# Abdominal aortic calcification as a potential predictor for postoperative atrial fibrillation in patients with aortic valve stenosis undergoing aortic valve replacement

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# ABSTRACT

**Background:** Postoperative atrial fibrillation (AF) is a common complication of cardiac surgery that has negative implications on patient outcomes. This study aimed to evaluate the effect of abdominal aortic calcification, measured using the Agatston Score, on patients undergoing aortic valve replacement for aortic valve stenosis. **Methods and Results:** This study included 183 patients who underwent aortic valve replacement. Preoperative characteristics and Agatston scores for abdominal aortic calcification were compared between patients with (n = 108) and without (n = 75) postoperative atrial fibrillation. Multivariate analysis showed that a high Agatston Score (derived by a cutoff point of 2767.65; odds ratio, 2.314; 95% confidence intervals (CI) , 1.063–5.041; *P* = 0.035), left atrial volumes (LAV) (derived by a cutoff point of 69.95; odds ratio, 3.176; 95% CI, 1.459–6.914; *P* = 0.004), and age (derived by a cutoff point of 75.5 years old, odds ratio, 3.465; 95% CI, 1.588–7.557; *P* = 0.003) were significant predictors of postoperative atrial fibrillation in patients with aortic valve stenosis, while the severity of abdominal aortic calcification, as measured using the Agatston Score, independently predicted postoperative atrial fibrillation during the second week following aortic valve stenosis. Patients with an Agatston Score exceeding 2767.65 should be considered at high risk and should receive appropriate management to improve outcomes.

Key words: Aortic Valve Stenosis, Valve disease, Atrial Fibrillation, Arrhythmia

# **INTRODUCTION**

Atrial fibrillation that occurs after surgery, known as postoperative atrial fibrillation (POAF), is a frequently encountered complication following cardiac surgical procedures. Studies have indicated that the occurrence of POAF ranges from 20–40% based on reported data, and the incidence can vary significantly depending on factors such as the specific type of cardiac surgery performed, the population under study, the method used to detect atrial fibrillation (AF), and the specific definition of AF utilized in different research studies<sup>9,22)</sup>. POAF contributes to immediate postoperative complications and poses a long-term risk for multiple adverse cardiovascular outcomes. These include recurrent AF, stroke, myocardial infarction, and mortality<sup>22)</sup>.

POAF can be attributed to two commonly recognized mechanisms: ectopic firing and reentry. These mechanisms arise from alterations in the atrial substrate, which can be influenced by preoperative, surgery-induced, and postoperative remodeling processes. These changes create a vulnerable environment within the atrium that facilitates the occurrence of POAF<sup>1,11</sup>. In our previous study, we observed that preoperative tissue Doppler atrial conduction time was a significant independent predictor of POAF. This finding was specifically observed in patients who underwent mitral valve surgery for mitral valve regurgitation or aortic valve replacement for aortic valve stenosis<sup>20,21)</sup>. Another study documented that the presence of abdominal aortic calcification (AAC) can serve as a potential risk predictor for cardiovascular disease<sup>6)</sup>, though there are no further reports on the association between AAC and POAF. Consequently, the objective of the current study was to examine the effect of AAC levels on the occurrence of POAF. Our study focused on assessing the correlation between preoperative AAC and the incidence of POAF in patients diagnosed with aortic valve stenosis (AS). The information obtained in this study may facilitate the development of prophylactic strategies that can be administered in a timely manner.

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## **MATERIALS AND METHODS**

#### Subjects

We conducted a retrospective study involving 186 consecutive patients diagnosed with severe AS who underwent aortic valve replacement (AVR) surgery at our hospital. The study period spanned from June 2009 to August 2022. The exclusion criteria for our study included patients with a prior history of permanent pacemaker or implantable cardioverter defibrillator implantation, those who did not undergo plain computed tomography (CT), and those who were using class I or III antiarrhythmic agents. Following the specified criteria, a total of three patients were excluded from the study because of the absence of a plain computed tomography (CT) scan. Of the 183 patients, 138 underwent isolated AVR, while the remaining 45 underwent a concomitant procedure, including coronary artery bypass grafting (CABG), other valve procedures, a maze procedure, replacement of the ascending aorta, or aortic root implantation.

We used the Agatston score (AgS) to describe the AAC level and collected patient characteristics including sex, age, AAC level, presence of hypertension, diabetes, hyperlipidemia, creatinine level, and preoperative dialysis. This retrospective study was approved by the institutional review board to utilize patient data for analysis and research purposes.

All patients included in the study were subjected to continuous electrocardiogram (ECG) telemetry monitoring for a minimum duration of two weeks after AVR. A diagnosis of atrial fibrillation (AF) was established when any episode lasted longer than five minutes. Cardiologists or anesthesiologists working in the cardiovascular intensive care unit (ICU) who were unaware of the study confirmed the diagnosis of AF and promptly initiated appropriate treatment using medications such as β-blockers, calcium antagonists, antiarrhythmic drugs, and/or defibrillation, if necessary. The patients were categorized into two groups based on the presence or absence of POAF. Various factors including patient characteristics, ECG findings, medication usage, and perioperative parameters were compared between the NPOAF (absence of POAF) and POAF (presence of POAF) groups. Furthermore, owing to the notable difference in the incidence of POAF between the first week postoperatively and later time points, we categorized the POAF group into two subgroups: the s-POAF group (patients with POAF solely within the first week after the operation) and the l-POAF group (patients with POAF lasting beyond the first week).

## Aortic abdominal calcification

A standardized imaging protocol was performed using a 320-detector row CT scanner (Aquilion One Vision; Toshiba Medical Systems, Otawara, Japan) for CT angiography. In our study, we employed AgS<sup>6)</sup> to assess the AAC volume. The AgS was calculated automatically by identifying calcifications within the abdominal aorta, specifically from the origin of the renal artery to the iliac bifurcation, based on an attenuation threshold of 130 Hounsfield units or higher.

#### Surgical technique

Prior to surgery, all preoperative cardiac medications (such as β-blockers, calcium-channel antagonists, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers), except nonsteroidal antiinflammatory drugs, were continued until the day before the procedure. The patients underwent AVR using standard surgical techniques. General anesthesia was induced and maintained with an intravenous infusion of fentanyl and propofol. Muscle relaxation was achieved by using pancuronium. Through median sternotomy, a cardiopulmonary bypass was established using the ascending aortic and bicaval or two-staged right atrial cannulae. Cardiac arrest was achieved through antegrade blood cardioplegia with or without intermittent retrograde cardioplegia. Transverse aortotomy was performed during the surgical procedure to remove the diseased aortic cusps with calcification. This was accomplished by using forceps and a Cavitron Ultrasonic Surgical Aspirator (SonoSurg; Olympus, Tokyo, Japan). Subsequently, the aortic valves were replaced with a bioprosthesis, mechanical prosthesis, or autologous pericardium, depending on the patient's condition. Following the operation, all patients were closely monitored in the intensive care unit (ICU) and gradually recovered from anesthesia within approximately 2 h or the following morning. Once stabilized, the patients were transferred to the general inpatient ward and subsequently enrolled in a rehabilitation program.

## Statistical analysis

Data are reported as mean ± standard deviation. Continuous variables that exhibited a normal distribution were analyzed using Student's t-test and analysis of variance, whereas those that did not conform to a normal distribution were analyzed using the Mann-Whitney Utest. Categorical variables were analyzed using either the chi-squared test or Fisher's exact test. Univariate and multivariate logistic regression analyses were conducted to identify the predictors of POAF, and odds ratios (OR) and 95% CI were calculated. Receiver operating characteristic (ROC) curves were generated to determine the optimal cut-off values for predicting POAF. Statistical analyses were performed using GraphPad Prism (version 6.01; GraphPad Software Inc., San Diego, CA, USA) and IBM SPSS Statistics 23 (IBM Corp., Armonk, NY, USA). Statistical significance was set at P < 0.05.

## **RESULTS**

## **Characteristics of patients**

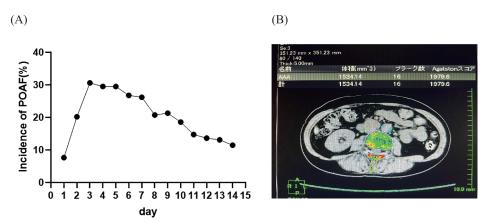
The study cohort consisted of 95 men and 88 women, with an overall mean age of  $74.2 \pm 8.7$  years. The patient characteristics and details of the surgical procedures are presented in Table 1. Patients in the POAF group were significantly older than those in the NPOAF group (67–78 years vs. 72–82 years; P < 0.001). Additionally,

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	No POAF	POAF	t-test	Univari	iate logistic regressio	n analysis
Characteristic	Characteristic $(n = 75)$ $(n = 108)$		<i>P</i> -value	OR	95%CI	Р
Age	73 (67–78)	77 (72–82)	$< 0.001^{b}$	1.079	1.038-1.122	< 0.001
Sex (male)	38 (51)	57 (53)	0.779 <sup>c</sup>	0.919	0.510 - 1.657	0.779
BMI (kg/m²)	23.3 (20.1-26.2)	23.4 (20.6-25.4)	0.724 <sup>b</sup>	1.004	0.923 - 1.092	0.920
BSA (m <sup>2</sup> )	$1.55 \pm 0.17$	$1.57 \pm 0.19$	0.612ª	1.532	0.298 - 7.883	0.610
Hypertension	55 (73)	75 (69)	$0.568^{\circ}$	0.826	0.429-1.592	0.569
Hyperlipidemia	39 (52)	60 (56)	0.635°	1.154	0.639-2.084	0.635
Diabetes	20 (27)	29 (27)	0.978 <sup>c</sup>	1.009	0.519 - 1.964	0.978
HbA1c	5.6 (5.4-6.2)	5.8 (5.4-6.3)	$0.577^{b}$	1.108	0.736 - 1.668	0.623
Smoking	30 (40)	39 (36)	0.593°	0.848	0.462 - 1.555	0.594
COPD	4 (5.3)	5 (4.6)	$1^{d}$	0.862	0.224-3.321	0.829
Creatinine	0.75 (0.68-0.96)	0.9 (0.72-1.19)	$0.006^{\mathrm{b}}$	1.146	0.943-1.392	0.170
Hemodialysis	5 (7)	12 (11)	$0.308^{\circ}$	1.750	0.590 - 5.194	0.313
ACEI/ARB	29 (39)	56 (52)	0.079 <sup>c</sup>	1.708	0.939 - 3.109	0.080
CCB	24 (32)	43 (40)	0.280 <sup>c</sup>	1.406	0.757 - 2.612	0.281
3-blocker	21 (28)	35 (32)	0.525°	1.233	0.647 - 2.351	0.525
Statin	20 (27)	42 (39)	0.086 <sup>c</sup>	1.750	0.921-3.324	0.087
PAF	2(3)	5 (5)	$0.702^{d}$	1.772	0.335-9.384	0.501
BNP	498 (274–1986)	861 (306-2947)	$0.073^{\mathrm{b}}$	1	1	0.156
CRP	0.07 (0.04-0.17)	0.085 (0.04-0.225)	$0.228^{\mathrm{b}}$	1.257	0.740 - 2.135	0.397
LAD	38 (35-42)	40.5 (37-45.75)	$0.018^{\mathrm{b}}$	1.045	0.993 - 1.099	0.090
LAV	59.4 (51.6-53.6)	73.9 (58.05-88.35)	$< 0.001^{\rm b}$	1.025	1.010 - 1.041	0.001
EF	65 (59–68)	63 (57.25-69)	$0.507^{\mathrm{b}}$	0.986	0.956 - 1.018	0.396
AgS	2215 (674-5388)	3848 (1631-6541)	$0.006^{\mathrm{b}}$	1	1	0.067

**Table 1** Characteristics of patients undergoing aortic valve replacement for aortic valve stenosis with POAF or sinus rhythm(no POAF)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; AgS, Agatston score of abdominal aortic calcification; BNP, brain natriuretic peptide; BMI, body mass index; BSA, body surface area; CCB, calcium-channel blocker; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; EF, ejection fractions; LAD, left atrial diameter; LAV, left atrial volume; PAF, paroxysmal atrial fibrillation; POAF, postoperative atrial fibrillation. a. Student's *t*-test; b. Mann-Whitney U test; c. Chi-square test; d. Fisher's exact test.



**Figure 1** (A) Overall incidence of postoperative atrial fibrillation (POAF) by day after surgery; (B) selection and calculation of Agatston score (blue area).

they exhibited higher creatinine levels, left atrial diameters, LAV, and Agatston scores. The other characteristics showed no significant differences between the groups.

## **Effect of factors in POAF**

The overall POAF occurrence rate in the 183 patients with AS was 59% (108/183) (Figure 1A). The AgS among patients with POAF was found to be 3848 (ranging from 1631 to 6541) (e.g, the AgS of a patient in Figure 1B). In contrast, patients without POAF had an AgS of 2215 (ranging from 674 to 5388). A significant difference was

observed between the two groups (z = -2.754, P = 0.006, Mann-Whitney U test).

To account for the significant variation in AgS, we utilized the common logarithm of AgS (lgAgS) for the logistic regression analysis. Univariate analyses (lgAgS: OR, 1.519; 95% CI, 1.077–2.142; P = 0.017) confirmed AgS as a potential risk factor for POAF. Multivariate logistic analyses showed that age (OR, 1.068; 95% CI, 1.023–1.115; P = 0.003) and LAV (OR, 1.024; 95% CI, 1.008–1.039; P = 0.003) were the only significant factors associated with POAF (Table 2).

Variable		Odds ratio	95% CI	<i>P</i> -value
Univariate	lgAgS	1.519	1.077-2.142	0.017
Multivariate	Age	1.068	1.023 - 1.115	0.003
	LAV	1.024	1.008 - 1.039	0.003
	lgAgS	1.208	0.825 - 1.770	0.331

**Table 2** Predictors of POAF (age, LAV, lgAgS)

POAF, postoperative atrial fibrillation; CI, confidence interval; lgAgS, common logarithm of Agatston Score; LAV, left atrial volume

Table 3 Predictors of POAF (level of age, LAV and AgS)

Variable		Odds ratio	95% CI	P-value
Univariate	Age level	3.145	1.703-5.809	< 0.001
	LAV level	3.165	1.699 - 5.897	< 0.001
	AgS level	2.344	1.283 - 4.286	0.006
Multivariate	Age level	3.100	1.586 - 6.058	0.001
	LAV level	3.446	1.772 - 6.704	< 0.001
	AgS level	1.698	0.879-3.281	0.115

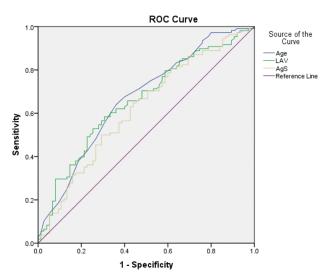
AgS level, Agatston Score level; POAF, postoperative atrial fibrillation; CI, confidence interval; LAV, left atrial volume

We then used the ROC curve to investigate changes in POAF for the different age ranges, LAV, and AgS and determined that their optimal cut-off points were 75.5 (sensitivity, 63.9%; specificity, 64%), 69.95 (sensitivity, 58.3%; specificity, 69.3%), and 2767.65 (sensitivity, 64.8%; specificity, 56%), respectively. (Figure 2). Using this threshold value, we evaluated all patients and labeled them as high (greater than or equal to the cutoff point) or low (less than the cutoff point). The follow analyses also showed that age (OR, 3.100; 95% CI, 1.586–6.058; P = 0.001) and LAV (OR, 3.446; 95% CI, 1.772–6.704; P < 0.001) were the only significant factors associated with POAF (Table 3).

To understand the effect of AgS on the different types of POAF, we subdivided patients with POAF. Among them, 47 patients (44%) had POAF only within the first week postoperatively, 10 patients (9%) had POAF in both the first and second weeks postoperatively, 50 patients (46%) had POAF only within the second week postoperatively, and 1 patient (1%) had POAF only at the 15<sup>th</sup> day postoperatively (Table 4). The compositions of the groups are listed in Table 5.

Additionally, significant differences were identified in terms of age, creatinine level, LAV, and AgS between the NPOAF and l-POAF groups (Tables 6–9). Only LAV showed significant differences between the NPOAF and s-POAF groups (Table 8) (univariate logistic regression: OR, 1.021, 1.003–1.040, P = 0.026)

Further analyses still showed age (OR, 1.098; 95% CI, 1.036–1.163; P = 0.001) and LAV (OR, 1.027; 95% CI, 1.009–1.044; P = 0.003) as the only two significant independent predictors for l-POAF (Table 10; to account for the significant variation in AgS, the common logarithm of AgS was used in calculation here). We then analyzed The differences between the two age groups were analyzed, LAV and AgS, in the l-POAF and NPOAF groups. Multivariate logistic analyses showed that age level (OR, 3.465; 95% CI, 1.588–7.557; P = 0.003), LAV level (OR,



**Figure 2** Area under the ROC curve for age was 0.668 (95% CI: 0.588–0.748; P < 0.001). The optimal cut-off to identify patients at high risk of POAF is 75.5 (sensitivity, 63.9%; specificity, 64%);

The area under the ROC curve for left atrial volume was 0.657 (95% CI:0.577–0.737; P < 0.001). The optimal cutoff for identifying patients at a high risk of POAF was 69.95 (sensitivity, 58.3%; specificity, 69.3%).

The area under the receiver operating characteristic (ROC) curve for the Agatston score was 0.62 (95% CI:0.537–0.703; P = 0.006). The optimal cutoff for identifying patients at a high risk of POAF was 2767.65 (sensitivity, 64.8%; specificity, 56%).

3.465; 95% CI, 1.459–6.914; P = 0.004), and AgS level (OR, 2.314; 95% CI, 1.063–5.041; P = 0.035) could be significant independent predictors of l-POAF (Table 11). Additionally, a positive correlation was observed between age and AgS levels ( $r^2 = 0.07483$ ; P < 0.001) (Figure 3). However, there was no positive correlation between age and LAV ( $r^2 = 0.008381$ ; P = 0.2177), LAD, or AgS levels ( $r^2 = 0.002274$ ; P = 0.5215).

Characteristic	NPOAF (n = 75)	s-POAF (n = 47)	l-POAF (n = 61)	<i>P</i> -value
Age	73 (67–78)	77 (70-81)	78 (70-81)	< 0.001 <sup>b</sup>
Sex (male)	38 (51)	28 (60)	29 (48)	0.428 <sup>c</sup>
BMI (kg/m <sup>2</sup> )	23.3 (20.1–26.2)	23.0 (20.5-25.3)	23.4 (20.8-25.7)	$0.551^{b}$
BSA (m <sup>2</sup> )	$1.55 \pm 0.17$	$1.56 \pm 0.18$	$1.57 \pm 0.19$	0.795ª
Hypertension	55 (73)	32 (68)	43 (71)	0.819°
Hyperlipidemia	39 (52)	27 (57)	33 (54)	0.847 <sup>c</sup>
Diabetes	20 (27)	12 (26)	17 (28)	0.977°
HbA1c	5.6 (5.4-6.2)	5.8 (5.4-6.3)	5.8 (5.5-6.3)	$0.852^{b}$
Smoking	30 (40)	19 (40)	20 (33)	0.650°
COPD	4 (5.3)	1 (2)	4 (7)	$0.625^{d}$
Creatinine	0.75 (0.68-0.96)	0.86 (0.71-1.09)	0.96 (0.72-1.26)	$0.014^{b}$
Hemodialysis	5 (7)	4 (9)	8 (13)	0.443°
ACEI/ARB	29 (39)	22 (47)	34 (56)	$0.150^{\circ}$
CCB	24 (32)	17 (36)	26 (43)	0.443 <sup>c</sup>
β-blocker	21 (28)	14 (30)	21 (34)	0.723°
Statin	20 (27)	14 (30)	28 (46)	0.051°
PAF	2(3)	1 (2)	4 (7)	$0.487^{d}$
BNP	498 (274–1986)	829 (345-2952)	890 (212-3089)	$0.170^{b}$
CRP	0.07 (0.04-0.17)	0.11 (0.03-0.45)	0.08 (0.04-0.16)	$0.339^{b}$
LAD	38 (35-42)	41 (36-45)	40 (37–49)	$0.06^{\mathrm{b}}$
LAV	59.4 (51.6-53.6)	74.7 (58.5-86.6)	73.2 (57.4–96.8)	$0.001^{b}$
EF	65 (59–68)	63 (57–68)	64 (57.5–69.8)	$0.623^{b}$
AgS	2215 (674–5388)	2917 (1364–5571)	4759 (2051–7992)	$0.002^{b}$

**Table 5** Characteristics of patients undergoing aortic valve replacement for aortic valve stenosis with sinus rhythm(NPOAF) and in the POAFI7D and POAFO7D groups

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; AgS, Agatston score of abdominal aortic calcification; BNP, brain natriuretic peptide; BMI, body mass index; BSA, body surface area; CCB, calcium-channel blocker; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; PAF, paroxysmal atrial fibrillation; EF, ejection fractions; LAD, left atrial diameter; LAV, left atrial volume; NPOAF, no postoperative atrial fibrillation; s-POAF, postoperative atrial fibrillation within 7 days after surgery; l-POAF, postoperative atrial fibrillation out of 7 days after surgery. a. Univariate analysis of variance; b. Kruskal-Wallis test; c. Chi-square test, exact significant; d. Fisher's exact test.

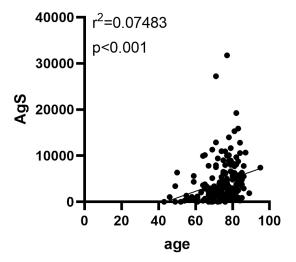


Figure 3 Correlation curve of age and AgS.

Table 4 Composition of groups

	No POAF	s-POAF	ŀ	POAF	
Criteria (d)	0	1–7	8–14	1–14	15
Patients	75	47	10	50	1

Criteria: post-operation time when POAF occurred

#### DISCUSSION

The results of this study indicate that advanced age and LAV could be independent predictors of POAF after AVR in patients with aortic valve stenosis. However, a high AAC level is associated with an increased risk of POAF that continues for two weeks following AVR. A high AgS score could indicate high stiffness in the aortic artery, possibly due to an increased afterload. This stiffness may contribute to the development of long-lasting POAF as a pre-existing condition of the aorta. In the first week after surgery, the impact of surgical stress is more significant than that of the preexisting aortic substrate; therefore, there may be no noticeable difference in AgS between the POAF and non-POAF groups. However, age and LAV might influence the patient's state throughout the course of the disease, including the time of anesthesia maintenance and the surgical procedure, resulting in a significant difference in age and LAV between the POAF and NPOAF groups. In the second week, AgS could become a potential factor that continuously promotes POAF. Moreover, conducting research that separates the influence of surgical stress from that of pre-existing factors is challenging. In our study, we focused on investigating preoperative factors to gain insights into the mechanisms underlying POAF.

Sample1-Sample2	Test Statistic	Std. Error	Std.Test Statistic	Sig.	Adj.Sig.
NPOAF-sPOAF	-22.014	9.846	-2.236	.025	.076
NPOAF-lPOAF	-37.399	9.125	-4.099	.000	.000
sPOAF-lPOAF	-15.385	10.272	-1.498	.134	.403

 Table 6
 Comparison of age among groups

Std. standard; Sig. significance; Adj, adjusted; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, postoperative atrial fibrillation within 7 days after surgery; lPOAF, postoperative atrial fibrillation out of 7 days after surgery.

Table 7 Comparison of creatinine among groups

Sample1-Sample2	Test Statistic	Std. Error	Std.Test Statistic	Sig.	Adj.Sig.
NPOAF-sPOAF	-16.510	9.852	-1.676	.094	.281
NPOAF-lPOAF	-26.119	9.131	-2.861	.004	.013
sPOAF-lPOAF	-9.608	10.278	935	.350	1.000

Std. standard; Sig. significance; Adj, adjusted; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, postoperative atrial fibrillation within 7 days after surgery; lPOAF, postoperative atrial fibrillation out of 7 days after surgery.

Table 8 Comparison of LAV among groups

Sample1-Sample2	Test Statistic	Std. Error	Std.Test Statistic	Sig.	Adj.Sig.
NPOAF-sPOAF	-26.390	9.855	-2.678	.007	.022
NPOAF-lPOAF	-30.527	9.133	-3.343	.001	.002
sPOAF-lPOAF	-4.138	10.281	402	.687	1.000

Std. standard; Sig. significance; Adj, adjusted; LAV, left atrial volume; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, postoperative atrial fibrillation within 7 days after surgery; lPOAF, postoperative atrial fibrillation out of 7 days after surgery.

Table 9	Comparison	of Agatston sc	ore (AgS) among groups	5

Sample1-Sample2	Test Statistic	Std. Error	Std.Test Statistic	Sig.	Adj.Sig.
NPOAF-sPOAF NPOAF-lPOAF	-8.983 -31.899	9.854 9.133	912 -3.493	.362 .000	1.000 .001
sPOAF-lPOAF	-22.916	10.281	-2.229	.026	.077

Std. standard; Sig. significance; Adj, adjusted; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, postoperative atrial fibrillation within 7 days after surgery; lPOAF, postoperative atrial fibrillation out of 7 days after surgery.

Table 10 Predictors of l-POAF (age, creatinine, LAV, lgAgS)

Variable		Odds ratio	95% CI	<i>P</i> -value
Univariate	Age	1.109	1.052-1.168	< 0.001
	Creatinine	1.185	0.963 - 1.457	0.109
	LAV	1.027	1.010 - 1.044	0.001
	lgAgS	2.028	1.203-3.419	0.008
Multivariate	Age	1.098	1.036 - 1.163	0.001
	LAV	1.027	1.009 - 1.044	0.003
	lgAgS	1.455	0.861 - 2.457	0.161

l-POAF, postoperative atrial fibrillation out of 7 days after surgery; AgS level, Agatston Score level; LAV, left atrial volume

Notably, our study is the first to establish a direct link between AAC levels and POAF occurrence after AVR. These findings contribute to our understanding of the effect of AAC on POAF and emphasize the significance of assessing AAC levels as a potential risk factor for patients undergoing AVR.

POAF, a common complication of cardiac surgery,

Table 11 Predictors of l-POAF (level of age, LAV, lgAgS)

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Variable		Odds ratio	95% CI	<i>P</i> -value
Univariate	Age level	3.644	1.787-7.433	< 0.001
	LAV level	3.043	1.502 - 6.166	0.002
	AgS level	3.294	1.600 - 6.780	0.001
Multivariate	Age	3.465	1.588 - 7.557	0.003
	LAV	3.176	1.459–6.914	0.004
	AgS level	2.314	1.063 - 5.041	0.035

l-POAF, postoperative atrial fibrillation out of 7 days after surgery; AgS level, Agatston Score level; LAV, left atrial volume

has significant implications for hospitalization costs and postoperative outcomes<sup>16)</sup>. Studies by Banach et al. and Filardo et al. showed that POAF increases the risk of stroke, hospital mortality, and long-term mortality in patients undergoing isolated AVR<sup>5,10)</sup>. Swinkels et al. highlighted the importance of restoring sinus rhythm to avoid adverse effects on long-term survival associated with new-onset POAF after AVR<sup>18)</sup>. In our study of 183 patients, 59% developed POAF, leading to a prolonged hospital stay. Thus, a proactive preoperative assessment and prophylactic management of POAF may improve patient prognosis and outcomes.

Numerous risk factors for POAF have been identified. Preoperative factors included older age, male sex, history of AF, LV failure, enlarged left atrium, chronic obstructive pulmonary disease, diabetes mellitus, obesity, and reoperation. Perioperative and postoperative factors include catecholamine use during surgery, respiratory failure, and postoperative LV diastolic dysfunction<sup>5,12</sup>. These findings indicate that POAF is a multifactorial condition, emphasizing the importance of considering all predictors in preoperative assessment. By identifying and addressing these risk factors, proactive measures can be implemented to mitigate the risk of POAF and improve patient outcomes.

Almuwaqqat et al. reported a relationship between POAF, central arterial stiffness, and AF risk; arterial stiffness increased LV end-systolic workload, resulting in left atrial and ventricular remodeling<sup>2)</sup>. The study conducted by Lage et al. highlighted the association between arterial stiffness and AF, indicating that increased arterial stiffness may contribute to the early stages of AF development<sup>15)</sup>. Furthermore, aortic calcification is closely related to aortic stiffness<sup>17)</sup>, and AAC has been identified as a risk predictor of cardiovascular disease<sup>6)</sup>. Building upon these findings, the present study and previous research on the detrimental effects of high AAC levels provide evidence that high AAC serves as a risk factor for the development of POAF following AVR. These findings emphasize the importance of considering the AAC level as a potential marker for assessing the risk of POAF in patients undergoing AVR.

Considering the insights provided by previous studies, it is advisable to assess AAC levels preoperatively as a part of patient risk management. Several methods can be employed to detect AAC, including plain lateral abdominal X-ray films, which offer a straightforward approach with a low radiation dose, but provide only semiquantitative results. Alternatively, CT-based examinations can be utilized by employing either manual or automatic algorithms that enable the rapid and reproducible detection and quantification of calcified areas within vessel walls. These methods facilitate a more comprehensive evaluation of AAC and aid in determining the patient's risk profile13). Recent advancements in imaging technology have made accurate and automated calculations and quantification of AAC levels possible. Sophisticated imaging devices such as computed tomography (CT) scanners equipped with specialized software algorithms can efficiently analyze the extent and severity of AAC. These advanced tools not only enhance the precision of AAC assessment but also save time by automating the process and reducing the need for manual calculations. Consequently, healthcare professionals can obtain reliable AAC measurements conveniently, enabling improved risk assessment and patient management<sup>23)</sup>. Considering the wide variation in AgS, we believe that lgAgS could be a better predictor of POAF

than the raw categories of atherosclerotic cardiovascular disease<sup>14)</sup>. Using an optimal cutoff point to evaluate the AgS level in patients may improve the accuracy of predicting POAF within the second week after AVR.

Several treatments have been shown to be effective in preventing POAF, including the use of  $\beta$ -blockers, sotalol, amiodarone, angiotensin II receptor antagonists, and temporary pacing<sup>3,4,7,8)</sup>. Crystal et al. reported a positive effect of postoperative  $\beta$ -blockers in reducing the incidence of POAF in patients undergoing CABG<sup>7)</sup>. Prophylactic use of  $\beta$ -blockers is the current strategy for preventing POAF in cardiac surgery. However, in our study, we did not find an association between oral βblocker use and the incidence of POAF. This could be attributed to factors such as AV block and heart failure, which may necessitate catecholamine infusion immediately after AVR surgery for aortic stenosis. Nevertheless, based on previous evidence, prophylactic administration of  $\beta$ -blockers is still recommended for the prevention of POAF after cardiac surgerv<sup>19)</sup>.

Additional studies are required to improve the accuracy of POAF prediction by AAC levels. We focused on predicting the risk of POAF in the first week postoperatively using intraoperative factors identified in our previous study and on adding AAC levels to develop a more useful model to predict the occurrence of POAF and administer suitable and timely treatment.

# CONCLUSION

In our retrospective study, we observed a higher likelihood of POAF occurring within the first week after surgery compared to the second postoperative week. POAF has a higher risk of recurrence in the second week after surgery in patients who already have AF within seven days postoperatively. Our findings suggest that advanced age and LAV are independent predictors of POAF in patients with AVS who underwent AVR. A high AAC level, as indicated by a high Agatston score, may be associated with the persistence of POAF for two weeks after aortic valve replacement in patients with aortic valve stenosis.

# **Ethical approval**

The study protocol was governed by the guidelines of the Japanese government and based on the Declaration of Helsinki. This study was approved by the Institutional Research and Ethics Committee of Hiroshima University Hospital.

## Data availability statements

The corresponding author of this article will provide the underlying data upon reasonable request.

# **Disclosure statement**

The authors declare that they have no conflicts of interest related to this study.

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