Different Influences of Left Ventricular Remodeling on Anterior and Posterior Mitral Leaflet Tethering – 3-D Echocardiography Quantitative Analysis –

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**Background:** Different influences of left ventricular (LV) remodeling on anterior and posterior mitral leaflet (AML and PML) tethering in ischemic mitral regurgitation (MR) has not been fully investigated. We hypothesized that progressive outward displacement of papillary muscles, including posterior vector, may cause greater tethering to PML compared to AML.

**Methods and Results:** In 79 patients with LV ejection fraction <50% and 20 controls, LV sphericity, AML and PML tethering angles, apical and posterior displacement of coaptation, mitral annular area, and severity of MR (vena contracta width) were measured using 3-D echocardiography. To examine different influences of LV remodeling on AML and PML tethering, interaction between AML/PML and LV sphericity was tested using multiple regression analysis. Both AML and PML tethering significantly increased with increased LV sphericity (r=0.59 and 0.65, P<0.001). Multiple regression yielded a significant interaction term between AML vs. LV sphericity and PML vs. LV sphericity (t=3.69, P<0.001), indicating greater influence from LV remodeling on PML compared to that for the AML. Multivariate analysis demonstrated independent contributions to MR severity from PML tethering primarily along with posterior and apical displacement of coaptation.

**Conclusions:** LV remodeling augments tethering of both AML and PML, with greater influence on PML. (Circ J 2012; 76: 2481–2487)

**Key Words:** Echocardiography; Heart failure; Mitral valve
Figure 1. Potential mechanism for different influences of left ventricular (LV) remodeling on anterior and posterior mitral leaflet (AML and PML) tethering. (Middle, Right) Posterior displacement of papillary muscles (PMs) may tether and pull both leaflets toward the line connecting the PM and annulus (red and blue broken lines for AML and PML, respectively), resulting in increased leaflet tethering angle between leaflet and annular line in mild LV remodeling. In contrast, the response of PM tethering angle (angle between red and black broken lines for AML and the angle between blue and black broken lines for PML, respectively) to progressive LV remodeling can be different between AML and PML. While PM tethering angle for AML may decrease with progressive LV remodeling, the PM angle for PML may progressively increase, suggesting that the influence of progressive LV remodeling on mitral leaflet tethering can be limited in the AML and greater in the PML, respectively.

Figure 2. 3-D echocardiography measurement of anterior mitral leaflet (AML) and posterior leaflet (PML) tethering. (A) In the 3-D data set, mitral valve (MV) en face view from the left ventricular (LV) side was obtained. (B) By rotating and manipulating a cross-sectional image, the commissure-commissure (CC) plane, including both commissures and LV apex, was obtained. (C) The antero-posterior (AP) plane, being perpendicular to the CC plane and cutting the central portion of the whole MV, was then obtained. (D) In this AP plane, the tethering angle of the AML and PML were measured, respectively. (E) Apical and posterior displacement of coaptation was also measured in this plane.
LV remodeling, the PM angle for PML may progressively increase. We, therefore, hypothesized that the influence of LV remodeling on mitral leaflet tethering, expressed by leaflet tethering angle, is greater for the PML compared to the AML. The purpose of this study was to compare the influence of LV remodeling on AML and PML tethering, respectively.

Methods

Subjects
Eighty-nine consecutive patients with LV dysfunction with ejection fraction (EF) <50% were studied using real time 3-D echocardiography (RT3DE). Due to the absence of normal sinus rhythm, 5 patients were excluded. Due to inadequate RT3DE, 5 patients were also excluded. The remaining 79 patients (42 with global LV dysfunction and 37 with segmental LV dysfunction) and 20 normal subjects constituted the study group. Informed consent was obtained in all patients and the institutional committee approved the study protocol.

Echocardiographic Data Acquisition
Conventional Doppler and 2-D echocardiography was performed in all subjects. Harmonic real-time transthoracic 3-D imaging was performed using a commercial ultrasound imaging system (IE33, Philips Medical Systems, Andover, MA, USA) equipped with a matrix-array transducer (X3-1, 1.9/3.8 MHz) with the patient in the left lateral decubitus position. Gain and compression controls as well as time gain compensation settings were optimized to enhance image quality. Pyramidal volume datasets were acquired from the LV apical window. Care was taken to include the entire LV cavity within the pyramidal scan volume. RT3DE datasets were acquired using a wide-angle (93±20°) acquisition mode, in which 4 wedge-shaped subvolumes (93±20° each) were obtained from 4 to 7 consecutive cardiac cycles during held end expiration. Acquisition was triggered to the electrocardiogram R-wave.

3-D MV and LV Measurement
Data were transferred to a personal computer for offline analysis using 3DQ ADV (QLAB, Philips Medical Systems). Mid-systole was defined as the middle echocardiographic frame with systolic mitral leaflet closure. LV end-systolic volume was obtained using the vena contracta width or the diameter=apico-basal LV diameter. Mitral regurgitation (MR) was quantified using the vena contracta width or the ratio of LV end-systolic volume to the spherical volume, with diameter=apico-basal LV diameter. Mitral regurgitation severity (steeper slope of the regression line) for the PML compared to that for the AML. The greater influence on PML remodeling, the PM angle for PML may progressively increase. We, therefore, hypothesized that the influence of LV remodeling on mitral leaflet tethering, expressed by leaflet tethering angle, is greater for the PML compared to the AML. The purpose of this study was to compare the influence of LV remodeling on AML and PML tethering, respectively.

Table 1. Subject Clinical Characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender (M/F)</th>
<th>LV</th>
<th>EDVI (ml/m²)</th>
<th>ESVI (ml/m²)</th>
<th>EF (%)</th>
<th>Sphericity</th>
<th>Location of LV dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>64±15</td>
<td>63/16*</td>
<td></td>
<td>110±55*</td>
<td>82±50*</td>
<td>28±11*</td>
<td>0.42±0.14*</td>
<td>Normal</td>
</tr>
<tr>
<td>58±13</td>
<td>11/9</td>
<td></td>
<td>44±6</td>
<td>18±3</td>
<td>60±5</td>
<td>0.24±0.04</td>
<td>Global</td>
</tr>
</tbody>
</table>

Table: Data are expressed as n or mean±SD. *P<0.05 vs. normal subjects. αi; anterior mitral leaflet tethering angle; αs; posterior mitral leaflet tethering angle; A-P, antero-posterior; C-C, commissure-commissure; EDVI, end-diastolic volume index; EF, ejection fraction; ESVI, end-systolic volume index; LV, left ventricular; MR, mitral regurgitation; NA, not applicable; VC, vena contracta.

Results

Patient Profile
Table 1 lists the subject characteristics. Generally, patients with LV dysfunction had greater LV dilatation, MV tethering, MAA, MR and greater reduction in LVEF compared to normal controls.

MV Tethering and LV Remodeling
The LV sphericity was significantly correlated with both AML and PML tethering (r=0.59 and 0.65, P<0.001; Figure 3). Multiple regression analysis yielded a significant interaction term between AML vs. LV sphericity and PML vs. LV sphericity (t=3.69, P<0.001), indicating greater influence from LV sphericity (steeper slope of the regression line) for the PML compared to that for the AML. The greater influence on PML...
tethering, however, may vary along the wide spectrum of LV sphericity. A significant and positive relationship existed between mid-systolic LV sphericity and AML tethering angle until the LV sphericity reached 0.38. After this point, even if LV sphericity increased further, no further increase in AML tethering developed. In contrast, a significant and positive relationship existed between PML tethering and LV sphericity even beyond the 0.38 LV sphericity cut-off.

Figure 3. Tethering of the anterior or posterior mitral leaflet (AML and PML) vs. left ventricular (LV) sphericity. LV sphericity is significantly correlated with both AML and PML tethering angle (P<0.01). The slope of the regression line is significantly steeper for the PML compared to the AML (interaction term, t=3.69, P<0.001). A significant and positive relationship existed between mid-systolic LV sphericity and AML tethering angle until the LV sphericity reached 0.38. After this point, even if LV sphericity increased further, no further increase in AML tethering occurred. In contrast, a significant and positive relationship existed between PML tethering and LV sphericity even beyond the 0.38 LV sphericity cut-off.

Figure 4. Apical or posterior displacement of coaptation vs. left ventricular (LV) sphericity. LV sphericity is significantly correlated with both apical and posterior displacement of the coaptation (P<0.001). The slope of the regression line is significantly steeper for posterior displacement (interaction term, t=3.54, P<0.001).
Predominant Posterior Mitral Leaflet Tethering

Figure 4. The slope of the regression line was significantly steeper for posterior displacement (t=3.54, P<0.001). Figure 5 shows representative patients. Mild LV remodeling (Figure 5 Middle) is associated with significant increase in both AML and PML tethering compared to the normal subject (Figure 5 Left). In contrast, the severe LV remodeling (Figure 5 Right) has a similar degree of AML tethering and apparently greater PML tethering in comparison to the mild LV remodeling (Figure 5 Middle).

Regarding annular dilatation, there was a significant cor-

Figure 5. Representative cases of left ventricular (LV) remodeling. (Middle) In mild LV remodeling, there is an increase in both anterior and posterior mitral leaflet (AML and PML) tethering. (Right) In advanced LV remodeling there is similar AML tethering but markedly increased PML tethering, demonstrating a greater influence on PML tethering from advanced LV remodeling.

Figure 6. Anterior mitral leaflet (AML) or posterior leaflet (PML) tethering angle vs. mitral regurgitant vena contracta (MRVC) dimension. VC dimension significantly correlated with both AML and PML tethering angle. Multivariate analysis identified independent and primary contributions to PML tethering angle.
Table 2. Determinants of MR Severity and PML Tethering

<table>
<thead>
<tr>
<th>Determinants of MR vena contracta width</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P value</td>
</tr>
<tr>
<td>α1</td>
<td>0.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>α2</td>
<td>0.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apical displacement of coaptation</td>
<td>0.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Posterior displacement</td>
<td>0.62</td>
<td>&lt;0.001</td>
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<tr>
<td>Annular area</td>
<td>0.39</td>
<td>&lt;0.001</td>
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B. Determinants of PML tethering angle α2

<table>
<thead>
<tr>
<th>Determinants</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDVI</td>
<td>0.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESVI</td>
<td>0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sphericity index</td>
<td>0.65</td>
<td>&lt;0.001</td>
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</table>

PML, posterior mitral leaflet. Other abbreviations as in Table 1.

Discussion

The present study has demonstrated that both AML and PML tethering are significantly correlated with LV dilatation. The influence from LV remodeling on the AML and PML, however, seems different. The slope of correlation with LV sphericity was significantly steeper for the PML compared to the AML. Similarly, the slope of correlation with LV sphericity was also significantly steeper in posterior displacement of coaptation compared to the apical displacement. These suggest a predominant influence from LV remodeling on the PML. This seems reasonable, because the PM displacement vector contains a posterior component, and severe displacement of the PM in the posterior direction is expected to cause progressive tethering especially to the PML (Figure 1). Of note, it is not clear whether the predominant influence on the PML similarly occurs throughout the entire range of LV sphericity. Because AML tethering seems to show plateau in the range of advanced LV sphericity while the PML tethering continues to increase even in that range, predominant PML tethering may mainly take place in the stage of advanced LV remodeling. Multivariate analysis identified independent and primary contributions to MR severity from PML tethering angle. These suggest that predominant PML tethering plays an important role, in the presence of AML tethering, in the development of ischemic MR.

Previous Studies

The present results are consistent with previous studies demonstrating the importance of geometric changes in the development of ischemic MR.1–12 There have been multiple reports of different severity or response of AML and PML tethering. Agricola et al for the first time evaluated AML and PML tethering separately. They demonstrated that predominant medial PM displacement specifically increases PML tethering.6 Multiple studies have demonstrated that annular size reduction by surgery increases PML tethering.13–18 We further demonstrated that LV remodeling has a greater influence on PML than AML tethering. Posterior displacement of the PMs relative to the posterior annulus seems to be a common mechanism to specifically augment PML tethering in the aforementioned situations. Of note, the larger annulus may not necessarily be associated with less PML tethering, as shown by the positive correlation between annular area and PML tethering in the present study. This suggests the superimposition of 2 opposite effects with regard to annular dilatation: effect 1, the attenuation of PML tethering by annular dilatation; and effect 2, the augmentation of PML tethering by associated LV remodeling. In the present study, the latter effect seems predominant. In patients who underwent restrictive annuloplasty for ischemic MR, Magne et al found that increased preoperative PML tethering was associated with greater LV remodeling, and adverse postoperative outcome with recurrent or persistent ischemic MR after the procedure.16 The present results suggest that PML tethering rather than AML tethering may better express LV remodeling. This can potentially explain the ability of PML tethering to predict outcome after surgical annuloplasty for ischemic MR in Magne et al study.16

Clinical Application

The present results have emphasized the important role of PML tethering in the development of ischemic MR. The results suggest benefits of addressing the subvalvular tethering in ischemic MR.19–24 Procedures targeted to outward displacement of PMs, as opposed to global LV dilatation or annular dilatation,25,26 seem reasonable to improve tethering of both AML and PML. Procedures specifically targeted to PML tethering also seem reasonable,27 especially in patients with annuloplasty and/or advanced LV remodeling. In ischemic MR, the regurgitant jet is usually directed posteriorly or centrally. Predominant PML tethering with relative AML prolapse can potentially explain the MR jet direction.

Study Limitations

Both AML and PML tethering reflect geometric alterations of the MV apparatus, including PM displacements. Geometric al-
tations can be heterogeneous among patients. The precise tethering pattern of whole MV leaflets can potentially express heterogeneous alterations of the geometry. For instance, Kwan et al have demonstrated asymmetrically predominant tethering in the medial half of the MV in patients with medial LV deformation or inferior myocardial infarction. The precise leaflet tethering pattern of whole leaflets and the geometric alterations of the MV apparatus, however, were not investigated in the present study. The present subjects had heterogeneous underlying disease with variable location and degree of LV dysfunction/dilatation. Therefore, the present hypothesis was not separately investigated according to the site or degree of LV dysfunction. Nevertheless, the purpose of the study was achieved by demonstrating a greater influence on PML tethering, compared to AML tethering, from LV remodeling, especially in the stage of advanced LV remodeling.

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References


