay (LOS), healthcare associated costs (HCAC), and inpatient mortality using a large, extensive validated administrative claims database.

Methods

The study was conducted using the National Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP) data set between 2011 and 2017.14 The population selected from the NIS data set for this study were patients with AS, with and without AF, undergoing TAVI or SAVR between 2011 and 2017. These data include male and female patients >18 years of age. These timeframes were chosen to allow a sufficient run-in period for adoption of TAVI throughout the United States, as well as the availability of procedural International Classification of Diseases, Ninth and Tenth Edition, Clinical Modification (ICD-9-CM and ICD-10-CM) codes from 2011 onward. This study was considered exempt from Institutional Review Board approval because HCUP-NIS contains de-identified patient information and is publicly available.

NIS data were queried using the ICD-9-CM and ICD-10-CM to identify the patients with AS, TAVI, SAVR, and AF, as listed in Supplementary Tables 1 and 2. Calculations of the CHA2DS2-VASc score were done following Supplementary Table 3 using the NIS database. The stroke data were evaluated along with its relation with anticoagulation status and CHA2DS2-VASc score, but the reliability of these data could not be confirmed (Supplementary Figure 1). Hence, these have not been included in the results or discussion section. The study was carried out following Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Descriptive statistics are presented as number (percentage) for categorical variables and as median with interquartile range (IQR) for continuous variables. Baseline characteristics were compared using the chi-square test for categorical variables and a Kruskal-Wallis equality-of-populations rank test for continuous variables. In addition to these analyses, we used the Friedman test to compare differences of continuous variables in some stratified groups. Bonferroni correction is used as a post hoc test after the Kruskal-Wallis equality-of-populations rank test or Friedman test. We did a survival analysis using the Kaplan-Meier method and followed the log-rank test. Furthermore, the Cox hazard model was used to minimize the impact of confounders. The included variables for the Cox hazard model were AF, age, gender, hospital region, bed size, race, primary payer, anticoagulant therapy, comorbidities, Elixhauser comorbidities scores (i.e., readmit and mortality score), permeant pacemaker implantation (PPM), cardiac resynchronization therapy pacemaker (CRT-P), implantable cardioverter-defibrillator (ICD), Cardiac Resynchronization Therapy with Defibrillator (CRT-P), and admission years. The results were displayed as the hazard ratio and 95% confidence interval (HR [95%CI]). For multivariable linear analysis, random-effects models were used to identify the predictors influencing LOS or adjusted healthcare associated costs. Regarding inpatient mortality, logistic regression analysis was used in this study. Data analyses were done with STATA v.15.1 (Stata-Corp, TX, USA). A 2-tailed priori p value of <0.05 was regarded as significant.

Results

A total of 742,168 patients had AS of which 645,909 patients met the exclusion criteria (Figure 1). Overall, the median (IQR) age of patients was 74 (66 to 81) years, and 62.1% (59,730 patients) were male. The most prevalent comorbidity was hypertension (65.5%; Table 1). In-hospital mortality for the complete cohort was 2.5%. The median (IQR) value of LOS and adjusted healthcare associated costs (HCAC) in the analyzed cohort were 6 (4 to 10) days and $44,299 ($34,006-59,585), respectively.

SAVR was performed in 69,266 patients (72.0%) and TAVI in 26,993 (28.0%), respectively. The patients who received SAVR were younger than those receiving TAVI (SAVR: 71 [63 to 78] years, TAVI: 82 [76 to 87] years; p <0.0001). There was a higher proportion of males in the SAVR group compared to TAVI (65.2 vs 54.1%, p <0.0001). Preexisting or new-onset AF was similar between the groups: 40.1% of patients in the SAVR group and 30.9% of patients in the TAVI group (Table 1). The median (IQR) LOS in the patients undergoing SAVR was significantly higher than those undergoing TAVI (SAVR: 7 [5 to 11] days, TAVI: 4 [2 to 7] days, p <0.0001) whereas the median (IQR) adjusted Healthcare associated costs in the patients with TAVI were significantly higher than those with SAVR (TAVI: $47,700 [37,290 to 60,988], SAVR: $42,803.6 [32,985 to 58,863], p <0.0001).

The patients with AF were older (76 [68-82] vs 72 [64-81] years, p <0.0001) and more likely to be males (with AF: 64.2%, without AF: 60.8%; p <0.001) than those without AF. The Elixhauser comorbidity readmission and mortality score in the patients with AF was significantly higher (Readmission: 31 [21 to 43] vs 28 [18 to 40] points, p <0.0001; Mortality: 16 [9 to 25] vs 14 [6 to 22] points, p <0.0001). LOS and adjusted Healthcare associated costs were also higher in the patients with AF than those without AF (LOS: 8 [5 to 12] vs 6 [4 to 9] days, p <0.0001; adjusted Healthcare associated costs: $46,792 [35,908 to 63,380] vs $42,880 [33,007 to 57,309], p <0.0001).

As shown in Figure 2, the median LOS (IQR) in the patients with AF and SAVR was 33% higher as compared with those without AF (8 [6 to 12] vs 6 [5 to 10] days; p <0.0001). Similarly, a 33.3% increase in LOS was seen in patients with AF patients who underwent TAVI than those without AF (5 [3 to 8] vs 3 [2 to 6] days; p <0.0001). The unadjusted linear analysis showed higher LOS in younger patients (Estimate: −0.03 days per year of age, p <0.0001) but it was no longer significant after the adjustments (Estimate: −0.002, p = 0.41) (Table 2). Patients in SAVR and AF group had the highest LOS as compared with other groups, even after adjustments (p <0.0001). The standardized regression coefficient after propensity score matching in the presence of AF was 0.08 (p <0.0001).

The presence of AF significantly increased the adjusted Healthcare associated costs in the patients undergoing both TAVI and SAVR (TAVI: $49,959.5 [38,932.0 to 64,201.4] vs 46,754.3 [36,613.2 to 59,442.2], p <0.0001; SAVR: $45,683.1 [35,154.4 to 63,026.1] vs 40,948.4 [31,762.3 to 55,853.9, p <0.0001) (Figure 3). The unadjusted linear analysis showed older patients had significantly higher adjusted Healthcare associated costs (Estimate: 74.5, p <0.0001) but after adjustments for other parameters the younger age group showed higher adjusted Healthcare associated costs (Estimate: −87.1, p <0.001) (Table 2). An unadjusted analysis also demonstrated the presence of AF significantly increased the adjusted Healthcare associated costs (Estimate: 5,045.0, p <0.0001). When the estimates for adjusted Healthcare associated costs were adjusted for potential confounders such as comorbidities, device implantations (i.e., PPM, CRT-P, ICD, and CRT-D), and admitted year, the presence of AF and/or SAVR were significant predictors of increased adjusted Healthcare associated costs. The standardized regression coefficient after propensity score matching in the presence of AF was 0.05 (p <0.0001).

As listed in Table 1, the rate of in-hospital mortality was highest in the group of patients undergoing TAVI with AF and lowest in the group undergoing TAVI without AF. Inpatient mortality was found to be significantly higher with increasing age and female gender in unadjusted analysis as well as in the post-adjustment model [(increasing age: OR [95%CI]:1.02 [1.01 to 1.02], p <0.0001 and 1.01 [1.01 to 1.02], p <0.0001; female gender: OR [95%CI]: 1.36 [1.26 to 1.48], p <0.0001) and OR [95%CI]: 1.40 [1.29 to 1.53], p <0.0001, respectively)]. When the TAVI group was used as a reference standard, mortality was higher in SAVR with and without adjustments (OR [95%CI]: 1.24 [1.12 to 1.36]; and OR [95%CI]: 1.53 [1.36 to 1.74]; both p <0.0001) (Table 3). The presence of AF was a predictor of increased in-hospital mortality in the unadjusted model (OR [95%CI]: 1.12 [1.03 to 1.21], p = 0.01), whereas it was found to be significantly lower after adjusting for all other parameters (OR [95%CI]: 0.89 [0.81 to 0.98], p = 0.002). The temporal trend for mortality in the patients undergoing TAVI or SAVR has shown a decrease from 2015 onward and was found to be lowest in 2017 (OR [95%CI]: 0.60 [0.50 to 0.73], p <0.0001).

Discussion

This study is a real-world analysis of the LOS, Healthcare associated costs, and in-hospital mortality in patients undergoing interventional procedures for significant AS. The key findings are as follows: (1) the co-existence or development of AF leads to a significantly higher inpatient LOS and Healthcare associated costs in patients undergoing both SAVR and TAVI; (2) when adjusted for all other variables, AF was not associated with increased in-hospital mortality; (3) patients undergoing SAVR were significantly younger than TAVI; and (4) SAVR has a higher LOS whereas TAVI has a higher Healthcare associated costs.

Increasing age is a risk factor for developing AF with a doubling of the incidence with each decade of life15 secondary to a higher increase in the number of comorbidities.16 AF worsens prognosis in patients with severe valvular heart disease17 including those undergoing SAVR and TAVI,18, 19, 20 although this may be owing to other comorbidities rather than the AF itself.7 This is the first study to document the real-world experience of AF independently prolonging LOS and increasing Healthcare associated costs when interventions are performed for significant AS.7,19,21 This information can be useful during the consent process, particularly when communicating with patients regarding the expected LOS and the associated Healthcare associated costs related to the procedure.

Our data suggested that about a third of the population undergoing SAVR or TAVI had AF. The presence of both AF and AS can cause challenges during the assessment. There can be an underestimation of valvular gradient owing to reduced forward flow in the absence of atrial systolic contribution to ventricular filling. Patients with AS have concentric hypertrophy and diastolic dysfunction. Atrial contribution, thus, may be more important in this subset of patients.7 Owing to the overlap of symptoms of AF and severe AS, more AS patients may be labeled as being symptomatic, pushing them toward valve replacement. Additionally, AF increases the mortality incidence in any degree of AS,17,22 therefore it is essential to analyze further the role of AF in severe AS independently and as a product of the co-existing conditions.

The stressors related to the procedure for treating AS have the potential to disrupt well-controlled ventricular rates in AF as well as induce AF by itself given the pro-inflammatory milieu in the periprocedural period. This could explain the increased LOS and subsequent increased Healthcare associated costs in patients undergoing TAVI or SAVR. This is a pertinent point that may explain why younger patients seemed to have higher Healthcare associated costs. The potential reasons for this may be a more robust sympathetic nervous system and inflammatory response as compared with older people leading to more difficulty in the management of the ventricular rate as well as the rhythm in the postoperative period. It may be useful to have a peri-admission evaluation to help with the management of preexisting AF. Perioperative β-blockers have been suggested for the reduction in the incidence of postoperative AF in patients undergoing coronary artery bypass grafting,23,24 but no randomized trials have been done in patients with valvular AS.

The in-hospital mortality associated with SAVR and TAVI increased with age, which may be explained by increasing comorbidities and frailty. When the overall risk factor profile of the patients was considered, AF was not found to increase in-hospital mortality. This finding is consistent with a recent study done in patients with aortic stenosis, where AF was not found to be significantly associated with mortality after multivariate analysis.[7] Okuno et al[25] have evaluated the effect of the association of AF (valvular or non-valvular) on mortality in patients undergoing TAVI at 30 days and 1 year. They have reported no significant effect of AF on short-term (30 days) mortality but significantly higher mortality at 1 year.

The main strength of this study is the large sample size with the absence of selection bias associated with clinical trials and selective publication of results from specialized centers. There is a wide representation of age and the United States's geographical representation. These findings are thus reflective of the real-world impact that AF has on the healthcare utilization costs and LOS for these procedures. Retrospective studies have well-known limitations. NIS is a de-identified administrative dataset and there is a possibility of under-coding and misinterpretation of procedure volumes, although we used validated codesets where possible. Our analysis focused primarily on American patients and, hence, may not be generalizable to other populations. The effect of the intervention on known comorbidities is unknown. Lack of control of these may by themselves predispose to AF, which may, therefore, confound the role that AF may play in prolonging primary outcomes. The uptake of AF ablation data, either surgical maze or catheter ablation, is limited in this setting of SAVR and TAVI (Supplementary Table 4). A more aggressive approach toward AF before SAVR or TAVI may reduce the length of stay for these patients, but that might come at a higher Healthcare associated costs. Moreover, information on the type of prosthesis used and their role in the recovery and discharge of the patient is unknown, making that an independent confounding factor.26 Distinguishing preexisting and peri-procedural AF was not possible.

In conclusion, the presence of AF in patients undergoing treatment for severe AS, either SAVR or TAVI, is independently associated with increased LOS and Healthcare associated costs, but with similar in-hospital mortality compared to those without AF. These findings should help improve communication with patients and during the process of obtaining informed consent.

Disclosures

The authors have no conflicts of interest to declare.

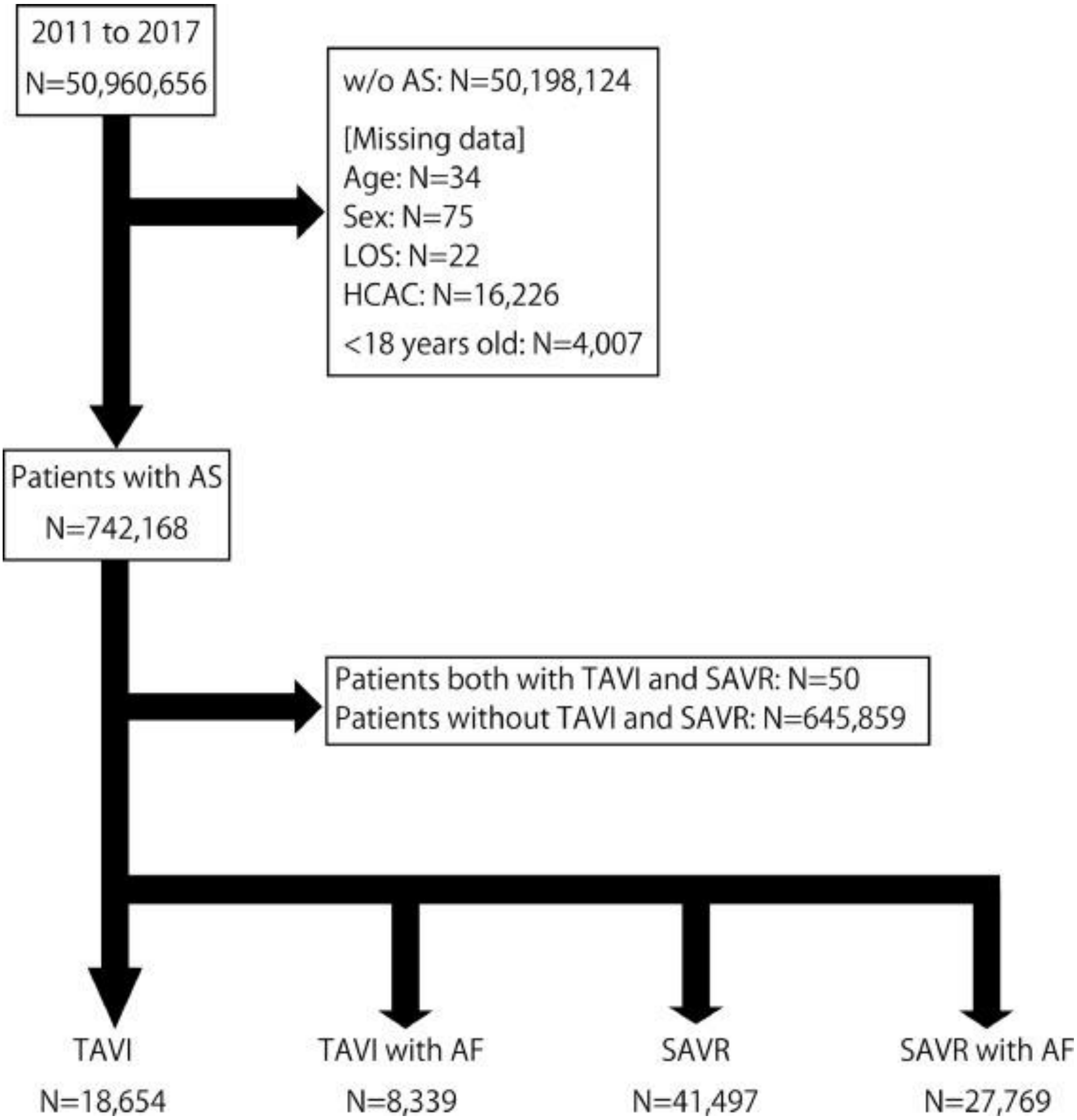

Figure 1 Study Flow Diagram

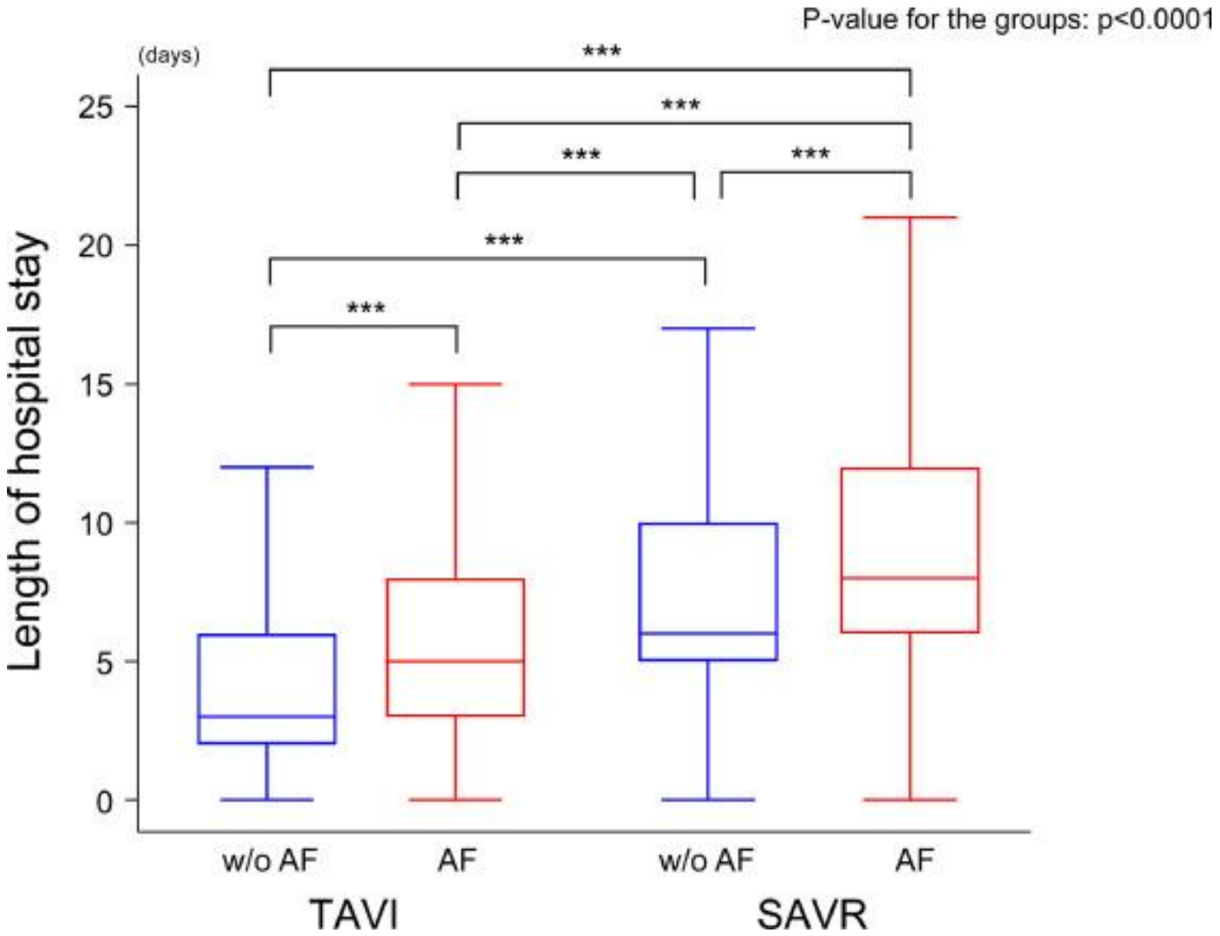

Figure 2. Differences in length of stay between patients with atrial fibrillation and those without atrial fibrillation.

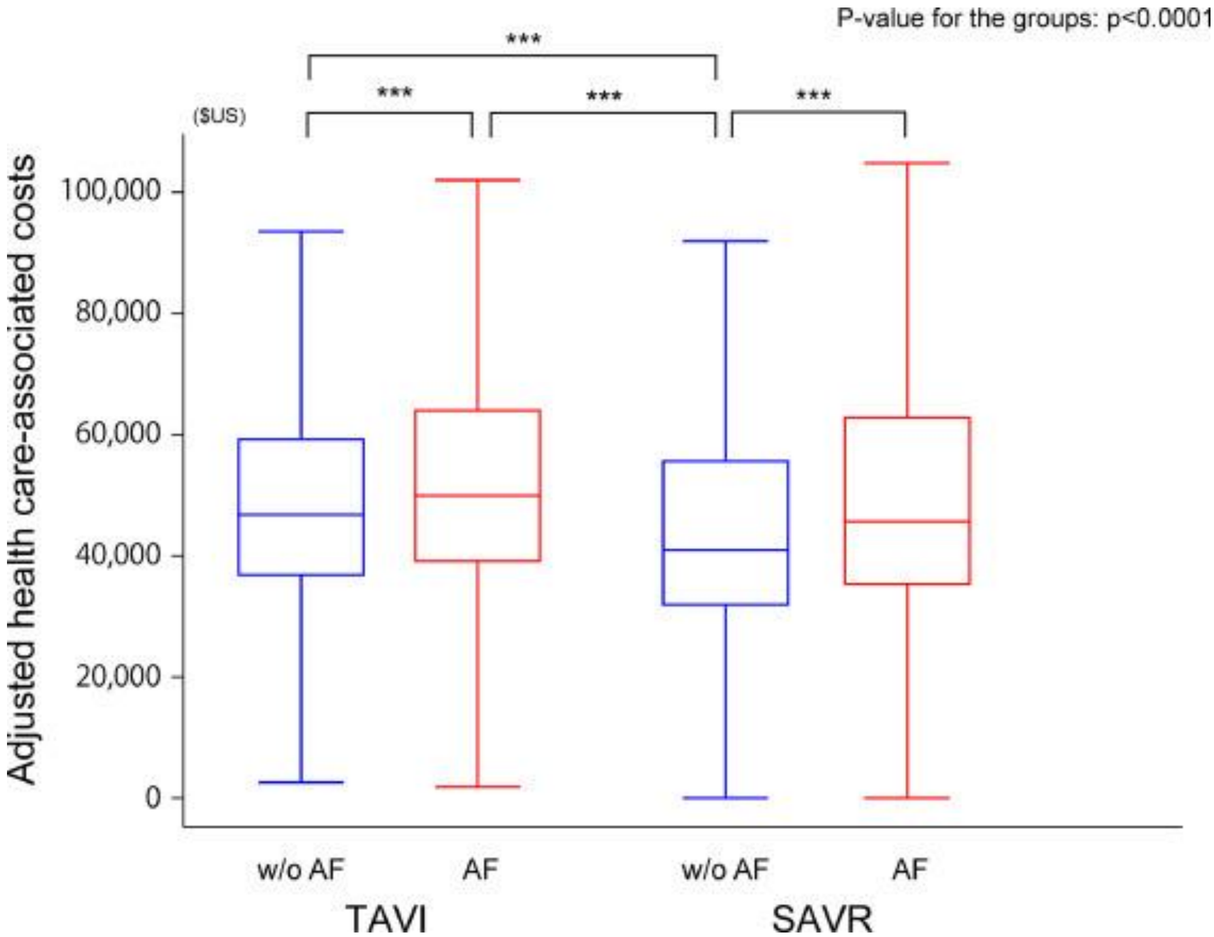

Figure 3. Differences of adjusted healthcare-associated cost between patients with atrial fibrillation and those without atrial fibrillation.

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Table 1. Clinical characteristics

	All (n=96,259)	TAVI w/o AF (n=18,654)	TAVI+AF (n=8,339)	SAVR w/o AF (n=41,497)	SAVR+AF (n=27,769)	p Value
Men	59,730 (62.1%)	9,872 (52.9%)	4,727 (56.7%)	26,674 (64.3%)	18,457 (66.5%)	<0.0001
Age (years)	74.0 (66.0–81.0)	82.0 * † ‡ (75.0–87.0)	83.0 † ‡ (78.0–87.0)	68.0 ‡ (60.0–76.0)	74.0 (67.0–80.0)	0.0001
Anticoagulant therapy	9,559 (9.69%)	1,475 (7.9%)	2,908 (34.9%)	1,709 (4.1%)	3,467 (36.3%)	<0.0001
In-hospital death	2,381 (2.5%)	350 (1.9%)	223 (2.7%)	1,078 (2.6%)	730 (2.6%)	<0.0001
Race						
White	76,997 (85.3%)	15,237 (85.9%)	7,126 (90.2%)	31,826 (82.2%)	22,808 (87.8%)	<0.0001
Black	3,998 (4.4%)	847 (4.8%)	186 (2.4%)	2,129 (5.5%)	836 (3.2%)	
Hispanic	5,049 (5.6%)	848 (4.8%)	251 (3.2%)	2,811 (7.3%)	1,139 (4.4%)	
Others	4,269 (4.7%)	807 (4.6%)	335 (4.2%)	1,938 (5.0%)	1,189 (4.6%)	
Comorbidities						
Anemia	18,442 (19.2%)	4,272 (22.9%)	1,994 (23.9%)	7,016 (16.9%)	5,160 (18.6%)	<0.0001
Chronic heart failure	42,627 (44.3%)	13,021 (69.8%)	6,505 (78.0%)	12,543 (30.2%)	10,558 (38.0%)	<0.0001
Chronic pulmonary disease	22,893 (23.8%)	5,601 (30.0%)	2,734 (32.8%)	8,488 (20.5%)	6,070 (21.9%)	<0.0001
Coagulopathy	27,267 (28.3%)	2,875 (15.4%)	1,588 (19.0%)	12,915 (31.1%)	9,889 (35.6%)	<0.0001
Diabetes mellitus	32,293 (33.6%)	6,927 (37.1%)	3,068 (36.8%)	13,346 (32.2%)	8,952 (32.2%)	<0.0001
Hypertension	63,071 (65.5%)	9,298 (49.8%)	4,870 (58.4%)	28,274 (68.1%)	20,629 (74.3%)	<0.0001
Renal failure	19,869 (20.6%)	6,088 (32.6%)	3,060 (36.7%)	5,820 (14.0%)	4,901 (17.7%)	<0.0001
Stroke	1,058 (1.1%)	290 (1.6%)	119 (1.4%)	384 (1.4%)	265 (1.0%)	<0.0001
Elixhauser comorbidity (points)						
Readmit score (30 d)	29.0 (20.0–41.0)	35.0 * † ‡ (24.0–47.0)	38.0 † ‡ (28.0–49.0)	25.0 ‡ (17.0–37.0)	29.0 (19.0–40.0)	0.0001
Mortality score (in-hospital)	14.0 (7.0–23.0)	15.0 * † ‡ (10.0–22.0)	18.0 † ‡ (12.0–25.0)	13.0 ‡ (4.0–21.0)	15.0 (7.0–25.0)	0.0001

AF = Atrial fibrillation; COPD = chronic obstructive pulmonary disease; SAVR = surgical aortic valve replacement; TAVI = trans catheter aortic valve implantation.

Table 2. Predictors of length of stay and adjusted healthcare costs

Empty Cell	**Model 1**		**Model 2**		**Model 3**		**Model 4**		**Model 5**	
Length of Stay										
Empty Cell	estimate	p value	estimate	p value	estimate	p value	estimate	p value	estimate	p value
Age	−0.03	<0.0001	0.02	<0.0001	0.006	0.006	−0.002	0.47	−0.002	0.41
Female	0.08	0.08	0.44	<0.0001	0.36	<0.0001	0.46	<0.0001	0.44	<0.0001
Types of patients										
TAVI	(ref.)		(ref.)		(ref.)		(ref.)		(ref.)	
SAVR	3.76	<0.0001	3.91	<0.0001	3.98	<0.0001	4.72	<0.0001	4.44	<0.0001
Presence of AF										
AF	2.11	<0.0001	1.76	<0.0001	1.84	<0.0001	1.43	<0.0001	1.26	<0.0001
Adjusted HAC										
Age	74.5	<0.0001	12.5	0.19	−35.2	0.002	−73.9	<0.0001	−87.1	<0.0001
Female	238.66	0.26	346.9	0.10	94.6	0.66	677.0	0.001	670.4	<0.0001
Types of patients										
TAVI	(ref.)		(ref.)		(ref.)		(ref.)		(ref.)	
SAVR	-1,220.9	<0.0001	-1,321.0	<0.0001	-1,223.4	<0.0001	1,108.7	<0.0001	459.1	0.10
Presence of AF										
AF	5,045.0	<0.0001	5,062.9	<0.0001	5,340.7	<0.0001	3,733.2	<0.0001	3,485.4	<0.0001

AF = atrial fibrillation; HAC = healthcare associated costs; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

Table 3. Predictors of in-hospital mortality

Empty Cell	**Model 1**		**Model 2**		**Model 3**		**Model 4**		**Model 5**	
Empty Cell	Or (95%CI)	p Value	Or (95%CI)	p Value	Or (95%CI)	p Value	Or (95%CI)	p Value	Or (95%CI)	p Value
Age	1.02 (1.01–1.02)	<0.0001	1.03 (1.02–1.03)	<0.0001	1.02 (1.02–1.03)	<0.0001	1.01 (1.01–1.02)	<0.0001	1.01 (1.01–1.02)	<0.0001
Female	1.36 (1.26–1.48)	<0.0001	1.35 (1.24–1.46)	<0.0001	1.32 (1.21–1.44)	<0.0001	1.42 (1.29–1.54)	<0.0001	1.40 (1.29–1.53)	<0.0001
Types of patients										
TAVI	(ref.)		(ref.)		(ref.)		(ref.)		(ref.)	
SAVR	1.24 (1.12–1.36)	<0.0001	1.67 (1.50–1.85)	<0.0001	1.67 (1.50–1.86)	<0.0001	1.73 (1.54–1.95)	<0.0001	1.53 (1.36–1.74)	<0.0001
Presence of AF										
AF	1.12 (1.03–1.21)	0.01	1.01 (0.92–1.10)	0.88	1.04 (0.95–1.13)	0.43	0.94 (0.86–1.03)	0.17	0.89 (0.81–0.98)	0.02

SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve implantation.