Determinants of Recurrent or Residual Functional Tricuspid Regurgitation After Tricuspid Annuloplasty

Shota Fukuda, MD; A. Marc Gillinov, MD; Patrick M. McCarthy, MD; William J. Stewart, MD; Jong-Min Song, MD; Takashi Kihara, MD; Masao Daimon, MD; Mi-Seong Shin, MD; James D. Thomas, MD; Takahiro Shiota, MD

Background—The durability of tricuspid valve (TV) repair by annuloplasty is limited. Identification of mechanisms of recurrent or residual tricuspid regurgitation (TR) after annuloplasty is necessary to improve results of TV repair. The purpose of this study was to investigate echocardiographic determinants of mid-term outcome after TV annuloplasty.

Methods and Results—This study consisted of 39 patients with functional TR who had echocardiography preoperatively, early postoperatively (5±2 days), and >1 year (20±6 months) after TV annuloplasty. Detailed echocardiographic measurements were performed, including TR severity, TV annular dimension, TV leaflet displacement, left ventricular (LV) function, and right ventricular (RV) function and pressures. Preoperative leaflet tethering height and area predicted early and mid-term outcome of annuloplasty. Early postoperative LV ejection fraction and TR severity influenced degree of TR >1 year after surgery. In addition, increased RV pressure was related to worse TR during late follow-up.

Conclusions—Although TV tethering is an important determinant of recurrent or residual TR, LV and RV function and pressures impact repair durability. These factors identify patients at risk for repair failure; such individuals require development of additional surgical strategies to improve results of tricuspid valve repair and close surveillance after surgery. (Circulation. 2006;114[suppl I]:I-582–I-587.)

Key Words: echocardiography † regurgitation † surgery † valves

Functional tricuspid regurgitation (TR) is common in patients with left-side valve disease and left ventricular (LV) dysfunction, and depending on its severity it can considerably decrease long-term survival.1,2 Several echocardiographic and angiographic studies have suggested important changes in the tricuspid valve (TV) geometry in patients with functional TR, including annular dilatation and tethering of the leaflets.3–5 These TV deformations may restrict the motion of the leaflets and decrease coaptation.

Clinical and surgical management of functional TR has evolved from conservative approaches4 (that is, no directed treatment and hope for spontaneous regression after correction of left-sided disease) to a more direct approach to the valve.6,7 TV annuloplasty is now recommended for treatment of functional TR at the time of cardiac surgery; however, residual regurgitation is common.8–11 We recently showed that the preoperative extent of tethering of the leaflets is associated with residual regurgitation early after TV annuloplasty.12 However, the mechanisms responsible for recurrent or residual TR at mid-term follow-up after annuloplasty have not been determined. Therefore, the purpose of this study was to investigate echocardiographic determinants of recurrent or residual TR >1 year after TV annuloplasty.

Methods

Study Population

Three-hundred forty-five patients with functional TR who had TV annuloplasty were initially enrolled from the Cleveland Clinic Foundation surgical and echocardiography databases from 2002 to 2004; both databases were approved by the Institutional Review Board for clinical research. In these 345 patients, we found 52 patients who had echocardiographic examination >1 year after TV annuloplasty at our institution. Follow-up echocardiographic examination was performed according to the recommendation by patient’s attending physicians. Patients with pacemaker wires across the TV preoperatively (n=4), congenital heart disease (n=3) and inadequate image quality of echocardiography (n=5) were excluded. One patient was also excluded because repeat open heart surgery was required during this follow-up period. The final population of this study consisted of 39 patients (18 male, 21 female; mean age 64±12 years). All patients had 2-dimensional transthoracic echocardiography preoperatively, early postoperatively (5±2 days), and >1 year (20±6 months) after surgery.

Types of TV Annuloplasty and Concomitant Surgical Procedures

TV ring annuloplasty was performed with the Carpentier ring in 6 patients, Cosgrove ring in 17 patients, and MCIII ring in 12 patients (Edwards Lifesciences, LLC, Irvine, Calif). The average ring size

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was 27±2 mm (range, 26 to 30 mm). The remaining 4 patients underwent suture annuloplasty, as described by Kay.\textsuperscript{12} Annuloplasty type mostly depended on device availability and surgeons’ preference in our institution. There were no significant differences in any preoperative parameters between patients with the Kay procedure and ring-annuloplasty.

The concomitant procedures performed at the time of TV annuloplasty were mitral valve surgery in 15 patients, aortic valve surgery in 3 patients, both mitral and aortic valve surgery in 6 patients, coronary artery bypass grafting in 1 patient, and combined valve surgery (mitral valve in 12, and aortic valve in 2) and coronary artery bypass grafting in 14 patients.

**Echocardiographic Measurements**

Two-dimensional transthoracic echocardiography was performed in a standard manner using Sonos 5500 (Philips Medical Systems, Andover, Mass), Sequoia 512 (Siemens, Mountainview, Calif), or Vivid 7 (GE Medical Systems, Milwaukee, Wis). After carefully choosing the highest possible quality image using our digital storing system, echocardiographic measurement was performed with the best frame in patients without atrial fibrillation. To minimize the effect of varied TV preload caused by irregular beats, the values of echocardiographic parameters were averaged over 5 cardiac cycles in patients with atrial fibrillation (preoperatively atrial fibrillation was observed in 6 (15%) patients, early postoperatively in 3 (8%) patients, and >1 year after the procedure in 2 (5%) patients).

Right ventricular (RV) fractional area change,\textsuperscript{11,14} the minimal TV annular dimension, the tethering height (the distance between the coaptation of the septal and anterior leaflets and the tricuspid annular plane),\textsuperscript{5,15} the tethering area (the area enclosed by the annular plane and septal and anterior leaflets), and the ratio of the maximal TR area on color flow mapping to RA area (%TR) were measured in the apical 4-chamber view, as previously described.\textsuperscript{10} LV ejection fraction was obtained using the Simpson method from apical 4-chamber and 2-chamber views. After recording TV systolic velocity with continuous-wave Doppler, RV systolic velocity was calculated using the simplified Bernoulli equation.

**Statistical Analysis**

Values are expressed as mean±SD. An unpaired t test was used to compare the continuous variables. One-factorial repeated measures analysis of variance was used to compare among 3 time points (preoperatively, early postoperatively, and >1 year after surgery). When differences were found, any 2 points were compared using Student t test with the Bonferroni correction. Linear regression was used for correlation of variables of interest. Multivariate stepwise linear regression analysis was performed to identify factors associated with TR severity >1 year after surgery. Significant variables on univariate analysis entered into models were LV ejection fraction, tethering height and area on preoperative echocardiography, LV ejection fraction and TR severity on early postoperative echocardiography, and the combination of mitral valve surgery and coronary artery bypass grafting. Differences were considered significant at P<0.05. We also examined the sensitivity and specificity of various cut-off points for prediction of moderate or severe TR (>20% TR) using receiver operating characteristic curves.

Inter-observer and intra-observer variability for measurement of TV annular dimension, and tethering height and area were obtained by analysis of 10 random images by 2 independent blinded observers and by the same observer at 2 different time points. The results were analyzed by both least squares fit linear regression analysis and the Bland-Altman method.

The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

**Results**

**Relationship of Clinical and Echocardiographic Findings to TR Severity >1 Year After Surgery**

Preoperatively, TV annular dimension and tethering height and area were 3.38±0.55 cm, and 0.53±0.40 cm and 0.88±0.98 cm², respectively.

| Table 1. Relationship of Clinical and Echocardiographic Parameters With TR Severity >1 Year After Annuloplasty |
|------------------------------|----------|-----------|-----------|
| Preoperative                 | t        | Univariate P  | Multivariate P |
| Age (years)                  | 0.23     | 0.2       |           |
| LV ejection fraction (%)     | 0.38     | 0.02      | 0.1       |
| RV fractional area change (%)| 0.21     | 0.2       |           |
| RA area (cm²)                | 0.27     | 0.1       |           |
| RV pressure (mm Hg)         | 0.01     | 0.9       |           |
| TV annular dimension (cm)   | 0.20     | 0.2       |           |
| TV tethering height (cm)    | 0.53     | <0.001    | 0.4       |
| TV tethering area (cm²)     | 0.53     | <0.001    | 0.9       |
| TR severity (%TR)           | 0.17     | 0.3       |           |
| Early postoperative         |          |           |           |
| LV ejection fraction (%)     | 0.46     | 0.003     | 0.002     |
| RV fractional area change (%)| 0.12     | 0.5       |           |
| RA area (cm²)                | 0.24     | 0.1       |           |
| RV pressure (mm Hg)         | 0.31     | 0.05      |           |
| TR severity (%TR)           | 0.60     | <0.001    | <0.001    |

LV indicates left ventricle; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation; TV, tricuspid valve.

In univariate analysis, the degree of TR >1 year after surgery was significantly related to LV ejection fraction (r=0.38, P=0.02), tethering height (r=0.53, P<0.001), and tethering area (r=0.53, P<0.001) on preoperative echocardiography, and to LV ejection fraction (r=0.46, P=0.003) and TR severity (r=0.60, P<0.001) on early postoperative echocardiography (Table 1). The combination of mitral valve surgery and coronary artery bypass grafting was performed in 12 (31%) patients. There was a significant difference in TR severity >1 year after the surgery between these 12 patients and the remaining 27 patients (19.9±15.5% versus 10.5±10.0%; P=0.03). Mitral valve surgery (14.6±12.9% versus 6.8±8.1%; P=0.2) or coronary artery bypass grafting alone (16.7±15.4% versus 11.3±10.2%; P=0.2) was not a significant factor on univariate analysis.

When significant variables on univariate analysis were analyzed by the multiple stepwise regression analysis, early postoperative LV ejection fraction (P=0.002) and TR severity (P<0.001) emerged as independent factors for TR >1 year after surgery (Table 1). The combination of mitral valve surgery and coronary artery bypass grafting turned out to be insignificant in multiple stepwise leaner regression analysis (P=0.07).

When only preoperative parameters (LV ejection fraction, and tethering height and area) were analyzed with multivariate stepwise linear regression analysis, tethering height was found to be the only independent predictor of TR severity >1 year after TV annuloplasty (P=0.001).

**Echocardiographic Predictors of Early and Mid-Term Outcome of TV Annuloplasty**

Intraoperative tranesophageal echocardiography was performed in 36 (92%) of 39 patients in this study. Only 1 (3%)
significant TR with sensitivity of 75% and specificity of 93% respectively (Table 2). Moreover, early postoperative LV function (39.4±12.4 mm Hg versus 12.4 mm Hg, P<0.04). Changes over time in LV ejection fraction, RV fractional area change, RA area, RV pressure, and TR severity after surgery are summarized in Figure 2. Repeated measures analysis of variance showed no significant differences in LV ejection fraction (P=0.2) and RV fractional area change (P=0.3) at the 3 time points. In contrast, RA area, RV pressure, and TR severity significantly decreased immediately after surgical procedure, and were relatively stable thereafter.

Reproducibility of Echocardiographic Measurements
Excellent correlation was observed in inter-observer and intra-observer echocardiographic measurements. They were r=0.85 and r=0.93 for TV annular dimension, r=0.92 and r=0.93 for tethering height, and r=0.96 and r=0.98 for tethering area, respectively. From the Bland-Altman method, inter-observer and intra-observer variabilities were 0.15 cm and 0.10 cm for TV annular dimension, 0.08 cm and 0.09 cm for tethering height, and 0.15 cm² and 0.07 cm² for tethering area, respectively.

Discussion
The present study investigated echocardiographic determinants of mid-term outcome of TV annuloplasty. Residual TR soon after annuloplasty and postoperative LV dysfunction were independent factors of recurrence/persistence of TR >1 year after TV annuloplasty. Although preoperative and postoperative RV pressures did not emerge as predictive factors, the increase in RV pressure after annuloplasty was associated with worse TR during this mid-term follow-up.

Mechanisms of Residual TR Early After TV Annuloplasty
It is well-known that significant TR that is not surgically corrected or that reappears after surgical management jeopardizes long-term outcome after cardiac surgery. TV annuloplasty is widely recommended for treatment of functional TR. The rationale for the currently used TV annuloplasty techniques is based primarily on the assumption that annular dilatation is the major cause of functional TR. Functional TR, however, frequently presents with tethering of the leaflets,3–5 which has not received much attention in the past. We recently showed that preoperative tethering of the leaflets is an independent predictor of residual TR early after annuloplasty.10 Current annuloplasty techniques might not be adequate to correct TR in patients with severe tethering.

Table 2. Echocardiographic Predictors of ≥Moderate TR Midterm After TV Annuloplasty

<table>
<thead>
<tr>
<th></th>
<th>Cut-Off Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Area Under Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative TV tethering height (cm)</td>
<td>0.51</td>
<td>75%</td>
<td>78%</td>
<td>0.81</td>
</tr>
<tr>
<td>Preoperative TV tethering area (cm²)</td>
<td>0.80</td>
<td>83%</td>
<td>85%</td>
<td>0.82</td>
</tr>
<tr>
<td>Postoperative LV ejection fraction (%)</td>
<td>36.6</td>
<td>75%</td>
<td>93%</td>
<td>0.88</td>
</tr>
<tr>
<td>Postoperative TR severity (%TR)</td>
<td>13.0</td>
<td>75%</td>
<td>67%</td>
<td>0.75</td>
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</tbody>
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LV indicates left ventricle; TR, tricuspid regurgitation; TV, tricuspid valve.

Figure 1. Regression plots showing correlation of changes in RV pressure with those in TR severity (%TR) during the follow-up period. Percent TR was defined as the ratio of the maximal regurgitant area to RA area. RV indicates right ventricle; TR, tricuspid regurgitation.

A patient had moderate TR on intraoperative evaluation. TR persisted early postoperatively in this patient.

Early postoperatively, severe TR was observed in 4 (10%) patients, moderate in 5 (13%), and mild TR in 30 (77%). Using receiver operating characteristic curves, the sensitivity and specificity in predicting moderate to severe TR were 67% and 90% for tethering height >0.68 cm, and 67% and 80% for tethering area >0.82 cm², respectively.

More than 1 year after surgery, severe TR was present in 2 (5.1%) patients, moderate TR in 10 (26%), and mild TR in 27 (69%). The sensitivity and specificity in predicting moderate to severe TR were 75% and 67% for early postoperative TR severity >13% TR, 75% and 78% for tethering height >0.51 cm, and 83% and 85% for tethering area >0.80 cm², respectively (Table 2). Moreover, early postoperative LV ejection fraction <36.6% was also a predictive factor of significant TR with sensitivity of 75% and specificity of 93% (Table 2).

Changes in TR Severity During Follow-Up
By univariate analysis, changes in RV pressure during the follow-up period significantly correlated with those in TR severity (r=0.56, P<0.001; Figure 1), whereas changes in LV ejection fraction (P=0.4), RV fractional area change (P=0.9), and RA area (P=0.2) were not associated. RV pressure during late follow-up was higher in patients with early postoperative moderate or severe LV dysfunction (ejection fraction <40%) than patients with preserved early postoperative LV function (39.4±12.4 mm Hg versus 29.3±14.4 mm Hg, P=0.04).

Changes in Other Echocardiographic Parameters After TV Annuloplasty

Reproducibility of Echocardiographic Measurements
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However, the mechanisms of recurrent or residual TR mid-term after annuloplasty are unclear.

**Risk Factors for Recurrent or Residual TR**

**Mid-Term After TV Annuloplasty**

In this report, residual TR soon after the procedure influenced mid-term outcome of TV annuloplasty. This finding is expected because significant TR early after the procedure may lead to a vicious cycle; residual TR causes volume overloading of the RV and further RV dilatation and dysfunction, resulting in more TR.

We demonstrated that LV dysfunction early postoperatively is also a risk factor for significant TR >1 year after TV annuloplasty. This supplements previous reports demonstrating that impaired LV systolic function is associated with an unfavorable long-term progress after TV annuloplasty.\(^9\,^{19,\,20}\) Severe LV systolic dysfunction is thought to be a consequence of longstanding pathological changes that are secondary to preoperative and postoperative pressure and/or volume overload. In addition, a dilated and elliptically shaped LV is frequently encountered in patients with severe LV dysfunction. These geometric LV abnormalities may affect RV geometry and function directly through the interventricular septum or pericardium, or indirectly by contributing to pulmonary hypertension.\(^21\,^{22}\) Weber et al examined the effect of altered LV geometry on RV pressure-volume relationships in a canine model.\(^22\) RV size, and shape were altered when LV geometry became abnormal, resulting in RV dysfunction in their study. Damiano et al showed that RV systolic pressure and pulmonary artery blood flow were affected by not only RV but also LV function in an experimental model.\(^23\) Such ventricular interactions between the LV and RV might explain the importance of LV dysfunction in risk stratification of patients with TV annuloplasty. Also, LV dysfunction

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**Figure 2.** Changes over time in LV ejection fraction (A), RV fractional area change (B), RA area (C), RV systolic pressure (D), and TR severity (E). Percent TR was defined as the ratio of the maximal regurgitant area to RA area. LV indicates left ventricle; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation; TV, tricuspid valve.
may cause high end-diastolic pressures and pulmonary hypertension, which may, in turn, affect RV size and function. As a matter of fact, we observed higher RV pressures >1 year after the procedure in patients with early postoperative LV dysfunction, as compared with patients having relatively preserved LV function.

**Importance of Pulmonary Hypertension Mid-Term After TV Annuloplasty**

This study demonstrated that the preoperative severity of pulmonary hypertension did not influence mid-term outcome of annuloplasty, which is consistent with the results of previous studies of TV surgery. However, we found that an increase in the severity of pulmonary hypertension caused worse functional TR during mid-term follow-up after TV annuloplasty. This finding was supported by previous observations, showing that changes in RV pressure were associated with severity of TR in patients with underlying left sided disease. In patients with mitral stenosis after percutaneous mitral valvuloplasty, greater reductions in transmural pressure gradients and RV pressure were observed in patients with resolution of functional TR, as compared with patients with persistent TR. Also, reduction of RV pressure after thromboendarterectomy in patients with chronic pulmonary hypertension was associated with reduction in functional TR without any changes of TV deformations. As a consequence, we conclude that the existence of severe pulmonary hypertension should not be considered a deterrent for recommending TV annuloplasty to patients with functional TR, and approaches alleviating pulmonary hypertension could potentially be a part of effective management strategies for patients after TV annuloplasty.

**Study Limitations**

This is an observational study. The number of patients was relatively small. Therefore, the effect of a wide variance of operative techniques for concomitant procedures and TV annuloplasty on the results of this study was unclear. Also, the relationship between recurrent mitral regurgitation and mid-term outcome after TV annuloplasty remained unclear. Further prospective study should be performed to confirm the results of this study in a much larger population.

Furthermore, this echocardiographic study was a retrospective analysis of a highly selected population. The majority of patients operated in the Cleveland Clinic Foundation were referred from outside hospitals in other states and, in many cases, other countries. They were thus usually followed-up by local cardiologists, not at our institution, especially when postoperative courses were benign. There might be overemphasis of surgical failure because successful patients were less likely to return for follow-up examinations. The purpose of this study was not to investigate the safety or effectiveness of TV annuloplasty; this is the subject of numerous studies in the literature.

TR is a dynamic lesion that is highly dependent on RV volume/pressure loading characteristics. Therefore, when echocardiographic examinations were performed, stable hemodynamic conditions were carefully confirmed during transthoracic echocardiographic examination. In addition, the echocardiographic evaluation postoperatively was performed on fully recovered and catecholamine-free patients except in 1 case (3%). This patient did not have residual TR.

Correlation of RV pressure increases and changes in TR severity was weak in this study. Considering the relatively small number of patients and complicated multiple factors, affecting on RV pressure and TR severity, this relatively weak relationship was expected, but its report may be of clinical value.

Two-dimensional echocardiography was used for assessment of RV geometry and function as well as TV deformation in this study. Changes in RV shape and size might result in papillary muscle dislocation and tethering of the leaflets. However, precise quantification of RV shape and size was technically difficult with 2-dimensional echocardiography because of associated complex anatomic geometry. Moreover, the posterior leaflet was not visualized from apical 4-chamber view. Three-dimensional imaging techniques may have the potential to provide more accurate information for RV function and geometry and on TV deformations.

**Conclusions**

Residual TR early after the procedure, which was associated with preoperative tethering of TV leaflets, and postoperative LV dysfunction predict mid-term outcome of TV annuloplasty. Increased RV pressure results in worse TR during mid-term follow-up. Additional repair techniques may be beneficial in patients with severe leaflet tethering and LV dysfunction. Close follow-up is required in patients in whom increased RV pressures after TV annuloplasty develop.

**Disclosures**

Drs Gillinov and McCarthy have served as consultants to Edwards Lifesciences, LLC. Dr McCarthy is an inventor of McCarthy tricuspid annuloplasty MCHI ring and receives royalties from Edwards Lifesciences, LLC.

**References**


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