Mitral Annular Dynamics in Myxomatous Valve Disease
New Insights With Real-Time 3-Dimensional Echocardiography

Jasmine Grewal, MD; Rakesh Suri, MD, DPhil; Sunil Mankad, MD; Akiko Tanaka, MD; Douglas W. Mahoney, MS; Hartzell V. Schaff, MD; Fletcher A. Miller, MD; Maurice Enriquez-Sarano, MD

Background—Mitral annulus is a complex structure of poorly understood physiology. Full-volume real-time 3-dimensional transesophageal echocardiography offers a unique opportunity to completely image and quantify mitral annulus size and motion.

Methods and Results—Real-time 3-dimensional transesophageal echocardiography of the mitral valve was acquired in 32 patients with myxomatous valve disease (MVD) and moderate to severe regurgitation, 15 normal control subjects, and 10 patients with ischemic mitral regurgitation of identical body surface area. Mitral annular dimensions (circumference, area, anteroposterior and intercommissural diameters, height, and ratio of height to intercommissural diameter ratio, which appraises annular saddle-shape depth) were measured throughout the cardiac cycle with dedicated quantification software. Compared with direct surgical measurement, 3-dimensional anterior annular dimension provided reliable measurements (mean difference, 0.1±0.01 mm; P=0.73; 95% confidence interval, ±4.4 mm). Annular dimensions were larger in MVD patients compared with control subjects in diastole (all P<0.05). Normal annulus displayed early-systolic anteroposterior (P<0.001) and area (P=0.04) contraction, increased height (P<0.001), and deeper saddle shape (ratio of height to intercommissural diameter, 15±1% to 21±1%; P<0.001), whereas intercommissural diameter was unchanged (P=0.30). In contrast, MVD showed early-systolic intercommissural dilatation (P=0.02) and no area contraction (P=0.99), height increase (P=0.11), or saddle-shape deepening (P=0.35). Late-systolic MVD annular saddle shape deepened but annular area excessively enlarged (P<0.04) as a result of persistent intercommissural widening (P<0.02). MVD annulus also contrasts with ischemic mitral regurgitation annulus, which, despite similar anteroposterior enlargement, is narrower and essentially adynamic. After MVD repair, the annulus remained dynamic without systolic saddle-shape accentuation (P=0.30).

Conclusions—Real-time 3-dimensional transesophageal echocardiography provides insights into normal, dynamic mitral annulus function with early-systolic area contraction and saddle-shape deepening contributing to mitral competency. MVD annulus is also dynamic but considerably different with loss of early-systolic area contraction and saddle-shape deepening despite similar magnitude of ventricular contraction, suggestive of ventricular-annular decoupling. Subsequent area enlargement may contribute to mitral incompetence. After mitral repair, MVD annulus remains dynamic without systolic saddle-shape accentuation. Thus, real-time 3-dimensional transesophageal echocardiography provides new insights that allow the refining of mitral pathophysiology concepts and repair strategies. (Circulation. 2010;121:1423-1431.)

Key Words: echocardiography • mitral valve • surgery • valves

The mitral annulus, a complex asymmetrical structure crucial to mitral valve competence, has been insufficiently studied. Tsakiris et al1 first described dynamic motion of normal mitral annulus in animal experiments >30 years ago. Pioneering echocardiographic work with 3-dimensional (3D) reconstruction defined complex mitral annulus geometry, with its “saddle shape,”2 a discovery that led to profound conceptual changes, particularly for mitral valve prolapse diagnosis.3 Sophisticated animal studies using sonomicrometry extended our comprehension of mitral annulus in the normal heart and in models of ischemic mitral regurgitation (IMR).4–6 The unique annular shape is considered important in reducing leaflet stress and enhancing valve competence during systole.7 These seminal efforts were essential in generating new advances, from the diagnosis of mitral prolapse to the development of deformable annular rings for mitral regurgitation (MR) repair. Nevertheless, the depth of knowledge about mitral annular physiology is limited. Pilot studies performed 3D reconstruction of mitral structure, particularly with MR induced by ischemia8,9 or cardiomyop-
However, the annular geometry and dynamics with MR resulting from myxomatous valve disease (MVD) are uncertain, despite the importance of annuloplasty in surgical treatment. Chief reasons for the paucity of data on mitral annular dynamics were technical. The complex annular shape hinders complete imaging by classic techniques. Discrete point annular delineation in multiple views, experimentally obtained with radiopaque markers, was particularly difficult in 2-dimensional (2D) echocardiographic studies, including our own. Widespread 3D reconstruction of individual-slice echocardiography was hindered by prolonged acquisition and computation times and by difficulty with ECG and respiratory gating, leading to major artifact. With the advent of novel real-time 3D, full-volume acquisition with transesophageal echocardiography (RT3DE), unparalleled high-quality, high-frame-rate imaging of the entire annular volume over full cardiac cycles is now possible. This advance, coupled with quantitative analysis software, heralds a new era of physiological assessment of mitral valvular and annular function. Thus, we aimed at investigating mitral annular size, shape, and motion over the cardiac cycle using RT3DE in patients with MVD compared with normal control subjects and patients with IMR.

### Clinical Perspective on p 1431

#### Methods

**Patient Population**

Consecutive patients referred for surgical repair of MR caused by MVD were enrolled prospectively the day of surgery. Patients with IMR referred for clinically indicated transesophageal echocardiography or cardiac surgery were also prospectively enrolled. Patients referred for transesophageal echocardiography and found to have no underlying structural cardiac disease or arrhythmias were included as control subjects. Exclusion criteria were contraindications to transesophageal echocardiography and the presence of mitral stenosis, aortic valve disease, tricuspid regurgitation more than mild, or pericardial or congenital heart disease. The Institutional Review Board at the Mayo Clinic approved the study. Written informed consent was obtained.

#### Transesophageal 2D and 3D Echocardiography

Intraoperatively, transesophageal 3D of mitral apparatus was acquired after anesthesia induction, endotracheal intubation, and complete echocardiography before cardiopulmonary bypass and after repair in a subset of patients as dictated by the availability of a 3D operator (S.M., J.G.). The ultrasound platform used for 2D and 3D acquisitions was the RT3DE imaging probe (model X72t) and the iE33 echocardiography imaging platform, both from Philips Medical Systems (Philips Medical Systems, Bothell, Wash). Live 3D zoom of the mitral valve included aortic valve and entire annulus throughout the cardiac cycle. Direct intraoperative measurement of the anterior intertrigonal arc circumferenza was taken by the surgeon (H.V.S., R.M.S.) using a flexible metric ruler. Care was taken to prevent annular distortion during measurement by avoiding excessive retraction of the left atrium. Surgical measurements were subsequently compared with corresponding RT3DE measurements to validate 3D measurements. RT3DE was similarly performed in IMR patients or control subjects. Preoperative transthoracic 2D echocardiography within 1 week determined left ventricular ejection fraction, end-systolic and end-diastolic dimensions, left atrial volume, and MR severity following the American Society of Echocardiography recommendations.

Full-volume 3D data sets were digitally stored and transferred to a workstation with Q-Laboratory Mitral-Valve-Quantification Software (Philips Medical Systems) for offline analysis. Three orthogonal mitral annulus images were displayed and subsequently modified to optimize visualization of the entire annulus (Figure 1). Mitral annular measurements were performed 6 times during the cardiac cycle in early, middle, and late diastole and early, middle, and late systole. Early diastole was identified with mitral valve opening, late diastole before mitral closure, and middle diastole as midway between these frames. Early systole was identified just before mitral closure, late systole on the frame preceding aortic closure, and middle systole midway between these frames. First, we marked 4 annular key reference points (anterolateral and postero medial hinge points of leaflet insertion, anterior and posterior points). Second, with 3 key orthogonal planes locked in, 7 rotational planes allowed marking of 14 markers around the annulus at leaflet insertion, thereby completing 18 total discretely marked points. Ascertain anatomic markings relied on a simultaneous view of point positioning in all planes, regardless of the plane marked. With complete 3D delineation of the annulus, the software calculated the annular parameters in 3D space, specifically annular area, circumference, intercommissural diameter, anteroposterior diameter, and height (Figure 2). Annular height was the instantaneous maximal vertical distance between the highest (anterior or posterior) and lowest

---

**Figure 1.** Atrial view of the mitral annulus in end diastole (row A) and end systole (row B) without (left) and with (right) measurement markers. Verification of correct position of mitral annulus markers was obtained in 3 orthogonal planes. A indicates anterior; P, posterior; AL, anterolateral; and PM, posteromedial.
The anterolateral or posteromedial points and was used to compute the
instantaneous ratio of annular height to intercommissural diameter, a
measure of annular saddle shape. Deeper saddle shape of the mitral
annulus is characterized by a more apical position of the medial and
lateral aspects of the annulus, whereas the anterior and posterior
aspects remain basal in position and thus translate as a higher
percentage of the ratio of annular height to intercommissural
diameter. Anterior annulus was directly measured in the short-axis
atrial view after complete annulus marking to ensure 3D (rather than
2D) measurement. Variability of measurement was determined by
repeating measurements on stored 3D data sets at least 1 week after
initial measurement by the same observer (intraobserver) and a
different observer (interobserver).

Statistical Analysis
The main analysis focused on characterizing MVD annulus and
comparing it with the annulus of normal control subjects and IMR
patients. Mean (SD) and numbers (percentages) summarize contin-
uous and categorical variables, respectively. Group comparisons of
baseline characteristics and of summarized (overall mean, diastolic,
and systolic dimensions) mitral annulus measures used \( t \) tests
or ANOVA with posthoc comparisons between specific groups when
appropriate. Intragroup comparisons of each annular measure be-
tween 2 points in the cardiac cycle used paired \( t \) tests. Repeated-
measures ANOVA analyzed differences in annular dynamics
through the cardiac cycle between groups. The Bland-Altman
method analyzed the association between intraoperative and 3D
measurements of the anterior annulus. Variability of measurements
was assessed by the Bland-Altman method and by the within-subject
coefficient of variation. Using the Bland-Altman method, we cal-
culated 95% confidence intervals of the variability range for absolute
dimensions. The within-subject coefficient of variation (calculated as
ratio of the SD of the measurement difference to the mean value of
all measurements) provides a scale-free and unitless metric of
variation expressed as a percentage, which is particularly useful
when the association between the variability magnitude and the value
of the parameter measured is uncertain at the outset. We measured
intraobserver reproducibility and interobserver reproducibility for
3D mitral valve annulus measurements in early diastole in 13
patients and expressed them using the coefficient of variation.
Values of \( P < 0.05 \) were considered statistically significant.

Results
Study Population
Characteristics of the 32 patients with MVD are compared
with those of the 15 control subjects and 10 IMR patients in
Table 1. Compared with control subjects, most clinical
characteristics of patients with MVD were similar except for
less diabetes mellitus and more frequent and severe symp-
toms. Patients with IMR were quite similar but tended to be
older with more diabetes mellitus and symptoms than patients
with MVD. Ejection fraction was identical between MVD
patients and control subjects but was lower in IMR patients.
Larger ventricular dimension resulting from volume overload
in MVD and IMR patients compared with control subjects did
not reach significance because of wide distributions, whereas
end-systolic diameter was higher in IMR patients. Trivial MR

Table 1. Participant Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>MVD Patients (n=32)</th>
<th>Control Subjects (n=15)</th>
<th>( P^* )</th>
<th>IMR Patients (n=10)</th>
<th>( P^† )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>62 (15)</td>
<td>57 (18)</td>
<td>0.33</td>
<td>72 (6)*</td>
<td>0.06</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>10 (31)</td>
<td>7 (46)</td>
<td>0.30</td>
<td>2 (20)</td>
<td>0.48</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.9 (0.3)</td>
<td>1.9 (0.2)</td>
<td>0.90</td>
<td>1.9 (0.1)</td>
<td>0.42</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>16 (50)</td>
<td>10 (67)</td>
<td>0.35</td>
<td>7 (70)</td>
<td>0.26</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>2 (6)</td>
<td>4 (27)</td>
<td>0.07</td>
<td>3 (30)</td>
<td>0.06</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>12 (38)</td>
<td>5 (33)</td>
<td>0.90</td>
<td>6 (60)</td>
<td>0.21</td>
</tr>
<tr>
<td>NYHA class, n (%)</td>
<td>0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>11 (34)</td>
<td>15 (100)</td>
<td></td>
<td>2 (20)‡</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>13 (41)</td>
<td>0 (0)</td>
<td></td>
<td>2 (20)</td>
<td></td>
</tr>
<tr>
<td>III/IV</td>
<td>8 (25)</td>
<td>0 (0)</td>
<td></td>
<td>6 (60)‡</td>
<td></td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>61 (7)</td>
<td>60 (1)</td>
<td>0.66</td>
<td>42 (11)†</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic dimension, mm</td>
<td>55.7 (6.9)</td>
<td>53.4 (3.4)</td>
<td>0.46</td>
<td>57.3 (8.5)</td>
<td>0.62</td>
</tr>
<tr>
<td>Systolic dimension, mm</td>
<td>35.8 (5.6)</td>
<td>34.6 (2.2)</td>
<td>0.62</td>
<td>42.7 (9.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Left atrial volume index, ml/m²</td>
<td>53.4 (20.1)</td>
<td>27.8 (5.5)</td>
<td>0.0005</td>
<td>42.7 (9.4)†</td>
<td>0.22</td>
</tr>
</tbody>
</table>

NYHA indicates New York Heart Association. Data are mean (SD) when appropriate.
*Control subjects versus MVD patients; †IMR patients versus MVD patients.
‡\( P < 0.05 \), IMR patients vs control subjects.
was documented in 5 control subjects; all others were free of MR. All patients with MVD or IMR had moderate to severe MR qualitatively. Quantitatively, effective regurgitant orifice area and regurgitant volume of 0.53 ± 0.22 cm² and 80 ± 32 mL/beat in MVD patients and of 0.34 ± 0.19 cm² and 54 ± 24 mL per beat (both $P = 0.05$) in IMR patients, respectively, displayed the expected differences between these conditions.17 MVD lesions were prolapse/flail of the P2 segment in 13 (41%), of the P3 in 5, of the A2 in 2, of the P1 in 1, and of multisegment in 11 (34%). All IMR lesions were of Carpentier type IIIb (systolic restriction).12 Of 15 control subjects with structurally normal hearts, evaluation was for infective endocarditis (n = 2), infective endocarditis (n = 2), and aortitis (n = 1), but these diagnoses were ultimately ruled out after comprehensive assessment.

**Mitral Annular Dimensions in MVD**

Comparison of direct intraoperative and 3D anterior-annulus length measurement showed good agreement (mean difference, 0.1 ± 0.1 mm; $P = 0.73$; 95% confidence interval, ±4.4 mm) between measurements. The Bland-Altman plot showed a random scatter of points around 0, indicating no systematic bias or measurement error proportional to the measurement value. Measurement variability (within-subject coefficient of variation and 95% confidence interval of the Bland-Altman method) for 3D annular measurements for interobserver differences was as follows: anteroposterior diameter, 5.7% and ±5.1 mm; intercommissural diameter, 4.3% and ±2.3 mm; height, 11% and ±1.9 mm; circumference, 5.3% and ±19.8 mm; and area, 5.5% and ±119 mm². Measurement variability for intraobserver differences was as follows: anteroposterior diameter, 1.6% and ±1.7 mm; intercommissural diameter, 2.1% and ±2.4 mm; height, 3.8% and ±0.7 mm; circumference, 1.8% and ±7.1 mm; and area, 2.0% and ±70 mm². Mitral annulus dimensions averaged over the entire cardiac cycle in control subjects and in MVD patients are shown Table 2. Compared with control subjects, MVD patients displayed larger annular circumference, area, and anteroposterior and intercommissural diameters. Overall, however, there was no statistically or clinically significant difference in annular height and saddle-shape depth (ratio of height to intercommissural diameter). Stratified by diastolic and systolic phases, annular area, circumference, and anteroposterior and intercommissural diameters remained larger in MVD patients than in control subjects in both systole and diastole. However, this stratified comparison showed new differences between MVD patients and control subjects. Indeed, in

### Table 2. Annular Dimensions Overall and Throughout the Cardiac Cycle Among Normal Subjects (n = 15) and MVD Patients (n = 32)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>All Cycle</th>
<th>Diastole</th>
<th>Systole</th>
<th>Early Diastole</th>
<th>Middle Diastole</th>
<th>Late Diastole</th>
<th>Early Systole</th>
<th>Middle Systole</th>
<th>Late Systole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Area, mm²</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1050 (123)*</td>
<td>1051 (146)*</td>
<td>1049 (109)*</td>
<td>0.87</td>
<td>1044 (156)*</td>
<td>1061 (136)*</td>
<td>1046 (180)*</td>
<td>1003 (135)*</td>
<td>1048 (130)*</td>
</tr>
<tr>
<td>MVD</td>
<td>1529 (303)</td>
<td>1498 (301)</td>
<td>1559 (354)</td>
<td>0.039</td>
<td>1479 (364)</td>
<td>1466 (318)</td>
<td>1536 (356)</td>
<td>1513 (344)</td>
<td>1577 (401)</td>
</tr>
<tr>
<td><strong>Anteroposterior diameter, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>32.4 (2.7)*</td>
<td>32.6 (3.0)*</td>
<td>32.3 (2.8)*</td>
<td>0.48</td>
<td>32.9 (3.1)*</td>
<td>32.7 (3.3)*</td>
<td>32.2 (3.6)*</td>
<td>30.0 (3.2)*</td>
<td>32.7 (2.7)*</td>
</tr>
<tr>
<td>MVD</td>
<td>38.3 (4.6)</td>
<td>38.6 (4.5)</td>
<td>38.1 (5.1)</td>
<td>0.40</td>
<td>39.0 (5.7)</td>
<td>38.5 (4.9)</td>
<td>37.8 (5.1)</td>
<td>37.0 (4.8)</td>
<td>38.3 (5.7)</td>
</tr>
<tr>
<td><strong>Intercommissural diameter, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>39 (2.4)*</td>
<td>39.3 (2.5)*</td>
<td>38.7 (2.5)*</td>
<td>0.18</td>
<td>39.0 (3.2)*</td>
<td>39.2 (1.9)*</td>
<td>39.5 (3.4)*</td>
<td>38.3 (3.8)*</td>
<td>38.7 (2.6)*</td>
</tr>
<tr>
<td>MVD</td>
<td>47.1 (5.3)</td>
<td>46 (5.3)</td>
<td>48.2 (5.9)</td>
<td>0.005</td>
<td>45.1 (5.7)</td>
<td>45.3 (5.6)</td>
<td>46.9 (5.8)</td>
<td>48.2 (6.5)</td>
<td>47.9 (6.7)</td>
</tr>
<tr>
<td><strong>Circumference, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>125 (8.7)*</td>
<td>123 (9.1)*</td>
<td>126 (8.4)*</td>
<td>0.001</td>
<td>122.4 (8.7)*</td>
<td>123.9 (8.9)*</td>
<td>123 (10)*</td>
<td>125.3 (8.7)*</td>
<td>127.6 (9.5)*</td>
</tr>
<tr>
<td>MVD</td>
<td>150 (16.8)</td>
<td>146.9 (16.2)</td>
<td>152.3 (17.9)</td>
<td>0.002</td>
<td>145.2 (17.5)</td>
<td>145.5 (16.2)</td>
<td>148.4 (17.9)</td>
<td>150.5 (16.7)</td>
<td>152.0 (22.4)</td>
</tr>
<tr>
<td><strong>Annular height, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>6.6 (1.5)</td>
<td>5.5 (1.7)†</td>
<td>7.6 (1.7)</td>
<td>0.002</td>
<td>5.1 (1.4)</td>
<td>5.6 (2.2)</td>
<td>5.9 (2.2)</td>
<td>8.0 (1.7)</td>
<td>7.9 (2.2)</td>
</tr>
<tr>
<td>MVD</td>
<td>7.3 (1.6)</td>
<td>6.8 (1.7)</td>
<td>7.7 (1.9)</td>
<td>0.003</td>
<td>6.7 (2.2)</td>
<td>6.7 (1.6)</td>
<td>6.8 (2.3)</td>
<td>7.2 (2.4)</td>
<td>7.4 (2.2)</td>
</tr>
<tr>
<td><strong>Ratio of height to intercommissural diameter</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>16.9 (3.4)</td>
<td>14.0 (4.0)</td>
<td>19.7 (3.6)†</td>
<td>0.0001</td>
<td>13.0 (3.6)</td>
<td>14.3 (5.3)</td>
<td>14.8 (5.5)</td>
<td>20.8 (4.5)*</td>
<td>20.1 (5.0)*</td>
</tr>
<tr>
<td>MVD</td>
<td>15.5 (3.6)</td>
<td>14.8 (3.5)</td>
<td>16.3 (4.4)</td>
<td>0.03</td>
<td>14.9 (4.7)</td>
<td>14.8 (3.5)</td>
<td>14.4 (4.6)</td>
<td>15.5 (5.3)</td>
<td>15.9 (5.2)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (SD).

*P<0.001, †P<0.01, ‡P<0.05, difference between normal and MVD.
systole, MVD patients compared with control subjects displayed unchanged height and smaller ratio of systolic height to intercommissural diameter, demonstrating dynamic differences between MVD patients and control subjects during the cardiac cycle.

**Mitral Annular Dynamics During the Cardiac Cycle in MVD**

**Overall Annular Changes From Diastole to Systole**

In control subjects, anteroposterior and intercommissural diameters did not change significantly from diastolic to systolic averages, but annular height increased markedly in systole with marked saddle-shape (ratio of height to intercommissural diameter) deepening (Table 2, third and fourth columns). Deeper saddle shape resulted in increased annular circumference without a change in area. In MVD patients, diastolic to systolic annulus changes did not affect anteroposterior diameter, but intercommissural diameter increased markedly, causing a substantial increase in annular circumference and area. Comparing MVD patients and control subjects showed that annular area, on average 43% larger in MVD patients in diastole, became 49% larger than in control subjects in systole. Annular height increased from diastole to systole in both groups but to a lesser degree in MVD patients (by 13% versus by 38%). Annular saddle shape also deepened in both groups in systole but less in MVD than in control subjects (by 10% versus by 43%).

**Timed Changes in Annular Dimensions Over the Cardiac Cycle**

Measurements performed in early, middle, and late diastole and systole provided further details about annular dynamics. There was no systematic trend for change in annular dimensions during diastole in any group.

In control subjects, early systole compared with diastole was marked by anteroposterior contraction ($P<0.001$), whereas intercommissural diameter remained unchanged ($P=0.30$), leading to early-systolic annular area contraction ($P=0.04$). Normal early-systolic annular height increase ($P<0.001$) led to deeper saddle shape (increased ratio of height to intercommissural diameter, $P<0.001$). Conversely, early-systolic annular circumference remained unchanged ($P=0.15$) despite anteroposterior contraction because of simultaneous saddle-shape accentuation. During the remainder of systole in control subjects, anteroposterior diameter returned to its diastolic size ($P=0.20$) with unchanged intercommissural diameter ($P=0.60$), leading to annular area return to its diastolic size ($P=0.10$). Annular height increase was sustained throughout systole ($P<0.001$) with sustained shape change (deeper saddle shape than diastole) throughout systole ($P<0.001$; Figure 3). In middle and late systole after dissipation of the anteroposterior annular contraction, sustained shape change led to increased circumference to a greater level than in diastole ($P=0.005$). Thus, the normal annulus displays a complex sequence of changes during systole (Figure 4A through 4D).

In MVD patients, the annulus was also dynamic, but systolic changes were different. Specifically, MVD early-systolic anteroposterior contraction was less apparent ($P=0.04$).

This lesser anteroposterior contraction, combined with early-systolic intercommissural diameter increase ($P=0.02$ versus diastole, $P=0.03$ versus control subjects), led to an absence of annular area early-systolic contraction ($P=0.99$). The lack of early-systolic annular height increase ($P=0.11$) in MVD patients caused failure of early-systolic saddle-shape deepening ($P=0.35$) in contrast to control subjects (both $P<0.001$ for lesser change versus control subjects). Later in systole, MVD patients displayed an anteroposterior diameter increase back to its diastolic size ($P=0.77$ versus diastole), but with persistent systolic intercommissural enlargement ($P=0.02$), annular area increased compared with diastole ($P=0.04$). Thus, although annular area increased between early and middle or late systole in both control subjects and MVD patients (all $P<0.05$), this resulted in a return to diastolic area in the normal annulus and in enlargement beyond diastolic area in MVD. Another MVD-specific change was that the annular height increase ($P<0.02$) was delayed (in middle and late systole) and minimal compared with control subjects ($P=0.03$). Consequently, saddle-shape deepening occurred later and was less pronounced in MVD patients compared with control subjects ($P<0.0001$). Because of these opposite changes (less saddle-shape deepening but more intercommis- sural diameter increase in MVD patients compared with control subjects), the systolic annular circumference increase was similar in control subjects and MVD patients ($P=0.50$). These considerably different annular dynamics are shown Table 2 and Figure 4.

**Mitral Valve Annular Characteristics in MVD Versus IMR Patients**

In diastole, IMR patients displayed annular enlargement (anteroposterior diameter, $37\pm7$ mm; $P=0.025$ versus control subjects) similar to MVD patients ($P=0.57$). However, IMR intercommissural diameter was not increased ($39.7\pm6.0$; $P=0.84$ versus control subjects) in contrast to MVD ($P=0.002$). Thus, IMR diastolic area ($1273\pm427$ mm$^2$; $P=0.05$) and circumference ($135\pm21$ mm; $P=0.03$) were
smaller than in MVD. In IMR, diastolic annular height also tended to be smaller (5.6 ± 2.5 mm; P = 0.08) than in MVD and was close to normal (P = 0.87), but because of intercommissural diameter differences, diastolic saddle shape was almost identical (13.7 ± 4.2%; P = 0.83 versus control subjects, P = 0.42 versus MVD patients).

Annular dynamics were also different, with IMR patients showing unchanged anteroposterior diameter throughout systole, particularly early systole (P = 0.27), which is probably not due to lack of statistical power because the magnitude of change (−0.9 mm) was smaller than in MVD patients (−1.6 mm) and control subjects (−2.3 mm). IMR annular height, which tended to increase between diastole and systole (5.6 ± 2.4 to 6.4 ± 2.2 mm; P = 0.07), remained lower than in MVD patients and control subjects in systole (P = 0.05). A slight systolic increase in intercommissural diameter in IMR patients (39.7 ± 6.3 to 40.9 ± 6.8 mm; P = 0.05) was of low magnitude (1.2 versus 2.2 mm in MVD patients versus −0.6 mm in control subjects; P = 0.03). Thus, the trend for systolic saddle-shape deepening in IMR (13.7 ± 4.2% to 15.5 ± 3.8%; P = 0.14) was insignificant, contrasting with the immediate increase in control subjects and the delayed increase in MVD patients (P = 0.003). Annulus area in IMR patients, similar to that in MVD patients, showed no systolic contraction (1261 ± 420 to 1286 ± 434; P = 0.15), particularly in early systole (P = 0.45), in contrast to control subjects. Thus, despite similar anteroposterior diameter enlargement in diastole, the wide but dynamic MVD annulus was profoundly different from the narrow and mostly adynamic IMR annulus.

**Post–Mitral Valve Repair MVD Annular Dynamics**

Twelve patients underwent postrepair imaging as dictated by the availability of a 3D transesophageal echocardiography probe operator. Mitral valve repair included leaflet correction followed by implantation of a standard-length 63-mm flexible C-shaped posterior annuloplasty band in all patients. All patients had a successful repair with no or trivial residual regurgitation. Annular dimensions measured over the cardiac cycle before and after repair in MVD patients are shown in Table 3. As expected, postrepair annular circumference, area, and anteroposterior and intercommissural diameters were reduced (all P < 0.001). Postoperatively, MVD annulus remained dynamic with a systolic increase in intercommissural diameter, circumference, and annular area (all P < 0.01). However, postoperatively, there were no contractile changes in anteroposterior diameter (in particular, no early systolic contraction). In addition, the annular saddle shape did not change preoperatively to postoperatively and did not show a

---

**Figure 4.** Sequential measurements of mitral annulus in 6 phases of the cardiac cycle: early, mid and late diastole (ED, MD, and LD) and systole (ES, MS, LS) for control subjects (solid dots) and patients with myxomatous valves (MVD; open dots). In each panel, P values apply to differences between control subjects and MVD patients in diastole (left) and systole (right). A, Changes in ratio of annular height to intercommissural diameter measuring saddle-shape depth, which increased markedly from late diastole to early systole in control subjects but mildly and belatedly in patients with MVD (P < 0.0001 for the difference in controls vs MVD). B, Variation of annular area over the cardiac cycle. Area decreased from diastole to early systole in control subjects (return to diastolic area) but is marked in MVD patients with late-systolic area larger than diastolic area (P = 0.06 for difference in control subjects vs MVD patients). C, Variation of anteroposterior (AP) diameter. AP decrease from diastole to early systole (both P < 0.01) is more pronounced in control subjects. D, Variation of intercommissural diameter over the cardiac cycle. There is no change over the cardiac cycle in control subjects. In MVD patients, intercommissural diameter increases from diastole throughout systole (P < 0.01 for the difference in control subjects vs MVD patients). *Significant within-group difference (P < 0.05) between systolic and mean diastolic measurements.
return of physiological early-systolic saddle-shape deepening (all \( P = 0.30 \)).

### Discussion

The present study aimed to define mitral annular characteristics and dynamics using RT3DE technology in MVD patients in contrast to normal control subjects and IMR patients. Direct comparison of intraoperative and RT3DE annular measurements demonstrated the accuracy of RT3DE. In the normal human, similar to previous animal models, mitral annulus is dynamic in systole compared with diastole. In contrast to control subjects, the annulus in MVD patients was larger in all dimensions, and although it remained dynamic, its phasic changes were different, with loss of regurgitation preventive mechanisms. In contrast to the wide and dynamic MVD annulus, IMR of similar anteroposterior diameter displays a narrow and mostly adynamic annulus. After repair, MVD annular dimensions were markedly reduced, yet the annulus remained dynamic. Thus, the MVD annulus is dynamic but profoundly different from the normal annulus and that of IMR and is an important contributor to the MR complicating MVD.

#### 3D Dynamics of the Normal Annulus

Our findings using new RT3DE to assess normal mitral annulus add to previous studies using quantification attempts in normal subjects with 2D\(^4,\)\(^15\) and 3D reconstruction.\(^2,\)\(^0,\)\(^10\) This improved technology demonstrates a sequence of normal mitral annulus conformational changes over the cardiac cycle. Although atrial contraction may theoretically affect annular shape, no change occurred between early and late diastole. Variation of annular size in diastole was doubtful because of the crude technology used in initial attempts to measure annular function.\(^15\) We cannot exclude changes of very small magnitude, but they would pale in comparison to impressive systolic changes. Normal annulus saddle-shape is accentuated in early systole, coinciding with ventricular myocardial contraction. Simultaneously, annular anteroposterior contraction and increased height occur without intercommissural change. This phenomenon was first described by Levine et al\(^2\) as elevation of annular anterior and posterior sectors with saddle nadir at commissures. Early-systolic anteroposterior contraction with fixed intercommissural diameter leads to early-systolic annular area contraction and approximates anterior and posterior leaflets. Thus, in the normal valve, when early-systolic ventricular pressure is relatively low and does not yet press the leaflets together,\(^14\) leaflet approximation by annular contraction may contribute to their coaptation\(^10\) and be temporarily important in preventing regurgitation. Deeper saddle shape may also contribute to coaptation because the central parts of the leaflets are positioned more apically, resulting in less chordal traction, and may participate in homeostasis of the ventriculomitral complex.\(^6\) After early contraction, there is progressive annular enlargement (increasing annular area and anteroposterior dimension) into late systole, whereas ventricular myocardium continues its contraction and shortening.\(^15\) We interpret these findings as likely related to increased annular traction by continued ventricular contraction with longitudinal ventricular shortening. Annular return to an area similar to diastole\(^15\) has little potential for inducing MR once the leaflets are firmly apposed by intraventricular pressure.\(^18\) Lack of area change (in late systole versus diastole) does not mean lack of annular stretch because deeper systolic saddle shape results in increased annular circumference. Such systolic stretching and diastolic recoil may be limited in fibrous or calcified annuli. Thus, improved 3D technology provides new insights into normal annulus dynamics, the complex changes of which converge toward mitral valve competence throughout systole.

#### 3D Dynamics of Mitral Annulus in MVD

Compared with control subjects, the annulus in MVD patients was larger throughout the cardiac cycle. However, putting
this enlargement in perspective with IMR shows that not all annular enlargements are identical. Indeed, although anteroposterior diameter in diastole was similar in IMR and MVD patients, MVD patients displayed enlarged intercommissural diameter that was absent in IMR patients, resulting in larger annular area and circumference. Although all groups had similar diastolic saddle shape, early-systolic normal saddle-shape deepening was absent in MVD and IMR patients. A more planar annulus, reported in IMR and cardiomyopathy, can now be extended to MVD and may be a common mechanism of early-systolic regurgitation, although the main mechanism of systolic MR in MVD (prolapse) has not yet fully developed. However, other changes are different in IMR and MVD. In IMR, minimal annular height and intercommissural diameter changes in opposite directions lead to adynamic annulus in term of saddle shape. In MVD, normal systolic annular height is ultimately achieved with late-systolic saddle-shape deepening but is of subnormal magnitude as a result of concomitantly increasing intercommissural diameter. Annular shape differences are associated with contraction differences. IMR annulus shows no area contraction and is mostly adynamic, probably related to poor ventricular function. Conversely, MVD annulus contracts in early systole anteroposteriorly but less than normal and is compensated for by intercommissural expansion, leading to absent overall annular area contraction, which is particularly remarkable with ventricular contraction similar to that in control subjects. Thus, in MVD, there is decoupling of annular and ventricular contraction, possibly caused by annular-ventricular disjunction, which is almost universally observed. During the remainder of systole in MVD, excessive annular area expansion contrasts with annular stability in control subjects and IMR patients, probably reflecting tissue deficiencies in MVD. Regardless of the mechanisms, in contrast to the normal annular dynamics that tend to prevent MR and to adynamic IMR annulus, MVD annulus is dynamic but with conformational changes that increase leaflet separation and MR. Hence, it is questionable whether maintaining preoperative MVD mitral annular dynamics after mitral repair is useful.

Annuloplasty rings are widely used in mitral repair, but their effects on annular function remain incompletely understood in humans. Valve repair with flexible posterior annuloplasty band insertion reduces annular area, circumference, and intercommissural and anteroposterior diameters compared with before repair and reaches levels slightly below those in control subjects. After repair, MVD systolic annular dynamics were maintained (systolic increase in intercommissural diameter and annular area) but without restoration of the dynamic annular saddle shape observed experimentally with flexible annuloplasty. Hence, in view of the excellent long-term results of repair in MVD and the absence of residual MR, restoration of normal annular saddle shape and dynamics may not be essential for durable repair in MVD. Leaflet stress depends on multiple factors, and preventing further saddle-shape loss while suppressing billowing may effectively reduce leaflet stress after repair. To improve repair procedures (surgical or percutaneous), 3D mitral characteristics before and after repair and their link to the repair outcome, ie, the recurrence of MR, should be established in future studies.

Limitations

Control patients were referred to transesophageal echocardiography for clinical indications and do not represent a random population sample. With normal echocardiography and no overt clinical abnormality, this subset represents a reasonable control group.

Other mitral measurements can be considered for valve anatomy and regurgitation. However, our study is not a dissertation on all aspects of MVD but specifically addresses annular physiology. Differences in MVD annulus and normal annulus were regarded mostly as differences in size and not function based on outdated technology. The observation of major alterations in MVD annular function should lead to future prospective studies with technically challenging sequential valvular, annular, and MR measurements. The IMR group is small and intended to contrast annular changes in MVD and IMR, which are profound. However, our study suggests that future long-term studies of IMR should shed light on the mechanism by which IMR repair succeeds or fails.

Conclusions

RT3DE imaging of mitral annulus shows that the normal mitral annulus is dynamic with complex changes throughout the cardiac cycle. Early-systolic anteroposterior diameter and area contraction with saddle-shape accentuation probably contribute to normal systolic mitral competency. MVD annulus is also dynamic but considerably different with loss of regurgitation preventive mechanisms. Loss of early-systolic area contraction and saddle-shape accentuation despite similar ventricular contraction suggests ventricular-annular decoupling in MVD. Toward end systole, the MVD annulus widens and enlarges beyond its diastolic dimension, potentially further contributing to leaflet separation. Despite similar anteroposterior enlargement, the wide and dynamic MVD annulus differs from the narrow and mostly adynamic IMR annulus. After mitral repair, MVD annulus remains dynamic in systole but without systolic saddle-shape accentuation. These new insights provided by RT3DE should lead to refined concepts for mitral pathophysiology and repair techniques.

Source of Funding

The study was funded by the Mayo Foundation.

Disclosures

None.

References

The mitral valve is formed by leaflets (1 anterior and 1 posterior) attached to the ventricular wall (by chordae and papillary muscles) and by the annulus, a fibrous ring-shaped structure that attaches leaflets to the base of the heart. The mitral annulus has been little studied because of the difficulty in imaging this wide structure completely and quickly enough.

Real-time 3-dimensional echocardiography is a new technology that allows imaging of a pyramid of the heart structure at high speed. We used this new technology to image the mitral annulus, to define its characteristics and dynamics in patients with myxomatous valve disease annulus in man, II: abnormalities in mitral valve prolapse. Circulation. 1982;65:713–719.


16. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster e, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440–1463.


Mitral Annular Dynamics in Myxomatous Valve Disease: New Insights With Real-Time 3-Dimensional Echocardiography
Jasmine Grewal, Rakesh Suri, Sunil Mankad, Akiko Tanaka, Douglas W. Mahoney, Hartzell V. Schaff, Fletcher A. Miller and Maurice Enriquez-Sarano

Circulation. 2010;121:1423-1431; originally published online March 15, 2010;
doi: 10.1161/CIRCULATIONAHA.109.901181
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 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/121/12/1423