Left Atrial Appendage Flow in Nonrheumatic Atrial Fibrillation*

Relationship With Pulmonary Venous Flow and ECG Fibrillatory Wave Amplitude

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Objective: This study was conducted (1) to examine the relationship between left atrial appendage (LAA) flow velocity and pulmonary venous flow (PVF) variables during nonrheumatic atrial fibrillation (AF), and (2) to determine whether a reduction in LAA flow is reflected by the fibrillatory wave amplitude on the surface ECG.

Background: Although LAA Doppler echocardiographic signals provide information regarding the velocity and direction of flow only for a localized narrow sample, systolic PVF represents in part the global left atrial function, mainly relaxation. Controversy exists about whether the amplitude of fibrillatory waves recorded on the surface ECG correlates with LAA flow velocity during AF.

Measurements and results: Thirty-three patients (20 men, 13 women; mean [± SD] age, 61 ± 11 years) with nonrheumatic AF undergoing transthoracic and transesophageal echocardiography were studied. A correlation between LAA flow velocity and systolic PVF variables (peak systolic velocity, R = 0.450, p = 0.009; velocity-time integral of systolic flow, R = 0.491, p = 0.004; systolic fraction of PVF, R = 0.627, p < 0.0001) was observed. Patients with a low LAA flow profile (< 25 cm/s) had a reduced systolic PVF. Longer AF duration and the occurrence of moderate mitral regurgitation were related to reduced LAA flow. AF was subdivided into coarse (peak-to-peak fibrillatory amplitude ≥ 1 mm) or fine (< 1 mm) in standard ECG lead V1. There was no association between the coarseness of AF and the LAA flow profile.

Conclusion: In patients with nonrheumatic AF, a reduction in LAA flow velocity correlates with a reduction in systolic PVF. These hemodynamic changes are not reflected by the ECG fibrillatory wave amplitude.

Key words: atrial fibrillation; ECG; left atrial appendage function; pulmonary venous flow; transesophageal echocardiography

Abbreviations: AF = atrial fibrillation; LAA = left atrial appendage; PVF = pulmonary venous flow; SEC = spontaneous echocardiographic contrast; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography; VTI = velocity-time integral

With the advent of transesophageal echocardiography (TEE), several flow patterns within the left atrial appendage (LAA) have been described in patients with sinus rhythm as well as atrial fibrillation (AF).1–3 LAA Doppler echocardiographic interrogation provides information regarding the velocity and

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ith the advent of transesophageal echocardiography (TEE), several flow patterns within the left atrial appendage (LAA) have been described in patients with sinus rhythm as well as atrial fibrillation (AF).1–3 LAA Doppler echocardiographic interrogation provides information regarding the velocity and direction of flow only for a localized narrow sample. In contrast, systolic pulmonary venous flow (PVF) represents in part global left atrial function, mainly relaxation.4 In patients undergoing cardioversion for AF, during sinus rhythm restoration of LAA function is accompanied by a normalization in transmitral flow and PVF pattern.5–8 Although AF has been shown to modify PVF,9–12 the association between LAA dysfunction expressed by a reduction in LAA flow velocity and PVF variables has not yet been systematically analyzed during AF.

Associations between AF causes,13 left atrial diameter,14–18 or atrial electrophysiology16,19 and fibrillatory

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wave amplitude have been investigated with conflicting results. Controversy also exists about whether LAA velocity correlates with the amplitude of fibrillatory waves recorded on the surface ECG.17,18

The purpose of this study was (1) to examine the relationship between LAA flow velocity and PVF variables during nonrheumatic AF, and (2) to determine whether a reduction in LAA flow is reflected by the fibrillatory wave amplitude on the surface ECG.

MATERIALS AND METHODS

Patients

The study group comprised 36 consecutive patients with nonrheumatic AF who underwent transthoracic echocardiographic (TTE) and TEE examination at our institution between February and July of 1998. All patients provided written informed consent.

Nonrheumatic AF was defined as AF in the absence of mitral stenosis, severe mitral regurgitation, or valve prosthesis. The duration of AF was calculated from the onset of symptoms or first ECG documentation to the performance of the echocardiographic examination. A detailed patient history was taken to identify associated cardiovascular morbidity and the use of anticoagulant or antiplatelet agents. None of the patients was taking any antiarrhythmic drugs during the study.

Three patients were excluded because of inadequate Doppler echocardiographic recordings from pulmonary veins. The remaining 33 patients formed the basis for this study.

Echocardiography

All patients were studied using a Sonotron Vingmed CFM 800 imaging system (Sonotron; Horten, Norway). Two-dimensional and Doppler TTE were performed before the TEE study with a 2.5- or 3.5-MHz transducer. Transthoracic measurements including left atrial diameter were obtained according to the standards of the American Society of Echocardiography.20,21 Left ventricular systolic function was defined as normal if there was no regional or global hypokinesis. If left ventricular dysfunction was present, it was quantified as mild, moderate, or severe.

TEE was performed using a 5-MHz multiplane phased-array transducer. Patients were studied in the fasted state after local anesthesia of the hypopharynx with 10% lidocaine spray. IV sedation was not routinely used.

The LAA was visualized from a transverse view, and flow profiles were obtained by pulsed Doppler echocardiographic interrogation at the orifice of the appendage with the lowest possible filter settings (5 to 10 cm/s). The maximal LAA area was determined by tracing a line from the top of the limbus of the left upper pulmonary vein along the whole appendage border.2 The flow profile was used to assess the LAA emptying velocity.

PVF was obtained by positioning the Doppler echocardiographic sample approximately 0.5 to 1 cm into the left upper pulmonary vein. Color Doppler echocardiographic imaging was used to determine a beam direction as parallel as possible to the PVF. Angle correction was not used. Measurements obtained from Doppler echocardiographic tracings included the peak velocity of flow waves and the velocity-time integral (VTI) for both systolic and diastolic flows. The systolic fraction of PVF was calculated as systolic VTI divided by the sum of the systolic and diastolic VTIs.11 Early systolic reverse flow was identified according to Paraskevaidis et al,12 and peak velocity was determined.

Specific attention was paid to the existence of spontaneous echocardiographic contrast (SEC) and any thrombus formation. SEC was ascertained by the presence of dynamic swirling smokelike echoes within the left atrium and the LAA using normal gain settings.22 Left atrial thrombus was diagnosed in the presence of a well-defined intracavitary echogenic mass, distinct from endocardium and pectinate muscles.

Mitral regurgitation was graded as mild or moderate depending on the width and depth of the regurgitation jets on color Doppler echocardiographic imaging.23

Representative transthoracic images and LAA images, as well as LAA flow and PVF signals (Fig 1), were digitized, stored on optical disk, and analyzed off-line with custom-made software.

In each patient, five consecutive cardiac cycles with stable flow signals obtained during end-tidal volume apnea were selected for analysis, and obtained values were averaged.

Electrocardiography

ECG recordings were performed in all patients before the echocardiographic examination. All recordings were made with the subject relaxed in a supine position after a 5-min equilibration period. A standard 12-lead ECG (Pagewriter XL; Hewlett Packard; Bad Homburg, Germany) was obtained at a paper speed of 50 mm/s and an amplitude of 10 mm/mV. Standard filter settings (0.5 to 40 Hz) were used. AF was subdivided into coarse and fine according to the method of Peter et al24 using lead V1. Coarse AF was defined as any peak-to-peak fibrillatory amplitude ≥ 1 mm. When all fibrillatory waves were < 1 mm, AF was classified as fine. Artifacts and T or U waves were carefully excluded. Fibrillatory waves were classified only in the T-QRS interval.

Interobserver Variability

Two independent observers measured left atrial diameter, LAA area, LAA flow velocity, PVF variables, and ECG fibrillatory amplitude. Interobserver variability was assessed by calculating the coefficient of variation. The coefficient of variation was < 5% for all measurements.

Two experienced echocardiographers evaluated all echocardiographic recordings for the presence of SEC, thrombus, degree of left ventricular function, and mitral regurgitation. Any discrepancy was resolved by consensus.

Data Analysis

All continuous variables are presented as mean ± SD. Correlation between LAA emptying velocity and PVF Doppler echocardiographic variables was evaluated by linear regression analysis. Clinical, echocardiographic, and ECG variables were compared for patients with a high LAA flow profile (LAA emptying velocity ≥ 25 cm/s) vs those with a low LAA flow profile (LAA emptying velocity < 25 cm/s).2 Differences between groups were assessed using Student’s t test for continuous variables and χ² test for categoric variables. A p value < 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

The clinical characteristics including TTE measurements of the 33 patients enrolled into the study were as follows. Their mean age was 61 ± 11 years (range, 39 to 80 years); 20 were men and 13 were...
women. AF duration ranged from 1 day to 13 years. In 9 patients, AF lasted < 6 months; the remaining 24 patients had a longer history of AF.

Cardiovascular conditions associated with AF included one or more of the following: essential hypertension (n = 18), coronary artery disease (n = 6), dilated cardiomyopathy (n = 5), and degenerative valvular heart disease (n = 7). Lone AF was present in four patients (12%). Cardiovascular comorbidity included stroke (n = 4) and transient ischemic attacks (n = 2). One patient suffered from hyperthyroidism.

Five patients received neither anticoagulant nor antiplatelet agents. Left atrial size measured 46 ± 5 mm. Moderate or severe left ventricular impairment was observed in 11 patients (33%). Moderate mitral regurgitation was found in five patients (15%) with left ventricular dysfunction.

AF was categorized as coarse in 16 patients (49%) and as fine in 17 patients (51%).

LAA Function and PVF

Mean LAA emptying velocity measured 25 ± 14 cm/s, showing a wide range between 10 and 52 cm/s.

LAA area measured 4.0 ± 2.0 cm². SEC was observed in 17 patients (51%), and LAA thrombus was detected in 8 patients (24%).

All patients had a biphasic PVF pattern, with one systolic and one diastolic forward wave. In all but four patients (86%), there was an early systolic reverse wave immediately after the onset of the QRS complex. Multiple backward waves corresponding with atrial contractions were observed in three patients (Fig 2). All of them had AF of short duration with high LAA flow profiles.

Variables of LAA function and PVF flow are summarized in Table 1. Systolic PVF expressed by peak velocity and VTI were lower than PVF during diastole.

The relationship between LAA flow velocity and PVF variables is depicted in Table 2. Correlations were observed between LAA flow velocity and systolic PVF variables. Among them, systolic fraction of PVF showed the closest relationship to LAA flow (Fig 3). This relationship was stable when analyzing all patients and patients with normal LV function separately. In contrast, diastolic PVF variables showed no correlation with LAA flow velocity.
Low and High LAA Flow Profiles

Two distinct LAA flow profiles were observed. There were 14 patients with a high-flow profile (LAA emptying velocity \( \geq 25 \text{ cm/s} \)) and 19 patients with a low-flow profile (LAA emptying velocity < 25 cm/s). The clinical, echocardiographic, and ECG characteristics of the two groups are summarized in Table 3. Patients with a high LAA flow profile exhibited a higher systolic PVF expressed by peak velocity, VTI, and systolic fraction of PVF. Longer AF duration and the occurrence of moderate mitral regurgitation were related to reduced LAA flow. In contrast, associated cardiovascular conditions, the use of anticoagulant and antiplatelet agents, and other echocardiographic variables including LAD, LAA area, and systolic left ventricular dysfunction were not different between groups. Diastolic PVF was similar between the two groups. Similarly, there was no difference in the occurrence of coarse or fine AF between the two groups.

LAA Function in Patients With AF

Different patterns of LAA filling and emptying as assessed by TEE have been described for patients in sinus rhythm as well as AF. In patients with AF, two flow patterns are known. Some patients may exhibit well-defined emptying and filling waves corresponding with LAA contractions, whereas in others, the LAA may act as a static pouch, and very low or no flow is observed.\(^{1-3}\) As with this study, a reduction in LAA flow velocity has been shown to depend on AF duration.\(^{25-27}\) In experimental and clinical sustained AF, a loss of contractile myofilaments has been found.\(^{28,29}\) The degree of contractile degeneration is reflected by the loss of mechanical LAA function expressed by a low LAA flow velocity. It has been shown by several investigators that the LAA dysfunction is of reversible nature. After cardioversion, a gradual recovery of contractile LAA function was observed. This was related to recovery from stunning of the left atrial chamber assessed by transmitral and PVF analysis.\(^{5-7}\)

PVF in Patients With AF

Doppler echocardiographic interrogation of PVF has been shown to be abnormal in various cardiac disorders such as constrictive pericarditis,\(^{30}\) hypertrophic and dilated cardiomyopathy,\(^{31,32}\) and cardiac amyloidosis.\(^{33}\) Approaches to quantify left atrial function from PVF in patients with AF are lacking. There are, however, several descriptive studies showing the influence of AF on PVF.\(^{9-12}\) Characteristic findings were the disappearance of atrial reverse flow, a decrease in systolic flow with a greater diastolic than systolic flow, a prolonged onset of systolic flow, and the appearance of an early systolic reverse flow.
A loss of the end-diastolic atrial reverse wave was observed in all our patients studied. This seems to be a typical finding in patients with AF. It can be explained by the loss of global active left atrial contractions. It is interesting to note that three of our patients exhibited multiple small reverse waves. Those waves seem to represent atrial contractions. This is supported by the fact that they corresponded to larger fibrillatory waves recorded on the ECG. All three patients had AF of short duration and preserved LAA function. Their systolic PVF was not reduced. One might speculate that left atrial contractions may still be present immediately after AF onset and diminish over time because of the loss of contractile filaments.

The measurements for systolic and diastolic PVF variables in this study are similar to those that have been reported previously. A reduction in systolic PVF expressed by reduced peak velocity, reduced VTI of systolic flow, and reduced systolic fraction of PVF were noted in previous studies and attributed to the existence of AF. We have observed a wide range of systolic PVF variables. The reduction of systolic PVF fraction corresponded closely to LAA dysfunction. Thus, PVF modification seems to reflect a change in left atrial function, mainly atrial relaxation, caused by the sustained arrhythmia rather than just a change in heart rhythm. This finding is supported by Hoit et al, who noted an increase in atrial stiffness after rapid atrial pacing in dogs, resulting in a reduction in systolic PVF.

Because severe mitral regurgitation also affects systolic PVF, those patients were not included in our study.

In contrast to systolic PVF, the diastolic PVF showed no relationship to LAA dysfunction. This observation is supported by findings from Ren et al, who showed similar diastolic PVF variables for patients in sinus rhythm and AF.

In all but three of our patients, an early systolic reverse wave was observed. Paraskevaidis et al described this wave in all 20 patients studied. The authors explained this finding as an abnormal motion of the mitral annulus toward the left atrium starting with the onset of ventricular contraction.

**LAA Function and Fibrillatory Wave Amplitude**

AF is characterized by disorganized atrial electrical activity. The ECG manifestation can be subdivided into coarse or fine AF according to the fibrillatory wave amplitude. Usually, standard ECG lead V1 is used for the analysis of AF characterization, and an amplitude greater than 1 mm describes AF as coarse.

Few studies have investigated the relationship between LAA flow velocity and fibrillatory wave amplitude during AF. The results of these studies are conflicting. Li et al have studied 78 patients with AF using TEE. They found that patients with coarse AF had a lower LAA velocity and subsequently higher rates of SEC as well as thrombus formation. In contrast, Blackshear et al, similar to our study, demonstrated no correlation between fibrillatory wave size and LAA flow velocity in 53 patients enrolled in the Stroke Prevention in Atrial Fibrillation III trial. In this study with an average

![Figure 3. Correlation between systolic fraction of PVF and LAA emptying velocity.](image-url)

Table 2—Correlation of PVF Doppler Echocardiographic Variables With LAA Emptying Velocity

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Patients</th>
<th>Normal LV Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early systolic flow velocity, cm/s</td>
<td>0.133</td>
<td>NS</td>
</tr>
<tr>
<td>Peak systolic velocity, cm/s</td>
<td>0.450</td>
<td>0.009</td>
</tr>
<tr>
<td>Peak diastolic velocity, cm/s</td>
<td>0.130</td>
<td>NS</td>
</tr>
<tr>
<td>VTI of systolic flow, cm</td>
<td>0.491</td>
<td>0.004</td>
</tr>
<tr>
<td>VTI of diastolic flow, cm</td>
<td>0.092</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic fraction of PVF, %</td>
<td>0.627</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

*LV = left ventricular; NS = not significant.
follow-up of 1.3 years, fibrillatory amplitude was not related to a thromboembolic risk.

The mechanisms behind the ECG manifestation of fibrillatory wave size or its relationship to echocardiographic variables are not fully understood. Strassburger and Klepzig35 have explained coarse AF by atrial hypertrophy. Although Morganroth et al16 have hypothesized that coarse AF reflects intra-atrial conduction abnormalities, coarse AF has been shown by others to correlate with more organized AF.19 Roithinger and colleagues19 studied 16 patients with nonrheumatic AF. They found that during organized right free-wall activation a stable 1:1 relationship to distinct fibrillatory waves in the ECG lead V1, similar to atrial flutter, was present. Patients with atrial flutter are known to have a higher LAA flow velocity than those with AF or fibrillation-flutter.36,37 Although in contrast to the findings of Li and colleagues,18 one would then expect a better LAA function in patients with coarse AF.38 Differences in recording techniques15,39 or cut values ranging from 0.05 mV40 to 0.12 mV19 to differentiate coarse from fine AF may also contribute to the conflicting results.

**Clinical Implications**

To the best of our knowledge, this study is the first to characterize the relationship between LAA flow and PVF variables in patients with AF. Patients with LAA dysfunction have a higher prevalence of SEC with subsequent thrombus formation and thrombo-embolic events,1–3 as well as a higher recurrence rate of AF after cardioversion.41–43 Although assessment of LAA flow only reflects a localized function, systolic PVF is a global marker for left atrial function. Therefore, the reduction in systolic PVF might be used as a variable for left atrial dysfunction and subsequently AF severity. In contrast, fibrillatory wave amplitude seems not to be associated with LAA flow profiles.

**Study Limitations**

Our study population represented a rather heterogeneous group of patients with different cardiac disorders. Factors other than left atrial dysfunction might have influenced PVF.10 The cause of AF, however, was restricted to patients with nonrheumatic causes. As the majority of our patients received anticoagulant medication and thrombus resolution with warfarin therapy has been described,44,45 the same prevalence of thrombus formation in patients with low and high LAA flow does not indicate conflicting data.

Both LAA function and PVF were assessed using TEE. Therefore, further studies must demonstrate the applicability of these results to transthoracic studies and the role of PVF variables in AF management. However, a close relationship between TTE-derived and TEE-derived measurements has been reported previously.46

Although 2-min recordings of LAA flow and PVF were made and representative tracings were selected for analysis, temporal variability of those measurements cannot be excluded.

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Similarly, intermittent changes in fibrillatory amplitude could not be excluded, even though short ECG segments are sufficient to distinguish coarse from fine AF.24 As already pointed out by Blackshear et al,17 nonsimultaneous ECG and echocardiographic variables were not synchronized in all recordings.
graphic examination does not exclude that a relationship between fibrillatory amplitude and LAA velocity may exist.

CONCLUSION

In patients with nonrheumatic AF, a reduction in LAA flow velocity correlates with a reduction in systolic PVF. These hemodynamic changes are not reflected by the ECG fibrillatory wave amplitude.

REFERENCES


