Short-Term Outcomes Following Percutaneous Left Atrial Appendage Closure in Patients With History of Valve Implantation

Left atrial appendage closure (LAAC) with the Watchman device has been shown to be noninferior to anticoagulation for the prevention of vascular events in patients with nonvalvular atrial fibrillation (AF).[1] In accordance with the growing evidence, LAAC has become the standard alternative in patients with AF who cannot tolerate long-term anticoagulation. Patients with history of valve implantation (HVI) are an important subgroup of patients who were underrepresented in the LAAC device studies. With the increasing prevalence of valve replacements, there is a growing need to understand the characteristics and outcomes of these subsets of patients. Therefore, our study aimed to describe the difference in short-term outcomes between patients with and without HVI who underwent percutaneous LAAC.

We conducted a retrospective cohort study using the Nationwide Readmissions Database (NRD) 2016-2017, a publicly available, population-based database provided by the Healthcare Cost and Utilization Project.[2] The International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System codes were used to identify patients ≥18 years of age with a primary diagnosis of AF (I48.0/I48.1/I48.2/I48.91) who underwent percutaneous LAAC (02L73DK). We divided eligible patients into two groups according to the presence or absence of HVI (Z95.2/Z95.3/Z95.4). The outcomes of interest were in-hospital adverse events and 30-day/180-day readmission outcomes after discharge. The composite outcome was defined as in-hospital death, ischemic stroke or transient ischemic attack (TIA), systemic embolism, bleeding requiring blood transfusion, pericardial effusion and/or cardiac tamponade treated with pericardiocentesis or surgery, and removal of embolized device. We presented the data on the national estimates using the discharge weights provided by the NRD and compared patient characteristics and outcomes between the groups. We also examined the association between HVI and the outcomes using multivariable logistic regression (for the in-hospital composite outcome) or multivariable Cox regression (for post-discharge readmission outcomes) with adjustment for all patient characteristics in Table 1 in the unweighted cohort.

Out of 15,399 eligible patients, 807 (5.2%) had HVI and 14,592 (94.8%) did not have HVI. Patients with HVI were older and mostly males when compared with those without HVI. Both groups predominantly had paroxysmal AF, but the prevalence of permanent and/or long term AF was higher in patients with HVI. The CHA_2DS_2-Vasc score was also higher in patients with HVI. Patients with HVI had higher prevalence of coronary artery bypass grafting and pacemaker or defibrillator implantation. Mitral regurgitation and pulmonary hypertension were also more frequent in patients with HVI. There was no significant difference in the in-hospital composite outcome between the groups (2.6% vs 2.2%, $p = 0.467$, adjusted odds ratio=1.10, 95% confidence interval [CI]=0.60 to 2.01). Despite similar 180-day any-cause readmission rates (28.6% vs 28.3%; adjusted hazard ratio=0.97, 95% CI=0.75 to 1.26), the rate of ischemic stroke or TIA was significantly higher at 180 days after discharge in patients with HVI when compared with patients without HVI (3.8% vs 1.3%, $p = 0.005$). The association between HVI and a higher rate of 180-day ischemic stroke or TIA remains significant after adjustment for patient characteristics (adjusted hazard ratio=3.00, 95% CI=1.40 to 6.45) (Table 1).

Our study is the first to evaluate the short-term outcomes of patients with HVI who underwent LAAC and shows that they have similar in-hospital and 30-day outcomes when compared with patients without HVI but a higher risk of ischemic stroke or TIA at 180 days after discharge. Patients with HVI have added factors that contribute to a prothrombotic state in addition to AF such as exposure to a foreign surface, possibility of pannus growth, and the local turbulence of blood flow around the implanted valve.[3] Patients with HVI may also have dilated cardiac chambers as a result of the prior valvular dysfunction which predisposes to thrombus formation. These factors could accentuate the risk of thrombus formation in patients with a new prosthetic device in the form of LAAC. Also, since LAAC only eliminates the possibility of thrombus formation in the left atrial appendage, other areas of forming a thrombus can still exist. The United States Food and Drug Administration currently recommends oral anticoagulation for minimum of 45 days and dual antiplatelet for up to 6 months following LAAC.[4] However, the findings of our study reiterate that the optimal duration of anticoagulation and antiplatelet therapy in patients with HVI who undergo LAAC remains unknown and needs to be further investigated.

Our study has limitations associated with its data source, which is based on International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System codes and so is unable to describe the details of HVI (e.g., location and type of implanted valve), laboratory and imaging results, indication and procedural details of LAAC, pre-/after-LAAC anticoagulant or antiplatelet therapy, out-of-hospital death, and long-term follow-up.

In conclusion, this nationwide study suggests that LAAC in patients with HVI is feasible and is associated with similar short-term outcomes but a higher 180-day risk of ischemic stroke or TIA when compared with patients without HVI.

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this study.

Disclosure

The authors declare no conflict of interest.

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Ethical approval: This study was exempted from the approval of the institutional review board because it used anonymized and de-identified data in a publicly available database.

Table 1
Patient characteristics and in-hospital and 30-day/180-day outcomes in patients undergoing percutaneous left atrial appendage closure with or without prior history of valve implantation

Variable	Prior Valve Implantation		p Value
	Yes (n=807)	No (n=14592)	
Age, (years), median (IQR)	79 (74−84)	76 (71−82)	<0.001
Men	528 (65.4%)	8722 (59.8%)	0.002
Type of atrial fibrillation			0.002
Paroxysmal	307 (38.0%)	6195 (42.5%)	
Persistent	179 (22.2%)	2894 (19.8%)	
Permanent/chronic	251 (31.1%)	3896 (26.7%)	
Unspecified type	71 (8.8%)	1607 (11.0%)	
CHA_2DS_2-Vasc score, mean ± SD	4.5 ± 1.6	4.1 ± 1.5	<0.001
Prior percutaneous coronary intervention	142 (17.6%)	2213 (15.2%)	0.061
Prior coronary artery bypass grafting	308 (38.2%)	2070 (14.2%)	<0.001
Prior pacemaker/defibrillator implantation	259 (32.1%)	3731 (25.6%)	<0.001
Prior cerebrovascular disease	200 (24.8%)	3543 (24.3%)	0.738
Mitral regurgitation	74 (9.2%)	982 (6.7%)	0.008
Tricuspid regurgitation	13 (1.6%)	349 (2.4%)	0.193
Pulmonary hypertension	77 (9.5%)	918 (6.3%)	<0.001
Carotid artery disease	14 (1.7%)	309 (2.1%)	0.521
Chronic pulmonary disease	191 (23.7%)	2834 (19.4%)	0.004
Renal failure	215 (26.6%)	2880 (19.7%)	<0.001
Liver disease	33 (4.1%)	329 (2.3%)	0.001
Anemia	141 (17.5%)	2142 (14.7%)	0.031
Obesity	105 (13.0%)	2129 (14.6%)	0.238
Hospital status			
Metropolitan teaching hospital	704 (87.2%)	12514 (85.8%)	0.233
Annual hospital procedural volume*			0.104
Lowest tertile (≤28 cases/year)	285 (35.3%)	5228 (35.8%)	
Middle tertile (29−57 cases/year)	260 (32.2%)	5115 (35.1%)	
Highest tertile (≥58 cases/year)	261 (32.3%)	4250 (29.1%)	
In-hospital adverse events			
Composite outcome of the following events	21 (2.6%)	322 (2.2%)	0.467
Adjusted OR (95% CI)	1.10 (0.60-2.01)	Reference	0.765
Death	≤10 (≤1.2%)†	24 (0.2%)	0.399
Ischemic stroke/transient ischemic attack	≤10 (≤1.2%)†	69 (0.5%)	0.272
Systemic embolism	0 (0%)	18 (0.1%)	>0.99
Bleeding requiring blood transfusion	≤10 (≤1.2%)†	72 (0.5%)	0.195
Pericardial effusion/cardiac tamponade treated with pericardiocentesis or surgically	≤10 (≤1.2%)†	134 (0.9%)	0.123
Removal of embolized device	≤10 (≤1.2%)†	37 (0.3%)	0.001
Length of stay ≥ 2 days	107 (13.3%)	1981 (13.6%)	0.828
30-day readmission after discharge‡	**(n=741)**	**(n=12948)**	
Any-cause readmission	79 (10.7%)	1192 (9.2%)	0.191
Adjusted HR (95% CI)	1.07 (0.79-1.45)	Reference	0.672
Ischemic stroke/transient ischemic attack§	≤10 (≤1.3%)†	47 (0.4%)	0.355
Adjusted HR (95% CI)‖	1.35 (0.31-5.95)	Reference	0.693
180-day readmission after discharge*	**(n=364)**	**(n=5935)**	
Any-cause readmission	104 (28.6%)	1677 (28.3%)	0.905
Adjusted HR (95% CI)	0.97 (0.75-1.26)	Reference	0.845
Ischemic stroke/transient ischemic attack§	14 (3.8%)	80 (1.3%)	0.001
Adjusted HR (95% CI)‖	3.00 (1.40-6.45)	Reference	0.005

Values are n (%) unless otherwise indicated. Categorical variables were compared using Fisher's exact test or chi-squared test. Continuous variables were compared using Mann−Whitney U test or Student t-test.

* Defined as the annual number of percutaneous left atrial appendage closure cases in each hospital in each year.

† Categorical variable cell with n≤10 was suppressed in compliance with the privacy protection policy of the Healthcare Cost and Utilization Project Data Use Agreement (2).

‡ Includes only patients who were discharged alive before December in each calendar year to allow for 30-day after-discharge follow-up in the Nationwide Readmissions Database because only patients' readmissions within a state during the same calendar year are identifiable in the Nationwide Readmissions Database (2).

§ Ischemic stroke/transient ischemic attack after discharge was identified using data on diagnoses recorded during readmissions.

‖ Patients were censored if they died during readmission without ischemic stroke/transient ischemic attack.

** Includes only patients who were discharged alive before July in each year to allow for 180-day follow-up after discharge in the Nationwide Readmissions Database. CI = confidence interval; HR = hazard ratio; IQR = interquartile range; OR = odds ratio; SD = standard deviation.

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Cardiorespiratory Fitness Attenuates the Increased Risk of Sudden Cardiac Death Associated With Low Socioeconomic Status

Emerging evidence suggests an inverse association between socioeconomic status (SES) and adverse cardiovascular disease (CVD) outcomes that is attributed primarily to poor lifestyle behaviors.[1] More recently, lower SES has been associated with an increased incidence of sudden cardiac death (SCD), an enormous public health concern that accounts for approximately 50% of all coronary heart disease-related death.[2] Cardiorespiratory fitness (CRF), which represents an integrity of cardiopulmonary and muscular system to perform and sustain physical activity, is independently associated with CVD risk factors and outcomes.[3] Importantly, higher CRF has been demonstrated to exert a favorable effect on the incidence of SCD, independently of potential CVD-related confounders,[4] but whether CRF also attenuates the incidence of SCD among underserved populations remains unclear. Thus, this prospective study tested the hypothesis that SES and CRF are independently associated with the incidence of SCD and that CRF attenuates the association between SES and the incidence of SCD.

This prospective study was based on a population-based sample of 2,368 men, aged 42 to 61 years, who were followed in the Kuopio Ischemic Heart Disease cohort. The Kuopio Ischemic Heart Disease study protocol was approved by the Research Ethics Committee of the University of Eastern Finland. SES was characterized using self-reported questionnaires via combined measures of income, education, occupation, occupational prestige, material standard of living, and housing conditions, and was categorized into tertiles as well as low SES and high SES based on median values. CRF was directly measured by peak oxygen uptake (VO_{2peak}) during progressive exercise testing to volitional fatigue. CRF was classified by tertiles of VO_{2peak} value based on age-specified CRF categories: low (22.2 ± 4.7 ml/kg per min), moderate (29.9 ± 3.2 ml/kg per min) and high (38.1 ± 5.5 ml/kg per min) as well as into unfit (24.3 ± 5.1 ml/kg per min) and fit (36.0 ± 5.8 ml/kg per min) categories based on median values of age-specific VO_{2peak} percentiles. The joint associations of SES and CRF with SCD were based on the following four possible combinations (High SES-Fit, Low SES-Fit, High SES-Unfit, and Low SES-Unfit).

SCD was defined as a fatal event that occurred within 1 hour after the onset of symptoms or within 24 hours when autopsy data did not reveal a noncardiac cause of SCD or after a fatal cardiac arrest following successful resuscitation from ventricular tachycardia and/or ventricular fibrillation. Data on SCDs were derived from interviews with family members, hospital records, death certificates, autopsy reports, and medico-legal documents. We used Cox proportional hazard models adjusted for potential confounders to determine the hazard ratios (HRs) and 95% confidence intervals (CIs) of SCD according to each exposure.

During a 27.6-year median follow-up, 268 SCD occurred. After adjusting for confounding factors (model 1), men with low SES were at increased risk for SCD (HR 1.38, 95% CI: 1.02 to1.87), but this association was attenuated (HR 1.33, 0.98 to 1.80) when additionally adjusted for CRF (model 2). Higher levels of CRF were associated with lower risk of SCD (HR 0.66, 0.46 to 0.95) after adjusting for potential confounders including SES. In joint associations of SES and CRF with SCD, low SES-Unfit had significantly higher risk of SCD (HR 2.04, 1.37 to 3.02), but low SES-Fit was not significantly associated with an increased risk of SCD (1.41, 0.92 to 2.16), compared with their high SES-Fit counterparts (Table 1).

The major findings of this prospective study were that both low SES and high CRF were significantly and independently associated with a higher and lower incidence of SCD, respectively, and that the association between SES and SCD was dependent on CRF. Most importantly, the novel findings of this prospective study were that the incidence of SCD associated with low SES was the highest in unfit men, while the incidence of SCD was significantly attenuated in fit men with low SES. Taken together, these findings from this prospective study extend the favorable impact of CRF on survival outcomes in socioeconomically disadvantaged populations, consistent with findings from a previous study, which found that moderate-to-high levels of CRF attenuate the incidence of CVD mortality in men with low SES.[5]

Lifestyle risk factors and disadvantaged neighborhood infrastructure may be implicated in the incidence of SCD in underserved populations,[1,2] thereby underscoring the need for policies and programs focused on modifying lifestyle risk factors that are associated with low SES in order to lower the incidence of SCD[1]. Furthermore, the levels of leisure-time physical activity appear to be relatively low in individuals with low SES,[6] suggesting that SES-related inequalities in physical activity levels may stem, in part, from differences in lifestyle behavior. Thus, our findings