

# Progression of Tricuspid Regurgitation After Repaired Functional Ischemic Mitral Regurgitation

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**Background**—Despite correction of left-sided cardiac lesions, associated functional tricuspid regurgitation (TR) that was surgically ignored can persist. It can also appear de novo. The aim of this study was to analyze TR in a group of patients who underwent successful revascularization and mitral valve repair (MVR) for functional ischemic mitral regurgitation (MR).

**Methods and Results**—Among 124 consecutive patients with MVR, 70 left the operating room with MR  $\leq$ 1+ and had a preoperative and follow-up transthoracic echocardiogram. Moderate or greater MR or TR was considered significant. Twenty-one patients (30%) had TR before surgery, and only 9 had TR repaired. The postoperative incidence of residual TR was not significantly different whether the tricuspid valve had been repaired (4 of 9 [44%]) or surgically ignored (8 of 12 [67%]). At last follow-up, 34 patients (49%) had significant TR. The incidence of TR increased from 25% at  $<$ 1 year to 53% between 1 and 3 years and 74% at  $>$ 3 years. Absence or presence of recurrent MR did not significantly affect TR (14 of 22 [64%] with MR versus 20 of 48 [42%] with no MR). Preoperative and postoperative tricuspid annulus size in patients with late TR was significantly larger than in patients without TR.

**Conclusions**—Functional TR is frequently associated with functional ischemic MR. After MVR, close to 50% of patients have TR. The incidence of postoperative TR increases with time. Preoperative tricuspid annulus dilation might be a predictor of late TR. (*Circulation*. 2005;112[suppl I]:I-453-I-457.)

**Key Words:** valves ■ regurgitation ■ ischemia ■ mitral valve ■ tricuspid valve

Functional tricuspid regurgitation (TR) is the most common type of tricuspid valve pathology and is usually associated with mitral valve disease.<sup>1-3</sup> Despite correction of left-sided lesions, associated functional TR that was surgically ignored can persist, or it can appear de novo.<sup>4-6</sup> The mechanism responsible for the development or persistence of functional TR after correction of mitral valve disease remains unclear. The aim of this study was to analyze TR in a group of patients who underwent successful revascularization and mitral valve repair using reducing ring annuloplasty (MVR) for functional ischemic mitral regurgitation (MR). An attempt was also made to find preoperative and postoperative echocardiographic differences between the 2 groups of patients separated by the presence or absence of follow-up TR.

## Methods

### Patients

From January, 1992, through December, 2001, 124 consecutive patients with functional ischemic MR underwent coronary artery bypass grafting (revascularization) and MVR with a flexible Duran ring (Medtronic, Inc) at our institution. Seventy patients were selected for the study. The study included all patients who (1) had no organic tricuspid disease as diagnosed by preoperative transthoracic echocardiography (TTE) and/or intraoperative transesophageal echo-

cardiography (TEE); (2) left the operating room with less than or equal to mild MR; (3) did not experience a recorded ischemic event during the postoperative period; and (4) had complete preoperative and follow-up TTE examinations. This last condition was the most frequent cause for exclusion. Moderate or greater MR or TR was considered significant. All patients were divided into 2 groups according to the last TTE. Those patients with significant follow-up TR were classified as the "TR group"; those without significant TR were the "no-TR group."

### Surgery

All patients were operated on with similar standard cardiopulmonary bypass with moderate hypothermia and antegrade and retrograde cold blood cardioplegia. All coronary and valve procedures were done under a single aortic cross clamp. A Duran flexible ring was used in all mitral valve repairs. Nine patients underwent tricuspid annuloplasty. A Duran ring was placed in 5 patients using sizes 27 (n=1), 29 (n=2), and 31 (n=2). In 4 cases, a de Vega tricuspid annuloplasty was performed. In all cases, the intraoperative TEE showed absent or trivial TR.

### Echocardiographic Measurements

Routine TTE examinations, which included 2-dimensional (2D) and Doppler echocardiography with color flow mapping, were performed in all patients using a standard scanner. All preoperative and last follow-up TTE examinations were reviewed by one single operator (A.M.), who measured the parameters listed below. The functional TR jet was observed in the apical 4-chamber view, the parasternal

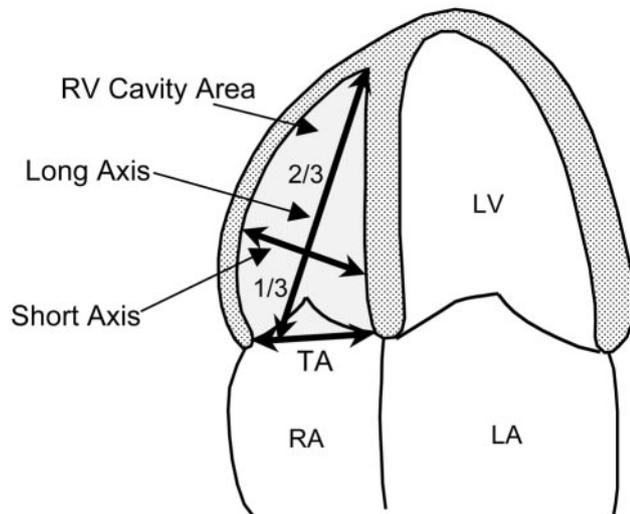
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**Figure 1.** Diagram of transthoracic echocardiographic parameters measured. RA indicates right atrium; LA, left atrium; and TA, tricuspid annulus diameter.

short-axis view at the level of the aortic valve, and the right ventricular (RV) inflow view. The view in which the spatial distribution of the jet was maximal was selected, and the maximal ratio of color Doppler regurgitant jet area to right atrial area was calculated. The severity of TR was graded as trivial when the jet area occupied <10% of the right atrial area, mild when it occupied 10% to <20%, moderate when it occupied 20% to <33%, and severe when it occupied  $\geq 33\%$ .<sup>7</sup> The severity of MR was determined by the ratio of maximum color Doppler regurgitant jet area to left atrial area. MR grade was estimated as trivial, mild, moderate, or severe on the basis of ratios of 0% to 10%, 10% to 20%, 20% to 40%, and greater than 40%, respectively.<sup>8</sup> The tricuspid annulus diameter was measured in the apical 4-chamber view in late diastole at the time of maximal tricuspid opening.<sup>9</sup> The RV end-systolic and end-diastolic cavity areas were traced in the apical 4-chamber view, and the percent change in area was calculated.<sup>10</sup> The RV long axis and short axis at the upper one-third level were measured in the mid-systolic apical 4-chamber view, and the RV sphericity index was calculated by the ratio of the short/long axis.<sup>11</sup> RV systolic pressures were estimated by continuous wave Doppler echocardiography using the modified Bernoulli equation ( $4 \times [\text{Peak TR velocity}]^2$ ), with 10 mm Hg added for the estimated right atrial pressure.<sup>12</sup> The end-diastolic, mid-systolic, and end-systolic frames were determined as the initial, middle, and last frame of tricuspid leaflet closure, respectively (Figure 1). Left ventricular (LV) ejection fraction was measured by the modified biplane Simpson method or the single plane area-length method.<sup>11</sup> Sixteen patients who had suboptimal echocardiographic windows leading to incomplete anatomic evaluation of RV were excluded from the study.

### Statistical Analysis

Data are expressed as mean  $\pm$  standard deviation. To assess differences between the groups, the Mann-Whitney test was used for continuous variables, and the  $\chi^2$  test was used for categorical variables. The Wilcoxon signed-ranks test was used to compare intragroup differences. A probability value of <0.05 was considered statistically significant. The tricuspid annulus diameter was normalized by body surface area (BSA) to compare differences between groups.

## Results

### Patient Characteristics and Clinical Results

The characteristics of the patients undergoing revascularization and MVRep are shown in Table 1. The TR group comprised 34 patients (49%), and the no-TR group included

**TABLE 1. Preoperative Data of Patients With Functional Ischemic Mitral Regurgitation Who Underwent Revascularization and Mitral Valve Repair Using Ring Annuloplasty**

Patient Data	TR (n=34)	No-TR (n=36)	P Value
Age, y	69.3 $\pm$ 9.2	64.9 $\pm$ 6.1	<0.05
Male/female, n	17/17	24/12	NS
NYHA functional class	2.8 $\pm$ 0.6	2.8 $\pm$ 0.7	NS
Preoperative TR $\geq$ moderate	12 (35.3%)	9 (25.0%)	NS
Tricuspid annuloplasty	4 (11.8%)	5 (13.9%)	NS
Follow-up period, mo	34.7 $\pm$ 23.7	19.9 $\pm$ 29.0	<0.01

Where applicable, data are shown as mean  $\pm$  SD or No. of patients. NYHA indicates New York Heart Association.

36 patients (51%). No significant differences were found between the groups in terms of sex, preoperative New York Heart Association functional class, incidence of significant preoperative TR, and percentage of tricuspid valve annuloplasties performed (TVRep). Two of 5 patients with a Duran ring and 2 patients with a de Vega annuloplasty developed recurrent TR. Age and length of follow-up period in the TR group, however, were significantly higher than in the no-TR group (Table 1). Although the mean New York Heart Association functional class was significantly ( $P < 0.0002$ ) better at last follow-up (2.0) than before surgery (2.9), 29 patients (41%) died after the last TEE.

### Tricuspid Annuloplasty

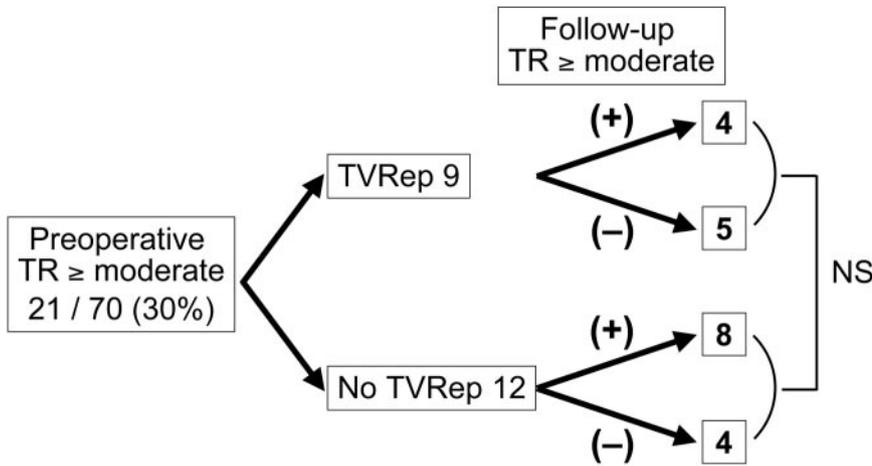
Twenty-one patients (30%) had moderate or greater preoperative TR, but only 9 underwent TVRep. Although immediately successful in all 9 patients, 4 (44%) developed significant TR at follow-up. This annuloplasty failure was similar in the patients with Duran ring (2 of 5) and de Vega (2 of 4) annuloplasties. Of the 12 patients with surgically ignored TR, 8 (67%) had significant TR at follow-up. There was no statistical difference whether the tricuspid valve had been repaired or ignored (Figure 2). The preoperative tricuspid annulus/BSA was significantly larger in patients who underwent annuloplasty than in those who did not ( $25.8 \pm 2.7$  mm versus  $20.7 \pm 2.7$  mm;  $P < 0.01$ ). In contrast, the annulus size was not significantly different between patients who underwent annuloplasty versus those that did not ( $24.9 \pm 7.3$  mm versus  $22.0 \pm 3.1$  mm). In patients without annuloplasty, however, annulus size increased significantly ( $P < 0.01$ ) from the preoperative value, while it did not in those with annuloplasty.

### Progression of TR After Mitral Valve Repair

The mean follow-up time was  $27.3 \pm 27.0$  months (range 1 to 105 months). The incidence of significant TR (as evaluated by the last follow-up TTE) after revascularization and MVRep was 25% (7 of 28) at less than 1 year, 53% (10 of 19) between 1 and 3 years, and 74% (17 of 23) at greater than 3 years. The difference between all groups was significant (Figure 3).

### Follow-Up MR and TR

Twenty-two of the 70 patients had significant recurrent MR at last follow-up (31%). Among them, 14 (64%) had significant follow-up TR. Among the 48 patients without MR, 20 (42%)



**Figure 2.** Evolution of functional tricuspid regurgitation after being repaired or ignored. TVRep indicates tricuspid valve annuloplasty.

had significant follow-up TR. This difference was not significant (Figure 4).

**Preoperative Echocardiographic Measurements**

No differences were found between the TR and no-TR groups in preoperative percentage TR jet area, RV area change, RV sphericity index, RV systolic pressures, and LV ejection fraction. The only preoperative difference found between the groups was a significantly larger tricuspid annulus/BSA in the TR group than in no-TR group (Table 2 and Figure 5).

**Follow-Up Echocardiographic Measurements**

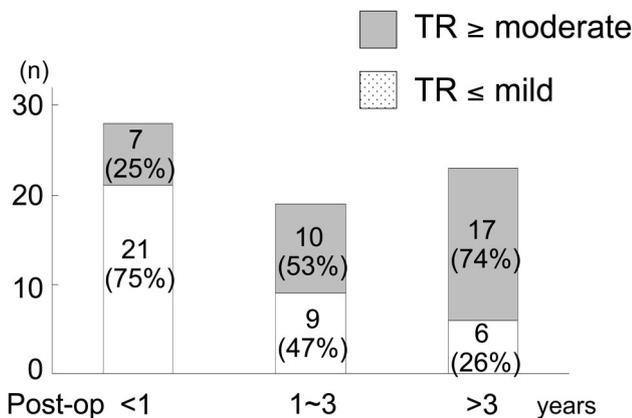
In the TR group, percentage TR jet area, tricuspid annulus/BSA, and RV sphericity index increased, and the RV area change decreased significantly from the preoperative value. In contrast, percentage TR jet area, tricuspid annulus/BSA, RV sphericity index, and RV area change did not vary in the no-TR group. In fact, at follow-up, percentage TR jet area, tricuspid annulus/BSA, and RV sphericity index in the TR group were significantly higher than in the no-TR group. Additionally, RV area change in the TR group was significantly lower than in the no-TR group. Although the RV systolic pressure and LV ejection fraction did not change in either group, at follow-up, the RV systolic pressure in the TR group was significantly higher than in the no-TR group. LV ejection fraction was not different between the groups (Table 2 and Figure 5).

**Discussion**

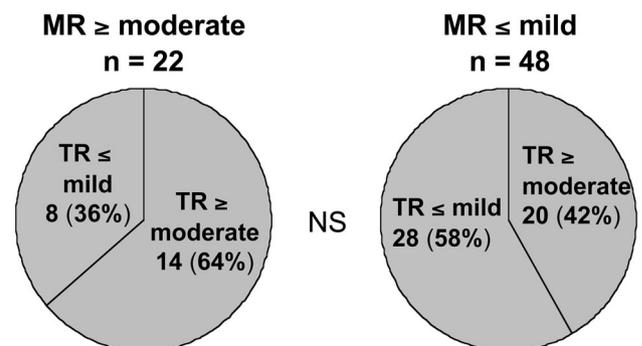
Tricuspid valve disease is not only underdiagnosed but it is also often surgically ignored. This is particularly relevant in cases of functional regurgitation, which is characterized by its variability and minimal clinical impact. Its presence is largely ignored and unreported. This lack of diagnosis is compounded at the time of surgery, when the changes in load under anesthesia minimize its degree. The aims of the present study were to determine the incidence of TR among patients referred for revascularization and MVRep for ischemic MR, to detect how many TRs were surgically treated or ignored, and to observe the late outcome in terms of presence or absence of TR after surgery. Intraoperative, post-repair TEE was used to select patients for the study who had a successful MVRep.

Our findings show that among the patients with functional ischemic MR who underwent revascularization and MVRep, the presence of significant functional TR was 30% before surgery. In more than half (57%), the regurgitation was ignored by the surgeon. These findings should alert both cardiologists and surgeons of the high incidence of ischemic functional TR. Whether a consequent aggressive repair attitude should be followed remains to be shown.

Surprisingly, after successful surgical revascularization and MVRep, close to 50% of the patients showed significant TR at their last TTE. The mechanism responsible for the persistence or development of new functional TR after correction of mitral valve disease of different etiologies has been extensively studied. Classically, functional TR has been



**Figure 3.** Presence of TR during the postoperative period.



**Figure 4.** Relationship between recurrent ischemic MR and late TR.

**TABLE 2. Preoperative and Late Transthoracic Echocardiographic Data of Patients**

	TR (n=30)			No-TR (n=24)		
	Pre-Op	Follow-Up	P Value	Pre-Op	Follow-Up	P Value
Percentage TR jet area, %	13.3±15.5	36.2±12.7†	<0.01	7.7±12.0	6.2±6.3	NS
Tricuspid annulus/BSA, mm/m <sup>2</sup>	22.0±2.9*	23.5±3.9†	<0.01	20.2±3.1	20.6±2.9	NS
RV sphericity index	0.38±0.06	0.44±0.06†	<0.01	0.39±0.11	0.39±0.07	NS
RV area change, %	38.8±9.2	29.1±10.2†	<0.01	36.0±12.8	39.3±11.3	NS
RV systolic pressure, mm Hg	53.6±15.1	51.1±12.2†	NS	43.9±15.1	39.3±11.3	NS
LVEF, %	42.4±13.0	40.5±14.9	NS	40.5±14.9	44.9±12.6	NS

Data are shown as mean±standard deviation. LVEF indicates left ventricular ejection fraction.

P values are shown for comparison between preoperative values (pre-op) and follow-up in the same group.

\*Difference between preoperative TTE in TR group and no-TR group ( $P<0.05$ ).

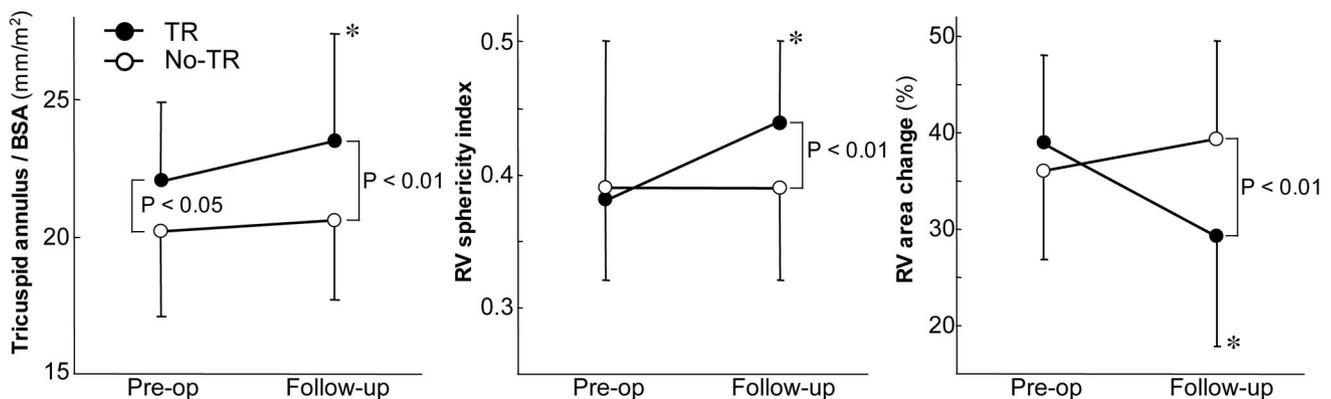
†Difference between follow-up TTE in TR group and no-TR group ( $P<0.01$ ).

related to RV pressure overload secondary to mitral valve disease, which induces RV and tricuspid annulus dilation. Correction of the left-sided lesion should reduce functional TR.<sup>1</sup> Sadeghi et al<sup>13</sup> reported that after significant pulmonary artery pressure reduction after pulmonary thromboendarterectomy, severe functional TR with a dilated annulus spontaneously improved. On the other hand, others have shown that pulmonary hypertension failed to be a significant determinant of functional TR.<sup>14,15</sup> Our data show that the presence or absence of residual MR did not affect the incidence of follow-up TR. Also, although the follow-up RV systolic pressure in patients with TR was significantly higher than in those without TR, no change was found between preoperative and late RV pressures within each group. These results do not show that revascularization and MVRep reduce RV pressure overload and prevent late TR. Although possibly because of irreversible pulmonary vasculature damage,<sup>5</sup> we speculate that the cause of the persistent elevated RV systolic pressure could also be nondetected LV failure.

Among the patients with follow-up TR, preoperative and follow-up tricuspid annulus dilation was significantly larger than in those without TR. This finding suggests that preoperative tricuspid annulus dilation might be a predictor of late TR. Previous investigators have shown that preoperative tricuspid annulus dilation was a risk factor for late TR in nonischemic patients.<sup>2,4,16–18</sup> Our results also show that patients with follow-up TR tend to be older than those without

follow-up TR. Therefore, it is possible that those patients with follow-up TR had been subjected to RV pressure overload for a longer time.

To our dismay, we found that the incidence of late TR was independent of whether the TR was surgically treated or ignored (44% versus 67%;  $P=NS$ ). Although this nonsignificant difference might become significant in a larger series of patients, the fact remains that in these patients, tricuspid annuloplasty is not as efficient as might be believed. Furthermore, the incidence of functional TR increased progressively from 25% at less than 1 year of follow-up to 53% between 1 and 3 years and 74% at more than 3 years of follow-up. Overall, functional ischemic TR increased from 30% before surgery to 50% during the follow-up period, and this was apparently independent of whether the TR was repaired or ignored. Recently, Matsuyama et al<sup>15</sup> reported that 16% of the patients who underwent nonischemic mitral valve surgery without tricuspid valve surgery developed 3 to 4+ TR at an 8-year follow-up, and in a study of 790 patients, McCarthy and associates<sup>19</sup> reported recurrence rates of 17% to 32% at 5 years according to the type of annuloplasty performed. In the present series, the rate of late TR was similar among patients with a flexible ring (2 or 5) or an encircling suture (2 of 4). Whether the degree of annulus reduction was a factor cannot be answered because of the small number of patients. These results suggest that a simple tricuspid reduction annuloplasty might not consistently protect against recurrent functional



**Figure 5.** Echocardiographic right ventricular data. Preoperative and late echocardiographic measurements in patients with (TR) and without follow-up TR (No-TR). \* $P<0.01$  versus preoperative values.

TR. Furthermore, similar disappointing results of mitral annuloplasty in patients with ischemic mitral regurgitation reinforce this skepticism.<sup>20,21</sup> These recurrence rates, observed in patients with different etiologies, are lower than our rates in a selected patient population that included only ischemic mitral disease. This difference might be because of ongoing ischemic remodeling cardiomyopathy that induces RV and LV geometric changes (which are not addressed by a simple annuloplasty). The very significant recurrent MR (31%) present in our patients reinforces the significance of ventricular geometric distortion.<sup>20,22,23</sup>

### Study Limitations

The present study is a retrospective analysis of routine clinical echocardiographic data. We investigated the presence of significant functional TR in patients with functional ischemic MR who underwent revascularization and MVRep. The grade of TR was evaluated only semiquantitatively, and the assessment of RV function was evaluated only by the percent change in RV cavity area, which was dependent on echocardiographic image quality. In addition, we did not investigate in detail geometric changes occurring in the tricuspid valve and the RV shape. The cusp coaptation point and its displacement from the annulus and papillary muscle displacement could not be calculated.<sup>14</sup> Finally, in the present study, the number of patients was relatively small, particularly the number of those who underwent tricuspid repair. Further larger and prospective studies are needed.

### Conclusions

The present retrospective study is a TTE analysis of 70 patients with functional ischemic MR who underwent successful revascularization and MVRep. Preoperative functional TR was present in 30% of the cases. The TR was surgically ignored in 57% of the cases. After surgery, the incidence of TR rose to close to 50%, independent of whether it was repaired or ignored. The presence of TR increased over time, reaching up to 70% at more than 3 years' follow-up. The presence or absence of postoperative TR was not related to the presence or absence of recurrent ischemic MR. The preoperative and postoperative tricuspid annulus dimension in patients with TR was significantly larger than in patients without TR.

### Acknowledgments

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