Left atrial size and function: assessment using echocardiographic automatic boundary detection

Peter B M Clarkson, Nigel M Wheeldon, Pitt O Lim, Stuart D Pringle, Thomas M MacDonald

Abstract

Objective—To evaluate the waveforms of left atrial area changes obtained by automated boundary detection with newly developed acoustic quantification technology.

Design—All subjects had measurements of left atrial areas taken in the apical four chamber, parasternal long axis, and parasternal short axis views using both conventional echocardiographic methods and automatic boundary detection on two occasions separated by at least a week. On the second visit measurements were also repeated in healthy volunteers after acute intravenous volume loading with 1 litre of saline over 2-5 minutes.

Setting—A university medical school echocardiographic laboratory.

Subjects—12 healthy male volunteers and 8 patients with cardiac disease (5 with congestive heart failure, 1 with mitral stenosis, and 2 with hypertensive left ventricular hypertrophy, and dilated left atria).

Results—There was close correlation between conventionally derived left atrial areas and those obtained by automatic boundary detection, particularly in the apical four chamber view (r = 0.98). Both inter and intra observer variabilities (coefficient of variation) for left atrial areas measured by automatic boundary detection were good (4.7-14.2% and 8.1-18.6% respectively). The reproducibility (coefficient of variation) for derived indices of left atrial function, however, was much poorer (10-4-104.8% and 12.5-88% respectively). After acute volume loading significant increases in left atrial area were observed at all stages in the cardiac cycle.

Conclusions—These data demonstrate that although the reproducibility of left atrial functional indices is poor, instantaneous left atrial cavity measurements with automatic boundary detection are reproducible. This suggests that automatic boundary detection may assist in serial non-invasive measurement of left atrial size to assess disease states and treatments.

Keywords: acoustic quantification; automated boundary detection; left atrial area changes

Although left atrial function has been extensively investigated by left atrial pressure measurements and several features of its performance as a reservoir, conduit, and augmenter of ventricular filling ("booster pump") have been described, little is known about left atrial volume because there are no simple non-invasive methods for continual assessment of left atrial volume. Though indirect attempts have been made to assess changes in left atrial volume by M mode echocardiography, whether this single measurement adequately expresses the corresponding variation in atrial volume is open to question. Combining transmitral Doppler flow profiles with pulmonary venous flow profiles, though more accurate in determining changes in left atrial volumes is both complex and limited by poor pulmonary flow profiles from transthoracic imaging. Nevertheless, quantitative real time imaging of the left atrium and on-line assessment of its function would be highly desirable to allow better understanding of left atrial function in normal and disease states.

Real time cross sectional echocardiographic imaging with automatic endocardial border detection has been shown accurately to assess cavity sizes, systolic and diastolic properties of the left ventricle, and also left atrial cavity sizes in the apical four chamber view better than off-line analysis of cross sectional images. However, automatic boundary detection has not been applied to either the parasternal short axis or parasternal long axis views of the left atrium, and thus the optimum use of automatic boundary detection in determining left atrial size and function is not known. This study is designed to (a) determine the inter and intra observer variability of automatic boundary detection in determining left atrial size and function in three different echocardiographic planes in patients and healthy controls, (b) compare the areas derived from automatic boundary detection with the areas derived by manual tracing in each imaging plane, and (c) after determining the optimal technique for assessing left atrial function to evaluate the effects of acute volume loading on left atrial size and function in healthy controls and compare the findings.
with transmitral and pulmonary venous Doppler flow profiles.

Methods

SUBJECTS
We studied 12 healthy male volunteers (age range 19–27 years) and eight patients with known cardiac disease (five with congestive cardiac failure, two with hypertensive left ventricular hypertrophy and dilated left atria, and one with mitral stenosis) in whom the left atrial cavity and walls were well visualised in conventional apical four chamber, parasternal long axis, and parasternal short axis views. Four patients were in sinus rhythm and four in atrial fibrillation. Each provided written informed consent, and the study was approved by the Tayside Committee on Medical Research Ethics. Physical examination, haematological and biochemical indices, the 12 lead electrocardiograph, and echocardiography were normal in all the healthy controls.

STUDY PROTOCOL
All subjects were studied on two separate days at least one week apart. Subjects were asked to refrain from alcohol, caffeine, and cigarettes for 24 h, and to fast for 2 h before each study day. On both study days subjects reported to the research laboratory and remained supine and inactive for the duration of each study. On the first visit after 30 minutes of supine bed rest conventional cross sectional echocardiography was performed, followed by echocardiography with automatic boundary detection of the left atrium in the apical four chamber, parasternal long axis, and parasternal short axis views. In the patient group echocardiography was performed in identical fashion on the second visit, without further interventions. In the healthy volunteers on the second visit a 16FG intravenous cannula was inserted into the right antecubital fossa. After 30 min of bed rest echocardiographic imaging was performed in identical fashion to that on the first study day. In addition transmitral and pulmonary venous Doppler flows were recorded. Once measurements were completed a litre of 0.9% saline was rapidly infused over 2–5 min, and the measurements were repeated as soon as the infusion was completed.

ECHOCARDIOGRAPHIC AUTOMATIC BOUNDARY DETECTION
All echocardiographic examinations were performed using a Hewlett-Packard Sonos 1500 with a 2-7/3-5 MHz transducer.

Automatic boundary detection involves discrimination of the tissue-blood boundary in every frame of the image caused by differences in the back-scattered signal strengths. After detection of boundaries a colour enhanced image is superimposed on the conventional cross sectional image, and the endocardial-blood interface displayed in real time. Software incorporated into the echocardiographic unit enables a region of interest to be specified by tracing an area using a track-ball. This permitted the instantaneous calculation and display of chamber cavity areas within the region of interest, together with display of the simultaneous electrocardiographic signal and the real time automatic boundary detection cross sectional image.

IMAGING PROTOCOL
All subjects were studied in the supine position rotated onto the left side, and recordings taken during quiet respiration.

Once an optional standard apical four chamber view of the heart was obtained automatic border detection was engaged. Careful adjustment of transmit power control, time gain compensation, and lateral gain compensation were required to optimise the image. To ascertain that the true cavity area of the left atrium was displayed by the automatic boundary detection we frequently switched to the conventional cross sectional image. Then the region of interest was traced along the atrial septum, posterior left atrial wall, lateral left atrial wall, and across the mitral annulus, the latter was placed according to its position at end diastole. A continuous wave form was thus obtained of left atrial area (fig 1A–C). Similar imaging was performed in the parasternal long axis and parasternal short axis with the region of interest drawn respectively around the boundary of left atrium and aortic root, posterior left atrial wall, lateral left atrial wall, and across the mitral annulus according to its position at end diastole, and for the parasternal short axis along the boundary of left atrium and aortic root, interatrial septum, posterior left atrial wall, and pulmonary artery.

To determine interobserver variability automatic boundary detection measurements were repeated in each subject by a second observer, on either the first or second visit. Transmitral Doppler flows were recorded by placing a pulsed wave Doppler sample volume in the inflow area of the left ventricle between the tips of the mitral valve, and its position was adjusted until maximum Doppler flow velocities were recorded. Doppler signals were traced using an analysis package built into the echocardiographic unit from which the time velocity integrals of the early filling (E) wave and atrial systolic (A) wave were calculated. To detect pulmonary venous flow the Doppler sample was placed in the orifice of the pulmonary vein in which the direction of flow was most closely aligned with the Doppler probe. In most volunteers this was the right upper pulmonary vein. Using the same analysis package the time velocity integrals of pulmonary venous systolic and diastolic forward flow and atrial flow reversal were calculated.

INDICES OF LEFT ATRIAL FUNCTION DERIVED FROM AUTOMATIC BOUNDARY DETECTION
Maximal atrial area, minimal atrial area, area at the end of the early emptying phase, and area at the onset of atrial systole were
recorded, and fractional indexes of left atrial area changes were calculated from these areas.

As previously described, a diastolic emptying index and systolic expansion index were defined respectively as the maximum atrial area minus the minimum atrial area divided by the maximum atrial area, and the maximum atrial area minus the minimum atrial area divided by the minimum atrial area. An atrial systolic emptying index was defined as the area at the onset of atrial systole minus the minimum atrial area divided by the area at the onset of atrial systole. The ratio of early emptying to atrial systolic emptying was defined as the maximum atrial area minus the area at the end of the early emptying phase divided by the change in area between the onset of atrial systole and the minimal atrial area.

In the four patients with atrial fibrillation it was possible only to determine maximum, and minimum left atrial areas, and therefore possible only to determine the diastolic emptying and systolic expansion indices.

To determine the accuracy of left atrial areas derived from automatic boundary detection the end diastolic and end systolic areas obtained instantaneously by automatic boundary detection were compared with the areas measured by manual tracing of the conventional echocardiographic images using non-simultaneous beats. This was performed in all subjects on the images obtained at baseline on the second visit. End systole was defined as the frame before mitral valve opening and end diastole as the time of the electrocardiographic R wave.

STATISTICAL ANALYSIS
All data were analysed using the Statgraphics software package (STSC Software Publishing Group, Rockville, Maryland, USA).

The intra-observer variabilities were calculated for echocardiographic automatic boundary detection indices measured on the first visit and baseline on the second visit. Inter-observer variabilities were calculated from the measurements obtained by both observers. One way analysis of variance was used to obtain the mean sum of squares for within subject variation (SD) where SD is the standard deviation. The coefficient of variation (cv) for within subject variability was then calculated as SD/global mean × 100%.

Analysis of variance and Bonferroni multiple range tests were performed to determine the significance of changes in Doppler flow and left atrial size function induced by acute volume loading.

Results

COMPARISON OF AUTOMATIC BOUNDARY DETECTION DERIVED AREAS WITH CONVENTIONALLY DERIVED AREAS (FIG 2)

The automatic boundary detection derived left atrial areas at end diastole and end systole correlated well with conventional measurement of the cross sectional echocardiographic

Figure 1 Automatic border detection and display of left atrial areas in (A) apical four chamber, (B) parasternal long axis, (C) parasternal short axis views.
Left atrial size and function: assessment using echocardiographic automatic boundary detection

Intra-observer reproducibility of automatic boundary detection derived areas (Table 1)

There was greater reproducibility of overall mean left atrial area (8.1-9.1%) than left atrial areas obtained in apical four chamber (8.6-12.9%), parasternal long axis (13.3-17.7%), or parasternal short axis (12.8-18.6%) views. Of the three single plane views, reproducibility was best for automatic boundary detection derived left atrial areas in the apical four chamber view. Derived indices of left atrial function were less reproducible irrespective of whether single views or the mean values were used.
From these results one can calculate that nine subjects would be required to detect a 10% change in mean left atrial area with 90% power at the 5% level. Larger numbers would be required to detect a 10% change in other automatic boundary detection derived indices (diastolic emptying index, 17 subjects; systolic emptying index, 39 subjects; atrial systolic emptying index, 36 subjects; early emptying/atrial systolic emptying index, 77 subjects).

### INTER-OBSERVER REPRODUCIBILITY OF AUTOMATIC BOUNDARY DETECTION DERIVED AREA (TABLE 2)

The reproducibility of measurements of left atrial areas between two observers performed on the same day was good in all imaging planes (4.7–14.2%) but best for mean left atrial areas. As with the intra-observer reproducibility, the derived indices of left atrial function were less reproducible.

### EFFECTS OF ACUTE VOLUME LOADING ON DOPPLER FLOW AND LEFT ATRIAL FUNCTION (TABLE 3, FIGURE 3)

Acute volume loading caused significant changes in the transmitral flow velocity integral, pulmonary venous systolic flow, early filling, and pulmonary venous atrial flow reversal. Non-significant increases in the transmitral flow velocity integral (P = 0.08) and pulmonary venous diastolic flow (P = 0.06) were also seen.

Acute volume loading increased left atrial areas throughout the cardiac cycle but had no significant effects on the diastolic emptying index, systolic expansion index, atrial systolic emptying index or ratio of early emptying to atrial systolic emptying. There were significant increases in both the total area change of the left atrium and the area change during atrial systole.

### Discussion

AUTOMATIC BOUNDARY DETECTION DERIVED LEFT ATRIAL AREAS

Figure 1 shows instantaneous changes in left atrial area throughout the cardiac cycle. At the onset of ventricular systole the left atrial area progressively increases, reaching its maximum dimension towards the end of ventricular systole. After mitral valve opening the left atrium empties rapidly—corresponding with the early filling wave (E wave) obtained with transmitral Doppler flow profiles—and the left atrial area rapidly decreases. During dias- tasis the left atrial area either remains constant or shows a small increase in area. At the end of diastasis, atrial systole begins, expelling blood into the left ventricle causing the left atrial area to decrease to its minimum dimension. The left atrial area curves thus obtained resemble the left atrial volume curves obtained with invasive angiographic techniques.

ASSESSMENT OF LEFT ATRIAL FUNCTION

Other echocardiographic techniques have been used in earlier studies in an attempt to quantify continuous left atrial volume changes, but all have major limitations. M mode recordings of left atrial dimensions at the level of the aortic valve have been used, and, though reproducible, concern has been voiced because these display left atrial size in only one dimension.

Changes in left atrial volume have been inferred from the transmitral flow profile. However, the area of the mitral annulus changes during diastole (by up to 12%); this makes assumptions about volume changes from a linear measurement inaccurate. In addition the left atrium functions not only as a pump but also as a conduit and reservoir, with blood entering the left atrium during passive atrial emptying, diastasis, and ventricular systole, and so the volume of the left atrium cannot be determined using Doppler without recordings of pulmonary venous flow.

A technique to calculate left atrial volumes using combined pulmonary venous flow and transmitral Doppler flow was recently described. This entails estimating left atrial end diastolic volume by cross sectional echocardiography together with digitisation and superimposition of pulmonary venous

### Table 1 Intra-observer variability (%) of left atrial areas and indices of left atrial function derived from automatic boundary detection

<table>
<thead>
<tr>
<th>Image plane</th>
<th>AAC</th>
<th>PSA</th>
<th>PLA</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum area</td>
<td>8.6</td>
<td>18.6</td>
<td>13.3</td>
<td>8.9</td>
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<tr>
<td>Minimum area</td>
<td>12.5</td>
<td>17.3</td>
<td>15.6</td>
<td>9.1</td>
</tr>
<tr>
<td>Area at end early emptying</td>
<td>12.9</td>
<td>13.0</td>
<td>17.7</td>
<td>8.4</td>
</tr>
<tr>
<td>Area at onset atrial systole</td>
<td>11.7</td>
<td>12.8</td>
<td>14.9</td>
<td>8.1</td>
</tr>
<tr>
<td>Diastolic emptying index</td>
<td>28.4</td>
<td>17.2</td>
<td>24.6</td>
<td>12.5</td>
</tr>
<tr>
<td>Systolic expansion index</td>
<td>47.0</td>
<td>23.4</td>
<td>38.3</td>
<td>19.0</td>
</tr>
<tr>
<td>Atrial systolic emptying index</td>
<td>28.2</td>
<td>33.5</td>
<td>24.1</td>
<td>18.5</td>
</tr>
<tr>
<td>Early emptying/atrial systolic emptying ratio</td>
<td>35.1</td>
<td>88.0</td>
<td>42.0</td>
<td>27.0</td>
</tr>
</tbody>
</table>

Values are expressed as percentage: AAC, apical four chamber; PSA, parasternal short axis; PLA, parasternal long axis; mean, average value of left atrial area from the three perpendicular imaging planes.

### Table 2 Inter-observer variability (%) for automatic boundary detection derived left atrial areas and indices of left atrial function

<table>
<thead>
<tr>
<th>Image plane</th>
<th>AAC</th>
<th>PSA</th>
<th>PLA</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum area</td>
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<td>12.5</td>
<td>7.4</td>
<td>5.0</td>
</tr>
<tr>
<td>Minimum area</td>
<td>11.9</td>
<td>11.0</td>
<td>7.3</td>
<td>7.3</td>
</tr>
<tr>
<td>Area at end early emptying</td>
<td>6.5</td>
<td>14.2</td>
<td>9.3</td>
<td>5.8</td>
</tr>
<tr>
<td>Area at onset atrial systole</td>
<td>4.7</td>
<td>13.0</td>
<td>9.8</td>
<td>4.9</td>
</tr>
<tr>
<td>Diastolic emptying index</td>
<td>20.5</td>
<td>10.5</td>
<td>15.4</td>
<td>10.4</td>
</tr>
<tr>
<td>Systolic expansion index</td>
<td>29.3</td>
<td>13.7</td>
<td>29.8</td>
<td>16.2</td>
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<tr>
<td>Atrial systolic emptying index</td>
<td>12.4</td>
<td>12.9</td>
<td>14.8</td>
<td>10.8</td>
</tr>
<tr>
<td>Early emptying/atrial systolic emptying ratio</td>
<td>50.5</td>
<td>36.9</td>
<td>104.8</td>
<td>29.8</td>
</tr>
</tbody>
</table>

See footnote to Table 1 for abbreviations.

### Table 3 Effects of volume loading on Doppler flow and on left atrial size and function

<table>
<thead>
<tr>
<th>E flow velocity integral (cm)</th>
<th>Before</th>
<th>After</th>
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</thead>
<tbody>
<tr>
<td>11.6</td>
<td>13.2**</td>
<td></td>
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<tr>
<td>A flow velocity integral (cm)</td>
<td>3.81</td>
<td>4.30</td>
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<tr>
<td>Pulmonary venous systolic flow (cm)</td>
<td>10.4</td>
<td>12.8**</td>
</tr>
<tr>
<td>Pulmonary venous diastolic flow (cm)</td>
<td>10.0</td>
<td>11.1</td>
</tr>
<tr>
<td>Pulmonary venous atrial flow reversal (cm)</td>
<td>1.92</td>
<td>2.3**</td>
</tr>
<tr>
<td>Maximum atrial area (cm²)</td>
<td>13.7</td>
<td>15.8*</td>
</tr>
<tr>
<td>Minimum atrial area (cm²)</td>
<td>9.3</td>
<td>10.4*</td>
</tr>
<tr>
<td>Area at onset early emptying (cm²)</td>
<td>10.2</td>
<td>12.8**</td>
</tr>
<tr>
<td>Area at onset atrial systole (cm²)</td>
<td>11.0</td>
<td>12.6**</td>
</tr>
<tr>
<td>Diastolic emptying index (%)</td>
<td>32.6</td>
<td>34.3</td>
</tr>
<tr>
<td>Systolic expansion index (%)</td>
<td>49.2</td>
<td>53.2</td>
</tr>
<tr>
<td>Atrial systolic emptying index (%)</td>
<td>16.2</td>
<td>17.9</td>
</tr>
<tr>
<td>Early emptying/atrial systolic emptying ratio</td>
<td>2.10</td>
<td>1.77</td>
</tr>
<tr>
<td>Total area change (cm²)</td>
<td>4.43</td>
<td>5.40*</td>
</tr>
<tr>
<td>Atrial systolic area change (cm²)</td>
<td>1.76</td>
<td>2.24**</td>
</tr>
</tbody>
</table>

Values are expressed as means. *P < 0.05, **P < 0.01.
and transmitral Doppler flow profiles. Left atrial volumes derived by this technique were morphologically similar to those obtained using angiographic techniques but underestimated the angiographic left atrial volume by up to 60%. In addition to the limitations of changes in the mitral valve annulus area, substantial changes in pulmonary vein area may also occur. The pulmonary veins provide a major component of compliance in the pulmonary venous system and are known to change shape from elliptical to circular in response to increased left atrial pressure.13

Automatic boundary detection of left atrial areas offers a potential method for evaluating left atrial function without the above methodological problems. In the present study we showed close correlations with conventional cross-sectional echocardiography. However, as with all transthoracic echocardiographic techniques, the left atrial appendage is not visualised, leading to underestimation of the true left atrial size. Since the left atrial appendage may be more distensible than the rest of the left atrium,14 automatic boundary detection may underestimate the reservoir capacity of the left atrium. In view of this we have not attempted to derive changes in left atrial volume from changes in left atrial area, although theoretically it should be possible to do so using the left atrial areas obtained from the three perpendicular planes. Further limitations to automatic boundary detection assessment of left atrial size and function are that the position of the region of interest can lead to either (a) underestimation of left atrial cavity area (to avoid including other cardiac cavities—for example, the left ventricle or right atrium within the left atrial measurement) or (b) overestimation of left atrial cavity in the case of pulmonary venous engorgement because it is difficult to draw a region of interest that completely excludes the pulmonary veins from the analysis.

**REPRODUCIBILITY OF INDICES OF LEFT ATRIAL FUNCTION DERIVED FROM AUTOMATIC BOUNDARY DETECTION**

In the present study, in a research setting, we showed good reproducibility of left atrial areas using automatic boundary detection. The variation in measurement was greatest for the parasternal short axis and parasternal long axis views, less in the apical four chamber, and least with the derived mean left atrial area. The reproducibility of derived indices of left atrial function was poor, however, with only slight differences between imaging planes. Again reproducibility was best using the mean of the three imaging planes. These data suggest that automatic boundary detection imaging provides a potential new tool for the assessment of left atrial function that may assist in studies requiring serial non-invasive measurements of left atrial function.

**VOLUME LOADING**

Previous studies of the effect of acute volume loading on left atrial function in dogs showed that under normal physiological conditions the left atrial pressure-volume curve is fairly flat, volume loading causing only small increments in left atrial pressure associated with quite large volume changes.2 Similar experiments, again in dogs, showed that the left atrium can expand by 60% in volume in the presence of acute mitral regurgitation.19

Less is known about changes in left atrial volumes in humans after volume loading, primarily because of differences in non-invasive assessment. In both the present study, and in previous studies16 acute volume loading increases the transmitral early filling wave, the pulmonary venous systolic forward flow, and atrial systolic flow reversal in the pulmonary venous flow profile, which suggests an increase in the conduit and booster pump functions of the left atrium. We found an increase in left atrial area throughout the cardiac cycle, together with increases in both total area change, and atrial systolic area change. No significant changes in other indices of left atrial function were seen. These findings are therefore consistent with Doppler data from Nishimura et al’s study,16 and other studies in which an increase in the reservoir capacity, conduit, and booster pump functions of the left atrium was shown.

It is likely that the left atrial areas measured after volume loading are overestimates because of difficulties in excluding portions of pulmonary vein from the region of interest. Because the pulmonary veins are highly compliant13 volume loading may lead to large changes in pulmonary venous area and thus increase the derived left atrial area.

A further limitation of this study is that comparisons of left atrial areas were open and not randomised for order. However, the study was performed for methodological validation rather than a true investigation of changes in left atrial size.

**CLINICAL APPLICATION**

Before the advent of echocardiographic auto-
matic boundary detection non-invasive quantitative real-time imaging of the left atrium and on-line assessment of both size and function has been impossible. Although the use of automatic boundary detection requires both high quality cross sectional echocardiographic pictures and a high level of technical expertise it takes far less time than manually tracing left atrial areas in each frame of the cardiac cycle.

Although echocardiographic automatic boundary detection for the assessment of the left atrium will, at present, remain a research technique there are several potential applications for this new technology: (a) it should allow better understanding of left atrial function in both normal and disease states; (b) changes in left ventricular compliance as a result of hypertension, cardiomyopathy, or ischaemia are likely to result in altered left atrial function, and thus echocardiographic automatic boundary detection provides a non-invasive tool to assess the diastolic interactions between the left atrium and left ventricle; (c) left atrial diameter on M mode echocardiography has been related to the incidence of atrial fibrillation and thrombus formation, and thus earlier or more subtle changes in left atrial size and function, as assessed by echocardiographic automatic boundary detection, may also predispose to atrial arrhythmias, and thrombus formation.

Conclusions

The results of this study show that measurement of instantaneous left atrial cavity area by echocardiographic automatic boundary detection correlates closely with measurement of instantaneous left atrial cavity area obtained with conventional echocardiographic techniques. The inter and intra observer variability for left atrial areas derived by automatic boundary detection was good though the reproducibility of derived indices of left atrial function was poor. This suggests that automatic boundary detection may assist in serial non-invasive measurements of left atrial size to assess disease states and therapeutic interventions. This study also shows that acute volume loading increases the reservoir capacity, conduit function, and booster pump function of the left atrium, results which largely confirm other studies.

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