Limitations of Echocardiography in the Assessment of Left Ventricular Size and Function in Aortic Regurgitation

ABDULLA M. ABDULLA, M.D., MARTIN J. FRANK, M.D., MARIO I. CANEDO, M.D., AND MIlTIADIS A. STEFADOUROS, M.D.

SUMMARY The optimal timing for prosthetic valve replacement in patients with aortic regurgitation (AR) depends on the identification of left ventricular (LV) enlargement and dysfunction. Whether this goal can be achieved reliably by echocardiography was evaluated in 22 patients with pure or dominant AR (AR group) in whom echocardiographic LV dimensions and performance indices were compared with corresponding dimension, volume and performance data obtained by single-plane and biplane angiography. Echocardiographic and single-plane angiographic comparisons were also made in 18 patients with diseases other than AR (non-AR group).

In the AR group, there was a moderately close correlation between the echocardiographic dimensions and single-plane right anterior oblique (RAO) angiographic volume (r = 0.80; p < 0.001). However, the standard error of estimate was large (SEE ± 60 ml) and did not justify the use of a regression formula for calculating LV volume from echocardiographic dimension in individual patients. Substituting biplane for RAO angiographic volume did not improve the correlation (r = 0.78, SEE ± 63 ml, p < 0.001). Moreover, in these patients, the echocardiographic calculation of LV ejection phase indices compared unfavorably with corresponding RAO (r = 0.31-0.38; p = NS), left anterior oblique (r = 0.54-0.56; p < 0.05), and biplane angiographic data (r = 0.53, 0.54; p < 0.05). In contrast, comparison between echocardiographic dimensions and RAO angiographic volumes in the non-AR group exhibited a higher degree of correlation (r = 0.94; p < 0.001) and the SEE was half that seen in the AR group (p < 0.001). Also, there was a clinically satisfactory correlation between echocardiographic and RAO angiographic indices of LV function (r = 0.81-0.84; p < 0.001).

We conclude that single echocardiographic measurements of LV dimensions and function indices are clinically unsatisfactory and potentially misleading in patients with AR. We postulate that this discrepancy may be related to the altered geometric configuration of the enlarged chamber in this disease state.

ALTHOUGH AORTIC REGURGITATION (AR) is easily diagnosed in most patients and its severity can usually be estimated at the bedside,¹ ² the clinical recognition of early left ventricular (LV) dysfunction remains a problem because of the unique nature of this lesion. Patients with hemodynamically significant AR respond to effort by redistributing rather than augmenting the total LV stroke volume, i.e., increasing forward flow at the expense of regurgitant flow.³ Thus, they are able to remain asymptomatic during effort for several years despite progressive deterioration of LV function.⁴ Dysfunction is often far advanced by the time radiographic enlargement, wide pulse pressure and electrocardiographic abnormalities become apparent.⁵ Because of the insidious nature of the transition from normal to overt LV dysfunction, there is a bias in some centers toward earlier valve replacement. However, the problems with available prosthetic valves make other clinicians reluctant to recommend surgery in the asymptomatic patient. Thus, the optimal time for valve replacement is controversial.⁶ ⁷

In addition to usual clinical criteria,⁶ indications for prosthetic valve replacement at our institution include angiographic demonstration of significantly increased LV end-diastolic and end-systolic volumes with an ejection fraction below 0.50 and LV end-diastolic pressure above 18 mm Hg, the latter two values representing 3 standard deviations from the normal mean values for our laboratory.⁹ Hence, a reproducible, noninvasive method that can estimate LV enlargement and detect myocardial dysfunction is needed to assist in the selection of patients for cardiac catheterization and valve replacement, and echocardiography appeared to be a logical choice.

Echocardiography does not measure LV volume per se, but a clinically useful estimate of LV volume can be provided from the LV internal dimension measured by this technique.¹⁰ ¹³ In addition, the performance of the left ventricle can be evaluated by use of this dimension directly, without the need for translating it into volume.¹⁴ ¹⁶ Although this may usually be the case, we have repeatedly been misled by echocardiographic estimates of LV size and function in patients with AR in whom subsequent cardiac catheterization provided angiographic data for comparison. A similar experience has been reported by Johnson et al.¹⁷ The present study was designed to extend and systematize our initial observations and to evaluate echocardiography in the assessment of the left ventricle in AR.

Methods

Study Groups

Thirty-one consecutive patients with hemodynamically significant (moderate to severe), isolated or
dominant chronic AR (AR group, table 1) were
studied by echocardiography and cardiac catheterization performed within 24 hours of each other. We excluded patients with atrial fibrillation, complete left bundle branch block, segmental LV wall motion abnormalities associated with coronary artery disease, technically unsatisfactory studies or a difference in heart rate in excess of 10% between procedures. In 22 patients (17 male) the data were considered suitable for analysis. The patients were 16-68 years old (mean 41 years). All patients were evaluated as candidates for aortic valve replacement. Eight patients were New York Heart Association functional class II and 14 were in class III. Coronary arteriograms were performed in all patients who were older than 40 years or had complained of chest pain. The coronary arteriograms were normal in all but three cases (table 1, patients 15, 20 and 21).

Another group of 18 patients with a wide range of LV volumes due to miscellaneous cardiac diseases other than AR were randomly selected and served as controls (non-AR group, table 2). Data obtained by the two methods were processed by different investigators working independently. LV dimensions and function indices obtained by echocardiography were compared with their angiographic counterparts using the least-squares method of linear regression analysis to determine the correlation coefficient.
### Table 2. Left Ventricular Angiographic and Echocardiographic Data in 18 Patients with Diseases other than Aortic Regurgitation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>End-diastole</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Dimension (cm)</td>
<td>Volume (ml)</td>
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<tr>
<td></td>
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<td>ECHO</td>
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<tr>
<td>18</td>
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**Mean**

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<th>Dimension (cm)</th>
<th>Volume (ml)</th>
<th>End-diastole</th>
<th>End-systole</th>
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<tr>
<td>6.3</td>
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**Difference (ECHO - ANGIO)**

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<th>(RAP)</th>
<th>&lt;0.001</th>
<th>NS</th>
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**Correlation (r) with ECHO dimension**

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<th>(RAP)</th>
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<th>&lt;0.001</th>
<th>&lt;0.001</th>
<th>&lt;0.001</th>
</tr>
</thead>
</table>

*Abbreviations: MR = mitral regurgitation; MS = mitral stenosis; CMP = congestive cardiomyopathy; HCVD = hypertensive cardiovascular disease; AS = aortic stenosis; ECHO = echocardiographic; ANGIO = angiographic; RAO and LAO = right and left anterior oblique angiograms, respectively.*

Differences were analyzed by the two-tailed *t* test, and the level of significance was set at *p* < 0.05. Values are expressed as mean ± SEM.

### Cardiac Catheterization and Angiography

All patients underwent routine diagnostic right- and left-heart catheterization. Cineangiography was performed in all patients in the 30–45° right anterior oblique (RAO) view, and in 14 patients (table 1) in the 50–60° left anterior oblique (LAO) position, with a 35-mm camera (60 frames/sec) during rapid (2–3 seconds) injection of 45–60 ml of sodium meglumine diatrizoate through a retrograde arterial catheter. There was an average delay of 15 minutes between the two studies. This time period is thought to be sufficient to allow the heart to return to baseline hemodynamic levels after the use of radiopaque contrast material.18, 19 Except for rotating the patient from one oblique position to another, no intervention was attempted that might possibly alter the hemodynamic status of the patient between the two angiograms. An electrocardiographic lead was recorded during LV opacification to permit selection of appropriate film frames for volume analysis, elimination of premature beats and first post premature sinus beats and calculation of heart rate during filming. In patients with AR, technically satisfactory angiograms were obtained in both oblique positions at identical heart rates in 14 patients. Aortic regurgitation was graded from mild (1+) to severe (4+) by analysis of aortic valvulograms from the magnitude and rapidity of retrograde opacification of the left ventricle relative to that of the aorta, as previously described.20

A 5-cm metal ring was placed at the center of the palpable apex of the left ventricle to obtain a correction factor for magnification in the RAO view.21 Catheter width was used to obtain corresponding cor-
rection factors for the LAO view. Single-plane LV volumes in the RAO position were calculated at end-diastole (EDV) and end-systole (ESV) by the area-length method described previously and corrected to equal the more accurate biplane volume by the formula of Kasser and Kennedy. This formula includes a correction for the known discrepancy between direct measurements and biplane estimates of LV volumes in postmortem hearts. The single-plane cineangiographic technique has been standardized and its accuracy validated in our laboratory by displaying a very good agreement with indicator-dilution estimate of volume. The minor diameters at end-diastole (Dd) and end-systole (Ds) were calculated in each oblique view by the formula: minor diameter = 4A/πL, where A is the area of the chamber as measured by planimetry and L is the long diameter drawn from the midpoint of the aortic valve to the apex, at the respective phase of the cardiac cycle.

The biplane volume was calculated by the formula: volume = (π/6) × L × D₁ × D₂, where L is the long diameter of the ventricle in the RAO view and D₁ and D₂ are the minor diameters in the RAO and LAO positions, respectively. Because there is also a consistent slight overestimate inherent in this method, the calculated volumes were corrected by the regression equation of Dodge et al.

The ejection fraction (EF) was calculated as (EDV - ESV)/EDV for the RAO single-plane and the biplane techniques using volume data obtained by the respective methods.

**Echocardiographic Examinations**

An Ekoline 20 ultrasonoscope (Smith Kline Instruments, Palo Alto, California) equipped with a 2.25-MHz focused transducer (Model C-12) and interfaced with a Cambridge physiologic recorder (Cambridge Scientific Instruments, Ltd., Cambridge, U.K.) was used to record the M-mode echocardiograms on a strip chart. Patients were examined in the supine position with the transducer applied along the left sternal border at that interspace from which the mitral echogram could be visualized with the transducer held perpendicular to the chest wall with only slight medial but no superior or inferior angulation. From this position the transducer was gradually tilted inferolaterally until the echoes of the mitral valve were replaced by those of the chordae tendineae with clear visualization of the endocardium of the left side of the interventricular septum and of the posterior LV wall; the vertical distance between these two structures was measured to the nearest 0.5 mm at the peak of the R wave of the simultaneously recorded ECG and also at the peak anterior motion of the posterior LV wall to obtain the end-diastolic (Dd) and the end-systolic (Ds) LV minor-axis dimensions, respectively (fig. 1). These dimensions were then averaged over five beats and used to calculate the systolic fractional shortening of LV minor dimension ([Dd - Ds]/Dd) and the LVEF using the formula: EF = (Dd² - Ds²)/Dd², which bypasses the need for translating dimensional to volume data. A third index of LV function, the mean circumferential fiber shortening rate, was not used in this study because its computation requires knowledge of the ejection time, the measurement of which from either the LV echogram or the LV angiogram is subject to sizable error.

**Results**

The results of echocardiographic (echo) and angiographic (angio) measurements of LV dimensions and volumes from the AR and non-AR groups are listed in tables 1 and 2, respectively.

Visual examination of the cineangiographic films failed to reveal regional contraction abnormalities of the LV wall in any of the 22 patients of the AR group. The end-diastolic and end-systolic outlines of the LV cavity of the 14 patients with AR who had technically satisfactory angiograms filmed in both the LAO and RAO projections are shown in figures 2A and B.

**Echocardiographic vs Angiographic Dimensions**

In the 22 patients of the AR group, the mean echo dimension was smaller than the RAO angio dimension by 1.2 cm at end-diastole (p < 0.005; table 1); when end-diastolic and end-systolic data were pooled to yield 44 data points, the echo dimension was smaller than the RAO angio dimension by 1.0 cm (p < 0.001) and the correlation coefficient relating these 44 pairs of values was r = 0.81 (p < 0.001).

Similar comparisons were made between the echo dimension and the angio dimension obtained in the LAO position in the 14 patients of the AR group for whom data were available. The echo dimension was
again smaller than the angio dimension (table 1), but the difference was about half that of the RAO comparison. Thus, considering end-diastolic and end-systolic data together (n = 28), the echo dimension was on the average 0.5 cm (p < 0.02) smaller than its LAO angio counterpart. However, despite a better approximation, the correlation between the two was worse (r = 0.68; p < 0.001) than that between echo and RAO angio dimensions.

Echocardiographic Dimensions vs Angiocardiographic Volumes

In the AR group there was a fair correlation between the echo dimensions and the angio LV volumes computed from the RAO projection at end-diastole (r = 0.55) or end-systole (r = 0.62); when end-diastolic and end-systolic data were considered together, the correlation improved (r = 0.80; SEE ± 60 ml; p < 0.001), but not to a point that would justify the use of a regression formula for calculating LV volume from echo dimension in individual patients (fig. 3). Substituting biplane angio for RAO angio volumes did not improve the correlation with echo dimensions (r = 0.78; SEE ± 63 ml; p < 0.001).

In contrast, similar comparison between echo dimensions and RAO angio volumes in the 18 patients of the non-AR group correlated better for end-diastolic (r = 0.90), end-systolic (r = 0.91) and combined data (r = 0.94; SEE ± 30 ml; p < 0.001) (fig. 3).

Echocardiographic vs Angiocardiographic Indices of LV Performance

In AR, the echocardiographic LVEF and fractional minor-axis shortening correlated poorly with the respective indices obtained by RAO angiography (r = 0.31-0.38; p > 0.05; table 3). Some improvement was noted when these echo indices were compared with the biplane angio EF (r = 0.54 and 0.53, respectively; p < 0.05) or with the LAO angio fractional shortening of the LV minor axis (r = 0.54 and 0.56, respectively; p < 0.05; table 3).

In contrast to these findings, in the non-AR group, the correlations between RAO angio EF and either the echo systolic fractional shortening (r = 0.83; p < 0.001) or the echo EF (r = 0.84; p < 0.001) were much better than in the AR group, and the difference between echo and RAO angio estimates of EF was trivial (3.8%; p > 0.05; tables 3 and 4).
Discussion

Using a single echocardiographic dimension to determine the volume of a cavity with as complex and irregular shape as that of the human left ventricle is a formidable problem without a satisfactory solution. In the past few years several formulas have been proposed to compute LV volume from the echocardiographic LV dimension, with various degrees of accuracy. Although useful in the majority of cases, these formulas may fail when applied to ventricles with a shape significantly different from the assumed shape of a normal left ventricle or with a nonuniform wall contraction. Even in the absence of these conditions, LV volume computed by these formulas for a given dimension may vary considerably.

Problems inherent in the calculation of LV volume can be avoided by using the measured echocardiographic dimension as an estimate of volume without attempting to compute the latter. Although the precise relation between dimension and volume is not known, both variables increase or decrease together so that comparison of the LV dimension of a patient, with the spectrum of LV dimensions obtained from normal hearts or from diseased hearts with known degree of cardiomegaly, may provide valid information concerning the absence or presence and the degree of LV enlargement. The success of this approach obviously depends on the presence of an acceptable degree of consistency in the relation between measured dimension and true volume, expressed in the form of a correlation coefficient high enough and a

<table>
<thead>
<tr>
<th>TABLE 3. Statistical Matrix of Correlation Between Echocardiographic and Angiographic Indices of Left Ventricular Performance</th>
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<tbody>
<tr>
<td><strong>AR group</strong></td>
</tr>
<tr>
<td>ECHO FS</td>
</tr>
<tr>
<td>ECHO EF</td>
</tr>
<tr>
<td><strong>Non-AR group</strong></td>
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<tr>
<td><strong>Fractional shortening</strong></td>
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<tr>
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<tr>
<td>Mean</td>
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<tr>
<td><strong>Non-AR group</strong></td>
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<tr>
<td>n</td>
</tr>
<tr>
<td>Mean</td>
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<tr>
<td>SEM</td>
</tr>
</tbody>
</table>

*p < 0.05.
†p < 0.001.
‡Nonsignificant (p > 0.05) correlation.
Abbreviations: EF = ejection fraction; FS = systolic fractional shortening of left ventricular minor dimension; ECHO = echocardiographic; ANGIO = angiographic; AR = aortic regurgitation; RAO and LAO = right and left anterior oblique angiograms, respectively.

Figure 3. Relation of the end-diastolic and end-systolic left ventricular (LV) volumes (ordinate) calculated by angiography to the respective echocardiographic LV minor-axis dimension (D) in 22 patients with isolated aortic regurgitation (AR) (left) and 18 patients with diseases other than aortic regurgitation (non-AR) (right). Dashed lines are two standard errors of the estimate above and below the mean.
standard error of estimate small enough to be of clinical value in individual cases. This requirement is indispensable because it guarantees that, over a wide range of LV sizes, ventricles with equal dimension would have equal or nearly equal volume, despite our inability to provide the exact numerical expression of the latter.

Because of these considerations we elected to examine the relation between echo LV dimension as such and angio LV volumes. Our data indicate that, although statistically significant, the relation is not close enough to inspire confidence in the use of echo dimensions to evaluate LV size in individual patients with AR, regardless of whether the RAO volume (r = 0.80; SEE ± 60 ml) or the biplane volume (r = 0.78; SEE ± 63 ml) was used for comparison with the echo LV dimension. In contrast, application of the same protocol in the group of patients with diseases other than AR resulted in a more consistent and, hence, clinically useful relation between echo LV dimension and angio volume (r = 0.94; SEE ± 30 ml). These findings suggest that factors related to the shape, pattern of wall contraction, or to other attributes of the left ventricle in AR, rather than methodologic errors in obtaining and processing the LV echogram and angiogram, are primarily responsible for the observed clinically unsatisfactory scatter in the relation between echo dimension and angio LV volume.

The reason for the unusually poor reliability of the echocardiographic estimate of volume in AR compared with other conditions may be related to differences in the shape of the enlarged left ventricle. Necropsy studies have shown that the enlargement in AR primarily involves the LV outflow tract, which becomes markedly elongated.30 Gould et al. have shown that the left ventricle in AR retains its ellipsoidal shape with a nearly normal end-diastolic LV major/minor axis ratio.31 However, when decompensation develops, the chamber gradually becomes spheroidal.32 In this study, the angio LV major/minor axis ratio at end-diastole in both the AR and non-AR groups was practically the same (1.64 ± 0.05 and 1.66 ± 0.04, respectively, p = NS), despite the fact that the LV volume in AR was 36% larger (p < 0.001). Furthermore, when the angio end-diastolic and end-systolic LV major/minor axis ratio was plotted against the respective volume, an inverse curvilinear relation was found between the two variables in both groups (fig. 4). Despite significant overlap between the two groups, trend line analysis showed that at any given volume the left ventricle in the AR group had a higher major/minor axis ratio, and hence a more ellipsoidal shape. This combination of an enlarged but relatively ellipsoidal left ventricle in AR with the attendant elongation of the chordae tendineae and papillary muscles would theoretically permit the echocardiographic landmark structures to be recorded over an unusually wide area and still fulfill the standard criteria of acceptance for purposes of measurement of LV dimension.33 Thus, more than one legitimate LV minor echo dimension could be ob-

tained from the same heart, leading to greater dispersion in the dimension-volume relation. In contrast, when LV enlargement develops in patients with other disease states, the chamber dilates in a spheroidal fashion, the papillary muscles ride higher on the walls of the left ventricle and the chordae tendineae are pulled more horizontally.33, 34 This decreases the angle that they form with the ultrasound beam and restricts the area where these structures can be recorded together with the septum and LV posterior wall endocardium and enhances the reproducibility and reliability of measuring the LV dimension.

Our data also indicate that echocardiography is unreliable for evaluating LV performance in AR, an experience similar to that reported by Johnson et al.17 Regional abnormalities of LV wall contraction in two patients with AR reported by Corya et al.35 and in four of the 20 patients with AR studied by Johnson et al.17 have been held responsible by the latter investigators for the discrepancy between echocardiographic and angiographic indices of LV performance. That factors other than nonuniform LV wall contraction may also cause such discrepancy is suggested by the fact that the problem was not alleviated when we recomputed the statistics of Johnson and co-workers after exclud-
ing the four patients who had regional wall abnormalities. In addition, a similar discrepancy was also present in our series of 22 patients with AR, none of whom were found to have abnormal contraction patterns. While the reason for the discrepancy is obscure, it is possible that the poor agreement between echo and angiocardiographic indices of function is a consequence of the unsatisfactory correlation between the primary dimensional and volume data obtained by the two techniques.

In conclusion, this study has shown that single M-mode echocardiographic estimates of LV volume and function are not accurate enough to be relied upon as an aid for making critical decisions in the management of AR. These findings do not rule out the possibility that such aid could be provided by serial longitudinal studies on individual patients with AR and initial evidence suggests that this may be the case. The usefulness of cross-sectional echocardiography in assessing the hemodynamic severity of AR and its effect on the anatomy and function of the left ventricle remains to be shown.

Acknowledgment

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