Mechanism of Recurrent/Persistent Ischemic/Functional Mitral Regurgitation in the Chronic Phase After Surgical Annuloplasty

Importance of Augmented Posterior Leaflet Tethering

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Background—Surgical annuloplasty can potentially hoist the posterior annulus anteriorly, exaggerate posterior leaflet (PML) tethering, and lead to recurrent ischemic/functional mitral regurgitation (MR). Characteristics of leaflet configurations in late postoperative MR were investigated.

Methods and Results—In 30 patients with surgical annuloplasty for ischemic MR and 20 controls, the anterior leaflet (AML) and PML tethering angles relative to the line connecting annuli, posterior and apical displacement of the coaptation and the MR grade were measured by echocardiography before, early after, and late after surgery. Early after surgery, grade of MR and AML tethering generally decreased ($P < 0.01$), whereas PML tethering significantly worsened ($P < 0.01$). Nine of the 30 patients showed recurrent/persistent MR late after surgery. Compared with patients without late MR, those with the MR showed similar reduction in the annular area, significant re-increase in posterior displacement of the coaptation, and progressive worsening in PML tethering ($P < 0.05$) late after surgery in comparison to the early phase. Both preoperative MR and late postoperative MR were significantly correlated with all tethering variables in univariate analysis. Although apical displacement of the coaptation was the primary determinant of preoperative MR ($r^2 = 0.60, P < 0.0001$), increased PML tethering was the primary determinant of late MR ($r^2 = 0.75, P < 0.0001$).

Conclusions—Whereas both leaflets tethering is related to preoperative ischemic MR, both leaflets tethering but with predominant contribution from augmented and progressive PML tethering is related to recurrent/persistent ischemic/functional MR late after surgical annuloplasty. (Circulation. 2006;114[suppl I]:I-529–I-534.)

Key Words: coronary disease ■ mitral valve ■ valvuloplasty

Although surgical annuloplasty for ischemic/functional mitral regurgitation (MR) is effective,1–3 a considerable number of patients show recurrent/persistent MR,3–6 which adversely affects mortality7 without established mechanism.

Mitral leaflet tethering by the outward displacement of papillary muscles (PM) caused by left ventricular (LV) remodeling is the basic mechanism of ischemic MR.8–14 Surgical annuloplasty, which may hoist the posterior annulus anteriorly without displacing the anterior annulus fixed at the aortic root, can potentially and specifically augment posterior leaflet (PML) tethering by increasing the distance between the PM tip and posterior annulus without affecting anterior leaflet (AML) tethering (Figure 1).15 We hypothesized that ischemic MR before surgical annuloplasty is related to both leaflets tethering, and that the MR afterward is also related to both leaflets tethering but with PML predominance. This hypothesis has been tested for persistent ischemic MR early after surgery.16 However, this has not been tested for recurrent/persistent MR in the chronic phase after surgery. Therefore, the purpose was to investigate leaflet configurations in patients with ischemic/functional MR before and late after surgical annuloplasty, and to clarify the characteristics of leaflet configurations responsible for recurrent/persistent ischemic MR.

Methods

Subjects
Subjects consisted of 51 consecutive patients who underwent surgical annuloplasty for ischemic/functional MR in our hospital and 20...
normal controls. Four patients with later cardiac death, 3 with concomitant chordal cutting, 1 with subsequent mitral valve replacement, 1 with ring detachment, 10 without echocardiographic evaluation in the chronic phase after the surgery, and 2 with suboptimal images were excluded. The remaining 30 patients with surgical annuloplasty and serial echocardiography up to the chronic phase comprised the study subjects. Patients' profiles are summarized in Table 1. Ischemic/functional MR was diagnosed by echocardiography with the following criteria: (1) the presence of LV dilatation and/or dysfunction; (2) the presence of apical displacement of mitral leaflets;8 and (3) the absence of organic leaflet lesions. Normal subjects had no known cardiovascular disease and normal echocardiogram. In addition to Carpentier Edwards rigid ring, posterior annuloplasty with a flexible linear reducer (stainless steel wire seemed with a polyester sheath) was performed. Coronary artery bypass grafting was performed in 27 and LV plasty with Dor’s, anterior wall overlapping,17 posterior aneurysm plication, or papillary muscle approximation was performed in 11 patients. Patients were managed with standard medications after surgery and no patient had a subsequent ischemic event. Written informed consent was obtained from all patients.

Echocardiography
Echocardiographic examinations were performed using commercially available scanners (ATL HDI 3000, Bothell, Wash; Toshiba SSH 380A, Tokyo, Japan; Philips Medical Systems Sonos 5500, Andover, Mass; Aloka SSD-5500, Tokyo, Japan; Siemens Sequoia 512, Mountain View, Calif) 1 week before, 2 to 8 weeks after, and 10 to 45 months after the surgery.

By biplane Simpson’s method, LV end-diastolic volume, end-systolic volume (ESV), and ejection fractions (EF) were obtained. LV short-to-long axis dimension ratio in the end-systolic apical 4-chamber view was defined as the LV sphericity. Mid-systolic mitral annular dimension in the apical 4-chamber and 2-chamber views was measured to calculate its area.18

Mitral Leaflet Configuration
Mitral leaflet configuration was quantified in the mid-systolic parasternal long-axis view (Figure 2). AML and PML tethering was measured as the angles α1 and α2, respectively. AML tethering from secondary chordae was measured as the bending angle β between tangent lines of proximal and distal AML.19 Posterio and apical displacement of the coaptation was measured as distances d1 and d2, respectively.

Quantification of MR
In the parasternal or apical long-axis view, MR was quantified by the narrowest jet origin or the vena contracta (VC) width.8 VC width >3 mm was considered significant.

Statistical Analysis
Results were expressed as mean±SD. Comparisons of continuous variables among >3 groups were performed by Kruskal-Wallis test. When this test was significant, Scheffe test was conducted for multiple comparisons. Wilcoxon test was used to compare preoperative, early postoperative, and late postoperative variables. Determinants of MR degree were explored by multiple stepwise regression analysis. A P<0.05 was considered significant. Echocardiographic measurements were averaged over 3 cardiac cycles. Inter-observer and intra-observer variability for measurement of d1, d2, α1, and α2 were 6.4 or 5.6%, 7.7 or 6.7%, 7.5 or 7.0%, and 6.7 or 6.1% of the mean value, respectively. 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
Incidence of Early and Late Postoperative Ischemic MR
Early after the surgery, severity of MR significantly decreased (VC width, 3.7±1.6 versus 0.2±0.8 mm; P<0.001) and 2 patients had persistent MR. Late after the surgery, the MR significantly re-increased (0.2±0.8 to 1.3±2.0 mm; P<0.01), resulting with 2 patients with early postoperative MR and significant MR, and an additional 7 in whom recurrent MR developed. These 9 patients comprised the group with late postoperative MR and the remaining 21 comprised the group without it (Table 1).

Changes in LV Volume, Mitral Leaflet Configuration, and MR in Patients Without and With Late Postoperative MR (Table 2)
Severity of MR significantly decreased early after surgery in both groups (P<0.01). Although patients without late MR did not show re-increase in the MR late after surgery, those with it had significant re-increase (P<0.01). The LVESV significantly decreased in both groups early after the surgery (P<0.05). Whereas patients without late MR had further reduction in LVESV late after surgery (P<0.05), those with the MR had re-increase but without statistical significance. LVEF significantly improved early after surgery only in patients without late MR (P<0.05). LVEF kept constant afterward in both groups. The mitral annulus area significantly decreased early after surgery (P<0.05) and kept constant afterward in both groups.

D1 significantly decreased early after surgery in both groups (P<0.05). Whereas D2 kept constant afterward in patients without late MR, it significantly re-increased in those with the MR (P<0.05). D2 significantly decreased early after surgery (P<0.01) and kept constant afterward in both groups. The α1 significantly decreased early after surgery in both groups (P<0.05). Although it kept constant afterward in patients without late MR, it re-increased in those with the MR but without statistical significance. The α2 significantly increased early after surgery in both groups (P<0.01). Patients without late MR did not show progressive increase in α2 afterward, but those with it showed significant progression.
(P<0.05). The \( \beta \) significantly increased early after surgery only in patients without late MR. Whereas it kept constant afterward in patients without late MR, it significantly decreased in those with the MR \((P<0.05)\).

Preoperatively, increase in \( \alpha_1 \) compared with mean normal value was comparable with that in \( \alpha_2 \) in both groups (no late MR, plus 22±6 versus 24±9 degree, not significant; late MR, plus 22±3 versus 24±7 degree, not significant). Therefore, preoperative tethering was similar between AML and PML. However, early after surgery, increase in \( \alpha_1 \) compared with mean normal value was significantly smaller than that in \( \alpha_2 \) in both groups (no late MR, plus 16±3 versus 56±5 degree, \( P<0.01 \); late MR, plus 17±6 versus 57±15 degree, \( P<0.01 \)). Therefore, early postoperative leaflet tethering was asymmetric with PML predominance, which showed significant progression only in patients with late MR \((57±15 to 81±10 degree, P<0.01)\).

Determinants of Preoperative and Late Postoperative MR (Table 3)

Multiple regression analysis identified primary independent contribution from increased \( d_2 \) for the preoperative VC width along with increased \( \alpha_1 \) and \( d_1 \), suggesting that combination of both leaflets tethering was the main determinant of preoperative MR.

Multiple regression analysis identified primary contribution from increased \( d_2 \) for the late postoperative VC width along with decreased \( \beta \) and increased \( d_1 \), suggesting that combination of both leaflets tethering but with predominant contribution from augmented PML tethering was the main determinant of the late MR (Figure 3).

Figure 4 demonstrates representative patients. Compared with the normal subject in the left upper panel, the patient with ischemic MR without annuloplasty in the right upper panel has similarly increased AML and PML tethering. The patient without late postoperative MR in the middle panels had predominant PML tethering. The patient in the lower panels with late MR had more advanced PML tethering and LV remodeling.

Change in LV Volume and Leaflet Tethering Late After Surgery

Reduction in LVESV late after surgery relative to preoperative phase was significantly correlated with less leaflet...
Discussion

Different Leaflet Configurations in Preoperative and Postoperative Ischemic/Functional MR

This study has demonstrated that ischemic MR without surgical ring annuloplasty is associated with approximately symmetrical AML and PML tethering. Early after the surgery, only PML tethering significantly increased in both patients without and with late MR. The PML tethering showed progressive worsening late after surgery in patients with late MR. Therefore, AML and PML tethering is asymmetric with PML predominance in patients with surgical annuloplasty and the asymmetry was progressive only in those with late recurrent/persistent MR. Posterior displacement of the coaptation after annuloplasty in patients with late MR can be explained as a result of restricted PML. This augmented PML tethering contributed to recurrent/persistent ischemic MR late after ring annuloplasty.

Relation to Previous Studies

Recurrent ischemic MR despite surgical annuloplasty is related to leaflet tethering by progressive LV remodeling. Green et al has observed restricted PML after surgical annuloplasty, which was related to early postoperative persistent ischemic MR. Results of this study are consistent with these and further revealed importance of augmented PML tethering for the recurrent/persistent ischemic MR in the chronic phase after surgical ring annuloplasty.

Clinical Implications

Although mitral annuloplasty may not directly relieve ventricular tethering, it is effective to repair ischemic/functional MR by reducing antero-posterior annular dimension to re-

### TABLE 2. Echocardiographic Findings Before and After Surgical Annuloplasty

<table>
<thead>
<tr>
<th></th>
<th>Late Postoperative MR (−), n=21</th>
<th>Late Postoperative MR (+), n=9</th>
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<tr>
<td></td>
<td>Control</td>
<td>Preoperative Early After Surgery Late After Surgery Preoperative Early After Surgery Late After Surgery</td>
</tr>
<tr>
<td>LVEDV/BSA (mL/m²)</td>
<td>52 ± 9</td>
<td>92 ± 16*</td>
</tr>
<tr>
<td>LVESV/BSA (mL/m²)</td>
<td>18 ± 4</td>
<td>62 ± 14*</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>66 ± 6</td>
<td>34 ± 8*</td>
</tr>
<tr>
<td>LV D/L</td>
<td>0.43 ± 0.06</td>
<td>0.62 ± 0.06*</td>
</tr>
<tr>
<td>MAA/BSA (cm²/m²)</td>
<td>5.6 ± 0.8</td>
<td>7.0 ± 1.4*</td>
</tr>
<tr>
<td>MR jet width/BSA (mm/m²)</td>
<td>0</td>
<td>2.1 ± 1.2*</td>
</tr>
<tr>
<td>Mitral leaflet configuration</td>
<td></td>
<td></td>
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<tr>
<td>d₁/BSA (mm/m²)</td>
<td>13.0±1.1</td>
<td>12.9±1.9</td>
</tr>
<tr>
<td>d₂/BSA (mm/m²)</td>
<td>3.9±0.7</td>
<td>6.6±1.0*</td>
</tr>
<tr>
<td>AML tethering α₁ (degree)</td>
<td>12±3</td>
<td>34±6*</td>
</tr>
<tr>
<td>β (degree)</td>
<td>186±4</td>
<td>150±8*</td>
</tr>
<tr>
<td>PML tethering α₂ (degree)</td>
<td>30±5</td>
<td>54±9*</td>
</tr>
</tbody>
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*P<0.05 relative to normal controls.
†P<0.05 relative to preoperative value.
‡P<0.05 relative to early postoperative value.
§P<0.05 relative to late postoperative MR (−).

AML indicates anterior leaflet; BSA, body surface area; D/L, short-to-long axis dimension ratio; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; LV, left ventricular; MAA, mitral annular area; MR, mitral regurgitation; PML, posterior leaflet.
store reduced coaptation by tethering. However, PML tethering was significantly increased afterward even in patients without postoperative MR. Therefore, mitral annuloplasty reduces antero-posterior annular diameter at the expense of augmented PML tethering. When the former effect is predominant, MR can be eliminated by ring annuloplasty. However, when the former is not predominant, recurrent MR may develop. Results of this study suggest need for aggressive undersized annuloplasty, because longer AML than antero-posterior annular diameter is required in the presence of restricted PML. At the same time, more posterior location of the coaptation than posterior annulus and significant bending of AML by tethering from basal chordae in patients with late MR suggest that considerably longer AML than annular diameter is required to prevent leakage. In addition, reduction in LVESV after the surgery was associated with less tethering. These also encourage interventions addressing ventricular tethering, such as LV plasty, chordal elongation or cutting, PM alignment, leaflet elongation, and others.

### Limitations

Multiple patients were excluded because of the lack of serial echocardiography; therefore, the incidence of recurrent/persistent MR may not be accurate. Blinded measure to surgical outcome was not performed because of black and white echo images and color images are on the same set of postoperative images. All patients with serial echocardiography after surgical annuloplasty for ischemic/functional MR were investi-
gated to address characteristics of recurrent/persistent MR with heterogeneous etiology and procedure. However, the small number of studied patients requires further investigations to address specific issues such as recurrent/persistent MR after isolated annuloplasty, effects of rigid and flexible ring annuloplasty with or without aggressive undersizing, and effects of different types of LV plasty in patients with specific etiologies such as different location of myocardial infarction or nonischemic LV dysfunction. Nevertheless, the purpose of this study was achieved by demonstrating significant contribution of augmented and progressive PML tethering for the recurrent/persistent ischemic MR in the chronic phase after surgical ring annuloplasty.

Sources of Funding

Y. Otsuji was supported by a grant-in-aid for scientific research 17500334 from Japan Society for the Promoting of Science, Tokyo, Japan.

Disclosures

This paper has no relation to any clinical trial registration.

References

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_Circulation_. 2006;114:I-529-I-534
doi: 10.1161/CIRCULATIONAHA.105.000729
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://circ.ahajournals.org/content/114/1_suppl/I-529

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