Progression of Isolated Tricuspid Regurgitation Late After Left-Sided Valve Surgery – Clinical Features and Mechanisms –

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Background: Severe tricuspid regurgitation (TR) sometimes develops late after left-sided valve surgery without left heart failure, pulmonary hypertension or rheumatic tricuspid valve. The purpose of the present study was to investigate clinical characteristics and mechanisms of severe isolated TR late after left-sided valve surgery.

Methods and Results: A total of 372 consecutive patients who underwent left-sided valve surgery between 1990 and 2003 and who were followed up with echocardiography for at least 5 years, were retrospectively investigated. The mean follow-up period was 9.4 years. Clinical background, preoperative and postoperative echocardiographic parameters were evaluated. Among the 372 patients, severe isolated TR was detected in 23 patients, which developed at a mean of 8.6 years after surgery. Twenty-two of 23 patients had undergone mitral valve surgery. Multivariate logistic regression analysis identified the presence of preoperative atrial fibrillation and preoperative ejection fraction as independent determinants for the development of severe isolated TR. In patients with severe isolated TR, the tricuspid annular diameter and the right atrial area were already enlarged early after surgery and both of these increased prior to TR progression.

Conclusions: Severe isolated TR developing late after mitral valve surgery is not uncommon, thus it is important to recognize this disease entity. Annular dilatation was the main cause of isolated TR and serial echocardiographic data are important to detect progression of isolated TR and to assess its mechanisms. (*Circ J* 2011; **75**: 2902–2907)

Key Words: Echocardiography; Surgery; Tricuspid regurgitation; Valvular disease

The tricuspid valve is often called a “forgotten” valve, because tricuspid regurgitation (TR) is usually a secondary, not primary disease. In addition, right heart failure due to TR is usually controllable for a long period with diuretic drugs; thus the course of TR over a long period of time may shed some light on this disease. In contrast, severe TR may often appear and progress late after left-sided valve surgery without significant left heart failure, pulmonary hypertension or rheumatic tricuspid valve.^{1–10} Moderate to severe TR has been reported to be associated with a poor prognosis^{11,12} and the degree of TR influences functional status after surgery.¹³

The purpose of the present study was to investigate the clinical characteristics and mechanism of severe isolated TR late after left-sided valve surgery.

Methods

Subjects

We retrospectively investigated 520 consecutive patients who underwent left-sided valve surgery between 1990 and 2003 in Tenri Hospital. Among these patients, follow-up with echocardiography was <5 years in 138 patients, and moderate to severe TR was detected early after surgery in 10 patients. Therefore, we finally studied 372 patients (204 male; mean age at surgery, 60 years; range, 18–82 years) who had no or mild TR early after surgery and who were followed up with echocardiography for at least 5 years. The mean follow-up period was 9.4 years (range, 5.0–18.8 years). Mitral valve surgery alone was performed in 173 patients, aortic valve surgery alone in

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147 patients, and both mitral and aortic valve surgery in 52 patients. Concomitant tricuspid annuloplasty was performed at the time of left-sided valve surgery in 54 patients. Preoperative cardiac rhythm was atrial fibrillation (AF) in 131 patients who underwent mitral valve surgery alone, in 26 patients who underwent aortic valve surgery alone, and in 42 patients who underwent both mitral and aortic valve surgery, making a total of 199 patients (Table 1). Maze procedures were performed in 24 of 199 patients with AF.

Clinical Features

In order to investigate the clinical features of patients who had progression of severe isolated TR after left-sided valve surgery, we examined the following factors by checking the previous clinical charts, electrocardiograms, and operation data base: age, cardiac rhythm, and tricuspid annuloplasty at the time of left-sided valve surgery, history of previous valve operations, types of left-sided valve surgery and underlying valve diseases.

The study protocol was approved by the institutional ethics committee at Tenri Hospital.

Echocardiographic Parameters

Development of severe TR during follow-up and the etiology of TR were examined. Severe isolated TR was defined as a TR jet area of $\geq 10 \text{ cm}^2$ without mitral or aortic valve dysfunction, left ventricular dysfunction, pulmonary hypertension, rheumatic tricuspid valve, transvenous pacemaker implantation or constrictive pericarditis. Pulmonary hypertension was defined as $\geq 40 \text{ mmHg}$ systolic pulmonary artery pressure, which was calculated from peak TR velocity.

In order to investigate the echocardiographic predictors of the development of severe isolated TR, preoperative echocardiographic parameters, such as left atrial diameter (LAD), left ventricular diastolic diameter, left ventricular systolic diameter, and ejection fraction (EF) were examined. LAD was measured from the parasternal long axis view at end-systole. Left ventricular dimensions were measured from the parasternal long axis view at the level of mitral leaflet tips. EF was measured using the modified Simpson's method.

Furthermore, chronological changes of the TR jet area, the tricuspid annular diameter, the right atrial area and the tenting area of the tricuspid valve were evaluated in patients with severe isolated TR in order to investigate the mechanisms of isolated TR after left-sided valve surgery. These parameters were measured 6 months–1 year, 5–7 years, and 10–15 years

Table 1. Baseline Subject Characteristics

Characteristics	n (%)
Age at operation (years)	60 $\pm$ 12 (18–82)
Male	204 (55)
Preoperative cardiac rhythm	
Sinus rhythm	173 (47)
AF	199 (53)
History of previous valve surgery	75 (20)
TAP	54 (15)
Left-sided valve surgery	
Mitral valve alone	173 (47)
Aortic valve alone	147 (39)
Mitral+aortic valve	52 (14)
Mitral valve surgery	
MVR	126 (56)
Repair	74 (33)
OMC	25 (11)

AF, atrial fibrillation; TAP, tricuspid annuloplasty; MVR, mitral valve replacement; OMC, open mitral commissurectomy.

after left-sided valve surgery. Because these parameters were not routinely measured, we remeasured these parameters from the original echocardiographic recordings. The TR jet area was traced from the view where the area was at a maximum. The tricuspid annular diameter, the right atrial area and the tenting area were measured from the 4-chamber view at end-systole. The tenting area was defined as the area enclosed by the annular line and septal and anterior leaflets.¹⁴ For each patient, we measured these parameters from the same view for the follow-up echocardiograms.

Statistical Analysis

Statistical analysis was performed using JMP version 6. Data are presented as mean $\pm$ SD. The difference in a parameter between early and late after left-sided valve surgery was determined using paired t-test analysis. The difference in a parameter between 2 groups was determined using unpaired t-test for continuous variables and Fisher's exact test for discrete variables. Logistic regression was used to assess the contribution of clinical features and preoperative echocardiographic parameters to the development of severe isolated TR during follow-up. We selected variables with $P < 0.05$ in univariate

Figure 1. Incidence of severe isolated tricuspid regurgitation (TR). PH, pulmonary hypertension.

Table 2. Comparison of Clinical and Echocardiographic Features

Characteristics	Severe isolated TR(+) (n=23)	Severe TR(-) (n=324)	P value
Age at left-sided valve surgery (years)	60±9	60±12	0.86
Male	10 (43)	188 (58)	0.20
Preoperative AF	22 (96)	136 (42)	<0.0001
History of previous valve surgery	6 (26)	66 (20)	0.59
TAP at left-sided valve surgery	4 (17)	42 (13)	0.53
Mitral valve surgery	22 (96)	184 (57)	<0.0001
MVR	13 (57)	103 (32)	0.021
Mitral stenosis	10 (43)	76 (23)	0.044
Preoperative echo parameters			
LVDd (mm)	56±10	57±11	0.72
LVDs (mm)	36±10	36±11	0.80
LAD (mm)	60±9	46±13	<0.0001
EF (%)	63±12	66±14	0.33

Data given as mean ± SD or n (%).

TR, tricuspid regurgitation; LVDd, left ventricular diastolic diameter; LVDs, left ventricular systolic diameter; LAD, left atrial diameter; EF, ejection fraction. Other abbreviations see in Table 1.

Table 3. Comparison of Clinical and Echocardiographic Features After Mitral Valve Surgery

Characteristics	Severe isolated TR(+) (n=22)	Severe TR(-) (n=184)	P value
Age at left-sided valve surgery (years)	61±10	58±12	0.31
Male	10 (45)	96 (52)	0.65
Preoperative AF	21 (95)	114 (62)	0.0014
History of previous valve surgery	5 (23)	54 (29)	0.62
TAP at left-sided valve surgery	4 (18)	40 (22)	0.99
MVR	13 (59)	103 (56)	0.82
Mitral stenosis	10 (45)	76 (41)	0.82
Preoperative echo parameters			
LVDd (mm)	56±10	57±9	0.65
LVDs (mm)	37±10	34±10	0.19
LAD (mm)	59±9	53±13	0.05
EF (%)	62±12	70±10	0.004

Data given as mean ± SD or n (%).

Abbreviations see in Tables 1,2.

models and included them simultaneously in multivariate models. Relative risks were calculated with 95% confidence intervals (CI). Statistical significance was set at $P<0.05$.

Results

Incidence of Isolated TR Late After Left-Sided Valve Surgery

Among the 372 study patients, severe TR was detected in 48 patients during follow-up. Among those patients, 21 had left heart failure and/or pulmonary hypertension, 2 had constrictive pericarditis, and 2 others underwent transvenous pacemaker implantation (Figure 1). Thus, severe isolated TR was detected in 23 (6.2%) of the 372 patients after left-sided valve surgery. Preoperative cardiac rhythm was AF in 22 of 23 patients. Maze procedures were performed in 1 of 22 patients with AF. Postoperative cardiac rhythm was AF in 21 of 23 patients with severe isolated TR.

Among the 23 patients, type of left-sided valve surgery was mitral valve surgery alone in 18 patients, both mitral and aortic valve surgery in 4 patients, and aortic valve surgery alone in 1 patient. Late progression of severe isolated TR was detected in 9.2% of the patients after mitral valve surgery.

Clinical and Echocardiographic Features of Isolated TR Late After Left-Sided Valve Surgery

Clinical background and preoperative echocardiographic parameters were compared between patients who had progression of severe isolated TR and those without severe TR. Patients who had progression of severe isolated TR had a higher rate of preoperative AF (96% vs. 42%, $P<0.0001$), mitral valve surgery (96% vs. 57%, $P<0.0001$), mitral valve replacement (57% vs. 32%, $P=0.021$) and mitral stenosis (43% vs. 23%, $P=0.044$) than those without severe TR. The preoperative LAD was larger in patients with severe isolated TR than in those without severe TR (60±9 mm vs. 46±13 mm, $P<0.0001$), but there were no differences in other echocardiographic parameters between the 2 groups (Table 2).

With the exception of 1 patient, all who had progression of severe isolated TR underwent mitral valve surgery. Therefore, clinical features and preoperative echocardiographic parameters were examined only among patients after mitral valve surgery. Preoperative AF was the only preoperative clinical determinant for the progression of severe isolated TR after mitral valve surgery (95% vs. 62%, $P=0.0014$). The preoperative LAD was larger (59±9 mm vs. 53±13 mm, $P=0.05$) and

preoperative EF was lower ($62\pm 12\%$ vs. $70\pm 10\%$, $P=0.004$) in patients with severe isolated TR than in those without severe TR after mitral valve surgery (Table 3).

Multivariate logistic regression analysis identified the presence of preoperative AF and a low EF as independent determinants for the development of severe isolated TR late after mitral valve surgery (AF: odds ratio [OR], 12.86; 95%CI: 1.91–109.45, $P=0.019$; EF: OR, 1.06; 95%CI: 1.01–1.16, $P=0.033$; Table 4).

Mechanisms of Severe Isolated TR

Severe isolated TR developed 3–18 years, at a mean of 8.6 years, after left-sided valve surgery. The tricuspid annular diameter and the right atrial area were already enlarged early after left-sided valve surgery, and both of these increased (tricuspid annular diameter, 31.2 ± 4.6 mm at 6 months, 35.9 ± 6.9 mm at 5 years, $P<0.0001$ vs. 6 months; and 38.2 ± 6.9 mm at 10 years after surgery, $P<0.0001$ vs. 6 months, $P=0.010$ vs. 5 years; right atrial area, 26.3 ± 12.7 cm² at 6 months, 33.1 ± 16.7 cm² at 5 years, $P=0.0002$ vs. 6 months; and 36.6 ± 15.4 cm² at 10 years after surgery, $P<0.0001$ vs. 6 months, $P=0.022$ vs. 5 years) prior to the progression of TR (TR jet area: 2.2 ± 1.5 cm² at 6 months, 8.2 ± 6.6 cm² at 5 years, $P<0.0001$ vs. 6 months; and 16.3 ± 7.3 cm² at 10 years after surgery, $P<0.0001$ vs. 6 months, $P<0.0001$ vs. 5 years). The tenting area was not large in patients with severe isolated TR and it did not increase (0.36 ± 0.21 cm² at 6 months, 0.34 ± 0.19 cm² at 5 years, and 0.34 ± 0.18 cm² at 10 years after surgery) despite the progression of TR (Figure 2).

Discussion

Severe TR often develops late after mitral valve surgery^{1–10} without significant left heart failure, valve dysfunction or pulmonary hypertension.

Incidence and Clinical Determinants of Severe Isolated TR

Because there are differences in the subject groups, follow-up period, and definition of significant TR, the incidence of significant TR varies among reports.^{1–10} Late severe TR has been reported in 14–43% of patients after mitral valve surgery, and in 7–27% of patients with left-sided valve surgery including

Table 4. Multivariate Logistic Regression Analysis for Severe Isolated TR After Mitral Valve Surgery

Characteristics	OR	95%CI	P value
Preoperative AF	12.86	1.51–109.45	0.019
Preoperative EF	1.06	1.01–1.16	0.033
Preoperative LAD	0.99	0.95–1.04	0.725

OR, odds ratio; CI, confidence interval. Other abbreviations see in Tables 1,2.

aortic valve surgery alone. According to changes in the etiology of mitral valve disease from rheumatic to degenerative disease, there is a possibility that the incidence of severe TR late after surgery may change.

In the present study, 48 of 372 patients (13%) after left-sided valve surgery had severe TR, and approximately half of them (6.2% of total patients) had severe TR without specific causes such as left heart failure or pulmonary hypertension, namely isolated TR. We focused on isolated TR because the mechanisms, prognosis and treatment may be different from TR associated with left heart failure or pulmonary hypertension.

Mitral valve surgery and AF were predictors of development of severe isolated TR. Severe isolated TR appeared in 9.2% of patients after mitral valve surgery, while in only one patient (0.8%) after aortic valve surgery alone. Only one patient with sinus rhythm had severe isolated TR in the present study. AF has been identified as a predictor of severe TR in many previous studies.^{1–5} The number of patients with preoperative AF was much lower in the group who underwent aortic valve surgery than in the group who underwent mitral valve surgery, which may have resulted in a low number of patients with severe isolated TR in the aortic valve surgery alone group.

In addition, preoperative LAD and EF were preoperative echocardiographic determinants for development of severe isolated TR after mitral valve surgery. Left atrial enlargement is considered to be related to the presence of AF. In addition, left atrial enlargement represents preoperative chronic pressure elevation of the left atrium, which might result in right ventricular dysfunction. A lower EF at the time of mitral valve surgery might represent a longer history of mitral valve disease

Figure 2. Chronological changes in tricuspid regurgitation (TR) jet area, tricuspid annular (TA) diameter, right atrial (RA) area, and tenting area of the tricuspid valve. The TA diameter and the RA area increased prior to the progression of TR. Red triangle, TR jet area; blue circle, RA area; green square, TA diameter; open square, tenting area.

or might represent more patients with mitral stenosis, which might result in more severe right ventricular dysfunction.

Mechanisms of Severe Isolated TR

Ton-Nu et al carried out research on the 3-D structure of the tricuspid annulus.¹⁵ Normal tricuspid annulus has a bimodal shape but the annulus becomes larger, more planar, and circular in patients with functional TR. Previous studies using 3-D echocardiography showed that tricuspid tethering was an important mechanism for functional TR.^{16,17} In the present study, however, the tenting area was not large in patients with severe isolated TR and it did not increase despite the progression of TR. In contrast, annular diameter and right atrial area increased prior to the progression of TR. In addition, the presence of AF was a strong predictor of the development of severe isolated TR. Therefore, it is thought that the annular dilatation was strongly related to the progression of severe isolated TR rather than tricuspid valve tethering. A full-volume 3-D echocardiography image is composed of 4 consecutive beats, therefore most patients with isolated TR after mitral valve surgery were not included in these previous studies because most of those patients had AF. Different subject groups may give different results for the mechanisms.

Severe TR is occasionally found in patients with lone AF,^{18,19} which may show a strong relationship between the development of TR and annular dilatation. The incidence of severe isolated TR, however, is much greater in patients after mitral valve surgery than in patients with lone AF. Therefore, other factors, such as right ventricular dysfunction, may be related to the progression of isolated TR after mitral valve surgery. Right ventricular dysfunction due to preoperative chronic pressure overload might persist after mitral valve surgery. Right ventricular dysfunction, however, is still difficult to evaluate on conventional echocardiography. Several studies have demonstrated that tricuspid annular velocity measured on tissue Doppler imaging is useful in evaluating right ventricular function.^{20,21} The right-sided Tei index has also been reported to be another useful index to evaluate right ventricular function.²² Because the present study was retrospective, we had no data on tricuspid annular velocity nor on right-sided Tei index.

The suggested mechanisms of progression of isolated TR are as follows: AF and/or right ventricular dysfunction promote dilatation of the tricuspid annulus, leading to the development of TR, which, in turn, accelerates dilatation of the tricuspid annulus. TR begets TR, thus it is somewhat a vicious cycle.

Prevention and Treatment of Severe Isolated TR

Several reports have demonstrated that mild to moderate TR uncorrected at the time of mitral valve surgery may lead to severe isolated TR late after surgery.^{3,6-8,10,23-25} They insisted that mild to moderate TR should be repaired during mitral valve surgery, but this remains controversial. In the present study, tricuspid annuloplasty at the time of left-sided valve surgery was not related to the prevention of severe isolated TR late after surgery. It may be because patients with moderate to severe TR early after left-sided valve surgery were excluded in the present study. In addition, tricuspid annuloplasty used to be performed with the De Vega procedure, not ring annuloplasty. A better long-term outcome has been reported for ring annuloplasty than for the De Vega procedure.^{26,27}

In the ESC guidelines, patients with more than a 2-degree TR or more than a 40-mm annular diameter are recommended (class IIa) to undergo tricuspid annuloplasty during mitral valve surgery,²⁸ but the recommendation level in the ACC/AHA guidelines for patients with the same criteria is class IIb.²⁹ Iso-

lated tricuspid surgery for severe TR has been reported to be associated with a high mortality rate.^{9,20,30-32} Furthermore, the prognosis of patients with severe isolated TR who did not undergo tricuspid valve surgery was reported to be worse than of those who underwent tricuspid valve surgery.³³ Therefore, it is thought that the indication for tricuspid ring annuloplasty during mitral valve surgery should be broadened to patients with AF, a large atrium and a low EF in spite of mild to moderate TR.

Study Limitations

The present study had several limitations, mainly based upon its retrospective nature. First, views of the tricuspid valve were limited in preoperative and postoperative echocardiograms. Therefore, the tricuspid annular diameter, right atrial area, and tenting area could not be measured from several different views. Second, we had no data on right ventricular function. Third, the technique for tricuspid annuloplasty at left-sided valve surgery changed according to the operative period, which might have influenced the incidence of late progression of severe TR. In addition, the incidence of isolated TR may depend on the etiology of mitral valve disease, but this could not be evaluated because it was at times difficult to clearly distinguish.

Conclusions

Severe isolated TR developing late after mitral valve surgery is not uncommon; thus it is important to recognize this disease entity. Tricuspid annular dilatation was the main cause of isolated TR after mitral valve surgery. Serial echocardiographic data are very important to detect late progression of isolated TR and to assess its mechanisms.

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