

Echocardiographic Assessment of Left Ventricular Remodeling: Are Left Ventricular Diameters Suitable Tools?

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Objectives. We sought to analyze the value of echocardiographic left ventricular (LV) diameters in assessing LV remodeling.

Background. LV diameters are easily measured and commonly used as a substitute for volumetric analysis to evaluate LV remodeling caused by ventricular overload or dysfunction. However, the impact of these measurements on outcome is disputed, suggesting that they may not adequately assess LV remodeling.

Methods. M-mode echocardiographically measured LV dimensions and the derived LV ejection fraction and end-systolic wall stress were compared with LV volumes and the derived LV ejection fraction and wall stress using the biplane Simpson rule. These measurements were made prospectively and simultaneously in 463 patients (289 men, 174 women; mean [\pm SD] age 62 ± 15 years), including 46 normal subjects, 52 with aortic regurgitation, 253 with mitral regurgitation and 112 with LV dysfunction.

Results. The correlation between diameter and volume was

good at end-systole ($r = 0.91$, $p < 0.0001$) and end-diastole ($r = 0.86$, $p < 0.0001$). However, the relation was exponential, and the 95% confidence interval increased with increasing diameter. The calculated LV ejection fraction and wall stress using LV diameter and volume correlated linearly with a limited range of error ($r = 0.96$, $SEE = 5\%$, $p < 0.0001$ and $r = 0.95$, $SEE = 20 \text{ g/cm}^2$, $p < 0.0001$, respectively).

Conclusions. For assessing LV remodeling, LV diameters measured by M-mode echocardiography allow acceptable estimation of LV ejection fraction and wall stress and correlate significantly with LV volumes but are hindered by a wide range of error for assessment of LV size, especially for enlarged ventricles, suggesting that measurement of LV volume should be the preferred method of echocardiographically assessing LV remodeling.

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Uncontrolled left ventricular (LV) remodeling, whether due to primary myocardial dysfunction (1-3) or valvular heart disease (4), is part of a vicious cycle that produces additional LV dysfunction (5-7) and has dismal consequences regardless of the symptom status of the patient (8). Most of the available information on the clinical impact of LV remodeling originated with studies using angiography (9-11), but echocardiography has gradually supplemented and often replaced angiography in assessing and monitoring LV remodeling, mainly because of its low risk and noninvasive nature. Although the validity of two-dimensional echocardiographic volumetric analysis has been established (12,13), M-mode-derived dimensions have been used as surrogates for volumes in the assessment of LV size and function. This approach is simple and has been successful to the point that LV diameter has been recommended as a criterion for surgical intervention in valvular heart disease (14). However, the use of LV diameters to

estimate LV size and function has not been validated fully. Moreover, in contrast to LV volumes (9-11), dimensions measured by M-mode echocardiography have been found to be mediocre and inconsistent predictors of outcome in patients with valvular heart disease, with (15-18) or without (19-21) surgical treatment, and in patients with primary LV dysfunction (22), suggesting that diameters may not adequately assess LV remodeling.

Standard software implementation in the echocardiographic hardware of the recommended methods of two-dimensional volumetric analysis (12) has allowed widespread availability of the volumetric measurement capability in routine practice. However, volumetric analysis is more labor-intensive and time-consuming than the acquisition of LV diameters, and the extent to which it should replace diameter analysis for assessing LV remodeling is unclear. Accordingly, we examined in a large prospective cohort the assessment of LV remodeling mechanics using LV diameters and volumes and hypothesized that LV diameters 1) are imperfect instruments for assessing LV size, but 2) provide an acceptable estimation of LV ejection fraction (LVEF) and wall stress.

Methods

Study patients. Patients were included prospectively in this study of LV remodeling. Inclusion criteria were 1) adequate

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Abbreviations and Acronyms

CI	= confidence interval
ESWS	= end-systolic wall stress
LV	= left ventricle, left ventricular
LVEF	= left ventricular ejection fraction

recording of LV diameter by M-mode echocardiography; 2) adequate quantitative assessment of the LV by two-dimensional echocardiography; and 3) normal cardiac function, isolated mitral or aortic regurgitation or primary LV dysfunction. Exclusion criteria were 1) inability to measure LV diameters or volumes; 2) previous valve repair or replacement; 3) regurgitation of both valves or associated with stenosis; 4) pericardial constriction or effusion; and 5) congenital heart disease with a shunt. The final study group comprised 463 patients (289 men, 174 women, mean [\pm SD] age 62 ± 15 years)—46 normal subjects, 52 patients with aortic regurgitation, 253 with mitral regurgitation and 112 with primary LV dysfunction. This group with diameters measurable by M-mode echocardiography represented 79% (463 of 588) of the patients who were referred to the echocardiography laboratory for a quantitative echocardiographic study. At the time of echocardiography, 387 patients were in sinus rhythm, 73 were in atrial fibrillation and 3 were in paced rhythm.

Echocardiographic analysis. A comprehensive Doppler echocardiographic study was performed, with multiple measurements of all variables averaged (at least three in sinus rhythm and six in atrial fibrillation) (23,24). M-mode measurements of the LV were obtained using guidance by two-dimensional echocardiography at end-systole and end-diastole, as recommended by the American Society of Echocardiography (25). Calculation of LVEF was done by taking the square of these diameters, with a correction for apical contraction (26,27). This method was modified so that the LVEF was initially estimated before it was calculated for each patient (28). If the calculated and estimated LVEFs were within 5% of one another, the measurements were accepted. If a discordance was noted, further imaging was performed until agreement was obtained for each patient. The final LVEF after all repeat imaging was used. The M-mode end-systolic wall stress (ESWS) of the LV was calculated using systolic diameter and wall thickness (29) and estimates of end-systolic LV pressure based on cuff blood pressure specific to the cardiac status of the patient (29,30).

LV end-systolic and end-diastolic volumes were measured using the modified biplane Simpson method (method of disks) using the apical four-chamber and two-chamber views (31). The total stroke volume of the LV was calculated as the difference between these volumes. The derived LVEF was calculated directly as the ratio of stroke volume to end-diastolic volume. The derived ESWS was calculated using the estimate of the end-systolic pressure based on cuff blood pressure (29,30) and a geometric factor based on the measured

length and calculated diameter of the LV using two-dimensional tracing of the LV (32).

Quantitative Doppler echocardiography was used to determine the regurgitant fraction of aortic or mitral regurgitation (33) based on mitral and aortic stroke volumes.

Statistical methods. Group data are presented as the mean value \pm SD or as a percentage. Group comparisons were based on chi-square analysis and analysis of variance, with subsequent two-tailed *t* tests. The associations between diameters and derived LVEF and wall stress measured by M-mode echocardiography (independent variables) and their two-dimensional counterparts (volumes, LVEF wall stress—dependent variables) were studied using linear and nonlinear regression analyses, and the closeness of the fit was analyzed using the 95% confidence interval (CI) of the estimated two-dimensional value from the M-mode value. Next, the residuals of the regression were plotted against the independent variable of the regression. To analyze for trends of increasing 95% CI with increasing levels of independent variables, the absolute value of the residuals or the difference was regressed over the independent variable. All grouped data are presented as the mean value \pm SD. A *p* value <0.05 was considered significant.

Results

Left ventricular remodeling. The baseline values of the clinical variables and the results of echocardiographic measurements for each subgroup are listed in Table 1. As compared with the 46 normal patients, the 417 patients with LV volume overload or dysfunction had significant LV remodeling on M-mode and two-dimensional echocardiography, emphasizing the ability of both techniques to detect LV remodeling.

Assessment of LV remodeling with diameter and volume.
Left ventricular size. Significant correlations were found between end-diastolic diameter and end-diastolic volume ($r = 0.86$, $p < 0.0001$) (Fig. 1A) and between end-systolic diameter and end-systolic volume ($r = 0.91$, $p < 0.0001$) (Fig. 2A), but the relation was curvilinear and the best fit was obtained with a logarithmic regression. Furthermore, the 95% CI increased progressively with higher end-diastolic or end-systolic diameter, and the regression of residuals by the diameters showed widening of the scatter of the residuals with increasing diameter (Fig. 1B and 2B). This widening was confirmed by the significant correlation between the absolute value of the residuals and the diameters ($r = 0.31$, $p = 0.0001$ and $r = 0.48$, $p = 0.0001$ for end-diastolic and end-systolic diameters, respectively). Table 2 lists the predicted values and 95% confidence intervals for the estimated volumes.

Despite the good correlation observed between diameter and volume, the correlation between end-diastolic LV diameter and regurgitant fraction was significant but mediocre ($r = 0.46$, $p < 0.0001$).

Left ventricular function. Similar to LV size, the values of LVEF and ESWS calculated using the diameters measured by M-mode echocardiography demonstrated a good correlation

Table 1. Baseline Characteristics of the Overall Study Group and the Four Groups of Patients

	Overall	Group				p Value
		Normal (n = 46)	AR (n = 52)	MR (n = 253)	LVD (n = 112)	
Age (yr)	62 ± 15	52 ± 15	57 ± 16	63 ± 14	65 ± 12	0.0001*
Gender (%male)	62	57	65	60	68	0.44
LVDD (mm)	59 ± 10	50 ± 5	58 ± 9	57 ± 8	66 ± 9	0.0001†‡
LVSD (mm)	39 ± 12	31 ± 5	37 ± 8	35 ± 7	56 ± 11	0.0001†‡
EF-m (%)	54 ± 17	62 ± 7	61 ± 8	62 ± 8	27 ± 9	0.0001‡
ESWS-m (kdynes/cm ²)	92 ± 42	72 ± 12	93 ± 27	74 ± 20	148 ± 50	0.0001‡§
EDV (ml)	216 ± 84	137 ± 32	216 ± 77	203 ± 68	279 ± 93	0.0001†‡
ESV (ml)	101 ± 75	53 ± 20	82 ± 39	71 ± 33	199 ± 86	0.0001†‡
EF-2D (%)	56 ± 17	62 ± 7	63 ± 8	65 ± 8	30 ± 9	0.0001‡
ESWS-2D (g/cm ²)	190 ± 65	163 ± 27	199 ± 45	161 ± 34	269 ± 75	0.0001‡§

*Normal and aortic regurgitation groups are different from mitral regurgitation and left ventricular dysfunction groups. †p < 0.05, normal group versus overall group. ‡p < 0.05, left ventricular dysfunction group versus overall group. §p < 0.05, aortic regurgitation group versus overall group. Data are presented as mean value ± SD, unless otherwise indicated. AR = aortic regurgitation; EDV = end-diastolic volume; EF-2D = ejection fraction by two-dimensional echocardiography; EF-m = ejection fraction by M-mode echocardiographic diameters; ESV = end-systolic volume; ESWS-m = end-systolic wall stress by M-mode echocardiographic diameters; ESWS-2D = end-systolic wall stress by two-dimensional echocardiography; LVD = left ventricular dysfunction; LVDD = left ventricular diastolic diameter; LVSD = left ventricular systolic diameter; MR = mitral regurgitation.

with the values obtained by the two-dimensional echocardiography (r = 0.96, p < 0.0001 [Fig. 3A] and r = 0.95, p < 0.0001 [Fig. 4A], respectively). Importantly, these relations were

linear, and the individual 95% CIs were narrow (Fig. 3A and 4A), with an SEE of 5% and 20 g/cm² for LVEF and ESWS, respectively. The regression of residuals to the independent

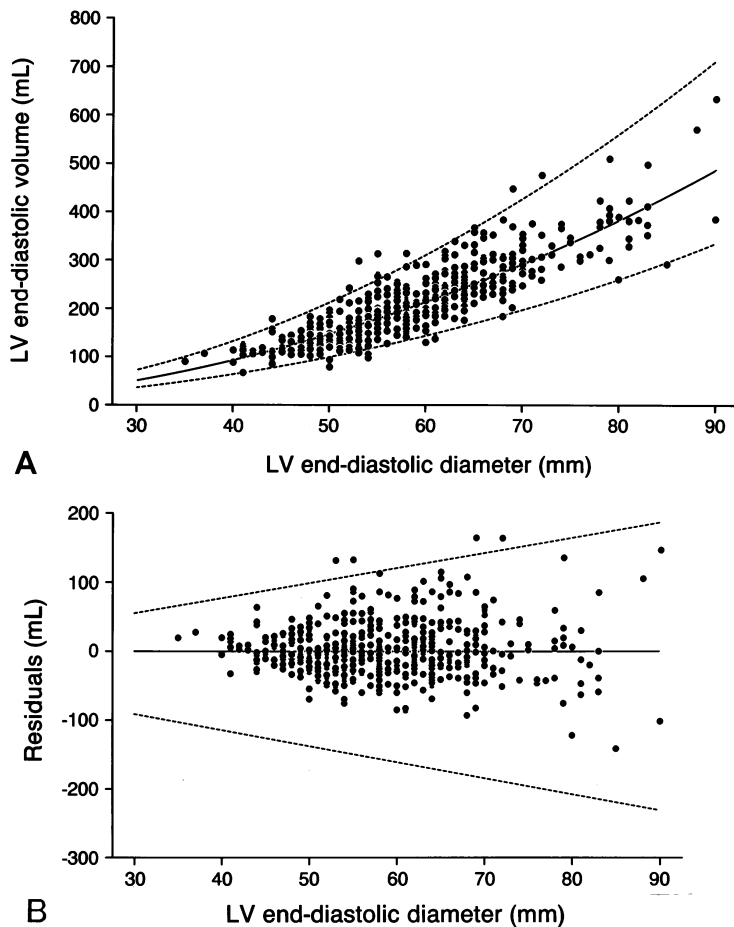


Figure 1. A, Correlation between LV end-diastolic diameter and volume. B, Scatterplot of residuals of the regression presented in A versus LV end-diastolic diameter. Dashed lines = 95% CI of these residuals based on the absolute residual regression.

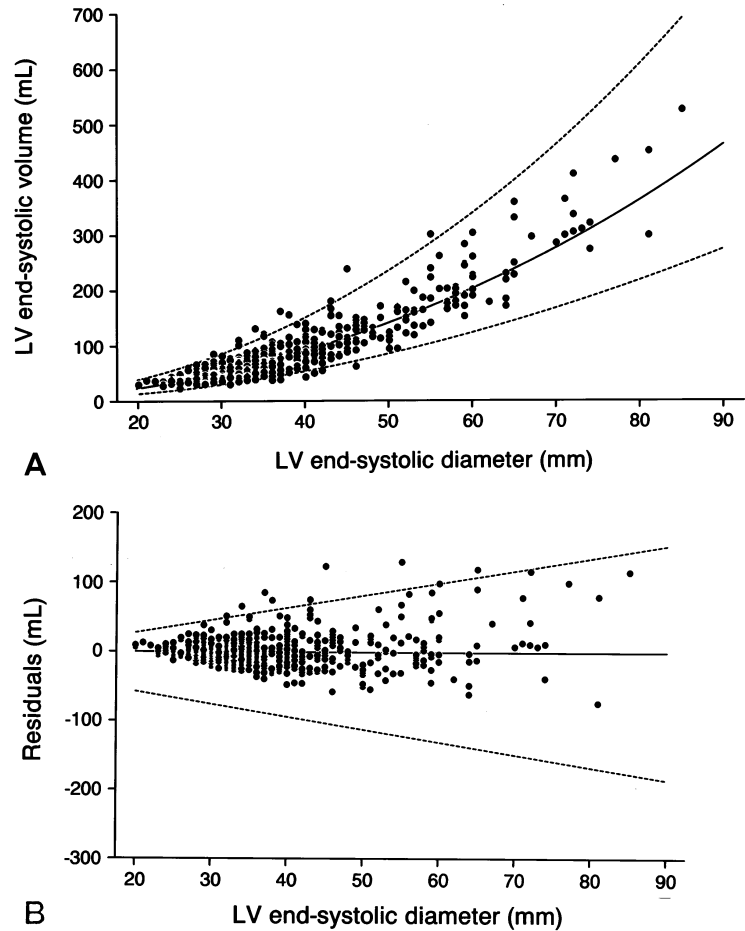


Figure 2. A, Correlation between LV end-systolic diameter and volume. B, Scatterplot of residuals of the regression presented in A versus LV end-systolic diameter. Dashed lines = 95% CI of these residuals based on the absolute residual regression.

variable (i.e., to LVEF and wall stress calculated using the diameters measured by M-mode echocardiography) showed no change in the scatter with increasing levels of EF ($p = 0.31$) (Fig. 3B) and a significant increase in the scatter with increasing levels of ESWS ($r = 0.26$, $p = 0.0001$) (Fig. 4B), which remained mild, however.

Discussion

With regard to assessing LV remodeling using LV diameters and volumetric measurement methods, the present study showed that 1) for the assessment of LV size, a good correlation was observed between the two methods at

end-diastole and end-systole, but with a curvilinear relation and marked widening of the 95% CI of the estimated volume with increasing diameter, and 2) in contrast, for the assessment of LVEF and ESWS, a strong correlation was noted between the two methods, with a linear relation and a narrow 95% CI.

LV remodeling. LV remodeling is the hallmark of LV overload (4) or dysfunction (1-3), whether patients are symptomatic or not (8). LV remodeling, whether due to primary valvular disease (5-7) or myocardial disease, is associated with progression of LV dysfunction (2,3,8) and a poor prognosis (1,2,34,35). Therefore, assessing the degree of LV remodeling and monitoring its progression are integral to the clinical

Table 2. Predicted Volume and 95% Confidence Interval for Discrete Values of Left Ventricular Diameter

LVDD (mm)	40	50	60	70	80
Predicted EDV (ml)	95	149	216	295	386
95% CI	66-138	103-217	149-313	203-428	266-561
LVSD (mm)	35	45	55	65	75
Predicted ESV (ml)	68	113	170	238	310
95% CI	41-113	68-189	102-284	143-398	185-518

CI = confidence interval; EDV = end-diastolic volume; ESV = end-systolic volume; LVDD = left ventricular diastolic diameter; LVSD = left ventricular systolic diameter.

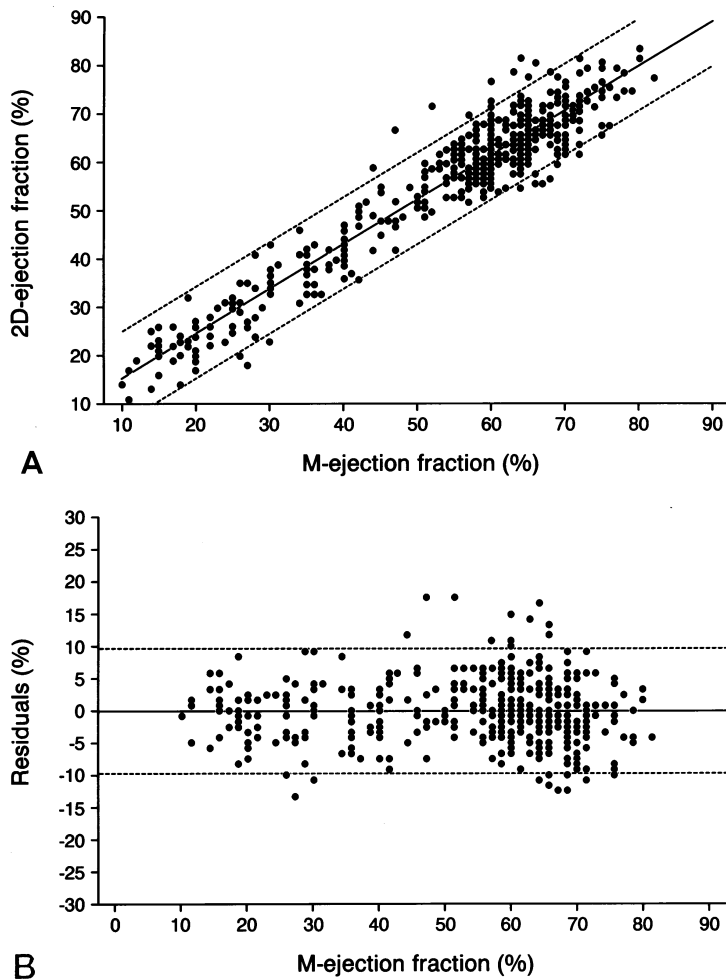


Figure 3. A, Correlation between LVEF calculated using LV diameter (M-ejection fraction) and volume (2D-ejection fraction). B, Scatterplot of residuals of the regression presented in A, versus the M-ejection fraction. **Dashed lines** = 95% CI of these residuals based on the absolute residual regression.

evaluation of patients with LV volume overload or dysfunction. On the basis of limited data derived from angiographic LV volumes for the assessment of LV remodeling and its impact on outcome (9–11), the degree of LV remodeling in valvular heart disease has been used as an objective criterion for the timing of surgical treatment (14). However, LV angiography has minimal but definite risks (36), and thus echocardiography has been widely used to monitor LV size and function. Diameters are easily measured with M-mode echocardiography and have been advocated as surrogates for LV volumes in the timing of surgery for valvular heart disease (14). In contrast, echocardiographic analysis of LV volumes is more time-consuming, and initial reports have emphasized its potential for underestimating LV volumes (37), thus limiting the widespread use of the technique. However, two series of facts may lead to reconsideration of the approach of using LV diameters for the assessment of LV remodeling: 1) The predictive value of LV diameters on the outcome of patients with mitral or aortic regurgitation treated surgically (15–18) or medically (19–21) or with LV dysfunction (22) has been inconsistent and controversial. Furthermore, LV volumes tend to decrease with treatment (38), but this effect could not be demonstrated using diameters measured by

M-mode echocardiography (22). These data raise concern that LV diameter may not appropriately reflect LV remodeling. 2) The methods of echocardiographically measuring LV volumes are now better codified (12) and are standard software in echocardiographic equipment. Furthermore, with current high resolution imaging, the method is accurate (13) and reproducible (39), and accordingly, it is essential to determine whether the simple measurement of LV diameter is an appropriate substitute for LV volume in assessing LV remodeling.

LV size and volume overload. Enlargement and hypertrophy are basic processes of LV remodeling, whether the initial disease is volume overload or dysfunction of the LV (1,2,4,34,40). However, this compensatory response that allows cardiac output to be maintained is not innocuous and may lead to increased wall stress (41) and progression of LV dysfunction (2,3,8), which can be reversed by promptly decreasing the size of the LV (7,30). Therefore, monitoring LV size is a major goal of cardiac imaging. Many formulas have been developed to estimate volume based on dimensions measured by M-mode echocardiography, but have been limited by their geometric assumptions (42,43). Although limited pilot data indicate an excellent correlation between LV diameter obtained by M-

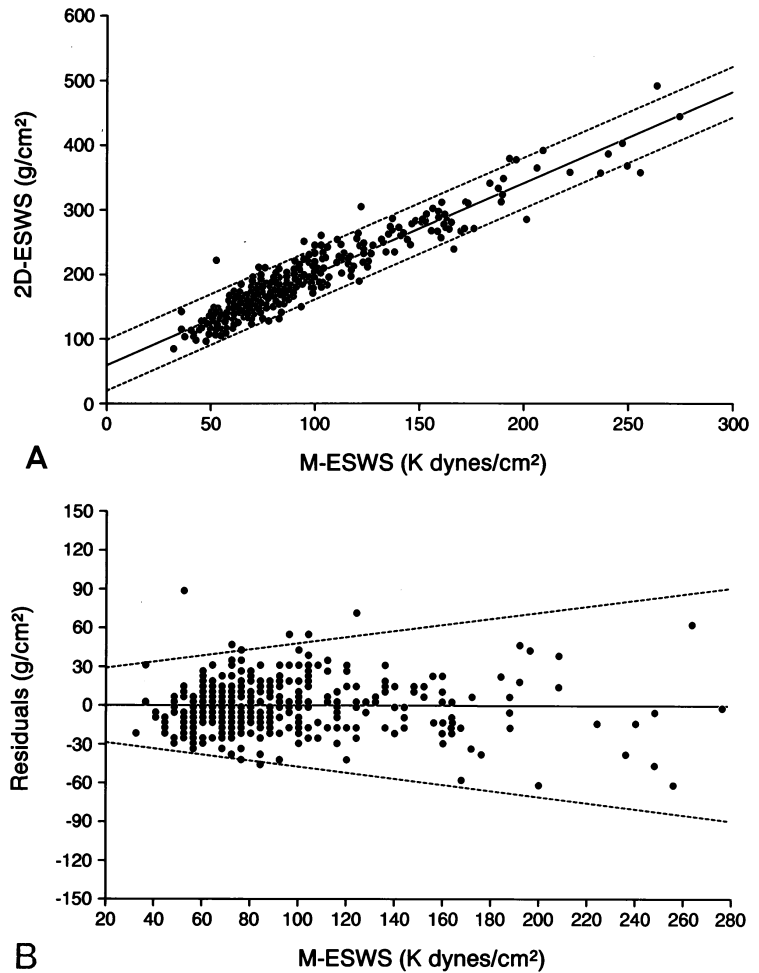


Figure 4. A, Correlation between LV ESWS calculated using LV diameter (M-ESWS) and volume (2D-ESWS). B, Scatterplot of residuals of the regression presented in A versus M-ESWS. Dashed lines = 95% CI of these residuals based on the absolute residual regression.

mode echocardiography and angiographic volume measurements (44), this correlation was not optimal for enlarged LVs (45). In the present study, the correlation between simultaneously measured LV diameters and volumes was good overall, suggesting that diameter can be used to diagnose enlargement of the LV. However, with the curvilinear relation observed, a small increase in diameter may correspond to a large increase in volume in enlarged ventricles. Furthermore, the 95% CIs of prediction of LV volume from diameter, which were acceptably narrow for diameters <60 mm, were wider for larger ventricles (46). Therefore, the diagnosis of advanced dilation of the LV, which may be associated with heightened risk (21,24,35), in particular, of sudden death (21), has a wide range of error when made on the basis of LV diameter. This large range of uncertainty may explain in part the limited and disputed predictive value of LV diameter for outcome (16,17). Consequently, for assessing LV remodeling due to overload or dysfunction and for follow-up of LV size, the preferred approach should be direct measurement of LV volumes. The value of LV volumes as a predictor of outcome should be tested in future studies.

LV diameters measured by M-mode echocardiography have been used to estimate the severity of regurgitation in

patients with aortic or mitral regurgitation (47). Despite the limitations of this approach (42), the trend is to relate an increase in LV diameter to the degree of regurgitation and to use a less aggressive surgical approach in patients with a mild increase in diameters. Importantly, the present study showed only a poor correlation between LV end-diastolic diameter and the regurgitant fraction measured by quantitative methods. Therefore, it should be emphasized that LV diameters obtained by M-mode echocardiography should not be used to estimate the severity of valvular regurgitations.

LV function. The use of M-mode echocardiographically derived LV diameter to calculate LVEF (44) has been hindered by the possibility of myocardial dyssynergy (48). Currently, these M-mode calculations are not used in isolation but are integrated into the results of a two-dimensional echocardiographic study. The procedure used in the present study combines an estimation of LVEF (28), a calculation using LV diameter (26,27) and the possibility of repeat imaging, which provides an opportunity for verifying the measurements. Under these circumstances, the LVEF calculated from LV diameters or volumes shows a good correlation with a relatively narrow and constant CI. Although the diameter method tends to slightly underestimate the volumetric LVEF (by two points,

on average), it appears to provide an acceptable alternative to the volumetric LVEF in routine practice.

LV wall stress, a measure of afterload, is an important determinant of systolic function. It is calculated from a complex formula that incorporates elements of LV size, geometry, hypertrophy and pressure. Originally, it was derived from angiographic data (32). As an alternative to using measurements made with invasive techniques, pilot data suggest that wall stress could be calculated from a simplified formula using the LV diameter measured by M-mode echocardiography (29). However, because two-dimensional echocardiography provides more information on the shape and length of the LV, it may be preferred to M-mode data for calculating wall stress (49). In the present study, a good and linear correlation was found between the two methods for calculating ESWS, and the 95% CI was relatively narrow. The two methods showed the characteristic changes of wall stress—that is, increased primary LV dysfunction and aortic regurgitation and normal mitral regurgitation. Therefore, the simplified M-mode echocardiographic method appears to provide an adequate estimate of ESWS.

Study limitations. The measurement of LV volume requires meticulous technique, and the volume may be overestimated by angiography (40) and underestimated by echocardiography (37). However, echocardiographic high resolution imaging and improvements in computer software allow accurate calculation of LV volumes (13). Furthermore, in the present study, the correlation between the derived stroke volume of the LV and the maximal stroke volume calculated simultaneously by Doppler echocardiography was excellent ($r = 0.97$, $SEE = 10$ ml, $p < 0.0001$) and confirmed the value of LV volume measurements made with two-dimensional echocardiography in the present study.

The calculation of LVEF using LV diameters is not based only on M-mode measurements but requires the interpretation of all two-dimensional echocardiographic views. Therefore, for calculating LVEF, the results of the present study emphasize that the diameter method is of value only if it is integrated into a two-dimensional echocardiographic study. These results further substantiate previous studies that have underlined the high prognostic value of LVEF calculated with this method (6,7,18,20).

Conclusions. The clinical implications for the assessment of LV remodeling due to valvular regurgitation or LV dysfunction are that LV diameter can be used to assess normal ventricular size and to diagnose LV enlargement, but because of the large range of error, this method is not suitable for precise assessment and follow-up of LV size in enlarged ventricles, for which volumetric analysis should be preferred. Importantly, LV diameter reflects poorly the degree of valvular regurgitation, for which quantitation of regurgitation should be preferred. However, acceptable estimates of LVEF and wall stress can be derived from LV diameter.

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