Left Atrial Spontaneous Echo Contrast in Patients With Rheumatic Mitral Valve Disease in Sinus Rhythm*  
Implication of an Altered Left Atrial Appendage Function in Its Formation

Yi-Heng Li, MD; Juely-Jen Huang, MD; Yu-Lin Ko, MD; Jiunn-Lee Lin, MD; Yung-Zu Tseng, MD, FCCP; Peiliang Kuan, MD; and Wen-Pin Lien, MD, FCCP

Thirty-nine patients who had rheumatic mitral valve disease in sinus rhythm were studied to compare echocardiographic and hemodynamic characteristics between those with and without left atrial (LA) spontaneous echo contrast. Patients were divided into two groups according to the presence (group 1, n=17) or absence (group 2, n=22) of the echo contrast. Transthoracic echocardiography and transesophageal echocardiography were performed in all patients within 1 week of cardiac catheterization study. Group 1 patients (5 men and 12 women; mean age, 47.7±13.1 years) showed smaller mitral valve area, greater transmitral valve pressure gradient, and absence of moderate to severe mitral regurgitation compared with group 2 patients (7 men and 15 women; mean age, 47.8±14.3 years). There was no significant difference in LA dimension, left ventricular end-systolic and end-diastolic dimensions, or in left ventricular ejection fraction between the two groups of patients. Left atrial appendage function was studied with Doppler in 26 patients. Patients (n=10) with LA spontaneous echo contrast had significantly lower LA appendage ejection fraction (20.34±10.76% vs 34.16±13.13%; p<0.05) and lower LA appendage peak emptying velocity (0.17±0.09 m/s vs 0.27±0.12 m/s; p<0.05) than those (n=16) without echo contrast. It is concluded that obstruction to mitral flow and altered LA appendage contractile function, not the LA size, are likely to be more important factors for the development of LA and LA appendage spontaneous echo contrast in patients with rheumatic mitral valve disease (predominant mitral stenosis) who are in sinus rhythm. These findings further substantiate that blood stasis in the LA cavity and the LA appendage is the mechanism fundamental to the formation of such spontaneous echo contrast.

*From the Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, Republic of China.
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Reprint requests: Dr. Lien, Dept of Internal Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei, 10016 Taiwan ROC

Spontaneous echo contrast in the left atrium (LA) is not an uncommon finding in patients with rheumatic mitral valve disease, as noted by transesophageal echocardiographic examinations.1,2 The clinical implications of such LA spontaneous echo contrast are its common association with LA thrombus formation and with subsequent systemic embolic phenomenon. In fact, LA spontaneous echo contrast has been reported to be an independent predictor for systemic arterial embolization in patients with mitral stenosis.2,3 A previous report3 has claimed the contribution of atrial fibrillation, LA enlargement, and severe mitral valve obstruction to the development of LA spontaneous echo contrast; atrial fibrillation is regarded as the most powerful single predictor. To our knowledge, there has been no report dealing with the characteristics of patients with rheumatic mitral valve disease in sinus rhythm who demonstrate such spontaneous echo contrast in the LA and LA appendage. This study was designed primarily to assess the echocardiographic features, including LA appendage function by Doppler, and hemodynamics of patients with rheumatic mitral valve disease in sinus rhythm who showed LA spontaneous echo contrast.

METHODS

Study Patients
A total of 39 patients with rheumatic mitral valve disease in sinus rhythm who were admitted to the National Taiwan University Hospital from January to December 1993 were
enrolled in this study. Their diagnosis of rheumatic mitral valve disease was based on clinical, electrocardiographic, roentgenologic, and echocardiographic examinations. All patients underwent cardiac catheterization studies. Four patients had undergone xenograft replacement at the mitral position and had developed xenograft dysfunction. The presence of sinus rhythm was confirmed by serial 12-lead electrocardiograms in all patients. Patients with previously documented atrial fibrillation or atrial flutter were excluded. All patients had mitral valve area ≥2.0 cm² as calculated by the Doppler method.4 Mitral regurgitation was categorized angiographically as grades 1 to 4, according to the criteria of Sellers et al.5 Of 35 patients with native valves, 7 had concomitant mitral regurgitation > grade 1. Among four patients with xenograft dysfunction, three had pure mitral stenosis and the remainder had grade 2 mitral regurgitation as well.

The 39 patients were classified into two groups based on the presence or absence of LA spontaneous echo contrast. Group 1 consisted of 17 patients (5 men and 12 women) with LA spontaneous echo contrast, ranging in age from 26 to 65 years (mean 47.7 ± 13.1). Of these, two were receiving oral anticoagulant treatment with warfarin at the time of study. Group 2 consisted of 22 patients (7 men and 15 women) without LA spontaneous echo contrast; their ages ranged from 31 to 79 years (mean 47.8 ± 14.3). At the time of study, one of them also was receiving oral anticoagulant treatment.

Echocardiographic Studies

Transthoracic M-mode echocardiography and two-dimensional echocardiography were performed in all patients using a color Doppler system (Aloka SSD 570, Aloka Corp Ltd, Tokyo, Japan) and a 2.5- or 3.75-MHz transducer. Patients were examined in the left lateral position, and standard left parasternal and apical views were used. Routine M-mode measurements were made according to the recommendations of the American Society of Echocardiography.6 Left ventricular ejection fraction was calculated by the method of Teichholz et al.7 The mitral valve area was measured by continuous-wave Doppler, according to the pressure half-time method.4 The mean transmitral pressure gradient was estimated from the maximal transvalvular flow velocity using a modified Bernoulli equation.8

Transesophageal echocardiography was done within 24 h of transthoracic study using the method described by Seward et al.9 Briefly, it was performed using a 5-MHz biplane transducer attached to the tip of a commercially available gastroscope that was connected to the same ultrasound imaging system. All patients had fasted for at least 4 h and had received local pharyngeal anesthesia with 2% lidocaine spray immediately before the insertion of the gastroscope. From the transgastric short-axis and four-chamber views, LA could be clearly visualized. The presence or absence of spontaneous echo contrast and/or thrombus was carefully examined and precise locations were specified if they were noted. The LA appendage was then examined by superior tilting of the gastroscope for detection of possible spontaneous echo contrast, thrombus, or both. The LA appendage area was measured by tracing a line from the limbus of the left upper pulmonary vein to the aorta at its shortest distance along the whole LA appendage endocardial border. The area was calculated by computed planimetry. The maximal LA appendage area was obtained at the onset of the p wave on electrocardiogram, while the minimal area was determined at the time of the QRS complex. The LA appendage ejection fraction (percent) was calculated as follows: (LA appendage maximal area)-(LA appendage minimal area)/(LA appendage maximal area) X 100. Pulse-wave Doppler study of the LA appendage flow was also performed. We placed the sample volume at the LA appendage cavity in proximity to its outlet, and Doppler flow pattern was recorded. In each case, peak emptying velocity was measured. A successive five values were averaged for the LA appendage areas and LA appendage flow, respectively.

Spontaneous echo contrast within the LA and LA appendage was diagnosed by the presence of dynamic clouds of echoes curling up slowly in a circular shape. The effect of excessive gain was excluded by adjusting the gain settings as required. The presence of thrombus was established by demonstrating an echogenic mass with echotexture different from that of the atrial wall despite alterations in gain settings. All the echocardiographic findings were carefully evaluated by two observers and any discrepancy in determination was resolved by consensus.

Cardiac Catheterization Study

Complete right and left heart catheterization was performed in each patient within 1 week of the echocardiographic studies. Pulmonary capillary wedge pressure, main pulmonary artery pressure, and left ventricular pressure were determined. Left ventriculography was performed in both oblique views, and the presence of mitral regurgitation, if any, was graded according to the criteria of Sellers et al.5

Systemic Arterial Embolization

The history of each patient was carefully reviewed for any suspicious event of systemic arterial embolization. All major embolic episodes were confirmed by surgery, angiography (peripheral artery), or both, or by computed tomography (brain) in addition to a history of clinical presentations typical of embolism.

Statistical Analysis

Statistical analyses were performed using the Student’s t test and χ² test. A probability value of less than 0.05 was considered statistically significant.

RESULTS

Clinical, Echocardiographic, and Hemodynamic Characteristics

The LA spontaneous echo contrast was detected in 17 (43.6%) of the 39 patients with rheumatic mitral valve disease in sinus rhythm by transesophageal echocardiography; none was detected by transthoracic echocardiography (p<0.001). All the spontaneous echo contrasts were present concomitantly in the LA and in the LA appendage. No spontaneous echo contrast in the LA appendage alone was observed. Of the 17 patients with spontaneous echo contrast (group 1), 2 were found also to have LA thrombus; both were confined to the LA appendage alone. No such thrombus, however, was found in the remaining 22 patients (group 2) without spontaneous echo contrast (p=not significant [NS]). Four patients gave a history of systemic arterial embolization, two each in both groups of patients (p=NS). The pertinent clinical profile, echocardiographic features, and hemodynamic data of the 39 patients are summarized in Table 1. Compared with the group 2 patients, patients in group 1 were characterized by smaller mitral valve area (p=0.003) and less severe mitral regurgitation (mitral regurgitation >grade 1, 1/17 vs 7/22; p=0.006). There was no significant difference
Table 1—Characteristics of Patients With (Group 1) and Without (Group 2) Left Atrial Spontaneous Echo Contrast*

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=17)</th>
<th>Group 2 (n=22)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>47.7±13.1</td>
<td>47.8±14.3</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>5/12</td>
<td>7/15</td>
<td>NS</td>
</tr>
<tr>
<td>Echo features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>42.3±6.6</td>
<td>47.0±7.8</td>
<td>NS</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>27.6±6.5</td>
<td>29.5±6.2</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>67.5±14.0</td>
<td>69.9±9.4</td>
<td>NS</td>
</tr>
<tr>
<td>LAD, mm</td>
<td>46.5±6.0</td>
<td>44.6±5.3</td>
<td>NS</td>
</tr>
<tr>
<td>MVA, cm²</td>
<td>0.9±0.3</td>
<td>1.3±0.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Transmital pressure gradient, mm Hg</td>
<td>12.2±6.0</td>
<td>6.2±3.8</td>
<td>0.002</td>
</tr>
<tr>
<td>LA thrombus</td>
<td>2/17</td>
<td>0/22</td>
<td>NS</td>
</tr>
<tr>
<td>Hemodynamic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PASP, mm Hg</td>
<td>42.7±11.7</td>
<td>37.9±15.3</td>
<td>NS</td>
</tr>
<tr>
<td>Mean PCWP, mm Hg</td>
<td>19.6±5.4</td>
<td>15.3±7.1</td>
<td>NS</td>
</tr>
<tr>
<td>MR&gt;grade 1</td>
<td>1/17</td>
<td>7/22</td>
<td>0.006</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>2/17</td>
<td>2/22</td>
<td>NS</td>
</tr>
</tbody>
</table>

*NS=not significant; LVEDD=left ventricular end-diastolic dimension; LVESD=left ventricular end-systolic dimension; LVEF=left ventricular ejection fraction; LAD=left atrial dimension; MVA=mitral valve area; PASP=pulmonary artery systolic pressure; PCWP=pulmonary capillary wedge pressure; MR=mitral regurgitation. Data are presented as mean±SD.

in age, gender, left ventricular end-systolic and end-diastolic dimension, left ventricular ejection fraction, or LA dimension between the two groups. Pulmonary artery systolic pressure or mean pulmonary capillary wedge pressure showed no significant difference. The transmitral valve pressure gradient, however, was significantly greater in group 1 than in group 2 patients (p=0.002).

Left Atrial Appendage Function

Twenty-six patients (10 in group 1 and 16 in group 2) were studied by Doppler for their LA appendage function during the transesophageal echocardiographic examinations. Characteristic biphasic LA appendage flow waves (Fig 1) could be clearly delineated in 25 patients. A so-called “akinetic” pattern (that is, no identifiable flow waves) was found in one other patient. As shown in Table 2, 10 patients (group 1) with LA spontaneous echo contrast had significantly lower LA appendage ejection fraction as well as lower LA appendage peak emptying velocity than did 16 patients (group 2) without LA spontaneous echo contrast (p<0.05 in both parameters). Although there existed considerable overlap between the two groups, the lower limit of LA appendage peak emptying velocity for patients without spontaneous echo contrast was approximately 0.15 m/s (Fig 2), and the LA appendage ejection fraction was approximately 20% (Fig 3). Six (60%) of the 10 patients in group 1 had LA appendage peak emptying velocity <0.15 m/s and LA appendage ejection fraction

![Figure 1](image1.png)  
**Figure 1.** Well-defined LA appendage emptying (arrow) and filling Doppler flow pattern in a patient with rheumatic mitral valve disease and sinus rhythm.

![Figure 2](image2.png)  
**Figure 2.** LA appendage peak emptying velocity of 26 patients with rheumatic mitral valve disease with (plus sign) and without (minus sign) LA spontaneous echo contrast.

Table 2—Comparison of Left Atrial Appendage Function in Patients With (Group 1) and Without (Group 2) Spontaneous Echo Contrast*

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=10)</th>
<th>Group 2 (n=16)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAA maximal area, (cm²)</td>
<td>9.91±3.75</td>
<td>8.20±2.99</td>
<td>NS</td>
</tr>
<tr>
<td>LAA minimal area, (cm²)</td>
<td>7.44±3.43</td>
<td>5.43±1.89</td>
<td>NS</td>
</tr>
<tr>
<td>LAA EF, %</td>
<td>20.34±10.76</td>
<td>34.16±13.13</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LAA peak emptying velocity, m/s</td>
<td>0.17±0.09</td>
<td>0.27±0.12</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*LAA=left atrial appendage; EF=ejection fraction. Data are presented as mean±SD.
Left Atrial Appendage Contractile Function in Rheumatic Mitral Valve Disease With Sinus Rhythm: Patients With Spontaneous Echo Contrast vs Those Without

Assessment of LA appendage contractile function in 26 patients with sinus rhythm found that patients with LA spontaneous echo contrast had significantly lower LA appendage ejection fraction and lower LA appendage peak emptying velocity than did those without such echo contrast. Recently, LA appendage and its contractile function have received much attention. Garcia-Fernandez et al. demonstrated the characteristic LA appendage Doppler flow patterns consisting of waves of filling and emptying in patients with sinus rhythm. They also found that larger LA appendage size was associated with a higher incidence of LA appendage echo contrast and thrombus formation. These results are consistent with those reported by Pollick and Taylor. In the present study, the mean LA appendage area of patients with LA appendage echo contrast was greater than that of those without the echo contrast; the difference between the two groups, however, did not reach a statistically significant level. In the previous study from our laboratory, impaired LA appendage contractile function was noted in patients with rheumatic heart disease, either of atrial fibrillation or sinus rhythm, when compared with those having no rheumatic heart disease. The present study dealt with rheumatic heart disease alone and we compared two groups of patients, one with the presence of LA spontaneous echo contrast and the other without. Rheumatic inflammatory process may involve both the LA and LA appendage resulting in impairment of LA and LA appendage contractile function. The condition with such change may worsen with subsequent occurrence of spontaneous echo contrast and, later, thrombus formation; this phenomenon probably begins with the LA appendage.

Correlation of Other Parameters With the Occurrence of Left Atrial Spontaneous Echo Contrast

The transmitral pressure gradient was greater and mitral valve area was smaller in those with spontaneous echo contrast, indicating that blood stasis in the LA cavity might be one of the mechanisms for the formation of such echo contrast. In fact, in these patients, significant mitral regurgitation (grade I of grading by Sellers et al.) was uncommon. The dimensions of the LA and left ventricle, as well as the left ventricular ejection fraction, did not differ between the two groups. The LA dimension has been reported to be greater in patients who had rheumatic mitral valve disease with atrial fibrillation and spon-

<20%; these values were noted only in 2 (12.5%) among the 16 patients without spontaneous echo contrast (group 2). There was, however, no significant difference between the two groups in the LA appendage areas.

**Discussion**

The present transesophageal echocardiographic study found LA spontaneous echo contrast in 43.6% of 39 patients with rheumatic mitral valve disease in sinus rhythm. This incidence was lower than in patients who had similar mitral valve lesions, but in atrial fibrillation (32 of 36 patients, 88%) as previously reported from this country. Interestingly, however, the spontaneous echo contrast in these patients was found concomitantly in the LA cavity and in the LA appendage; two of those with such echo contrast also showed evidence of thrombus formation confined to the LA appendage. Thus, hemodynamic characteristics of the LA appendage may play an important role in the formation of spontaneous echo contrast as well as the formation of thrombi in those with sinus rhythm. Previous reports on rheumatic mitral valve disease have emphasized the contribution of atrial fibrillation, LA enlargement, and severe mitral valve obstruction to the formation of LA spontaneous echo contrast; atrial fibrillation is regarded as the single most powerful predictor. In these reports, however, most patients with LA spontaneous echo contrast were in atrial fibrillation. Are there the same contributing factors for LA echo contrast formation in patients with rheumatic mitral valve disease and sinus rhythm?
tainous echo contrast;\textsuperscript{10,11} this seems not always the case in those with sinus rhythm. The LA size may be a less important factor for LA spontaneous echo contrast formation in patients having rheumatic mitral valve disease and sinus rhythm.

**Limitation of the Study**

For assessment of LA size, the standard M-mode criteria\textsuperscript{6} were used in this study. Although these criteria provide a good indicator for LA dilatation and have been used in many previous reports,\textsuperscript{2,3,11} LA area/volume measured by two-dimensional echo in the apical four-chamber view might be a better indicator for the LA dilatation. The mean LA dimension was equally increased (>40 mm) in our two groups of patients, irrespective of the presence or absence of spontaneous echo contrast. We dealt with patients in sinus rhythm rather than in atrial fibrillation; this might be the reason why the LA and LA appendage sizes did not correlate with spontaneous echo contrast, as shown by previous studies. However, this issue needs to be clarified by future study with more patients. In our practice, a large or huge LA is relatively uncommon in patients with rheumatic mitral valve disease (predominant mitral valve obstruction) in sinus rhythm.

In the present study, a small number of patients (two in group 1 and 1 in group 2 patients) were receiving oral anticoagulant treatment with warfarin at the time of study. The effect of anticoagulation in patients who have rheumatic heart disease in sinus rhythm with concomitant impaired LA appendage function cannot be evaluated in this small patient population.

**Clinical Implications**

In patients with rheumatic mitral valve disease, serial assessment of LA appendage contractile function may be important for prediction of the occurrence of spontaneous echo contrast in the LA and LA appendage. This is also true in patients with sinus rhythm. In the absence of a significant mitral regurgitation, for those patients with progressively deteriorating LA appendage contractile function, and occurrence of the intracavitary spontaneous echo contrast, early institution of anticoagulant therapy might be indicated for prevention of intracavitary thrombus formation and later occurrence of systemic arterial embolization, a not uncommon hazardous complication of rheumatic heart disease. However, the effect of this therapeutic strategy still needs further confirmation. For patients with symptomatic mitral valve obstruction with the echocardiographic evidence of intracavitary echo contrast or thrombus formation, of course, early surgery or interventional transvenous mitral commissurotomy is mandatory.

**Acknowledgment**

The authors thank Miss Mei-Huei Feng and Miss Yu-Hui Liu for their continuing help in the echocardiography laboratory.

**References**

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