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Echocardiography

ORIGINAL INVESTIGATIONS

Assessment of Echocardiographic Left Atrial Size: Accuracy of M-Mode and Two-Dimensional Methods and Prediction of Diastolic Dysfunction

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Background: Despite the American Society of Echocardiography recommendation to use left atrial volume indexed for body surface area (LAVI) for quantification of left atrial size, a variety of methods are used in clinical practice. Our objectives were to evaluate the accuracy of M-mode and two-dimensional (2D) echocardiographic LA size estimates to LAVI and to determine their ability to predict left ventricular diastolic dysfunction. Methods: In 150 consecutive patients, LA diameter (LAD), LA diameter indexed for body surface area (LADI), LA area in the apical two- and four-chamber views (LAA 2c and LAA 4c), biplane area–length LA volume (LAV), and LAVI were obtained. The accuracy of these methods to quantify LA enlargement by LAVI, correlation with clinical parameters, and ability to act as a surrogate for diastolic dysfunction were determined using Pearson correlation coefficients along with univariate and multiple logistic analysis. Results: The true degree of LA size (with LAVI as standard) was identified by LAD in 45%, LADI in 42%, LAA 4c in 43%, and LAA 2c in 41%. All methods showed positive correlation with age, E/E′, mitral regurgitation, and right atrial size and negative correlation with ejection fraction. LAVI was the strongest method to predict any ($c = 0.655$, $P = 0.012$) or moderate–severe ($P = 0.856$ and $P < 0.001$) diastolic dysfunction. All methods have greater capacity to identify moderate or severe diastolic dysfunction than any degree of diastolic dysfunction alone. Conclusions: One-dimensional and 2D methods inaccurately quantify LA size and are inferior to LAVI to predict diastolic dysfunction. (Echocardiography 2012;29:379-384)

Key words: left atrial volume, diastolic dysfunction

Left atrial (LA) enlargement has been demonstrated to predict stroke, atrial fibrillation, heart failure, and mortality.[1–5] LA enlargement has also been shown to serve as a marker for the magnitude and duration of left ventricular (LV) diastolic dysfunction.[6] Two-dimensional (2D) echocardiography provides multiple measurements for assessment of LA size. Among these measurements, left atrial volume indexed for body surface area (LAVI) has the strongest association with cardiovascular disease[7] and is the most sensitive in predicting cardiovascular outcomes.[8] Despite the American Society of Echocardiography (ASE) recommendation of LAVI for quantification of left atrial size,[9] individual echocardiography laboratories still use a variety of one-dimensional (1D)_ linear and 2D area measurements.

The primary objective of our study was to evaluate the accuracy of these measurements of left atrial size compared to LAVI. Furthermore, we examined the relative capacity of each of the measurement strategies to predict diastolic dysfunction.

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Methods:

Patient Selection:

This study was reviewed and approved by the University Hospitals Case Medical Center Institutional Review Board. One hundred fifty-six consecutive adults presenting for transthoracic echocardiography to the University Hospitals Case Medical Center Echocardiography Laboratory for any indication were prospectively evaluated. The only exclusion criterion was image quality that prevented accurate assessment of left atrial size and this occurred in six of the patients. Clinical parameters collected included age, sex, height, weight, and cardiac rhythm during the procedure.

Echocardiography:

All LA size measurements were made by one of the two echocardiographers at LV end-ventricular systole and LA size was classified as normal, mildly enlarged, moderately enlarged, or severely enlarged based on the ASE guidelines for the given

TABLE I

Normal Values of Left Atrial Size Adapted from the American Society of Echocardiography[9]

	Women				Men			
	Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal	Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal
LAD (cm)	2.7–3.8	3.8–4.2	4.3–4.6	$\geq$4.7	3.0–4.0	4.1–4.6	4.7–5.2	$\geq$5.2
LADI (cm/m^2)	1.5–2.3	2.4–2.6	2.7–2.9	$\geq$3.0	1.5–2.3	2.4–2.6	2.7–2.9	$\geq$3.0
LAA (cm^2)	$\leq$20	20–30	30–40	>40	$\leq$20	20–30	30–40	>40
LAV (mL)	22–52	53–62	63–72	$\geq$73	18–58	59–68	69–78	$\geq$79
LAVI (mL/m^2)	22 $\pm$ 6	29–33	34–39	$\geq$40	22 $\pm$ 6	29–33	34–39	$\geq$40

LAD = left atrial diameter; LADI = left atrial diameter indexed for body surface area; LAA = left atrial area; LAV = biplane area–length LA volume; LAVI = left atrial volume indexed for body surface area.

measurement[9] (Table I). These measurements included LA diameter (LAD), LA diameter indexed for body surface area (LADI), LA area in the apical two- and four-chamber views (LAA 2c and LAA 4c), biplane area–length LA volume (LAV), and LA volume indexed for body surface area (LAVI). LAD was recorded from the anteroposterior linear dimension in the parasternal long-axis view. LAV was obtained using the biplane area–length formula of (0.85 $\times$ [LA area in apical four chamber view] $\times$ [LA area in the apical two chamber view])/shortest length from the mitral annulus midplane to the superior border of the LA in the four- and two-chamber views.

A composite of mitral inflow peak E velocity to peak A velocity ratio (E/A), mitral inflow deceleration time (DT), and an average of the lateral and medial mitral annular velocities (E′) with tissue Doppler imaging were used to grade diastolic dysfunction as normal, grade I, grade II, or grade III.[10] Patients with grade I diastolic dysfunction (mild or impaired relaxation) was characterized by a mitral E/A ratio of <1.0, DT > 240 msec, and an E′ < 8 cm/sec. Grade II diastolic dysfunction (moderate or pseudonormal) was defined as a mitral E/A ratio of 1.0–1.5 with either a 50% decrease with Valsalva or an E′ < 8 cm/sec. Grade III diastolic dysfunction (severe or restrictive) was characterized by an E/A ratio > 2 and DT < 150 msec.

Left ventricular ejection fraction was determined by 2D semiquantitative measures (i.e., an eyeball estimate or “biretinal algorithm”) while mitral regurgitation,[11] left ventricular hypertrophy,[9] and right atrial size[9] were quantified by methods established by the ASE.

Statistical Analysis:

Continuous variables are presented as means $\pm$ standard deviation (SD) and categorical variables are presented as the percentage of the group total. Weighted kappa statistics were used to evaluate the agreement between the categorical measurements and LAVI. Pearson correlation coefficients were employed to analyze correlations between the LA size measurements and pertinent clinical and echocardiographic variables. Univariate analysis for the predictive abilities of the LA measurements for diastolic dysfunction was determined with Mann-Whitney statistics. Multiple logistic regression analysis incorporated the stated variables impact of the LA measurement to predict diastolic dysfunction. A Bland–Altman analysis was performed in 20 randomly selected patients to measure the interobserver agreement.

Results:

Baseline Characteristics:

The clinical and echocardiographic characteristics of the 150 patients in the study are listed in Table II. Indications for echocardiography included chest pain or myocardial infarction (22%), heart failure (19%), dyspnea (17%), syncope/arrhythmia (10%), valvular disease (9%), and stroke (7%). Other indications accounted for 8%.

Accuracy of Methods to Predict LA Enlargement:

The sensitivity, specificity, positive predictive value, and negative predictive value of the various methods to detect any abnormality in LA size (mild, moderate, or severe enlargement) using LAVI as the “gold-standard” are displayed in Table III. LAD had a sensitivity of 73% and a specificity of 63% to predict abnormal LA size. LAA 4c and LAA 2c had a specificity of 0.98 and 0.96, respectively.

Table IV lists the sensitivity for each method in identifying the specific degree of LA enlargement (identified by LAVI) along with the correlation and agreement between each measurement and LAVI. Of note, no patients with moderate enlargement by LAVI were identified as having moderate enlargement by either 2D area assessment. Severe

TABLE II

Clinical and Echocardiographic Characteristics ($n = 150$)

Clinical parameters	
Age (years)	62.8 ± 18.2
Female gender, n (%)	87 (58)
Body surface area (m^2)	1.92 ± 0.27
Height (cm)	168.2 ± 10.2
Weight (kg)	86.3 ± 23.5
Atrial fibrillation, n (%)	13 (9)
Echocardiographic parameters	
LV ejection fraction (%)	54.9 ± 13.1
LV end-diastolic diameter (cm)	4.7 ± 0.8
LAD (cm)	4.1 ± 0.8
LADI (cm/m^2)	2.1 ± 0.4
LAA two-chamber (cm^2)	20.4 ± 5.9
LAA four-chamber (cm^2)	19.6 ± 5.5
LAV (mL)	67.27 ± 30.3
LAVI (mL/m^2)	34.9 ± 14.96
Mitral E/E′ ratio	12.5 ± 8.2
Diastolic dysfunction grade	
Normal, n (%)	56 (37)
Grade I	65 (43)
Grade II	16 (11)
Grade III	10 (6)
Indeterminate	3 (2)
Mitral regurgitation	
None, n (%)	53 (35)
Trace	29 (19)
Mild	49 (33)
Moderate	16 (11)
Severe	3 (2)
Left ventricular hypertrophy	
None, n (%)	77 (51)
Eccentric hypertrophy	29 (19)
Concentric hypertrophy	15 (10)
Concentric remodeling	29 (19)

Data expressed in mean ± SD unless specified. E/E′= ratio of mitral inflow peak E velocity to average of tissue Doppler mitral annular velocities; LAA = left atrial area; LAD = left atrial diameter; LADI = left atrial diameter indexed for body surface area; LAV = biplane area–length LA volume; LAVI = left atrial volume indexed for body surface area; LV = left ventricular.

enlargement on LAVI was identified as severe in 40% with LAD and in only 2% and 5% of LAA 4c and LAA 2c, respectively. All grades of LA size (normal, mildly enlarged, moderately enlarged, severely enlarged) by LAVI were accurately identified by LAD in 45% of the patients, LADI in 42%, LAA 4c in 43%, and LAA 2c in 41%. The correlation coefficients between LAD, LADI, LAA 4c, LAA 2c, and LAV and LAVI were 0.63, 0.61, 0.81, 0.87, and 0.93, respectively. The agreements between LAD, LADI, LAA 4c, LAA 2c, and LAV and LAVI as categorical variables (normal, mild, moderate, and severe) were 0.41, 0.25, 0.28, 0.31, and 0.78.

Correlation between LA Size and Various Parameters:

Pearson correlation coefficients for the measurements of LA size and various clinical and echocardiographic variables are shown in Table V. Age, E/E′, mitral regurgitation, and right atrial size were positively correlated with LA size in all measurements. Left ventricular size was positively correlated with LA size in all measurements except for LADI. Left ventricular ejection fraction was negatively correlated with LA size in all measurements. There was no correlation between left ventricular hypertrophy and LA size.

LA Size as a Surrogate for Diastolic Dysfunction:

The ability of LA size to predict diastolic dysfunction of any degree and for moderate or severe only is shown in Table VI. LA size had better predictive accuracy for moderate or severe diastolic dysfunction than for any degree of diastolic dysfunction alone. Table VII displays the effect of LA size added to a multiple logistic regression model to predict any type of diastolic dysfunction. A model using age, E/E′, EF, and the presence of LVH and atrial fibrillation without inclusion of LA size had C-statistic of 0.912 ($P < 0.05$) to predict any diastolic dysfunction. Adding the various LA size measurements did not greatly improve the

TABLE III

Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value of the Various Methods to Detect Any Abnormality in LA Size Defined by LAVI

	Sensitivity (95% CI)	Specificity	PPV	NPV
LAD	0.73 (0.63–0.81)	0.63 (0.49–0.75)	0.78 (0.67–0.85)	0.57 (0.43–0.69)
LADI	0.40 (0.29–0.50)	0.87 (0.74–0.94)	0.84 (0.70–0.93)	0.45 (0.35–0.55)
LAA 4c	0.67 (0.56–0.76)	0.98 (0.89–1.00)	0.98 (0.91–1.00)	0.62 (0.51–0.72)
LAA 2c	0.68 (0.57–0.77)	0.96 (0.86–0.99)	0.97 (0.89–0.99)	0.63 (0.51–0.73)
LAV	0.93 (0.85–0.97)	0.91 (0.79–0.97)	0.95 (0.87–0.98)	0.88 (0.75–0.94)

LAA 2c = left atrial area in the apical two-chamber view; LAA 4c = left atrial area in the apical four-chamber view; LAD = left atrial diameter; LADI = left atrial diameter indexed for body surface area; LAV = left atrial volume; NPV = negative predictive value; PPV = positive predictive value.

TABLE IV

Sensitivity, Correlation, and Agreement for Each Method in Regard to LAVI

	Sensitivity for Specific Degree of LA Enlargement					Correlation	Agreement
	Normal (n = 54) (%)	Mild (n = 29) (%)	Moderate (n = 30) (%)	Severe (n = 37) (%)	All (n = 150) (%)	Pearson Coefficient*	Kappa (95% CI)*
LAD	63	38	23	40	45	0.63	0.41 (0.31–0.51)
LADI	87	14	7	24	42	0.61	0.25 (0.15–0.35)
LAA 4c	98	38	0	2	43	0.87	0.28 (0.22–0.35)
LAA 2c	96	28	0	5	41	0.87	0.31 (0.24–0.38)
LAV	91	48	27	97	71	0.93	0.78 (0.72–0.84)

CI = confidence interval; other abbreviations as in Table III.
*P-value < 0.001.

TABLE V

Correlation between Measurement Methods and Clinical and Echocardiographic Variables

	Age	E/E′	LV Size	EF	LVH	MR	RA
LAD							
r	0.306	0.447	0.307	−0.192	0.031	0.339	0.521
P-value	<0.001	<0.001	<0.001	0.019	0.706	<0.001	<0.001
LADI							
r	0.410	0.536	−0.042	−0.049	0.120	0.426	0.229
P-value	<0.001	<0.001	0.613	0.549	0.144	<0.001	0.005
LAA 4c							
r	0.374	0.437	0.345	−0.289	0.008	0.476	0.681
P-value	<0.001	<0.001	<0.001	<0.001	0.921	<0.001	<0.001
LAA 2c							
r	0.300	0.397	0.421	−0.322	−0.033	0.401	0.679
P-value	<0.001	<0.001	<0.001	<0.001	0.686	<0.001	<0.001
LAV							
r	0.328	0.429	0.389	−0.303	−0.021	0.427	0.680
P-value	<0.001	<0.001	<0.001	<0.001	0.801	<0.001	<0.001
LAVI							
r	0.411	0.507	0.248	−0.256	0.030	0.527	0.583
P-value	<0.001	<0.001	0.002	0.002	0.712	<0.001	<0.001

EF = ejection fraction; LAVI = left atrial volume indexed for body surface area; LVH = left ventricular hypertrophy; MR = mitral regurgitation; RA = right atrial size. Other abbreviations as in Tables II and III. LV size = LV end-diastolic dimension.

predictive capacity of the model, although LAA 4c, LAV, and LAVI contributions were statistically significant.

Interobserver Agreement:

The Bland–Altman plot (Fig. 1) indicates sufficient agreement between the reader measurements of LAVI as the bias was −0.19. The 95% limits of agreement between the two readers ranged from −6.65 to 6.26 mL/m.[2]

Discussion:

Our study demonstrates the relatively poor ability of the various methods of LA chamber quantification to describe the true degree of LA enlargement in a large heterogeneous population of patients. The specificity for LADI, LAA 4c, LAA 2c, and LAV to identify individuals with normal LA size is fair; however, when LA enlargement is present, it is not accurately defined by these 1D and 2D assessments.

Previous studies have demonstrated the discordance between 1D and three-dimensional (3D) LA measurements.[6,12] Our study displays similar statistics in 1D assessment; however, we also demonstrate incremental correlations when additional planes are added to measurement, consistent with the asymmetric process of left atrial remodeling.

Although 2D assessment as a continuous variable was moderately correlated with LADI, a categorical assessment was not. Only 1 of the 37 patients (2.7%) with severe left atrial enlargement by LADI was classified as having severe left atrial enlargement by LAA 4c. Two of these 37 patients (5.4%) were identified by LAA 2c. This

TABLE VI

C-Statistic for Measurement Method to Predict Degrees of Diastolic Dysfunction

	Any Diastolic Dysfunction*	P-Value	Moderate–Severe Diastolic Dysfunction*	P-Value
LAD	0.632	0.04	0.777	<0.001
LADI	0.654	0.003	0.775	<0.001
LAA 4c	0.618	0.035	0.854	<0.001
LAA 2c	0.609	0.068	0.780	<0.001
LAV	0.636	0.061	0.845	<0.001
LAVI	0.655	0.012	0.856	<0.001

Abbreviations as in Table III.
*C-statistic.

TABLE VII

Multivariate Logistic Regression to Predict Any Degree of Diastolic Dysfunction

	C-statistic	P-Value	Difference
Model with age, E/E′, EF, LVH, and rhythm only	0.912	<0.05	n/a
LAD	0.917	0.06	0.005
LADI	0.912	0.28	0
LAA 4c	0.922	<0.05	0.01
LAA 2c	0.917	0.08	0.005
LAV	0.917	<0.05	0.005
LAVI	0.918	<0.05	0.006

Abbreviations as in Tables II, III, and V.

misclassification hinders accurate risk stratification as categorical assessment of LADI has demonstrated worse cardiovascular outcomes with increasing LA size.[13] Tsang et al. have reported an adjusted hazard ratio of 2.0 for future cardiovascular events in patients with mild LA enlargement. This rises to 3.4 with moderate LA enlargement and 6.6 for severe LA enlargement.

Left atrial size is paramount in the evaluation of diastolic dysfunction as it represents the cumulative effects of chronically elevated left ventricular filling pressures. LAVI has been shown to be a stronger predictor of diastolic dysfunction than LAD[6] and the American Society of Echocardiography utilizes LAVI in its algorithm for defining diastolic dysfunction.[14] We demonstrate that 1D measurements (LADI) are equally effective to 3D volume assessments (LAVI) for describing any degree of diastolic dysfunction when LAD is indexed for body surface area. However, it should be noted that LADI remains inferior to LAVI to predict moderate and severe diastolic dysfunction. All LA size measurements are better able to predict "moderate or severe diastolic dysfunction" than "any degree of diastolic dysfunction." While LAVI remains the most robust measurement, the LAA 4c is nearly equivalent in its ability to predict moderate or severe diastolic dysfunction.

Limitations:

There are a few limitations to our study. Importantly, although LAVI is the echocardiographic "gold-standard" and has been shown to be well correlated with MRI,[15] it still underestimates true LA size.[16] Hence, the 1D and 2D measurements reflect their accuracy to identify LAVI rather than absolute LA size. Real time 3D echocardiographic measurements may be useful in this regard. Also, like all methods of LA volume determination, the volume of the LA appendage is excluded from measurements. Our previous work suggests that, especially at high LA volumes, the contribution of the LA appendage to overall volume cannot necessarily be ignored.[17] Finally, a formal sample size was not calculated prior to our study.

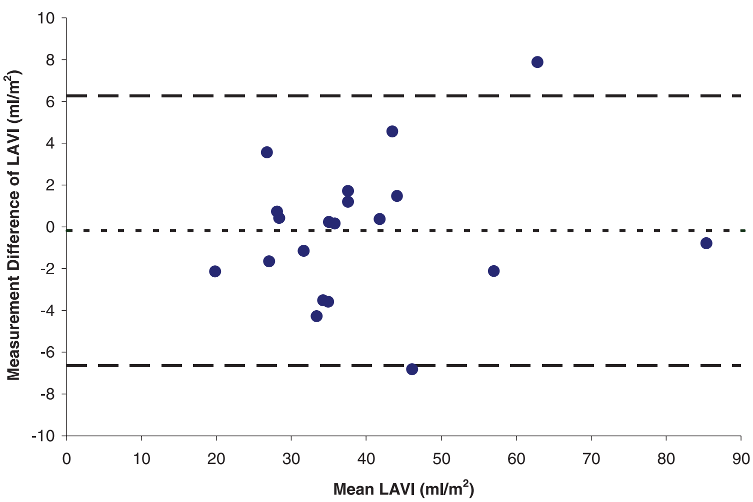

Figure 1. Bland–Altman plot. The difference between the mean left atrial volume index measured by the two readers was −0.19. The 95% limits of agreement between the two methods ranged from −6.62 to 6.26 mL/m^2.

Conclusions:

We conclude that variability in the different methods for obtaining left atrial size is significant. The echocardiographer must realize that they are most likely incorrect in their categorization of left atrial size when using methods other than LAVI, especially when LA size is abnormal. Although these methods are simpler to obtain than LAVI, our data emphasize the ASE recommendation for determining LA size based on LAVI. Furthermore, LAVI serves as the best measure to predict diastolic dysfunction. Reporting based on 1D or 2D assessment should be eliminated to provide uniform and accurate risk stratification.

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