Percutaneous Mitral Valvuloplasty Versus Surgical Treatment in Mitral Stenosis With Severe Tricuspid Regurgitation

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Background—The persistence of significant tricuspid regurgitation (TR) after percutaneous mitral valvuloplasty (PMV) is known to be an independent predictor of adverse outcome in mitral stenosis (MS). However, it remains unclear whether mitral valve (MV) surgery combined with surgical correction of TR is the better treatment option than PMV in patients with severe MS and severe functional TR.

Methods and Results—We included a total of 92 consecutive patients (18 men, age 49 ± 13 years) with severe MS and severe functional TR, who were potential candidates for PMV from 1997 to 2005, and the exclusion criteria were defined as the presence of left atrial thrombi, mitral regurgitation grade ≥ 3, echo score > 10, and left ventricular ejection fraction (EF) < 35%. PMV was performed on 48 patients (PMV group), and MV surgery combined with tricuspid valve (TV) repair was performed on 44 patients (TVP group). The clinical events were defined as death, repeat surgical or percutaneous intervention, and readmission because of heart failure. There were no significant differences between the 2 groups in terms of gender, baseline EF, and baseline severity of pulmonary hypertension, but patients in the TVP group were older and had a higher echo score and a higher incidence of atrial fibrillation than those in the PMV group. During follow-up of 57 ± 35 months, 2 deaths occurred in the TVP group, and there were 2 deaths, 7 cases of heart failure requiring surgical intervention in the PMV group. The difference of event rates between the 2 groups showed borderline significance (P = 0.05), but no difference in mortality was observed. The estimated actuarial 7-year event-free survival rate was 77 ± 8% in the PMV group and 95 ± 3% in the TVP group. Severe TR was improved to mild or absent TR in 43 (98%) patients in the TVP group, and this was significantly higher than in the PMV group (22/48, 46%; P < 0.001). In the TVP group, the right ventricle (RV) size was significantly decreased in 18 (90%) patients among 20 patients with preoperative significant RV enlargement. On stepwise multivariate logistic regression analysis, TVP group and baseline sinus rhythm were independent predictors for improvement of TR (P < 0.001).

Conclusions—TV repair combined with MV surgery was related to better clinical outcomes than PMV alone, and we recommend that this surgical option should be considered preferentially in severe MS with severe functional TR, especially if atrial fibrillation or enlarged RV is associated. (Circulation. 2007;116[suppl I]:I-246–I-250.)

Key Words: surgery □ valvuloplasty □ mitral stenosis □ tricuspid regurgitation

Functional tricuspid regurgitation (TR) is frequently associated with severe mitral stenosis (MS), 1–4 because significant MS can cause pulmonary venous and arterial hypertension resulting in right ventricle (RV) dysfunction and tricuspid annular dilatation. The clinical importance of associated TR has been well appreciated, as persistent TR contributes to increased morbidity and mortality despite adequate surgical and percutaneous intervention of the mitral valve (MV) disease. 5–8

Although percutaneous mitral valvuloplasty (PMV) has become the treatment of choice in selected patients with severe MS, 9–11 its inability to correct the associated tricuspid valve disease can be an inherent limitation, and persistent significant TR after PMV is known as an independent predictor of an adverse outcome. 5,6 However, it is unclear whether MV surgery with simultaneous surgical correction of TR would be the better treatment option in patients who are potential candidates for PMV, because MV surgery has the morbidity and mortality related with operation, and regression of TR may result from improvement of pulmonary hypertension by PMV. 12,13 We therefore examined the hypothesis that MV surgery with tricuspid valve (TV) repair is

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related with more favorable clinical outcomes by reducing functional TR more effectively than PMV alone. We also analyzed the effects of clinical, echocardiographic, and procedural variables on clinical outcome and improvement of TR in patients with severe MS and severe functional TR.

Methods

Study Population
We included a total of 92 consecutive patients (18 men, age 49±13 years) with severe MS (MV area <1.2 cm^2) and severe functional TR, who were potential candidates for PMV from 1997 to 2005. The criteria for exclusion in the study were defined as a total echocardiographic score >10, mitral regurgitation ≥grade 3, left atrial thrombi, significant aortic valvular disease, and left ventricular (LV) ejection fraction ≤35%. The decision to recommend PMV alone or combined MV surgery and TV repair was at the discretion of the attending physician.

Percutaneous Mitral Valvuloplasty
The PMV was performed using either the double balloon or the Inoue balloon technique, as described previously. The procedure was performed by two experienced interventional cardiologists during which conventional hemodynamic parameters were monitored. A successful immediate result was defined as a MV area ≥1.5 cm^2 or an increase of ≥50% after PMV with mitral regurgitation less than grade 3.

Surgical Procedure
All patients underwent normothermic cardiopulmonary bypass with intermittent cold blood cardioplegia. In all patients undergoing mechanical mitral valve replacement (MVR), the posterior leaflet was preserved. After MVR, TV repair was performed using the De Vega tricuspid annuloplasty or Carpentier-Edward and Duran ring annuloplasty. After tricuspid annuloplasty, cold saline solution was rapidly flushed into the right ventricle to test the competence of the tricuspid valve. The maze operation was performed on selected patients with atrial fibrillation as described previously.

Echocardiographic Evaluation
Echocardiographic evaluation was performed before and after either PMV or surgery, and then annually during the follow-up. Two-dimensional echocardiography and Doppler color flow imaging were performed on all patients with a Hewlett-Packard Sonos 2500 or 5500 imaging system equipped with a 2.5-MHz transducer (Hewlett-Packard, Andover, Mass). Transesophageal echocardiography was performed on all patients to detect left atrial thrombi. The morphological features of the MV were categorized as described previously, and the total echocardiographic score was obtained by adding the score for each of the following individual morphological features: leaflet mobility, thickness, calcification, and subvalvular lesions. The MV area was measured by direct planimetry of the mitral orifice. Mitral regurgitation was detected and semiquantitatively graded with color flow imaging.

RV size and TR were evaluated in the apical four-chamber view. TR was graded as trace, mild, moderate, and severe when the jet area occupied 10%, 10% to 20%, 20% to 33%, or >33% of the right atrial area, respectively, in correlations with surgical and angiographic data. The right atrial area was traced from the same frame as the maximal jet area. TR was defined as having improved when the regurgitation was trace or mild on the 1-year follow-up echocardiography. The RV was considered significantly enlarged when the dimension of RV which equaled to or was greater than the dimension of LV. The tricuspid annular diameter was measured at the time of maximal tricuspid opening as the distance from the insertion of septal tricuspid leaflet to the insertion of anterior tricuspid leaflet. RV systolic pressures were estimated by continuous wave Doppler using the simplified Bernoulli equation (4×[peak TR velocity]²), with 10 mm Hg added for the estimated right atrial pressure. RV systolic pressure was considered to be equal to the pulmonary artery systolic pressure unless there was significant pulmonary stenosis.

Clinical Follow-Up
The clinical follow-up ranged from 6 to 114 months. Data were obtained during visits to the outpatient clinic or by telephone interview. The clinical events were defined as death, repeat surgical or percutaneous intervention, and readmission because of symptomatic heart failure.

Statistical Analysis
Numerical data expressed as mean±SD values. Continuous variables were compared using the Student paired and unpaired t tests. The χ² test and Fisher exact test compared frequency ratios between groups. Wilcoxon signed-rank test was used to assess the follow-up change in RV size and progression of TR. Multiple stepwise logistic regression analysis was used to identify independent predictors for improvement of TR. Kaplan-Meier analysis was used to determine the event-free survival rate, and differences in survival rates between groups were analyzed by the log-rank test. A probability value <0.05 was considered to be significant.

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

Results

Baseline Characteristics
The PMV was performed on 48 patients (PMV group), whereas 44 patients received MVR combined with TV repair (TV group). The baseline clinical and echocardiographic characteristics of the study population were summarized in the Table. There were no significant differences between the 2 groups in terms of gender, predicted surgical mortality calculated by logistic Euroscore, LV ejection fraction, severity of pulmonary hypertension, tricuspid annular diameter, incidence of significant RV enlargement, or MV area, but patients in the TVP group were significantly older and had a

<table>
<thead>
<tr>
<th></th>
<th>TV Group (n=44)</th>
<th>PMV Group (n=48)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>54±12</td>
<td>44±11</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender, male</td>
<td>11 (25%)</td>
<td>7 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>38 (86%)</td>
<td>26 (54%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Logistic Euroscore</td>
<td>1.9±0.8</td>
<td>1.7±0.8</td>
<td>NS</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>61±10</td>
<td>54±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>55±7</td>
<td>57±8</td>
<td>NS</td>
</tr>
<tr>
<td>Mitral valve area, cm^2</td>
<td>1.0±0.3</td>
<td>0.9±0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Mean mitral PG, mm Hg</td>
<td>13±7</td>
<td>13±6</td>
<td>NS</td>
</tr>
<tr>
<td>Echo score</td>
<td>9.1±1.0</td>
<td>7.9±1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak TR velocity, m/sec</td>
<td>3.1±0.7</td>
<td>3.3±0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic PAP, mm Hg</td>
<td>48±19</td>
<td>54±20</td>
<td>NS</td>
</tr>
<tr>
<td>Tricuspid annulus diameter, mm</td>
<td>39±7</td>
<td>36±6</td>
<td>NS</td>
</tr>
<tr>
<td>RV enlargement, %</td>
<td>20 (45%)</td>
<td>13 (27%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

LV indicates left ventricle; PG, pressure gradient; TR, tricuspid regurgitation; PAP, pulmonary artery pressure; RV, right ventricle.
In the PMV group, the valve area was increased from a baseline of 0.9 cm² immediately after PMV (P < 0.001), and an immediate successful result of PMV was achieved in 95% (57/60) of the patients. In the TVP group, there was no operative mortality.

Clinical follow-up was completed with 91 (99%) patients, with a mean follow-up period of 57±35 months. There were 2 patient deaths in the TVP group: 1 patient died of severe LV dysfunction at 2 months, and the other patient died of gastrointestinal bleeding at 1 year after MVR. In the PMV group, there were 2 deaths from heart failure at 2 and 3 years after PMV. The estimated actuarial 7-year survival rate was 95±3% in the TVP group and 95±4% in the PMV group (P = NS). There were no other clinical events in the TVP group during follow-up, and in the PMV group, there were 2 cases of heart failure and 5 cases who underwent MVR combined with TV repair (3 cases of severe TR, 1 case of mitral restenosis with severe TR, and 1 case of severe MR and severe TR). The event rate was 19% in the PMV group and 5% in the TVP group, and the difference of event rates between the 2 groups showed borderline significance (P = 0.05). The estimated actuarial 7-year event-free survival rate was 77±8% in the PMV group and 95±3% in the TVP group, and the difference did not reach the statistical significance (Figure 1A).

Because the incidences of baseline atrial fibrillation differed between the 2 groups, subgroup analysis was performed according to cardiac rhythm. In patients with atrial fibrillation, the event rate was significantly higher in the PMV group (7/26) than in the TVP group (2/38, P < 0.05) and the estimated actuarial 7-year event-free survival rate was also significantly lower in the PMV group (70±11%) than in the TVP group (94±4%) (Figure 1B). In patients with sinus rhythm, the event rates were similar in the PMV and TVP groups (2/22 and 0/6, respectively), and the estimated actuarial 7-year event-free survival rates did not differ significantly between the 2 groups.

**Impact of TV Repair on Improvement of TR and RV Remodeling**

Severe TR was improved to mild or absent TR on 1-year follow-up echocardiography in 43 (98%) patients in the TVP group, and this was significantly higher than in the PMV group (22/48, 46% P < 0.001; Figure 2). The tricuspid annular diameter was decreased significantly from 38.5±6.6 to 28.5±6.2 mm in TVP group (P < 0.001), but was unchanged in the PMV group (36.4±5.9 to 36.7±6.1 mm, P = NS). In the PMV group, RV size was increased significantly in 5 patients and decreased significantly in 5 patients, respectively (P = NS), but RV size was significantly decreased in 18 (90%) patients among 20 patients with preoperative significant RV enlargement in TVP group (P < 0.001). A stepwise multivariate logistic regression analysis revealed that TVP group and baseline sinus rhythm were significant predictors for improvement of TR (P < 0.001). TR improvement rates of among patients with atrial fibrillation were 97% in the TVP group and 23% in the PMV group (P < 0.001), whereas improvement rates in patients with sinus rhythm did not differ significantly between the TVP and PMV groups (100% versus 73%, P = NS). During annual echocardiographic follow-up, mild TR had progressed to moderate TR in 7 patients and to severe TR in 1 patient, and moderate TR had progressed to severe TR in 2 patients in the PMV group (P < 0.05), and in the TVP group, mild TR was progressed to moderate TR in 2 patients with persistent atrial fibrillation (P = NS). The maze operation was performed in combination with MVR and TV repair on 21 patients, and atrial fibrillation was converted to sinus rhythm in 16 (76%) patients. The RV size and progression of TR did not differ significantly between patients who did and did not have the maze operation.

**Discussion**

This study demonstrates that MVR combined with TV repair is related to better clinical outcomes than PMV alone by improving TR more effectively in patients with severe MS and severe functional TR.

TR in patients with MV disease may be attributable to rheumatic involvement of the valve or to functional TR; in the majority of cases it is functional, being a consequence of RV dysfunction and tricuspid annulus enlargement secondary to pulmonary hypertension. The importance of significant TR was often neglected, but clinical recognition of TR has assumed increasing importance because it affects the outcome of MV surgery in several ways: (1) functional TR may persist or recur despite correction of MV disease, (2) significant persistent TR can also contribute to progression of RV
cardiomyopathy that results in further aggravation of TR, and
(3) significant TR can increase morbidity and mortality
independent of pulmonary hypertension and LV ejection
fraction. Based on these findings, it has become common
practice to detect and correct significant functional TR at the
time of initial MV surgery. However, MVR with surgical
correction of TR has not been previously compared with
PMV in patients who are potential candidates for PMV. In
this study, TV repair was effective at decreasing the tricuspid
annular diameter and TR, and these significant changes could
lead to a reduction in RV size, prevention of TR progression,
and finally more favorable clinical outcomes compared with
PMV alone. From the results of this study, we suggest that
this surgical option should be considered preferentially,
especially if significant TR is associated with enlarged RV.

Percutaneous mitral valvuloplasty (PMV) has been ac-
cepted as an effective method of treating hemodynamically
significant MS, but Sagie et al reported that significant TR
was closely associated with suboptimal immediate results and
poor late outcome after PMV. They also reported that
significant TR did not substantially decrease or resolve after
PMV in the majority of patients. We agree with their opinion
that the structural changes in RV may become irreversible,
causin significant functional TR to persist even after relief
of the increased pulmonary artery pressure. However, we
could observe regression of TR after PMV alone in a
subgroup of younger patients with sinus rhythm. In previous
studies, the regression of TR after PMV varied considerably
with the baseline characteristics of the study patients, and a clinically useful marker is needed to differentiate
chronic advanced disease from an acute decompensated state.
In this study, cardiac rhythm was significantly and independ-
ently related with improvement of TR, and in atrial fibril-
lation, clinical outcomes were also significantly worse in the
PMV group than in the TVP group. It is also well known that
atrial fibrillation is closely related to atrial dilatation, with
long-standing pressure elevation and chronic atrial fibrillation
also leading to atrial and tricuspid annular dilatation further. Therefore, we suggest that the presence of atrial fibrillation is
a useful clinical marker for identifying those patients with
chronic advanced structural changes. Additionally, the throm-
boembolic risk related to atrial fibrillation also affects the
clinical benefits of PMV, because atrial fibrillation exposes
the patient to a life-long risk of thromboembolism and anticoagulation-related bleeding after successful PMV in the
same way as MVR. The surgical option has another advan-
tage in patients with atrial fibrillation, because the maze
operation can be performed in combination with MV surgery.
It has been reported that the maze operation prevented
complications related to atrial fibrillation, such as heart
failure and thromboembolism, by converting atrial fibrillation
to sinus rhythm. Moreover, Kim et al recently reported
that atrial fibrillation was significantly higher in patients with postoperative atrial fibrillation, and that the
maze operation could prevent progression of TR.

Study Limitations
This study was subject to the limitations inherent to a
nonrandomized study, including selection bias. Although the
baseline characteristics were more unfavorable in the TVP
group than in the PMV group (in terms of being older and
having a higher echo score and higher incidence of atrial fibrillation), this study could show that TV repair was more
effective in improving TR, and it was associated with better
clinical outcomes than PMV. This study had a relatively
small number of patients, and no difference in mortality was
observed. Further prospective randomized studies are needed
to confirm our results.

Figure 2. Severe functional TR and RV enlargement were significantly decreased by TV repair on postoperative 1-year and 5-year
follow-up echocardiography (A). Severe TR and RV size were unchanged after PMV alone (B).
Conclusions

TV repair combined with MV surgery was related to better clinical outcomes than PMV alone by improving TR more effectively in severe MS with severe functional TR, and we recommend that this surgical option should be considered preferentially, especially if atrial fibrillation or enlarged RV is associated.

Disclosures

None

References

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