Geometric Differences of the Mitral Apparatus Between Ischemic and Dilated Cardiomyopathy With Significant Mitral Regurgitation

Real-Time Three-Dimensional Echocardiography Study

Jun Kwan, MD; Takahiro Shiota, MD; Deborah A. Agler, RDCS; Zoran B. Popović, MD; Jian Xin Qin, MD; Marc A. Gillinov, MD; William J. Stewart, MD; Delos M. Cosgrove, MD; Patrick M. McCarthy, MD; James D. Thomas, MD

Background—This study was conducted to elucidate the geometric differences of the mitral apparatus in patients with significant mitral regurgitation caused by ischemic cardiomyopathy (ICM-MR) and by idiopathic dilated cardiomyopathy (DCM-MR) by use of real-time 3D echocardiography (RT3DE).

Methods and Results—Twenty-six patients with ICM-MR caused by posterior infarction, 18 patients with DCM-MR, and 8 control subjects were studied. With the 3D software, commissure-commissure plane and 3 perpendicular anteroposterior (AP) planes were generated for imaging the medial, central, and lateral sides of the mitral valve (MV) during mid systole. In 3 AP planes, the angles between the annular plane and each leaflet (anterior, Aα; posterior, Pα) were measured. In ICM-MR, Aα measured in the medial and central planes was significantly larger than that in the lateral plane (39 ± 5°, 34 ± 6°, and 27 ± 5°, respectively; P < 0.01), whereas Pα showed no significant difference in any of the 3 AP planes (61 ± 7°, 57 ± 7°, and 56 ± 7°, P > 0.05). In DCM-MR, both Aα (38 ± 8°, 37 ± 9°, and 36 ± 7°, P > 0.05) and Pα (59 ± 6°, 58 ± 5°, and 57 ± 6°, P > 0.05) revealed no significant differences in the 3 planes.

Conclusions—The pattern of MV deformation from the medial to the lateral side was asymmetrical in ICM-MR, whereas it was symmetrical in DCM-MR. RT3DE is a helpful tool for differentiating the geometry of the mitral apparatus between these 2 different types of functional mitral regurgitation. (Circulation. 2003;107:1135-1140.)

Key Words: mitral valve ▪ echocardiography ▪ cardiomyopathy

Functional mitral regurgitation (MR), which occurs as a consequence of regional or global left ventricular (LV) dysfunction despite a structurally normal mitral valve (MV), is a common complication in patients with ischemic heart disease or idiopathic dilated cardiomyopathy. Its presence increases long-term risk and mortality even after surgical valve repair.1–5 Several competing geometric and hemodynamic factors have been separately proposed to cause functional MR: dilatation of the mitral annulus, tethering of leaflets by the displaced papillary muscles (PMs), and ventricular dysfunction with reduced transmural pressure to close the leaflets.6–11 With recent advances in 3D imaging techniques, geometric changes of the mitral apparatus accompanied by distortion of the LV chamber from which the PMs arise have been explored.12–17 In these studies, leaflet tethering by the displaced PMs due to regional or global LV dysfunction has been suggested as a main mechanism of functional MR. However, the geometry of the mitral apparatus accompanied by regional or global LV dilatation has not been clarified differentially. We hypothesized that the geometry of the MV related to unilateral PM displacement (regional LV dysfunction) would be different from that related to bilateral PM displacement (global LV dysfunction) on the basis of anatomic knowledge that each PM distributes the chordae only to the ipsilateral half of both leaflets. Therefore, the present study was conducted to elucidate and compare the geometry of the mitral apparatus in patients with significant MR caused by ischemic cardiomyopathy (ICM-MR) and MR due to dilated cardiomyopathy (DCM-MR) by use of real-time 3D echocardiography (RT3DE).

Methods

Population
We prospectively enrolled patients with significant functional MR (grade >2 on a 0 to 4 scale) from November 2000 to December 2001 who had RT3DE. The patient population was divided into 2 groups: 26 patients in the group with ICM-MR (age 64 ± 10 years, 5 females) and 18 patients in the group with DCM-MR (age 64 ± 10 years, 5 females).
and 18 patients in the group with DCM-MR (age 58±13 years, 5 females). In this study, ICM-MR was defined as significant functional MR (regurgitant orifice area [ROA] >0.15 cm²) with regional (posterior wall) LV dysfunction caused by coronary artery disease, whereas DCM-MR was defined as significant functional MR with global LV dysfunction without coronary artery disease. Inclusion criteria were (1) structurally normal MV, (2) technically adequate color flow Doppler image for proximal isovelocity surface area (PISA), (3) technically adequate RT3DE image of the LV chamber and the mitral apparatus to allow analysis of 3D geometry, and (4) normal sinus rhythm. Exclusion criteria were (1) clinical and echocardiographic evidence of other cardiac disease, such as organic valvular or infiltrative heart disease, and (2) morphological abnormalities of the mitral apparatus, such as chordae rupture, MV prolapse, or restricted leaflet due to degenerative calcification. In addition, 8 subjects (age 38±5 years, 1 female) with normal mitral apparatus on RT3DE were included as control subjects.

2D Measurements
2D echocardiography was performed with a phased-array ultrasound sector scanner of a Sequoia 512 (Acuson) with a 3.5- to 5-MHz probe. LV end-diastolic volume (EDV) and end-systolic volume (ESV) were measured by the biplane Simpson disk method. Ejection fraction was calculated by the equation 100×(EDV−ESV)/EDV. The characteristics (origin, number, and direction) of MR jets were estimated by color flow Doppler images on a parasternal short-axis view at the MV level and on multiple apical views. Degree of MR was quantified by ROA by the PISA method.

Real-Time 3D Echocardiography

Volumetric Image Acquisition
An RT3DE imaging system with a 2.5-MHz handheld transducer was used to image the mitral apparatus (Volumetric Medical Imaging Inc). For all patients, transthoracic volumetric images were obtained with the apical view. Care was taken to include the entire MV in the volumetric data set during a single cardiac cycle. The volumetric frame rate was 17 to 22 frames/second, with an imaging depth of 12 to 16 cm. All volumetric images were digitally stored on magneto-optical disk and transferred into a personal computer for offline analysis.

3D Measurements
We used 3D computer software (TomTec, Co) to define measurement planes. First, mid sístole of the heart cycle was defined. Then, a cross-sectional plane of the MV that clearly visualized both mitral commissures was used to define the commissure-commissure (CC) plane, a plane that passes through both commissures and the LV apex. Finally, 3 anteroposterior (AP) planes perpendicular to the CC plane were defined for imaging of the geometry of the medial, central, and lateral sides of the leaflets (Figure 1). The sphericity of the LV chamber at the level of the PMs was calculated by the ratio of the LV chamber width measured at the level of the PMs to the height of the level from the mitral annulus (Figure 2). The degree of circularization of the annulus was calculated by the ratio of the AP dimension to the CC dimension of the annulus (Figure 2). Mitral annular area (MAA) was then calculated with the simplified equation MAA = 3.14×CC dimension×AP dimension/4. The degree of leaflet tethering was estimated by measuring the angle at which each leaflet met the annular plane (anterior leaflet, Ao; posterior leaflet, Po; Figure 2) in all 3 AP planes. MV tenting area (MVTa), the area enclosed by the annular plane and 2 leaflets, and MV tent height (MVTht), the distance between the leaflet coaptation and the mitral annular plane, were also measured in all 3 AP planes (Figure 2).

Statistical Analysis
Data are expressed as mean±SD. Group comparison of continuous variables was performed by Student’s t test or by repeated-measures ANOVA followed by post hoc testing, as appropriate. Group comparisons of categorical variables were performed by Fisher exact test. In both patient groups, we assessed univariate regression with ROA as a dependent variable and other measurements. Then, multivariate analysis based on stepwise multiple regression analysis was done to assess major determinants of MR severity among measurements with significant univariate correlations (P<0.05) with ROA. A value of P<0.05 was considered significant.

Results

Geometry of the LV Chamber and Mitral Annulus
Geometric measurements of the LV chamber and the mitral annulus in the 3 groups are summarized in the Table. The volume and sphericity of the LV chamber significantly increased in both DCM-MR and ICM-MR compared with controls but increased more in DCM-MR than in ICM-MR. Global LV systolic function was impaired more severely in DCM-MR than in ICM-MR. CC dimension, AP dimension, and mitral annular area were significantly larger in DCM-MR than in ICM-MR, although without a significant difference in circularization of the annulus.

MV Deformation
In controls, both Aoα (21±3°, 23±5°, and 23±3°, P>0.05) and Poα (32±5°, 32±6°, and 34±4°, P>0.05) revealed no significant differences from the median to the lateral plane by ANOVA (Figure 3). In ICM-MR, Aaa significantly (P<0.01) increased in the medial and central planes but insignificantly increased (P>0.05) in the lateral plane compared with controls, with a significant difference from the medial to the lateral plane (39±5°, 34±6°, and 27±5°, respectively; P<0.01), whereas Poa significantly (P<0.01) increased in all 3 AP planes without a significant difference among the planes (61±7°, 57±7°, and 56±7°, P>0.05; Figure 3). Accordingly, the pattern of MV deformation from the medial to the lateral plane was asymmetrical in ICM-MR (Figure 4). In DCM-MR, both Aaa and Poo significantly (P<0.01) increased
in all 3 AP planes compared with controls, without significant differences from the medial to the lateral plane (Aα: 38 ± 8°, 37 ± 9°, and 36 ± 7°, P > 0.05; Pα: 59 ± 6°, 58 ± 5°, and 57 ± 6°, P > 0.05; Figure 3), which resulted in a symmetrical pattern of MV deformation (Figure 4). MVTα and MVTht were significantly increased in both ICM-MR and DCM-MR compared with controls, without significant differences (P < 0.05) from other planes, whereas they consistently increased in all 3 AP planes without significant difference between planes (P > 0.05) in DCM-MR (Figure 5).

**MR Jet Characteristics and MR Severity**

In ICM-MR, ROA ranged from 0.15 to 0.57 cm² (0.35 ± 0.13 cm²), which was not significantly different from DCM-MR, where it ranged from 0.15 to 0.53 cm² (0.34 ± 0.16 cm²; P > 0.05). In ICM-MR, 24 of 26 patients showed 2 separated jets, one from the medial side and the other from the lateral side of the MV, whereas in DCM-MR, a single wide, central jet extending from the medial to the lateral side was observed in 10 of 18 patients, and 2 separate central jets that originated from both sides were observed in 8 of 18 patients (Figure 6). Among 24 ICM-MR patients with 2 jets, the lateral jet was significantly larger than the medial jet in 21 (ROA 0.28 ± 0.11 versus 0.11 ± 0.04 cm², P < 0.01). In DCM-MR, MR in patients with a single jet was larger than that in patients with 2 jets (ROA 0.40 ± 0.17 versus 0.25 ± 0.04 cm², P < 0.01).

**Determinants of MR Severity**

In DCM-MR, both LV volume indices (end-diastolic and end-systolic) and sphericity of the LV chamber at the level of the PM showed significant correlation (P < 0.05) with ROA, whereas only the latter showed significant correlation in ICM-MR (P < 0.05). In DCM-MR, all measurements of the MV (MVTα, MVTht, Aα, and Pα) in the 3 AP planes correlated significantly (P < 0.05) with ROA, whereas all measurements but Aα showed significant correlation (P < 0.05) with ROA in ICM-MR. In both patient groups, all measurements of the mitral annulus except the degree of circularization showed significant correlation (P < 0.05) with ROA. When we explored the main determinants using multivariate stepwise linear regression analysis with the geometric measurements that showed significant correlations with MR severity, MVTα measured in the medial AP plane was found to be the strongest determinant of MR severity in both ICM-MR (r = 0.79) and DCM-MR (r = 0.87; Figure 7).

**Geometric Measurements of LV Chamber and Mitral Annulus**

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 8)</th>
<th>ICM-MR (n = 26)</th>
<th>DCM-MR (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROA, cm²</td>
<td>0.35 ± 0.13</td>
<td>0.34 ± 0.16</td>
<td></td>
</tr>
<tr>
<td>LV chamber</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDVI, mL/m²</td>
<td>106 ± 19</td>
<td>200 ± 88*</td>
<td>312 ± 121*</td>
</tr>
<tr>
<td>ESVI, mL/m²</td>
<td>41 ± 10</td>
<td>148 ± 71*</td>
<td>248 ± 102*</td>
</tr>
<tr>
<td>EF, %</td>
<td>63 ± 4</td>
<td>28 ± 7*</td>
<td>21 ± 7*</td>
</tr>
<tr>
<td>Sphericity</td>
<td>1.28 ± 0.04</td>
<td>1.65 ± 0.14*</td>
<td>1.83 ± 0.18*</td>
</tr>
<tr>
<td>Mitral annulus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC dimension</td>
<td>2.8 ± 0.1</td>
<td>3.1 ± 0.1*</td>
<td>3.3 ± 0.2*</td>
</tr>
<tr>
<td>AP dimension</td>
<td>2.4 ± 0.1</td>
<td>2.8 ± 0.2*</td>
<td>3.0 ± 0.2*</td>
</tr>
<tr>
<td>Circularization</td>
<td>0.83 ± 0.02</td>
<td>0.89 ± 0.03</td>
<td>0.91 ± 0.04*</td>
</tr>
<tr>
<td>MAA, cm²</td>
<td>5.2 ± 0.3</td>
<td>6.8 ± 0.6*</td>
<td>7.7 ± 1.0*</td>
</tr>
</tbody>
</table>

EDVI indicates LV end-diastolic volume index; ESVI, LV end-systolic volume index; EF, ejection fraction; and MAA, mitral annular area.

*P < 0.05 vs controls; †P < 0.05 vs DCM-MR.
the edges of the 2 mitral leaflets in conjunction with annular dilatation. As in DCM-MR, significant annular circularization in ICM-MR as much as that in DCM-MR might be one of the contributing factors to cause significant MR despite less enlargement of the mitral annulus.

Geometry of the MV (Tethering) at Mid Systole

The hypothesis we tried to test was that the leaflet tethering produced by unilateral and asymmetrical PM displacement due to regional (posterior) LV dysfunction might be different from that which occurs with bilateral and symmetrical PM displacement due to global LV dysfunction. We observed a significant difference in MV deformation between the 2 patient groups. The pattern of MV deformation from the medial to the lateral side of the MV was different and asymmetrical in ICM-MR, showing funnel-shaped deformity on the medial side and prolapse-like deformity on the lateral side. In contrast, it was almost symmetrical in DCM-MR, showing funnel-shaped deformity from the medial to the lateral side. These findings are in agreement with previous observations from in vitro experiments.

MR Jet Characteristics and Evolution of MR Severity

In most patients with ICM-MR, 2 separate jets, one from the medial side and the other from the lateral side, were observed. In particular, the lateral jet was characterized by an eccentric posterior jet, which has been described in previous reports. As mentioned above, each side of the MV was deformed in a different way, with funnel-shaped deformity on the medial side and prolapse-like deformity on the lateral side. These 2 separated leaflet asynergies with different geometry generated 2 different jets, the medial one away from the corresponding commissure in the central direction and the lateral one away from the lateral commissure in the posterior direction. Interestingly, patients with a larger lateral jet tended to have less impaired LV systolic function than those with a smaller lateral jet (ejection fraction 30% versus 19%). This finding supports the suggestion that LV systolic pressure probably acts on prolapse-like leaflet asynchrony in an opposite way from funnel-shaped leaflet asynchrony.

Determinants of MR Severity

In DCM-MR, LV chamber volume and sphericity at the level of the PM significantly correlated with MR severity, whereas...
only the latter showed a significant correlation in ICM-MR. This finding suggests that in ICM-MR, MR severity is mainly associated with regional geometry of the LV chamber rather than global geometry. The finding of the present study that MVTa was the strongest determinant of MR severity is consistent with that of a previous clinical study performed in 128 patients with systolic LV dysfunction in which 2D echocardiography was used. In addition, we observed that the slope of the regression line between MVTa and MR severity was steeper in ICM-MR than in DCM-MR (Figure 7), which suggests that MR became more severe in ICM-MR with the same increment of MVTa as in DCM-MR.

**Study Limitations**

In the present study, we did not assess the degree of displacement of either PM. Instead, we assumed, on the basis of several previous reports demonstrating PM displacement in global and regional LV dysfunction, that both PMs would be displaced bilaterally and symmetrically in DCM-MR, whereas only the posterior PM would be displaced, unilaterally and asymmetrically, in ICM-MR with posterior myocardial infarction.

In estimating MR severity in the patients with 2 jets, we estimated MR severity by the sum of 2 ROAs. However, this method has not yet been validated. Furthermore, in some patients, the smaller jet was too small to obtain proximal convergence flow images that were clear enough for determination of ROA. In those patients, MR severity was then estimated only by quantification of the larger jet while the smaller and negligible jet was ignored.

Finally, in the present study, the population studied was relatively small, and further investigation with a larger population is required in the future.

**Clinical Implications**

Recognition of the difference in mitral geometry and MR jet characteristics between ICM-MR and DCM-MR should give new insight for a better understanding of the mechanism in these 2 different types of functional MR caused by 2 different geometric conditions of the LV chamber. With regard to surgical treatment, currently there is no difference in strategy between ICM-MR and DCM-MR (annular size reduction for both). It has been shown that MR persists or worsens at long-term follow-up after annular size reduction by annuloplasty. Recently, several new reconstructive surgical procedures for ICM-MR have been proposed using an animal model. However, the clinical value of these new procedures remains to be verified. Reconstructive surgery for functional MR must rely on the morphological basis of the mitral apparatus. Therefore, a better and more detailed recognition of the geometric difference of the mitral apparatus should be achieved to develop new surgical strategies for these 2 different types of functional MR. RT3DE would be a unique and helpful tool to meet these challenges in the clinical setting.

**Conclusions**

In ICM-MR, the LV chamber and mitral annulus were less enlarged than in DCM-MR despite the presence of virtually the same grade of MR. In ICM-MR, the pattern of MV deformation from the medial to the lateral side of the MV was asymmetrical (significant tethering of both leaflets on the medial side, but significant tethering of only the posterior leaflet on the lateral side), whereas it was symmetrical in...
DCM-MR (significant tethering of both leaflets on both sides). RT3DE is a helpful tool for differentiating the geometry of the mitral apparatus between these 2 different types of functional MR.

Acknowledgments
This work was supported in part by grant NCC9-60 and NCC9-58 from the National Aeronautics and Space Administration, Houston, Tex.

References
Geometric Differences of the Mitral Apparatus Between Ischemic and Dilated Cardiomyopathy With Significant Mitral Regurgitation: Real-Time Three-Dimensional Echocardiography Study

Jun Kwan, Takahiro Shiota, Deborah A. Agler, Zoran B. Popovic, Jian Xin Qin, Marc A. Gillinov, William J. Stewart, Delos M. Cosgrove, Patrick M. McCarthy and James D. Thomas

_Circulation_. 2003;107:1135-1140; originally published online February 17, 2003; doi: 10.1161/01.CIR.0000053558.55471.2D

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2003 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/107/8/1135

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/