

The Natural History of
Tricuspid Regurgitation After
Mitral Valve Surgery

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Table of Contents

I. INTRODUCTION -----	3
II. MATERIALS AND METHODS -----	5
III. RESULTS -----	7
IV. DISCUSSION -----	14
V. CONCLUSION -----	17
REFERENCES -----	18

LIST OF FIGURES

Figure 1. Changes of severity of tricuspid regurgitation during follow-up after mitral valve surgery-----	9
Figure 2. Kaplan-Meier analysis of survival free from cardiovascular events including cardiovascular death and reoperation during follow-up period -----	13

LIST OF TABLES

Table 1. Baseline Characteristics of the Study Population -----	7
Table 2. Underlying Valve Diseases at the Time of Surgery -----	8
Table 3. Types of Valve Surgery -----	8
Table 4. Main Clinical and Echocardiographic Characteristics According to the Presence of Late Tricuspid Regurgitation ----	10
Table 5. Independent Factors for the Development of Late Significant Tricuspid Regurgitation -----	12

Abstract

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Background: We investigated the incidence and predictors of development of significant tricuspid regurgitation (TR) late after mitral valve surgery.

Methods and Results: A retrospective analysis was performed on a total of 334 patients who underwent mitral valve surgery between 1992 and 1995. Development of late TR was evaluated in the echocardiographic examination with a mean follow-up duration of 10.3 ± 2.1 years. Seventy percent of study population completed ten-year echocardiographic follow-up. Significant TR was found in 128 patients (38.3%). Patients with late TR showed advanced age (47 ± 14 vs 44 ± 12 yrs, $p=0.040$), a higher prevalence of atrial fibrillation (89 vs 62%, $p<0.001$), a greater left atrial dimension (59 ± 13 vs 56 ± 11 mm, 0.015), a higher mean right atrial pressure (12 ± 9 vs 8 ± 5 mmHg, $p<0.001$), a more frequent prior history of valve surgery (46 vs 31%, $p=0.005$), and a higher prevalence of preoperative TR (35 vs 14% $p<0.001$). In multivariate analysis, preoperative atrial fibrillation (Odds ratio 4.55; 95% C.I. 1.88-11.0; $p=0.001$), preoperative TR (Odds ratio 2.29; 95% C.I. 1.08-4.84; $p=0.03$), and preoperative mean right atrial pressure (Odds ratio 1.07; 95% C.I. 1.01-1.13; $p=0.014$) emerged as independent determinants for the development of late TR.

Patients with late TR showed lower survival rate free from cardiovascular events than those without TR.

Conclusions: Development of TR late after mitral valve surgery is common and associated with poor prognosis. Preoperative atrial fibrillation, TR and mean right atrial pressure were identified as independent predictors.

Key words: tricuspid regurgitation; echocardiography; heart valve surgery

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I. INTRODUCTION

Tricuspid regurgitation (TR) is a common finding in patients undergoing mitral or combined mitral/aortic valve surgery.^{1,2} Although TR may decrease gradually after mitral valve surgery with reduction of right ventricular pressure or volume overload,³ TR does not always regress after adequate correction of the underlying lesions.^{4,5} TR often progresses late after surgery without mitral valvular dysfunction even after tricuspid annuloplasty. Furthermore, TR can appear de novo during postoperative follow-up. Because it is well known that progression of TR badly affects the long-term mortality and morbidity and surgical correction of TR after mitral valve surgery carries disappointingly high mortality and morbidity,⁶⁻⁹ the prevention of late TR is clinically important. Therefore, the information regarding the incidence and predictors of progression or development of late TR is important for determining optimal operative timing for underlying mitral valve disease and surgical strategy regarding associated TR at the time of initial surgery. Several previous reports were limited due to relatively small study population,^{5,10} short-term follow-up,¹¹ or lack of reliable echocardiographic data.¹² Therefore, the present study was performed to investigate the incidence of significant TR late after

mitral valve surgery and identify preoperative predictors in a large number of patients with long-term echocardiographic examination.

II. METHODS

Study population

This study was based on our consecutive experience with patients who underwent surgical correction for mitral valve disease from January, 1992 to December, 1995. During this time period, a total of 478 patients underwent surgery for mitral or combined mitral/aortic valve disease in our institution and was initially considered eligible for the study. Among them, we excluded the patients who underwent combined tricuspid valve replacement (n=19), correction of congenital anomaly (n=21), or coronary artery bypass graft surgery (n=12). fifty-seven patients who were lost to follow-up and 35 patients who died within five years after surgery were also excluded. Accordingly 334 patients (133 male, 39.8%) who completed at least 5-year follow-up comprised the study population.

Baseline Data Procurement

We reviewed patients' hospital records and our database of cardiac surgery focusing on the following parameters; age at surgery, sex, body weight, height, heart rhythm, type of surgery, and history of prior cardiac surgery. Preoperative cardiac catheterization was performed in all patients and parameters including pulmonary capillary wedge pressure, systolic pulmonary artery pressure, and right atrial pressure were obtained. Preoperative echocardiographic examination was performed in all patients by skilled echocardiographers and interpreted by experienced cardiologists. Left ventricular end-systolic and end-diastolic diameter, left ventricular ejection fraction, left atrial dimension, and valvular functions were evaluated. The etiology of the valvular disease was confirmed on the basis of the surgical observation and/or the pathological findings. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital.

Follow-up Echocardiographic Examination

After discharge from the hospital, comprehensive 2-dimensional and Doppler echocardiographic examinations were repeated every one or two years by skilled echocardiographers in a standard manner using commercially available echocardiographic devices. The presence of TR as well as its severity was assessed using multiple transthoracic windows. Maximal TR jet area in any view was used to semiquantitatively estimate TR grade using the standard color Doppler technique. The grade of TR was classified as none, trivial, mild, mild to moderate, moderate, moderate to severe, or severe in each patient. For the simplicity of statistical analysis, significant TR was defined as more than mild in degree. Maximal TR jet velocity was obtained from the continuous-wave Doppler and was employed for calculating systolic pulmonary artery pressure. The latest echocardiographic examination was regarded as the end of the follow-up period.

Statistical Analysis

Continuous variables are expressed as mean \pm SD, and categorical variables as percentages. Multiple logistic regression analysis utilizing the forward stepwise selection process, including all significant parameters by univariate analysis and previously known confounding variables, was undertaken to determine the parameters associated independently with the presence of significant TR late after surgery. Cumulative survival rate was estimated by Kaplan-Meier method and compared between the groups with and without late TR using the log-rank test. SPSS 13.0 (SPSS Inc., Chicago, Illinois) was used for the statistical analyses and a p value of <0.05 was considered statistically significant.

III. RESULTS

Baseline Characteristics

Baseline characteristics of 334 patients are summarized in Table 1. Mean follow-up duration was of 10.3 ± 2.1 (range, 5-14) years. Mitral valve surgery was performed in 219 patients (mitral valve replacement or mitral valve repair) and combined mitral and aortic valve in 115 patients.

Table 1. Baseline Characteristics of the Study Population

Characteristics	Number (%)
Sex (male)	133 (39.8)
Age (years)	44.8 ± 12.9
Weight (Kg)	54.6 ± 9.4
Height (cm)	160.6 ± 8.4
Duration of follow up (year)	10.3 ± 2.1
Preoperative electrocardiography	
Sinus rhythm	93 (27.8)
Atrial fibrillation	241 (72.2)
Preoperative echocardiography	
LV Ejection Fraction (%)	60.0 ± 12.4
LV end-diastolic diameter (mm)	55.6 ± 11.6
Left atrial dimension (mm)	57.3 ± 11.9
Presence of significant TR	73 (21.9)
Preoperative cardiac Catheterization	
Pulmonary artery systolic pressure (mmHg)	46.7 ± 19.6
Pulmonary capillary wedge pressure (mmHg)	22.1 ± 8.6
Mean right atrial pressure (mmHg)	9.8 ± 7.1

LV denotes left ventricle and TR, Tricuspid Regurgitation

Preoperative diagnoses according to the type of valve disease and the procedures performed for underlying valvular diseases are described in detail in Table 2 and 3. The causes of mitral valve disease were rheumatic in 172 patients (51.5 %), prosthetic valve failure in 111 (33.2 %), mitral valve prolapse in 31 (9.3 %), and other causes in 20 (6.0%).

Table 2. Underlying Valve Diseases at the Time of Surgery

	Normal AV	AR	AS	ASR
MR	82 (24.5%)	34 (10.2%)	1 (0.3%)	4 (1.2%)
MS	63 (18.8%)	26 (7.8%)	3 (0.9%)	12 (3.6%)
MSR	59 (17.7%)	21 (6.3%)	1 (0.3%)	28 (8.4%)

MR denotes mitral regurgitation; MS, mitral stenosis; MSR, combined mitral stenosis and regurgitation; AV, aortic valve; AS, aortic stenosis; AR, aortic regurgitation; ASR: combined aortic stenosis and regurgitation

Table 3. Types of Valve Surgery

	AVR	Aortic valve repair	Without AV surgery
MVR	103 (30.8%)	2 (0.6%)	170 (50.9%)
Mitral valve repair	7 (2.1%)	3 (0.9%)	49 (14.7%)

MVR denotes mitral valve replacement; AV, aortic valve; AVR: aortic valve replacement

In preoperative echocardiography, 73 patients (21.9 %) had significant TR and 16 patients (4.8 %) had severe TR. At the time of mitral valve surgery, tricuspid annuloplasty was performed in 47 patients. Preoperative electrocardiogram showed atrial fibrillation in 241 patients (72.2 %).

Development of Late TR

Among 334 patients, 234 patients (70 %) completed 10-year echocardiographic follow-up. Long-term echocardiographic follow-up was not available in 28 patients who did not undergo echocardiographic examination due to the absence of any symptoms or signs of cardiac problems. Thus, these patients were regarded as those without significant TR. At the last follow-up, significant TR was found in 128 patients (38.3 %), among whom severe TR was present in 43 patients (12.9 %).

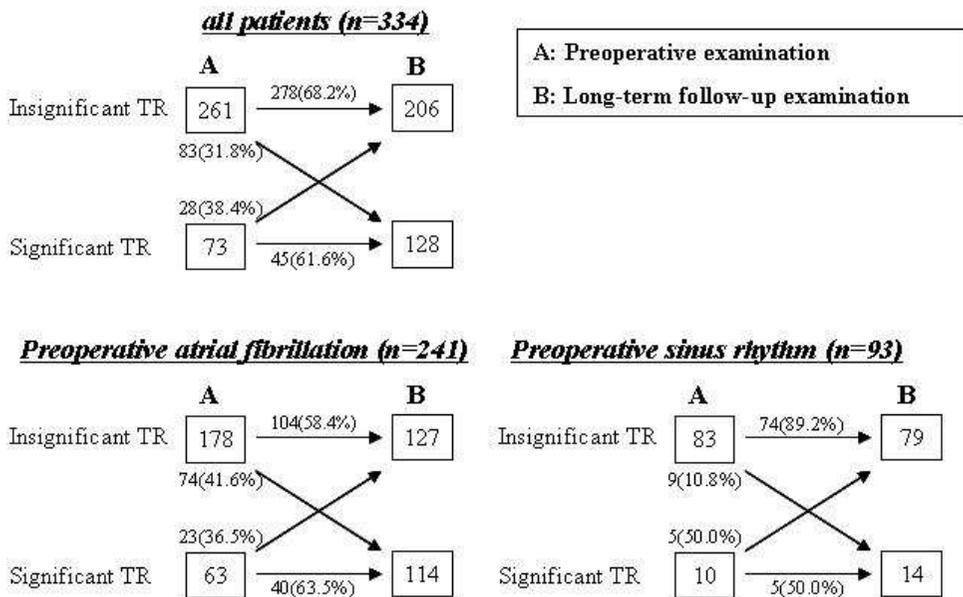


Figure 1. Changes of severity of tricuspid regurgitation during follow-up after mitral valve surgery.

Among 261 patients without preoperative TR, 83 patients (31.8 %) newly developed significant TR during follow-up, whereas 45 patients (61.6 %) out of 73 patients with preoperative TR showed late TR. (Fig. 1)

Table 4. Main Clinical and Echocardiographic Characteristics According to the Presence of Late Tricuspid Regurgitation

Characteristics	TR (+) (n=128)	TR (-) (n=206)	P value
Male : Female	48: 80	85: 121	0.57
Age (years)	46.7 ± 13.6	43.7 ± 12.3	0.040
Weight (kg)	53.6 ± 8.5	55.1 ± 9.9	0.17
Height (cm)	160.0 ± 8.4	161.0 ± 8.5	0.33
Previous valve surgery	59 (46.1%)	63 (30.6%)	0.005
Preoperative AF	114 (89.1%)	127 (61.7%)	<0.001
Preoperative echocardiographic data			
LVEF (%)	59.8 ± 12.4	60.1 ± 12.4	0.84
LVEDD (mm)	54.3 ± 11.4	56.5 ± 11.7	0.13
LA size (mm)	59.5 ± 12.8	56.0±11.2	0.015
TR > mild	45 (35.2%)	28 (13.6%)	<0.001
Preoperative cardiac catheterization data			
PASP (mmHg)	47.3 ± 19.3	46.4 ± 19.9	0.69
mPCWP (mmHg)	22.2 ± 9.1	22.0 ± 8.4	0.81
mRAP (mmHg)	12.2 ± 9.4	8.3 ± 4.7	<0.001

TR denotes tricuspid regurgitation; MV, mitral valve; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LA, left atrium; PASP, pulmonary artery systolic pressure; mPCWP : mean pulmonary capillary wedge pressure; mRAP, mean right atrial pressure

The characteristics according to the presence of late TR are summarized in Table 4. Patients with late TR showed advanced age (46.7 ± 13.6 vs 43.7 ± 12.3 years, p=0.040), a higher prevalence of atrial fibrillation (89.1 vs 61.7 %, p<0.001), a greater left atrial dimension (59.5 ± 12.8 vs 56.0 ± 11.2 mm, p=0.015), a higher

mean right atrial pressure (12.2 ± 9.4 vs 8.3 ± 4.7 mmHg, $p < 0.001$), a more frequent prior history of valve surgery (44.4 vs 26.4 %, $p = 0.001$), and a higher prevalence of preoperative significant TR (35.2 vs 13.6 % $p < 0.001$). However, rheumatic etiology, left ventricular ejection fraction, systolic pulmonary artery pressure, and pulmonary capillary wedge pressure were not significantly different between the groups.

Independent Factors Determining Late Significant TR (Table 5)

To identify independent clinical and echocardiographic factors for the development of late significant TR, we performed multivariate logistic regression analysis using clinical, echocardiographic and cardiac catheterization parameters that were found to be significant in univariate analysis, such as age, gender, history of previous valve surgery, the performance of mitral valve surgery, the presence of atrial fibrillation, left atrial size, presence of preoperative significant TR, and mean right atrial pressure. Preoperative atrial fibrillation (Odds ratio 4.55; 95% C.I. 1.875-11.044; $p = 0.001$), preoperative significant TR (Odds ratio 2.29; 95% C.I. 1.079-4.837; $p = 0.031$), and preoperative mean right atrial pressure (Odds ratio 1.07; 95% C.I. 1.014-1.128; $p = 0.014$) emerged as independent determinants for the development of late TR.

Table 5. Independent Factors for the Development of Late Significant Tricuspid Regurgitation

Risk factors	Odds ratio	95% CI	P value
<i>Univariate analysis</i>			
Age	1.018	1.001-1.036	0.041
Female	1.171	0.744-1.841	0.50
Weight	0.982	0.958-1.008	0.17
Height	0.986	0.958-1.014	0.33
Prosthetic valve failure	1.833	1.156-2.908	0.010
Previous valve surgery	1.941	1.229-3.065	0.004
Preoperative AF	5.065	2.719-9.435	<0.001
Preoperative echocardiographic data			
LVEF	0.998	0.980-1.017	0.84
LVEDD	0.984	0.964-1.004	0.13
LA size	1.025	1.005-1.047	0.016
TR > mild	3.466	2.022-5.941	<0.001
Preoperative cardiac catheterization data			
PASP	1.002	0.990-1.015	0.69
mPCWP	1.003	0.975-1.032	0.81
mRAP	1.098	1.044-1.156	<0.001
<i>Multivariate analysis</i>			
Preoperative AF	4.551	1.875-11.044	0.001
Preoperative significant TR	2.285	1.079-4.837	0.031
Preoperative mRAP	1.069	1.014-1.128	0.014

MV denotes mitral valve; AF : atrial fibrillation; ; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LA, left atrium; PASP, pulmonary artery systolic pressure; mPCWP : mean pulmonary capillary wedge pressure; mRAP, mean right atrial pressure

Clinical Events during Follow-up

Among 334 patients, 56 patients died during the follow-up period. The causes of death were heart failure in 8, cerebrovascular events in 9, myocardial infarction in 2, endocarditis in 9, malignancy in 4, accidents in 1, liver disease in 4, infection in 2, others in 10 and unknown in 8. During the follow-up period, reoperation for isolated TR was performed in 20 patients. Difference in survival free from cardiovascular events including cardiovascular death and reoperation was compared with the log-rank test and found to be lower in patients with late TR. (Fig. 2)

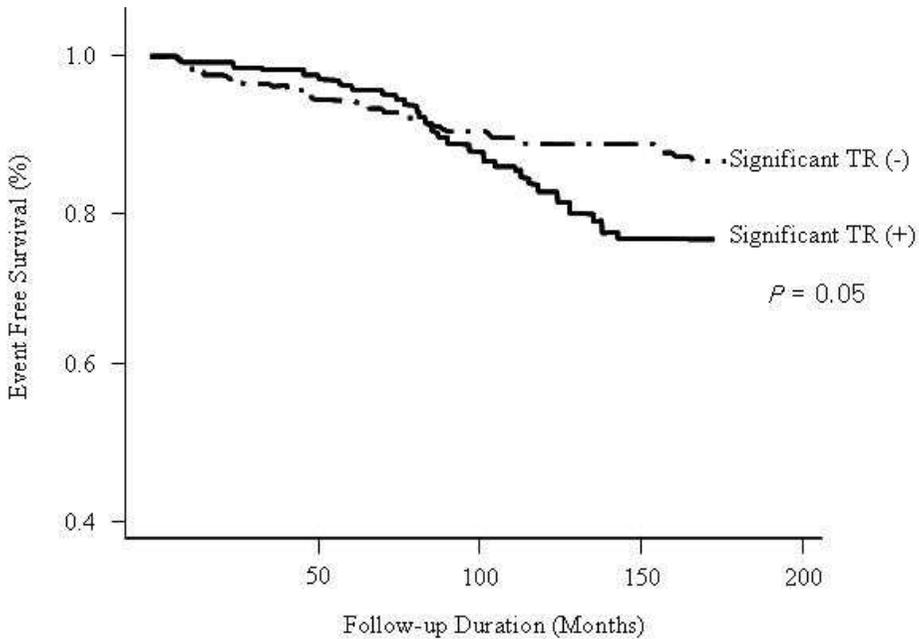


Figure 2. Kaplan-Meier analysis of survival free from cardiovascular events including cardiovascular death and reoperation during follow-up period

IV. DISCUSSION

In the present study we found that the prevalence of TR more than mild degree was 38 % in long-term echocardiographic follow-up after mitral valve surgery. The prevalence of severe TR was 13 %. Preoperative TR did not regress or progressed in 62 % of patients with preoperative TR and TR appeared de novo in 32 % of patients without preoperative TR. The predictors for the progression or development of late TR were preoperative atrial fibrillation, preoperative significant TR, and preoperative mean right atrial pressure. This is one of the largest studies evaluating TR late after surgery with long-term echocardiographic follow-up, which strengthens our findings.

Progression or development of late TR is a common and important echocardiographic finding following mitral valve surgery. It is associated with an impairment of exercise capacity⁶ and a poor prognosis. Moderate or greater TR was associated with worse prognosis, even in the absence of ventricular dysfunction or pulmonary hypertension.¹³ Furthermore, significant TR increases morbidity and mortality despite the adequate correction of underlying valve diseases.¹⁴ The reported incidences of TR late after surgery varied from 16 to 67 % according to the study population, definition of significant TR, and follow-up duration.^{5,10-12} Matsuyama et al. reported incidence of 16 %. In the study, the follow-up duration was relatively short and they did not include patients with concomitant tricuspid annuloplasty who were likely to have significant TR preoperatively.¹¹ In contrast, Porter et al. reported a much higher incidence of 67 % in their study, where the study population was relatively small while the follow-up duration was relatively long.⁵ In the present study we reported the prevalence of late TR to be approximately 38 % during a mean follow-up duration of 10.3 years. We believe that a follow-up duration of ten years is sufficient to detect patients who will develop clinically significant TR after mitral valve surgery, because it is unlikely that patients that do not progress beyond mild TR ten years after surgery would rapidly progress to severe TR during further follow-up.

Identification of predictors for late TR is important for guidance of therapy and for predicting prognosis. Previous studies have shown that preoperative significant TR, atrial fibrillation, advanced age or huge left atrium were significant predictors.^{5,11,12} In the present study, although many parameters were significant in univariate analysis, multivariate analysis revealed that preoperative atrial fibrillation, significant TR, and mean right atrial pressure were statistically significant predictors for the development of late TR. It is of interest to note that many patients with preoperative TR developed late TR despite concomitant tricuspid annuloplasty. Atrial fibrillation is not only a marker of the duration of underlying valve disease but also a factor that predisposes progressive atrial remodeling.¹⁵⁻¹⁸ Therefore, our findings suggest the importance of right ventricular and right atrial function as a determinants of late TR. Although the underlying mechanism for late TR is not well described, it is usually considered as 'functional' because tricuspid valve is morphologically normal in most patients. Therefore, right ventricular dysfunction and the tricuspid annular dilation have been regarded as important determinants of late TR.^{10,19}

Because corrective surgery for late TR carries high operative mortality and morbidity,^{8,9,20} the prevention of late TR development may be important clinically. Currently, tricuspid annuloplasty has been widely performed as a safe and effective surgical tool for reducing tricuspid annular diameter. However, the indication for tricuspid annuloplasty has not been well established. Although preoperative TR severity and the tricuspid annular dimension usually serve as guide to surgery,²¹ tricuspid annuloplasty has not been successful in a substantial number of patients,²² which may be due to right ventricular dysfunction precipitating progressive right ventricular remodeling. Therefore, careful monitoring for detecting predictors for late TR and timely surgical correction of underlying mitral valve disease may help to prevent the development of TR late after surgery and improve long-term prognosis.

Limitations

Several limitations of the study need to be addressed. First, this study is limited by its retrospective nature. However, the preoperative, operative and postoperative findings were prospectively summarized in the database system designed and maintained throughout the study period, which is an advantage of single-center study. Second, quantifications of TR grade were not performed. Although quantification may be more appropriate and provide an objective means for evaluating TR, the semi-quantitative evaluation of TR is a widely used method in clinical practice.

V. CONCLUSION

Our data demonstrated that progression or development of TR late after mitral valve surgery was common with the prevalence of 38 % and associated with poor prognosis. Preoperative atrial fibrillation, significant TR, and mean right atrial pressure were identified as independent predictors.

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승모판막 수술후 발생하는 삼첨판막 폐쇄부전의 자연경과

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곽 재 진

배경 및 목적: 승모판막 수술후 뒤늦게 발생하는 삼첨판막 폐쇄부전의 빈도와 예측인자를 알아보려고 하였다.

방법 및 결과: 1992 년부터 1995 년 사이에 승모판막 수술을 받은 334 명의 환자를 대상으로 후향적 연구를 하였다. 삼첨판막 폐쇄부전의 평가는 심초음파를 이용하였고 평균 추적관찰 기간은 10.3 ± 2.1 년이었다. 전체환자중 약 70%가 수술 후 약 10 년째 심초음파를 시행하였다. 의미있는 뒤늦은 삼첨판막 폐쇄부전은 128 명(38.3%)에서 관찰되었고, 이들은 삼첨판막 폐쇄부전이 없는 환자들에 비해 나이가 많았고(47 ± 14 vs 44 ± 12 yrs, $p=0.040$), 심방세동이 더 흔했으며(89 vs 62%, $p<0.001$), 좌심방이 더 심하게 확장되어 있었고(59 ± 13 vs 56 ± 11 mm, 0.015), 평균 우심방압이 더 높았으며(12 ± 9 vs 8 ± 5 mmHg, $p<0.001$), 심장판막수술을 과거에 받았었던 경우가 더 많았고(46 vs 31%, $p=0.005$), 수술전부터 삼첨판막 폐쇄부전을 가지고 있었던 경우가 많았다(35 vs 14% $p<0.001$). 로지스틱 회귀분석에 의하면 뒤늦은 삼첨판막폐쇄부전의 독립적인 예측인자는 수술전 심방세동(Odds ratio

4.55; 95% C.I. 1.88-11.0; $p=0.001$), 수술전 삼첨판막 폐쇄부전(Odds ratio 2.29; 95% C.I. 1.08-4.84; $p=0.03$), 그리고 수술전 높은 평균 우심방압(Odds ratio 1.07; 95% C.I. 1.01-1.13; $p=0.014$) 으로 나타났다. 또한 뒤늦은 삼첨판막 폐쇄부전이 나타난 경우 그렇지 않은 경우에 비해 심장혈관질환 관련 예후가 나쁜 경향이 있었다.

결론: 승모판막 수술후 뒤늦게 나타난 삼첨판막 폐쇄부전은 비교적 흔하며 예후가 좋지 않다. 또한 수술전 심방세동, 의미있는 삼첨판막 폐쇄부전, 높은 평균 우심방압이 독립적인 예측인자임을 알 수 있었다.

핵심되는 말: 삼첨판막 폐쇄부전; 심장초음파; 심장판막수술