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Reconsideration of Echocardiographic Standards for Mitral Valve Prolapse: Lack of Association Between Leaflet Displacement Isolated to the Apical Four Chamber View and Independent Echocardiographic Evidence of Abnormality

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Mitral valve prolapse by current echocardiographic criteria can be diagnosed with surprising frequency in the general population, even when preselected normal subjects are examined. In most of these individuals, however, prolapse is present in the apical four chamber view and absent in roughly perpendicular long-axis views. Previous studies have shown that systolic annular nonplanarity can cause apparent prolapse in the four chamber view without actual leaflet displacement above the most superior points of the anulus, and there is evidence for such nonplanarity in vivo. It is then reasonable to ask whether superior leaflet displacement limited to the four chamber view has any pathologic significance or complications. The purpose of this study, therefore, was to address the following *hypothesis*: that patients with superior leaflet displacement confined to the four chamber view have no higher frequency of associated echocardiographic abnormalities than do patients without displacement in any view. Such abnormalities, which would provide independent evidence of mitral valve pathology or dysfunction, include leaflet thickening, left atrial enlargement and mitral regurgitation.

Leaflet displacement was measured in the parasternal long-axis and apical four chamber views in 312 patients who were studied retrospectively and selected for the absence of forms of heart disease other than mitral valve prolapse. Leaflet thickness and left atrial size were measured and mitral regurgitation was graded. Patients with leaflet displacement limited to the four chamber view were no more likely to have associated abnormalities than were patients without displacement in any view (0 to 2% prevalence, $p > 0.5$). In contrast, patients with leaflet displacement in the long-axis view were significantly more likely to have associated abnormalities (12 to 24%, $p < 0.005$), the frequency of which increased with the extent of leaflet displacement in that view ($p < 0.0001$). These results suggest that displacement limited to the apical four chamber view is, in general, a normal geometric finding unassociated with echocardiographic evidence of pathologic significance.

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Prolapse is defined as the displacement of a body part from its usual or normal position or relations (1). Mitral valve prolapse, therefore, involves mitral leaflet displacement beyond the normal range of leaflet motion relative to some reference structure, usually taken to be the mitral anulus. Because two-dimensional echocardiography is ideally suited to define the leaflets and anulus, it has been widely applied to assess their relation in evaluating patients for possible prolapse. Recently, however, concern has arisen that, in the absence of a well defined normal range of leaflet motion, current echocardiographic standards are creating considerable iatrogenic disease in otherwise normal patients (2-4).

Initial two-dimensional echocardiographic studies (5,6) showed that the normal mitral leaflets coapted on the ven-

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tricular side of (below) a line connecting the annular hinge points in the parasternal long-axis view; leaflet displacement above this line correlated with angiographic prolapse (6). Subsequently, superior leaflet displacement in the apical four chamber view rapidly became accepted as the diagnostic standard (7,8), in part because of its greater yield of positive findings (7–10). The diagnostic equivalence of these two roughly perpendicular views, however, implicitly assumed that the mitral anulus must be planar so that leaflet-annular relations would be comparable in the two views.

Two observations challenge the validity of this assumption. First, by these criteria, mitral valve prolapse has been found in ≥11 to 13% of the general population, including preselected normal subjects, thus suggesting that these criteria may be too sensitive for abnormality (2–4). Second, prolapse is frequently diagnosed in the four chamber view and absent in roughly orthogonal long-axis views, a finding that is unexpected if the mitral anulus is a plane (3,8,9).

Evidence has been previously reported (11) of systolic mitral annular nonplanarity, which can explain the discrepancy of leaflet-annular relations in orthogonal views. Specifically, if the leaflets and anulus lie along a saddle surface, which is concave downward in one plane and upward in a perpendicular plane, then the leaflets will appear to lie *above* the edges of the structure in a section through the first plane and *below* them in a section through the perpendicular plane (Fig. 1). In a long-axis or anteroposterior view containing the highest points of the anulus (11–13), the leaflets lie below the annular hinge points, but in a four chamber or mediolateral view, the leaflets appear to rise above the low points of the anulus. Thus, the appearance of prolapse can occur without localized leaflet distortion or displacement above the most superior points of the anulus.

These results raise the possibility that superior leaflet displacement limited to the four chamber view may constitute a normal geometric finding without pathologic significance. Recent studies (2–4) have shown such displacement to be within the normal range in a *statistical* sense, by its frequent occurrence in preselected normal subjects (3) and healthy individuals on routine examination (2,4). However, a study limited to normal subjects cannot determine whether this finding is normal in a *medical* sense, by lack of association with independent evidence of valvular disease or dysfunction. The purpose of this study, therefore, was to address the following *hypothesis*: that superior leaflet displacement confined to the four chamber view is not associated with other, independent echocardiographic evidence of intrinsic mitral valve pathology or dysfunction — specifically, leaflet thickening, mitral regurgitation and left atrial enlargement without other cause.

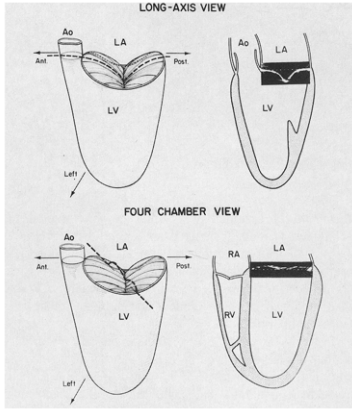

Figure 1. Discrepancy of leaflet-annular relations in two-dimensional echocardiographic views (long-axis and four chamber) of an in vitro model (left) with a saddle-shaped anulus and leaflets that are concave toward the left ventricle (LV), reflecting its distending pressure. The highest points of the saddle (farthest from the apex) are considered to be located anteriorly (Ant.) and posteriorly (Post.), with medial and lateral low points consistent with in vivo observations (11–13). **The heavy interrupted lines on the left** indicate the plane of view. **On the right,** echocardiographic images of the model are shown along with diagrams of surrounding structures. The **dotted lines** in the echocardiographic images demarcate an apparent annular plane in each view; they were manually placed with the aid of the echocardiographic instrument. Ao = aorta; LA = left atrium; RA = right atrium; RV = right ventricle. (Reprinted with permission from the American Heart Association, Inc. [11].)

Methods

Patient selection. Patients with no apparent structural heart disease other than mitral valve prolapse by existing two-dimensional echocardiographic criteria were collected by retrospective review of the log of patients referred for echocardiographic examination, beginning with the most recent patient and proceeding in reverse order. An initial consecutive collection of 222 patients, covering 6 weeks, contained 135 patients with a structurally *normal* heart and no systolic leaflet displacement above the annular hinge points in either the apical four chamber or the parasternal long-axis view (*Group 1*). 57 patients with leaflet displacement confined to the four chamber view (*Group 2*) and 30 patients with displacement in the long-axis view, with or without associated four chamber view displacement (*Group 3*). Because of the small number of patients in Group 3, an additional set of 90 consecutive patients with long-axis view displacement was added to that group from patients studied

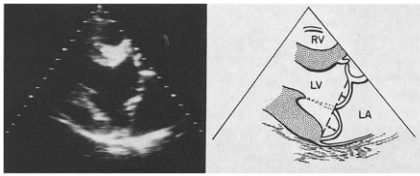

Figure 2. Measurement of leaflet displacement above a line connecting the annular hinge points in the parasternal long-axis view (**left**) and line drawing (**right**). Hinge points were determined by review of the videotaped images and displacement measured as shown in the video frame in which it was maximal. Abbreviations as in Figure 1.

during the preceding 18 weeks, during which equipment, personnel, scanning techniques and interpretive criteria remained unchanged. Although the main hypothesis related primarily to the similarity of Groups 1 and 2, these additional Group 3 patients allowed us to explore more fully the relation between long-axis view displacement and prevalence of abnormalities.

In total, 312 patients were studied who had no primary cardiac disease by echocardiography other than the diagnosis of mitral valve prolapse by existing criteria. In particular, associated conditions that could cause leaflet thickening, regurgitation or atrial enlargement, such as rheumatic valve disease or ischemic heart disease with papillary muscle dysfunction, had been excluded. Age of the patients ranged from 2 to 78 years (mean 35). Ninety-three were male and 209 female. Reasons for referral included evaluation of suspected prolapse, heart murmur, palpitation or other symptoms and routine evaluation. Patients had normal sinus rhythm when scanned.

Echocardiography. All patients had been studied with a commercially available phased-array sector scanner operating at 2.5 to 3.5 MHz. Studies included the apical four chamber view, defined to include the apex of the heart and to maximize its long axis and the mitral and tricuspid excursions (14,15), and the parasternal long-axis view, defined to include the left ventricular long axis and aortic root and to maximize ventricular short-axis diameter and mitral leaflet excursion (14,15). Doppler studies had been performed in 208 patients. The decision to perform a Doppler study was based primarily on the availability of personnel and equipment; in particular, Doppler studies were performed on 90 (67%) of the 135 patients with no leaflet displacement (Group 1)—the same proportion as in the entire study group. Mitral regurgitation was searched for with the Doppler sample volume on the atrial side of the valve. The sample volume (3 to 5 mm in axial length) was scanned in an expanding radial arc in the apical four chamber, apical long-axis and parasternal long-axis views.

To explore the relation between patterns of leaflet displacement and associated abnormality, the following measurements were made from videotaped images with a Microsonics Easy-View II off-line analysis system:

1. *The displacement of each leaflet* in the parasternal long-axis and apical four chamber views was measured above a line connecting the midportions of the annular hinge points as determined by real time review of the images. This measurement was made to the ventricular border of each leaflet in the video frame demonstrating maximal superior systolic displacement (Fig. 2 and 3).

2. *The thickness of both mitral leaflets* was determined in the long-axis view with the leaflet perpendicular to the beam (Fig. 4); maximal thickness of the midportion of the leaflet was measured and isolated focal thickenings ignored.

3. *Three maximal systolic left atrial dimensions were measured (Fig. 5).* An expression of left atrial volume was obtained by multiplying the product of these three orthogonal dimensions by $\pi/6$ (that is, $(4\pi/3)(1/2)^3$, to give the volume of an ellipsoid with these diameters [16]).

4. *The superior extent of mitral regurgitant flow* was graded by pulsed Doppler ultrasound on a scale of 1+ to 4+ by dividing the left atrium into fourths with 1+ regurgitation, for example, being limited to the region just above the mitral valve (17–19). Regurgitation was not diagnosed if flow was limited to the time of mitral valve closure at the onset of systole (20).

Normal ranges for the measured dimensions have been determined in this laboratory in 77 normal adults and 193 children (3,21,22).

Analysis of data. Patients were classified into the three groups described on the basis of their leaflet-annular relations (superior systolic leaflet displacement in no view, in the four chamber view only or in the parasternal long-axis view). The vast majority (113 of 120) of patients in Group 3 had displacement in both the parasternal long-axis and apical four chamber views.

Evidence of associated echocardiographic abnormalities included increased leaflet thickness (≥5 mm) and increases in any left atrial dimension (21) or their volumetric product (>43 ml). Mitral regurgitation was analyzed as any regurgitation (1+ to 4+) and separately as 2+ to 4+ regurgitation, given the findings in a review of 7,000 patients in this laboratory that up to 1+ regurgitation can be observed in 19% of patients with an otherwise normal heart in the

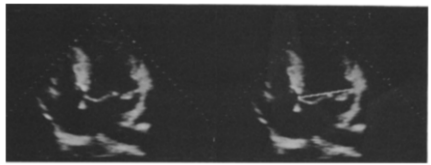

Figure 3. Measurement of leaflet displacement in the apical four chamber view (**left**). A line connecting the annular hinge points has been overlaid on the video image (**right**) to facilitate the measurement.

echocardiographic referral population, and similar findings by other groups (23–26).

The proportion of patients with a given abnormality, such as left atrial enlargement, was calculated for each group. These proportions were compared by Fisher's exact test. To afford protection from multiple comparisons, significance was assessed at $p < 0.005$ for these tests (27).

Multiple linear regression analysis was used to determine the correlation between the presence or absence of associated abnormalities on the one hand, and the measured leaflet displacements, age, gender and body surface area on the other (RS1 package; Bolt, Beranek and Newman, Inc.). The regression model also included two factors reflecting the leaflet-annular relations under investigation. These factors were the product of leaflet displacement in the two views studied for each leaflet. Each factor became zero if there was no leaflet displacement or displacement occurred in only one view. For the purpose of this analysis, the presence or absence of associated abnormality was expressed as a variable equal to 0 in the absence of associated abnormality and equal to 1 if any abnormality was present. To compare the contributions of various factors with the presence of abnormality, the regression coefficient of each factor was multiplied by the standard deviation of that factor in the population to give dimensionless regression coefficients that could then be compared.

Two independent observers measured the leaflet displacements and other linear dimensions in 10 patients to determine interobserver variability. For each type of dimension (leaflet displacement, leaflet thickness and left atrial dimension) the measurements of the two observers were subtracted from one another, and the standard deviation of the differences calculated to express interobserver variability. Similarly, one observer repeated the measurements 1 month later to determine intraobserver variability.

Results

Patient characteristics. By definition, patients in Group 1 had no leaflet displacement. In Group 2, leaflet displacement in the four chamber view ranged from 2 to 5 mm. In Group 3, displacement in the long-axis view ranged from 2 to 12 mm, and in the four chamber view, from 0 to 15 mm. Body surface area and gender were not significantly different among the groups by analysis of variance ($p > 0.2$). Age was not significantly different between Groups 1 and 2 (31 ± 16 versus 29 ± 14 years, $p > 0.05$), but was higher in Group 3 (41 ± 18, $p < 0.01$ compared with the other two groups).

Associated abnormalities (Table 1). There were no differences between patients in Groups 1 and 2 with respect to any of the associated abnormalities ($p > 0.5$). In each of these two groups, the proportion of patients with abnormalities (including mitral regurgitation >1+ in severity) was equal to or close to zero. The proportion of patients with 1+ mitral regurgitation is consistent with the experience of this and other laboratories in otherwise normal individuals referred for echocardiography (23–25).

Patients in Group 3 were significantly more likely to have the associated abnormalities studied ($p < 0.005$). Further, the frequency of abnormality progressively increased with the degree of leaflet displacement in that view (Fig. 6). These trends were significant at $p < 0.0001$ by Fisher's exact test. Only seven patients had leaflet displacement (3 to 5 mm) in the parasternal long-axis view only (too few to be compared

Figure 4. Measurement of leaflet thickening in the parasternal long-axis view (**left**) and line drawing (**right**). Arrow denotes the measured width of the anterior mitral leaflet. Abbreviations as in Figure 1.

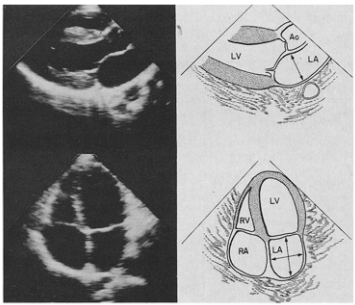

Figure 5. Measurement of left atrial dimensions. The anteroposterior dimension is measured in the parasternal long-axis view (**upper panels**) as indicated by the **arrow** in the line drawing (**upper right**). In the apical four chamber view (**lower panels**), the mediolateral (**horizontal arrow**) and inferosuperior (**vertical arrow**) dimensions are measured as shown in the line drawing (**lower right**). Abbreviations as in Figure 1.

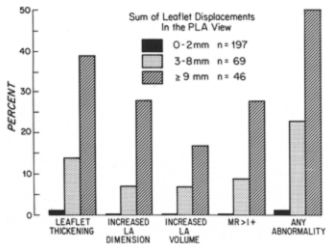

Figure 6. Frequency of associated abnormalities as a function of the degree of leaflet displacement in the parasternal long-axis (PLA) view. The 312 patients are grouped according to the sum of leaflet displacements (anterior plus posterior leaflets) in the long-axis view. The height of the **bars** expresses the percent of each group having a given abnormality. LA = left atrium; MR = mitral regurgitation.

as a separate group). Of these, one had leaflet thickening, none had left atrial enlargement and three of five studied by Doppler ultrasound had 1+ mitral regurgitation.

Effect of age. To assure that the higher proportion of patients with associated abnormality in Group 3 was not solely due to the older age of that group, patients were classified into those above and below the age 40 years or, alternatively, above and below age 60 years. Patients in Group 3 continued to have the preponderance of associated abnormality in each age range. This was confirmed quantitatively by log-linear analysis of the proportion of patients with each abnormality as a function of displacement group and age range (BMDP4F package, University of California, Los Angeles, 1981), which showed that none of the differences in proportions of patients with abnormalities are related to age (age interactions not significant, $p > 0.1$).

Multiple regression analysis. The factors correlating most strongly with the presence of any associated abnormality were posterior leaflet displacement in the long-axis view, the posterior leaflet displacement product defined previously, age and gender. The relative contributions of these factors, normalized so that the lowest was 1, were 1.9 for posterior leaflet displacement, 1.6 for the posterior leaflet displacement product, 1.1 for age and 1.0 for male gender. The regression model predicted the presence of associated abnormality with a correlation coefficient of 0.62 ($p < 0.0001$). (After the stronger contribution of the posterior leaflet had

Table 1. Echocardiographic Findings in the Three Leaflet Displacement Groups

	Group 1 (no displacement)	Group 2 (A4C only)	Group 3 (PLA at least)
No. of patients	135	57	120
Increased leaflet thickness	1 (0.7%)	0	29 (24%)
Increased LA dimension	3 (2%)	0	19 (16%)
Increased LA volume	0	0	14 (12%)
Mitral regurgitation/no. of Doppler studies	7/90 (8%)	2/31 (6%)	35/87 (40%)
MR >1+/Doppler studies	0/90	0/31	14/87 (16%)
	$p > 0.5$	$p < 0.005$	
		$p < 0.005$	

A4C = apical four chamber view; LA = left atrium; MR = mitral regurgitation; PLA = parasternal long-axis view.

been accounted for, the contribution of the anterior leaflet no longer appeared because the two were correlated [r = 0.8].)

Mitral regurgitation. The comparison of regurgitation was performed only in patients studied by Doppler ultrasound (Table 1). Within each group, the patients who were or were not studied by Doppler ultrasound were not significantly different with respect to any of the other characteristics measured: leaflet displacement, leaflet thickness and left atrial dimensions ($p > 0.05$ by analysis of variance). Because the two sets of patients were otherwise comparable, it is unlikely that any important change in the frequencies of regurgitation would have occurred had Doppler studies been performed in all patients; in particular, the prominent disparity in the frequency of regurgitation between Group 3 and the other two groups, and the similarity between Groups 1 and 2, would not be likely to change.

Observer variability. Interobserver variability was 0.5 mm for leaflet displacement, 0.3 mm for leaflet thickness and 1.5 mm for left atrial dimensions. The corresponding intraobserver variabilities were 0.5 mm, 0.4 mm and 1.7 mm.

Discussion

Mitral valve prolapse, originally believed to be uncommon (28,29), has evolved into a pervasive clinical problem (2,3,30). By current criteria, individuals who are apparently in good health are diagnosed as having disease (2–4,30–37) and ascribed an uncertain prognosis, including endocarditis, stroke and sudden death (28,29,38–41).

Basic problems of definition and diagnostic standard underlie the clinical perplexity (42,43). Mitral valve prolapse is a displacement of the mitral leaflets from their usual or normal relation to surrounding structures (1), generally taken to be the mitral annulus. Therefore, its proper diagnosis requires both a technique that can display the fundamental anatomic leaflet-annular relations and a knowledge of the normal range of leaflet motion.

Present criteria for diagnosing mitral prolapse. Two-dimensional echocardiography has provided a noninvasive technique capable of simultaneously visualizing the mitral leaflets and anulus and determining their relation (5,6); however, the range of normal has not been defined by this technique. Instead, it has been assumed that any leaflet displacement to the atrial side of the annular plane is abnormal and that prolapse can be diagnosed with equal validity in all tomographic views of the valve, with the diagnostic standard being taken as the view showing displacement most often—namely, the apical four chamber view (7,8).

By these criteria, prolapse can be diagnosed with surprising frequency in apparently healthy individuals (2–4), although results are not uniform (44). For example, prolapse could be diagnosed by existing criteria in 13% of 193 children preselected by their physicians to be normal, and in 34% of those aged 10 to 18 years (3). Moreover, 24 children had findings of prolapse in the four chamber view whereas only 3 had them in a long-axis view (3). This discrepancy in leaflet-annular relations is unexpected if the anulus is a plane, as has been implicitly assumed.

Role of annular shape in echocardiographic diagnosis. Previous work has shown that systolic annular nonplanarity can produce *apparent* prolapse in the four chamber view without actual leaflet displacement above the most superior points of the three-dimensional anulus (Fig. 1). This relates to the saddle-like systolic shape of the anulus, as suggested by animal experiments (12,13) and demonstrated in a series of patients (11). Annular nonplanarity is also reasonable because the *circumference* of the base of the ventricle decreases in systole (12,45) whereas the *length* of leaflet attached to the ventricle remains constant (the leaflet does not contract). To accommodate this constant length within a smaller circumference requires deforming it out of a plane. These annular studies can explain the clinically observed discrepancy of leaflet-annular relations in orthogonal views without the need to postulate localized leaflet distortion.

The current study. This study is a logical sequel to the annular work. Its purpose was to determine whether superior systolic leaflet displacement limited to the four chamber view may constitute a normal geometric finding without pathologic significance. The study of preselected normal children described previously (3) suggests that such displacement is normal in the *statistical* sense. However, those conclusions cannot be generalized to the echocardiographic referral population, which has not been so selected. Therefore, we addressed the question of whether superior displacement limited to the four chamber view could be considered normal by virtue of its lack of association with other *independent* evidence of mitral valve disease or dysfunction.

This retrospective study demonstrates that patients with displacement limited to the apical four chamber view are no more likely to have associated abnormalities connoting mitral valve pathology or dysfunction than are patients with no displacement in any view and no other echocardiographic evidence of heart disease. In both groups, the proportion of patients having leaflet thickening, left atrial enlargement or mitral regurgitation >1+ in severity ranged from 0 to 2%. On the other hand, patients with leaflet displacement in the parasternal long-axis view, with or without associated displacement in the four chamber view, *are* more likely to have these abnormalities, the frequency of which increases with greater degrees of displacement.

These results suggest that leaflet displacement limited to the apical four chamber view is a normal geometric finding without associated evidence of pathologic significance. Because prolapse is an abnormality by definition, these findings suggest that it cannot be diagnosed in the four chamber view alone.

Multiple regression analysis showed that the most impor-

tant factor predicting the presence of associated abnormalities was posterior leaflet displacement. This is consistent with the angiographic-pathologic studies of Ranganathan et al. (46) and the autopsy series of Davies et al. (47), which showed predominant distortion of the posterior leaflet and posteromedial scallop in patients with moderate to severe degrees of prolapse. (This does not imply that anterior leaflet displacement is unimportant, but simply reflects its lower numerical contribution to the regression model and its correlation with posterior leaflet displacement in the long axis view.) The increase in associated abnormalities with age and male gender is consistent with observations that complications, such as ruptured chordae tendineae and severe mitral regurgitation, occur most often in older men (48–55). This reinforces the concept that such complications relate to valvular "wear and tear" (53,56) because the magnitude and duration of hemodynamic stresses are likely to be greater in older men, whose systemic blood pressure may have been relatively high for many years (53,57,58).

Eliminating the diagnosis of prolapse confined to the four chamber view dramatically reduces its prevalence in the prospective study of normal children cited previously (3). In the current study, no serial prospective studies were performed to exclude the possibility that abnormalities may subsequently develop in patients with displacement in the four chamber view. The absence of abnormalities in the Group 2 patients *regardless of age*, which ranged up to 87 years, suggests that the development of associated abnormalities is unlikely; however, these considerations emphasize the need for prospective study.

Long-axis view leaflet displacement. Although the conclusions regarding the four chamber view are clearly evident from these data, *it is not obvious at what point leaflet displacement determines abnormality in the long-axis view.* As Figure 6 shows, the relation between displacement and abnormality appears to be a continuous one. In the individual patient, the presence of associated abnormalities may depend on a variety of other factors, such as leaflet morphology and hemodynamic stress. These relations are best established by prospective study of a larger population; such a study can further refine diagnostic criteria *within* the group with long-axis view displacement as the range of normal leaflet motion is more sharply defined.

A small number of patients were found to have displacement limited to the long-axis view, only one of whom had leaflet thickening. It would seem reasonable to speculate that such patients would have a net three-dimensional leaflet displacement less than that of patients with displacement in two perpendicular views, and would be less likely to have associated abnormalities; however, it must be emphasized that the group is *too small* to warrant such conclusions, which are also best established by a large population study. (Of note is that Panidis et al. [55], for example, found significant mitral regurgitation only in patients with displacement in two views.)

Although a full appreciation of three-dimensional structural relations requires reconstruction of the tomographic images, it is unlikely that such an approach will reveal that annular nonplanarity *masks* subtle degrees of prolapse in the long-axis view: if that were the case, such patients should have displacement above the low points of the anulus in the four chamber view, which is not associated with abnormalities, as this study has shown.

Standards for prolapse. Any study of mitral prolapse is made more difficult by the multiplicity of diagnostic techniques and often discordant criteria (59), many derived from patients coming to surgery or angiography and extrapolated to the general population with loss of specificity (60). No definitive standard has achieved universal acceptance, partly because most patients diagnosed as having prolapse follow a benign course that precludes tissue diagnosis (30,51). As Lucas and Edwards (61) have emphasized, "when a patient has a systolic click, a systolic click-murmur, and/or a mitral valve prolapse demonstrated by an imaging technique, a precise anatomical state cannot be presumed." Auscultatory criteria, for example, have a sensitivity and specificity that appear to depend on the population and examiners (59). Of particular note in contemplating an auscultatory standard are the following: 1) the frequency with which auscultatory findings occur in otherwise healthy individuals when closely examined (31,62); 2) the frequent discordance between auscultatory and echocardiographic findings (31,37), although results are variable (59,63); and 3) the considerable variation in such findings over time, as documented by Devereux et al. (56,59). Symptoms previously linked to prolapse, on the other hand, have been shown to occur as frequently in its absence (37,63–65).

The lack of a universally accepted, nonechocardiographic standard highlights the need to search for independent evidence of abnormality to separate normal variants from findings with pathologic significance. This study has tried to identify associations between leaflet geometry and evidence of valvular disease or dysfunction — in particular, leaflet thickening and significant regurgitation — factors that are clinically important in determining prognosis (51), the need for surgery and, as some studies suggest, antibiotic prophylaxis (53,66–68). In this retrospective study, auscultatory and phonocardiographic data were not available and, even if they had been, the approach would have been the same. The case can be put more strongly: even if patients in Group 1 or 2 had a click or a systolic murmur, there would be no solid basis for ascribing to them an *abnormality* of the mitral valve (prolapse) in the presence of normally thin leaflets, competent valve closure and either no displacement or a geometry described frequently in normal subjects and consistent with annular nonplanarity.

Study patients. Because of the selection criteria used, the results are applicable most properly to patients without echocardiographic evidence of heart disease other than mitral valve prolapse. It may therefore be possible that prominent, localized prolapse of a leaflet scallop may be evident only in the four chamber view in patients *with* other forms of heart disease. This is consistent with clinical observations, particularly of the posterior leaflet, in occasional patients with evidence of chordal rupture, infective endocarditis or papillary muscle disruption related to ischemic heart disease, although this possibility can be minimized by mediolateral scanning in the long-axis orientation (69).

As previously noted, an initial consecutive collection of 222 patients in Groups 1, 2 and 3 led to a disproportion among groups, with only 30 patients in Group 3. This collection was sufficient to address the primary hypothesis that abnormalities occur with comparable frequency in Groups 1 and 2. However, we extended the consecutive collection of Group 3 patients to strengthen the intergroup comparison and to explore the relation between long-axis view displacement and prevalence of abnormalities. This should not interfere with the conclusions derived for the following reasons: 1) *Within each group*, patients are consecutive: Group 2 patients, for example, have not been selected for the absence of regurgitation, nor Group 3 patients for its presence, so that each group is a representative consecutive sample of patients with a particular geometry. 2) *The major null hypothesis being tested*, as stated earlier, relates specifically to Groups 1 and 2, which were truly consecutive. Group 3 simply proves what is already known: that there *are* patients with mitral valve prolapse who have associated pathologic consequences. 3) The 90 patients added to Group 3 do not pose a problem because equipment, personnel, scanning techniques and interpretive criteria did not change during the 6 months of the entire collection. There were no significant differences between the initial 30 and subsequent 90 patients in Group 3 with respect to any of the abnormalities studied ($p > 0.6$ by Fisher's test), gender distribution ($p > 0.05$ by Fisher's test), age or body surface area ($p > 0.15$ by Student's t test). Indeed, all the differences between Group 3 and the other two groups listed in Table 1 persist at least at the $p < 0.05$ level if only the initial 30 patients are used, with the exception of regurgitation >1+ in severity in Group 3 versus Group 2 (3 of 23 versus 0 of 31, $p \sim 0.07$ because of the low number of positive end points and consequent low power of the test, suggesting the need for more patients).

In the initial group of 222 patients, the percent having long-axis view displacement (30 of 222, or 13.5%) may appear high; however, it is not surprising because of the high frequency of referral for suspected prolapse and the exclusion of patients with all other cardiac disease.

Conclusions. Patients with superior systolic mitral leaflet displacement on echocardiography confined to the four chamber view are no more likely to have associated abnormalities connoting mitral valve pathology or dysfunction than are patients with no displacement in any view and no other form of heart disease. These results suggest that, as a rule, displacement in this view is a normal geometric finding without pathologic significance. Because mitral prolapse is by definition an abnormality, our findings challenge its diagnosis based solely on the four chamber view in many otherwise normal individuals.

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