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# Impact of the Maze Operation Combined With Left-Sided Valve Surgery on the Change in Tricuspid Regurgitation Over Time

Hyung-Kwan Kim, MD; Yong-Jin Kim, MD; Kwang-Il Kim, MD; Sang-Ho Jo, MD; Ki-Bong Kim, MD; Hyuk Ahn, MD; Dae-Won Sohn, MD; Byung-Hee Oh, MD; Myoung-Mook Lee, MD; Young-Bae Park, MD; Yun-Shik Choi, MD

**Background**—Atrial fibrillation (AF) has been reported to be a predisposing factor for the progression of TR in patients with previous mitral or combined mitral/aortic valve surgery. We hypothesized that the maze operation (MAZE) can prevent the progression of tricuspid regurgitation (TR) in these patients.

**Methods and Results**—We analyzed 170 patients (age,  $45.5 \pm 10.9$  years) who had undergone mitral or combined mitral/aortic valve surgery. On the basis of preoperative rhythm, patients were divided into 3 groups; GrI was composed of 44 patients with sinus rhythm, GrII of 48 who had undergone MAZE, and GrIII of 78 with AF who had not undergone MAZE. Echocardiographic examinations were performed before, immediately after, and  $92.2 \pm 17.2$  (range, 50 to 131) months after surgery. Preoperative and immediate postoperative clinical and echocardiographic parameters were similar among the groups. Insignificant TR at the immediate postoperative examination worsened with time in 7.3% of GrI (3 of 41), 12.8% of GrII (6 of 47), and 38.8% of GrIII (26 of 67) patients at the final examination ( $P=0.63$  for GrI versus GrII,  $P=0.001$  for GrI versus GrIII,  $P=0.005$  for GrII versus GrIII). The incidence of significant TR at the final echocardiographic examination was higher in GrIII (39.7%) compared with GrI (9.1%) and GrII (14.6%) ( $P=0.001$  for GrI versus GrIII,  $P=0.005$  for GrII versus GrIII), whereas GrI and GrII did not show any difference ( $P=0.63$ ). By multivariate analysis, the only factor identified to prevent TR progression was the group factor (GrI and GrII versus GrIII,  $P=0.002$  and  $P=0.005$ , respectively). In a subgroup analysis of GrII according to the presence or absence of atrial mechanical activity, the absence of atrial mechanical activity was identified as an independent parameter for the progression of TR ( $P=0.001$ ).

**Conclusions**—AF predisposes patients undergoing mitral valve surgery to the progression of TR, which can be prevented by MAZE. This additional benefit of MAZE is largely dependent on the restoration and maintenance of atrial mechanical function. (*Circulation*. 2005;112[suppl I]:I-14-I-19.)

**Key Words:** fibrillation ■ echocardiography ■ surgery

Tricuspid regurgitation (TR) is a common finding in patients undergoing mitral or combined mitral/aortic valve surgery.<sup>1,2</sup> Although TR may decrease gradually after mitral or combined mitral/aortic valve surgery with reduction of right ventricular pressure or volume overload, TR does not always regress after adequate repair of the underlying lesions.<sup>3,4</sup> TR often progresses late after surgery without left-sided valvular dysfunction, even after tricuspid annuloplasty. Because the persistence or progression of TR badly affects the long-term mortality and morbidity, the prevention and management of functional TR are crucial in these patients.<sup>5</sup>

Atrial fibrillation (AF), a common arrhythmia in patients with left-sided valve diseases, has been identified as an independent predictor of survival.<sup>6,7</sup> Although increased mor-

bidity and mortality in patients with AF is attributed mainly to heart failure or thromboembolism,<sup>8</sup> AF itself is recognized as a factor that predisposes a patient to the progression of TR,<sup>6</sup> which can impair the quality of life and reduce survival.

Since Cox et al<sup>9</sup> introduced the maze operation (MAZE) for the surgical correction of AF, its effectiveness and safety have been well demonstrated,<sup>10–15</sup> and thus it has been widely performed in combination with surgery for underlying structural heart disease. It is hitherto unknown, however, whether MAZE can prevent late TR long after surgery. In addition, because it is well established that MAZE does not always restore atrial mechanical function,<sup>13–16</sup> we sought to evaluate whether the presence of atrial mechanical activity contributes to the effect of MAZE on the progression of TR. Therefore, we designed this study to evaluate whether MAZE can

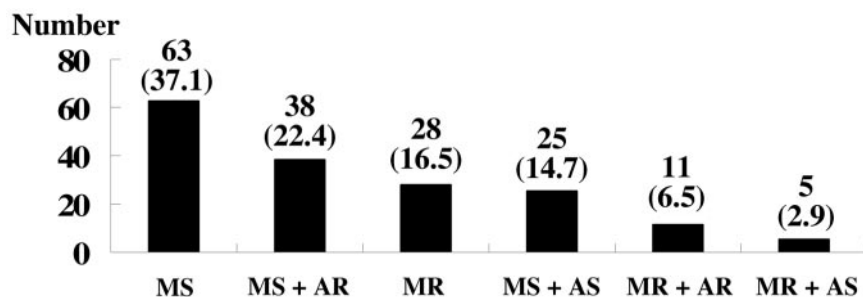
From the Department of Internal Medicine (H.-K.K., Y.-J.K., K.-I.K., S.-H.J., D.-W.S., B.-H.O., M.-M.L., Y.-B.P., Y.-S.C.), and the Department of Thoracic Surgery (K.-B.K., H.A.), Seoul National University College of Medicine, Seoul, Korea.

Correspondence to Yong-Jin Kim, MD, Division of Cardiology, Department of Internal Medicine, Seoul National University College of Medicine, 28 Yongon-dong, Chongno-gu, Seoul, 110-744, Korea. E-mail kimdamas@snu.ac.kr

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**Figure 1.** Preoperative diagnosis according to the type and hemodynamic severity of mitral and aortic valve disease. The number in parenthesis represents percentage. MS indicates mitral stenosis; MR, mitral regurgitation; AS, aortic stenosis; and AR, aortic regurgitation.

prevent the progression of TR in patients undergoing mitral or combined mitral/aortic valve surgery, and if so, whether progression of TR would be affected by the restoration of atrial mechanical function.

## Methods

### Study Population

Three hundred twenty four patients were operated on for mitral or combined mitral/aortic valve disease from January, 1994, to December, 1997. Hospital records were reviewed before enrollment in the study, and clinical variables including age, sex, hypertension, body mass index, smoking habit, and diabetes mellitus were investigated.

Patients with documented organic disease in the tricuspid valve, the absence of either a hospital record or echocardiographic data, or an implanted pacemaker were excluded. Those who had received tricuspid valve replacement were also excluded. Using the exclusion criteria above, 170 patients aged  $45.5 \pm 10.9$  years (range, 17 to 69) were included in the study. On the basis of preoperative rhythm, 44 patients were allocated to the sinus rhythm group (GrI) and 126 to the AF group. The AF group was further divided into patients with (GrII,  $n=48$ ) and without (GrIII,  $n=78$ ) combined MAZE (Cox III type). During follow-up, sinus conversion occurred in 7 patients with preoperative AF without undergoing MAZE, and these patients were subsequently included in GrIII. On the other hand, AF developed in 1 patient with preoperative sinus rhythm. This patient was included in GrI for analysis. The decision as to whether to perform MAZE was made solely by surgeons' preference (H.A. and K.B.K.). MAZE (Cox III type) was performed as described in detail previously.<sup>10</sup>

### Echocardiographic Examinations

Two-dimensional and Doppler echocardiographic examinations were performed in a standard manner using commercially available echocardiographic devices before and immediately after surgery as a part of routine clinical care. All examinations were recorded on super-VHS videotape.

TR was assessed using multiple transthoracic windows, and the maximal jet area in any view was used to estimate the regurgitation grade using the standard color Doppler technique. The grade of regurgitation was classified and coded as 0 (none), 1 (trivial), 2 (mild), 3 (moderate), 3.5 (moderate to severe), and 4 (severe) in each patient. For statistical analysis, significant TR was defined as more than mild in degree. TR maximal velocity was obtained from the continuous-wave Doppler of the TR signal and was used to calculate systolic pulmonary artery pressure (sPAP). Final echocardiographic examinations were performed in all recruited patients in the fashion described above. Right atrial (RA) mechanical activity was determined by the presence of late diastolic tricuspid inflow (A wave) in the last follow-up echocardiogram, with a sample volume placed at the tip of tricuspid valve.

### Statistical Analysis

All values are expressed as mean  $\pm$  SD or percentages. The comparative analysis of the 3 groups was done by analysis of variance with the Sheffé post hoc test for continuous variables, and the  $\chi^2$  test or Fisher's exact test was used for categorical variables. To compare

preoperative and postoperative variables within each group, we used the paired *t* test or the Mann-Whitney U test.

Multiple logistic regression analysis using the forward stepwise selection process, including all significant parameters by univariate analysis and previously known confounding variables, was undertaken to determine which clinical and echocardiographic parameters were independently associated with the presence of significant TR long after surgery. SPSS 11.0 (SPSS Inc) was used for the statistical analyses and a probability value of  $<0.05$  was considered statistically significant.

## Results

### General Features

All 170 patients were followed-up for an average of  $92.2 \pm 17.2$  (range, 50 to 131) months. Follow-up durations were not different for the 3 groups ( $91.9 \pm 17.4$  in GrI,  $88.3 \pm 13.5$  in GrII, and  $95.2 \pm 18.8$  in GrIII;  $P=0.09$ ). Preoperative diagnosis in the 170 patients according to the type and hemodynamic severity of valve disease is shown in Figure 1. Tricuspid valve annuloplasty (De Vega type in 30 patients, Kay type in 2 patients) was carried out in 32 patients (3 patients in GrI, 11 in GrII, and 18 in GrIII). Of the 170 study patients, 4 underwent reoperation for severe TR during the follow-up period, all of whom were from GrIII.

The procedures used for underlying valve lesions are shown in Table 1. Mechanical prostheses, especially bileaflet tilting discs (St Jude bileaflet valve and Carbomedics valve), were used in the majority of patients for both mitral and aortic valve surgery. The main clinical characteristics of the 3 groups are summarized in Table 2. Patient age was slightly higher in patients from GrII and GrIII than in GrI, and digoxin was more often prescribed in GrIII than in GrI or GrII. The other clinical parameters were similar in the 3 groups.

**TABLE 1. Surgical Procedures Used for Correcting Underlying Left-Sided Valve Disease**

Procedure	Group			P Value
	GrI (n=44)	GrII (n=48)	GrIII (n=78)	
MVR	33 (75)	39 (81.3)	68 (87.2)	0.10
Mitral valve repair	7 (15.9)	9 (18.8)	6 (7.9)	0.07
AVR	11 (25)	12 (25%)	29 (37.2)	0.15
Aortic valve repair	1 (2.3)	4 (8.3)	0 (0)	0.28
TV annuloplasty	3 (6.8)	11 (22.9)	18 (23.7)	0.02

Values are presented as n (%). AMVR indicates mitral valve replacement; AVR, aortic valve replacement; TV, tricuspid valve.

TABLE 2. Clinical Characteristics of the 3 Groups

	Group			P Value
	GrI (n=44)	GrII (n=48)	GrIII (n=78)	
Age, y	40±12	46±8*	48±10†	<0.001
BMI, kg/m <sup>2</sup>	21.5±2.7	22.6±2.8	21.3±2.9	0.09
Male:female	19:25	18:30	29:49	0.79
Diabetes mellitus, n (%)	0 (0)	1 (2.1)	4 (5.1)	0.10
Hypertension, n (%)	4 (9.1)	9 (18.8)	10 (12.8)	0.70
Smoking status, n (%)				
Ever smoker	9 (20.5)	8 (17.4)	15 (19.2)	0.85
Never smoker	32 (72.7)	35 (76.1)	58 (74.4)	
Unknown	3 (6.8)	3 (6.5)	5 (6.4)	
Medications during follow-up, n (%)				
ACEIs or ARBs	3 (6.8)	9 (18.8)	19 (24.4)	0.22
β-blockers	7 (15.9)	7 (14.6)	9 (11.5)	0.32
CCBs	3 (6.8)	7 (14.6)	10 (12.8)	0.97
Diuretics	6 (13.6)	15 (31.3)	22 (28.2)	0.39
Warfarin	37 (84.1)	40 (83.3)	72 (92.3)	0.44
Aspirin	3 (6.8)	3 (6.3)	1 (1.3)	0.39
Digoxin	8 (18.2)	6 (12.5)	48 (61.5)‡	<0.001
Amiodarone	6 (13.6)	10 (20.8)	13 (16.7)	0.88

BMI indicates body mass index; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor blockers; CCBs, calcium channel blockers.

\* $P<0.05$  vs GrI; † $P<0.01$  vs GrI; ‡ $P<0.001$  vs GrI and GrII.

### Echocardiographic Findings Other Than TR Grade

All preoperative and immediate postoperative echocardiographic parameters were similar in GrII and GrIII. Preoperative left atrial (LA) size was higher in GrIII than in GrI, which persisted to the immediate postoperative examinations. At the final examination, left ventricular ejection fraction (LVEF) was higher and LA size was smaller in GrI than in the other 2 groups. No significant differences were found regarding LV dimensions between the 3 groups, whereas sPAP was highest in GrIII, followed by GrII and then GrI. Comparisons of echocardiographic findings are shown in Table 3.

### Change of TR Grade Over Time

Preoperatively, significant TR was found in 12 patients in GrI (27.3%), 8 in GrII (16.7%), and 26 in GrIII (33.3%) ( $P=0.33$

in GrI versus GrII,  $P=0.62$  in GrI versus GrIII, and  $P=0.09$  in GrII versus GrIII). Immediately after surgery, 3 patients in GrI (6.8%), 1 in GrII (2.1%), and 11 in GrIII (14.1%) had significant TR ( $P=0.55$  in GrI versus GrII,  $P=0.36$  in GrI versus GrIII, and  $P=0.09$  in GrII versus GrIII). At the last follow-up, significant TR was present in 4 patients in GrI (9.1%), 7 in GrII (14.6%), and 31 in GrIII (39.7%) ( $P=0.63$  in GrI versus GrII,  $P=0.001$  in GrI versus GrIII, and  $P=0.005$  in GrII versus GrIII).

The majority of preoperative insignificant TR remained stable at the immediate postoperative examination (100% for GrI, 97.5% for GrII, and 96.2% for GrIII). Insignificant TR at the examination immediately after surgery, however, was aggravated) at the final examination in 7.3% of GrI (3 of 41), 12.8% of GrII (6 of 47), and 38.8% of GrIII (26 of 67) ( $P=0.63$  in GrI versus GrII,  $P=0.001$  in GrI versus GrIII, and

TABLE 3. Comparison of Echocardiographic Data

	Preoperative				Immediate Postoperative				Last Follow-Up			
	GrI	GrII	GrIII	P Value	GrI	GrII	GrIII	P Value	GrI	GrII	GrIII	P Value
LVEDD,mm	35.0±10.8	37.0±8.5	35.2±8.8	0.53	35.3±9.6	32.1±6.6	34.5±7.8	0.13	30.4±8.0	33.8±6.3	33.0±8.5	0.09
LVEDD,Mm	54.5±12.8	53.5±9.0	52.5±10.0	0.61	50.1±8.1	46.9±6.4	48.8±7.8	0.14	49.5±7.7	50.2±6.3	50.0±7.8	0.91
LVEF,%	57.2±9.4	53.4±9.3	56.1±11.2	0.18	49.9±12.5	52.4±9.5	49.7±13.2	0.44	62.6±10.4	54.6±9.6*	56.1±11.8*	0.001
LA size, mm	51.0±10.7	56.8±8.4	60.3±12.2*	<0.001	41.4±8.4	46.4±7.8	49.1±9.3*	<0.001	46.6±8.7	52.5±7.0†	55.4±10.5‡	<0.001
TR grade	1.8±1.3	1.6±0.9	2.1±1.1	0.09	1.0±0.8	1.1±0.6	1.5±1.0†	0.008	1.3±0.8	1.7±0.9	2.3±1.1‡§	<0.001
sPAP, mm Hg	42.3±32.1	39.5±14.4	47.7±23.6	0.22	19.2±18.0	27.8±13.4	29.8±19.6†	0.035	25.0±12.4	33.3±10.1*	41.5±12.8‡	<0.001

LVEDD indicates left ventricular end-systolic diameter; LVEDD, left ventricular end-diastolic diameter. Other abbreviations as defined in text.

\* $P<0.01$  vs GrI; † $P<0.05$  vs GrI; ‡ $P<0.001$  vs GrI; § $P<0.01$  vs GrII; || $P<0.005$  vs GrII.

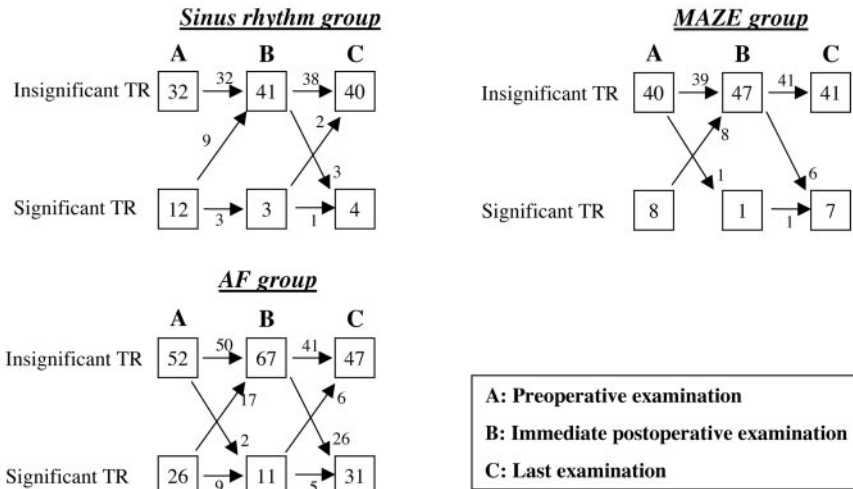


Figure 2. Outcome of preoperative TR in the 3 groups.

$P=0.005$  in GrII versus GrIII; Figure 2). Figure 3 shows serial changes of TR grade, sPAP, and LA size over time.

### Independent Factors Determining Late Significant TR

To identify independent clinical and echocardiographic factors for late significant TR, we performed multivariate analysis using clinical parameters, namely age, sex, presence of hypertension, presence of diabetes mellitus, smoking status, digoxin use, warfarin use, amiodarone use, group factor, tricuspid annuloplasty, and the type of prosthesis, and echocardiographic parameters, namely the presence of preoperative significant TR, preoperative LVEF, preoperative LA size, and preoperative sPAP. The only determinant for preventing late significant TR was the group factor (Table 4). In this model, MAZE was found to reduce the risk of late significant TR in GrII by 79% compared with GrIII.

### Subgroup Analysis According to Atrial Activity

GrII was categorized into 2 subgroups; GrIIa consisted of 38 patients who maintained sinus rhythm with discernible RA mechanical activity at the last follow-up, whereas the other group, GrIIb, comprised 10 patients without RA mechanical activity, who were in AF (5 patients), accelerated junctional

rhythm (2 patients), or sinus rhythm (3 patients). No significant differences were noted between these 2 subgroups in terms of echocardiographic and clinical parameters except age (Table 5). Patients in GrIIa had a significantly smaller LA size preoperatively and lower TR grade at the final follow-up than those in GrIIb ( $55.6 \pm 8.3$  mm versus  $61.1 \pm 7.7$  mm,  $P=0.038$ , and  $1.5 \pm 0.7$  versus  $2.4 \pm 1.1$ ,  $P=0.025$ , respectively). Multivariate logistic regression analysis of age, sex, diabetes mellitus status, hypertension status, smoking status, warfarin use, digoxin use, amiodarone use, tricuspid annuloplasty, duration of AF, preoperative LVEF, preoperative LA size, presence of preoperative significant TR, preoperative sPAP, and the type of prosthesis and subgroup factor (GrIIa and GrIIb) showed that the subgroup factor ( $P=0.001$ ,  $R^2=0.623$ ) was an independent parameter that has a significant impact on late TR.

### Discussion

The principal findings of the present study are that (1) AF affects the worsening of TR over time in patients undergoing mitral valve surgery, and it can be possibly prevented by MAZE, and (2) the recovery and maintenance of atrial mechanical activity are of great value for such a benefit. To

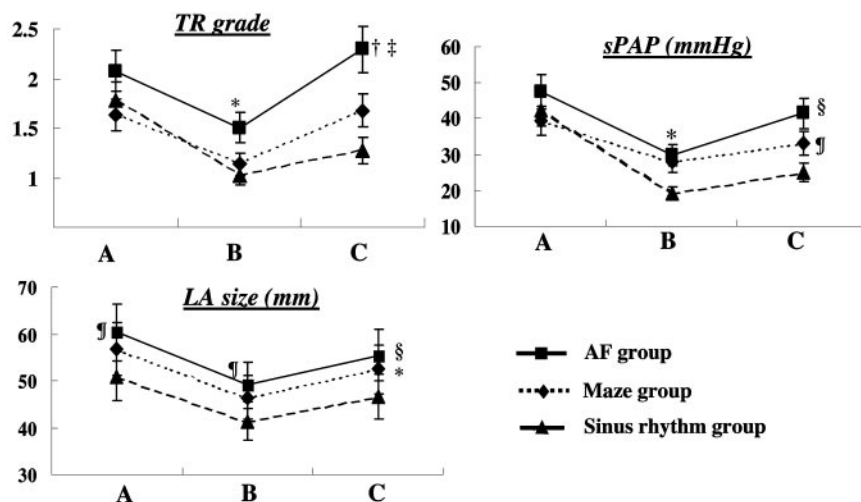


Figure 3. Changes in TR grade, sPAP, and LA size with time. A shows preoperative evaluation; B, immediate postoperative evaluation; and C, evaluation at the final follow-up. \* $P<0.05$  vs sinus rhythm group; † $P<0.001$  vs sinus rhythm group; ‡ $P<0.01$  vs maze group; § $P<0.001$  vs sinus rhythm group; ¶ $P<0.01$  vs sinus rhythm group.



**TABLE 4. Multivariate Logistic Regression Analysis for Independent Factors for the Development of Late Significant Tricuspid Regurgitation**

Independent Factors	Exponential Coefficient ( $\beta$ )	95% CI	P Value
Group			
GrI	0.150	0.045 to 0.505	0.002
GrII	0.211	0.072 to 0.619	0.005
GrIII	1 (Reference)	...	...

CI indicates confidence interval.  $R^2=0.289$  for model.

our knowledge, this is the first study that shows the impact of MAZE on TR progression after mitral valve surgery.

### AF and Late Tricuspid Regurgitation After Surgery

The importance of significant TR in patients with mitral valve surgery is due to its close relation to morbidity and mortality<sup>5,6,17,18</sup> irrespective of sPAP and LVEF.<sup>18</sup> Moreover, significant TR can increase morbidity and mortality despite the adequate correction of underlying valve diseases.<sup>19</sup> The

**TABLE 5. Clinical and Preoperative Echocardiographic Parameters in the Subgroups of GrII**

	Group IIa (n=38)	Group IIb (n=10)	P Value
Age, y	45±8	53±6	0.004
BMI, kg/m <sup>2</sup>	22.4±3.0	23.2±2.1	0.41
Male:female	15:23	3:7	0.58
Diabetes mellitus, n (%)	1 (2.8)	0 (0)	0.59
Hypertension, n (%)	8 (22.2)	1 (10.0)	0.39
Smoking status, n (%)			
Ever-smoker	7 (19.5)	1 (10.0)	0.97
Never-smoker	27 (75.0)	8 (80.0)	
Unknown	2 (5.6)	1 (10.0)	
Medications during follow-up, n (%)			
ACEIs or ARBs	7 (18.4)	2 (20.0)	0.83
$\beta$ -blockers	6 (15.8)	1 (10.0)	0.49
CCBs	6 (15.8)	1 (10.0)	0.49
Diuretics	10 (26.8)	5 (50.0)	0.16
Warfarin	32 (84.2)	8 (80.0)	0.75
Aspirin	2 (5.3)	1 (10.0)	0.97
Digoxin	4 (10.5)	2 (20.0)	0.78
Amiodarone	7 (18.4)	3 (30.0)	0.71
Preoperative echocardiographic parameter			
LVESD, mm	36.9±8.5	37.3±9.5	0.97
LVEDD, mm	53.3±8.7	54.4±10.7	0.81
LVEF, %	52.8±9.7	55.5±7.6	0.36
LA size, mm	55.6±8.3	61.1±7.7	0.04
TR grade	1.6±0.9	1.8±0.8	0.36
sPAP, mm Hg	38.5±14.8	42.9±13.3	0.50

Abbreviations as in Table 2 and Table 3.

information regarding the underlying mechanism and risk factors for the progression of TR after surgery is scarce, however. In our study, patients in GrIII demonstrated a higher TR grade at the final follow-up than those in the other 2 groups, and multivariate analysis confirmed AF as the only independent factor for late significant TR.

The mechanism of the progression of TR after surgery in patients with AF is elusive. It has been reported that atrial sizes are closely associated with AF<sup>20–22</sup> and that chronic AF induces mechanical and electrical remodeling of both atria, leading to further atrial dilatation.<sup>23,24</sup> As Vaturi et al<sup>20</sup> suggested, RA dilation may induce tricuspid annulus dilation with resultant TR progression with time. Also, LA dilation is frequently associated with an LA pressure elevation, which can be transmitted backwards passively or trigger pulmonary arteriolar constriction, leading to increased right ventricular afterload and eventually right-sided chamber enlargement that can contribute to the development of late significant TR. Mitral annulus distortion by mitral valve repair or replacement is another potential cause of LA pressure increment.<sup>25</sup>

### Additional Benefits of MAZE Beyond the Elimination of AF

Cox et al<sup>9</sup> introduced MAZE in 1991 as a surgical means of effectively controlling AF in combination with surgical management of mitral valve in patients with mitral valve disease. The procedure involves the creation of a maze by making multiple incisions on both atria, thus allowing sinus node impulse to be conducted to the atrioventricular node without creating a reentry circuit.<sup>26</sup> It has been reported that sinus rhythm is recovered and maintained in approximately 80% of cases.<sup>13,16,27,28</sup> The conventional benefit of MAZE is the elimination of AF, and it thus prevents subsequent complications related to AF, such as heart failure and thromboembolism.<sup>29</sup> In addition to these conventional benefits of MAZE, our study suggests that it can prevent the progression of TR after mitral valve surgery. Patients in GrII in our series showed a substantially (79%) reduced risk of late significant TR compared with patients in GrIII. Risk reduction, however, did not reach the extent achieved in GrI (risk reduction of 85% in GrI versus 79% in GrII), which is likely to be due to the possible difference in atrial mechanical function between the 2 groups. In subgroup analysis of GrII, we also found that the presence of atrial mechanical activity is a strong protective factor against the progression of TR, which implies that the additional benefit of MAZE stems mainly from the restoration and maintenance of atrial mechanical function.

### Limitations

Several limitations of the study need to be acknowledged. First, this study is limited by its retrospective nature. The decision to perform MAZE was not randomized. Because the decision was entirely dependent on the preference of the 2 surgeons, however, the clinical and echocardiographic variables were not significantly different between GrII and GrIII. Therefore, we believe that the validity of our findings is unlikely to be altered by the retrospective study design. A prospective, randomized, controlled study is needed to confirm our results. Second, more detailed quantifications of TR

grade, for example regurgitant fraction and proximal isovelocity surface area, were not performed. Although such techniques may be more appropriate and provide an objective means for evaluating TR severity, the semiquantitative evaluation of TR is a widely used method in clinical practice.

## Conclusions

Our data demonstrate that AF predisposes patients undergoing mitral or combined mitral/aortic valve surgery to TR progression, and that this can be possibly prevented by MAZE largely by the restoration and maintenance of atrial mechanical function. Prospective, randomized, clinical trials are warranted to further confirm our findings.

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