Predictor of atrial fibrillation recurrence in patients who underwent a tricuspid valve operation with modified Cox maze procedure

Minjung Bak MD1  | Dong Seop Jeong MD2  | Sung-Ji Park MD1  | Boram Park3  | Jeong Hun Seo MD4  | Ilkun Park MD2  | Jihoon Kim MD1  | Su Ryeun Chung MD2  | Eun Kyoung Kim MD1  | Kiick Sung MD2

1 Division of Cardiology, Department of Internal Medicine, Cardiovascular Imaging Center, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
2 Department of Thoracic and Cardiovascular Surgery, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
3 Statistics and Data Center, Samsung Medical Center, Seoul, Republic of Korea
4 Division of Cardiology, Department of Internal Medicine, Kangwon National University Hospital, Chuncheon-si, Gangwon-do, Republic of Korea

Correspondence
Sung-Ji Park, MD, PhD, Division of Cardiology, Department of Internal Medicine, Cardiovascular Imaging Center, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul, Republic of Korea.
Email: tyche.park@gmail.com
Dong Seop Jeong, MD, Department of Thoracic and Cardiovascular Surgery, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea.
Email: opheart1@gmail.com

Abstract
Background: Recurrence of any atrial arrhythmia after surgical ablation is known as a negative predictor of cardiovascular events and total mortality. However, there have been no focused studies for atrial fibrillation (AF) recurrence prediction in patients with significant tricuspid regurgitation (TR), and the risk-benefit estimation of surgical ablation in tricuspid valve (TV) surgery is not fully established.

Method: We screened 385 patients who underwent a TV operation between 2001 and 2017. After excluding patients who did not undergo a maze operation, 158 patients were enrolled. Enrolled patients were divided by recurrence of AF. We analyzed the difference between the AF recurrence group and no AF recurrence group, and AF recurrence factors in terms of clinical risk factors and echocardiographic risk factors. The hazard ratio (HR) and 95% confidence intervals (CIs) were presented using a Cox proportional hazard model.

Results: Among 158 patients, AF recurred in 65 patients within 10 years. For AF prediction, age was most the important clinical factor and right atrium (RA) diameter was the most important echocardiographic parameters. In patients with a larger RA diameter over 49.2 mm, the prevalence of AF recurrence was higher (HR 4.322, 95% CI [2.185–8.549], log rank p value < .001). In clinical outcome, there was no significant difference between the AF recurrence group and the no recurrence group in terms of death, TR recurrence, heart failure, and stroke. However, the risk of permanent pacemaker (PPM) insertion was higher in the AF recurrence group (HR 10.240, 95% CI [1.257–83.480], log rank p value .007) compared to the no recurrence group.

Conclusion: Age and RA enlargement are key predictors of AF recurrence after TV operation with the CM procedure in patients with significant TR.

KEYWORDS
atrial fibrillation, maze, right atrium diameter, structural heart disease, tricuspid valve operation
1 | INTRODUCTION

Ablation of atrial fibrillation (AF) can reduce the risk of cardiovascular events compared to medical treatment, and recurrence of any atrial arrhythmia after ablation can be a predictor of cardiovascular events and total mortality. The benefits of surgical ablation in structural heart disease (SHD) are well recognized, and more than half of the patients with AF undergoing open-heart surgery have concomitant AF surgery these days. Despite ablation, the risk of AF recurrence still remains, and AF recurrence can have negative effects on survival, heart failure exacerbation, and stroke risk.

AF recurrence risk estimation after ablation is not fully established yet as much as its importance. AF recurrence risk estimation is important in respect to decision to additional procedure or decision to continue the anticoagulation. For now, analysis of AF recurrence is usually conducted in patients who undergo general cardiac surgery or mitral valve surgery. However, as far as my knowledge, there is no concerted study for patients with significant tricuspid valve (TV) disease.

The Maze operation is controversial in patients with significant tricuspid regurgitation (TR) resulting from SHD due to concern of recurrence of AF regardless of the Maze operation. There is no established risk benefit estimation for Maze operation in TV surgery. Therefore, in this study, we analyzed predictors of AF recurrence after a modified Cox Maze (CM) procedure in patients with AF who underwent a TR operation and attempted to identify clear cutoffs for the benefits and safety of the CM procedure in TV surgery.

2 | METHODS

2.1 | Study subject and data collection

We retrospectively investigated 385 patients who underwent a TV operation between 2001 and 2017 at Samsung Medical Center in Seoul, South Korea. We enrolled 158 patients who had significant TR with AF who underwent TV repair or replacement and CM procedure. Patients who did not have the CM procedure, did not have a follow-up ECG after 3 months post-op, or had inadequate echocardiographic measurements were not included. Patients were divided by recurrence of AF within 10 years after the TV operation with CM procedure (Figure 1).

The primary endpoint was AF recurrence. We analyzed the difference between the AF recurrence group versus no recurrence group and analyzed the AF recurrence factor in terms of clinical and echocardiographic risk factors. After that, subgroup analysis was done between types of SHD, and between isolated TR and non-isolated TR.

The medical records of the enrolled patients were carefully reviewed by research coordinators. Mortality data for patients who were lost to follow-up were confirmed by National Death Records. The study protocol was approved and the requirement for informed consent of the individual patients was waived by the Institutional Review Board of Samsung Medical Center. This study was conducted according to the principles of the Declaration of Helsinki. (IRB No. 2020-12-054)

2.2 | Surgical technique

Detailed techniques of the cryo-maze procedure were described in our previous report. The cryo-maze procedure was performed with an N2O-based cryoprobe or an argon-based cryoprobe according to surgeons’ preference.

Usually, five lesions were created, including pulmonary vein isolation, mitral isthmus, posterior part of left atrium extending to the left atrial (LA) appendage to box the lesion, cavo-tricuspid-isthmus, and superior vena cava to inferior vena cava (IVC) line. Ablation time was 180 sec. After completion of this procedure, additional cardiac procedures including valve surgery, CABG, or ASD closures were performed.
The opening LA appendage was internally obliterated without an excision using a running 3-0 monofilament suture.

2.3 Definitions

AF recurrence was defined as restoration of AF rhythm at least one time in follow up electrocardiography (ECG) more than 3 months after the operation. Patients who never returned to sinus rhythm were counted in the AF recurrence group and recurrence day was set as zero. All of the ECG taken in outpatient clinic and admission period were included in analysis of AF recurrence after the index procedure. Median follow up duration was 7.6 years.

SHD in this study was defined as more than a moderate degree of valve disease, previous cardiac operation history, or congenital heart such as like atrial septal defects (ASD). Isolated TR without SHD indicates secondary TR caused by AF. Significant VHD indicates more than a moderate degree of valve disease.

Chronic kidney disease was defined as a glomerular filtration rate (GFR) < 60 ml/min/1.73 m² over 3 months and a disease code in medical record. Coronary artery disease was defined as over 50% stenosis in at least one coronary artery on computed tomography (CT) angiography or coronary angiography. TR recurrence was defined as reappearance of more than a moderate degree of TR after restoration to a minimal or mild degree at early after surgery. Stroke was defined as a neurological deficit of abrupt onset caused by ischemia or hemorrhage within the brain.

2.4 Echocardiographic evaluation

Two-dimensional echocardiography was performed using commercially available equipment (Vivid 7, GE Medical Systems, Milwaukee, WI; Acuson 512, Siemens Medical Solution, Mountain View, CA; or Sonos 5500, Phillips Medical System, Andover, MA). Left ventricular end-diastolic dimension (LVEDD) and LV end-systolic dimension (LVESD) were obtained from parasternal views according to the American Society of Echocardiography (ASE) guidelines. LV ejection fraction (EF) was calculated from two-dimensional recordings using the modified biplane Simpson’s method. Relative wall thickness (RWT) and left ventricular mass (LVM) were calculated from linear dimensions using the ASE-recommended formula. LA volume was assessed by the modified biplane area-length method and was indexed to body surface area. Early diastolic mitral inflow velocity (E) was measured using the pulsed wave Doppler method by placing the sample volume at the level of the mitral valve leaflet tips. Tissue Doppler-derived early diastolic mitral annular velocity (e’) was measured from the septal corner of the mitral annulus in the apical four-chamber view. We calculated the E/e’ ratio as an index of left ventricular filling pressure. LA diameter was measured in the apical 4 chamber view or parasternal long axis view at end systole phase and LA diameter over 40 mm was defined as LA enlargement (LAE). RA diameter was measure in a dedicated right heart view from an apical 4 chamber view that includes the entire RA and was not fore-shortened at the end ventricular systole phase from the inner edge to the inner edge at the mid-atrial level. Right ventricular (RV) diameter, Tricuspid annular plane systolic excursion (TAPSE), and TDI-derived tricuspid lateral annular systolic velocity (TV s’) were also measured in a dedicated right heart view. A RA diameter over 45 mm was defined as RA enlargement (RAE). Right ventricular systolic pressure (RVSP) was estimated by maximal TR velocity. RA pressure in RVSP measurement were assumed by IVC diameter and the presence of plethora. IVC diameter was measured at the junction of the hepatic vein approximately 3 cm from the RA in a standard subcostal view at end expiration, perpendicular to the IVC long axis. Quantitative and qualitative measurements of TR severity were performed according to American Society of Echocardiography guidelines.

2.5 Statistical analysis

All data are presented as mean ± SD or median (IQR) for continuous variables and as number and percentage for categorical variables. Continuous variables were evaluated using student t-test or Mann Whitney U test. Categorical variables were compared between groups using the Chi-square test or Fisher’s exact test.

The cumulative incidence of all events was presented as Kaplan-Meier estimate and compared using a log-rank test. The univariable and multivariable Cox proportional hazard model was applied to estimate the hazard ratio (HR) and 95% confidence interval (CI) for AF recurrence. Variance inflation factors (VIF) were used for estimating multi-collinearity between variables. For clinical factors and echo parameters, the final multivariable regression model was determined by backward variable selection method with entry criteria of p-value < .05 and elimination criteria of p value > .10.

The C index or concordance C was considered an overall measure of discrimination in survival analysis, and we tested whether there was a difference between two correlated overall C indices. The optimal cutoff values of RA diameter for predicting AF recurrence was calculated to maximize the product of sensitivity and specificity using receiver operating characteristic (ROC) curves.

All p-values were two-sided, and p-values < .05 was considered statistically significant. Statistical analyses were performed using R Statistical Software (version 3.6.0; R Foundation for Statistical Computing, Vienna, Austria) and SPSS statistics 20 (SPSS Inc., Chicago, IL).

3 RESULTS

3.1 Predictors of AF recurrence

Among 158 patients who underwent TVR or TV repair with CM procedure, 136 patients (86.1%) of them had SHD and the remainder (n = 22) had isolated TR without SHD. A total 134 patients (84.8%) of them did a TR repair and the remaining 24 patients (15.2%) did a TV replacement. Eleven (7.0%) patients did an ASD closure operation and 8 (5.1%) patients did a concomitant CABG. A total 65 of 158 patients (41.1%)
### TABLE 1 Baseline clinical characteristics between no AF recurrence group and AF recurrence group

| Variable                  | No AF recurrence (n = 93) | AF recurrence (n = 65) | p value |
|---------------------------|---------------------------|------------------------|---------|
| **Demographics**          |                           |                        |         |
| Age                       | 57.4 ± 12.0               | 61.0 ± 10.5            | .051    |
| Sex (female)              | 61 (65.6%)                | 40 (61.5%)             | .602    |
| **Cardiovascular risk factors** |                        |                        |         |
| Persistent AF             | 65 (95.6%)                | 52 (100%)              | .345    |
| DM                        | 12 (12.9%)                | 8 (12.3%)              | .912    |
| HTN                       | 20 (21.5%)                | 14 (21.5%)             | .996    |
| CKD                       | 6 (6.5%)                  | 1 (1.5%)               | .241    |
| Stroke Hx.                | 9 (9.7%)                  | 8 (12.3%)              | .600    |
| CAD                       | 2 (2.2%)                  | 3 (4.6%)               | .403    |
| Previous cardiac op       | 8 (8.6%)                  | 5 (7.7%)               | .838    |

**Echocardiographic parameters**

| Variable                  | No AF recurrence (n = 93) | AF recurrence (n = 65) | p value |
|---------------------------|---------------------------|------------------------|---------|
| LVEF (%)                  | 55.8 ± 9.8                | 56.6 ± 8.2             | .759    |
| LAD (mm)                  | 57.3 ± 9.8                | 59.1 ± 10.7            | .266    |
| LAVI (ml/m²)              | 98.2 ± 47.9               | 120.9 ± 88.7           | .316    |
| LAE                       | 92 (98.9%)                | 60 (92.3%)             | .082    |
| RAD (mm)                  | 51.7 ± 8.6                | 58.6 ± 11.5            | .001    |
| RAE                       | 89 (95.7%)                | 64 (98.5%)             | .649    |
| LVEDD (mm)                | 52.1 ± 9.0                | 51.9 ± 9.6             | .843    |
| LVESD (mm)                | 34.6 ± 7.3                | 34.9 ± 8.5             | .822    |
| LVMi (g/m²)               | 109.1 ± 42.0              | 114.6 ± 48.9           | .755    |
| RVSP (mmHg)               | 47.8 ± 17.5               | 52.3 ± 18.4            | .119    |
| E (m/sec)                 | 1.64 ± .5                 | 1.53 ± .61             | .244    |
| e’ (m/sec)                | .087 ± .082               | .084 ± .027            | .779    |
| E/e’                      | 22.9 ± 12.0               | 20.6 ± 14.9            | .089    |
| DT (msec)                 | 438.0 ± 277.4             | 440.0 ± 336.5          | .708    |
| Significant MS            | 37 (39.8%)                | 24 (36.9%)             | .716    |
| Significant MR            | 44 (47.3%)                | 32 (49.2%)             | .812    |
| Significant AS            | 11 (11.8%)                | 5 (7.7%)               | .396    |
| Significant AR            | 17 (18.3%)                | 10 (15.4%)             | .634    |
| Severe TR                 | 57 (61.3%)                | 48 (73.8%)             | .168    |
| Isolated TR               | 11 (11.8%)                | 11 (16.9%)             | .363    |

**Concomitant procedure**

| Variable                  | No AF recurrence (n = 93) | AF recurrence (n = 65) | p value |
|---------------------------|---------------------------|------------------------|---------|
| ASD closure               | 4 (4.3%)                  | 7 (10.8%)              | .202    |
| CABG                      | 2 (2.2%)                  | 6 (9.2%)               | .065    |
| AVR                       | 19 (20.4%)                | 13 (20.0%)             | .947    |
| MVR                       | 55 (59.1%)                | 45 (69.2%)             | .195    |
| DVR                       | 18 (19.4%)                | 12 (18.5%)             | .888    |
| TVR                       | 14 (15.1%)                | 10 (15.4%)             | .955    |

(Continues)

### TABLE 1 (Continued) Surgical information

| Variable                  | No AF recurrence (n = 93) | AF recurrence (n = 65) | p value |
|---------------------------|---------------------------|------------------------|---------|
| EuroScore                 | 5.2 ± 2.1                 | 5.5 ± 2.1              | .278    |
| pump time                 | 149.0 [122.0–189.5]       | 154.0 [120.0–208.0]    | .458    |
| ACC time                  | 115.0 [97.0–152.0]        | 117.0 [93.5–155.5]     | .690    |

Data are presented as mean ± standard deviation, median [25 percentile – 75 percentiles] or n (%).

Abbreviations: ACC, aortic cross clamping; AF, atrial fibrillation; AR, aortic regurgitation; AS, aortic stenosis; ASD, atrial septal defect; AVR, aortic valve replacement; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; DT, deceleration time; DVR(AVR and MVR), double valve replacement; E, early diastolic mitral inflow velocity; e’, early diastolic mitral annular tissue velocity; HTN, hypertension; LAD, left atrium diameter; LAE, left atrium enlargement; LAVI, left atrium volume index; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVEDS, left ventricular systolic diameter; LVMI, left ventricular mass index; RAE, right atrium enlargement; RAD, right atrium diameter; RVSP, right ventricular systolic pressure; MR, mitral regurgitation; MS, mitral stenosis; MVR, mitral valve replacement; TR, tricuspid regurgitation; TV, tricuspid valve; TVR, tricuspid valve replacement.

Statistical significance was defined as p < .05 by student t-test or Mann Whitney U test (continuous variables) or the Chi-square test or fisher’s exact test (categorical variables). The values in bold indicate statistical significance (p < .05).

In baseline characteristics analysis, the AF recurrence group had a larger RAD. There was no significant difference in age, sex, DM, HTN, CKD, stroke history, coronary artery disease, previous cardiac operation history, concomitant procedure, or surgical information between the AF recurrence group and the no recurrence group. With respect to echocardiographic parameters, except for RAD, there were no significant differences between the AF recurrence group and the no recurrence group. Left atrium diameter (LAD), left atrium volume index (LAVI), and left ventricular ejection fraction (LVEF) were not significantly different between two groups. In addition, the proportion of patients with significant valve disease such as more than a moderate degree of mitral stenosis (MS), mitral regurgitation (MR), aortic stenosis (AS), aortic regurgitation (AR), and isolated TR were also not significantly different between the two groups (Table 1).

In a multivariable Cox regression model among clinical factors (Table 2), age was significant risk factor for AF recurrence after adjusting relevant factors. Among echocardiographic parameters, LAVI, RAD, and RVSP were important risk factors for AF recurrence in the multivariable model (Table 3). The C-index value of age for predicting AF recurrence was 59.6%. When this prediction value of age was combined with significant echocardiographic parameters, only RAD had an additive value to the C index, at 69.2% (p < .008, when compared to the C-index of age alone, which was 59.6%) (Figure 2).

The C index value of solitary RAD was 66.5%. The cut-off value for RAD was 49.2 mm, and AF recurred more than four times in
TABLE 2  Clinical risk factor for AF recurrence

| Variable            | Univariable analysis | Multivariable analysis |
|---------------------|----------------------|------------------------|
|                     | HR                   | 95% CI                 | p value | HR                   | 95% CI                 | p value |
| Age                 | 1.037                | 1.014–1.062            | .002    | 1.039                | 1.015–1.063            | .001    |
| Male Sex            | 1.261                | .755–2.107             | .375    | 1.533                | .915–2.570             | .104    |
| DM                  | 1.131                | .537–2.382             | .746    | 1.533                | .915–2.570             | .104    |
| HTN                 | 1.249                | .684–2.282             | .470    | 1.249                | .684–2.282             | .470    |
| CKD                 | .329                 | .046–2.372             | .270    | .329                 | .046–2.372             | .270    |
| Stroke Hx.          | 1.290                | .612–2.717             | .503    | 1.290                | .612–2.717             | .503    |
| CAD                 | 2.177                | .675–7.017             | .193    | 2.177                | .675–7.017             | .193    |
| Previous cardiac op | 1.124                | .450–2.805             | .802    | 1.124                | .450–2.805             | .802    |
| TV operation method | 1.342                | .637–2.825             | .439    | 1.342                | .637–2.825             | .439    |

Abbreviations: CI, confidence interval; HR, hazard ratio; other abbreviations are listed in Table 1.

TABLE 3  Echocardiographic Risk Factor for AF Recurrence

| Variable          | Univariable analysis | Multivariable analysis |
|-------------------|----------------------|------------------------|
|                    | HR                   | 95% CI                 | p value | HR                   | 95% CI                 | p value |
| LVEF (%)          | 1.000                | .973–1.027             | .986    | 1.000                | 1.002–1.010            | .004    |
| LAVI (ml/m²)      | 1.004                | 1.000–1.007            | .029    | 1.004                | 1.002–1.010            | .004    |
| RAD (mm)          | 1.048                | 1.027–1.070            | <.001   | 1.048                | 1.034–1.090            | <.001   |
| LVEDD (mm)        | .993                 | .965–1.022             | .629    | .993                 | .965–1.022             | .629    |
| RVSP (mmHg)       | 1.015                | 1.001–1.030            | .033    | 1.015                | 1.007–1.040            | .006    |
| Severe TR         | 1.491                | .853–2.608             | .161    | 1.491                | .853–2.608             | .161    |
| ASD               | 1.648                | .709–3.831             | .246    | 1.648                | .709–3.831             | .246    |

Abbreviations: CI, confidence interval; HR, hazard ratio; other abbreviations are listed in Table 1.

patients with RAD over 49.2 mm (HR 4.322, 95% CI [2.185–8.549], p value < .001). (Figure 3) When comparing the C index value of solitary echocardiographic parameters for AF recurrence prediction, RAD showed superior predictive value over LAVI (p value = .043, Figure S1).

In subgroup analysis according to valve disease, LAVI and RAD were higher in AF recurrence group compared to non-recurrence group in every subgroup with or without statistical significance (Table S1). In comparison of C index value of LAVI and RAD, C index of RAD was numerically higher than C index of LAVI in every subgroup and statistical significance was prominent in significant mitral regurgitant group (Table S2).

In subgroup analysis between SHD (n = 136, 86.1%) and isolated TR (n = 22, 13.9%), RAD could predict AF recurrence in SHD (HR 1.052, 95% CI [1.028–1.076], p value < .001), and could not in the isolated TR group (HR 1.009, 95% CI [1.096–1.027], p value = .724). The interaction p-value of RA diameter and the presence of isolated TR for AF recurrence was insignificant at .098 (Table S3). In patients with isolated TR, The RA diameter of the AF recurrence group (65.5 ± 14.1 mm) was numerically higher than that of the no recurrence group (60.8 ± 8.8 mm) but there was no significant difference (p value = .353).

Comparing right heart-related echocardiographic parameters between the AF recurrence group and the no AF recurrence group, only IVC diameter showed a significant difference. The IVC diameter was higher in the AF recurrence group, although the RV dysfunction incidence estimated by TAPSE and TVs’ did not differ significantly. Differences of RV size and TV annulus size were also insignificant (Table 4).

When the analysis was performed with 145 patients excluding 13 who had SR and returned to AF during the window period, or who had never received SR, the results did not change significantly. Age (HR 1.038, 95% CI [1.012–1.064], p value = .004) and RAD (HR 1.047, 95% CI [1.025–1.069], p value < .001) were still factors significantly associated with AF recurrence (Table S2). For 145 patients, the optimal cutoff point for AF recurrence was 49 mm, and the probability of AF recurrence was 4.1 times in those with a preoperative RAD diameter of more than 49 mm (Figure S3).

3.2 | Clinical outcome

In long term, event rates of TR recurrence, HF admission and ischemic stroke were not related with AF recurrence. Instead, the possibility of PPM insertion within the same period happened more frequently in the AF recurrence group. In analysis of PPM insertion events, patient who needed PPM due to sick sinus syndrome during initial
FIGURE 2  C index comparison for AF recurrence. Abbreviations: AUC, area under curve; AF, atrial fibrillation; LAVI, left atrium volume index; RAD, right atrium diameter; RVSP, right ventricular systolic pressure. Statistical significance between AUC values was defined as $p < .05$ by the DeLong test. The values in bold indicate statistical significance ($p < .05$).

FIGURE 3  Comparison of AF recurrence according to RA enlargement. Abbreviations: AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio; RA, right atrium; RAD, right atrium diameter.

TABLE 4  Right heart-related echocardiographic parameters comparison between no AF recurrence group and AF recurrence group

| Variable          | No AF recurrence ($n = 93$) | AF recurrence ($n = 65$) | $p$ value |
|-------------------|-----------------------------|--------------------------|-----------|
| TAPSE (mm)        | $15.0 \pm 3.6$              | $16.7 \pm 5.1$           | .271      |
| TV S' (m/s)       | $0.093 \pm .023$            | $0.090 \pm .020$         | .736      |
| TV annulus (mm)   | $40.8 \pm 7.3$              | $42.4 \pm 7.9$           | .531      |
| IVC diameter (mm) | $24.5 \pm 4.8$              | $27.3 \pm 5.8$           | .008      |
| RV basal diameter (mm) | $47.5 \pm 8.1$            | $51.0 \pm 10.1$          | .106      |
| RV mid diameter(mm) | $40.1 \pm 6.1$            | $44.9 \pm 10.4$          | .115      |
| RV dilatation     | 40 (43.0%)                  | 37 (57.8%)               | .068      |
| RV dysfunction    | 18 (19.4%)                  | 11 (17.2%)               | .831      |

Data are presented as mean ± standard deviation or n (%). Abbreviations: IVC, inferior vena cava; RV, right ventricle; TAPSE, Tricuspid annular plane systolic excursion; other abbreviations are listed in Table 1. Statistical significance was defined as $p < .05$ by student t-test or Mann Whitney U test (continuous variables) or Chi-square test or fisher’s exact test (categorical variables). The values in bold indicate statistical significance ($p < .05$).
TABLE 5  Comparison of 10 years clinical outcomes between no AF recurrence group and AF recurrence group

| Event                        | No AF recurrence (n = 93, n = 91) | AF recurrence (n = 65, n = 61) | Univariable analysis | Log-rank p value |
|------------------------------|----------------------------------|--------------------------------|----------------------|------------------|
| All death (n = 158)          | 15 (26.7%)                       | 13 (23.5%)                     | 1.106  .525–2.334  .791 .791 |
| TR recurrence (n = 158)       | 9 (11.0%)                        | 8 (14.6%)                      | 1.277  .492–3.313  .615 .614 |
| Heart failure admission (n = 158) | 6 (7.0%)                        | 7 (12.3%)                      | 1.635  .549–4.870  .377 .373 |
| PPM insertion (n = 152)       | 1 (2.4%)                         | 7 (16.0%)                      | 10.240 1.257–83.480  .030 .007 |
| Ischemic stroke (n = 158)     | 0 (0.0%)                         | 0 (0.0%)                       | .607  .054–6.791  .686 .683 |

Values are estimated n (%). Cumulative incidence of events were presented as Kaplan-Meier estimates.

Abbreviations: AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio; PPM, permanent pacemaker; TR, tricuspid regurgitation.

FIGURE 4  Incidence of PPM insertion according to AF recurrence. Abbreviations: AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio; PPM, permanent pacemaker;

hospitalization period were excluded. In patients of AF recurrence group, seven patients (16.0%) had a PPM insertion after discharge, while only one patient (2.4%) of no AF recurrence group needed PPM insertion. In the Cox proportional hazard model, the HR for PPM insertion in the AF recurrence group was 10.240 (95% CI [1.257-83.480], log rank p value = .007) (Table 5, Figure 4).

3.3 | Surgical outcome

During TV operation with CM procedure, there was no mortality case. There was one redo MVR (mitral valve replacement) case for bleeding control and three reoperation cases (1.9%) due to hemothorax. Sick sinus syndrome requiring PPM insertion occurred at six patients (3.8%) and AV block was not observed. There was no brain infarction and there were four cases of brain hemorrhage (2.5%) without neurologic sequela. Among four cases of brain hemorrhage, one patient needed burr hole operation during hospitalization period. CRRT needed at three patients who had chronic kidney disease before operation. Two patients needed MCS after operation for short period (Table 6).

4 | DISCUSSION

In this study, we investigated predictors of AF recurrence and the safety and efficacy of a modified Cox maze procedure in patients with AF who underwent a TV operation. The major findings of this study were as follows: 1. RA enlargement is key predictor of AF recurrence after a TV operation with CM procedure in patients with significant TR, 2. AF recurred more than four times more commonly in patients with RAD over 49.2 mm.

4.1 | Predictors of AF recurrence

AF recurrence analysis based on echocardiographic parameters has been well-studied recently. Risk models like the APPLE score and
TABLE 6 Post operation complication rate

| Complication                      | Incidence |
|-----------------------------------|-----------|
| Re-operation                      | 1 (6.6%)  |
| Tracheostomy                      | 0 (0.0%)  |
| Bleeding requiring re-operation   | 3 (1.9%)  |
| Sick sinus syndrome               | 6 (3.8%)  |
| AV block                          | 0 (0.0%)  |
| Infarction                        | 0 (0.0%)  |
| Brain hemorrhage                  | 4 (2.5%)  |
| ARF requiring CRRT                | 3 (1.9%)  |
| Requiring MCS after Op            | 2 (1.3%)  |
| Mediastinitis                     | 0 (0.0%)  |

Values are estimated n (%).

Abbreviations: AV, atrioventricular; ARF, acute renal failure; CRRT, continuous renal replacement therapy; MCS, mechanical circulatory support.

MB-LATER score consist of clinical risk factors and echocardiographic parameters, and show superiority over the CHADS2 and CHA2DS2VASc scores. These new risk prediction models use LA diameter as a scoring factor. LA diameter, LAVI, and LA strain are well known for AF recurrence prediction in both lone AF and AF in SHD. Besides LAVI, RA area, AF duration, and size of F-wave are known for predicting AF recurrence. The relationship between RAD in AF occurrence was observed in mitral valve surgery, catheter ablation and hypertrophic cardiomyopathy. However, there are few studies that directly compare RAD with other echocardiographic parameters like LAD, LAVI, or RVSP.

In this study, RAD was most powerful predictor of AF recurrence among clinical and echocardiographic parameters. LAVI which is traditional predictor of AF recurrence had less discriminative value than RAD in patients with over moderate degree TR. The reason why LAVI has less effective predictive power compared to RAD is that 81% patients had left-sided valve disease and the median value of LAVI was 88.5 ml/m2, which is two times higher than the upper limit of normal range. In left side heart disease, LA enlargement precedes to right heart remodeling. This progressed LA remodeling compared to RA makes LAVI has less discriminative value than RA diameter. Superiority of predictive power of RAD over LAVI was consistent in any type of valvular heart disease such as significant MS, MR, AS, and AR.

In subgroup analysis of isolated TR in this study, RAD was not a statistically significant factor predicting AF recurrence. Considering that even LAVI, which is a known predictor of AF recurrence in lone AF, was not significant indicator of AF recurrence (HR 1.000, 95% CI [0.983–1.018], p value < .969) in the isolated TR group, irrelevance of RAD could come from small number of patients with isolated TR (n = 22, 13.9%).

The cut-off value of RAD for AF recurrence was 49.2 mm in this study. When deciding whether to perform a CM procedure in patients with more than a moderate degree of TR and AF, RAD could be an important factor for decision making based on this study’s result since RAD alone has good predictive value with 66.5% for AF recurrence.

4.2 Relation of RA pressure and AF recurrence

LA pressure is known higher in AF recurrence group after ablation as is LA volume index, but relation between RA pressure and AF recurrence has not established yet. In AF recurrence group of this study, diameters of IVC and RA were higher than no AF recurrence group. Dilated IVC represents elevated RA pressure. In circumstance of AF, atrial pressure is elevated with non-homogeneous contractility of atrium and elevated both atrial pressure lead to both atrial enlargement. Progression of TR in AF is related with both bi-atrial enlargement and tricuspid annulus dilatation. Changed hemodynamics of atrium in AF could induced additional metabolic requirement, ischemia, and fibrosis and this change could irreversible change in atrium that is resistant to ablation treatment. Although there is no direct measurement of RA pressure in this study, we confirmed that RA pressure implied by IVC diameter was higher in AF recurrence group as is RA diameter.

4.3 Relation of PPM insertion and AF recurrence

AF is commonly associated with sick sinus syndrome. Histopathologic change damage to the sinus node, the perinodal tissue and the sinus node artery is associated with persistent AF. Atrial myocardial structural relation to sinus node dysfunction (SND) is primarily in the RA and RA stretching is known to cause SND. Electrical remodeling secondary to AF also could contribute to SND.

In this study, AF recurrence group has higher rate of PPM insertion during follow up period. The association between AF recurrence and high incidence of sick sinus syndrome after maze was addressed in previous study. Electrical remodeling by AF and histopathological change of atrium could contribute to higher incidence of sick sinus syndrome requiring PPM insertion in AF recurrence group.

4.4 Safety and efficacy of modified Cox maze procedure in TR operation

The pathophysiology of AF is reentry and atrial ectopic activity. Ablation for arrhythmia targets rhythm control by isolation of focal atrial ectopic activity. Concomitant surgical ablation of AF is recommended with level of evidence grade I in open surgical ablation and level II evidence in closed surgical ablation. However, the beneficial effect of the maze procedure in TV surgery has not been discussed. In this study, the success rate of the CM procedure in TV surgery was 58.9% (93/158) without mortality. Although there were cases of brain hemorrhage, acute renal injury requiring renal replacement therapy in few patients, there was no major sequela in these patients which needed permanent dialysis or neurologic rehabilitation. A total 41.1% recurrence rate of AF at 10 years is comparable to other results of CM procedure during mitral valve surgery and catheter ablation. This study result proved safety and efficacy of CM procedure in TV surgery.
4.5 | Limitations

The study has several limitations that need to be addressed. First, this is single center study, so center characteristics could be reflected here. However, a relatively long follow-up duration after surgery (median 7.9 years) is strength of this study, We need external validation moving forward. Second, RAD could be affected by volume status, but there was no measurable value that reflects volume status of patients in our data. We should assume that all patients have euvolemic status before surgery. Third, because of the limitations of a retrospective study, we could not identify the value of the RA volume index (RAVI). Since RA size has fewer clinical implications than LA size, RAVI was not included in routine protocol. We could include RAVI measurements in a prospective study later. Fourth, there was a limitation in subgroup analysis in patients with isolated TR (n = 22) due to the relatively small number of patients. Although we could not reach valuable conclusions in the isolated TR subgroup, it is meaningful that AF recurrence factors are analyzed in end-stage SHD accompanied by significant TR, and in the isolated TR subgroup, it is meaningful that AF recurrence factors are analyzed in end-stage SHD accompanied by significant TR, and this differs from the common-sense view that LA size is most important among echocardiographic parameters in AF recurrence prediction.

5 | CONCLUSION

RA enlargement is key predictor of AF recurrence after a modified Cox Maze procedure in patients with significant TR. We can use RA size in clinical risk prediction models to create a risk-benefit estimation of the CM procedure in patients with significant TR and AF.

CONFLICTS OF INTEREST

None of the authors have any conflicts of interest to declare.

ORCID

Sung-Ji Park MD https://orcid.org/0000-0003-3345-2516

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SUPPORTING INFORMATION
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