Left Atrial Appendage Function and Thrombus Formation in Atrial Fibrillation-Flutter: A Transesophageal Echocardiographic Study

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Objectives. The purpose of this study was to investigate left atrial appendage size, function and thrombus prevalence in patients with atrial “fibrillation-flutter.”

Background. Thrombus formation and peripheral embolization in atrial fibrillation are related to left atrial appendage dysfunction. Embolization occurs less frequently in atrial flutter. It is not known whether the atrial appendage in fibrillation-flutter, which has an intermediate appearance on the surface electrocardiogram (ECG), has distinct characteristics that could affect thrombus formation.

Methods. Sixty-one patients with atrial tachyarrhythmias underwent transesophageal echocardiographic examination of the left atrial appendage. Appendage area, peak emptying velocity and the presence of thrombus and spontaneous echo contrast were determined. The results for 14 patients with fibrillation-flutter (based on ECG fibrillatory wave characteristics) were compared with those for 30 patients with atrial fibrillation and 17 patients with atrial flutter.

Results. Both fibrillation-flutter and atrial fibrillation were associated with chaotic appendage flow patterns with similarly low peak emptying velocities (18 ± 8 and 17 ± 10 cm/s, mean ± 1 SD), respectively. Atrial flutter was associated with a regular pattern of appendage contraction and a significantly higher peak emptying velocity (42 ± 18 cm/s, p < 0.0001). Mean appendage area was similar for fibrillation-flutter and fibrillation (6.3 ± 2.2 and 6.7 ± 2.1 cm², respectively) but was significantly smaller for atrial flutter (5.3 ± 1.4 cm², p < 0.05). The prevalence of left atrial appendage thrombus was similar for fibrillation-flutter and atrial fibrillation (40% and 29%, respectively), whereas no patient with atrial flutter had a thrombus (p < 0.05). Similarly, the presence of spontaneous echo contrast was higher for fibrillation-flutter (50%) and atrial fibrillation (40%) than for atrial flutter (6%, p < 0.05).

Conclusions. Left atrial appendage size and function in atrial fibrillation-flutter are indistinguishable from those of typical atrial fibrillation, and the frequency of thrombus and spontaneous echo contrast is similarly high. This is in contrast to atrial flutter, which is characterized by a smaller, more contractile left atrial appendage and a lower frequency of thrombus and spontaneous echo contrast.

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similar to atrial fibrillation or atrial flutter in regard to left atrial appendage size, function and thrombus formation.

Methods

Study patients. Over a 10-month period from August 1992 through May 1993, 63 patients (33 men, 30 women; mean \[\pm 1 SD\] age 67 \(\pm 12\) years) with atrial tachyarrhythmias, consecutively referred to the echocardiography service for transesophageal echocardiography, were prospectively studied. Two patients were excluded because of an eccentric mitral regurgitant jet that did not permit adequate Doppler interrogation of the left atrial appendage. Patients were classified into three groups based on their surface ECG: atrial fibrillation, fibrillation-flutter and atrial flutter. Baseline clinical characteristics were determined from chart review and patient interviews. Reasons for referral are listed in Table 1. The study protocol was approved by the Institutional Review Board of Columbia-Presbyterian Medical Center. Informed consent was obtained from each patient.

Electrocardiography. Twelve-lead ECGs and 6-s rhythm strips were obtained immediately after completion of the echocardiographic study in all patients. For our study, atrial fibrillation-flutter was defined by prominent fibrillatory waves in lead V\(_1\), having a maximal amplitude >1.0 mm (measured as previously described by Peter et al. [24]), an average cycle length \(<176\) ms (f-wave rate >340 beats/min), irregular f-f intervals and varying f-wave configuration. Atrial flutter and atrial fibrillation were defined using standard criteria (21). No patient shifted between atrial fibrillation and flutter during the ECG. Tracings were reviewed by two experienced electrophysiologists (J.C. and J.R.) who were unfamiliar of the echocardiographic results.

Previous ECGs were available for 34 of the 61 cases. All tracings done within the preceding 1 year were reviewed to determine possible alternation between arrhythmias and to assist in determining the duration of arrhythmia when not obvious from clinical history or chart review.

Transesophageal echocardiography. Studies were performed using a biplane 5-MHz phased-array transesophageal probe (Hewlett-Packard Sonos 1000). Images of the left atrial appendage were obtained in the transverse and longitudinal planes and recorded on \(\frac{1}{2}\)-in. VHS tape for analysis. The boundary of the base of the appendage was defined by a line drawn from the limbus of the left upper pulmonary vein to the exteriormost portion of the mitral annulus, just medial to the circumflex artery in the AV groove. Maximal left atrial appendage area was determined at end-systole by computed planimetry (average of three consecutive values). Peak left atrial appendage emptying velocity was measured by placing a pulsed wave Doppler sample volume just inside the base of the appendage. A mean value was obtained by averaging the peak deflection per cardiac cycle over five consecutive cycles. Measurements obtained in the longitudinal plane were used for analysis.

Thrombi were defined as masses adherent to the wall of the left atrial appendage with either independent motion or different echogenic density. Particular attention was paid to differentiation from pectinate muscles. Spontaneous echo contrast was defined as slowly swirling smokelike echoes within the appendage (Fig. 1). The gain was continuously adjusted to ensure the best possible visualization and avoid noise artifact. A consensus of two experienced echocardiographers (M.D. and S.H.) was used to define the presence or absence of thrombi and spontaneous echo contrast. Mitral regurgitation was assessed qualitatively on the basis of maximal area of the regurgitant jet (27). Recent transthoracic echocardiograms (within 2 weeks of the transesophageal studies) were available for 30 of the 61 cases for determination of left atrial dimensions in the parasternal long-axis view.

Statistical analysis. Data are expressed as a mean value ± 1 SD. Single-factor analysis of variance was used to compare continuous variables among three groups. Unpaired Student \(t\) test was used to compare continuous variables between two groups. The chi-square test was used for comparison of categoric variables, replaced by Fisher exact test in case of
Table 2. Clinical Variables: Group Comparisons

<table>
<thead>
<tr>
<th></th>
<th>AF (n = 30)</th>
<th>FF (n = 14)</th>
<th>AFL (n = 17)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>69 ± 10</td>
<td>65 ± 15</td>
<td>64 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>16/14</td>
<td>6/8</td>
<td>10/7</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>92 ± 10</td>
<td>85 ± 18</td>
<td>98 ± 18</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (53%)</td>
<td>7 (30%)</td>
<td>5 (29%)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>4 (13%)</td>
<td>1 (7%)</td>
<td>8 (47%)</td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>Neurovascular event</td>
<td>7 (23%)</td>
<td>6 (43%)</td>
<td>2 (12%)</td>
<td>NS</td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>8 (27%)</td>
<td>3 (21%)</td>
<td>4 (24%)</td>
<td>NS</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>12 (40%)</td>
<td>5 (36%)</td>
<td>6 (35%)</td>
<td>NS</td>
</tr>
<tr>
<td>Anticoagulation (&gt;21 days)</td>
<td>17 (57%)</td>
<td>4 (29%)</td>
<td>6 (36%)</td>
<td>NS</td>
</tr>
<tr>
<td>New arrhythmia (&lt;7 days)</td>
<td>4 (13%)</td>
<td>1 (7%)</td>
<td>5 (29%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*AF = atrial fibrillation; VS = versus atrial flutter and fibrillation-flutter versus atrial flutter. Abbreviations as in Table 1. Data presented are mean values ± 1 SD or number (%)."
The mean value of peak emptying velocity for all patients with thrombus was significantly lower than for patients without thrombus (15 ± 7 vs. 28 ± 17 cm/s, p < 0.005). The mean value of peak emptying velocity for patients with spontaneous echo contrast was also lower than for those without thrombus (12 ± 5 vs. 30 ± 16 cm/s, p < 0.0001). Left atrial appendage area and left atrial dimension did not differ significantly between patients with and without thrombus.

Significant (more than mild) mitral regurgitation was present in 20 patients (33%). Only one of these patients (5%) had spontaneous echo contrast compared with 19 of 41 patients (46%) with mild or no regurgitation (p = 0.01). A similar relation was not observed between mitral regurgitation and thrombus (p = 0.2).

**Discussion**

The ECG in atrial fibrillation is generally characterized by small baseline undulations of variable amplitude and morphology. These correspond to rapid, chaotic atrial depolarizations of irregular amplitude and cycle length, with an atrial "rate" greater than 330 beats/min on the atrial electrogram (26). Atrial activity in typical atrial flutter has a characteristic morphology on the ECG and is seen on the atrial electrogram as depolarizations of constant morphology and cycle length with rates between 240 and 340 beats/min, though more rapid forms can exhibit rates of 340 to 430 beats/min (28). Atrial fibrillation and atrial flutter are usually easily distinguishable. However, relatively nonchaotic forms of atrial fibrillation exist in which distinct, more uniform

**Figure 2.** Left atrial appendage Doppler flow pattern in a patient with atrial fibrillation. Irregular emptying (above the baseline) and filling (below the baseline) waves with low, variable velocity are identified. Vertical markers correspond to 20 cm/s.

**Figure 4.** Doppler flow pattern of a patient with atrial flutter. A regular emptying/filling pattern is present, and a dominant deflection of uniform velocity per cardiac cycle can be seen (>).

**Figure 5.** Comparison of left atrial appendage peak emptying velocities. Crossbars represent mean values ±1 SD. *p < 0.0001, atrial fibrillation and fibrillation-flutter versus atrial flutter.
atrial activity is seen on both the surface ECG and the atrial electrogram, periodically resembling atrial flutter (29). In addition, the alternation between atrial fibrillation and atrial flutter is not uncommon (30), and simultaneous coexistence of the two rhythms within a single atrium has been demonstrated (31,32). Thus, in certain cases a form intermediate between atrial fibrillation and atrial flutter, or "fibrillation-flutter," might be considered to exist.

Although it is generally accepted that organized atrial activity does not exist in atrial fibrillation, our study and others (5-8,10,11) demonstrate that discrete mechanical activity can exist in the left atrial appendage in atrial fibrillation, contributing to irregular flow. This study also demonstrates, however, that this activity is not related to the morphologic type of atrial fibrillation. Fibrillation-flutter, as we have defined it, is no more likely to have left atrial appendage mechanical activity than typical atrial fibrillation. The similarly high prevalence of thrombus and spontaneous echo contrast found in both groups is likely related to this finding. Notably, the fibrillation-flutter group was similar to the atrial fibrillation group with regard to all variables examined, including clinical heart failure and hypertension) and echocardiographic variables (left atrial dimension) that have been shown to be predictive of thromboembolism in atrial fibrillation (13,33). The findings in this study suggest that the risk of cardioembolic events in fibrillation-flutter is similar to that of atrial fibrillation and that indications for anticoagulation should also be similar. In addition, we found that regular and efficacious left atrial appendage contraction is present in atrial flutter, which may help explain the absence of thrombi seen in our study and the relatively small risk of cardioembolic events associated with this rhythm.

Appendage emptying velocity and thrombus. In this study, left atrial appendage thrombus presence was associated with low peak emptying velocity, found in patients with atrial fibrillation and fibrillation-flutter. No thrombus was found in the atrial flutter group, which had a higher emptying velocity. Velocities for atrial fibrillation and fibrillation-flutter were consistently low, and no significant difference was found between those with and without thrombi in these groups (15 ± 7 vs. 19 ± 11 cm/s, p = 0.08). Thus, although poor appendage contractility may be a prerequisite for thrombus formation, other factors such as duration of arrhythmia, anticoagulation status, and etiology of heart disease may also play a role in the groups with low velocity.

Doppler flow patterns. We have assumed that the Doppler flow patterns in the appendage are a result of active appendage contraction. Rapid oscillations of appendage area were observed by two-dimensional imaging in nearly all patients with atrial flutter (simultaneous with observed flutter-waves) and in several patients with atrial fibrillation and fibrillation-flutter, which would be difficult to explain by a purely passive mechanism. However, it is likely that passive emptying and filling contribute to some degree to the flow velocities generated. This could help explain the presence of the dominant deflection seen in atrial flutter, which occurred in diastole in 12 of 13 cases. Other investigators have recognized a minor early diastolic Doppler wave in sinus rhythm (9-11), and it has been suggested that the filling left ventricle compresses the medial wall of the appendage, causing some passive emptying in atrial fibrillation as well (5). In addition, early diastolic atrial blood flow over the appendage orifice has been proposed to facilitate passive emptying according to the Bernoulli principle (9). Augmented appendage emptying in atrial flutter in our study occurred more frequently in late to end-diastole (75%) rather than early diastole (25%).

Spontaneous echo contrast and mitral regurgitation. The presence of spontaneous echo contrast has been found to be predictive of thromboembolic events and is associated with left atrial thrombus formation (34). In our study a high prevalence of echo contrast was seen in the left atrial appendage of patients with both atrial fibrillation and fibrillation-flutter, and the presence of echo contrast was strongly associated with low emptying velocity. Because identification of spontaneous echo contrast may be less subjective than identification of small appendage thrombi, its presence might be a more reliable indicator of poor left atrial appendage function, though additional factors such as mitral regurgitation and/or stenosis and left ventricular dysfunction are probably related to its formation.

One-third of all patients in our study had more than mild mitral regurgitation. Although mitral regurgitation does not appear to affect appendage flow velocity (10), it has been shown to be associated with a lower frequency of left atrial spontaneous echo contrast (34). Similarly, we have observed a possible protective affect of mitral regurgitation against appendage spontaneous contrast formation, though this was not observed for thrombus formation.

Prevalence of appendage thrombus. In the present study, the number of patients with either atrial fibrillation or fibrillation-flutter who had left atrial appendage thrombi was notably high (16/44, 36%). In four previous studies, thrombi were found in 13% to 28% of patients with atrial fibrillation (5-7,35). This may have several explanations: 1) our study included a large number of patients referred for cerebrovascular events of presumed cardiac etiology, and nearly all had concomitant cardiovascular disease (only three patients had "lone" atrial fibrillation); 2) unlike previous studies using monoplane transesophageal echocardiographic probes, we used a biplane probe, which may increase the sensitivity for detecting small thrombi; and 3) the overwhelming majority (80%) of patients had chronic arrhythmias (duration >1 month), and 32% were not therapeutically anticoagulated.

The incidence of spontaneous echo contrast and that of thrombus in the combined atrial fibrillation/fibrillation-flutter group were similar (36% and 31%, respectively) in our study. Previous studies have demonstrated a prevalence of spontaneous contrast between 15% and 64% in atrial fibrillation (5-8,10,11), generally much higher than the prevalence of appendage thrombus. In addition to the unusually high prevalence of thrombus in our study already noted, this may be explained by the following: 1) in contrast to several of the studies cited, we reported spontaneous contrast to be
present if it was identified within the body of the appendage, not if it was present only within the main left atrial cavity, and 2) a large number of patients had significant mitral regurgitation, which might have reduced the incidence of spontaneous contrast.

Conclusions. Left atrial appendage function in atrial fibrillation-flutter is indistinguishable from that of typical atrial fibrillation and is significantly diminished compared with that seen in atrial flutter. The prevalence of thrombus and spontaneous echo contrast within the left atrial appendage is similarly high in this group. This suggests that the risk of cardiac embolism in fibrillation-flutter is similar to that of typical atrial fibrillation (and is lower for atrial flutter), and spontaneous echo contrast within the left atrial appendage is similarly high in this group. This suggests that the risk of cardiac embolism in fibrillation-flutter is similar to that of typical atrial fibrillation (and is lower for atrial flutter), and therefore indications for anticoagulation should not differ.

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References