Clinic value of left atrial appendage flow velocity for predicting cardioversion success in patients with non-valvular atrial fibrillation

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Background Echocardiographic parameters for predicting cardioversion outcome in patients with non-valvular atrial fibrillation are not accurately defined.

Objective To evaluate the role of left atrial appendage flow velocity detected by transoesophageal echocardiography for prediction of cardioversion outcome in patients with non-valvular atrial fibrillation enrolled in a prospective, multicentre, international study.

Methods Four hundred and eight patients (257 males, mean age: 66 ± 10 years) with non-valvular atrial fibrillation lasting more than 48 h but less than 1 year underwent transthoracic echocardiography and transoesophageal echocardiography before either electrical (n=324) or pharmacological (n=84) cardioversion.

Results Cardioversion was successful in restoring sinus rhythm in 328 (80%) and unsuccessful in 80 patients (20%). Mean left atrial appendage peak emptying flow velocity was significantly higher in patients with successful than in those with unsuccessful cardioversion (32.4 ± 17.7 vs 23.5 ± 13.6 cm·s⁻¹; P<0.0001). At multivariate logistic regression analysis, three parameters proved to be independent predictors of cardioversion success: the atrial fibrillation duration <2 weeks (P=0.011, OR=4.9, CI 95%=1.9–12.7), the mean left atrial appendage flow velocity >31 cm·s⁻¹ (P=0.0013, OR=2.8, CI 95%=1.5–5.4) and the left atrial diameter <47 mm (P=0.093, OR=2.0, CI 95%=1.2–3.4). These independent predictors of cardioversion success outperformed other univariate predictors such as left ventricular end-diastolic diameter <58 mm, ejection fraction >56% and the absence of left atrial spontaneous echo contrast.

Conclusion In patients with non-valvular atrial fibrillation, measurement of the left atrial appendage flow velocity profile by transoesophageal echocardiography before cardioversion provides valuable information for prediction of cardioversion outcome.


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Key Words: Transoesophageal echocardiography, atrial fibrillation, cardioversion.

Introduction

There are few clinical and echocardiographic predictors of cardioversion success in patients with non-valvular atrial fibrillation, such as the duration of the atrial fibrillation and the diameter of the left atrium[1,2].

Moreover, the predictive value of these parameters is far from optimal[3]. In order to minimize patient risk and to reduce health care costs it is essential to establish more precise predictors of cardioversion outcome. In recent years transoesophageal echocardiography has become an accepted tool in the management of patients with atrial fibrillation by screening for left atrial appendage thrombi and allowing earlier cardioversion[4–7]. Furthermore, the assessment of thrombembolic risk by measurement of left atrial appendage velocities during transoesophageal echocardiography in atrial fibrillation has become widely accepted[8–10].


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Recent studies have suggested that the conversion (drug induced or electrical) from atrial fibrillation to sinus rhythm may be predicted by evaluating left atrial appendage velocities before cardioversion[11,12]. However, this finding has been challenged by other reports[13,14], and the conclusions are weakened by the small sample size, heterogeneous patient population and retrospective design of the available studies[11–14]. Prospective studies are needed at this point to clarify the predictive capability of left atrial appendage velocities for cardioversion success and their additional value, if any, over other established echocardiographic and clinical predictors. To this purpose, we evaluated in a prospective, four centre, international study design 408 consecutive patients with non-valvular atrial fibrillation lasting <1 year prior to the pharmacological or electrical cardioversion attempt. Transeosophageal echocardiography was performed 24 h before the cardioversion attempt with commercially available ultrasonographic systems (Hewlett Packard Sonos 2500 and 5500, Acuson XP128 and Sequoia; ATL HDI 9). The indication for transoesophageal echocardiography in all cases involved ruling out intracardiac thrombi before the cardioversion attempt. Transeosophageal echocardiography

### Methods

#### Study group

Four hundred and eight patients with non-valvular atrial fibrillation lasting longer than 48 h and less than 1 year were recruited consecutively from the Albert Szent-Györgyi Medical University, Szeged, Hungary, the SS. Annunziata Hospital, Savigliano, Italy, the Mauriziano Umberto I' Hospital, Turin, Italy and the Institute of Clinical Physiology, Pisa, Italy between December 1997 and October 2000. Exclusion criteria were: duration of atrial fibrillation of >1 year, unknown duration of atrial fibrillation, organic valvular heart disease, presence of prosthetic valve, pericarditis, pericardial effusion, acute myocarditis, acute myocardial infarction, chronic obstructive lung disease, pulmonary embolism, congenital heart disease, recent heart surgery, latent or manifest hyperthyroidism, permanent pacemaker treatment, sick sinus syndrome and presence of atrial thrombus found by transoesophageal echocardiography. The patients' demographic and clinical characteristics are shown in Table 1.

#### Echocardiography

Echocardiographic variables

### Table 1  Clinical and echocardiographic variables in patients with and without successful cardioversion (n=408)

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>All patients n=408</th>
<th>Success n=328</th>
<th>Failure n=80</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>66 ± 10</td>
<td>66 ± 10</td>
<td>65 ± 9</td>
<td>ns</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>257 (63%)</td>
<td>205 (63%)</td>
<td>52 (65%)</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>33 (8%)</td>
<td>25 (8%)</td>
<td>8 (10%)</td>
<td>ns</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>235 (58%)</td>
<td>196 (60%)</td>
<td>39 (49%)</td>
<td>ns</td>
</tr>
<tr>
<td>Ischaemic heart disease (%)</td>
<td>46 (11%)</td>
<td>38 (12%)</td>
<td>8 (10%)</td>
<td>ns</td>
</tr>
<tr>
<td>Prior myocardial infarction (%)</td>
<td>29 (7%)</td>
<td>26 (8%)</td>
<td>3 (4%)</td>
<td>ns</td>
</tr>
<tr>
<td>Atrial fibrillation duration (days)</td>
<td>46 ± 75</td>
<td>40 ± 66</td>
<td>81 ± 107</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Atrial fibrillation duration &gt;2 weeks</td>
<td>302 (74%)</td>
<td>229 (70%)</td>
<td>73 (91%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Transthoracic echocardiographic variables

| LA diameter (mm)                           | 45 ± 6.0           | 44.6 ± 5.9   | 46.6 ± 6.1  | <0.01   |
| LA diameter >47 mm (%)                     | 136 (33%)          | 97 (30%)     | 39 (49%)    | <0.01   |
| % LVEF                                     | 54.3 ± 12.7        | 54.9 ± 12.8  | 52.1 ± 12.0 | <0.077  |
| LV EDD (mm)                                | 54.1 ± 7.4         | 53.6 ± 7.3   | 55.9 ± 7.6  | <0.05   |
| LV EDD >58 mm (%)                          | 116 (28%)          | 85 (26%)     | 31 (39%)    | <0.01   |
| LVS thickness (mm)                         | 10.9 ± 1.9         | 11 ± 1.9     | 11 ± 1.8    | ns      |
| LV PW thickness (mm)                       | 10.3 ± 3.3         | 10.3 ± 3.5   | 10.3 ± 3.4  | ns      |

### Transoesophageal echocardiographic variables

| Presence of left atrial SEC (%)            | 233 (57%)          | 178 (54%)    | 55 (69%)    | <0.05   |
| Degree of mitral valve regurgitation (%)  | 334 (82%)          | 273 (83%)    | 61 (76%)    | ns      |
| Medium                                     | 55 (13%)           | 39 (12%)     | 14 (18%)    | ns      |
| Severe                                     | 21 (5%)            | 16 (5%)      | 5 (6%)      | ns      |
| Mean LAA peak anterograde flow (cm . s⁻¹)  | 30.6 ± 17.2        | 32.4 ± 23.5  | 23.5 ± 13.6 | <0.001  |
| Mean LAA peak anterograde flow <31 cm . s⁻¹ (%) | 244 (60%)        | 178 (54%)    | 66 (83%)    | <0.001  |

LA=left atrium; LVEF=left ventricular ejection fraction; LV PW=left ventricular posterior wall; LVS=left ventricular septum; LV EDD=left ventricular end-diastolic diameter; SEC=spontaneous echo contrast; LAA=left atrial appendage.
was performed with bi- or multiplane probes with a 5·0 or 7·0 MHz transducer. The following transthoracic echocardiographic measurements were taken by parasternal long-axis view from 2-D targeted M mode tracings according to the recommendations of the American Society of Echocardiography[15]: left atrial diameter, left ventricular end-diastolic and end-systolic diameter, left ventricular septal and posterior end-diastolic wall thickness, ejection fraction (according to the Quinones formula).

The two dimensional biplane area–length method was used to calculate the ejection fraction in patients with previous infarction. All transthoracic echocardiographic indices were measured offline, using the integrated software of the echocardiographic equipment and were calculated as the average of five consecutive cardiac cycles. Following transthoracic echocardiography and after a 6 h fast all patients underwent examination by transoesophageal echocardiography. During the transoesophageal echocardiography, images were analysed on-line, by an experienced observer, for the presence of intracardiac thrombus. In order to view the maximal size and to obtain the highest resolution of the left atrial appendage, the most appropriate section was used for the analysis. The gain was continuously adjusted to ensure the best possible visualization and to avoid noise artifact. A thrombus was considered to be present when a well-circumscribed echodense intracavitary mass that was acoustically distinct from the underlying endocardium was detected[16].

Patients demonstrating intracardiac thrombus during transoesophageal echocardiography were excluded from the study. Videotape and/or digitally stored images were subsequently analysed off-line for the presence of left atrial spontaneous echo contrast and mitral valve regurgitation grade by two independent observers, unaware of the patients’ history. Spontaneous echo contrast was defined as an intracavitary swirling smoke-like echo within the left atrium or left atrial appendage[17]. Mitral regurgitation was qualitatively graded by colour flow Doppler mapping as none, mild, moderate or severe on the basis of regurgitant jet area and spatial distribution of the regurgitant flow[18]. Differences between observers were resolved by consensus; if observers could not agree, a third more experienced observer reviewed the study and his judgement was binding. Left atrial appendage velocity profiles were obtained by pulsed-wave Doppler interrogation from 1 cm within the orifice of the left atrial appendage and analysed off-line from videotape or digitally stored images by a single observer, A.P., unaware of the patients’ history. Left atrial appendage peak emptying velocities were averaged with each RR interval over a minimum of five consecutive cardiac cycles[11,12].

Figure 1 Pulsed Doppler tracing of the left atrial appendage obtained by transoesophageal echocardiography in atrial fibrillation. It shows high peak emptying flow velocity signals in a patient with successful cardioversion. The mean left atrial appendage peak anterograde flow velocity was 52 cm . s⁻¹.
Cardioversion

All patients underwent either pharmacological (n=84) or electrical cardioversion (n=324). The physician in charge decided on which to choose. Electrical cardioversion was performed in the coronary care unit or electrophysiology laboratory after the induction of anaesthesia (propofol 0.8 to 1.4 mg·kg⁻¹) and an initial synchronized direct current shock at 150 J from the anterior-lateral paddle position. If necessary, the procedure was repeated with 200, 300, and up to a maximum of 360 J. In no instance was endotracheal intubation necessary. Pharmacological cardioversion was attempted with intravenous propafenone (n=30), oral quinidine sulphate in combination with metoprolol if a high ventricular rate was present (n=25), intravenous and/or oral amiodarone (n=21) and flecainide (n=8). All patients underwent permanent electrocardiographic monitoring during the cardioversion procedure. Continuous electrocardiographic monitoring was performed after successful restoration of sinus rhythm for 24 h to assess maintenance of sinus rhythm. Successful cardioversion was defined as a stable sinus rhythm lasting for at least 1 day after successful conversion[19,20]. All patients had an appropriate anticoagulation level at the point of cardioversion — including those with a short duration of atrial fibrillation, who were treated by intravenous heparin and subsequent oral anticoagulation therapy. Oral anticoagulation was prolonged for 4 weeks after successful restoration of sinus rhythm and continuously maintained in those in whom cardioversion failed.

Statistical analysis

All data are expressed as means ± standard deviation. Statistical significance was assessed by Student’s t-test for continuous variables. Comparison of proportions was performed using chi-square analysis. Receiver–operating characteristic analysis was used to determine the optimal cut-off value for prediction of cardioversion with respect to the left atrial parasternal diameter, left ventricular end-diastolic dimension, ejection fraction, the mean left atrial appendage peak anterograde flow velocity, and the duration of atrial fibrillation. The best cut-off value was defined as the point with the highest sum of sensitivity and specificity. Univariate and multivariate logistic regression analysis for assessment of cardioversion success was performed using an SPSS 9.0 software package. All tests were two-sided, and a P value <0.05 was considered significant.
**Results**

**Cardioversion**

Thirty five out of 84 patients (42%) who underwent attempted pharmacological cardioversion had less than 2 weeks atrial fibrillation; 71 out of 324 patients (22%) who underwent attempted electrical cardioversion also had less than 2 weeks atrial fibrillation. Cardioversion was successful in 328 (80%) and unsuccessful in 80 (20%) patients. Electrical cardioversion effectively restored the sinus rhythm in 266 of 324 patients (82%) with an average of 2.5 shocks (range 1–4) and a cumulative 552 ± 314 J energy dose. During attempted pharmacological cardioversion, 62 of 84 patients (74%) converted to sinus rhythm. There were no important side effects during either pharmacological or electrical cardioversion.

**Clinical parameters and successful cardioversion**

There were no differences in age, sex and underlying diseases between patients with and without successful conversion (Table 1). Successfully converted patients had shorter atrial fibrillation duration than those whose cardioversion failed (Table 1). On the basis of a receiver–operating characteristic analysis, an atrial fibrillation duration cut-off value of 2 weeks provided the best separation between patients with and without successful restoration of sinus rhythm (shorter in patients with successful cardioversion) (Table 1).

**Echocardiographic parameters and successful cardioversion**

On the basis of transthoracic echocardiographic parameters, successfully cardioverted patients had a lower left ventricular end-diastolic diameter and left atrial parasternal diameter. Left ventricular ejection fraction tended to be higher in patients with successful cardioversion, whereas left ventricular wall thickness was not related to the outcome of cardioversion (Table 1). On the basis of a receiver–operating characteristic analysis, cut-off values of a left atrial diameter <47 mm, a left ventricular end-diastolic diameter <58 mm and a left ventricular ejection fraction >56% provided the best separation between patients with and without successful cardioversion. Transoesophageal echo parameters could also distinguish between the two groups on the basis of the mean left atrial appendage peak anterograde flow (higher in patients with cardioversion success) and the presence of left atrial spontaneous echo contrast (less frequent in patients with cardioversion success), whereas no difference could be observed when the degree of mitral valve regurgitation was considered (Table 1). Typical examples of high and low flow velocity profiles of the left atrial appendage in atrial fibrillation, obtained by pulsed Doppler during transoesophageal echocardiography in patients with and without successful cardioversion are shown in Figs 1 and 2, respectively. According to a receiver–operating characteristic analysis (Fig. 3), a mean left atrial appendage peak anterograde flow velocity >31 cm·s⁻¹ could best distinguish between patients with and without successful cardioversion (Table 1).

**Prediction of cardioversion by integrated clinical, transthoracic and transoesophageal echocardiographic variables**

Univariate logistic regression analysis revealed that the mean left atrial appendage peak anterograde flow velocity >31 cm·s⁻¹ was the most powerful predictor of successful cardioversion, followed by atrial fibrillation duration <2 weeks, left atrial diameter <47 mm, left ventricular ejection fraction >56%, absence of left atrial spontaneous echo contrast during transoesophageal echocardiography and the left ventricular end-diastolic diameter <58 mm (Table 2). By multivariate logistic regression analysis, three parameters proved to be independent predictors of cardioversion success: atrial fibrillation duration <2 weeks, followed by the mean left atrial appendage peak anterograde velocity >31 cm·s⁻¹ and left atrial parasternal diameter <47 mm (Table 2).

**Discussion**

The results of our study show that measurement of the left atrial appendage emptying velocity profile by
transoesophageal echocardiography in patients with non-valvular atrial fibrillation before cardioversion provides valuable additional information for prediction of cardioversion success.

**Comparison with previous studies**

Left atrial appendage flow velocities in patients with atrial fibrillation are highly variable, with high flow velocity at one end (velocities similar to, or even higher, than those observed in sinus rhythm), and minimal to absent flow velocities at the other end of the spectrum. This represents the wide continuum of left atrial appendage contractile dysfunction in patients with atrial fibrillation, from relatively preserved contraction to complete paralysis of the appendage.

Previous studies have already demonstrated that left atrial appendage velocity is related to the left atrial size and the duration of atrial fibrillation, all of which are predictors of cardioversion success. Furthermore, recent reports have suggested that the success of cardioversion (drug induced or electrical) in patients with non-valvular atrial fibrillation may be predicted by assessing left atrial appendage function before cardioversion, although this was not a uniform observation. Mitusch et al. reported transoesophageal echocardiographic data from 93 patients with non-valvular atrial fibrillation. They found a significant difference in left atrial appendage peak emptying velocity between patients with and without successful cardioversion. Although our results are consistent with those of Mitusch et al., one should consider that in the majority of their patients atrial fibrillation duration was longer than 1 year and, moreover, in half of those who converted to sinus rhythm the left atrial appendage velocity was measured only after restoration of the sinus rhythm, creating a methodologically heterogeneous study group.

Our data are also in keeping with the results obtained by Tabata et al. assessing the left atrial appendage flow velocities by transoesophageal echocardiography before cardioversion in patients with non-valvular atrial fibrillation. However, they studied only a small group of patients (n=26) which weakened their conclusion. In contrast, in a study of 82 patients with atrial fibrillation <6 months, Perez et al. found no relationship between left atrial appendage flow velocities and outcome of the cardioversion. However, in this study the small number of patients with failure of cardioversion (n=7) led to a high level of beta-error: i.e. high probability of rejecting as false an existing difference between groups. In another study of 62 patients with non-valvular atrial fibrillation, Verhorst et al. were unable to show a difference in left atrial appendage velocity values between successful and unsuccessful cardioversion groups, but the left atrial appendage flow velocities tended to be higher in patients who converted to sinus rhythm. Similarly, as reported in previous studies, we also found that the duration of atrial fibrillation is a predictor of successful conversion. However, in a substantial number of patients with atrial fibrillation of non-valvular aetiology, the duration of the atrial fibrillation is either unknown or cannot be determined accurately, which weakens the clinical value of this parameter.

In broad terms, our results are therefore consistent with previous reports. However, our study is also unique for several reasons: (1) the prospective, multicentre design; (2) the large number of patients enrolled (408, whereas previous studies enrolled 25 to 82 patients); (3) the strict selection criteria. The relatively large sample size allowed us to demonstrate that the mean left atrial appendage peak emptying velocity has independent and additive prognostic value over other clinical and echocardiographic predictors.

**Study limitation**

The study population may appear heterogeneous with regard to the clinical parameters such as duration of atrial fibrillation, mode of cardioversion, type of chemical cardioversion protocol, but it corresponds to the

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**Table 2 Univariate and multivariate predictors of successful cardioversion outcome**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>P value</th>
<th>Chi-square</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular end-diastolic diameter &lt;58 mm</td>
<td>0.0236</td>
<td>5.1</td>
<td>1.8 (1.1-3.0)</td>
</tr>
<tr>
<td>Absence of left atrial SEC during TEE</td>
<td>0.0201</td>
<td>5.4</td>
<td>1.9 (1.1-3.1)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction &gt;56%</td>
<td>0.0029</td>
<td>8.8</td>
<td>2.1 (1.3-3.5)</td>
</tr>
<tr>
<td>Left atrial diameter &lt;47 mm</td>
<td>0.0013</td>
<td>10.3</td>
<td>2.3 (1.4-3.7)</td>
</tr>
<tr>
<td>Atrial fibrillation duration &lt;2 weeks</td>
<td>0.0001</td>
<td>15.6</td>
<td>6.6 (2.6-16.7)</td>
</tr>
<tr>
<td>Mean peak anterograde LAA flow velocity &gt;31 cm . s⁻¹</td>
<td>0.0001</td>
<td>19.2</td>
<td>4.0 (2.1-7.4)</td>
</tr>
</tbody>
</table>

**Multivariate predictors**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>P value</th>
<th>Chi-square</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrial diameter &lt;47 mm</td>
<td>0.0093</td>
<td>6.8</td>
<td>2.0 (1.2-3.4)</td>
</tr>
<tr>
<td>Mean peak anterograde LAA flow velocity &gt;31 cm . s⁻¹</td>
<td>0.0013</td>
<td>10.4</td>
<td>2.8 (1.5-5.4)</td>
</tr>
<tr>
<td>Atrial fibrillation duration &lt;2 weeks</td>
<td>0.0011</td>
<td>10.6</td>
<td>4.9 (1.9-12.7)</td>
</tr>
</tbody>
</table>

SEC=spontaneous echocontrast; TEE=transoesophageal echocardiography; LAA=left atrial appendage.
variable clinical situations encountered in hospital practice. The conclusions of this study can therefore be reasonably applied to the general population of patients with non-valvular atrial fibrillation of less than 1 year. Use of some antiarrhythmic drug at the point of electrical cardioversion might have some influence on conversion rate; however, available data in the literature on this issue are still controversial. A potential limitation of the study is the unavoidable uncertainty inherent in estimating the arrhythmia duration and this may lead to underestimation of the true time length of atrial fibrillation. The presented results on pharmacological and conventional electric cardioversion do not apply necessarily to recent and newer types of electrical cardioversion such as transthoracic biphasic waveform or transvenous low energy internal cardioversion.

Left atrial appendage areas have not been assessed in our study; however, these measurements are inherently prone to substantial interobserver variability during both data registration and off-line analysis, possibly due to the complex three-dimensional anatomy of the left atrial appendage. In contrast, assessment of left atrial appendage function by Doppler echocardiography during transesophageal echocardiography could be easily performed, was reproducible and clinically highly relevant.

Conclusion

Our study demonstrates that the left atrial appendage flow velocity pattern determined by transesophageal echocardiography before cardioversion has an independent value in predicting cardioversion success in patients with non-valvular atrial fibrillation of less than 1 year’s duration. This value is incremental over important predictors derived from clinical history and transthoracic echo, such as duration of atrial fibrillation and left atrial dimension.

Dr Atila Pálinkás was supported by the educational grant “Eötvös” of the Hungarian Government.

References


