

Surgical Ablation of Atrial Fibrillation in Patients Undergoing Bioprosthetic Valve Replacement

WonKyung Pyo, M.D., Sung Jun Park, M.D., Wan Kee Kim, M.D.,
Ho Jin Kim, M.D., Joon Bum Kim, M.D., Ph.D., Sung-Ho Jung, M.D., Ph.D.,
Suk Jung Joo, M.D., Ph.D., Cheol Hyun Chung, M.D., Ph.D., Jae Won Lee, M.D., Ph.D.

*Department of Thoracic and Cardiovascular Surgery, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea*

Background: Scarce data have been reported on the efficacy of concomitant atrial fibrillation (AF) ablation in patients undergoing bioprosthetic valve replacement. **Methods:** From 2001 and 2014, 146 consecutive patients (69.3±9.4 years, 84 females) who underwent bioprosthetic heart valve replacement concomitant with AF ablation were assessed. We evaluated long-term rhythm and valve-related outcomes. **Results:** During 49.1 months of follow-up (interquartile range, 22.5–96.8 months), 7 in-hospital and 49 (6.7% per person-year) post-discharge deaths occurred. The thromboembolic event-free survival rate at 5 years was 79.2%±3.5%. The freedom from AF recurrence rate at 5 years was 59.8%±4.9%. Multivariate analysis showed that old age (hazard ratio [HR], 1.06; 95% confidence interval [CI], 1.02–1.11; p=0.002), previous cardiac operation (HR, 3.01; 95% CI, 1.22–7.43; p=0.02), and a large left atrial (LA) dimension (HR, 1.02; 95% CI, 1.00–1.05; p=0.045) were significantly associated with AF recurrence. **Conclusion:** The overall long-term clinical outcomes in these predominantly elderly patients undergoing AF ablation concomitantly with bioprosthetic valve replacement were satisfactory; however, AF recurrence was frequent. Older age, a history of prior cardiac surgery, and large LA size were associated with an increased risk of AF recurrence.

Key words: 1. Arrhythmia surgery
2. Anticoagulants
3. Bioprosthesis
4. Atrial fibrillation
5. Surgical ablation

Introduction

Surgical atrial fibrillation (AF) ablation has been accepted as the most effective procedure to restore sinus rhythm [1-3]. According to several randomized controlled trials and meta-analyses, the addition of AF ablation to mitral valve (MV) surgery reduces the postoperative AF recurrence rate and improves sur-

vival [4,5]. Theoretically, the addition of AF ablation in patients requiring bioprosthetic heart valve replacement may be beneficial by decreasing their likelihood of requiring lifelong systemic anticoagulation.

However, the outcomes of surgical ablation are known to be highly variable according to patients' baseline profile, including factors such as pre-operative left atrial (LA) size, duration and pattern of

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Corresponding author: Jae Won Lee, Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea (Tel) 82-2-3010-3584 (Fax) 82-2-3010-6966 (E-mail) jwlee@amc.seoul.kr

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AF, and age [6,7]. In general, patients who receive valve replacement with a bioprosthetic valve tend to be older and to have multiple comorbidities, with a somewhat shorter life expectancy. Nevertheless, little is known about the true efficacy of concomitant AF ablation in elderly patients undergoing bioprosthetic valve replacement.

Therefore, we present our long-term surgical experiences of AF ablation in patients undergoing bioprosthetic valve replacement, with the goal of evaluating the impact of AF ablation on patients' outcomes.

Methods

1) Study population

Using our institutional electronic database and chart review, we obtained the records of 227 consecutive patients who underwent bioprosthetic replacement of a left-side heart valve concomitantly with AF ablation from January 2001 to December 2014. After exclusion of patients with infective endocarditis, concomitant aortic procedures, and intra-cardiac septal defects, a total of 146 patients were identified. To estimate individual baseline risk for stroke, the CHADS2-VASc score was calculated for each patient (Fig. 1).

The study protocol was approved by the Institutional Review Board of Asan Medical Center (IRB approval no., 2016-0862). The requirement for informed consent from individual patients was omitted because of the retrospective design of this study.

2) Surgical procedures

For aortic valve (AV) replacement, median full sternotomy (n=65) was solely used. For MV replacement, both median full sternotomy (n=78, 80.4%) and a right thoracotomy approach (n=19, 19.6%) were performed. Cardiopulmonary bypass was established by arterial cannula insertion at the distal ascending aorta with single right atrial appendage or bi-caval venous drainage techniques for the patients who underwent sternotomy. The femoral vessel approaches were used with or without internal jugular vein cannulation in the patients who underwent right thoracotomy.

Among the 97 patients (66.4%) who underwent isolated or concomitant MV replacement, 36 (37.1%) had both mitral stenosis and insufficiency, 22

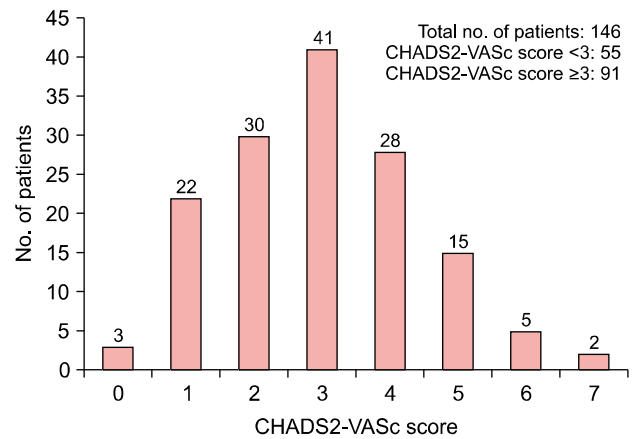


Fig. 1. Distribution of patients by CHADS2-VASc scores.

(22.7%) had mitral stenosis, and 29 (29.9%) had isolated mitral insufficiency. Ten patients (10.3%) had a history of MV surgery or intervention: MV replacement in 2, MV repair in 3, and percutaneous mitral valvuloplasty in 5. A total of 71 (81.6%) of the 87 patients with native valve disease without a previous MV operation had rheumatic pathology. The decision to perform valve repair or replacement was made based on the severity and the mode of the MV dysfunction. The most crucial indicator for rheumatic MV repair was flexibility of the anterior leaflet. Simple commissurotomy was performed in carefully selected patients with stenosis when fibrotic lesions were limited to the commissural sites. Although age was not a major determinant for rheumatic MV repair, younger patients were more likely to undergo repair surgery, as their MV anatomy tends to be more favorable. In contrast, patients with severe rheumatic fibrosis extending to the subvalvular apparatus or predominant stenotic lesions with diffuse leaflet calcification were not considered to be suitable candidates for repair surgery. In certain patients, MV repair was initially attempted, but failed due to severe thickening or retraction of the leaflets. Nevertheless, the final decision on reparability depended on the attending surgeon's discretion.

The lesion sets for the surgical ablation were performed as described previously [8,9]. In brief, right-side ablation was most commonly performed on the beating heart after establishment of cardiopulmonary bypass support, and the lesion included a right atrial free-wall incision, cavo-tricuspid isthmus isolation, and a linear line towards the superior vena

cava. Left-side ablation was performed after cross-clamping the aorta. The lesion included a box lesion isolating the pulmonary veins, a linear lesion connecting the box lesion to the LA appendage orifice, and another linear lesion connecting the pulmonary vein box lesion to the MV annulus.

The choice of whether to perform biatrial or LA-isolated surgical ablation was determined based on individual patients' baseline risk factors for AF recurrence, such as large LA size, old age, long duration and a fine wave pattern (<1 mm) of AF, and the presence of a right-side heart lesion. Patients with atrial flutter or at a high risk of AF recurrence were more likely to undergo biatrial ablation. In patients with paroxysmal AF, LA ablation was favored. Nevertheless, the final decision to perform biatrial or LA ablation was made at the attending surgeon's discretion. Biatrial and LA-isolated ablation was performed in 88 patients (60.3%) and 54 patients (37.0%), respectively. The decision to preserve or to reset the LA appendage was made based on demographic and clinical factors. LA appendage resection was preferred in patients at high risk for thromboembolism, as indicated by thrombi in the LA, comorbidities such as diabetes mellitus, old age, and an advanced degree of tricuspid insufficiency or pulmonary hypertension. However, the final decision was at the discretion of the attending surgeon considering each patient's baseline profile. LA appendage resection was performed in 54 patients (37%). The LA size was reduced in 41 patients (28.1%) by resecting the redundant atrial tissue between the posterior mitral annulus and the inferior pulmonary veins to retain an LA size of less than 4 cm to prevent macro-reentry.

From 2001 to 2005, a modified version of the Cox maze III procedure was performed utilizing liquid nitrogen-based cryo-ablation (Frigitronics Cardiac Cryosurgical System 200, Frigitronics; Cooper Surgical, Shelton, CT, USA) at -70°C . Since 2005, surgical ablation was most commonly performed using an argon-based cryoablation system (SurgiFrost; Medtronic, Minneapolis, MN, USA) at -120°C via the endocardial approach (n=129, 86.3%). Between 2004 and 2008, the microwave energy transfer method was used in limited cases (n=17, 11.6%), utilizing FLEX 4 microwave ablation probes (Afx Inc., Fremont, CA, USA). Since 2008, surgical ablation has most often

been performed employing the argon-based cryoablation system via the endocardial approach (n=129, 86.3%).

3) Outcomes of interests and follow-ups

The primary outcomes of interest were death and valve-related events. Early mortality was regarded as any death that occurred in-hospital or within 30 days of surgery. Valve-related events were defined as reoperation of the operated valve, thromboembolic events, anticoagulation-related bleeding complications, and infective endocarditis, as defined in the Society of Thoracic Surgeon Guidelines [10].

The secondary outcome of interest was rhythm status. In general, patients' rhythm status was evaluated by a follow-up 12-lead electrocardiogram at 3, 6, 12, 18, and 24 months postoperatively and every year thereafter. Twenty-four-hour Holter monitoring was conducted for patients in whom sinus rhythm was considered to have been restored to evaluate the possibility of AF undetected by routine electrocardiogram. Any of the 3 potential AF rhythms (AF, atrial flutter, or atrial tachycardia lasting more than 30 seconds) detected on Holter monitoring was regarded as AF recurrence. Early AF was defined as any AF event that occurred during the initial post-ablation blanking period of 3 months, and late AF was defined as any episode of AF, atrial flutter, or atrial tachycardia detected after the initial blanking period. AF recurrence was defined as any AF documented by electrocardiography after 3 months postoperatively.

4) Postoperative management

Warfarin was routinely administered to patients undergoing bioprosthetic valve replacement for 3–6 months with a target international normalized ratio (INR) of 1.5–2.5. The continuation of warfarin was determined considering coexisting risk factors for thromboembolism, postoperative rhythm status, and the presence/absence of atrial kicking.

The patients displaying atrial tachyarrhythmia were managed with class I/III anti-arrhythmic drugs or electrical cardioversion to restore sinus rhythm. For patients with AF despite antiarrhythmic management, rate control methods with anticoagulation therapy were considered.

Table 1. Baseline characteristics of the patients

Characteristic	Value
Age (yr)	69.3±9.4
Female gender	84 (57.5)
Diabetes mellitus	32 (21.9)
Hypertension	62 (42.5)
Chronic obstructive pulmonary disease	36 (24.7)
End-stage renal disease	2 (1.4)
History of stroke	27 (18.5)
Previous cardiac surgery	7 (4.8)
Hemoglobin (g/dL)	12.8±1.7
Creatinine (mg/dL)	1.0±0.5
Body mass index (kg/m ²)	22.7±3.4
Echocardiographic findings	
LV ejection fraction (%)	53.9±9.7
LV end-systolic dimension (mm)	36.5±9.1
LV end-diastolic dimension (mm)	53.7±9.6
Left atrial dimension (mm)	56.2±10.8
Tricuspid regurgitation ≥grade 3	66 (45.2)
CHAD2-VASc score	
<3	55 (37.7)
≥3	91 (62.3)
European System for Cardiac Operative Risk Evaluation II	
<3	76 (52.1)
≥3	70 (47.9)

Values are presented as mean±standard deviation or number (%). LV, left ventricle.

5) Statistical analysis

Continuous variables are expressed as mean±standard deviation or medians with ranges. Categorical variables are presented as percentages and frequencies. The Kaplan-Meier method was used to assess the conditional probability of survival or freedom from valve-related complications, and the log-rank test was used to compare intergroup differences.

To determine the risk factors for AF recurrence, a stepwise backward multivariate Cox regression analysis was performed. For this analysis, baseline variables with a p-value ≤0.20 in univariate regression models were included in the multivariate models. Thereafter, a stepwise backward elimination technique was performed to leave only variables with a p-value <0.10 in the final multivariate model.

Data were analyzed with SPSS software ver. 12.0 (SPSS Inc., Chicago, IL, USA) and R statistical software ver. 3.3.1 (<https://www.r-project.org/>). All reported p-values were 2-tailed, and p-values ≤0.05

Table 2. Operative details of the patients

Variable	Value
Aortic valve replacement	49 (33.6)
Mitral valve replacement	81 (55.5)
Aortic and mitral valve replacements ^{a)}	16 (11.0)
Concomitant procedures	
Tricuspid valve repair	75 (51.4)
Tricuspid valve replacement	4 (2.7)
Coronary arterial bypass graft	20 (13.7)
Total pump time (min)	165.8±51.9
Cardiac ischemic time (min)	113.6±38.4
Minimally invasive surgery	19 (13.0)
Surgical ablation details	
Lesions	
Bilateral ablation	88 (60.3)
Left atrium-isolated ablation	54 (37.0)
Energy source	
Cryoablation	126 (86.3)
Microwave	17 (11.6)
Left atrial reduction	41 (28.1)
Left atrial appendage resection	54 (37.0)

Values are presented as number (%) or mean±standard deviation. ^{a)}Combined aortic and mitral valve replacements.

were considered to indicate statistical significance.

Results

1) Baseline characteristics and operative profiles

The baseline demographic and clinical characteristics of the patients are summarized in Table 1. The mean age of the patients was 69.3±9.5 years and 84 (57.2%) were women. Baseline echocardiographic data revealed that 42 patients (28.8%) had an LA diameter larger than 60 mm. Operative details are listed in Table 2. Single AV and MV replacements were performed in 49 patients (33.6%) and 81 patients (55.5%), respectively. Double-valve replacements were performed in 16 patients (11.0%). Bilateral ablation was performed in 88 patients (60.3%), while left-side ablation was carried out in 54 patients (37.0%).

2) Clinical outcomes

Early mortality occurred in 7 patients (4.8%). Early complications were observed in 25 patients (17.1%) (Table 3). The follow-up was complete in 118 patients (80.8%). During a median follow-up of 49.1 months (interquartile range, 22.5–96.8 months),

49 patients (6.7%/person-year [PY]) died and 32 (4.4%/PY) experienced major valve-related complications, including thromboembolic events (n=3, 0.4%/PY), anticoagulation-related hemorrhage (n=17, 2.5%/PY), prosthetic valve endocarditis (n=4, 0.6%/PY), and an unplanned valve reoperation (n=8, 1.2%/PY). Fig. 2

Table 3. Clinical outcomes	
Clinical outcomes	Value
Early outcomes	
Early mortality (< 30 day)	7 (4.8)
Early major complications	
Stroke	3 (2.1)
Low-cardiac output syndrome	5 (3.4)
Permanent pacemaker insertion	4 (2.7)
Acute kidney injury	13 (8.9)
Pneumonia	2 (1.4)
Wound infection	3 (2.1)
Bleeding events	14 (9.6)
Late outcomes	
Late death	49 (31.5)
Valve-related complications	
Thromboembolic events	3 (0.4) ^{a)}
Anticoagulation-related hemorrhage	17 (2.5) ^{a)}
Prosthetic valve endocarditis	4 (0.6) ^{a)}
Reoperation	8 (1.2) ^{a)}
Other complications	
Congestive heart failure	15 (2.2) ^{a)}
Permanent pacemaker insertion	9 (1.3) ^{a)}

Values are presented as number (%) or number (%/person-year).
^{a)}%/person-year.

depicts the Kaplan-Meier plots for overall survival (Fig. 2A) and thromboembolic event-free survival (Fig. 2B). The overall survival and thromboembolic free-survival rates at 5 years were 80.6%±3.4% and 79.2%±3.5%, respectively.

The average CHADS2-VASc score and European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) of the study cohort was 3.0±1.5 and 3.5±2.8, respectively. A total of 3 stroke events (0.42%/PY) were observed in patients with a high CHADS2-VASc score (≥3, n=91), while no stroke events occurred in patients with a low CHADS2-VASc score (<3, n=55; p=0.009). There were 32 (9.9%/PY) deaths among patients with a high CHADS2-VASc score (≥3, n=91) and 24 (5.8%/PY) deaths among patients with a low CHADS2-VASc score (<3, n=55; p=0.25). In the subgroups categorized according to the EuroSCORE II, superior overall survival was observed for the low-risk EuroSCORE II subgroup (<3, n=76; 4.4%/PY; p=0.025) in comparison to the high-risk EuroSCORE II subgroup (≥3, n=70; 8.03%/PY). Fig. 3 depicts Kaplan-Meier plots for the overall survival and thromboembolic event-free survival rates according to the CHADS2-VASc score and EuroSCORE II.

3) Rhythm outcomes

During the initial blanking period of 3 months, early AF events were detected in 88 patients (60.3%). Additional AF recurrences were documented in 53 patients (39.6%) during the follow-up period (Table 4). The risk of AF recurrence did not sig-

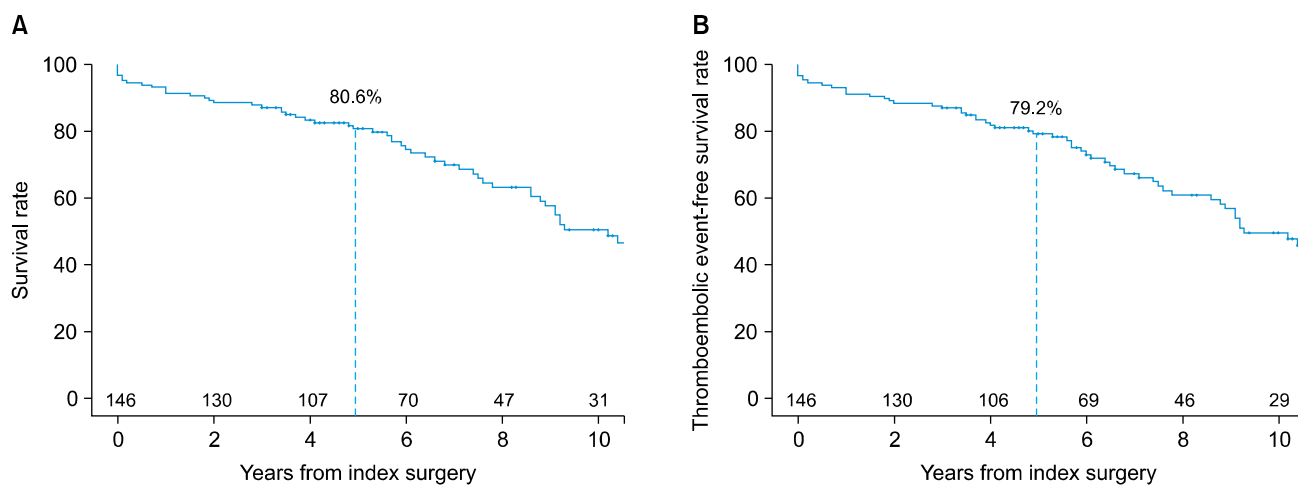


Fig. 2. Kaplan-Meier curves delineating the rates of (A) overall survival and (B) thromboembolic event-free survival in patients undergoing bioprosthetic valve replacement and atrial fibrillation ablation.

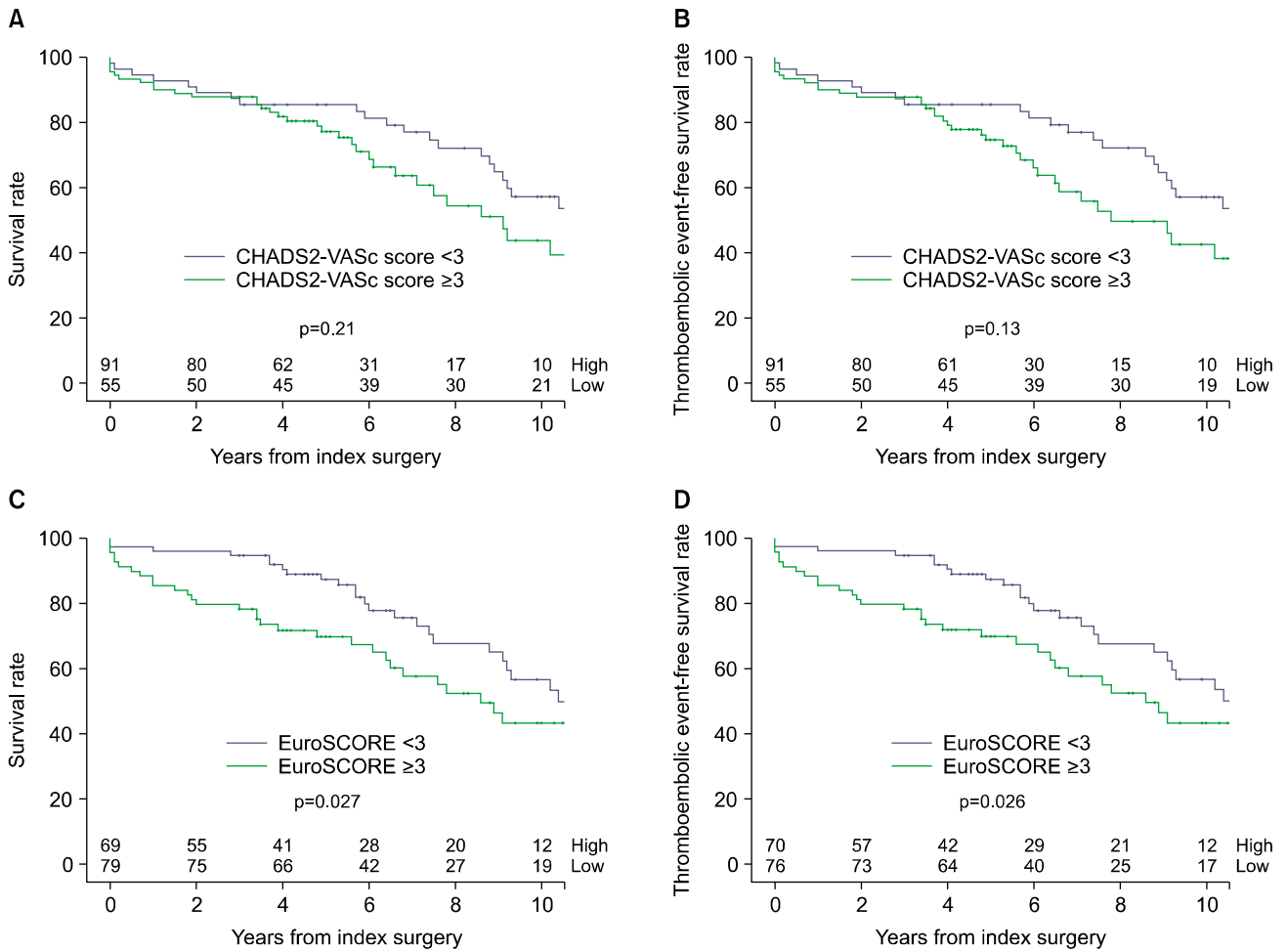


Fig. 3. Kaplan-Meier plots for the rates of (A) overall survival and (B) thromboembolic event-free survival according to the CHADS2-VASc score and EuroSCORE II. EuroSCORE II, European System for Cardiac Operative Risk Evaluation II.

Table 4. Rhythm outcomes (total N=134)	
Rhythm outcomes	No. (%)
Sinus rhythm	68 (50.8)
Atrial fibrillation	
At immediate postoperative state	88 (60.3)
Recurrence	53 (39.6)
Pacemaker rhythm	13 (9.7)

nificantly differ between left-only versus bilateral ablation (hazard ratio [HR], 1.33; 95% confidence interval [CI], 0.76-2.32; p=0.32). The freedom from AF recurrence rates at 1 and 5 years were 83.0%±3.3% and 59.8%±4.9%, respectively (Fig. 4). A permanent pacemaker was implanted in 9 patients throughout the follow-up period. In the multivariate analysis, old age (HR, 1.06; 95% CI, 1.02-1.11; p=0.002), a pre-

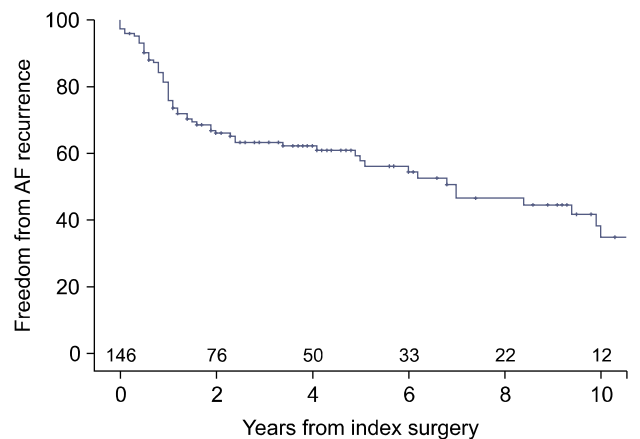


Fig. 4. Kaplan-Meier curve for freedom from AF recurrence among patients undergoing bioprosthetic valve replacement and AF ablation. AF, atrial fibrillation.

Table 5. Univariate and multivariate analyses for atrial fibrillation recurrence

Variable	Univariate		Multivariate	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Age	1.06 (1.02–1.10)	<0.001	1.06 (1.02–1.11)	0.002
Previous cardiac operation	3.09 (1.31–7.28)	<0.001	3.01 (1.22–7.43)	0.02
Left atrium dimension	1.91 (1.12–3.25)	0.002	1.02 (1.00–1.05)	0.045
Tricuspid valve insufficiency	1.14 (0.92–1.34)	0.30		
Left ventricular ejection fraction	0.99 (0.96–1.02)	0.70		
Bilateral ablation	1.33 (0.76–2.32)	0.32		
Cardiac ischemic time	1.00 (0.99–1.04)	0.47		

CI, confidence interval.

vious cardiac operation (HR, 3.01; 95% CI, 1.22–7.43; p=0.02), and a large LA dimension (HR, 1.02; 95% CI, 1.00–1.05; p=0.045) were significantly associated with AF recurrence (Table 5). The most suitable cut-off value of the LA dimension for AF recurrence in our patients was 57.5 mm (sensitivity, 54.4%; specificity, 73.0%; area under the curve, 0.65; p=0.002; lower bound, 0.56; upper bound, 0.75). LA appendage resection did not reduce the rate of AF recurrence; instead, it significantly increased the risk of AF recurrence (HR, 2.18; 95% CI, 1.2–4.0; p=0.01). However, since the surgical ablation lesions were not uniformly applied to all patients, the influence of LA appendage resection on AF recurrence should be carefully interpreted.

4) Anticoagulation treatment

At the time of discharge, 138 of 139 patients (99.3%) were on oral anticoagulation, while 1 was lost to follow-up. Among those 138 patients, anticoagulation-related bleeding occurred in 17 patients (2.37%/PY). Of these, 1 (5.8%) died of bleeding, and 5 stopped anticoagulation immediately due to a life-threatening bleeding event. After discharge from the hospital, discontinuation of anticoagulation therapy was achieved in 93 patients (67.4%). However, 11 of 93 (11.9%) resumed anticoagulation therapy due to several reasons, including 5 redo MV replacements, 3 AF recurrences, 1 case of LA thrombus detection on echocardiography, and 1 case of pulmonary thromboembolism. As a result, 82 patients (59.4%) were documented to have discontinued anticoagulation therapy at the last follow-up. Among the 60 patients who continued anticoagulation therapy at the last follow-up, supplementary aspirin was pre-

Table 6. Anticoagulation or antiplatelet treatments at last follow-up (total N=138)

Anticoagulation treatment	No. (%)
Warfarin (N=60)	
Warfarin only	56 (40.6)
Warfarin with aspirin	2 (1.4)
Warfarin with aspirin and clopidogrel	2 (1.4)
Alternative treatments (N=42)	
NOAC only	6 (4.3)
NOAC with aspirin	1 (0.7)
Aspirin only	27 (19.6)
Aspirin with clopidogrel	8 (5.8)

NOAC, novel oral anticoagulant.

scribed in 2 (1.4%). Table 6 summarizes the state of anticoagulation or antiplatelet treatment at the last follow-up.

Discussion

Surgical AF ablation is well known to be closely associated with improvements in symptoms and hemodynamics, as well as clinical outcomes such as overall survival and the risk of thromboembolic events, when restoration of normal sinus rhythm is successfully achieved in patients with chronic AF. Furthermore, theoretically, elderly patients with AF undergoing valve replacement with a bioprosthesis would receive additional benefits from restoration of sinus rhythm due to the elimination of the necessity of lifelong anticoagulation. Meanwhile, rhythm outcomes after surgical AF ablation procedures are known to be strongly affected by patients' baseline profiles, including factors such as preoperative LA size, duration and pattern of AF, and age [6,7]. In general,

patients who receive valve replacement with a bioprosthetic valve tend to be older and to have multiple comorbidities, with a somewhat shorter life expectancy. However, the efficacy of AF ablation procedures in terms of overall outcomes and rhythm outcomes in this subset of patients has not been thoroughly examined, meaning that the degree to which this procedure is actually beneficial is also not completely understood.

In the present study, we investigated clinical outcomes, as well as rhythm outcomes, in patients who underwent a concomitant surgical AF ablation procedure during bioprosthetic valve replacement. The overall clinical outcomes, including all-cause death (6.7%/PY) and valve-related events (4.4%/PY), were acceptable considering the relatively old age of the patients (69.3±9.5 years) and their high level of baseline comorbidities. The high prevalence of CHADS2-VASc scores of ≥3 (91, 62.3%) and EuroSCORE II values of ≥3 (67, 45.9%) represents the high baseline risk profile of these patients. There have always been safety issues around the addition of an AF ablation procedure, particularly in patients with a high risk profile. Despite the concerns that concomitant AF ablation may increase cardiac ischemic time, which would further aggravate cardiac dysfunction and could possibly be associated with early mortality and morbidity, concomitant AF ablation during bioprosthetic valve replacement does not seem to impose further risks. It seems to be possible to perform the surgical AF ablation procedure in a safe manner without further risks even in elderly, high-risk patients.

Meanwhile, as could have been expected, the rhythm outcomes may seem disappointing, with a freedom from AF recurrence rate of 59.8%±4.9% at 5 years, compared to the outcomes of previous studies performed on patients with valvular AF undergoing MV surgery [11-13]. In other words, however, approximately 60% of patients could have attained AF-free status after AF ablation without additive safety issues. Therefore, 56.5% of patients (78 of 138) were able to discontinue warfarin as of the last follow-up. However, it also seems that particular caution is required before discontinuation of warfarin even in the subset of patients in whom restoration of sinus rhythm is achieved. In our observations, late recurrence of AF also occurred even 5 years after in-

dex surgery, as shown by the Kaplan-Meier curves, and, furthermore, among the 93 patients who initially discontinued warfarin, 4 should have resumed systemic anticoagulation due to recurrent AF or an LA thrombus. For these reasons, particular care should be used when deciding whether to discontinue warfarin, and further watchful observation seems to be required after discontinuation.

In the multivariate analysis, older age, a history of prior cardiac surgery, and large LA size were identified as independent and significant risk factors for postoperative AF recurrence after the maze procedure. These findings are consistent with our previous reports. Old age may correspond to a longer duration of AF, and the surrounding inflammatory responses following prior cardiac surgery may contribute to the long-term rhythm outcomes. Although the long-term rhythm outcomes seemed to be less favorable than expected, we believe that even elderly patients who should undergo bioprosthetic valve replacement can receive benefits from concomitant AF ablation without additional risks if the patients are properly selected and the procedure is appropriately performed.

1) Limitations

This was a retrospective and observational study, meaning that undetected baseline factors may have influenced the clinical outcomes. Since the present study included nearly 15 years of follow-up, heterogeneous surgical procedures and medical management strategies may have been present. Considering the lower target INR compared with Western countries, our results on thromboembolic events may not be generally applicable. A further study comparing clinical outcomes with or without the maze procedure with a randomized controlled design is needed in order to evaluate the efficacy of surgical ablation thoroughly.

2) Conclusion

The overall long-term clinical outcomes in these predominantly elderly patients undergoing AF ablation concomitantly with bioprosthetic valve replacement were satisfactory; however, AF recurrence was frequent. Old age, a history of prior cardiac surgery, and large LA size were associated with an increased risk of postoperative AF.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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ORCID

WonKyung Pyo: <https://orcid.org/0000-0002-5769-052X>
Sung Jun Park: <https://orcid.org/0000-0002-0244-062X>
Wan Kee Kim: <https://orcid.org/0000-0002-1452-8055>
Ho Jin Kim: <https://orcid.org/0000-0002-0809-2240>
Joon Bum Kim: <https://orcid.org/0000-0001-5801-2395>
Sung-Ho Jung: <https://orcid.org/0000-0002-3699-0312>
Suk Jung Joo: <https://orcid.org/0000-0003-4291-302X>
Cheol Hyun Chung: <https://orcid.org/0000-0001-8981-6011>
Jae Won Lee: <https://orcid.org/0000-0003-0751-2458>

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