Left Atrial Maximum Volume Is a Recurrence Predictor in Lone Atrial Fibrillation
An Acoustic Quantification Study

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SUMMARY

Predictors of recurrence in lone atrial fibrillation have not been clearly identified. Acoustic quantification (AQ) is a promising method in the assessment of left atrial (LA) volumes. The purpose of the present study was to investigate the potential of LA volumes obtained by standard manual tracing and AQ methods in predicting AF-recurrence after restoring the sinus rhythm in patients with lone AF, and to test the agreement between the two approaches. Standard echocardiography combined with AQ was performed in 28 patients with lone AF one hour after the sinus rhythm was regained, and in 10 controls. LA volumes were determined by conventional manual tracing and AQ methods. AQ waveforms of LA were obtained by drawing a region of interest around the LA border. The agreement of the two methods was tested by Bland-Altman analysis. Patients were followed up for 6 months for the occurrence of AF recurrence. A good correlation was observed between AQ and manual tracing methods in determining both minimal ($r=0.59$) and maximal ($r=0.88$) LA volumes. Patients with AF recurrence had a significantly larger maximum LA volume as assessed with both methods ($P<0.05$ for both). M-mode derived LA dimension and isovolumic relaxation time were additional predictors of recurrence in patients with lone AF. In lone AF, patients prone to recurrence could be predicted by determining LA maximum volume assessed either by AQ or manual tracing methods. AQ provides on-line, accurate estimation of LA volumes. (Jpn Heart J 2002; 43: 241-248)

Key words: Lone atrial fibrillation, Echocardiography, Acoustic quantification

Atrial fibrillation (AF) is the most commonly encountered sustained arrhythmia, affecting 0.9% of the general population.1) Although it is frequently associated with systemic hypertension, structural heart disease, pulmonary disease, and metabolic or endocrine disease,1,2) it occurs as an isolated event termed "lone AF" in about 30% of patients. Restoring the sinus rhythm and preventing relapses are desirable endpoints of AF management. Therefore, the identification of patients

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prone to recurrence is of clinical importance. Although some clinical variables such as left atrial (LA) size, longer arrhythmia history, low functional capacity and concomitant rheumatic mitral disease have been reported to predict recurrence in the overall AF population, predictors of recurrence in patients with lone AF have not yet been clearly demonstrated.\(^2\)\(^-\)\(^7\)\)

Acoustic quantification (AQ) is an echocardiographic modality that allows a rapid, on-line determination of the volumes and functions of a selected cardiac chamber with accuracies comparable to those achieved with standard off-line volume analysis.\(^8\)\(^,\)\(^9\)\) The present study was designed to investigate whether the LA volumes assessed both by manual tracing and AQ methods would predict the AF relapses of patients suffering an acute episode of lone AF.

**METHODS**

**Patient selection:** One hundred and twenty-one patients with atrial fibrillation admitted to our emergency room with palpitations between October 1999 and January 2001 were initially evaluated. Patients were excluded from the study if they had mitral and/or aortic valve disease (33), ischemic (23) or hypertensive (19) heart disease, a clinical history of hyperthyroidism (4), Wolf-Parkinson-White syndrome (6), or diabetes mellitus (8). Coronary artery disease was excluded by the history, clinical evaluation, ECG, and exercise stress test that was performed after the restoration of sinus rhythm (SR). Systemic hypertension (>160/90 mmHg), pulmonary artery disease, hyperthyroidism, diabetes and anemia were eliminated by appropriate tests. The remaining 28 (9 women, mean age: \(39.4\pm6.9\), 29-52 years) consecutive patients were enrolled into the study group with the diagnosis of lone AF that was defined as the absence of structural heart disease based on clinical interrogation, physical examination, chest x-ray, routine blood chemistry, and transthoracic echocardiography. Ten age and sex matched healthy individuals served as a control group.

**Cardioversion:** Six patients spontaneously regained SR before the onset of treatment. In 17 patients, SR was restored within 24 hours of pharmacological cardioversion that was performed with IV procainamide (100 mg every 5 minutes; maximum dose of 1 g). Five patients who did not respond to procainamide in 24 hours were treated with successful DC cardioversion. The total amount of electrical energy used for cardioversion was \(245\pm183\) joules per patient. Patients who underwent either chemical or electrical cardioversion were given hydroquinidine retard (250 mg) twice daily after the restoration of SR. All study patients were followed up to six months for any AF recurrence; and they were classified into two groups according to the presence or absence of AF recurrence within 6 months. Group 1 included 17 patients who experienced recurrence; the remaining
11 free of recurrence formed group 2.

**Standard echocardiography:** Patients underwent two-dimensional, M-mode, and Doppler echocardiography 1 hour after the restoration of SR. All examinations were performed in the left lateral recumbent position using a commercially available echocardiographic system (Sonos 1500, Hewlett-Packard, Andover, Massachusetts) equipped with 2.5 and 3.5 MHz phased-array transducers. Subjects were asked to avoid deep inspiration during the recordings that were stored on half-inch super VHS magnetic tapes for later analysis by an independent observer in a blinded manner. M-mode derived LA anterior-posterior dimension was measured in the parasternal long axis view.\(^{10}\) Left ventricular ejection fraction was calculated using the Teichholz formula. Transmitral spectral flow patterns were recorded by placing a 0.5- to 1.0-cm pulsed wave Doppler sample volume between the mitral leaflet tips, where maximal flow velocity was recorded. The measurements represent the mean of at least three consecutive cardiac cycles, and include peak early (E) diastolic velocity, and isovolumic relaxation time (IVRT), which was measured as the time-interval between the end of aortic flow and the onset of diastolic flow. Following obtaining the best image of LA from the apical four chamber window, maximal and minimal LA volumes were measured by carefully tracing its edges manually and applying the biplane area-length method.\(^{11,12,13}\) Maximal LA volume was measured at the frame of mitral valve opening. The minimal LA volume was measured at the frame of the mitral valve closure.

**Automated boundary detection of left atrium:** To perform an optimal acoustic quantification study, the overall gain, time gain compensation, and lateral gain controls were optimized. Automated boundary detection was activated and performed on the LA in an apical four-chamber view.\(^{13}\) The region of interest was set around the interatrial septum, mitral annulus, and LA walls. Care was taken to exclude the pulmonary veins and right atrium. From the on-line–acquired AQ waveforms during the cardiac cycle, minimal and maximal LA volumes at end-diastole and systole were determined with reference to the frames of mitral valve opening and closure (Figure 1).

**Statistical analysis:** The results are expressed as the mean±SD. The variables were compared using an unpaired Student's *t* Test. Recurrence correlation was evaluated with the Spearman correlation and linear regression analysis. Significance was set at a *P* value <0.05. The agreement between two methods of volume determinations was assessed using the analysis proposed by Bland and Altman.\(^{14}\)
RESULTS

A comparison of the baseline demographic and echocardiographic parameters is displayed in Table I. The two groups and controls were similar in terms of age, gender and heart rate (after the rate control) at the echocardiographic examination. Left ventricular dimensions, ejection fraction, and early transmitral Doppler diastolic velocity were comparable between the patients who did and did not experience an AF recurrence during the 6 month follow-up. LA anterior-posterior diameter was found to be significantly increased in group 1 (3.9±1.6 cm vs. 3.5±1.1; P<0.05). Among the parameters of left ventricular function, an IVRT that was significantly longer in group 1 was the only parameter that was different between the two groups (93±12 ms vs. 77±9 ms; P<0.05).

In patients with lone AF, there was a good correlation between AQ and conventional manual tracing methods for the determination of both minimal (r=0.59) and maximal (r=0.88) LA volumes (Figure 2). Patients with lone AF recurrence had a significantly larger maximum LA volume as assessed with both methods (P<0.05 for both) (Table).

Figure 1. Left atrial acoustic quantification waveforms recorded after the restoration of sinus rhythm in a patient with lone fibrillation.
Figure 2. Bland-Altman plots of minimum (top) and maximum (bottom) left atrial LA volumes determined by conventional manual tracing and acoustic quantification methods.
DISCUSSION

The present study has demonstrated that there is good agreement between manual tracing and AQ methods in determining LA minimal and maximal volumes. LA maximal volume soon after the sinus rhythm is restored—assessed either by conventional manual tracing or on-line AQ—is a predictor of AF recurrence during the 6 month follow-up. M-mode derived LA dimension and IVRT were additional parameters discriminating the two groups.

LA size and functions are affected by various disease states such as left ventricular systolic and diastolic dysfunction, cardiomyopathy, and valvular, ischemic, and hypertensive heart disease. LA dilatation is usually recognized on the M-mode and two-dimensional echocardiogram; ultrafast computerized tomography, magnetic resonance imaging and radionuclide methods have also been introduced to identify changes in LA volumes and functions. In routine clinical practice, the most commonly used approach has been the manual tracing method, which includes tracing the LA inner surface on a two-dimensional echocardiographic window providing the best image of the LA. The off-line and time-consuming nature of this measurement has made the more recent AQ method attractive, because it allows instantaneous cavity measurements to provide on-line assessment of chamber volumes. AQ studies have mostly focused on left ventricular functions; there are, to our knowledge, few studies in the literature applying this method to determine LA volumes in rhythm disturbances.

**Table.** Comparison of Demographic and Echocardiographic Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n=17)</th>
<th>Group 2 (n=11)</th>
<th>Control (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>38±8</td>
<td>37±5</td>
<td>38±6</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>11/6</td>
<td>8/3</td>
<td>7/3</td>
</tr>
<tr>
<td>HR</td>
<td>72±9</td>
<td>69±8</td>
<td>65±8</td>
</tr>
<tr>
<td>V-LA max-MT (mL)</td>
<td>48±4*</td>
<td>39±2</td>
<td>38±3</td>
</tr>
<tr>
<td>V-LA max-AQ (mL)</td>
<td>46±3*</td>
<td>35±2</td>
<td>33±2</td>
</tr>
<tr>
<td>V-LA min-MT (mL)</td>
<td>22±1</td>
<td>18±3</td>
<td>19±2</td>
</tr>
<tr>
<td>V-LA min-AQ (mL)</td>
<td>21±3</td>
<td>19±2</td>
<td>20±2</td>
</tr>
<tr>
<td>d-LA (cm)</td>
<td>3.9±1.6*</td>
<td>3.5±1.1</td>
<td>3.4±0.9</td>
</tr>
<tr>
<td>LVDD (cm)</td>
<td>5.2±0.5</td>
<td>5.0±0.7</td>
<td>4.9±0.5</td>
</tr>
<tr>
<td>EF (%)</td>
<td>65±6</td>
<td>67±4</td>
<td>64±7</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>70±6</td>
<td>73±7</td>
<td>72±7</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>93±12*</td>
<td>77±29</td>
<td>75±7</td>
</tr>
</tbody>
</table>

HR=heart rate; V=volume; LA=left atrium; MT=manual tracing; AQ=acoustic quantification; d=diameter; LVDD=left ventricular end-diastolic diameter; EF=ejection fraction; E=early diastolic velocity of transmitral flow, respectively; IVRT=isovolumic relaxation time. *Significantly different from both group 2 and controls (P<0.05).
agreement we observed between manual tracing and AQ methods in determining LA volumes is consistent with the findings of Zhang, et al who compared both techniques in patients with coronary artery disease with sinus rhythm.\(^{24}\)

Although prophylactic antiarrhythmic therapy lowers the relapses, the recurrence rate of AF is still high, predominantly occurring within the first month after cardioversion. Some clinical variables predicting the chance of maintaining sinus rhythm have been suggested, including the duration of AF, LA size, presence of rheumatic valvular disease, and low functional capacity.\(^{3,4}\) However, the data at hand fails to elucidate the specific recurrence predictors of lone AF, which by definition excludes the presence of any underlying heart disease. Our results emphasize that patients are more prone to AF recurrence if they had an increased anterior-posterior LA diameter, large maximal LA volume, and long IVRT. On the other hand, minimal LA volume was only slightly and insignificantly increased in group 1. This could be explained by the absence of an identifiable heart disease or long-standing AF that might potentially result in persistent morphological changes in atrial musculature, which might disturb its pump performance. A long IVRT in a subset of patients supports the hemodynamic study of Jais, et al who found that the end-diastolic left ventricular pressure and the nadir of the left atrial Y descent were significantly higher in lone AF patients versus controls, even though the patients were free of any evidence of diastolic dysfunction according to echocardiographic criteria.\(^{25}\)

**Study limitations:** In our study, LA volumes obtained by AQ were compared with those derived by manual tracing as a gold standard. Although a good correlation has been reported between LA volumes determined by manual tracing and angiography, this comparison fails to perfectly validate the accuracy of AQ in determining LA volumes. Furthermore, AQ is gain dependent and influenced by the respiratory cycle, image quality, and the variable distance of cardiac structures from the transducer. Finally, our study group was small and the study gives no information about a follow-up longer than 6 months.

**Conclusion:** In patients suffering an acute lone AF, LA maximal volume and M-mode diameter, and IVRT assessed after the restoration of sinus rhythm are predictors of AF recurrence during a 6 month follow-up. There was a good correlation between AQ and manually derived LA volumes, and the on-line and rapid features of AQ make it potentially useful for rapidly obtaining LA volumes.

**REFERENCES**