

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 is a common complication of cardiac surgery and has negative implications for patient outcomes. This study aimed to evaluate the impact of abdominal aortic calcification, measured by the Agatston Score, in patients undergoing aortic valve replacement for aortic valve stenosis.

Methods and Results: A total of 183 patients undergoing aortic valve replacement were included. Preoperative characteristics and Agatston Score of abdominal aortic calcification were compared between patients with (n=108) and without (n=75) postoperative atrial fibrillation. Multivariate analysis showed that the high level of Agatston Score (derived by a cutoff point at 2767.65 Agatston Score, odds ratio, 2.314; 95% CI, 1.063-5.041; P = 0.035), LAV (derived by a cutoff point at 69.95, odds ratio, 3.176; 95% CI, 1.459-6.914; P = 0.004) and age (derived by a cutoff point at 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 the second week after surgery.

Conclusions: Age and left atrial volume could be independent predictors for post operative atrial fibrillation in aortic valve stenosis patients, while the severity of abdominal aortic calcification, as measured by 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 high risk and receive appropriate management to improve outcomes.

Key words: Aortic Valve Stenosis; valve disease; Atrial Fibrillation; arrhythmia; ROC Curve

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 falls within a range of 20% to 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.^[9,22] 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.^[22]

POAF is attributed to two commonly recognized mechanisms: ectopic firing and re-entry. 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 atria, facilitating the occurrence of POAF.^[1,11] In our previous study, we observed that the preoperative tissue Doppler atrial conduction time emerged as a significant independent predictor of POAF. This finding was noted specifically in patients undergoing mitral valve surgery for mitral valve regurgitation or aortic valve replacement for aortic valve stenosis.^[20,21] Another study has documented that the presence of abdominal aortic calcification (AAC) can serve as a potential risk predictor for cardiovascular disease,^[6] but there are no further reports on the association between AAC and POAF. Consequently, the objective of our current study was to examine the impact of AAC level on the occurrence of POAF. In particular, 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 gained from this study may allow us to develop prophylactic strategies that can be administered in a timely manner.

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 Hospital. The study period spanned from June 2009 to August 2022. Exclusion criteria for our study included patients with a prior history of permanent pacemaker or implantable cardioverter defibrillator implantation, those who did not undergo a plain computed

tomography (CT) scan, and individuals who were using class I or III antiarrhythmic agents. Following the specified criteria, a total of three patients were excluded from the study due to the absence of a plain computed tomography (CT) scan. Out of the total 183 patients, 138 individuals underwent isolated AVR, while the remaining 45 patients underwent a concomitant procedure, which included coronary artery bypass grafting (CABG), other valve procedures, maze procedure, replacement of the ascending aorta, or aortic root implantation.

We used the Agatston score (AgS) to describe the level of AAC and collected patient characteristics including sex; age; AAC level; presence of hypertension, diabetes, and hyperlipidemia; creatinine level; and pre-operative dialysis. This retrospective study received approval from 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 following AVR. The diagnosis of atrial fibrillation (AF) was established when any episode lasted longer than five minutes. Cardiologists or anesthesiologist working in the cardiovascular intensive care unit (ICU), who were unaware of the study, confirmed the AF diagnosis and promptly initiated appropriate treatment using medications such as β -blockers, calcium antagonists, anti-arrhythmic drugs, and/or defibrillation if necessary. 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 (absent of POAF) and POAF (present of POAF) groups. Furthermore, due to the notable difference in the incidence of POAF between the first week post-surgery and later timepoints, we categorized the POAF group into two subgroups: s-POAF group (patients with POAF solely within the first week after the operation) and l-POAF group (patients with POAF lasting beyond the first week).

Aortic Abdominal Calcification

The standardized examination protocol for imaging 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 the AgS^[6] to assess the volume of AAC. 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, were continued until the day before the procedure, with the exception of nonsteroidal anti-inflammatory drugs. The patients underwent AVR using standard surgical techniques. General anesthesia was induced and maintained with the intravenous infusion of fentanyl and propofol. Muscle relaxation was achieved using pancuronium. Through a median sternotomy, cardiopulmonary bypass was established using ascending aortic and bicaval or two-staged right atrial cannulae. Cardiac arrest was achieved through antegrade blood cardioplegia, with or without

intermittent retrograde cardioplegia. During the surgical procedure, a transverse aortotomy was performed to remove the diseased aortic cusps with calcification. This was accomplished using forceps and the Cavitron Ultrasonic Surgical Aspirator (SonoSurg, Olympus, Tokyo, Japan). Subsequently, aortic valves were replaced with either 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 hours or by the following morning. Once stabilized, patients were transferred to the general inpatient ward and subsequently enrolled in a rehabilitation program.

Statistical Analysis

The data are reported as the mean \pm standard deviation. Continuous variables that exhibited a normal distribution were analyzed using Student's t-test and analysis of variance, while those that did not conform to a normal distribution were analyzed using the Mann-Whitney U-test. Categorical variables were analyzed using either a Chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were conducted to identify the predictors of POAF, with odds ratios (OR) and 95% confidence intervals (CI) calculated. Receiver operating characteristic (ROC) curves were generated to determine the optimal cutoff values for predicting POAF. Statistical analyses were performed using GraphPad Prism statistical software (version 6.01; GraphPad Software Inc., San Diego, CA, USA) and IBM SPSS Statistics 23 (IBM Corp., Armonk, NY, USA). P-values below 0.05 were considered statistically significant.

RESULTS

Characteristics of Patients

The study cohort consisted of 95 men and 88 women, with an overall mean age of 74.2 ± 8.7 years. Patient characteristics and details of the surgical procedures are presented in Table 1. Patients in the POAF group were found to have a significantly higher age compared to the NPOAF group (ranging from 67 to 78 years old versus 72 to 82 years old, $P < 0.001$). Additionally, they exhibited higher levels of creatinine, left atrial diameter, left atrial volume (LAV) and Agatston score. The other characteristics showed no significant differences between the groups.

Effect of factors in POAF

The overall occurrence rate of POAF in 183 AS patients was 59% (108/183), as shown in Fig. 1(A). The AgS among patients with POAF was found to be 3848 (ranging from 1631 to 6541) (For example, AgS of a patient, Fig. 1(B)). In contrast, patients without POAF had an AgS of 2215 (ranging from 674 to 5388). There was a significant difference 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 logistic regression analysis. By univariate analyses (lgAgS: OR, 1.519; 95% CI, 1.077-2.142; P = 0.017), we confirmed AgS as a potential factor of POAF. The follow multivariate logistic analyses showed 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) as the only two significant factors for POAF (Table 2).

We then used the ROC curve to investigate changes in POAF under different levels of age, LAV and AgS and determined that the optimal cut-off point of them was 75.5 (sensitivity, 63.9%; specificity, 64%), 69.95 (sensitivity, 58.3%; specificity, 69.3%) and 2767.65 (sensitivity, 64.8%; specificity, 56%; Fig. 2). Using this threshold value, we evaluated all patients and labeled them with high level (bigger than or equal with the cut-off point) and low level (smaller than the cut-off point). The follow analyses also showed 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) as the only two significant factors for POAF (Table 3).

To insight the effect of AgS between the different types of POAF patients, we subgroup the POAF patients. Within them, 47 patients (44%) only had POAF within the first week post-operation, 10 patients (9%) had POAF in both the first and the second weeks post-operation, 50 patients (46%) only had POAF within the second week post-operation, and 1 patient (1%) had POAF only at the 15th day post-operation (Table 4). The composition of groups is shown in Table 5.

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

Following 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, we utilized the common logarithm of AgS in calculation here). Then we analyzed the difference between the two level of age, LAV and AgS in l-POAF group and NPOAF group. Multivariate logistic analyses showed age level (OR, 3.465; 95% CI, 1.588-7.557; P = 0.003), LAV level (OR, 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 the significant independent predictors for l-POAF (Table 11). Additionally, there was a positive correlation observed between age and AgS ($r^2= 0.07483$; P < 0.001) (Fig. 3). But there was no positive correlation between age and LAV ($r^2=0.008381$; P=0.2177), LAV and AgS ($r^2=0.002274$; P=0.5215).

DISCUSSION

The results of this study indicate that a high level of age and LAV could be two independent predictors for POAF following AVR in aortic valve stenosis patients. While high level of AAC is associated with an increased risk of POAF that continues for 2 weeks following AVR. High AgS could indicate a high stiffness in the aortic artery,

possibly due to increased afterload. This stiffness may contribute to the development of long-lasting POAF as a pre-existing condition in the aorta. In the initial week after surgery, the impact of surgical stress is more significant than the pre-existing aortic substrate, so there may be no noticeable difference in AgS between the POAF and non-POAF groups. However, the age and LAV might influence the patients' state throughout the course of disease, include the time of anesthesia maintain and surgical procedure, resulted to the significant difference in age and LAV between POAF group and No POAF group. As the second week progresses, AgS could become a potential factor continuously promoting POAF. Moreover, conducting research that separates the influence of surgical stress from pre-existing factors is challenging. In our work, we focus on investigating preoperative factors to gain insights into the mechanisms underlying POAF. Notably, our study is the first to establish a direct link between AAC level and the occurrence of POAF after AVR. These findings contribute to our understanding of the impact of AAC on POAF and emphasize the significance of assessing AAC level as a potential risk factor in patients undergoing AVR.

POAF, a common complication following cardiac surgery, has significant implications on hospitalization costs and postoperative outcomes. ^[16] Studies by Banach et al. and Filardo et al. have shown that POAF increases the risk of stroke, hospital mortality, and long-term mortality in patients undergoing isolated AVR. ^{[5][10]} S 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. ^[18] In our study of 183 patients, 59% developed POAF, leading to a prolonged hospital stay. Thus, proactive preoperative assessment and prophylactic management of POAF could improve patient prognosis and outcomes.

Numerous risk factors have been identified for the development of POAF. Preoperative factors encompass older age, male gender, prior AF history, LV failure, enlarged left atrium, chronic obstructive pulmonary disease, diabetes mellitus, obesity, and reoperation. Perioperative and postoperative factors involve the use of catecholamines during surgery, respiratory failure, and postoperative LV diastolic dysfunction. ^[5,12] These findings indicate that POAF is a multifactorial condition, emphasizing the importance of considering all these predictors in the preoperative assessment. By identifying and addressing these risk factors, proactive measures can be taken to mitigate the occurrence of POAF and improve patient outcomes.

Almuwaqqat et al. reported a relationship of POAF with central arterial stiffness and AF risk; arterial stiffness increased LV end-systolic workload resulted to left atrial and ventricular remodeling. ^[2] 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. ^[15] Furthermore, it is known that aortic calcification is closely related to aortic stiffness, ^[17] and AAC has been identified as a risk predictor for cardiovascular disease. ^[6] Building upon these findings, the present study and previous research on the detrimental effects of high AAC provide evidence that a high AAC level serves as a risk factor for the development of POAF following AVR. These findings emphasize the importance of considering AAC level as a potential marker for assessing the risk of POAF in patients undergoing AVR

procedures.

Considering the insights provided by previous studies, it is advisable to assess the AAC level preoperatively as part of the risk management for patients. Several methods can be employed to detect AAC, including plain lateral abdominal X-ray films, which offer a straightforward approach with low radiation dose but provide only semiquantitative results. Alternatively, CT-based examinations can be utilized, employing either manual or automatic algorithms that enable rapid and reproducible detection and quantification of calcified areas within the vessel walls. These methods facilitate a more comprehensive evaluation of AAC and aid in determining the patient's risk profile.^[13] With recent advancements in imaging technology, accurate and automated calculation and quantification of the AAC level have become 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, reducing the need for manual calculations. As a result, healthcare professionals can obtain reliable AAC measurements more conveniently, enabling improved risk assessment and management for patients.^[23] Considering the wide variation in AgS, we think that IgAgS could be a better predictor for POAF than raw categories for atherosclerotic cardiovascular disease.^[14] Using an optimal cut-off point to evaluate the AgS level of patients may improve the accuracy of predicting POAF within the second week after AVR surgery.

Several treatments have been shown to be effective in preventing POAF, including the use of β -blockers, sotalol, amiodarone, angiotensin-II receptor antagonists, and temporary pacing.^[3,4,7,8] Crystal et al. reported a positive effect of postoperative β -blockers in reducing the incidence of POAF in patients undergoing CABG.^[7] Prophylactic use of β -blockers is a current strategy for preventing POAF in cardiac surgery. However, in our study, we did not find an association between oral β -blocker 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, the prophylactic administration of β -blockers is still recommended in the prevention of POAF after cardiac surgery.^[19]

Additional studies are needed to improve the accuracy of prediction of POAF by AAC level. We are focused on predicting the risk of POAF in the first week post-surgery using intraoperative factors identified in our previous study, and on adding AAC level 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 recurring in the second week post-surgery in patients who already

have AF occurrence within 7 days post-operation. Our findings suggest that high level of age and LAV could be two independent predictors for POAF in patients with AVS underwent AVR. While high level of AAC, indicated by a high Agatston score, may be associated with the persistence of POAF for a duration of 2 weeks following aortic valve replacement in patients with aortic valve stenosis.

Ethical Approval

The study protocol was governed by the guidelines of the Japanese government, based on the Helsinki Declaration. The 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.

REFERENCES

- [1] Andrade, J., Khairy, P., Dobrev, D. and Nattel, S. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. *Circ Res.* 2014;114:1453-1468.
- [2] Almuwaqqat, Z., Claxton, J.S., Norby, F.L., Lutsey, P.L., Wei, J., Soliman, E.Z. et al. Association of arterial stiffness with incident atrial fibrillation: a cohort study. *BMC Cardiovasc Disord.* 2021;21:247.
- [3] Arsenault, K.A., Yusuf, A.M., Crystal, E., Healey, J.S., Morillo, C.A., Nair, G.M. et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. *Cochrane Database Syst Rev.* 2013;2013:CD003611.
- [4] Auer, J., Weber, T., Berent, R., Puschmann, R., Hartl, P., Ng, C-K. et al; Study of Prevention of Postoperative Atrial Fibrillation. A comparison between oral antiarrhythmic drugs in the prevention of atrial fibrillation after cardiac surgery: the pilot study of prevention of postoperative atrial fibrillation (SPPAF), a randomized, placebo-controlled trial. *Am Heart J.* 2004;147:636-643.
- [5] Banach, M., Goch, A., Misztal, M., Rysz, J., Jaszewski, R. and Goch, I.H. Predictors of paroxysmal atrial fibrillation in patients undergoing aortic valve replacement. *J Thorac Cardiovasc Surg.* 2007;134:1569-1576.

- [6] Criqui, M.H., Denenberg, J.O., McClelland, R.L., Allison, M.A., Ix, J.H., Guerci, A. et al. Abdominal aortic calcium, coronary artery calcium, and cardiovascular morbidity and mortality in the Multi-Ethnic Study of Atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2014;34:1574-1579.
- [7] Crystal, E., Connolly, S.J., Sleik, K., Ginger, T.J. and Yusuf, S. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: a meta-analysis. *Circulation.* 2002;106:75-80.
- [8] Dahl, J.S., Videbæk, L., Poulsen, M.K., Pellikka, P.A., Veien, K., Andersen, L.I. et al. Prevention of atrial fibrillation in patients with aortic valve stenosis with candesartan treatment after aortic valve replacement. *Int J Cardiol.* 2013;165:242-246.
- [9] Dobromir, Dobrev., Martin, Aguilar., Jordi, Heijman., Jean-Baptiste, Guichard. and Stanley, Nattel. Postoperative atrial fibrillation: mechanisms, manifestations and management. *Nat Rev Cardiol.* 2019;16:417-436.
- [10] Filardo, G., Hamilton, C., Hamman, B., Hebel, R.F., Asams, J. and Grayburn, P. New-onset postoperative atrial fibrillation and long-term survival after aortic valve replacement surgery. *Ann Thorac Surg.* 2010;90:474-479.
- [11] Heijman, J., Guichard, J.B., Dobrev, D. and Nattel, S. Translational challenges in atrial fibrillation. *Circ Res.* 2018;122:752-773.
- [12] Handa, N., Miyata, H., Motomura, N., Nishina, T., Takamoto, S. and Japan Adult Cardiovascular Database Organization. Procedure- and age-specific risk stratification of single aortic valve replacement in elderly patients based on Japan Adult Cardiovascular Surgery Database. *Circ J.* 2012;76:356-364.
- [13] Imaoka, Y., Ohira, M., Nakano, R., Shimizu, S., Kuroda, S., Tahara, H, Ida, K. et al. Impact of abdominal aortic calcification among liver transplantation recipients. *Liver Transpl.* 2019;25:79-87.
- [14] Janjua, S.A., Massaro, J.M., Chuang, M.L., D'Agostino, R.B., Hoffmann, U. and O'Donnell, C.J. Thresholds for abdominal aortic calcium that predict cardiovascular disease events in the Framingham Heart Study. *JACC Cardiovasc Imaging.* 2021;14:695-697.
- [15] Lage, J.G.B., Bortolotto, A.L., Scanavacca, M.I., Bortolotto, L.A. and da Costa. Darrieux, F.C. Arterial stiffness and atrial fibrillation: a review. *Clinics (Sao Paulo).* 2022;77:100014.
- [16] Mahoney, E.M., Thompson, T.D., Veledar, E., Williams, J. and Weintraub, W.S. Cost-effectiveness of targeting patients undergoing cardiac surgery for therapy with intravenous amiodarone to prevent atrial fibrillation. *J Am Coll Cardiol.* 2002;40:737-745.

- [17] McEniery, C.M., McDonnell, B.J., So, A., Aitken, S., Bplton, C.E., Munnery, M. et al; Anglo-Cardiff Collaboration Trial Investigators.. Aortic calcification is associated with aortic stiffness and isolated systolic hypertension in healthy individuals. *Hypertension*. 2009;53:524-531.
- [18] Swinkels, B.M., de. Mol, B.A., Kelder, J.C., Vermeulem, F.E. and Ten. Berg, J.M. New-onset postoperative atrial fibrillation after aortic valve replacement: effect on long-term survival. *J Thorac Cardiovasc Surg*. 2017;154:492-498.
- [19] Sakamoto, A., Kitakaze, M., Takamoto, S., Namiki, A., Kasanuki, H., Hosoda, S. and JL-KNIGHT study group. Landiolol, an ultra-short-acting beta(1)-blocker, more effectively terminates atrial fibrillation than diltiazem after open heart surgery: prospective, multicenter, randomized, open-label study (JL-KNIGHT study). *Circ J*. 2012;76:1097-11
- [20] Takahashi, S., Fujiwara, M., Watadani, K., Taguchi, T., Katayama, K., Takasaki, T. et al. Preoperative tissue Doppler imaging-derived atrial conduction time can predict postoperative atrial fibrillation in patients undergoing aortic valve replacement for aortic valve stenosis. *Circ J*. 2014;78:2173-2181.
- [21] Takahashi, S., Katayama, K., Watanabe, M., Kodama, H., Taguchi, T., Kurosaki, T. et al. Preoperative tissue Doppler imaging-derived atrial conduction time predicts postoperative atrial fibrillation in patients undergoing mitral valve surgery for mitral valve regurgitation. *Circ J*. 2016;80:101-109.
- [22] Wang, H., Zhang, Y., Xin, F., Jiang, H., Tao, D., Jin, Y. et al. Calcium-induced autonomic denervation in patients with post-operative atrial fibrillation. *J Am Coll Cardiol*. 2021;77:57-67.
- [23] Yoon, Y.E., Han, W.K., Lee, H.H., Chang, M-Y., Huh, K.H., Jung, D.C. et al. Abdominal aortic calcification in living kidney donors. *Transplant Proc*. 2016;48:720-724.

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

Characteristic	No POAF (n = 75)	POAF (n = 108)	t-test...	Univariate logistic regression analysis		
			P-value	OR	95%CI	P
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 ^c	0.919	0.510-1.657	0.779
BMI (kg/m ²)	23.3 (20.1-26.2)	23.4 (20.6-25.4)	0.724 ^b	1.004	0.923-1.092	0.920
BSA (m ²)	1.55 ± 0.17	1.57 ± 0.19	0.612 ^a	1.532	0.298-7.883	0.610
Hypertension	55 (73)	75 (69)	0.568 ^c	0.826	0.429-1.592	0.569
Hyperlipidemia	39 (52)	60 (56)	0.635 ^c	1.154	0.639-2.084	0.635
Diabetes	20 (27)	29 (27)	0.978 ^c	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 ^c	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 ^b	1.146	0.943-1.392	0.170
Hemodialysis	5 (7)	12 (11)	0.308 ^c	1.750	0.590-5.194	0.313
ACEI/ARB	29 (39)	56 (52)	0.079 ^c	1.708	0.939-3.109	0.080
CCB	24 (32)	43 (40)	0.280 ^c	1.406	0.757-2.612	0.281
β-blocker	21 (28)	35 (32)	0.525 ^c	1.233	0.647-2.351	0.525
Statin	20 (27)	42 (39)	0.086 ^c	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 ^b	1	1	0.156
CRP	0.07 (0.04-0.17)	0.085 (0.04-0.225)	0.228 ^b	1.257	0.740-2.135	0.397
LAD	38(35-42)	40.5(37-45.75)	0.018 ^b	1.045	0.993-1.099	0.090
LAV	59.4(51.6-53.6)	73.9(58.05-88.35)	<0.001 ^b	1.025	1.010-1.041	0.001
EF	65(59-68)	63(57.25-69)	0.507 ^b	0.986	0.956-1.018	0.396
AgS	2215 (674-5388)	3848 (1631-6541)	0.006 ^b	1	1	0.067

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.

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

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

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	<i>P</i> -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

Table 4. Composition of groups

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

Criteria: post-operation time when POAF occurred

Table 5. Characteristics of patients undergoing aortic valve replacement for aortic valve stenosis with sinus rhythm (NPOAF) and in the s-POAF and l-POAF groups

Characteristic	NPOAF (n = 75)	s-POAF (n = 47)	l-POAF (n = 61)	P-value
Age	73 (67-78)	77 (70-81)	78 (70-81)	<0.001 ^b
Sex (male)	38 (51)	28 (60)	29 (48)	0.428 ^c
BMI (kg/m ²)	23.3(20.1-26.2)	23.0(20.5-25.3)	23.4(20.8-25.7)	0.551 ^b
BSA (m ²)	1.55 ± 0.17	1.56 ± 0.18	1.57 ± 0.19	0.795 ^a
Hypertension	55 (73)	32 (68)	43 (71)	0.819 ^c
Hyperlipidemia	39 (52)	27 (57)	33 (54)	0.847 ^c
Diabetes	20 (27)	12 (26)	17 (28)	0.977 ^c
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 ^c
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 ^c
ACEI/ARB	29 (39)	22 (47)	34 (56)	0.150 ^c
CCB	24 (32)	17 (36)	26 (43)	0.443 ^c
β-blocker	21 (28)	14 (30)	21 (34)	0.723 ^c
Statin	20 (27)	14 (30)	28 (46)	0.051 ^c
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 ^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

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, patients with POAF solely within the first week after the operation; l-POAF, patients with POAF lasting beyond the first week. a. Univariate analysis of variance; b. Kruskal-Wallis test; c. Chi-square test, exact significant; d. Fisher's exact test.

Table 6. Comparison of age among groups

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

Std. standard; Sig. significance; Adj, adjusted; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, patients with POAF solely within the first week after the operation; IPOAF, patients with POAF lasting beyond the first week.

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-IPOAF	-26.119	9.131	-2.861	.004	.013
sPOAF-IPOAF	-9.608	10.278	-.935	.350	1.000

Std. standard; Sig. significance; Adj, adjusted; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, patients with POAF solely within the first week after the operation; IPOAF, patients with POAF lasting beyond the first week.

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-IPOAF	-30.527	9.133	-3.343	.001	.002
sPOAF-IPOAF	-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, patients with POAF solely within the first week after the operation; IPOAF, patients with POAF lasting beyond the first week.

Table 9. Comparison of Agatston score (AgS) among groups

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

Std. standard; Sig. significance; Adj, adjusted; POAF, postoperative atrial fibrillation; NPOAF, no postoperative atrial fibrillation; sPOAF, patients with POAF solely within the first week after the operation; IPOAF, patients with POAF lasting beyond the first week.

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

Variable		Odds ratio	95% CI	P-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, patients with POAF lasting beyond the first week; AgS level, Agatston Score level; LAV, left atrial volume

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

Variable		Odds ratio	95% CI	P-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, patients with POAF lasting beyond the first week; AgS level, Agatston Score level; LAV, left atrial volume

Fig. 1 (A)

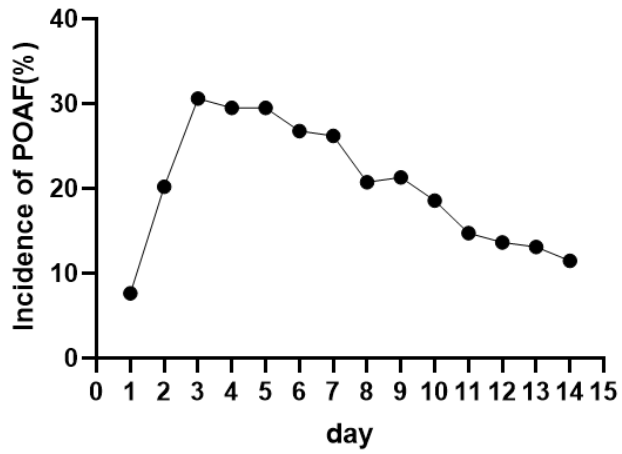


Fig. 1(B)

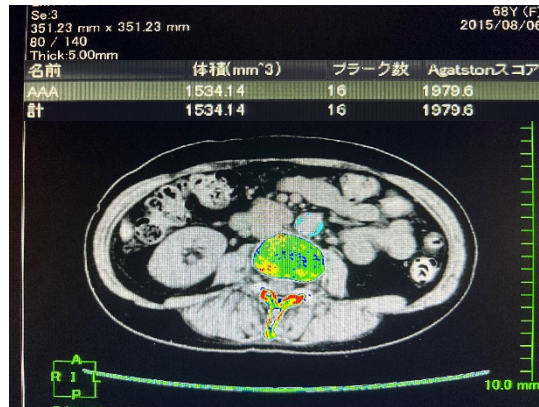


Fig. 2

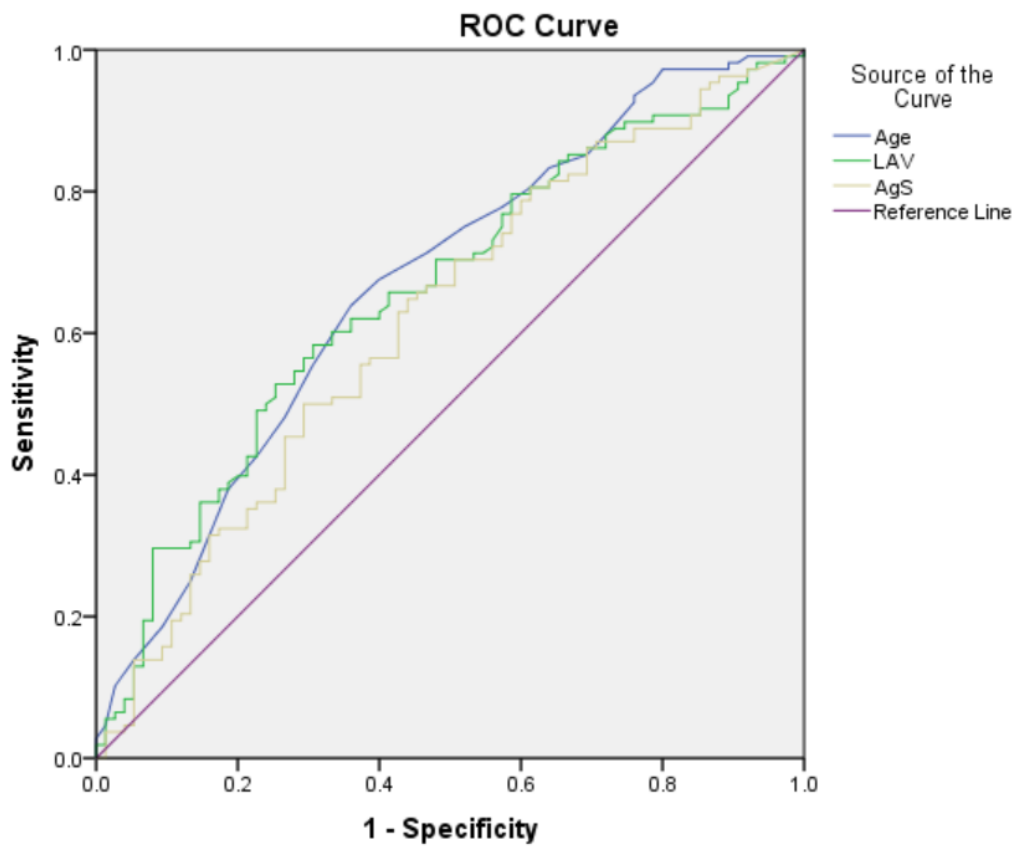


Fig. 3

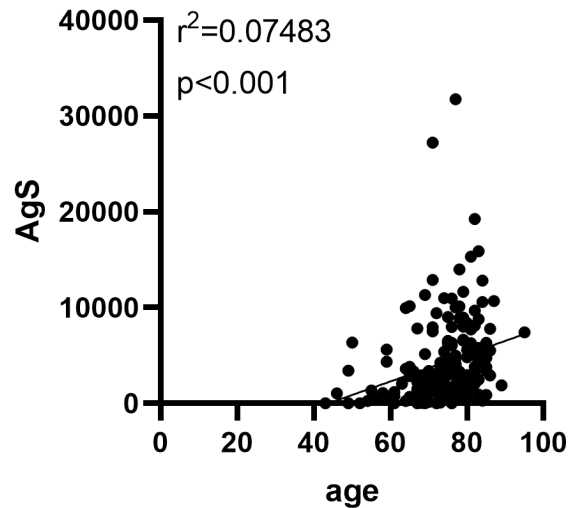


Fig. 1. (A) Overall incidence of postoperative atrial fibrillation (POAF) by day after surgery; (B) selection and calculation of Agatston score (blue area).

Fig. 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%);

Area under the ROC curve for left atrial volume was 0.657 (95% CI: 0.577-0.737; $P < 0.001$). The optimal cut-off to identify patients at high risk of POAF is 69.95 (sensitivity, 58.3%; specificity, 69.3%);

Area under the receiver operating characteristic (ROC) curve for Agatston score was 0.62 (95% CI: 0.537-0.703; $P = 0.006$). The optimal cut-off to identify patients at high risk of POAF is 2767.65 (sensitivity, 64.8%; specificity, 56%);

Fig. 3. Correlation curve of age and AgS.