Three-Dimensional Echocardiographic Analysis of Mitral Annular Dynamics
Implication for Annuloplasty Selection

Melissa M. Levack, MD*; Arminder S. Jassar, MD*; Eric K. Shang, MD; Mathieu Vergnat, MD; Y. Joseph Woo, MD; Michael A. Acker, MD; Benjamin M. Jackson, MD; Joseph H. Gorman III, MD; Robert C. Gorman, MD

Background—Proponents of flexible annuloplasty rings have hypothesized that such devices maintain annular dynamics. This hypothesis is based on the supposition that annular motion is relatively normal in patients undergoing mitral valve repair. We hypothesized that mitral annular dynamics are impaired in ischemic mitral regurgitation and myxomatous mitral regurgitation.

Methods and Results—A Philips iE33 echocardiographic module and X7–2t probe were used to acquire full-volume real-time 3-dimensional transesophageal echocardiography loops in 11 normal subjects, 11 patients with ischemic mitral regurgitation and 11 patients with myxomatous mitral regurgitation. Image analysis was performed using Tomtec Image Arena, 4D-MV Assessment, 2.1 (Munich, Germany). A midsystolic frame was selected for the initiation of annular tracking using the semiautomated program. Continuous parameters were normalized in time to provide for uniform systolic and diastolic periods. Both ischemic mitral regurgitation (9.98 ± 155 cm²) and myxomatous mitral regurgitation annuli (13.29 ± 3.05 cm²) were larger in area than normal annuli (7.95 ± 1.40 cm²) at midsystole. In general, ischemic mitral regurgitation annuli were less dynamic than controls. In myxomatous mitral regurgitation, annular dynamics were also markedly abnormal with the mitral annulus dilating rapidly in early systole in response to rising ventricular pressure.

Conclusions—In both ischemic mitral regurgitation and myxomatous mitral regurgitation, annular dynamics and anatomy are abnormal. Flexible annuloplasty devices used in mitral valve repair are, therefore, unlikely to result in either normal annular dynamics or normal anatomy. (Circulation. 2012;126[suppl 1]:S183–S188.)

Key Words: dynamics ■ echocardiography ■ mitral valve ■ valvuloplasty

It has been well reported in the literature that the mitral valve annulus assumes a complex, saddle-shaped 3-dimensional geometry, which alters configuration throughout the cardiac cycle.1–4 Annular dynamic motion has been thought to contribute to leaflet coaptation, valve competence, adequate diastolic filling of the left ventricle, and effective left ventricle systolic ejection.5,6 Previous experimental work in theoretical studies, animal models, and clinical echocardiographic studies have shown that the normal annulus contracts during early systole and deepens in saddle shape thereby improving leaflet coaptation.4,7,8 This physiology has been shown to be altered in animal models of ischemic mitral regurgitation (IMR) with the annulus dilating, flattening, and losing its ability to alter its annular height and saddle geometry throughout the cardiac cycle.9 More recently, with advances in real-time 3-dimensional echocardiography (3DE), investigators have begun studying the dynamic effects of the mitral annulus in clinical scenarios including IMR, nonischemic dilated cardiomyopathy, and myxomatous mitral regurgitation (MMR).7,10,11

As the clinical interest in accurately describing annular physiology has increased, so has the interest in developing a better understanding of how modern mitral valve repair techniques affect this physiology. Annuloplasty rings are routinely used in mitral valve (MV) repair surgery to restore annular size and geometry in both IMR and MMR and the design of 3-dimensional saddle-shaped rings has been shown to restore annular height.12 The use of flexible annuloplasty devices had been advocated by some based on the belief that they preserve annular dynamics. We hypothesized that mitral annular dynamics are impaired in both IMR and MMR. In this study, we describe the dynamic motion of normal, IMR,
and MMR annuli for a variety of measured parameters throughout the cardiac cycle using real-time 3DE and high-resolution, semiautomated annular tracking.

Methods

Patients
A total of 33 patients undergoing cardiac surgery for all causes were enrolled in this study, which was approved by the University of Pennsylvania School of Medicine Institutional Review Board. Patients were divided into 3 groups based on baseline physiology: normal physiology (N=11), IMR (N=11), or MMR (N=11). Patients were excluded from the normal group if they had any evidence on prior echocardiography of MV disease (including more than mild regurgitation or stenosis), depressed ejection fraction (defined as <40%), prior history of MV surgery, rheumatic valve disease, or endocarditis. Inclusion criteria for the ischemic group included history of coronary artery disease documented by angiography or prior documented history of myocardial infarction with or without previous intervention and moderate or greater functional mitral regurgitation on echocardiography. Inclusion criteria for the myxomatous group included documentation of P2 prolapse or flail and moderate or greater mitral regurgitation on echocardiography. Patients were excluded from these pathologic cohorts if they had a history of MV surgery, mitral stenosis, rheumatic valve disease, endocarditis, or were in atrial fibrillation at the time of image acquisition. Written informed consent was obtained from each subject.

Image Acquisition
Real-time 3DE images were acquired through a midesophageal view with a Philips iE33 (Andover, MA) ultrasound system equipped with a 2- to 7-MHz X7-2t transesophageal echocardiography matrix transducer. Electrocardiographically gated full-volume loops were acquired over 4 cardiac cycles at a frame rate of 17 to 30 frames/s prior to cannulation for cardiopulmonary bypass. Color flow Doppler images of the MV were acquired after adjusting the Nyquist limit to approximately 60 cm/s.

Image Analysis
Each full-volume data set was exported offline to an Image Arena, 4D-MV Assessment, 2.1 (Tomtec Imaging Systems, Munich, Germany) software workstation for image analysis. The highest quality data set was selected for each subject. A mid-systolic frame was selected for the initiation of annular tracking using the semiautomated program, which marks 80 points around the circumference of the annulus to create a static 3-dimensional mitral model. Manual edits of the 3-dimensional model were performed to ensure adequate automation. Dynamic models were then created from the 80 circumferential points using 3-dimensional speckle tracking algorithms, which track the annulus throughout each frame of the cardiac cycle. Manual edits of the dynamic models were performed in cases in which gross discontinuity of the tracking was observed; however, given the superiority of the tracking algorithms, this adjustment was rarely needed (Figure 1). Measured parameters were automatically generated from the resultant models including annular area, annular circumference, septolateral diameter (anteroposterior diameter), and MV transverse diameter (anterolateral–posteroomedial diameter). Annular height was determined from the actual Cartesian coordinates of the 80 circumferential points. For each patient, the dynamic data sets were time-shifted such that end systole became the first time point. The data were then normalized in time to provide for uniform systolic and diastolic periods such that the end diastolic data point moves to the midpoint of the cycle. Continuous parameters were computed at interval time points after having rotated the annulus such that its least squares plane lay on the XY axis. A smoothing spline was used to approximate the data. This spline was weighted at the end points to ensure that the curve began and ended at the end systolic value. The slopes of the curves were computed using a gradient function and recorded for determining rate of annular change.

Statistical Analysis
All statistical analysis was performed using Matlab 7.11 (The MathWorks Inc, Natick, MA). Continuous variables are reported as mean±SD. Categorical variables are reported as percentages and were compared using a Fisher exact test. A multivariate analysis of variance was performed to determine significance between groups for both static and dynamic measurements. If significance was determined by multivariate analysis of variance, individual one-way analyses of variance were performed followed by post hoc testing using a Bonferroni correction where appropriate. A probability value <0.05 was considered statistically significant.

Results
Three-dimensional dynamic mitral models were created for all 33 patients. Preoperative patient characteristics are presented in Table 1. There were no differences in sex between cohorts. Patients in the MMR cohort were slightly younger than patients in the IMR cohort. Ejection fraction was decreased in the IMR cohort relative to the normal and MMR cohorts.

Figure 1. A, Four annular points are identified by the user for the initiation of semiautomated annular tracking. After the initiation step, the automatic tracking feature marks 80 points around the circumference of the annulus to delineate annular geometry. B, Top, Side view of completed 3-dimensional dynamic mitral model used for annular analysis and (Bottom) surgeon’s view of 3-dimensional mitral valve reconstruction superimposed on 3-dimensional echocardiography image.
Table 1. Preoperative Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>IMR</th>
<th>MMR</th>
<th>P Value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63.7±16.8</td>
<td>72.8±8.7</td>
<td>57.7±14.5</td>
<td>0.32</td>
</tr>
<tr>
<td>Women</td>
<td>45.5%</td>
<td>36.4%</td>
<td>27.3%</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>65.7±15.0</td>
<td>34.5±14.7</td>
<td>60.9±9.6</td>
<td></td>
</tr>
<tr>
<td>MR grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>100%‡</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>...</td>
<td>54.5%</td>
<td>27.3%</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>...</td>
<td>45.5%</td>
<td>72.7%</td>
<td></td>
</tr>
</tbody>
</table>

IMR indicates ischemic mitral regurgitation; MMR, myxomatous mitral regurgitation; ANOVA, analysis of variance.

*p<0.05 by ANOVA; post hoc analysis showed P<0.03 for IMR versus MMR.
† P<0.001 by ANOVA; post hoc analysis showed P<0.05 for normal versus IMR and IMR versus MMR.
‡ P<0.05 by Fisher exact probability test for all groups.

Static Annular Geometry Comparison

The static annular measurements in the 3 study groups differed significantly by multivariate analysis of variance (P<0.001). These results are summarized in Table 2. Both IMR and MMR annuli were larger than normal annuli for a variety of measured parameters based on the static midsystolic frame. Two-dimensional annular area tended to be larger in the ischemic group (9.98±1.55 cm² versus 7.95±1.40 cm² in the normal group). Septolateral diameter was 3.46±0.29 cm in the ischemic group versus 2.84±0.25 cm in the normal group (P<0.001). Annular height showed a decreasing trend from 6.84±1.55 mm in normals to 5.92±1.15 mm in ischemics. Annular height to septolateral diameter ratio was significantly reduced from 0.24±0.05 to 0.17±0.03 (P<0.001). Interestingly, there was no significant difference in MV transverse diameter. These findings confirm that IMR annuli lose 3-dimensional geometry and remain relatively narrow by dilating in an anterior to posterior direction. Similar trends were noted in the MMR annuli. Two-dimensional annular area for the myxomatous cohort was 13.29±3.05 cm² versus 7.95±1.40 cm² (P<0.001) when compared with normal annuli. Annular circumference, septolateral diameter, and MV transverse diameter were also increased in a statistically significant fashion. At the midsystolic frame, annular height was similar between the myxomatous group and the normal group; however, annular height to septolateral diameter ratio was significantly different. MMR annuli were similar to IMR in terms of dilatation in the septolateral dimension (3.67±0.51 cm versus 3.46±0.29 cm, P=0.57); however, they demonstrated greater widening in the anterolateral–posteromedial direction than patients with IMR (4.46±0.50 cm versus 3.65±0.29 cm, P<0.001).

Normal Annular Dynamic Motion

Normal mitral annuli demonstrated early systolic area contraction when the cardiac cycle was normalized to align MV closing for all patients. Early systolic contraction was followed by gradual annular area increase until end systole. The 2-dimensional annular area fraction change defined as (area maximum−area minimum)/area maximum was 19.02±4.94%. Additionally, as demonstrated in Figure 2, normal annuli demonstrated early systolic narrowing in the septolateral direction followed by a gradual increase in diameter. This followed along with progressive systolic increases in annular height. In contrast, the dimensions of the MV transverse diameter changed little over time corroborating the findings that as annular height increases with a relatively fixed annular width, the relative saddle shape becomes more accentuated throughout systole. By multivariate analysis of variance (P=0.02), there was a significant difference in annular parameters among the normal, IMR, and MMR groups.

Ischemic Annular Dynamic Motion

As demonstrated in Figure 2, IMR annuli appeared less dynamic than normal annuli with decreased motion in a variety of directions. The annular area contracted less during early systole when compared with controls in terms of area. Average 2-dimensional annular area fraction change was 10.26±6.58%. The IMR annulus also displayed a decreased shortening in the septolateral direction and reduced ability to increase annular height.

Myxomatous Annular Dynamic Motion

Annuli in the MMR group demonstrated a different pattern of behavior from either the normal patients or ischemic patients, as also demonstrated in Figure 2. Although MMR appeared larger than both the normals and ischemics, they maintained the ability to contract and modify shape. MMR expand rapidly during systole. The maximum rate of increase (max Δy/Δx) for septolateral diameter, MV transverse diameter, annular circumference, and annular area in the MMR group was 4.53±1.76 cm/s, 2.68±1.55 cm/s, 8.09±3.37 cm/s and 15.61±6.95 cm²/s, respectively, as compared with 3.17±1.46 cm/s, 1.44±0.63 cm/s, 5.25±1.97 cm/s, and 7.81±3.83 cm²/s in the normal group. This shows that there is a rapid rise in annular dilatation in multiple directions as the left ventricular...

Table 2. Midsystolic Annular Dimensions

<table>
<thead>
<tr>
<th>Annular Parameter</th>
<th>Normal</th>
<th>IMR</th>
<th>MMR</th>
<th>P Value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annular height, mm</td>
<td>6.84±1.55</td>
<td>5.92±1.15</td>
<td>6.45±1.42</td>
<td>0.32</td>
</tr>
<tr>
<td>Septolateral diameter, cm</td>
<td>2.84±0.25</td>
<td>3.46±0.29</td>
<td>3.67±0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Annular height to septolateral ratio</td>
<td>0.24±0.05</td>
<td>0.17±0.03</td>
<td>0.18±0.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral valve transverse diameter, cm</td>
<td>3.49±0.39</td>
<td>3.65±0.29</td>
<td>4.46±0.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2D mitral annular area, cm²</td>
<td>7.95±1.40</td>
<td>9.98±1.55</td>
<td>13.29±3.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3D mitral annular area, cm³</td>
<td>8.24±1.47</td>
<td>10.22±1.55</td>
<td>13.56±3.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Annular circumference, cm</td>
<td>10.64±1.00</td>
<td>11.66±0.90</td>
<td>13.48±1.50</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P<0.001 by MANOVA for the entire table; P values presented are those of one-way ANOVA.
IMR indicates ischemic mitral regurgitation; MMR, myxomatous mitral regurgitation; ANOVA, analysis of variance; MANOVA, multivariate analysis of variance.
*Significance (P<0.05) between normal and IMR by post hoc testing.
†Significance (P<0.05) between normal and MMR by post hoc testing.
pressure increases (Figure 2). Two-dimensional average annular area fractional change was 20.87 ± 8.05%.

**Discussion**

In the current study, we analyzed the dynamic motion of the MV annulus in a comprehensive manner in both normal and pathological patient cohorts. Our results demonstrate that mitral annular dynamics are abnormal in patients with both IMR and MMR. The ischemic annulus is adynamic relative to the normal annulus and therefore loses its ability to modify shape throughout the cardiac cycle as it dilates and flattens. The myxomatous annulus is also severely dilated and exhibits rapid expansion during systole, including in the anterolateral-posteromedial direction, which is not part of normal physi-
ology. These patterns of abnormal behavior may be important factors in contributing to the degree of mitral regurgitation witnessed in these pathologies.

There have been a number of previous studies in the literature that have sought to accurately describe annular dynamic motion in both normal and pathological valves. One of the limitations of previous work has included the fact that some authors only report data on a few measured annular parameters, which only modestly describe annular physiology. Other studies have been limited in terms of annular dynamics by using a minimum number of circumferential reference points or in terms of reporting only a limited number of static time points (end diastole, midsystole, end systole, midsystole, etc.) throughout the cardiac cycle. One of the advantages to this study was that we used 3DE with innovative tracking features to accurately follow the annulus throughout time and reported all clinically relevant parameters in a continuous fashion throughout the cardiac cycle.

The current work is limited by a relatively small clinical population; furthermore, the control population did not consist of disease-free individuals. To obtain transesophageal 3DE studies on patients with “normal mitral valves,” patients undergoing cardiac surgery for causes unrelated to mitral valve pathology were deemed “normal.”

Despite these limitations, the normal patient group demonstrated early systolic annular contraction and anteroposterior shortening similar to what has been described by Grewal et al. In their study, they reference the fact that early annular contraction aids in approximating the leaflets when ventricular pressures are low, thereby serving to prevent early systolic valve incompetence. Moreover, Grewal described myxomatous annular dynamics. Our study expands on those results in demonstrating inherent dynamic annular differences between normal and myxomatous valves. Additionally, rather than extract annular measurements at single time points from 3DE, measurements were performed throughout every frame of the cardiac cycle (regardless of number of frames) and normalized across patient populations for a continuous rather than discrete analysis. These data are also consistent with reports demonstrating reduced geometric deformation in ischemic mitral regurgitation.7,14

There is an ongoing debate in the literature regarding the failure rates and long-term clinical outcomes of MV repair procedures performed with either flexible or rigid annuloplasty rings. Yamaura et al15 reported that mitral annular dynamics are preserved in patients who receive a flexible ring as compared with those who receive a rigid ring. Additionally, early reports suggested that the use of a flexible ring in degenerative valve disease may improve left ventricle systolic function defined strictly by echocardiographic criteria.16 As such, the past 20 years have seen a number of partial and complete flexible ring designs aimed at maintaining physiological annular motion. More recently, follow-up clinical studies analyzing the long-term data have been described. For example, Silberman et al17 compared flexible versus rigid annuloplasty in repair of ischemic mitral regurgitation. They found that clinical and hemodynamic results are better with rigid annuloplasty. In their study, both ring types reduced MR post repair; however, a more pronounced reduction was noted with the rigid group as well as a decreased incidence of recurrence in the rigid group. Chang et al18 performed a prospective, randomized study, which looked at the long-term results of both ring types for all causes of MV repair. They found no differences between annuloplasty types; however, they did not perform subanalyses on patients with ischemic or degenerative disease. Moreover, their study demonstrated a nonsignificant trend favoring the rigid annuloplasty group. As such, flexible annuloplasty devices have not been shown to improve clinical outcomes.18–20

The findings of this study suggest that re-establishing normal systolic annular saddle shape in patients requiring MV repair is probably the best approach for improving valve function. Such a strategy has been shown to reduce annular strain, optimize leaflet stress profiles, and increase leaflet coaptation area.24 Maintenance of annular function as a goal of ring annuloplasty may not benefit patients with already abnormal dynamics.

In conclusion, both IMR and MMR annular dynamics and anatomy are abnormal. Flexible annuloplasty devices used in MV repair are, therefore, unlikely to result in either normal annular dynamics or normal anatomy.

Sources of Funding
This work was supported by grants from the National Heart, Lung and Blood Institute of the National Institutes of Health, Bethesda, MD (HL63954, HL73021, and HL103723). R. Gorman and J. Gorman are supported by individual Established Investigator Awards from the American Heart Association, Dallas, TX. A. Jassar was supported by a postdoctoral fellowship from the American Heart Association.

Disclosures
None.

References
Three-Dimensional Echocardiographic Analysis of Mitral Annular Dynamics: Implication for Annuloplasty Selection


_Circulation_. 2012;126:S183-S188
doi: 10.1161/CIRCULATIONAHA.111.084483
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 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/126/11_suppl_1/S183

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/