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Associations between new-onset postoperative atrial fibrillation and changes in left ventricular mass index in patients undergoing transcatheter aortic valve replacement

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Abstract

Background New-onset postoperative atrial fibrillation (POAF) is common after transcatheter aortic valve replacement (TAVR). At present, the impact of POAF on cardiac remodeling after TAVR has not been thoroughly studied.

Objectives To investigate the impact of POAF on cardiac remodeling and its association with clinical outcomes after TAVR.

Methods 601 patients undergoing TAVR for severe aortic stenosis were evaluated. Of these, 253 patients were identified to have POAF, which was categorized as normal left ventricular mass index (LVMI) in 54 (21%) and high LVMI in 199 (79%). The primary endpoint was a composite of all-cause death, heart failure rehospitalization and disabling stroke. Reverse remodeling was assessed by transthoracic echocardiography.

Results In POAF patients, the 3-year cumulative incidence of primary composite outcome in the high LVMI subgroup was significantly higher than that in the normal LVMI subgroup (9.3 ± 3.3% vs. 13.5 ± 3.9%; $p = 0.02$). The incidence of LVMI regression after TAVR was lower in patients with POAF than in those without (65.6 ± 3.0% vs. 82.6 ± 2.7% at 3 years; $p = 0.029$). Furthermore, the 3-year cumulative incidence of the primary composite outcome and cardiovascular death was highest in the group of POAF without LVMI regression. Baseline LVMI (β = -1.73, $p < 0.001$) and POAF (β = -1.46, $p < 0.001$) were independent predictors of change in LVMI at one year.

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Conclusions Patients with POAF had less LVMI regression and impaired cardiac reverse remodeling after TAVR, which increased the incidence of all-cause death and heart failure rehospitalization. Therefore, clinicians should be more proactive in monitoring and treating POAF after TAVR.

Keywords Transcatheter aortic valve replacement, Aortic stenosis, Postoperative atrial fibrillation, Cardiac reverse remodeling

Introduction

Aortic stenosis (AS) is the most common native valve disease of the elderly. In early stages of AS, left ventricular (LV) ejection fraction (LVEF) and cardiac output may be maintained. However, when increasing wall stress exceeds the compensating mechanisms of the left ventricle, LV systolic function declines because of afterload mismatch and patients experience typical symptoms of chronic heart failure [1]. In patients with severe symptomatic AS and an intermediate to high surgical risk, transcatheter aortic valve replacement (TAVR) progressively became the standard of care over surgical aortic valve replacement (SAVR) [2–3].

New-onset postoperative atrial fibrillation (POAF) is a common complication of TAVR, with an estimated incidence of 16–51.1% [4]. New-onset POAF refers to the detection of atrial fibrillation (AF) after TAVR in patients without previously diagnosed AF [5]. Studies have shown that POAF in patients undergoing TAVR is associated with worse outcomes, including higher rates of all-cause death, rehospitalization for heart failure, cerebrovascular events, and major bleeding [6–7].

Cardiac reverse remodeling after TAVR has been consistently demonstrated in many studies, as measured by improvement in left ventricular mass index (LVMI) [8–9]. Atrial fibrillation (AF) is negatively correlated with cardiac reverse remodeling outside of TAVR populations [10–11]. However, the effect of POAF on cardiac remodeling after TAVR has not been fully studied. Therefore, the aim of this study was to investigate the effect of POAF on cardiac remodeling after TAVR and its association with clinical outcomes.

Methods

Study population

This study was approved by the Institutional Review Board of Southwest Hospital of Third Military Medical University (approval number: KY20210158) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Southwest Hospital of Third Military Medical University waived the need for informed consent.

We conducted a single-center, retrospective, and observational study of patients who underwent TAVR for severe pure/predominant AS in our institution between January 2018 and June 2021 (Fig. 1). For the purpose of the present study, we did not select patients with mixed aortic valve disease, defined as severe AS plus moderate or greater aortic regurgitation (AR). Patients were excluded from the analysis in case of: (i) prior cardiac surgery, such as aortic valve replacement (AVR); (ii) undergoing simultaneous procedures, such as percutaneous coronary intervention (PCI) or other transcatheter valve interventions; (iii) history of endocarditis; (iv) history of permanent or paroxysmal atrial fibrillation; (v) patients who have used antiarrhythmic drugs before TAVR.

After screening, a total of 601 patients were included in the final analysis. Of these, 437 patients (238 in the No POAF group and 199 in the POAF group) had high LVMI, and 164 patients (110 in the no POAF group and 54 in the POAF group) had normal LVMI. High LVMI was defined as LVMI > 115 g/m^2 in men and > 95 g/m^2 in women [12].

AF was diagnosed in accordance with the current European Society of Cardiology Guidelines [13] as an irregular RR interval, the absence of P waves, an unidentifiable isoelectric line, atrial rhythm greater than 300 b.p.m. or an interval between two atrial activations of less than 200 ms and lasting at least 30 s. Flutter episodes were included as AF episodes. All patients were routinely monitored with telemetry for the first 3 days after TAVR and longer if there had been cases of arrhythmia. Thereafter, a standard 12-lead electrocardiogram (ECG) was recorded every 12 h. We classified the occurrence of AF within the first 7 days following TAVR in the patients with no previous known AF as New-onset POAF. All patients were followed for AF occurrences for 12 months. Arrhythmia episodes were documented either on planned visits (3, 6, and 12 months) or on unplanned visits, according to the physician's judgment. During each visit, a clinical assessment, 12-lead ECG, and 24-h rhythm monitoring (Holter) were scheduled. The patients who developed POAF were treated with antiarrhythmic drugs, and electrical cardioversion was considered when AF was not controlled after 1–2 days of medical treatment. AF therapy (rhythm versus rate control) was at the discretion of the treating physician based on the patient´s clinical symptoms, left atrial size, comorbidities and age. A total of six patients received amiodarone as rhythm control therapy, and cardioversion was performed in a total of five patients with POAF after TAVR. These patients were also included in our subsequent analysis. New AF between hospital discharge and follow-up was not

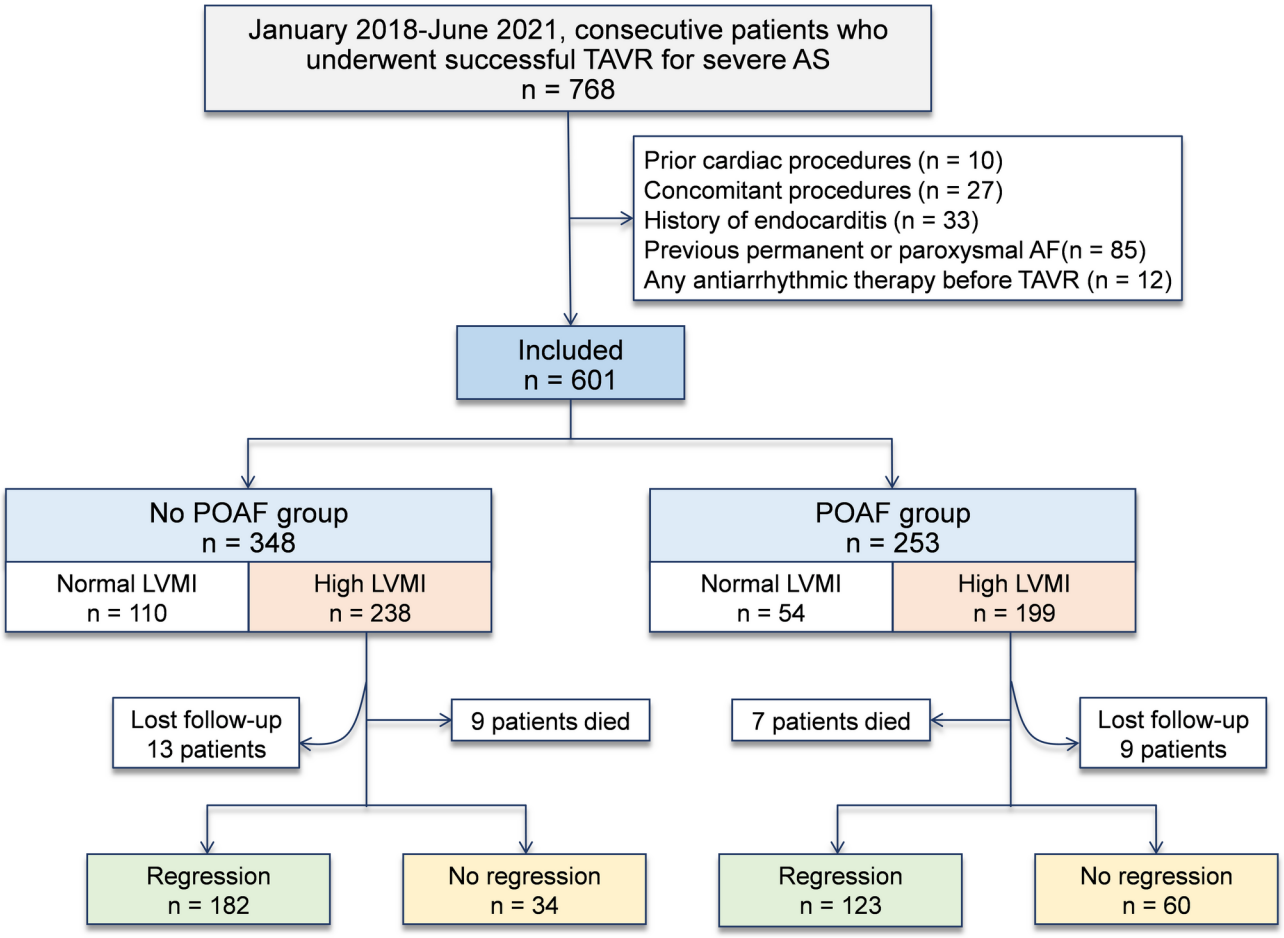

Fig. 1 The flowchart of the study. AS, aortic stenosis; LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation

diagnosed. Of these 253 POAF patients, 50 patients had paroxysmal AF, 63 patients had persistent AF and 140 patients had permanent AF.

Anticoagulation was started, unless contraindicated, immediately after the diagnosis of POAF and continued for at least 1 month. In case of short episodes (12 h) of AF, the potential risks/benefits of anticoagulation were evaluated in each patient, and the decision was finally made by the physician responsible for the patient. Warfarin was used as anticoagulant therapy in all cases, with the objective of an international normalized ratio between 2 and 3. Intravenous heparin was administered until therapeutic anticoagulation levels were achieved.

Two-dimensional transthoracic echocardiography

Transthoracic echocardiography was performed by the high-end equipment (Vivid E95, GE-Healthcare) by two specialist sonographers at baseline (the last examination before TAVR), before discharge (within one week after TAVR), at 3, 6, and 12 months after TAVR and every 6 months thereafter.

Left ventricular (LV) ejection fraction (LVEF), left ventricular end systolic volume (LVESV), and left atrial volume (LAV) were estimated by biplane Simpson method. LVESV and LAV were divided by body surface area (BSA) to acquire LVESVI and LAVI. 2D speckle tracking longitudinal strain analysis was performed on the apical two-, three-, and four- chamber views to calculate by LV global longitudinal strain (GLS) [14]. LV mass was calculated by the modified American Society of Echocardiography formula and subsequently indexed to BSA [14]. LV mass was calculated with the formula recommended by the American Society of Echocardiography (ASE) and was indexed to the body surface area as follows: LV mass = 0.8×1.04 $[(\mathrm{LVDd} + \mathrm{LVPWTd} + \mathrm{IVSTd})^3 - (\mathrm{LVDd})^3] + 0.6$, where LVDd was the LV diastolic diameter, IVSTd was the diastolic interventricular septal wall thickness and LVPWTd was the diastolic LV posterior wall thickness. LV mass index (LVMI) regression was defined as a ≥ 15% decrease in LVMI at 1 year follow-up with respect to the baseline value [15]. All other measurements were performed according to the European Association of Cardiovascular

Imaging and American Society of Echocardiography guidelines [14].

Follow-up

Patients were followed up postoperatively up to June 2024 by direct interview. In Fig. 1, a total of 348 patients in the No-POAF group were divided into normal LVMI group ($n = 110$) and high LVMI group ($n = 238$), and 225 (94.5%) patients in the high LVMI group completed follow-up. The 253 patients in the POAF group were divided into normal LVMI group ($n = 54$) and high LVMI group ($n = 199$), and 190 (95.5%) patients in the high LVMI group completed follow-up.

Clinical follow-up including assessment of symptoms and adverse events was performed at 1, 3, 6, and 12 months after TAVR and every 6 months thereafter. A 12-lead ECG was routinely performed at each follow-up visit. The main outcome measures were the composite of all-cause death, disabling stroke, or heart failure (HF) rehospitalization. Secondary measures included each component of the primary endpoint, and nondisabling stroke, transient ischemic attack (TIA), and major bleeding as defined by the International Society on Thrombosis and Hemostasis. All-cause death included aortic valve procedure-related death, sudden death, death caused by heart failure and death due to aortic valve endocarditis. Heart failure rehospitalization was defined as hospitalization for worsening heart failure requiring intravenous drug therapy. The cause of death was classified according to the Valve Academic Research Consortium definitions and was adjudicated by an independent clinical event committee.

Statistical analysis

The categorical variables were presented as numbers (percentages) and were compared using a χ^2 test or Fisher's exact test. The continuous variables were expressed as mean (SD) or median (IQR). Based on their distributions, the continuous variables were compared using the student's *t*-test or the Wilcoxon rank sum test between two groups, and the one-way analysis of variance or the Kruskal-Wallis test between four groups. Analyses of time-related clinical events used Kaplan-Meier analyses with log-rank tests. Linear regression analysis by Enter model was performed to establish univariate and multivariate predictors of change in LVMI after TAVR. Univariate predictors with $p < 0.05$ were included in the multivariate analysis. The univariate predictors were included in the univariable model involving the following potential independent clinically relevant variables: age, sex, body mass index (BMI), echocardiographic parameters, presence of other valve diseases, aetiology of AS, medical history and comorbidities, as shown in Table 1. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina). A value of $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

Table 1 shows the perioperative patient characteristics. The patients in the high LVMI subgroup were older, more often female, and had higher STS risk score than those in the normal LVMI subgroup for patients with and without POAF. No significant differences were found about procedural details and 30-day outcomes across groups. Myocardial infarction in the absence of obstructive coronary artery disease before TAVR is found in 3.3% of all patients with acute infarction who are referred for coronary angiography.

Clinical outcomes

There was no significant difference in the 3-year cumulative incidence of the primary composite outcome between the normal LVMI and high LVMI subgroups in patients without POAF (Fig. 2A). However, in POAF patients, the 3-year cumulative incidence of primary composite outcome in the high LVMI subgroup was significantly higher than that in the normal LVMI subgroup ($9.3 \pm 3.3\%$ vs. $13.5 \pm 3.9\%$; $p = 0.02$; Fig. 2B). The incidence of each component of composite outcomes (death, stroke, and rehospitalization for heart failure) was shown in Table 2.

Associations between clinical outcomes and LVMI regression

The incidence of LVMI regression after TAVR was lower in patients with POAF than in those without ($65.6 \pm 3.0\%$ vs. $82.6 \pm 2.7\%$ at 3 years; $p = 0.029$; Fig. 3). Furthermore, the 3-year cumulative incidence of the primary composite outcome (Fig. 4A) and cardiovascular death (Fig. 5A) was highest in the group of POAF without LVMI regression. There was no significant difference in the incidence of all-cause death (Fig. 4B) and cerebrovascular events (Fig. 5B) across groups.

Cardiac reverse remodeling

At baseline, all patients completed echocardiography. At 1 year, 228 (95.8%) people in the POAF-high LVMI group and 193 (97.0%) people in the POAF-high LVMI group completed echocardiogram follow-up. Figure 6 shows the changes in echocardiographic parameters in patients with and without AF. At one year after TAVR, LVMI, LV GLS and LVEF were significantly improved in No AF patients compared with AF patients (LVMI: -12.4 ± 5.3 vs. -5.5 ± 5.7 g/m^2, $p = 0.011$; LV GLS: -2.5 ± 2.7 vs. $-0.3 \pm 1.9\%$, $p = 0.015$; LVEF: $+6.9 \pm 4.6$ vs. $-2.3 \pm 3.8\%$, $p = 0.017$). Furthermore, LVESVI and LAVI were significantly reduced in the patients without POAF versus those with (LVESVI:

Table 1 Perioperative patient characteristics

Variables	All (*n* = 601)	No POAF			POAF		
		Normal LVMI (*n* = 110)	High LVMI (*n* = 238)	*p* value	Normal LVMI (*n* = 54)	High LVMI (*n* = 199)	*p* value
Age (years)	76.0 ± 8.1	73.4 ± 8.2	77.5 ± 8.9	< 0.001	74.2 ± 7.4	79.5 ± 7.6	0.0051
Male	239 (39.8)	56 (50.1)	82 (34.5)	< 0.001	29 (53.7)	72 (36.2)	< 0.001
BSA (m^2)	1.48 ± 0.18	1.51 ± 0.18	1.43 ± 0.18	0.648	1.52 ± 0.19	1.42 ± 0.17	0.703
Hypertension	464 (77.2)	80 (72.7)	178 (74.8)	0.725	40 (74.1)	166 (83.4)	0.044
Diabetes mellitus	188 (31.3)	34 (30.9)	77 (32.4)	0.554	17 (31.5)	60 (30.1)	0.613
Coronary artery disease	269 (44.8)	46 (41.8)	105 (44.1)	0.884	26 (48.1)	92 (46.2)	0.459
CKD (eGFR < 60 ml/min/1.73 m^2)	233 (38.8)	38 (34.5)	77 (32.4)	0.623	23 (42.6)	95 (47.7)	0.537
History of cerebrovascular events	89 (14.8)	13 (11.8)	33 (13.9)	0.913	10 (18.5)	33 (16.5)	0.581
COPD	203 (33.8)	35 (31.8)	80 (33.6)	0.759	18 (33.3)	70 (35.2)	0.813
NYHA functional class III/IV	179 (29.8)	19 (17.3)	70 (29.4)	< 0.001	17 (31.5)	73 (36.7)	< 0.001
NT-proBNP (pg/ml)	1792 (593–3908)	1232 (511–1936)	2538 (926–5302)	< 0.001	1362 (496–3637)	2845 (973–6985)	< 0.001
CHA_2DS_2-Vasc score	4.2 ± 1.4	4.0 ± 1.3	4.0 ± 1.2	0.568	4.5 ± 1.6	4.6 ± 1.5	0.674
STS risk score	6.9 (4.0–10.5)	6.1 (4.4–10.1)	6.7 (4.0–10.3)	0.021	6.9 (4.2–10.5)	7.5 (4.3–10.6)	0.013
Echocardiographic characteristics							
AV peak velocity (m/s)	4.58 ± 0.72	4.59 ± 0.64	4.62 ± 0.75	0.387	4.47 ± 0.78	4.52 ± 0.73	0.425
Mean AV pressure gradient (mmHg)	51.4 ± 19.5	51.5 ± 18.3	52.4 ± 19.2	0.412	49.9 ± 19.6	52.7 ± 19.9	0.529
AV area (cm^2)	0.63 ± 0.18	0.62 ± 0.17	0.63 ± 0.18	0.724	0.65 ± 0.19	0.63 ± 0.18	0.656
LV GLS (%)	-15.3 ± 4.1	-15.3 ± 4.3	-15.4 ± 4.2	0.672	-15.1 ± 4.3	-15.3 ± 4.0	0.659
LVEF (%)	52.3 ± 7.8	53.3 ± 13.2	52.8 ± 13.1	0.538	52.9 ± 13.4	49.3 ± 14.6	0.653
LVESVI (ml/m^2)	46.2 ± 17.8	45.2 ± 18.5	47.2 ± 17.6	0.516	45.2 ± 17.2	45.5 ± 16.8	0.687
LVEDVI (ml/m^2)	96.9 ± 19.3	94.7 ± 18.9	98.6 ± 18.8	0.587	95.5 ± 19.7	96.4 ± 19.6	0.492
LVMI (g/m^2)	136.3 ± 21.6	103.8 ± 10.5	150.8 ± 29.5	< 0.001	104.6 ± 10.2	163.8 ± 35.8	< 0.001
SVI (ml/m^2)	51.6 ± 8.8	53.6 ± 8.4	49.6 ± 9.5	0.362	51.8 ± 8.3	48.4 ± 9.7	0.441
LAVI (mL/m^2)	51.3 ± 16.6	45.4 ± 16.2	44.8 ± 16.8	0.419	59.3 ± 19.6	65.9 ± 17.7	0.685
Mitral regurgitation ≥ moderate	78 (13.0)	8 (7.2)	22 (9.2)	0.039	8 (14.8)	40 (20.1)	0.016
Tricuspid regurgitation ≥ moderate	45 (7.5)	5 (4.6)	15 (6.3)	0.040	4 (7.4)	21 (10.6)	0.027
Procedural characteristics and 30 day-outcomes							
Transfemoral access	532 (88.5)	101 (91.8)	210 (88.2)	0.763	46 (85.2)	175 (87.9)	0.812
Implanted valve size							
20 mm	36 (6.0)	6 (5.5)	12 (5.1)	0.67	4 (7.4)	14 (70.3)	0.516
23 mm	242 (40.3)	48 (43.6)	107 (45.0)	0.595	19 (35.2)	68 (34.2)	0.628
26 mm	237 (39.4)	39 (35.5)	87 (36.6)	0.543	23 (42.6)	88 (44.2)	0.669
29 mm	86 (14.3)	17 (15.5)	32 (13.4)	0.732	8 (14.8)	29 (14.6)	0.645
Major vascular complication	35 (5.8)	7 (6.4)	13 (5.5)	0.698	3 (5.6)	12 (6.0)	0.697
Myocardial infarction	20 (3.3)	3 (2.7)	7 (2.9)	0.783	2 (3.7)	8 (4.0)	0.886
Disabling stroke	16 (2.7)	3 (2.7)	5 (2.1)	0.542	2 (3.7)	6 (3.0)	0.516
Moderate-severe PVL	14 (2.3)	2 (1.8)	4 (1.7)	0.553	2 (3.7)	6 (3.0)	0.497
Major bleeding	27 (4.5)	4 (3.6)	10 (4.2)	0.498	3 (5.6)	10 (5.0)	0.531
ICU stay (day)	2.0 ± 1.1	1.8 ± 1.1	2.0 ± 1.0	0.523	1.9 ± 1.0	2.2 ± 1.2	0.673
Length of hospital stay (day)	4.5 (2.3–5.8)	4.1 (2.1–5.5)	4.8 (2.5-6.0)	0.462	4.3 (2.5–5.8)	4.9 (2.3–6.2)	0.508
Medications at discharge							
ACE inhibitor/ARB	436 (72.5)	47 (42.7)	189 (79.4)	< 0.001	21 (38.9)	179 (89.9)	< 0.001
Beta blocker	435 (72.3)	42 (38.2)	178 (74.8)	< 0.001	29 (53.7)	186 (93.4)	< 0.001
Diuretics	162 (27.0)	12 (10.9)	66 (27.7)	< 0.001	9 (16.7)	75 (37.7)	< 0.001
SGLT2i	53 (8.8)	8 (7.3)	20 (8.4)	0.694	5 (9.3)	20 (10.1)	0.792

Values are number (%), mean (SD) or median (IQR).

ACE, angiotensin-converting enzyme, ARB angiotensin II receptor blocker; AV, aortic valve, BSA, body surface area; CKD, chronic kidney disease; COPD, chronic obstructive lung disease; GLS, global longitudinal strain; LAVI, left atrial volume index; LV, left ventricular; LVEDVI, left ventricular end-diastolic volumes index; LVEF, left ventricular ejection fraction; LVESVI, left ventricular end-systolic volume index; LVMI, left ventricular mass index; NYHA, New York Heart Association; NOAC, non-vitamin K antagonist oral anticoagulant agent; PCI, percutaneous coronary intervention; POAF, postoperative atrial fibrillation; STS, Society of Thoracic Surgeons; SVI, left ventricular stroke volume index; PVL, paravalvular leak; SGLT2i, sodium-glucose transport protein 2 inhibitor; VKA, vitamin K antagonist

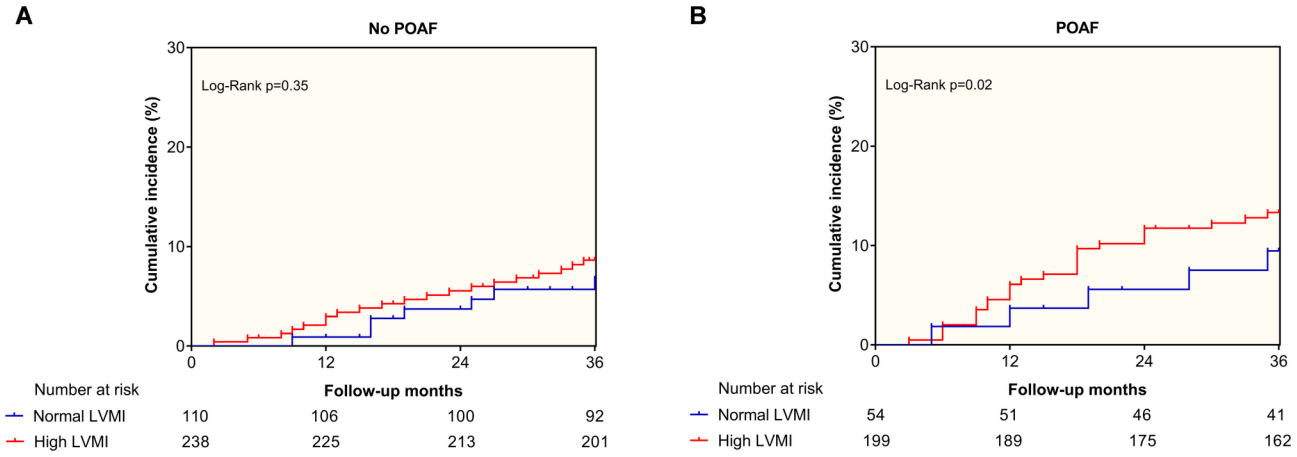

Fig. 2 Cumulative incidence of the primary composite outcome (all-cause death, disabling stroke, and rehospitalization due to heart failure) for patients with normal LVMI versus high LVMI in No POAF group (**A**) and POAF group (**B**). LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation

Table 2 The incidence of each component of composite outcomes (all-cause death, stroke, and rehospitalization due to heart failure) at 3 years

No POAF		**Normal LVMI (*n* = 110)**	**High LVMI (*n* = 238)**	***p* valve**
	Total	7 (6.4)	20 (8.4)	0.012
	All-cause death	2 (1.8)	9 (3.8)	0.009
	Disabling stroke	3 (2.7)	5 (2.1)	0.476
	Rehospitalization due to heart failure	2 (1.8)	6 (2.5)	0.033
POAF		Normal LVMI (*n* = 54)	High LVMI (*n* = 199)	p valve
	Total	5 (9.3)	26 (13.1)	0.007
	All-cause death	1 (1.9)	7 (3.5)	0.015
	Disabling stroke	2 (3.7)	6 (3.0)	0.538
	Rehospitalization due to heart failure	2 (3.7)	13 (6.5)	0.024

Values are number (%). LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation

-8.2 ± 4.1 vs. +1.3 ± 1.5 ml/m^2, $p = 0.008$; LAVI: -6.5 ± 12.8 vs. -1.3 ± 15.7%, $p = 0.022$). Baseline LVMI (β = -1.73, $p < 0.001$) and POAF (β = 1.46, $p < 0.001$) were independent predictors of change in LVMI at one year (Table 3).

Discussion

The main findings of this study are: (1) POAF after TAVR was associated with an increased risk of all-cause mortality and HF rehospitalization. (2) The incidence of LVMI regression was lower in POAF patients, which was associated with worse clinical outcomes. (3) POAF after TAVR was associated with impaired cardiac reverse remodeling.

The mean age of the cohort in our study (76 years) appears younger than that even in contemporary TAVR practice. The European Society of Cardiology guidelines recommend TAVR for patients aged ≥ 75 years [2]. The American College of Cardiology/American Heart Association guidelines recommend transfemoral TAVR is recommended for those aged 65 to 80 years age [3]. The mean age in the other TAVR observational study cohorts was also younger, at 69.0 [16] and 77 years [17], respectively. A plausible explanation could be that this study included a relatively younger but high-risk population with major organ dysfunctions (e.g., malignancy, neurological impairment, gastrointestinal disease, or frailty) who were deemed less suitable for surgery.

The frequency of POAF in our study (42%) was much higher than previously published clinical trials and other observational studies (10-30%) [18–19]. This may be due to a variety of reasons: (1) non-femoral approach is one of the major predictors for POAF and this study included much higher number of patients with non-femoral approach [20]. (2) Previous clinical trials had considered NOAF only if their patients were found to have NOAF on discharge [21]. In our study, patients were monitored using in-hospital continuous ECG telemetry after TAVR, which may also lead to a higher detection rate of NOAF. (3) Some studies also demonstrated POAF rates as high as 41-59% with TAVR within 2 weeks of the procedure [22–24].

LV pressure unloading after TAVR is an important driving factor of LV mass regression [25]. In addition, because TAVR reduced LV wall stress and intracavitary pressure, improvements in diastolic subendocardial perfusion were observed shortly after surgery, thereby enhancing LV longitudinal function [26]. Thus, when the cause of LV dysfunction is afterload mismatch rather than irreversible myocardial damage (due to fibrosis or co-existing coronary artery disease), postoperative function can improve almost immediately. Many studies have shown that a greater decrease in LV mass 30 days after TAVR was associated with lower hospitalization rates in patients with severe symptomatic AS and severe LV hypertrophy [27–28]. However, residual

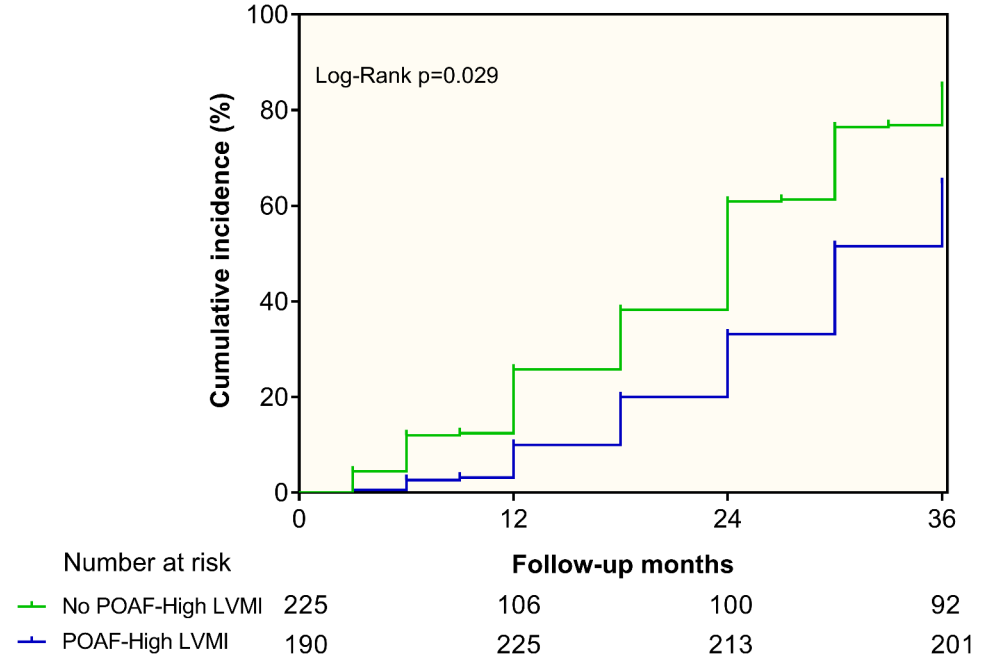

Fig. 3 Postoperative LVMI regression in patients with and without POAF. LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation

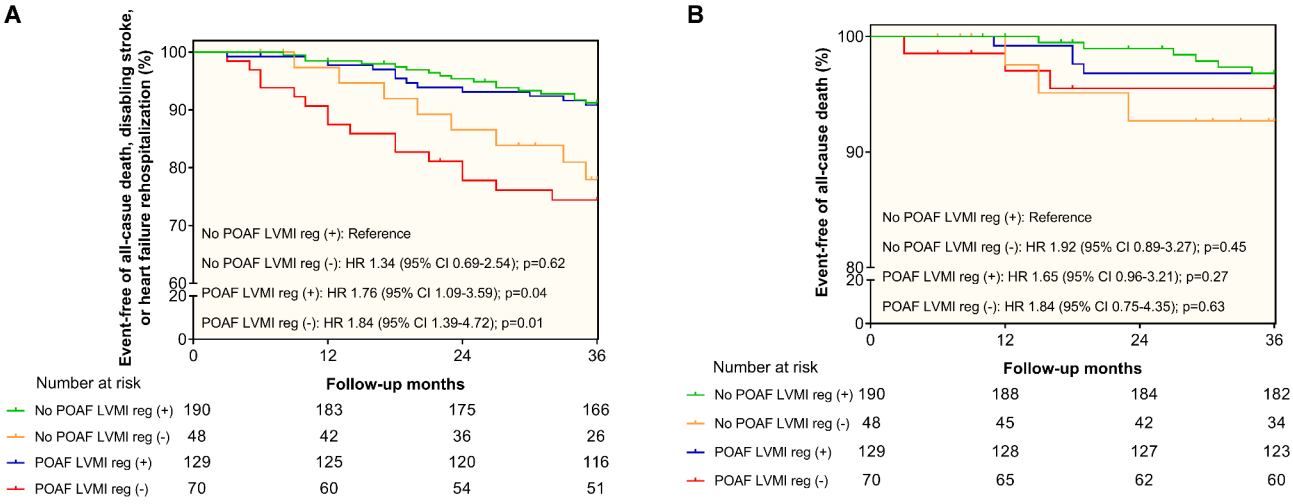

Fig. 4 Kaplan–Meier estimated event-free of all-cause death, disabling stroke, and heart failure rehospitalization (**A**) and event-free of all-cause death (**B**) in patients with and without POAF and LVMI regression. LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation

severe LV hypertrophy after TAVR was associated with a 71% increase in all-cause and cardiovascular mortality and an 89% increase in the risk of rehospitalization [29]. Thus, reverse remodeling has been linked to a substantial impact on clinical outcomes.

In many previous studies, both pre-existing AF and new-onset POAF have been reported to be associated with increased mortality, rehospitalization due to HF and stroke after TAVR [30–32]. Risk of stroke after TAVR can be affected by various factors, including antithrombotic regimens. Patients with AF and high CHA2DS2-Vasc score who underwent TAVR are currently recommended to receive a single oral anticoagulant or combination of an anticoagulant with an antiplatelet agent [33]. In addition, no bleeding events have been recorded in patients undergoing catheter ablation of AF treated with rivaroxaban in the 12-month follow-up [34]. In our study, more than 60% of the patients with POAF were treated with oral antiplatelet agents, which may have contributed to the low incidence of postoperative stroke.

The renin–angiotensin–aldosterone system (RAAS) inhibition was found to be associated with LV mass regression and improved clinical outcome after TAVR [35]. However, the present study showed that therapy

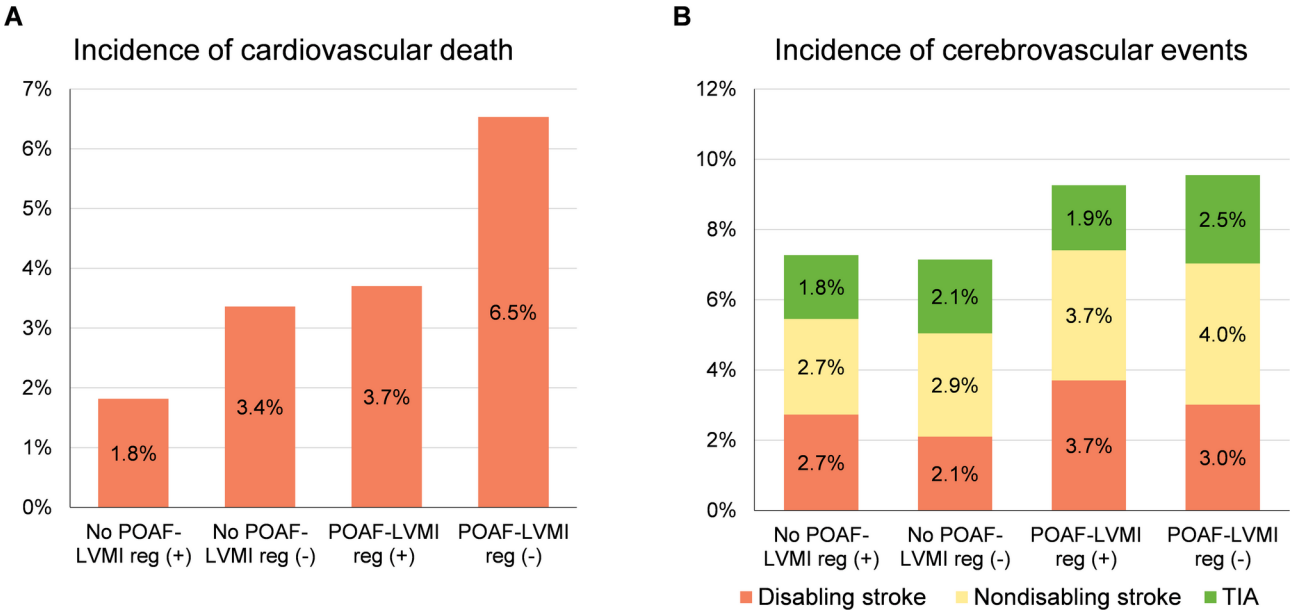

Fig. 5 Incidence of cardiovascular death (**A**) and cerebrovascular events (**B**) according to preoperative LVMI regression in patients with and without POAF. LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation; TIA, transient ischemic attack

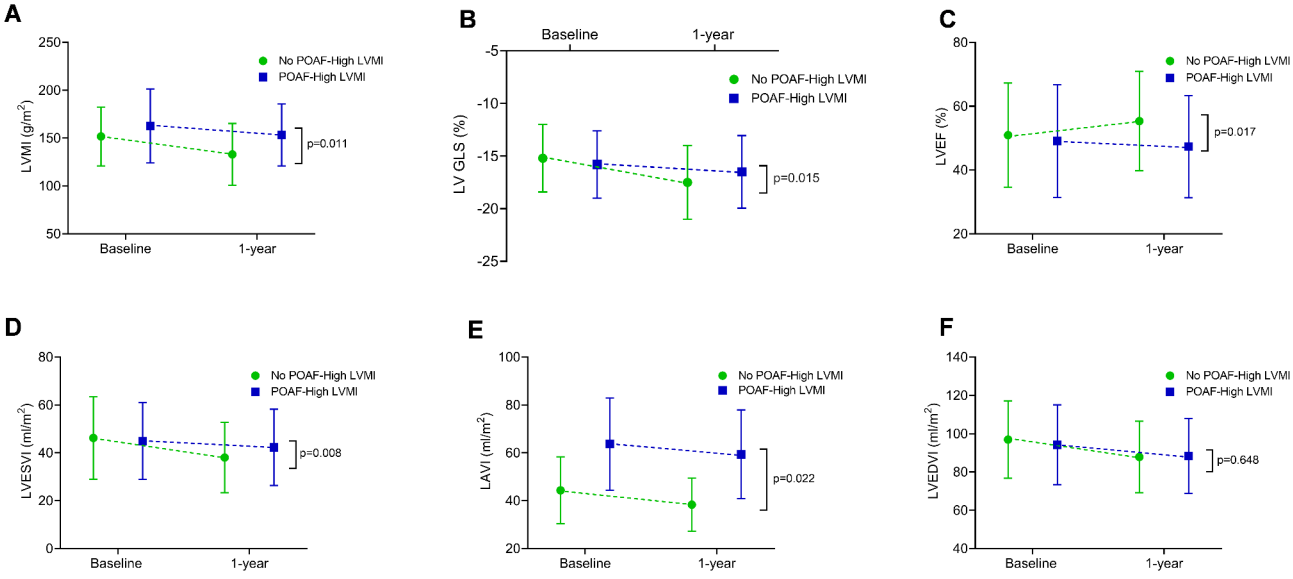

Fig. 6 Changes of echocardiographic parameters following TAVR in LVMI (**A**), LV GLS (**B**), LVEF (**C**), LVESVI (**D**), LAVI (**E**), and LVEDVI (**F**) in patients with and without POAF and high LVMI. GLS, global longitudinal strain; LAVI, left atrial volume index; LV, left ventricular; LVEDVI, left ventricular end-diastolic volumes index; LVEF, left ventricular ejection fraction; LVESVI, left ventricular end-systolic volume index; LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation; TAVR, aortic valve replacement

with ACE inhibitor or ARBs was not a significant predictor of change of LVMI, which was consistent with previous research [36]. Studies have shown that AF can lead to progressive ventricular remodeling through tachycardia and irregular ventricular rhythm [37]. Irregular cycle length in AF is known to result in poor hemodynamics including increased LV pressure [38], which leads to increased wall stress and thickness [39]. Furthermore, LV fibrosis in patients with AF may reflect the same process in the LV that leads to atrial fibrosis and triggers AF recurrence [40] AF-related ventricular remodeling leads to myocardial fibrosis, ventricular dilatation, and mitral and tricuspid regurgitation, all of which impair ventricular diastolic and systolic function [41]. After catheter ablation of patients with systolic dysfunction, it was found that LVEF increased significantly in non-fibrotic patients compared to fibrotic patients [42]. In addition, patients with mild LV interstitial fibrosis showed a

Table 3 Univariate and multiple regression analysis for the change of LVMI

Variables	Univariate analysis		Multiple analysis	
	β (95% CI)	*p* value	β (95% CI)	*p* value
Age	0.05 (−0.62 to 1.96)	0.443		
Male	−2.98 (−4.53 to 5.70)	0.607		
Coronary artery disease	−3.54 (−8.22 to 3.98)	0.896		
Hypertension	0.28 (-0.96 to 1.84)	0.279		
Baseline LV GLS	−1.80 (−3.62 to 2.79)	0.313		
Baseline LVMI	−2.68 (−4.53 to −1.89)	< 0.001	−1.73 (−3.53 to −0.998)	< 0.001
POAF	2.73 (1.13 to 3.38)	< 0.001	1.46 (1.29 to 2.75)	< 0.001
Postprocedural perivalvular leakage	−1.16 (−6.81 to 1.13)	0.259		
ACE inhibitor/ARB	−1.07 (−3.16 to 1.35)	0.458		

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CI, confidence interval; HR, hazard ratio; LV, left ventricular; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; POAF, postoperative atrial fibrillation. Postprocedural perivalvular leakage refers to the abnormal gap between the artificial heart valve ring and the patient's own ring tissue after heart valve replacement, causing blood leakage through the gap

greater degree of LV reverse remodeling after TAVR, as indicated by more significant improvement in LVMI and GLS [43].

In our study, the cumulative rate of adverse events over 3 years was similar to that previously reported by Izumi et al. [44], who found that the freedom rate from the primary outcome at 12 years was 83.9% vs. 74.3% for patients with LVMI < 102 g/m^2 and those with LVMI ≥ 102 g/m^2, respectively, both of which were around 10% at 3 years. What's more, cardiac reverse remodeling was significantly impaired in patients with POAF in the present study. Ross Agner et al. [45] reported that AF patients had significantly impaired LVMI regression after AVR compared with patients in sinus rhythm, which is consistent with our results. Studies of other diseases, such as arterial hypertension, have found significant LVMI regression in AF patients under antihypertensive medication [46–47]. In turn, another study found a 2% prevalence of AF in patients with LVMI regression, however, 17% in those with LVMI progression [48]. The possible explanation is that LVMI regression reduces LV filling pressure associated with unfavorable left atrial remodeling.

There is increasing evidence that the restoration of sinus rhythm after AF promotes cardiac reverse remodeling and improves clinical outcomes [49]. McCarthy et al. showed that long-term survival was significantly higher in patients who underwent surgical ablation of AF combined with SAVR than in patients without ablation. Furthermore, survival rates were comparable between patients with AF treated by ablation and those without [50]. Another study showed that after SGLT2i therapy initiation, larger reduction was recorded for AF episodes, reduced from 4 [3;8] to 0 [0;3] (*P* value < 0.001) [51]. Therefore, in clinical practice, the restoration of sinus rhythm in POAF patients after TAVR should be strongly advocated to avoid worsening of ventricular dysfunction.

Study limitations

This study has several limitations. First, the cohort consisted of a younger but high-risk population, which may limit generalizability. Second, the incidence of POAF in this study (42%) is much high. This may be due to the fact that this study is a single-center retrospective study, which needs to be verified by multi-center studies with larger samples in the future. Third, only echocardiographic measurements were analyzed in this study. Future studies using cardiac magnetic resonance imaging are needed for accurate assessment of left ventricular mass. Four, arterial afterload and myocardial fibrosis also affected reverse cardiac remodeling after TAVR. Therefore, it was difficult to determine whether changes in LVMI were secondary to POAF or due to other factors. Five, the exact duration of most patients with severe AS was unclear. Thus, the relationship between the duration of AS and the progression of reverse remodeling could not be further analyzed. Finally, this was a single-center study with a small sample size, which raises concerns about selection bias, variability of the procedure, and limited external validity. In the future, we will verify this in a multicenter prospective large sample cohort.

Conclusions

Patients with POAF had less LVMI regression and impaired cardiac reverse remodeling after TAVR, which increased the incidence of all-cause death and heart failure rehospitalization. Therefore, clinicians should be more proactive in monitoring and treating POAF after TAVR.

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No.

Author contributions

YNW and WC were responsible for the study concept and design. HJZ, LFT, and MG were responsible for the acquisition and analysis of data. All authors contributed to the interpretation of the data. HJZ and JL drafted the manuscript. The corresponding authors attest that all listed authors meet authorship criteria. All authors read and approved the final manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding authors upon reasonable request.

Declarations

Ethical approval and consent to participate
This retrospective study was approved by the Institutional Review Board of Southwest Hospital of Third Military Medical University (approval number: KY20210158) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Southwest Hospital of Third Military Medical University waived the need for informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
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