Quantitative echocardiography of the mitral complex in dilated cardiomyopathy: the mechanism of functional mitral regurgitation

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With the technical assistance of Patricia A. Trim

ABSTRACT We sought to elucidate the mechanism of mitral regurgitation (MR) in dilated cardiomyopathy (DCM). Quantitative two-dimensional echocardiographic examinations were performed in 27 patients, 18 with DCM (nine with MR on physical examination, nine without MR) and nine without underlying heart disease. The MR and "no MR" patients were clinically comparable. Spatial reconstructions from multiple apical cross sections were used to estimate the mitral leaflet area needed to occlude the orifice for a given mid-systolic coaptation configuration (LEAF), as well as mitral annular area index, left ventricular volume, and left atrial volume. Similarly, reconstructions from parasternal short-axis views were used to estimate central chordae tendineae length and angulation. From selective parasternal views papillary muscle (PM) length and contraction and the tethering length from the PM base to the annular plane were measured. The MR group was characterized by markedly enlarged occlusional leaflet area (LEAF 19.8 ± 3.1 in MR vs 13.8 ± 2.8 in no MR group vs 6.3 ± 0.9 cm² in normal group; p < .01), striking mitral annular dilatation (mid-systolic annular area index 7.5 ± 0.8 in MR vs 4.6 ± 0.9 in no MR group vs 2.9 ± 0.4 cm²/m² in normal group; p < .01), and left atrial enlargement (end-systolic left atrial volume 129 ± 39 in MR vs 73 ± 14 in no MR group vs 29 ± 5 ml in normal group; p < .01). Chordal length and angulation, PM length, contraction, and tethering length, and left ventricular volume were not significantly different in the MR vs the no MR group. Noncoaptation of the mitral leaflets at their free margins was not observed in any MR patient. With the use of stepwise linear regression LEAF was determined chiefly by annular size (R² .868), with left ventricular size having little additional influence (R² increment .071). Thus, DCM is associated with enlargement of the mitral anulus, which is more pronounced in those patients with MR. Based on the quantitative estimates of occlusional leaflet area, we postulate that mitral leaflet tissue can stretch somewhat to accommodate dilatation of the mitral complex, but as the requirement for occlusional leaflet area increases less tissue is available for coaptation. Thus, although coaptation continues to occur, the valvular seal becomes ineffective once a critical LEAF is reached. The chief determinant of LEAF is the mitral anulus size, while left ventricular size is a less important factor.

less, the mitral anulus normally shortens along its posterolateral segment during atrial and early ventricular systole, thereby reducing the valvular orifice. Anular dilatation and hypokinesis therefore may contribute to mitral insufficiency, particularly in the presence of leaflet tethering abnormalities. Indeed, the benefit of mitral annuloplasty in various forms of MR has been reported.

Our laboratory group has reported on an echocardiographic method of reconstructing and measuring the mitral anulus in man. After initial success with annular measurement, attention was turned to the mechanism of MR in dilated cardiomyopathy as an appropriate area of investigation. We hypothesized that certain clear anatomic differences might exist between patients with dilated cardiomyopathy with and without MR and that discerning these differences might yield insights into the pathophysiologic characteristics of the disease. Methods of quantitating the other features of the mitral apparatus were developed, and a comprehensive echocardiographic study was performed. The results of this study suggest a more important role for mitral annular dilatation in functional MR than has been appreciated heretofore.

Materials and methods

Patient selection. Patients with dilated cardiomyopathy who showed no clinical or echocardiographic evidence of coronary or primary valvular disease were enrolled in the study. The nine subjects in the “no MR” group had no detectable systolic murmur when examined separately by two cardiologists, while the nine in the MR group had easily detectable typical high-pitched apical holosystolic murmurs radiating to the axilla (grade 2/6 or greater) the presence of which were confirmed with phonocardiographic examination. Several patients with faint apical systolic murmurs not easily recorded on a phonocardiogram were excluded from the study. No patient was studied during an acute exacerbation of heart failure, and only one patient (in the MR group) had clinical and contrast echocardiographic evidence of associated tricuspid regurgitation. Nine age-comparable normal control subjects were enlisted from the hospital wards or from the medical staff. Subjects with technically unsatisfactory echocardiograms were excluded from the study. All subjects gave written informed consent.

Echocardiographic measurements. A two-dimensional echocardiographic system (Varian 3000) was used and recordings were made on half-inch videotape (Sony). The images could be redisplayed in real time, slow motion, or as single frames. Annular and central chordal measurements were taken directly off the screen with a large protractor and/or ruler, while other measurements required tracings on transparencies. Except when specified otherwise, measurements were averaged over 4 sinus or 8 atrial fibrillation beats. The screen height relative to the observer was adjusted to minimize parallax. Vertical and horizontal screen calibrations were repeatedly measured by imaging a 30 mm in diameter wire ring in a water-filled chamber.

Mitral anulus. This method has been described in detail in a prior communication from this laboratory. Briefly, subjects were studied in the left lateral decubitus position. With an inclinometer12 six separate apical recordings were obtained at 30 degree rotational intervals around the anular circumference. Each apical view was selected to maximize the anular diameter at a given rotational orientation and was recorded during held expiration. By convention, a hinge point was defined as the center of the triangular tissue supporting the base of a leaflet, as identified in cross section. At a given point in the cardiac cycle diameters between the two hinge points measured at 30 degree rotational intervals were assumed to bisect each other, and a smooth circumference was drawn to connect the outer edges of these diameters. In the original method11 the assumption of diameters bisecting other diameters was made at only one point in the cardiac cycle, namely end-isovolumetric relaxation, and a floating reference frame was used at other points in the cardiac cycle. In this study this assumption was extended to reconstruction at points of maximum and minimum anular size, i.e., use of a fixed reference frame throughout the cardiac cycle was assumed to be adequate. Also, only two points in the cardiac cycle were measured, namely maximum anular size (at the peak of the P wave, or peak of R wave in atrial fibrillation) and minimum anular size (at ventricular midsystole). The area and circumference of each anular outline was obtained by computerized planimetry. This method yielded the midsystolic and middiastolic anular areas indexed to body surface area (Amax and Amin), the fractional contraction in this area from maximum to minimum (FAC), and the midsystolic and middiastolic anular circumferences (Amin and Amax).

Leaflet coaptation. By convention, the apical views obtained with the inclinometer mentioned above were labeled 8', 9', 10', 11', 12', and 1'. Each view subtends 30 degrees of arc on two sides of the rotational center so that six views complete a 360 degree rotation. In general, the 12' view corresponds to a conventional four-chamber view, and the 9' view corresponds to a conventional two-chamber apical view. With the use of tomographic planes relatively perpendicular to the mitral closure line, the apical recordings obtained above at 10', 11', and 12' were used to study leaflet coaptation. In each recording the leaflet coaptation angle A and perpendicular distance from the anular plane D were measured at midsystole and averaged (figure 1). A and D were further averaged over the 10', 11', and 12' views.

Occlusive leaflet area (LEAF). The leaflet contour in a given apical view obtained as described above may be approximately described by the four heights h1, . . . , h4 and the three radii r1, . . . , r3 (figure 2). Assuming that this contour is swept through 30 degrees of rotation about the origin of r1, the area produced can be calculated as the sum of fractions of cone or frustum areas according to

\[
A = \frac{\pi}{12} \left( r_1^2 + r_2^2 \right) \left( h_1^2 + (r_1 - r_2)^2 \right)^{1/2} + r_3 \left( h_3^2 \right)^{1/2} + \left( r_1 + r_2 \right) \left( h_2^2 + (r_1 - r_2)^2 \right)^{1/2} + r_3 \left( h_3^2 \right)^{1/2} + \left( r_1 + r_2 \right) \left( h_2^2 + (r_1 - r_2)^2 \right)^{1/2} + r_3 \left( h_3^2 \right)^{1/2}
\]

The approximate LEAF would then be the sum of the fractional areas over the six apical rotational views. For this method only one representative midsystolic frame per view was analyzed, without multiframe averaging, and a programmable calculator was used to expedite the analysis. Note that this measurement does not account for leaflet infolding or compression of leaflet tissue at the line of coaptation; hence the term occlusive leaflet area. Presumably this LEAF is the minimum area needed to occlude the mitral orifice for a given midsystolic leaflet configuration and is less than the total leaflet tissue area anatomically present.

Left ventricular and atrial volumes. With the 9' and 12' views obtained as described above, left ventricular and left atrial endocardial outlines were obtained. The ventricular outlines were obtained at ventricular end-systole and end-diastole, while the
atrial outlines were obtained at ventricular end-systole. By convention, papillary muscles were included within the ventricular outlines and the mitral annular plane was taken as the division between the ventricle and atrium. Average volumes were calculated by a computer-accessed Dodge biplane formula, yielding the end-systolic and end-diastolic left ventricular volumes (LVS and LVD), the left ventricular ejection fraction (EF), and the end-systolic left atrial volume (LA).

Central chordal length (LC) and eccentricity (E). The three-dimensional orientations of chordae tendineae with respect to the annular plane are not well defined on any one two-dimensional echocardiographic view. However, a hypothetical central chordal line may be defined and measured by the following (figure 3). The central chordal line is that line from a papillary muscle tip to the midpoint of the corresponding half mitral systolic closure line. We hypothesize that this defined line roughly corresponds to the critical areas of tendon insertion of Brock or the strut chordae of Lam et al. and gives a measurement of overall chordal length and orientation. The method of measurement of the length and angulation of this central chordal line was as follows:

(1) A conventional parasternal long-axis view was recorded for several beats during held expiration (figure 4). On later review of the recording mitral annular hinge points were identified, along with the mitral valve closure point. For a representative beat a line was drawn through the two annular hinge points at midsystole, and the angle between this and the line from the sector origin to the mitral valve closure point was measured.

FIGURE 1. Schematic representation of an apical four-chamber echocardiographic image. H = annular hinge point; LV = left ventricle; LA = left atrium; RV = right ventricle; RA = right atrium.

FIGURE 2. A typical midsystolic leaflet contour as imaged with an apical long-axis view. This contour may be characterized by the radii \( r_1, ..., r_3 \) and the heights \( h_1, ..., h_4 \). \( O \) is the rotational center for this contour.

FIGURE 3. Schematic representation of two parasternal short-axis views in three-dimensional space, one at the mitral level (M), and one at the papillary muscle level (P). \( \alpha \) is the angle between these two planes. A central chordal line (CL) connects a papillary muscle tip to the midpoint of the corresponding half mitral closure line (MCL), shown here for the posteromedial papillary muscle (PM). AL = anterolateral papillary muscle.

(2) With the same chest position, but rotating the transducer 90 degrees, a conventional short-axis view showing the mitral closure line was then obtained (plane M in figure 3). After setting the gain for optimal endocardial and leaflet visualization approximately 10 cardiac cycles were recorded during held expiration. With the transducer located over the same position on the chest wall the transducer was angled apically in an axis of rotation parallel to the original mitral plane so as to just visualize the superior tips of the papillary muscles (plane P in figure 3). At this orientation the angle of plane rotation \( \alpha \) was measured with a precision inclinometer (adapted from a Lietz model 8047-15 Abney hand level and accurate to 10 to 20 min of rotation). Approximately 10 beats were then recorded during held expiration. The above maneuvers were repeated until about three or four recording pairs were obtained with reproducible angles (usually \( \pm 1 \) degree).

(3) Later the recordings were reviewed and four cardiac cycles in normal sinus rhythm or eight cycles in atrial fibrillation were chosen for analysis. To assure that the axis of plane rota-
tion was parallel to the original mitral plane only recording pairs in which mitral and papillary level endocardial outlines were concentric were analyzed (a condition met in most recording pairs). The polar coordinates \((r_p, \theta_p)\) of the center of a papillary muscle group were then measured at mid-systole along with the coordinates \(r_m, \theta_m\) of the midpoint of the corresponding half mitral closure line, as hand drawn and visually determined.

(4) For a given set of mitral and papillary recordings the parameters \(\rho_p, \theta_p, r_m, \theta_m\) for the posteromedial muscle; \(r_p, \theta_p, r_m, \theta_m\) for the anterolateral group; and the angles \(\alpha\) and \(\beta\) were thus obtained. Each \(r, \theta\) coordinate was transformed to X,Y coordinates according to \(X = C_r \cos \theta, Y = C_r \sin \theta\), where \(C_r\) and \(C_\theta\) are the respective horizontal and vertical screen calibrations (repeatedly checked by imaging a wire circle of 10 mm diameter in water). Given the \(\alpha\) angle between the mitral and papillary planes the three-dimensional coordinates of these points were calculated (such that \(Z = 0\) corresponds to the mitral plane and the papillary plane in negative Z space) according to

\[
(X,Y,Z)_m = (X_m, Y_m, 0), \quad \text{and} \quad (X,Y,Z)_p = (X_p, Y_p \cos \alpha - Y_p \sin \alpha)
\]

These coordinates were then transformed to the frame of reference in which \(Z = 0\) corresponds to the annular plane rotating the angle \(\beta\) around the X axis from the mitral closure plane according to

\[
(X,Y,Z)_T = (X, Y \cos \beta + Z \sin \beta, Z \cos \beta - Y \sin \beta)
\]

Four sets of coordinates therefore resulted: \(\rho_p, \theta_p, r_m, \theta_m\), \(X_m, Y_m, \theta_m\), \(X_p, Y_p, \theta_p\), these are the mitral and papillary coordinates defining the posteromedial and anterolateral central chordal lines.

(5) Given the mitral and papillary coordinates for the posteromedial central chordal line, its length was calculated as:

\[
L^{PM} = \left( (X_{PM} - X_p^2) + (Y_{PM} - Y_p^2) + (Z_{PM} - Z_p^2) \right)^{1/2}
\]

\(E\) was defined as the angle with respect to a line perpendicular to the annular plane (i.e., \(E = 0\) for a line perpendicular to the annular plane). The \(E\) of the posteromedial central chordal line was therefore calculated as:

\[
E^{PM} = 90^\circ - \sin^{-1} \left( \frac{Z_{PM} - Z_p}{L^{PM}} \right)
\]

Similar calculations were used for determination of the anterolateral central chordal line. These calculated parameters were then averaged over three to four reproducible recording pairs.

Adjacent left ventricular wall motion and cross-sectional areas. With the papillary level short-axis views obtained as described above, endocardial tracings were drawn so as to include the papillary muscles inside the outlines (figure 5). For a given endocardial outline the centers of each papillary muscle group were visually determined. A line was then drawn through these two points and a second line was drawn perpendicular to the first so as to divide the endocardial outline into two equal areas (as visually determined and verified within 10% by planimetry). A third line was in turn drawn perpendicular to the second so as to divide the endocardial outline into two equal areas. This method of identifying a floating reference frame was performed independently at end-diastole and end-systole. The areas of the two posterior quadrants, including the posteromedial and anterolateral papillary muscles, respectively, were planimetered, yielding end-systolic cross-sectional quadrant area adjacent to the papillary muscles \(A_{mn}\) and end-diastolic cross-sectional quadrant area adjacent to the papillary muscles \(A_{max}\) for each papillary muscle group. Fractional area contraction of each quadrant was calculated as \(FACA = (A_{max} - A_{mn})/A_{max}\).

\(A_{mn}/A_{max}\). The utility of such a quantitative approach has been demonstrated recently.\(^{18}\)

Direct long-axis papillary muscle views. The individual posteromedial and anterolateral papillary muscles were selectively imaged along their respective long axes by the following method.\(^{19}\) First, from a conventional parasternal short-axis view both papillary muscles were identified. The transducer was then rotated counterclockwise for the posteromedial or clockwise for the anterolateral papillary muscle, and the muscle was visualized continuously until its long axis was reached. Fine angle adjustments were made so as to optimally show chordae tendinae and their directions of systolic stress, which extend in the same direction as the papillary muscle long axis to the mitral leaflets.

Once a selective view was obtained and gain was adjusted for optimal endocardial and leaflet visualization, multiple cardiac cycles were recorded at held expiration (figure 6). The papillary muscle length from base to tip (LP) was measured at middias-

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**Figure 5.** Schematic representation of a typical parasternal short-axis view of the left ventricle at the papillary muscle level. A line is drawn through the centers of the two papillary muscles. The line A is then drawn perpendicular to this line so as to cut the endocardial area in half. A second line B is then drawn perpendicular to A, also so as to cut the endocardial area in half. The area of each quadrant including a papillary muscle is measured at end-systole and end-diastole. \(PM = \) posteromedial papillary muscle; \(AL = \) anterolateral papillary muscle.

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**Figure 6.** Schematic representation of a selective papillary muscle view at mid-systole. A line is drawn along the central chordal direction from the papillary muscle base to the annular plane. The LP, LD, and the LBA may be measured directly.
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tole and midsystole along its long axis, often requiring visual averaging between the two heads in a bifid muscle. Middiastole was used since rapid leaflet motion during early diastole precludes chordal definition, and since there may be papillary tension at end-diastole due to presystolic mitral valve closure. Midsystole was used to correlate with midsystolic measurements obtained as described above. The distance from the base of the papillary muscle to the annular plane along the mean chordal line (LBA) was also measured at middiastole and midsystole. Finally and also at midsystole, the chordal length (LD) was measured directly from the tip of the papillary muscle to the area of chordal insertion near the coaptation point of the mitral valve. The length LD was expected to correlate roughly with the parameter LC calculated indirectly as described above.

**In vitro studies and variability of measurements.** The central chordal reconstruction method was tested by imaging a wire model with a circle to define a plane and an attached chord of known length (20 mm) and annulation (60 degrees). This model was imaged in water, with the same field depth as found in the patient measurements (about 10 cm). The model was reconstructed with methods used above seven separate times, yielding a chord length of 18.2 ± 2.2 mm and annulation of 62.7 ± 3.7 degrees. These figures agree well with the actual measurements considering the limitations imposed by the resolution in two-dimensional echocardiography.

Inter- and intraobserver variability in echocardiographic interpretation was studied in the central chordal reconstruction and the selective papillary muscle views. For this purpose the same tape recordings were analyzed independently; variability in obtaining multiple recordings at different settings was not studied. Independent measurements were made by two different observers for intraobserver studies; repeat measurements by the same observer after a 1 month interval were used for intraobserver studies. Linear regression analysis was used to calculate the correlation coefficient r, the slope of the line m, and the intercept b. In addition, for each comparison the mean percentage error was calculated.

For the central chordal reconstruction the LC and E were calculated for the posteromedial chord in two MR and one no MR patients and two normal subjects a total of 16 times. For the selective papillary muscle view, LP, LBA, and chordal length were measured for the posteromedial papillary muscle once in each of six MR and four no MR and four normal subjects. The results of the regression analysis showed satisfactory inter- and intraobserver correlation, with r values ranging from .80 to .97, m values near unity (range .72 to 1.16) and b values near zero. The overall mean percentage area was about 10% (range 5% to 15%). Thus, at least in terms of echocardiographic interpretation and screen measurement variability, these parameters were satisfactory for use in intergroup comparison.

**Data analysis.** Data are expressed in tables, graphs, and in the text as mean ± SD. A one-way analysis of variance of each parameter was performed between the MR, no MR, and normal groups. If the null hypothesis was rejected at the 5% level, pairwise t tests were used to determine the location and significance of differences and the resulting p values were corrected by a Bonferroni factor of 3. The corrected t tests were taken to reject the null hypothesis if the 5% level was reached. For many of the measurements there were noncomparable variances between the heart disease and normal groups, so the Welch statistic was used for analysis of variance and t testing when appropriate.

For the purpose of intergroup comparisons the values obtained for the LC, LD, E, LP, LBA, Amin, Amax, and FACa in the posteromedial and anterolateral papillary muscles were averaged for each patient. With the addition of the remaining parameters (FAC, Amin, Amax, Cmin, Cmax, A, D, LEAF, LA, LVS, LVD, and EF) there were a total of 20 parameter values compared among the three patient groups. The effect of so many compared variables on the statistical analysis is an appropriate concern. Consideration of the nature of the measurements revealed that there were 12 relatively independent categories: annulus size and motion, chordal length and annulation, coaptation angle and distance from the annular plane, papillary muscle length, tethering length, left ventricular size and motion, leaflet area, and left atrial size. Most values for these parameters had nonequal means in the three groups, as shown by initial analysis of variance. However, we elected not to apply an additional factor to correct subsequent t test p values for the effect of multiple variables. Our rationale was that the power of analysis was already limited by the use of small patient groups and the conservative Welch statistic. Thus, we judged that an overly conservative use of the Bonferroni correction would introduce too great a type II error in the analysis.

The relationship between certain pairs of measurements was tested with linear regression analysis, including calculation of the SEE. The dependent variables, LEAF, Amax, and D were analyzed by multivariate linear regression analysis and the multiple regression coefficient R2 was calculated for each addition of an independent variable. In the numerical analysis programs P7D, P1R, and P2R in the BMDP Statistical Software were used.

**Results**

Twenty-seven subjects were studied, nine with MR, nine without MR, and nine age-comparable normal subjects. Tables 1 and 2 detail the clinical characteristics of the cardiomyopathy patients. The MR and no MR groups were comparable in age, NYHA functional class, chest x-ray cardiothoracic ratio, and left ventricular EF. Atrial fibrillation was present in one patient from each heart disease group, and all others were in sinus rhythm. A total of eight patients had previous normal coronary angiograms, and the three MR patients who underwent catheterization showed only moderate angiographic mitral reflux. One of the 27 subjects was female (patient 2 in the no MR group), and the mean age of the normal subjects was 56 ± 12 years (tables 1 and 2).

Table 3 summarizes the results in the three groups. The comparison of measurements between the MR and no MR groups is most salient to the mechanism of functional MR. Note that all the values determined for the various categories only four were significantly different between these two groups: values for the parameters annular size, leaflet area, coaptation distance from the annular plane, and left atrial size. For example, Amin was 7.5 ± 0.8 vs 4.6 ± 0.9 cm²/m² (p < .001), LEAF 19.8 ± 3.0 vs 13.8 ± 2.8 cm² (p < .001), D 13 ± 1 vs 9 ± 2 mm (p < .05), and LA 129 ± 39 vs 73 ± 14 ml (p < .001) in the MR vs the no MR groups. Furthermore, each of these four parameters was highly discriminating, with little overlap in measurements between the groups (figure 7). There were no significant differences in mitral annular contrac-
TABLE 1
Summary of clinical data for the MR group

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Presumed etiology</th>
<th>NYHA</th>
<th>S1</th>
<th>Rhythm</th>
<th>CTR</th>
<th>RAEF</th>
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<tr>
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<tr>
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<td>0.10</td>
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NYHA = New York Heart Association functional class; S1 = auscultatory third heart sound; CTR = cardiothoracic ratio on standard chest film; HTN = hypertension; Idio = idiopathic; NSR = normal sinus rhythm; AF = atrial fibrillation.

As LP and LBA, were relatively symmetrical, but there was relatively little shortening of these parameters from midystole to middiastole in normal subjects or heart disease patients (average LPS 14 ± 3 mm, LPD 13 ± 4 mm and LBAS 46 ± 7 mm, LBAD 47 ± 6 mm in the MR group; LPS 9 ± 2 mm, LPD 10 ± 2 mm and LBAS 35 ± 4 mm, LBAD 37 ± 4 mm in the normal group). Thus, in intergroup comparisons only the systolic lengths LPS and LBAS were studied. There was relative symmetry in left ventricular motion adjacent to the papillary muscles, where FACAPM = m × FACAPRM + b on regression analysis, with b = 0.028, m = 0.935, r = .967, and SEE = 0.05. This confirms the existence of symmetrical hypokinesis in the patients with nonischemic dilated cardiomyopathy.

The mean chordal length values for LC and LD agreed well in each group. There was only rough correlation, however, with LC = m × LD + b, m = 0.74, b = 4.5, r = .63, and SEE = 3.0. The central chordal line is a hypothetical chordal parameter, and close correlation with directly visualized chordae is not necessarily expected.

Table 4 shows the results of stepwise linear regression analysis. LEAF correlated strongly with ALmin (R2 .868), with minor additional influence from left ventricular size (averaged between end-systole and end-diastole to correlate with midystole, incremental R2 .071). LBAS, and E had no additional influence on LEAF. Annular area correlated somewhat with left atrial size (R2 .669), but there was no additional influence from left ventricular size. D correlated with ALmin (R2 .756), but there was no further influence from left ventricular or atrial sizes. Another parameter, termed RAEF (the radionuclide or angiographic left ventricular EF), was measured in 16 cardiomyopathy patients and after univariate regression it showed excellent cor-

TABLE 2
Summary of clinical data for the no MR group

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Presumed etiology</th>
<th>NYHA</th>
<th>S1</th>
<th>Rhythm</th>
<th>CTR</th>
<th>RAEF</th>
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</thead>
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<td>+</td>
<td>NSR</td>
<td>0.57</td>
<td>0.18</td>
</tr>
<tr>
<td>7</td>
<td>53</td>
<td>Idio</td>
<td>3</td>
<td>+</td>
<td>NSR</td>
<td>0.55</td>
<td>0.27</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>Alcohol</td>
<td>4</td>
<td>+</td>
<td>NSR</td>
<td>0.64</td>
<td>0.10</td>
</tr>
<tr>
<td>9</td>
<td>69</td>
<td>Alcohol</td>
<td>3</td>
<td>+</td>
<td>NSR</td>
<td>0.72</td>
<td>0.16</td>
</tr>
<tr>
<td>Mean</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.61</td>
<td>0.21</td>
</tr>
<tr>
<td>± SD</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.08</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Abbreviations are as in table 1.
Table 3

Summary of measurement results in the three subject groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MR</th>
<th>p value for</th>
<th>No MR</th>
<th>p value for</th>
<th>Normal</th>
<th>p value for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral annular size and contraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAC (cm²/m²)</td>
<td>0.06±0.06</td>
<td>NS</td>
<td>0.07±0.05</td>
<td>.01</td>
<td>0.17±0.06</td>
<td>.01</td>
</tr>
<tr>
<td>Amin (cm²/m²)</td>
<td>7.5±0.8</td>
<td>.001</td>
<td>4.6±0.9</td>
<td>.01</td>
<td>2.9±0.4</td>
<td>.001</td>
</tr>
<tr>
<td>Amax (cm²/m²)</td>
<td>8.1±1.1</td>
<td>.001</td>
<td>4.9±1.0</td>
<td>.05</td>
<td>3.5±0.5</td>
<td>.001</td>
</tr>
<tr>
<td>Cmin (cm)</td>
<td>13.6±1.0</td>
<td>.001</td>
<td>10.6±1.1</td>
<td>.001</td>
<td>8.5±0.5</td>
<td>.001</td>
</tr>
<tr>
<td>Cmax (cm)</td>
<td>14.1±1.2</td>
<td>.001</td>
<td>10.9±1.0</td>
<td>.01</td>
<td>9.3±0.5</td>
<td>.001</td>
</tr>
<tr>
<td>Chordal length and eccentricity</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LC (mm)</td>
<td>18±3</td>
<td>NS</td>
<td>18±2</td>
<td>.01</td>
<td>13±4</td>
<td>.05</td>
</tr>
<tr>
<td>LD (mm)</td>
<td>16±4</td>
<td>NS</td>
<td>18±2</td>
<td>.05</td>
<td>14±3</td>
<td>NS</td>
</tr>
<tr>
<td>E (degrees)</td>
<td>39±5</td>
<td>NS</td>
<td>41±10</td>
<td>NS</td>
<td>37±14</td>
<td>NS</td>
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<td>Papillary muscle and tethering length</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>LPS (mm)</td>
<td>14±3</td>
<td>NS</td>
<td>16±4</td>
<td>.01</td>
<td>9±2</td>
<td>.01</td>
</tr>
<tr>
<td>LBAS (mm)</td>
<td>46±7</td>
<td>NS</td>
<td>49±5</td>
<td>.001</td>
<td>35±4</td>
<td>.01</td>
</tr>
<tr>
<td>Leaflet area and coaptation characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LEAF (cm²)</td>
<td>19.8±3.0</td>
<td>.01</td>
<td>13.8±2.8</td>
<td>.001</td>
<td>6.3±0.9</td>
<td>.001</td>
</tr>
<tr>
<td>A (degrees)</td>
<td>62±10</td>
<td>NS</td>
<td>63±12</td>
<td>.05</td>
<td>47±11</td>
<td>.05</td>
</tr>
<tr>
<td>D (mm)</td>
<td>13±1</td>
<td>.05</td>
<td>9±2</td>
<td>.05</td>
<td>6±1</td>
<td>.001</td>
</tr>
<tr>
<td>Left atrial volume</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA (ml)</td>
<td>129±39</td>
<td>.001</td>
<td>73±14</td>
<td>.01</td>
<td>29±5</td>
<td>.001</td>
</tr>
<tr>
<td>Left ventricular size parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amin (cm²)</td>
<td>6.9±1.5</td>
<td>NS</td>
<td>6.4±2.3</td>
<td>.001</td>
<td>1.3±0.7</td>
<td>.001</td>
</tr>
<tr>
<td>Amax (cm²)</td>
<td>8.8±1.6</td>
<td>NS</td>
<td>7.6±2.5</td>
<td>.001</td>
<td>2.9±0.9</td>
<td>.001</td>
</tr>
<tr>
<td>LVS (ml)</td>
<td>223±77</td>
<td>NS</td>
<td>186±64</td>
<td>.001</td>
<td>44±14</td>
<td>.001</td>
</tr>
<tr>
<td>LVD (ml)</td>
<td>276±73</td>
<td>NS</td>
<td>226±73</td>
<td>.001</td>
<td>96±20</td>
<td>.001</td>
</tr>
<tr>
<td>Left ventricular motion parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACa</td>
<td>0.22±0.08</td>
<td>NS</td>
<td>0.16±0.09</td>
<td>.001</td>
<td>0.54±0.14</td>
<td>.001</td>
</tr>
<tr>
<td>EF</td>
<td>0.20±0.05</td>
<td>NS</td>
<td>0.18±0.06</td>
<td>.001</td>
<td>0.55±0.11</td>
<td>.001</td>
</tr>
</tbody>
</table>

LC, LD, E, LPS, LBAS, Amin, Amax, and FACa results for the posteromedial and anterolateral papillary muscles were averaged in each patient.

relation with FACa (RAEF = m × FACa + b, b = 0.03, m = 1.02, r = .937, SEE = 0.03), but poor correlation with echocardiographically measured EF (r = .385).

Discussion

Left ventricular dilatation complicating cardiomyopathy is a common cause of clinically apparent MR.2 The exact mechanism of such functional MR has evaded cardiologists for generations.4 Ventricular dilatation may cause alterations in all six elements of the mitral valve complex, but the particular anatomic changes responsible for valvular incompetence have not been identified. Drawing inferences from the comparison of cardiomyopathic patients with and without MR (as determined on physical examination), the results of this study clearly implicate mitral annular dilatation in the genesis of functional mitral incompetence. In fact, markedly elevated values in four interrelated parameters characterize the MR group: leaflet area, anulus area, the distance from coaptation in the left ventricle to the annular plane, and left atrial volume.

A fundamental observation in this study is that cardiomyopathic patients with MR have markedly larger occlusional leaflet areas than patients without MR, and that both of these groups have significantly larger areas than normal. This suggests that mitral leaflet tissue may stretch to accommodate dilatation in the mitral apparatus,21 as may the chordae tendineae and papillary muscles. However, a sizeable amount of leaflet area is required for coaptation to seal the valve in the face of high ventricular pressures,1 perhaps corresponding to the anatomic "rough zone" on the mitral leaflets.22 Thus, as more and more leaflet tissue is needed to simply occlude the orifice, less and less is available for the coaptation zone so that once a certain range in occlusional leaflet area is reached coaptation becomes ineffective. This situation, in which leaflets meet but are not sealed, would yield relatively small regurgitant orifices, and would translate into the mild to moderate degree of MR present in cardiomyopathic patients. However, noncoaptation, i.e., a situation in which
portions of the leaflet edges actually fail to meet, was not observed in any of our patients. With the use of the multivariate analysis described above, mitral annular area was found to be the chief determinant of the occlusional leaflet area, with only minor contributions from left ventricular size. Thus, mitral annular size appears to have a crucial role in determining the requirement for occlusional leaflet area, and therefore in the mechanism of functional MR. Analogous findings have been reported in patients with functional tricuspid regurgitation. In addition, the variation in the D value among the three groups may reflect indirect influence of annular size on this parameter. Consider a hypothetical situation in which the anulus dilates while tethering and leaflet area remain constant. Contrary to what would be expected, the effect would be to reposition leaflet tissue so that coaptation occurs more deeply in the left ventricle (figure 8). This would magnify the effect of mitral annular dilatation on the requirement for occlusional leaflet area. Indeed, regression analysis showed that D depended chiefly on $A_{\text{L min}}$ ($R^2 = 0.756$), with no further influence from left ventricular or atrial volumes.

The mitral anulus is a partly fibrous junction of left

**TABLE 4**

Results of stepwise linear regression analysis

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent (incremental $R^2$) variable</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEAF (cm$^2$)</td>
<td>$A_{\text{L min}}$ (0.868) (LVS + LVD)/2 (0.071) LBAS (−) E (−)</td>
<td>1.56</td>
</tr>
<tr>
<td>$A_{\text{L min}}$ (cm$^2$/m$^2$)</td>
<td>LA (0.669) (LVS + LVD)/2 (−)</td>
<td>1.22</td>
</tr>
<tr>
<td>D (mm)</td>
<td>$A_{\text{L min}}$ (0.756) (LVS + LVD)/2 (−) LA (−)</td>
<td>1.55</td>
</tr>
</tbody>
</table>

The variable (LVS + LVD)/2 is used as a correlate to other measurements obtained at midsystole.
atrium and ventricle that attaches to the mitral leaflets and the aortic root. Dense collagen is present in the two fibrous trigones on either side of the aortic root, but the posterolateral anulus contiguous with the posterior left atrial wall may have relatively sparse connective tissue. An intricate motion pattern results from the atrioventricular connection: the anulus is maximal just at the peak of the P wave and at this time atrial systole causes significant contraction in annular size, the contraction continuing until a minimum is reached at early to midventricular systole. During the later phases of ventricular systole the anulus begins to enlarge, reflecting an increment in left atrial size despite continued left ventricular contraction. The anulus suddenly contracts during early diastole, presumably due to sudden left atrial diastolic emptying, and the cycle is repeated. According to the regression analysis, annular area depended chiefly on left atrial volume, with no additional influence from left ventricular volume. While this might reflect problems in the left ventricular volume measurement, it emphasizes the important influence of the left atrium on mitral annular size as suggested in the annular contraction pattern. The regression equation so derived was not accurate, with an $R^2$ of only .669, implying that other factors influence the variability of annular area. Perhaps, analogous to findings in patients with mitral prolapse, differing connective tissue characteristics would help explain the remaining variation in annular size.

A final problem of circularity remains in interpreting the relationship between left atrial size and MR. Left atrial enlargement could be a consequence or a cause of MR, and discerning between these two options was impossible in this study. Since the MR and no MR groups were clinically comparable, it seems unlikely that more severe heart failure accounted for the difference in left atrial size. However, this noninvasive study did not provide hemodynamic measurements to address this question. Perhaps a circular relationship is more realistic than a simple causal one since certain patients might be more prone to annular enlargement and the accompanying functional MR that leads to additional left atrial enlargement, increased annular dilatation, and even further regurgitation. Indeed, there is a clinical impression that “mitral regurgitation begets more mitral regurgitation.”

Comment on several of the technical aspects of the study are warranted. While quantitation of MR would have been desirable, this is notoriously difficult and the current best technique of indirectly measuring regurgitant flow could not be used in several patients who refused to undergo cardiac catheterization or in whom it was contraindicated. In an effort to obtain correlates to the presence or absence of MR only patients with unmistakable murmurs on physical examination were included in the MR group, while the no MR patients had no discernible murmurs. Also, although patients with silent mitral insufficiency were not excluded totally, none of the patients studied were clinically in the extreme low-output state associated with this finding.

In addition, significant coronary disease was not a rigorously applied criterion for exclusion in 10 of the 18 cardiomyopathy patients studied. However, if severe left ventricular failure is caused by coronary disease, it is usually in the setting of one or more recognizable transmural infarctions. The absence of distinct dyskinetic segments on the echocardiogram, as well as the rarity of electrocardiographic Q waves, indicated that there was no ischemic heart disease in our patients as did the absence of angina or a history of infarction. Although atrial fibrillation may conceivably contribute to mitral incompetence because of resultant loss in annular contraction, such a causal relationship is not recognized clinically. Thus, patients in atrial fibrillation were not excluded from this study. Indeed, only one of nine patients in each cardiomyopathy group was in this rhythm, and fractional annular contraction in these two was reduced comparably to that in the other patients.

Although direct screen measurements or tracings were crude in technique, with care to avoid parallax they proved superior to the light-pen system available to us. In fact, indirect phantom measurements so ob-
tained were used to evaluate the central chordal reconstruction, yielding surprisingly good results within the general resolution limits of two-dimensional echocardiography. The central chordal reconstruction was technically demanding but feasible, limited chiefly by nonunique definition of the mitral closure plane and papillary muscle tip coordinates. However, averaging over several reconstructions helped compensate for these problems. We also found selective papillary muscle imaging feasible, but there were problems of papillary muscle definition in certain patients, and of chordal definition during systole. The minimal contraction of LP and LBA from mid-diastole to midsystole was of interest but may have related to resolution limits and the taking of a midsystolic rather than an end-systolic measurement. The nature of papillary muscle contraction is controversial and, in view of high tension in the systolic ventricle, papillary contraction may be isometric during early systole before ejection occurs. Although in vitro testing of these methods by imaging animal hearts in water is desirable, we found such studies impractical since a beating heart is necessary for identification of mitral complex structures. We chose a biplane apical technique for left ventricular volume measurement partly for convenience, but the EF so obtained had less-than-desirable accuracy as tested against RAIF, the radionuclide or angiographic EF. Several authors have suggested that incorporating short-axis information is beneficial and the excellent fit of RAIF to FAC, probably because of superior endocardial definition in this view, confirms this. However, the LVSs and LVDs, and EFs so obtained were presumably satisfactory for intergroup comparisons. Although never reaching statistical significance, the MR group tended to have slightly greater ventricular motion compared with the no MR group, perhaps reflecting the unloading effect of MR.

The conclusion drawn from this study contrasts with that from a previous autopsy study. Postmortem changes conceivably may occur, but echocardiographic and autopsy measurements of the mitral annular circumference in normal patients are similar. The annular circumference reported by Bulkley and Roberts in patients with dilated cardiomyopathy with or without MR (11 cm, range 10 to 14) correlates well with the measurements in our no MR group ($C_{max}$ 10.9 ± 1.0 cm). Therefore, the disagreement between results of the two studies may reflect differences in patient selection; perhaps our MR patients had more prominent MR and associated anatomic abnormalities. Our findings also contrast with those of a previous echocardiographic study. However, the mitral anulus is an elliptical two-dimensional structure so that single diameter measurements may be misleading. Furthermore, apical views are probably superior to parasternal views for identifying mitral annular hinge points. A current hypothesis is that papillary muscle displacement in dilated cardiomyopathy causes chordal malorientation that results in mitral insufficiency. The implied mechanism is that the chordal tension vector is oblique, with a resultant smaller vector perpendicular to the annular plane. This would yield a weakened tethering action and perhaps mitral valve prolapse. However, the pattern in our patients was just the opposite since the mitral leaflets were pulled deeply into the left ventricle. Also, there was no significant difference in chordal E values in our three groups, perhaps due to scaling of the mitral apparatus with dilatation causing angles to remain relatively constant. Because of more vigorous ventricular contraction in normal subjects, however, the chordal E would be less than that in cardiomyopathy patients at end-systole. Finally, in comparing our results with previously published data, the normal annular area indexes obtained here agreed nearly exactly with the data obtained previously in this laboratory. The normal end-systolic LA obtained here was comparable to a previously reported value, and the normal chordal length obtained was comparable to the lengths of rough zone chordae tendinae in an autopsy study.

Note that one patient in the no MR group had markedly elevated values for leaflet area, anulus area, and the distance from coaptation to the annular plane. This patient was carefully reexamined to make sure MR had not been missed. In normal sinus rhythm no murmurs were detectable, but during a run of trigeminy a faint systolic murmur was noted during each postextrasystolic beat. While this may have been due to an outflow murmur, we suspect this patient was on the threshold of mitral incompetence and that the increment in end-diastolic ventricular volume after an extrasystole was sufficient to induce mild MR. The concept of regurgitation threshold as implied in the mechanism we propose may also relate to the impact of medical therapy on functional mitral insufficiency. The beneficial effect of vasodilator therapy on secondary MR is well known, and results of animal studies have implied that vasodilator therapy actually reduces the mitral regurgitant orifice via effects on the anulus and subvalvular apparatus.

In conclusion, although this is the first clinical study to emphasize a role for annular dilatation in functional MR, this concept is not a new one. In 1956 Friedberg wrote: "Relative or functional mitral insufficiency oc-

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curs commonly as a result of pronounced dilatation of the left ventricle, due to hypertensive, coronary or aortic valvular disease, usually in association with left ventricular failure. Imperfect valvular closure under such circumstances is due to dilatation of the mitral ring and to retraction of the cusps by chordae and papillary muscles as the ventricular chamber elongates.” Our analysis, as presented above, only serves to substantiate this intuitive perception.

We thank Drs. Donald Guthrie and Stanton Glantz for helpful discussion concerning statistical analysis and Dr. Mark Schwab for assistance in accessing the UCLA computer system. We are grateful to Kaye Cherry and Cindy Ventuleth for secretarial assistance.

References

34. Folland ED, Parisi AF, Moynihan PF, Jones DR, Feldman CI, Tow DE: Assessment of left ventricular ejection fraction and volumes by real-time two-dimensional echocardiography. A comparison of cine-anigraphic and radionuclide techniques. Circulation 60: 760, 1979
Quantitative echocardiography of the mitral complex in dilated cardiomyopathy: the mechanism of functional mitral regurgitation.
C M Boltwood, C Tei, M Wong and P M Shah

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