On-line Assessment of Left Atrial Area and Function by Echocardiographic Automatic Boundary Detection

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Background. **Direct assessment of left atrial (LA) function has not been previously performed by noninvasive techniques; rather, LA function has been evaluated only indirectly via the analysis of transmitral flow velocity by Doppler. The recent development of real-time two-dimensional echocardiographic automatic boundary detection suggests that LA dimensions can be measured instantaneously to provide on-line assessment of its systolic and diastolic functions.**

Methods and Results. **We performed echocardiographic assessment of LA dimensions and function with automatic boundary detection in 45 patients by using the apical four-chamber view. Thirty-seven patients had structural or functional cardiac abnormalities, 35 patients were in sinus rhythm, and 10 patients had atrial fibrillation. Moderate to severe mitral regurgitation (MR) was noted in 16 patients. We also studied 10 control subjects to assess normal values of LA cavity area and indexes of function. From the instantaneously derived LA area, we derived indexes of systolic atrial expansion and diastolic atrial emptying. There were excellent correlations between the on-line–derived LA areas and those measured off line from videotaped images of conventional echocardiography (r=.91 for end-diastolic and .93 for end-systolic areas; SEE, 4.0 and 3.8 cm^2, respectively). Patients in atrial fibrillation had depressed diastolic emptying index (0.17±0.05) compared with those in sinus rhythm (0.28±0.12; P<.02). Furthermore, patients with chronic MR exhibited larger LA cavity areas and depressed systolic and diastolic LA function as compared with those without MR. In addition, the Doppler-determined mitral E/A ratio was related to the ratio of early diastolic-to-late diastolic change in LA cavity area (r=.79; SEE 0.6; n=35).**

Conclusions. **Instantaneous LA cavity area measurement by echocardiographic automatic boundary detection is accurate and feasible in patients with diverse cardiac disorders. Patients with atrial fibrillation had a depressed diastolic emptying index and those with significant mitral regurgitation had depressed systolic expansion index as well. LA functional indexes in both systole and diastole can be derived providing an approach for quantitative evaluations of left atrial–left ventricular interactions based on geometric assessment noninvasively. (*Circulation*. 1993;88:1142-1149.)**

Key Words • left atrial function • echocardiography • automatic boundary detection

The left atrial (LA) function has been assessed under experimental and clinical conditions, and several features of its performance as a reservoir, conduit, and booster pump have been described.[1-15] Despite some invasively determined volumetric descriptions in the literature, no invasive measurement is routinely performed to evaluate LA function directly. Noninvasive evaluation of left atrial size was initially carried out with M-mode and later, two-dimensional echocardiography.[16,17] Other investigators have used two-dimensional echocardiography to estimate LA volumes and ejection fraction using analytic methods such as modified Simpson's rule.[18-20] Indirectly, LA function has also been evaluated with the use of pulsed Doppler echocardiography by means of mitral flow velocities during atrial systole (A wave).[21-23] Nevertheless, quantitative real-time imaging of the LA and on-line assessment of its function has, heretofore, not been possible. We and others have recently reported on the development of real-time two-dimensional echocardiographic imaging with automatic boundary detection (ABD), which accurately estimates left ventricular areas, fractional area change, and left ventricular filling patterns.[24-28] The applicability of real-time ABD to derive LA area and function instantaneously may provide a noninvasive tool to assess the diastolic interaction between the left ventricle and the left atrium.

Thus, to define the accuracy of real-time ABD for measurement of the LA, we compared LA-ABD measurements to conventional off-line two-dimensional echocardiographic measurements off line at end diastole and end systole and the relation between changes in the instantaneous LA area during diastole and the transmitral inflow velocities obtained with pulsed Doppler under conditions of normal sinus rhythm, atrial fibrillation, and mitral regurgitation (MR) in patients.

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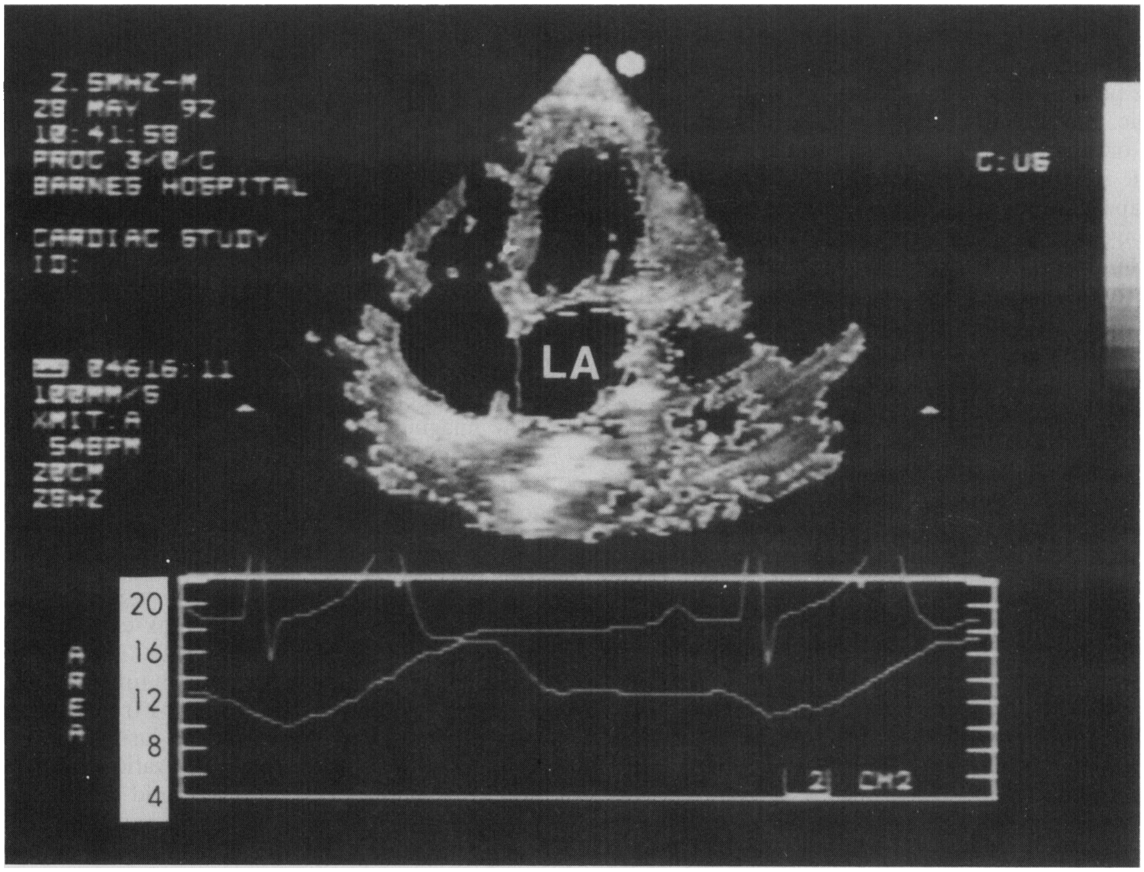

FIG 1. *Conventional two-dimensional echocardiographic image with the automatic boundary detection algorithm operating providing instantaneous left atrial (LA) dimensions in centimeters squared (bottom panel). The LA cavity area increases throughout systole and decreases during diastole in a biphasic fashion (rapid ventricular filling in early diastole and atrial contribution to filling in late diastole).*

Methods

Patient Population

We studied 45 patients (nonconsecutive) in whom the LA cavity and walls were adequately visualized from conventional apical four-chamber views. This criterion was met in this group after 55 patients were initially screened. Sinus rhythm was present in 35 patients, and 10 had atrial fibrillation. The mean age was 57.8±10.1 years (range, 22 to 86). Structural or functional cardiac abnormalities were detected in 37 patients, including wall motion abnormalities in 14, dilated or hypertrophic cardiomyopathy in 13, and valvular heart disease in 10 patients; 8 patients had normal two-dimensional echocardiograms. Doppler color-flow imaging disclosed moderate to severe MR in 16 patients and trivial or no MR in 29. Pulsed Doppler recordings of mitral flow velocity were obtained in all patients. We also studied 10 normal volunteers (mean age, 35.2±8.5 years) to assess normal values of LA area and indexes of left atrial function. Among the 55 subjects studied (45 patients and 10 volunteers), there were 32 women and 23 men.

Echocardiographic Automatic Boundary Detection

A commercially available echocardiographic system (Hewlett-Packard Sonos 1500) with a 2.5-MHz transducer was used in this study. The quantitative integrated backscatter imaging circuitry, developed at Washington University[29-31] and validated by others,[32,33] uses a relatively long integration time of 3.2 microseconds to obtain multiple data points of ultrasonic backscatter along each A-line in the echocardiographic field of view before the creation of the integrated backscatter image. Automatic boundary detection is then made possible by discrimination of the tissue-blood boundary in every frame of the image caused by differences in the backscattered signal strength. Reliable boundary detection results in part from the reduction of speckle noise in the integrated backscatter image. After detection of the boundaries, a brightly colored pixel is superimposed upon the conventional two-dimensional image, and the endocardial-blood border is displayed in real time. Novel software incorporated in the system allows the user to position a cursor with a trackball and draw a region of interest along tissue-blood boundaries around the blood pool cavity of interest. This permits the instantaneous computation of chamber cavity areas within the region of interest and the instantaneous display of the measurement in a continuously changing waveform along with the simultaneous ECG signal and the real-time ABD two-dimensional image (Fig 1).

Imaging Protocol

Standard two-dimensional imaging was performed using multiple views (parasternal, apical, and subcostal). Color-flow imaging was used for determining the

presence and qualitative estimation of MR (trivial or moderate and severe). Pulsed Doppler was performed from the apical four-chamber view with the sample volume positioned at the mitral leaflet tips to record the diastolic mitral inflow velocities. The cardiac rhythm (sinus or atrial fibrillation) was also noted for each patient. All images were recorded on half-inch VHS videotape. For quantitative LA measurements, we used the conventional apical four-chamber view. The ABD algorithm was then engaged using lateral gain compensation to enhance edge detection of the atrial septum and lateral LA wall. Optimal use and careful adjustments with lateral gain compensation and time gain compensation (vertical) and time gain compensation (horizontal) prevented overlap from right atrium or left ventricular blood pools (respectively) within the LA chamber. Minor adjustment in time gain compensation and transmit power controls were usually required to optimize the image. We frequently switched to the conventional two-dimensional image to ascertain that the true cavity area of the left atrium was being displayed by ABD imaging. When this was verified, a region of interest was traced along the atrial septum, posterior atrial wall, lateral LA wall, and across the mitral annulus, proceeding then to on-line graphical display of the instantaneous LA area in centimeters squared (Fig 1). The boundary near the mitral annulus was placed, judging from the end-diastolic frame. This decision was reached to avoid including LV cavity area within the LA measurement while accepting some degree of underestimation of the true cavity area of the atrium.

Comparison of On-line ABD and Conventional Imaging-Derived Area

Two types of comparisons were made to ascertain if the ABD-derived LA areas corresponded to the LA areas depicted in the conventional two-dimensional images. First, we compared LA areas at end diastole and end systole obtained instantaneously by ABD with the areas measured off line by planimetry of the conventional echocardiographic images using nonsimultaneous beats. End diastole was defined as the smallest LA cavity area at the time of the ECG R wave, and end systole was defined as the frame before the mitral valve opening judged from the real-time echocardiographic image. In separate measurements, the ABD-derived area was also instantaneously displayed along with the simultaneous two-dimensional image in conventional gray scale format. This format permitted off-line measurement of LA areas at end diastole and end systole in the same cardiac cycle as the ABD-derived areas by recording on tape the conventional image and the ABD-derived data. The conventional image was then analyzed off line using a trackball-cursor to trace the LA chamber area from three beats in a standard manner using still frames. The graphic display of ABD-derived instantaneous LA area was displayed at the same time for comparison. To ensure that the operator was not biased in tracing the conventional two-dimensional image, the ABD graphical display was concealed by covering that portion of the video screen until the off-line measurements of the conventional two-dimensional image were completed. The mean values (±SD) of end-diastolic and end-systolic LA area by both methods were compared by regression analysis.

Indexes of LA Function

The ABD-derived areas (end diastolic, end systolic) were used to compute fractional indexes of LA area changes. A diastolic atrial emptying index was defined as the end-systolic area minus end-diastolic area divided by end-systolic area (Fig 2). The systolic atrial expansion index was defined as end-systolic area minus end-diastolic area divided by end-diastolic area (Fig 2). The diastolic atrial emptying index was compared among patients with sinus rhythm and those with atrial fibrillation. The systolic atrial expansion index was compared among patients with moderate to severe MR (by color-flow imaging) and those with trivial or no MR. The mean values of these indexes (±SD) were compared using the Student's *t* test for unpaired data with significance determined at $P<.05$.

Mitral Flow Velocity and LA Diastolic Area

The mitral blood flow velocity was measured with pulsed Doppler to obtain the peak early diastolic (E) and late diastolic (A) flow velocity. The ABD-derived areas were measured at the point in time just before and after the LA area changes resulting from rapid ventricular filling and again before and just after atrial contraction (Fig 3). We derived the ratio of the LA area change that occurs because of rapid ventricular filling (early diastole) to the area change resulting from atrial contraction (D/AC). This D/AC ratio was compared with the Doppler E/A ratio. The mean values of these measurements (±SD) were compared by regression analysis.

Results

The ABD study was adequate in all 55 subjects, obtaining on-line tracking of at least 80% of the perimeter of the LA chamber endocardial-blood boundary. The remaining LA borders were approximated by lateral gain compensation. The time to perform quantitative ABD imaging of the LA did not exceed 7 minutes in any of the patients or subjects.

Validation of ABD-Derived LA Area

The ABD on-line–derived areas at end diastole and end systole correlated well with conventional off-line measurements of two-dimensional echocardiographic images in the 45 patients (Fig 4). The correlations were very close for both the data obtained nonsimultaneously and the data obtained from the same cardiac cycle. Although the mean values of LA areas obtained with ABD were slightly smaller than that obtained by conventional two-dimensional imaging, the differences were not statistically significant when two observers performed the off-line analysis, and when their results were averaged, there was still a good correlation between off-line and on-line LA area measurements (Fig 5). LA end-diastolic and end-systolic areas in the 10 volunteers were 7.8±2.4 and 13.6±2.7 cm^2, respectively.

Parameters of LA Function

Normal volunteers and atrial fibrillation. Measurements of LA function in the 10 normal volunteers disclosed a diastolic atrial emptying index of 0.44±.09

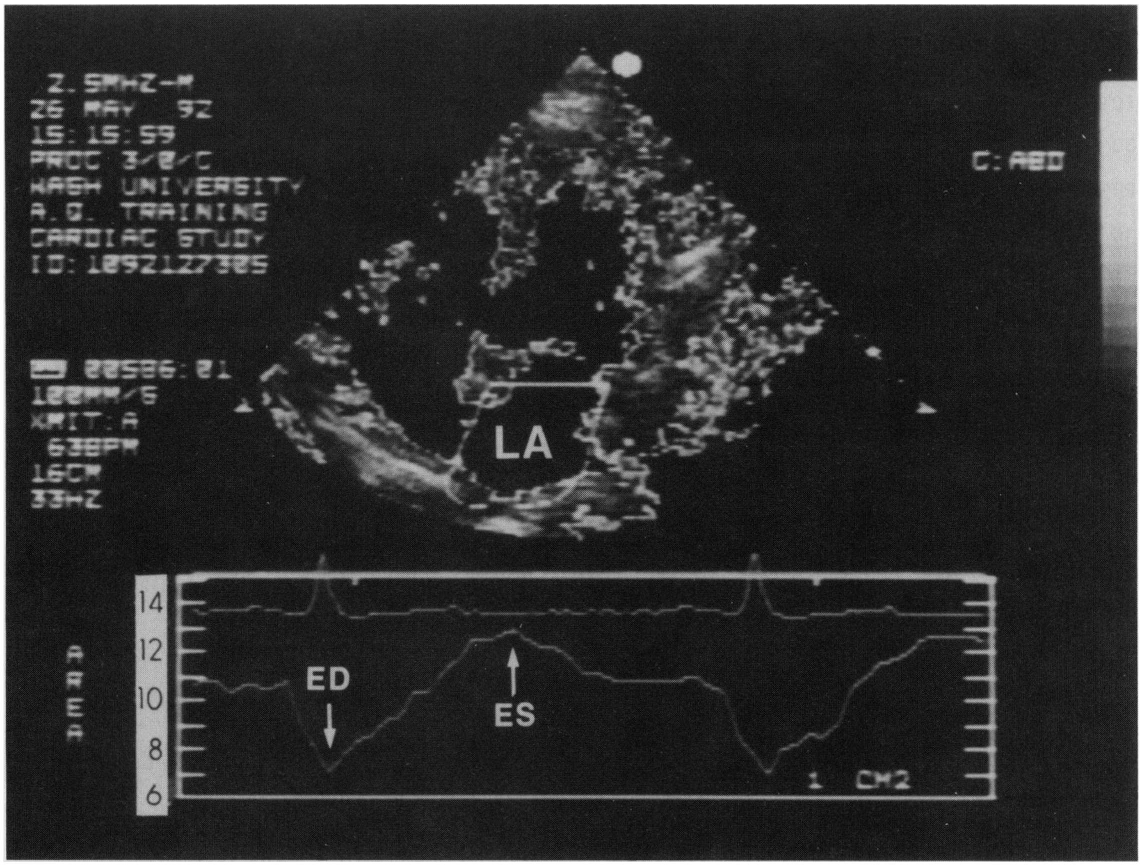

FIG 2. *Echocardiographic automatic boundary detection image (top) with the region of interest drawn around the left atrium (LA) and the instantaneous cavity area displayed (bottom). The diastolic emptying index was derived by subtraction of the end-diastolic (ED) left atrial area from the end-systolic (ES) left atrial area divided by the ES area (in percent). The systolic expansion index was derived by subtraction of the end-diastolic left atrial area from the end-systolic left atrial area divided by the ED area (in percent).*

and a systolic expansion index of 0.81±0.32. In the patient population (n=45), the diastolic emptying index was significantly greater in patients with sinus rhythm compared with those with atrial fibrillation (0.28±0.12 versus 0.17±0.05; $P<.02$). This is in keeping with the hemodynamic impairment in atrial emptying caused by loss of atrial contraction during atrial fibrillation. The ABD on-line display waveform did not display changes in LA cavity area during late diastole in any of the patients with atrial fibrillation.

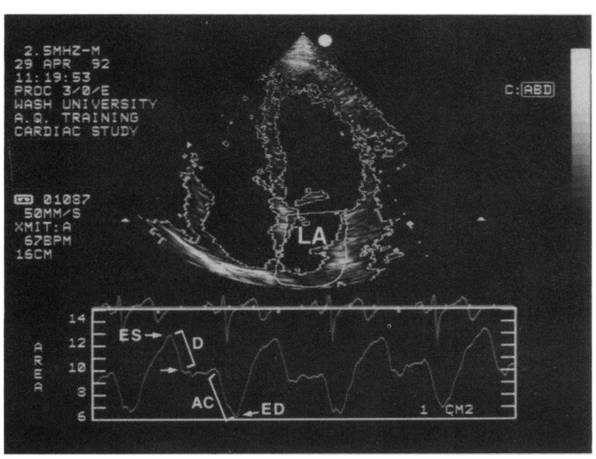

FIG 3. *The extent of left atrial (LA) area change resulting from rapid ventricular filling (D) divided by the LA area change that results from atrial contraction (AC) were measured, their quotient (D/AC) used as a ratio, compared with the transmitral Doppler flow velocity (MV) E/A ratio.*

Mitral regurgitation. The end-systolic LA area was significantly greater in patients exhibiting moderate or severe MR compared with those without MR (28±7.4 versus 23±7.4 cm^2; $P<.05$). The absolute increase in LA cavity area from end diastole to end systole was lower in patients with significant MR compared with those without or with trivial regurgitation (4.8±2.2 versus 6.4±2.0 cm^2; $P=.02$). We did not study patients with acute MR. The systolic expansion index was significantly greater in patients without significant MR compared with those with significant MR (0.47±0.28 versus 0.23±0.13; $P<.005$). The diastolic emptying index was also lower in patients with significant MR compared with those without or with trivial MR (0.18±0.07 versus 0.30±0.12; $P=.001$). Among patients without MR and a low expansion or emptying index, all except one had either myocardial dysfunction (wall motion abnormalities or cardiomyopathy) or atrial fibrillation and all except one had LA end-systolic areas >20 cm^2. Although MR was not present at the time of the LA function study, it was not possible to determine if individual patients had had MR at any time in their clinical history.

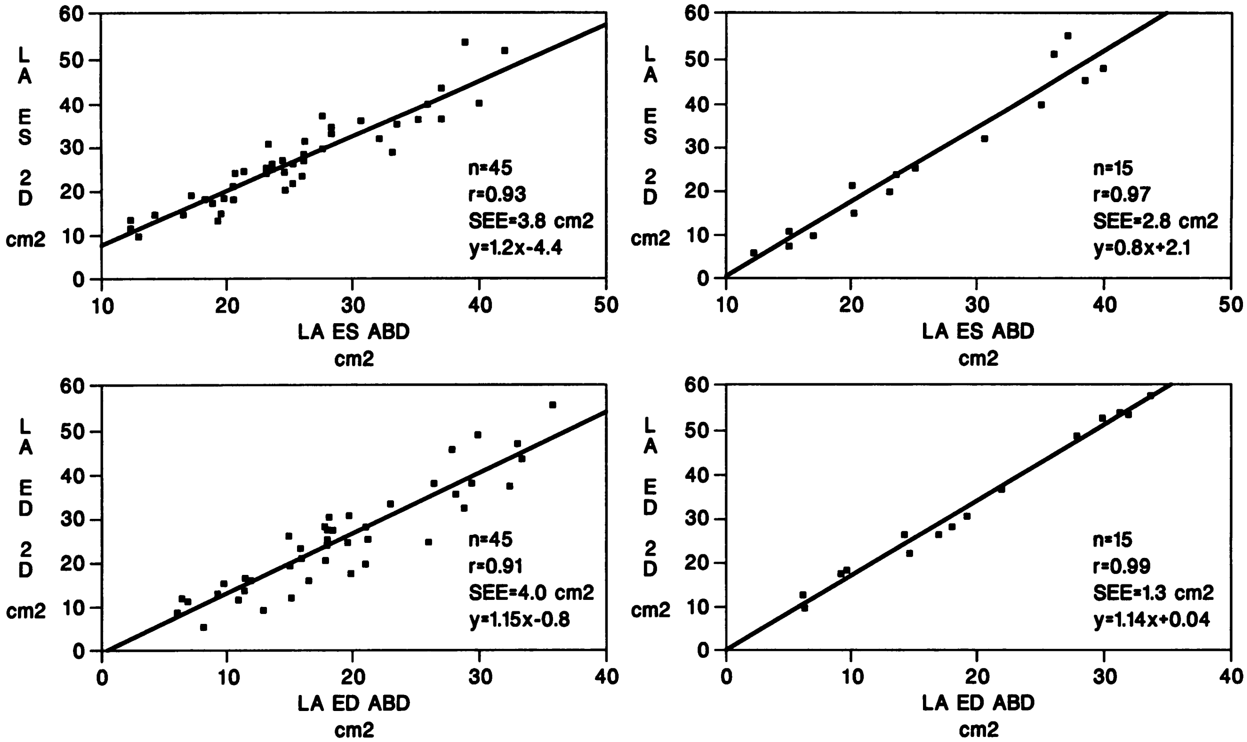

FIG 4. *Line plots show comparison of left atrial (LA) cavity area at end systole (ES, top panels) and end diastole (ED, bottom panels) in nonsimultaneous (left) and simultaneous beats (right). ABD, automatic boundary detection.*

Doppler mitral flow and diastolic LA area. The ABD graphic display of LA area waveform during diastole was used to yield the ratio of early diastolic change in cavity area to the change in area caused by atrial contraction (D/AC). This ratio correlated closely with the Doppler-determined mitral inflow velocity E/A ratio (r=.79, SEE 0.6; n=35; Figs 6, 7, and 8).

Discussion

The development of real-time two-dimensional echocardiographic ABD provides the opportunity for the routine acquisition of quantitative information regarding cardiac chamber dimensions and function at the time of the study.[24,28] The results of the current study extend this work to application of real-time quantitation of LA size and function. The close correlation of the measurements demonstrate that the technique provides accurate on-line information for determination of LA chamber area. Excellent correlations with low standard error of the estimates were obtained in patients by using measurements from nonsimultaneous beats or the same cardiac cycle. The slightly larger cavity areas measured off line may have resulted from difficulty in visualization in stop-frame images of the basal aspect of LA (pulmonary vein region) or variability in mitral valve position because of our decision to place the region of interest at

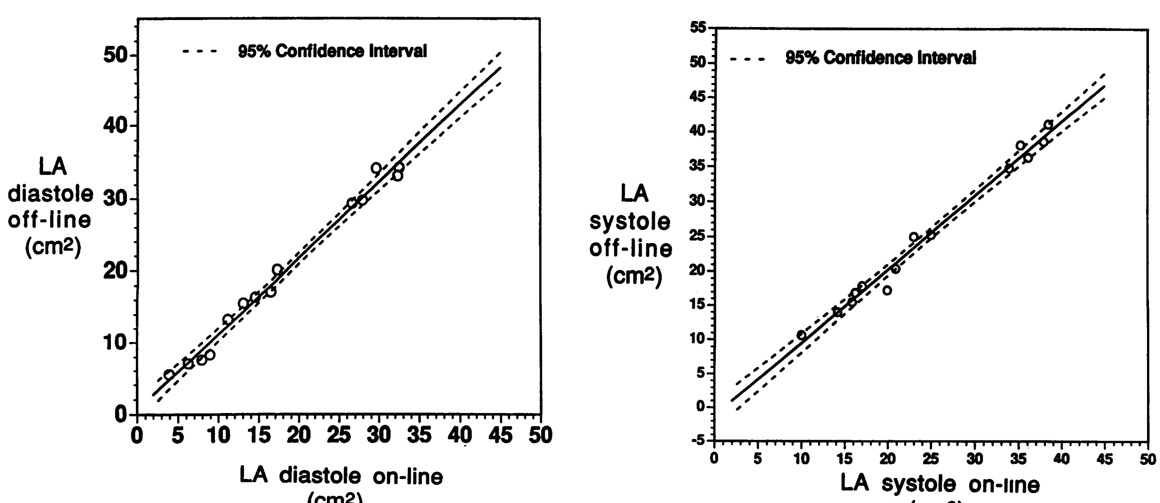

FIG 5. *Line plots show analysis of (two observers averaged) off-line left atrial (LA) area measurement (two observers averaged) compared with automatic boundary detection–derived LA area (dotted lines are 95% confidence intervals).*

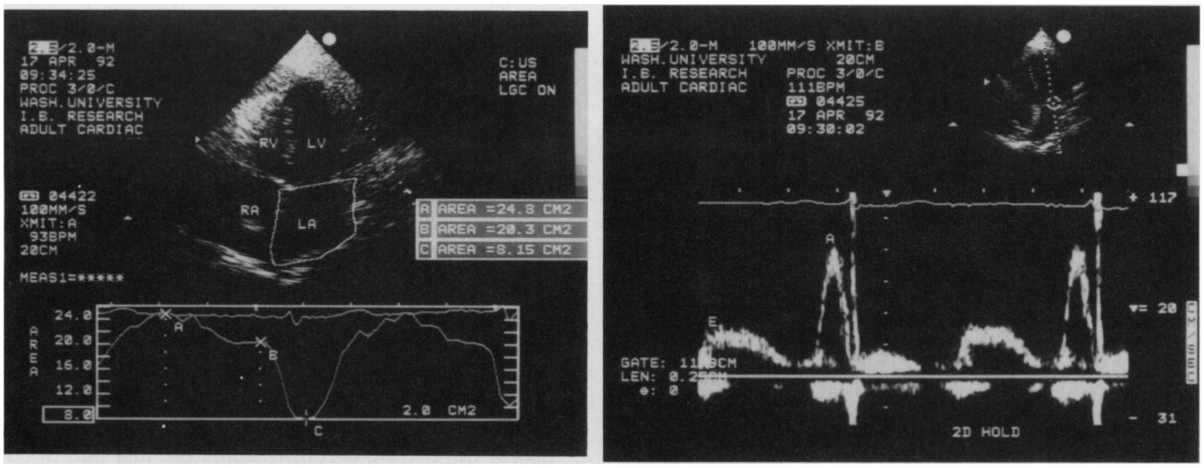

FIG 6. *Left: Two-dimensional echocardiography; representative example in a patient with extensive left ventricular (LV) wall motion abnormalities, of instantaneous left atrial (LA) cavity area change in diastole demonstrating a small change in area during rapid ventricular filling (A to B, or D in Fig 3), and a relatively large component of atrial cavity contraction (B to C, or AC in Fig 3). RV, right ventricle; RA, right atrium. Right: Corresponding transmitral Doppler flow velocity spectra obtained in the patient depicted in the left panel showing corresponding small E and large A wave components.*

the boundary of the annulus in end diastole. The graphic display of instantaneous LA area change during the cardiac cycle also represents a significant advancement. This information has not been available with conventional two-dimensional echocardiography unless tedious frame-by-frame digitizing was performed, as in the study Gehl et al.[18]

Assessment of LA function has been the subject of experimental and clinical investigations using angiographic, hemodynamic, and radionuclide ventriculographic measurements of LA volume or pressure changes, respectively.[1-15] Essentially, LA function exhibits three components: a phase of reservoir or expansion during systole, a conduit phase during diastole, and the active contractile component (when sinus rhythm is present) during late diastole.[2-5] This active contractile component of the LA has an important role in patients with ventricular dysfunction as a "booster pump" to augment ventricular volume.[7-9] Other studies[6,13,14] have reported on diverse hemodynamic conditions associated with a large atrial contribution to ventricular filling, as observed on the LV pressure tracing. Real-time ABD on-line display of LA area may further clarify our understanding about LA function. The systolic expansion or reservoir capacity of the LA is linked to the pulmonary venous inflow. The instantaneous measurement of LA systolic area by ABD coupled with Doppler assessment of instantaneous pulmonary vein-to-LA pressures changes via pulmonary venous inflow velocities lends itself for evaluation of LA compliance. Further evidence that the ABD display of LA area changes reflect atrial function is reflected by the close correlations obtained with the independent Doppler mitral flow velocity measurements (E/A ratio) despite nonsimultaneous data (Fig 8). Early work by Hitch and coworkers[8] in dogs demonstrated that maximal LA volume was achieved during ventricular relaxation before mitral valve opening. In that study, LA emptying

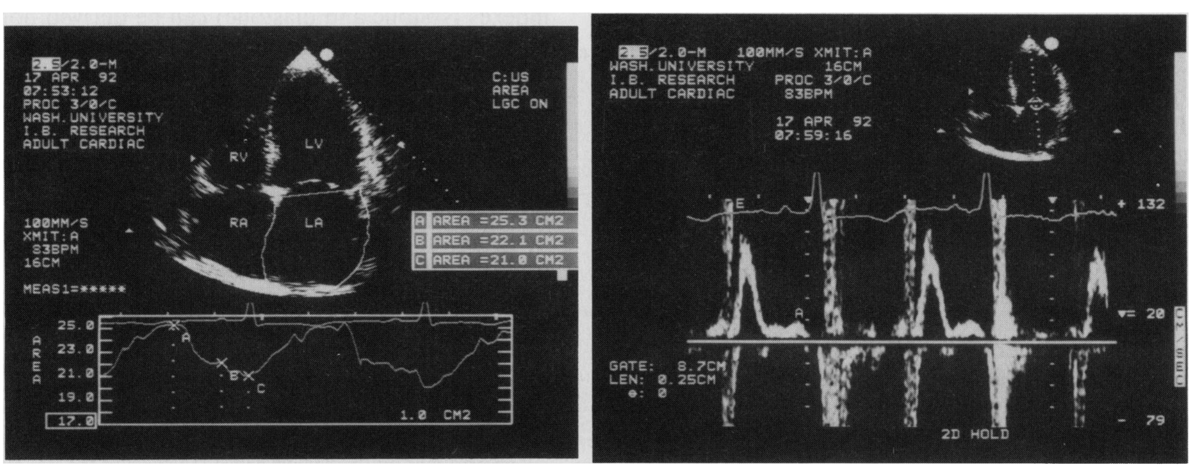

FIG 7. *Left: Two-dimensional echocardiography; instantaneous left atrial (LA) cavity area in a patient with dilated cardiomyopathy and chronic mitral regurgitation in whom the rapid filling phase is associated with the largest change in LA area (A to B), with a small component caused by atrial contribution to ventricular filling in late diastole (B to C). LV, left ventricle; RV, right ventricle; RA, right atrium. Right: Corresponding transmitral Doppler flow velocity spectra obtained in the patient depicted in the left panel showing a corresponding large E and small A wave.*

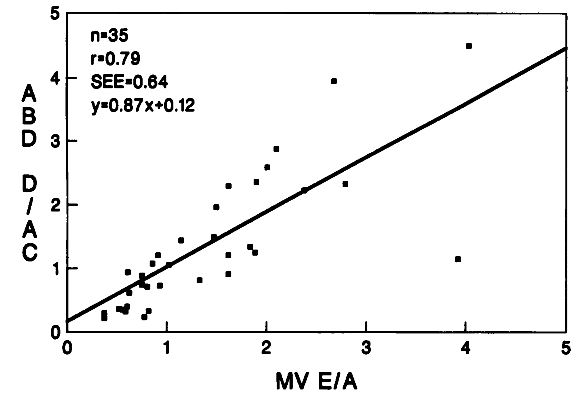

FIG 8. *Line plot shows relation between the ratio of early diastolic change in left atrial (LA) area to change caused by LA contraction (D/AC) and the Doppler E/A ratio. ABD, automatic boundary detection; MV, mitral valve.*

occurred in two stages and corresponded to mitral flow measured by an electromagnetic flow transducer. In our study, many patients exhibited changes in LA area during rapid ventricular filling or during atrial contraction that corresponded to the amplitude of the transmitral flow velocities determined by Doppler (Figs 6 and 7). The patients with atrial fibrillation exhibited no change in LA area during mid or late diastole. Not surprisingly, atrial fibrillation conferred lower values of ABD-determined diastolic atrial emptying compared with measurements obtained in patients with sinus rhythm.

Braunwald and coworkers[1] described the LA function on the basis of a Frank-Starling curve analogous to that of the left ventricle. Later work by Williams et al[3] demonstrated that LA contraction was augmented by increased venous return or by inotropic agents. However, LA distention beyond the peak length-action tension curve may be associated with atrial failure. Payne and colleagues[5] demonstrated that enhanced LA systolic shortening occurs early after volume loading, but further volume expansion resulted in higher LA pressure with reduced atrial shortening. Sasayama and coworkers[11] studied dogs with acutely induced MR and reported increased LA expansion and shortening from the baseline state when the regurgitant volume was small, but with large increases in regurgitant volume, both parameters fell significantly from the baseline state. Further studies by the same investigators in a model of chronic MR demonstrated improved LA compliance as increases in diameter were observed without changes in pressure.[12] Our group of patients with MR exhibited not only lower values of the ABD-determined systolic atrial expansion (probably reflecting long-standing MR and increased LA compliance) but also a reduced diastolic emptying index compared with patients without MR. This impaired LA function observed in patients with significant chronic MR is therefore consistent with previous experimental work.[11,12] In the group of patients without MR, we also observed some patients with impaired LA expansion and emptying. All of these patients also exhibited segmental or global dysfunction with cardiomyopathy. It is conceivable that these patients with dilated and dysfunctional ventricles may have had MR before the time of our study. Alternatively, increased LA pressures in patients with dysfunctional ventricles may have altered LA function despite the absence of MR at the time of our study.

Limitations of the Study

With any new technique, there is a considerable learning phase necessary to perform ABD studies with accuracy. As described, the operator must carefully examine the conventional echocardiographic image in real time to ascertain that the image portrayed by ABD is a very close approximation of the former. This is best accomplished by turning the displayed borders on and off in multiple occasions before acquiring the graphic quantitative area data. The settings of the time gain compensation, lateral gain compensation, and transmit power have to be carefully adjusted, just like in conventional echocardiography, to avoid overestimation or underestimation of the true cavity areas. Furthermore, the indexes described here for LA function are undoubtedly influenced by loading conditions and the left ventricular diastolic function itself. Further studies where instantaneous dimensions and pressures are correlated via ABD imaging[27] may result in improved nonejection phase indexes of LA function.

The LA areas obtained in this study were based on the two-dimensional LA image from the apical four-chamber view, but different absolute areas may be obtained from other image orientations. Furthermore, absolutely precise statements concerning timing of cardiac events cannot be made when using ABD imaging. There is a 30-millisecond delay between the anatomic change in the area as seen in the image and the inscription of this area change in the physiological tracings. This delay occurs because it typically takes 30 milliseconds to create one image frame before the physiological dimension information is updated.

Conclusions

Results of this study demonstrate that instantaneous LA cavity area measurements by ABD are accurate and feasible during echocardiographic examination of patients with diverse cardiac disorders. The LA functional indexes (systolic and diastolic) can be derived noninvasively to determine alterations in function in patients with MR, atrial fibrillation, and ventricular dysfunction even in the absence of MR. Thus, ABD imaging provides a new tool to quantitatively evaluate the LA-LV interactions and to assist in the assessment of therapeutic interventions providing serial noninvasive measurements of LA function.

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