

EDITORIAL COMMENT

Assessment of Echocardiographic Left Atrial Size

How Accurate Do We Need to Be?*

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Certainty is the most vivid condition of ignorance and the most necessary condition for knowledge.

—Kedar Joshi (1)

Growing interest in left atrial (LA) size is motivated by the recognition of its importance as: 1) a predictor of cardiovascular morbidity and mortality (2); 2) a biomarker integrating the magnitude and duration of diastolic left ventricular (LV) function (3); and 3) a determinant of success of the various procedures available for the treatment of atrial fibrillation (4). Many laboratories continue to use 1- and 2-dimensional measurements of the left atrium despite the greater accuracy and stronger association

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with cardiovascular disease of the LA volume index measured by biplane 2-dimensional echocardiography (2DE). Many studies have demonstrated discordance between 1-, 2-, and 3-dimensional (biplane) LA measurements (5); misclassification of categorical severity is common and has implications for risk stratification and prediction of diastolic dysfunction (5). Inaccuracies owing to geometric assumptions and foreshortening of the LA cavity with biplane volume methods result in a considerable underestimation of LA volume compared with computed tomography (CT) and cardiac magnetic resonance (CMR) (6,7). These limitations are theoretically overcome by 3-dimensional imaging; in-

deed, reconstructive freehand 3-dimensional echocardiography (3DE) was shown to reduce (but not eliminate) the underestimation of CMR LA volume (8), albeit with greater variability than 2-dimensional methods. More recently, using 64-slice multidetector CT as a reference standard, real-time (RT) 3DE LA volume estimates were shown to be more accurate and underestimate volumes less than biplane 2DE (6), and in a small number of patients studied with CMR as the reference standard, RT3DE correlated better with less variability than biplane 2DE (7).

In this issue of *JACC*, Mor-Avi et al. (9) prospectively validate RT3DE LA volume software (Tomtec 3D LA function, Tomtec Inc., Hamden, Connecticut) against 2DE biplane volume and CMR in 92 patients referred for clinically indicated CMR. Echocardiographic and CMR imaging were performed on the same day, and maximum and minimum LA volumes were compared. Correlation with CMR was greater for RT3DE than 2DE for both maximum ($r = 0.93$ vs. 0.74) and minimum ($r = 0.88$ vs. 0.82) volumes. 2DE systematically underestimated maximum and minimum volumes (biases of -31 ml and -16 ml, respectively), whereas biases with RT3DE were negligible (-1 ml and 0 ml, respectively). However, despite minimal biases with RT3DE, the wide limits of agreement indicate that the imaging modalities are not interchangeable. Using a threshold of 34 ml/m² (a value that implies diastolic dysfunction) to define an abnormal LA size for all 3 modalities, overall agreement with CMR was better for 3DE than 2DE ($\kappa = 0.88$ vs. 0.71) as was the agreement for classifying the LA as enlarged.

Although this is not the first study to validate RT3D LA volume measurements, it is important because it is the largest, is international in scope,

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and uses software customized for LA volume determination. However, it is unclear whether these results can be extrapolated to volume analysis using the widely available QLABS program (Philips Medical Systems, Andover, Massachusetts), which may underestimate volume because the software was designed for LV volume analysis and was applied to the left atrium. Curiously in this study, inter- and intraobserver variability of biplane 2DE and RT3DE were similar and approximately twice as great as CMR, and RT3DE test-retest variability was 11%. Although this variability may be clinically acceptable, it is surprising in view of previous studies that showed better test-retest variability (10) and better interpretative variability (2,7) with RT3DE than with 2DE. Such test performance is necessary to reliably detect changes in LA volume in response to treatments in individual patients.

A few cautions regarding the use of RT3DE LA volumes merit emphasis. Data extrapolated from biplane 2DE should be used cautiously if the American Society of Echocardiography–recommended LA volume cutoff of 34 ml/m^2 is used in the diagnosis of diastolic dysfunction (9). It would have been interesting to see how often RT3DE reclassified the pattern of diastolic dysfunction in this study. Recently, Stefano et al. (5) found that LA size using 1-dimensional, 2-dimensional, and biplane 2DE had better predictive accuracy for moderate or severe diastolic dysfunction than for any degree of diastolic dysfunction alone, but the LA area from the 4-chamber view alone performed as well as biplane 2DE. Whether there is incremental value of RT3DE over 2DE techniques is uncertain; RT3DE maximum LA volume correlated poorly with worsening LV diastolic dysfunction measured with E/e' (11).

Similarly, it is difficult to extrapolate cut points derived from the large body of outcome data that were obtained using biplane 2DE. Outcome data using RT3DE are scant. Suh et al. (2) found that RT3DE (also measured with dedicated Tomtec software) was a better predictor of cardiovascular events than biplane 2DE in a group of patients with severe LV dysfunction followed for approximately 1 year; unlike 2DE, RT3DE-indexed LA volume was an independent risk factor on multivariable analysis. Caselli et al. (12) also reported a better correlation with major adverse cardiovascular events when LA volumes were obtained with RT3DE than biplane 2DE in 178 outpatients followed for 45 months. Although these data need to be confirmed, they do

suggest a clinically important incremental benefit of RT3DE.

Although there are considerable data that support the use of the maximum LA volume, theoretical considerations and a growing literature suggest that perhaps minimum LA volume should be the parameter of interest (11–14). For example, LA elastance measurements and atrial ejection force, which reflect the inotropic state of the LA, are closely related to the minimum LA volume. Moreover, minimum LA volume is measured at end-diastole after being exposed to LV diastolic pressure; indeed, minimum, not maximum, LA volume was a sensitive and specific measure that predicted an elevated pulmonary wedge pressure (13) and was a significant correlate of diastolic dysfunction (11). In addition, RT3DE minimum LA volume was the best independent predictor of major adverse cardiovascular events (12), and biplane minimum LA volume was a better predictor of new-onset atrial fibrillation and flutter than maximum LA volume, although reproducibility was worse (14). Thus, it is notable that minimum LA volume was reported in the current study. Although biases with CMR and RT3DE for maximum and minimum LA volumes were similar, correlations with CMR and limits of agreement were better for maximum volumes; unfortunately, variability data were not reported for minimum LA volumes.

An unresolved question is whether the LA appendage contributes meaningfully to LA volume measurement. Although most investigators exclude the appendage as recommended, other investigators have included the appendage in the analysis (2). Our previous work suggests that, especially at high LA volumes, the contribution of the LA appendage to overall volume cannot necessarily be ignored (15).

A concern with the current study was the apparent inability to derive functional LA volumes (i.e., volumes reflecting the reservoir, conduit, and booster pump functions of the LA), which should be possible theoretically from RT3DE volume-time curves of the LA and LV. LA reservoir function has been particularly useful as a powerful, independent predictor of new-onset atrial fibrillation and flutter in the community (16) and of post-operative atrial fibrillation (interestingly, minimum, but not maximum, LA volume was also predictive) (17). Recently, total LA emptying volumes and fraction, measures of reservoir function, were analyzed using RT3DE and were shown to be related to diastolic LV dysfunction (11).

Finally, it is pertinent to ask how much certainty is needed to conclude that the left atrium is enlarged, particularly when existing cut points are known to have predictive accuracy. Mor-Avi et al. (9) convincingly demonstrated that RT3DE more accurately measures LA volume than bi-plane 2DE. However, it is unclear whether the incremental benefit of RT3DE for LA volume

measurement is valuable clinically. Stated another way, just how accurate do we need to be to be certain?

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