Annular Geometry in Patients With Chronic Ischemic Mitral Regurgitation

Three-Dimensional Magnetic Resonance Imaging Study

Shuichiro Kaji, MD; Michihiro Nasu, MD; Atsushi Yamamura, MD; Kazuaki Tanabe, MD; Kunihiko Nagai, MD; Tomoko Tani, MD; Koichi Tamita, MD; Kenichi Shiratori, MD; Makoto Kinoshita, MD; Michio Senda, MD; Yukikatsu Okada, MD; Shigefumi Morioka, MD

Background—Although animal studies showed that annular remodeling may be related to the pathogenesis of chronic ischemic mitral regurgitation (CIMR), little was known in humans. A better understanding of the precise 3D geometry of the mitral valvular-ventricular complex in CIMR is needed to devise a better surgical technique. The purpose of the study was to elucidate mitral annular geometry in patients with CIMR using cardiac MRI.

Methods and Results—Thirty-eight patients with previous inferior or posterior myocardial infarction were studied. With the 3D reconstruction of the mitral annulus and subvalvular apparatus from a series of longitudinal cine MRIs, end-systolic mitral annulus dimensions and 3D geometry were calculated. Patients were grouped by mitral regurgitation grade using echocardiography (≥2+, n=15 versus ≤1+, n=23). Both septal-lateral and commissure-commissure mitral annular diameters were significantly greater in CIMR(+) patients (35±5 versus 30±4 mm, P=0.005; 46±6 versus 39±4 mm, P<0.001, respectively). The length of the fibrous annulus was significantly larger in CIMR(+) patients (28±3 versus 24±3 mm; P<0.001). The height of the annular “saddle horn” above a best-fit plane was lower in CIMR(+) patients (4.2±1.2 versus 6.0±1.8 mm; P=0.002), and the annular height to commissural width ratio was significantly lower in CIMR(+) patients (12±3 versus 21±5%; P<0.001).

Conclusions—Patients with CIMR had greater septal-lateral and commissure-commissure mitral annular dimension, larger intertrigonal distance, and flattened saddle shape of mitral annulus. These associated geometric alterations may be important in the pathogenesis of CIMR. (Circulation. 2005;112[suppl I]:I-409–I-414.)

Key Words: coronary disease | ischemia | magnetic resonance imaging | mitral valve | regurgitation

Ischemic mitral regurgitation is a common and important complication of ischemic heart disease, associated with excess mortality independent of underlying left ventricular (LV) dysfunction.1 Because altered annular geometry often contributes to leaflet malcoaptation in chronic ischemic mitral regurgitation (CIMR),2 ring annuloplasty is the preferred treatment for CIMR. However, as many as 30% of patients3 after ring annuloplasty have residual or recurrent mitral regurgitation (MR), which is associated with a poor prognosis. Recent animal studies explored the precise geometric change of annular remodeling in ischemic MR to provide a more rational basis for optimal annuloplasty ring selection and sizing.4,5 In these studies, annular dilatation of the septal-lateral distance and annular flattening have been suggested as a mechanism of ischemic MR. However, human data describing 3D annular geometry in CIMR has not been well known.

Cardiac MRI has been reported to be useful for the assessment of mitral annular function. Although the previous technique required long acquisition time, recent advances of the steady state free precession sequence for cine MRI allows rapid acquisition and good image quality. This sequence has been reported to be useful for geometrical assessment of the mitral apparatus.6 Therefore, the present study was conducted to elucidate 3D mitral annular geometry in patients with CIMR using cardiac MRI.

Methods

Patient Population
We prospectively enrolled 38 patients with prior inferior or posterior myocardial infarction who had cardiac MRI. Inclusion criteria were as follows: (1) segmental LV wall motion abnormality of the inferior or posterior wall; (2) structurally normal mitral valve; (3) technically adequate cardiac MRIs to allow analysis of 3D geometry; and (4) normal sinuses rhythm. Exclusion criteria were as follows: (1) recent myocardial infarction (≤1 month); (2) clinical evidence of other cardiac disease; and (3) morphological abnormalities of the mitral apparatus. A conventional echocardiographic study was obtained including standard 2D images and color Doppler. MR severity was
assessed qualitatively according to the recommendation of American Society of Echocardiography for each study as none (0), mild (+1), moderate (+2), or severe (+3). Patients were divided into 2 groups on the basis of severity of MR: 23 patients who had no significant MR [MR ≤1; “CIMR(−)” group], and 15 patients with chronic ischemic MR [MR ≥2; “CIMR(+)” group]. Written informed consent was obtained from each patient.

Cardiac MRI
Images were acquired on a 1.5T MRI system (Echospeed; GE Healthcare) using a phased-array coil during repeated breath-holds (~10 s). Steady state free precession cine images were acquired in multiple long-axis (every 6 mm) and short-axis planes (every 10 mm). If the breath-holding position of a slice was judged to be different (>5 mm) from the others or image quality was inadequate for segmentation because of various artifacts, the slice was reacquired. The following parameters were used: an echo-time of 8.0 ms, an acquisition matrix of 256×128, and a field of view of 32 cm.

LV Volume
With the MASS Analysis software, the myocardial borders were planimetered on all of the short-axis cine images to determine LV volume and ejection fraction.

3D Measurements
3D reconstruction was performed using a commercially available DICOM viewer, and the image analysis was performed with MATLAB (The MathWorks). First, a cross-sectional plane of the mitral valve that clearly visualized both mitral commissures was obtained from multiple long-axis, end-systolic images using a multiplanar reformation (Figure 1). The end-systolic phase was defined as the cardiac phase with the smallest LV cavity volume. In this plane, the 8 points along the mitral annulus were determined as follows: (1) middle of septal annulus; (2) right trigone; (3) posteromedial commissure; (4) lateral annulus; (5) middle of lateral annulus; (6) lateral annulus; (7) anterolateral commissure; and (8) left trigone (Figure 2). Then, 5 anteroposterior planes, which pass through each 5 points (nos. 1, 2, 3, 7, and 8) and were perpendicular to this plane, were defined for imaging of the geometry of the mitral annular points. 3D coordinates of these 8 points were determined on these images (Figure 3). In addition, the end-systolic positions of anterior and posterior papillary muscle (PM) tips closest to the base of the heart were determined using multiplanar reformation. The septal-lateral diameter of the annulus was measured as the distance between the 2 points in the middle of the septal and lateral mitral annulus, respectively (nos. 1 and 5). The commissure-commissure diameter was measured as the distance between the 2 annular commissural points (nos. 3 and 7). The mitral annular area was calculated as the sum of the areas of 8 triangles formed by consecutive adjacent point pairs on the annulus and the annular centroid. The perimeter of the fibrous annulus was defined as the sum of distances between the points from trigone to trigone (nos. 2 to 1 and nos. 1 to 8). The perimeter of the muscular annulus was defined as the sum of the distances between the points along the muscular annulus. Height of the midseptal annulus (no. 1 or saddle horn) was defined as the distance of point no. 1 above a best-fit plane to the points of the muscular annulus. In addition, an annular height to commissural width ratio (AHCWR) was calculated as described previously by dividing the height of the annulus perpendicular to the least-squares fitting plane to all of the annular points by the commissure-commissure diameter. The leaflet tethering distances were measured as the distances between both PM tips and the midseptal annulus point.

Accuracy of Measurements in 3D Reconstructed Images
To evaluate the accuracy of measurements in 3D reconstructed images, we used the whole-heart MRI technique. This technique was developed for coronary imaging and has been introduced by Weber et al. Whole-heart MRI can provide 3D visualization of the entire heart with high-spatial resolution (reconstructed voxel size=1.1×1.8×1.3 mm³) within a single acquisition using the navigator respiratory gating technique, which enables measurements of mitral annular geometry. Therefore, we obtained whole-heart MRI in 6 patients and compared 30 distances between the points (septal-lateral, commissure-commissure, intertrigone, and trigones to lateral annulus: nos. 2 to 4 and nos. 8 to 6) measured in 3D reconstructed images with those in 3D whole-heart images. Because whole-heart MRI was originally developed for coronary imaging, we measured distances in mid-diastolic images.

Statistical Analysis
All of the values are expressed as mean ±1 SD. Differences between categorical parameters were assessed by use of χ² analysis or
Results

Table 1 summarizes patient characteristics and hemodynamic data. LV end-diastolic and end-systolic volumes were significantly larger in CIMR(+) patients than CIMR(−) patients, whereas ejection fraction was significantly lower in CIMR(+) patients.

Table 2 summarizes mitral annular dimensions at end-systole. Both septal-lateral and commissure-commissure diameters and mitral annular area were significantly greater in CIMR(+) patients. The length of the fibrous annulus was significantly larger in CIMR(+) patients. The height of the annular saddle horn was lower in CIMR(+) patients. In addition, AHCWR was significantly lower in CIMR(+) patients (Figures 4 and 5). The posterior PM-tethering distance was significantly greater in CIMR(+) patients, whereas there was no significant difference in the anterior PM-tethering distance between both groups.

MR grade (0–3) significantly correlated with septal-lateral (r=0.40, P=0.015) and commissure-commissure (r=0.42, P=0.011) diameters, mitral annular area (r=0.48, P=0.003), fibrous annular length (r=0.47, P=0.004), saddle horn height (r=−0.43, P=0.009), AHCWR (r=−0.61, P=0.0002), and posterior PM-tethering distance (r=0.49, P=0.003).

The distances measured with 3D reconstruction of cine MRI correlated and agreed well with those measured with 3D whole-heart MR images (y=1.02x-1.08, r=0.99, SEE=

TABLE 1. Patient Characteristics and Hemodynamics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CIMR(−) (n=23)</th>
<th>CIMR(+) (n=15)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>65±13</td>
<td>66±9</td>
<td>0.748</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>19/4</td>
<td>13/2</td>
<td>0.999</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.67±0.15</td>
<td>1.66±0.19</td>
<td>0.751</td>
</tr>
<tr>
<td>HR, min⁻¹</td>
<td>69±8</td>
<td>63±11</td>
<td>0.196</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>93±37</td>
<td>151±65</td>
<td>0.001</td>
</tr>
<tr>
<td>LVEDVI, mL/m²</td>
<td>56±21</td>
<td>91±37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>44±33</td>
<td>91±65</td>
<td>0.005</td>
</tr>
<tr>
<td>LVESVI, mL/m²</td>
<td>26±19</td>
<td>55±38</td>
<td>0.004</td>
</tr>
<tr>
<td>EF, %</td>
<td>56±16</td>
<td>44±15</td>
<td>0.030</td>
</tr>
<tr>
<td>MR grade (0−3)</td>
<td>0.5±0.5</td>
<td>2.3±0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BSA indicates body surface area; HR, heart rate; LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVESV, left ventricular end-systolic volume; LVESVI, left ventricular end-systolic volume index; EF, ejection fraction.

TABLE 2. Mitral Annular and Papillary Muscle Geometry

<table>
<thead>
<tr>
<th>Variables</th>
<th>CIMR(−) (n=23)</th>
<th>CIMR(+) (n=15)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anular S-L, mm</td>
<td>30±4</td>
<td>35±5</td>
<td>0.005</td>
</tr>
<tr>
<td>Annular C-C, mm</td>
<td>39±4</td>
<td>46±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral annular area, cm²</td>
<td>8.5±1.4</td>
<td>11.6±2.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrous perimeter, mm</td>
<td>24±3</td>
<td>28±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Muscular perimeter, mm</td>
<td>88±9</td>
<td>100±15</td>
<td>0.004</td>
</tr>
<tr>
<td>APM tethering distance, mm</td>
<td>35±5</td>
<td>35±4</td>
<td>0.956</td>
</tr>
<tr>
<td>PPM tethering distance, mm</td>
<td>38±5</td>
<td>44±4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Saddle horn height, mm</td>
<td>6.0±1.8</td>
<td>4.2±1.2</td>
<td>0.002</td>
</tr>
<tr>
<td>AHCWR, %</td>
<td>21±5</td>
<td>12±3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

S-L indicates septal-lateral dimension; C-C, commissure-commissure dimension; APM, anterior papillary muscle; PPM, posterior papillary muscle.
1.1 mm, \( P < 0.0001 \); Figure 6A); the mean difference between measurements by the 2 different methods was 0.9 ± 0.6 mm (Figure 6B).

**Discussion**

This study provides novel insight into the mitral annular geometry of patients with CIMR by comparing with patients who did not develop CIMR after inferior or posterior myocardial infarction. 3D reconstruction of cine MRIs revealed that the patients with CIMR had greater septal-lateral and commissure-commissure mitral annular dimension, larger intertrigonal distance, and flattened saddle shape of mitral annulus. These associated geometric alterations may be important in the pathogenesis of CIMR, and a better understanding of mitral annular geometry may allow a more rational design of annuloplasty rings or new approaches to ischemic MR.

**Cardiac MRI**

2D and 3D echocardiography has been used to investigate the pathophysiology of ischemic MR for human studies.\(^2\)\(^9\)\(^–\)\(^11\) Although 2D echocardiography is expeditious, mobile, and relatively inexpensive, it cannot assess the 3D geometry of the mitral apparatus.\(^12\) 3D echocardiography can overcome the limitations of 2D echocardiography. However, limited image resolution because of parallel processing, limited acoustic window, and relatively low frame rate are major limitations of 3D echocardiography.

Recent advance of the steady state free precession sequence for cine MRI has shown the advantages of short acquisition time and good image quality. For each slice location, it takes \( \approx 10 \) s in a breath hold to acquire a cine MRI of 20 frames per heart beat. Yu et al\(^6\) reported the usefulness of cine MRI in the 3D analysis of mitral apparatus. Considering the relatively short acquisition time and adequate quality of reconstructed images, cardiac MRI can be used as a clinical tool to assess mitral annular geometry in patients with ischemic MR.

**Annular Dilatation**

The role of annular dilatation in the pathogenesis of ischemic MR is still debated. Otsuji et al\(^12\) reported that leaflet tissue redundancy protects against leaflet malcoaptation in isolated annular dilatation. In addition, limited annular dilatation, or dilatation primarily in the commissure-commissure dimension,\(^12\)\(^11\) may not be sufficient to cause MR. However, annular dilatation, even in the commissure-commissure direction, may exacerbate leaflet malcoaptation by exhausting the supply of redundant leaflet tissue. Moreover, commissure-commissure annular dilatation may contribute to malcoaptation of the individual scallops of the posterior leaflet.\(^14\)

In the present study, both septal-lateral and commissure-commissure diameters of mitral annulus were significantly greater in patients with CIMR. Although the septal-lateral diameter is often implicated in leaflet malcoaptation in acute and chronic ischemic MR,\(^4\)\(^15\) the mechanistic importance of commissure-commissure annular dilatation has been debated.\(^13\) A human study with 3D echocardiography reported that commissure-commissure dimension was significantly larger in patients with significant MR caused by ischemic cardiomyopathy.\(^11\) On the other hand, Tibayan et al\(^4\) reported that commissure-commissure annular dilatation was similar in CIMR(+) and CIMR(−) groups using a model of ovine chronic inferior infarction. They suggested that remodeling in commissure-commissure dimension is not sufficient to produce MR. Recent experimental animal studies have demonstrated that reduction of septal-lateral diameter alone decreased CIMR.\(^16\) Furthermore, Byrne et al\(^17\) reported that
percutaneous device replacement reduced septal-lateral dimension and was associated with reduced CIMR. Therefore, although both septal-lateral and commissure-commissure diameters were larger in patients with CIMR, septal-lateral mitral annular dilatation may play a more prominent role in CIMR.

Controversy exists regarding fibrous annular dilatation in patients with CIMR. It has been reported that the fibrous portion of mitral annulus, which corresponds to the intertrigonal distance, is fixed and does not dilate. However, dilatation of the fibrous annulus has been reported in humans with dilated cardiomyopathy of ischemic and idiopathic etiologies. In the current study, the perimeter of the fibrous portion of mitral annulus in patients with CIMR was significantly larger than patients without CIMR. Tibayan et al demonstrated the dilatation of the intertrigonal distance in the setting of CIMR using an ovine experimental model. Our results were consistent with their study. Although additional studies with serial observations of mitral annulus are necessary, our data suggest that a complete ring would be better suited to the surgical repair of CIMR.

**Annular Flattening**

The saddle shape of the mitral annulus has been confirmed by 3D echocardiography, marker fluoroscopy, and sonomicrometry. This saddle shape contributes to leaflet curvature, which, theoretically, reduces leaflet stress in finite element models. The previous reports studying the change in shape of the mitral annulus in the sheep and ovine model of acute and chronic MR demonstrated that the annulus flattened in the acute and chronic disease process. Their findings were consistent with the results of our study. In the current study, saddle horn height and AHCWR were significantly lower in patients with CIMR. In addition, a human 3D echocardiography study comparing the mitral annular shape in healthy subjects and patients with different degrees of functional MR reported that functional MR was associated with a decrease in annular height. Therefore, this clinical and experimental evidence indicates that annular saddle shape may contribute to valve competence, and the annular flattening may potentially increase leaflet closing stress.

Our findings suggest that mitral repair for ischemic MR should aim to restore the physiological saddle shape of the annulus by means of a new designed ring. Such a design would decrease leaflet stress, which might, in turn, potentially reduce the incidence of long-term structural valve deterioration.

**PM Geometry**

Previous studies have described the role of PM displacement in the development in CIMR. Tibayan et al reported that sheep with CIMR after inferior myocardial infarction demonstrated greater posterior PM displacement, particularly lateral movement of the posterior PM. A clinical echocardiographic study demonstrated predominant contributions from both PM displacement with inferoposterior segmental dysfunction. In the current study, posterior PM to saddle horn was significantly larger in CIMR(+) patients, whereas anterior PM to saddle horn did not differ significantly. Our results are consistent with those of these previous studies.

**Study Limitations**

We compared only mid-diastolic data between 3D reconstructed images and 3D whole-heart images in the validation study. The accuracy of mid-diastolic points might be different from those of end-systolic points. Additional development of a MRI technique can provide a more accurate validation study. Although the in-plane spatial resolution was relatively high (1.3×2.5 mm²), the through-plane resolution was relatively low (slice thickness of 6 mm) because of the requirement of reasonable scan time for the patients. The low through-plane and anisotropic spatial resolution might compromise the accuracy of 3D measurements. In addition, the difference in breath-hold position between slices may have an effect on the reconstruction images. However, the previous study reported that differences because of breath-hold positions were negligible and that 3D reconstruction of intracardiac anatomy from a series of 2D MR images was feasible and clinically useful. In the current study, the images were reacquired when obvious differences (>5 mm) in breath-hold positions were noted. Moreover, the measurements in 3D reconstructed images showed a close correlation with those from 3D whole-heart images in our validation study. Therefore, it seems likely that 3D reconstruction from a series of 2D cine images can provide an accurate evaluation of mitral annular geometry.
References


Annular Geometry in Patients With Chronic Ischemic Mitral Regurgitation: Three-Dimensional Magnetic Resonance Imaging Study
Shuichiro Kaji, Michihiro Nasu, Atsushi Yamamuro, Kazuaki Tanabe, Kunihiko Nagai, Tomoko Tani, Koichi Tamita, Kenichi Shiratori, Makoto Kinoshita, Michio Senda, Yukikatsu Okada and Shigefumi Morioka

Circulation. 2005;112:I-409-I-414
doi: 10.1161/CIRCULATIONAHA.104.525246
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
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/112/9_suppl/I-409

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/