Transoesophageal echocardiography-guided cardioversion of atrial fibrillation or flutter

Selection of a low-risk group for immediate cardioversion

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Aims Despite exclusion of left atrial thrombi by transoesophageal echocardiography, cardioversion-related thromboembolism has been reported in atrial fibrillation or flutter. To define a low-risk group for cardioversion without previous anticoagulation, patients were selected for immediate cardioversion if there were no thrombi, no echo spontaneous contrast and the outflow velocity of the left atrial appendage was greater than 0.25 m.s\(^{-1}\) on transoesophageal echocardiography.

Methods and Results Two hundred and forty-two consecutive patients referred for cardioversion of atrial fibrillation or flutter with a duration of more than 2 days and no anticoagulation therapy were examined with transoesophageal echocardiography. After the transoesophageal echocardiography examination, patients who were eligible for immediate cardioversion were anticoagulated with low molecular weight heparin (dalteparin) subcutaneously, together with warfarin prior to cardioversion. Dalteparin treatment was continued until the patient had reached therapeutic prothrombin values.

Based on the transoesophageal echocardiographic findings the patients were divided into two groups: immediate cardioversion, group A, with a mean age of 62 ± 13 years (n = 162); or conventional warfarin treatment before cardioversion, group B, with a mean age of 67 ± 10 years (P < 0.05) (n = 80). In group A, lone atrial fibrillation or flutter was more common (53%; 95% CI: 45–61) compared to group B (34%; 95% CI: 23–44, P < 0.05), while heart disease was more common in group B (45%; 95% CI: 34–56) compared to group A (31%; 95% CI: 24–39, P < 0.05). Echocardiography revealed thrombi in 5% (95% CI: 2.6–8) of the patients, left atrial size was larger, fractional shortening lower, and a higher proportion had impaired left ventricular function in group B. No thromboembolic event occurred at or after cardioversion in any of the patients; however, before planned cardioversion one transitory ischaemic attack, one lethal stroke and one cardiac death occurred in three of the patients with thrombi despite warfarin therapy. One-month follow-up maintenance of sinus rhythm was 75% in group A compared to 45% in group B (P < 0.01).

Conclusion After using our transoesophageal echocardiographic exclusion criteria (no thrombi, no spontaneous echo contrast and left atrial appendage outflow velocity ≥0.25 m.s\(^{-1}\)) cardioversion can safely be performed in 2/3 of patients with atrial fibrillation or flutter without previous anticoagulation therapy. These patients maintained sinus rhythm significantly better after 1 month compared to patients with prolonged warfarin therapy before cardioversion.

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Key Words: Transoesophageal echocardiography, cardioversion, anticoagulation, thrombi, sinus rhythm.

See page 795 for the Editorial comment on this article

Introduction

The risk of systemic thromboembolism during chronic atrial fibrillation is about 5% year\(^{-1}\). To decrease this risk, restoration of sinus rhythm is commonly attempted. Current standard care for cardioversion in atrial fibrillation includes 3 weeks of therapeutic anticoagulation therapy before and 4 weeks after cardioversion\(^6\).

Transoesophageal echocardiography is a sensitive tool for identification of thrombus formation in the left atrium and left atrial appendage\(^7,8\). The safety of
transoesophageal echocardiography-guided cardioversion without previous anticoagulation in patients without a thrombus has been reported in several studies but also questioned in some reports since patients have suffered cardioversion-related embolic events even when no thrombi were found before cardioversion. Immediately following conversion to sinus rhythm, however, atrial mechanical function is not fully restored and embolic episodes may therefore be blamed on inadequate anticoagulation therapy after establishing sinus rhythm.

In addition to documented thrombus formation, the presence of spontaneous echo contrast and low outflow velocities in the left atrial appendage have been associated with an increased risk of thromboembolism.

Although no randomized study has yet been published concerning the safety of transoesophageal echocardiography-guided cardioversion of chronic atrial fibrillation or flutter, the available literature has been widely interpreted as a reliable proof of its safety, and also by us. To ensure safe cardioversion without risk of subsequent thromboembolism in patients without previous anticoagulation therapy, however, we only allow cardioversion in patients without thrombus formation, without spontaneous echo contrast and with a left atrial appendage outflow velocity ≥ 0.25 m·s⁻¹. If these criteria are not fulfilled, traditional pre-treatment with warfarin is given. Furthermore, immediately following transoesophageal echocardiography-documented exclusion of these potential thromboembolic indicators, all patients are given low molecular weight heparin (dalteparin) together with warfarin until a therapeutic prothrombin value is reached in order to prevent subsequent thrombus formation. This treatment is maintained for at least 4 weeks following conversion to sinus rhythm.

Although we and others have adopted transoesophageal echocardiography-guided cardioversion using the above defined safety criteria, there is still a need for further documentation of the safety of this procedure. Therefore we report the results of transoesophageal echocardiography-guided cardioversion of chronic atrial fibrillation or flutter in the consecutive series of our initial 242 patients.

**Methods**

**Indications for transoesophageal echocardiography before conversion of atrial fibrillation**

Patients with non-rheumatic atrial fibrillation or flutter of >48 h duration and no anticoagulant medication were routinely screened with transoesophageal echocardiography for possible thromboembolic risk before cardioversion. Patients with atrial arrhythmias together with haemodynamic instability requiring electrical conversion regardless of the echocardiographic findings, patients with previous a cardioembolic event, known rheumatic valvular disease, contraindications to transoesophageal echocardiography or long-term treatment with warfarin were excluded from transoesophageal echocardiography.

**Transoesophageal echocardiography criteria for conversion**

The qualifications for immediate cardioversion without previous treatment with warfarin were: (i) the absence of thrombus formation in the left atrium or appendage, (ii) no spontaneous echo contrast detected, and (iii) emptying velocities in the left atrial appendage exceeding 0.25 m·s⁻¹.

**Acute antithrombotic regimen**

If patients were accepted for immediate cardioversion, treatment with dalteparin was started, 200 U·kg⁻¹·1 subcutaneously (maximum dosage 18 000 U), together with warfarin before cardioversion. Dalteparin was given daily as a single dose until the patient had reached a therapeutic prothrombin value. Warfarin was given for 1 month after the cardioversion.

**Transthoracic echocardiography**

Using a Hewlett-Packard Sonos 2500 equipped with a 2.5 or 3.5 MHz transducer, a standard transthoracic echocardiographic examination was performed prior to the transoesophageal echocardiography.

Long- and short-axis views were obtained from the parasternal window and dimensions of the left atrium and chamber were measured according to standard criteria. In patients lacking an optimal parasternal view, measurements were made from the subcostal view. Fractional shortening was measured as LVEDd-LVESd/LVEDd as a systolic index.

Left ventricular regional and global systolic function were assessed from the apical two- and four-chamber view. Left ventricular systolic function was defined as impaired if there was evidence of global or regional hypokinesia in more than one segment of the left ventricle.

**Transoesophageal echocardiography**

Examination was made with a 5 MHz multiplane probe (model 21364 A) after sedation with midazolam 2 mg, intravenously. The hypopharynx was anaesthetized with 10% topical lidocaine, and 0.2 mg glycopyrolate was given intravenously before examination.
Basal short-axis, four-chamber and transgastric short-axis views, as well as views from the thoracic aorta were obtained. Shunt flow was investigated with colour Doppler and contrast echocardiography. Recordings were made after rapid injection of 10 ml agitated saline, with and without Valsalva. A patent foramen ovale was considered present when three or more microbubbles were visible in the left atrium within three cardiac cycles of their appearance in the right atrium. The extent of valvular regurgitation was assessed by colour Doppler and graded between 0 (none) and 3 (severe). The presence of protruding plaques (>5 mm) in the ascending aorta was noted.

Any presence of spontaneous echo contrast in the left and right atrium, including the appendages, was noted. Spontaneous echo contrast was defined as dynamic ‘smoke-like’ echoes within the atria or appendages, distinct from excessive gain settings\(^\text{[19]}\). No specific grading was made other than intermittent or continuous.

The left atrial appendage was visualized from the horizontal plane (0\(^\circ\)) and inspected continuously during stepwise rotation of the imaging sector by 5–10\(^\circ\) to 180\(^\circ\).

A thrombus was defined as an echo-dense mass with a uniform texture different to that of the atrial or appendage wall\(^\text{[20]}\). Specific care was taken to differentiate between a thrombotic mass and the pectinate muscles in the tip of the left atrial appendage. The area of the left atrial appendage was measured manually by planimetry, using the integrated software equipment in the echocardiographic machine. The base of the left atrial appendage area was defined as extending from the top of the limbus, between the left superior pulmonary vein, along the shortest line to the aorta. The cavity area was traced along the endocardial border of the left atrial appendage.

The Doppler flow of the left atrial appendage was studied with the sample volume positioned at the base of the left atrial appendage. The peak emptying and filling velocities were measured. Velocities were averaged over 3–5 cardiac cycles.

**Direct current cardioversion**

Direct current cardioversion was carried out within 6–8 h of the transoesophageal echocardiography using the standard method\(^\text{[25]}\), with an initial energy of at least 50 J for atrial flutter and 200 J for atrial fibrillation.

**Follow-up**

A follow-up examination was made at the outpatient clinic with an electrocardiogram after 1 week and 1 month. If, at 1 month the patient had sinus rhythm, warfarin therapy was terminated. If the atrial fibrillation or flutter had relapsed, warfarin therapy was continued and a decision was made as to whether a new cardioversion should be performed.

Cardioversion-related embolism was defined as a clinically evident acute cerebrovascular or systemic ischaemic event during the 1-month period after cardioversion.

**Statistics**

All data are expressed as means and 95% confidence intervals. Continuous variables were compared with the Mann–Whitney U-test for unpaired samples. Comparisons of categorical data were made with the Chi-square test or Fisher’s exact test (Stat View II; Abacus Concepts; Berkeley, CA, U.S.A.). A P value of <0.05 was considered significant.

A confidence interval for the percentage of patients in whom an embolic event occurred after cardioversion was calculated with an exact binomial procedure.

Stepwise logistic regression with SAS software (SAS version 6.12 institute, Gary, N.C.) was performed to find possible correlations of eligibility for immediate cardioversion. The factors analysed were: duration of arrhythmia, new onset of arrhythmia, fractional shortening, presence of heart disease, presence of hypertension, lone atrial arrhythmia, atrial flutter, size of the left atrium, age and impaired left ventricular function.

**Results**

**Material and clinical characteristics**

(Table 1)

From April 1995–December 1997, 242 patients were consecutively investigated with transoesophageal echocardiography in order to guide the choice of anticoagulation and time of direct current conversion. Two hundred and two patients were in atrial fibrillation whilst 40 had atrial flutter.

Contraindications for immediate cardioversion were lacking in 162 patients (group A) while the remaining 80 patients had one or more contraindications (group B).

Patients in group A were significantly younger than those in group B (62 ± 13 years and 67 ± 10 years, respectively, \(P < 0.05\)). The proportion of males/females did not differ between the groups (45/117 and 24/56, respectively, \(P = \text{ns}\)). Underlying and concomitant diseases differed between the two groups. Thus lone atrial fibrillation/flutter was significantly more common in group A (\(P = 0.05\)) whilst a history of heart disease was more common in group B (\(P = 0.05\)). No difference in history of hypertension was found between the groups.

In group A, atrial flutter was more common compared to group B 34/162 vs 6/80 (\(P < 0.01\)). Patients without a history of previous episodes of atrial fibrillation or atrial flutter were significantly more common in group B, 74/80, than in group A, 99/162 (\(P < 0.01\)).

Six of the 162 patients in group A reverted spontaneously to sinus rhythm, while the conversion attempt
failed to restore sinus rhythm in 11. In one case, conversion was achieved with a pharmaceutical agent (Sotalol iv). Thus, altogether sinus rhythm was restored in 151 patients of group A. In eight patients, a transoesophageal echocardiography examination was made even though the patients had been treated with warfarin for more than 1 week. These patients were examined because of a non-therapeutic prothrombin value. After exclusion of a thrombus, patients with spontaneous echo contrast or low velocities in their left atrial appendage were accepted for cardioversion if the prothrombin value was therapeutic at cardioversion. In these cases patients were not treated with dalteparin.

Five of 80 patients who were assigned to treatment with warfarin before direct current cardioversion (group B) reverted spontaneously to sinus rhythm, six failed to reach sinus rhythm at direct current conversion and two died before direct current conversion could be attempted. Clinical reasons motivated cancellation of the attempted direct current conversion in nine patients. Thus, ultimately 58 of the 80 patients were direct current converted to sinus rhythm and 63 reached sinus rhythm altogether.

The duration of the arrhythmia until the time of transoesophageal echocardiography in those who successfully underwent cardioversion did not differ significantly between the groups, group A (n=145) 42±59 days (range 3–365) compared to group B, 71±132 days (range 3–1095) Table 2. However, duration of arrhythmia at the time of direct current conversion differed significantly between the two groups: group A, 42±59 days (range 3–365) compared to group B, 157±144 (range 27–878), P<0.01. This difference was attributable to the duration of the warfarin therapy before cardioversion, 88±56 days (range 21–273), Fig. 1.

No differences were found in treatment with anti-thrombotic medication before the transoesophageal echocardiography examination. Thus 47/145 patients in group A were treated with acetylsalicylic acid compared to 24/58 (ns) in group B.

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**Table 1 Clinical and arrhythmia characteristics in patients selected for immediate cardioversion (A) and patients treated conventionally with warfarin before cardioversion (B)**

<table>
<thead>
<tr>
<th></th>
<th>Immediate group (A) (n=162)</th>
<th>Warfarin group (B) (n=80)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n % (95% CI)</td>
<td>n % (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>128 79 (73–85)</td>
<td>74 94 (86–98)</td>
<td>&lt;0·01*</td>
</tr>
<tr>
<td>Atrial flutter</td>
<td>34 21 (15–27)</td>
<td>6 6 (2–13)</td>
<td>&lt;0·01*</td>
</tr>
<tr>
<td>First episode atrial arrhythmia</td>
<td>99 61 (54–69)</td>
<td>58 73 (63–82)</td>
<td>&lt;0·01*</td>
</tr>
<tr>
<td>Lone atrial fibrillation/flutter</td>
<td>86 53 (45–61)</td>
<td>27 34 (23–44)</td>
<td>&lt;0·01*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>44 27 (20–34)</td>
<td>31 39 (28–49)</td>
<td>ns*</td>
</tr>
<tr>
<td>History of heart disease</td>
<td>51 31 (24–39)</td>
<td>36 45 (34–56)</td>
<td>&lt;0·05*</td>
</tr>
<tr>
<td>Coronary insufficiency</td>
<td>22 14 (8–19)</td>
<td>16 20 (11–29)</td>
<td>ns*</td>
</tr>
<tr>
<td>Valvular disease</td>
<td>10 6 (2–10)</td>
<td>1 1 (0–4)</td>
<td>ns**</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>3 2 (0–4)</td>
<td>8 10 (3–17)</td>
<td>&lt;0·01**</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>6 4 (1–7)</td>
<td>4 5 (0–10)</td>
<td>ns**</td>
</tr>
<tr>
<td>Alcohol-induced</td>
<td>4 2 (0–5)</td>
<td>2 3 (0–6)</td>
<td>ns**</td>
</tr>
<tr>
<td>Hyperthyroidism (corrected)</td>
<td>2 1 (0–3)</td>
<td>2 3 (0–6)</td>
<td>ns**</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4 2 (0–5)</td>
<td>3 4 (0–8)</td>
<td>ns**</td>
</tr>
</tbody>
</table>

*Chi-square test; **Fisher’s exact test.

**Table 2 Characterization of atrial arrhythmias in patients ultimately undergoing direct current cardioversion with the two different treatment regimen**

<table>
<thead>
<tr>
<th></th>
<th>Immediate group (A) (n=145)</th>
<th>Warfarin group (B) (n=58)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n % (95% CI)</td>
<td>n % (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>112 77 (70–84)</td>
<td>53 91 (84–98)</td>
<td>&lt;0·05#</td>
</tr>
<tr>
<td>First episode of atrial fibrillation</td>
<td>89 61 (53–69)</td>
<td>47 81 (71–92)</td>
<td>&lt;0·01#</td>
</tr>
<tr>
<td>Atrial flutter (%)</td>
<td>33 23 (16–30)</td>
<td>5 9 (2–16)</td>
<td>&lt;0·01#</td>
</tr>
<tr>
<td>Duration (days)</td>
<td>42±59 (range 3–365)</td>
<td>71±132 (range 3–1095)</td>
<td>ns*</td>
</tr>
<tr>
<td>Median (days)</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Unknown duration</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

*Mann–Whitney test, #Chi-square test.
Thrombi were noted in 14/242 (6%) of all patients; all but one had spontaneous echo contrast, and the mean outflow velocity of the left atrial appendage was 0.18 ± 0.06 m·s⁻¹.

Spontaneous echo contrast was considered a contraindication for immediate cardioversion and was found in 75/80 in group B. Forty-two of these patients also had an emptying velocity of <0.25 m·s⁻¹ in the left atrial appendage. In 5/80 patients the only risk factor noted was a low velocity flow in the left atrial appendage. Three patients were cardioverted even though spontaneous echo contrast was noted; in these cases the spontaneous echo contrast was intermittent, only seen in some cardiac cycles. Transoesophageal echocardiography was performed since the patients had non-therapeutic prothrombin values during treatment with warfarin.

The size of the left atrium was larger in group B, 47 ± 5.7 mm compared to group A, 44 ± 6.6 (P<0.01). The area of the left atrial appendage was also larger in group B compared to group A, 5.0 ± 5.7 cm² vs 4.0 ± 1.3 cm² (P<0.001). The dimensions of the left ventricle did not differ, but fractional shortening was lower in group B, and there was a higher proportion of patients with an impaired left ventricular function in group B, 39/80 compared to 28/162 in group A (P<0.001). No difference was found in the prevalence of a patent foramen ovale or protruding aortic plaques between the groups.

The results of the logistic regression are listed in Table 4. Atrial flutter was an independent positive predictor for immediate cardioversion, while age, duration and

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**Table 3** Echocardiographic and Doppler measurements in patients for immediate cardioversion (A) and patients treated conventionally with warfarin before cardioversion (B)

<table>
<thead>
<tr>
<th></th>
<th>Immediate group (A)</th>
<th>Warfarin group (B)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=162)</td>
<td>(n=80)</td>
<td></td>
</tr>
<tr>
<td>LVEDd (mm)</td>
<td>51 (50–52)</td>
<td>53 (51–54)</td>
<td>ns</td>
</tr>
<tr>
<td>Lad (mm)</td>
<td>44 (43–45)</td>
<td>47 (46–48)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>LAA area (cm²)</td>
<td>04 0 (3.3–4.2)</td>
<td>5.0 (4.5–5.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>FS (%)</td>
<td>32.8 (31.3–34.3)</td>
<td>26.1 (24.8–28.1)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Impaired left ventricular function</td>
<td>17% (11–23)</td>
<td>49% (38–60)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LAA outflow velocity (m·s⁻¹)</td>
<td>0.40 (0.38–0.43)</td>
<td>0.24 (0.22–0.26)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LAA inflow velocity (m·s⁻¹)</td>
<td>0.43 (0.41–0.46)</td>
<td>0.28 (0.25–0.31)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>27% (20–34)</td>
<td>31% (22–41)</td>
<td>ns#</td>
</tr>
<tr>
<td>≥ moderate PFO</td>
<td>19% (13–25)</td>
<td>14% (6–21)</td>
<td>ns#</td>
</tr>
<tr>
<td>Protruding aortic plaque</td>
<td>16% (10–22)</td>
<td>25% (16–34)</td>
<td>ns#</td>
</tr>
</tbody>
</table>

LVEDd=left ventricular end-diastolic diameter, Lad=left atrium diameter, LAA=left atrial appendage, FS=fractional shortening, PFO=patent foramen ovale. Figures in brackets indicate 95% CI.

* Mann–Whitney test; # Chi-square test.
impaired left ventricular function were negative predictors for immediate cardioversion.

**Thrombi**

In 14 (6%) patients a thrombus was found in the left atrial appendage, three of the 14 patients being in atrial flutter. Eight of 14 patients had a follow-up transoesophageal echocardiography. No thrombus was found in six of these, five underwent successful cardioversion, and in one, cardioversion failed. In two patients, the thrombus was still visible on the follow-up transoesophageal echocardiography, in one patient the cardioversion was cancelled and in the other, cardioversion was carried out successfully after a further 2 months of therapy with warfarin.

Of the remaining six patients, one patient underwent transoesophageal echocardiography after a transient ischaemic attack associated with spontaneous reversion to sinus rhythm. No remaining thrombus could be seen. Two further patients died, one of a stroke, the other from a myocardial infarction 2 days after the transoesophageal echocardiography. Autopsy showed an occluded right coronary artery and a thrombus in the left atrial appendage. In the remaining three patients, cardioversion was cancelled for clinical reasons and no follow-up transoesophageal echocardiography was performed.

**Cardioversion and follow-up (Table 5)**

Of the examined patients, 145/162 proceeded to immediate cardioversion in group A and 58/80 were pretreated with warfarin. In group A, 115/145 had atrial fibrillation while 30 had atrial flutter. The proportion of atrial flutter (30/145) differed significantly from that in group B (5 of 58), (P<0.05). Atrial arrhythmia occurred for the first time more often in the conservative group (47/58) than in the immediate group (89/145) (P<0.01).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio 95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial flutter</td>
<td>5.407 1.609–25.324</td>
</tr>
<tr>
<td>Duration of arrhythmia</td>
<td>0.996 0.992–1.000</td>
</tr>
<tr>
<td>Impaired left ventricular function</td>
<td>0.170 0.078–0.356</td>
</tr>
<tr>
<td>Age</td>
<td>0.964 0.932–0.993</td>
</tr>
</tbody>
</table>

**Table 4 Logistic regression analysis of clinical factors for choice of immediate cardioversion following transoesophageal echocardiography**

**Table 5 Follow-up one month after cardioversion**

<table>
<thead>
<tr>
<th></th>
<th>Immediate group (A) (n=145)</th>
<th>Warfarin group (B) (n=58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm</td>
<td>109</td>
<td>26</td>
<td>0.01#</td>
</tr>
<tr>
<td>Antiarrhythmic therapy</td>
<td>66</td>
<td>22</td>
<td>ns#</td>
</tr>
<tr>
<td>Embolic episode</td>
<td>0</td>
<td>0</td>
<td>ns#</td>
</tr>
</tbody>
</table>

Only patients with arrhythmia of new onset

<table>
<thead>
<tr>
<th></th>
<th>Immediate group (A) (n=145)</th>
<th>Warfarin group (B) (n=58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm (%)</td>
<td>65</td>
<td>21</td>
<td>0.01#</td>
</tr>
<tr>
<td>Antiarrhythmic therapy (%)</td>
<td>29</td>
<td>13</td>
<td>ns#</td>
</tr>
</tbody>
</table>

#Chi-square test.
Dalteparin was given before cardioversion in group A together with warfarin and was continued for a mean period of 4 ± 2 days (range 0–10 days). In the majority (80%) dalteparin was given for 3–6 days. In nine patients only warfarin and no dalteparin was given after cardioversion. Figure 2.

Fifty-eight patients in group B were ultimately cardioverted, the delay from transoesophageal echocardiography to cardioversion being 88 ± 56 days (range 21–270 days).

At the 1-month follow-up no embolic events were reported in either of the groups. Sinus rhythm was registered in 109/145 (75%) in the immediate group compared to 26/58 (41%) in the conservative group (P < 0.001). The use of antiarrhythmic drugs did not differ between the groups, 60/145 (45%) in the immediate group compared to 22/58 (38%); ns in the conservative group.

Discussion

The safety of transoesophageal echocardiography-guided cardioversion of atrial fibrillation/flutter has been addressed in several studies, but thromboembolic complications have been reported in up to 6–7% of cases in clinical studies. The small numbers of patients in these studies have made it difficult to interpret these complications, however. Since our study was started, isolated case reports have been published describing embolic events in patients despite anticoagulation treatment, both in atrial fibrillation and atrial flutter. Our study strongly supports the supposition that the careful use of transoesophageal echocardiography and meticulous anticoagulation from the moment of transoesophageal echocardiography allows direct cardioversion in the majority of patients, without risk of conversion-related thromboembolism.

We also observed an improved maintenance of sinus rhythm in patients with immediate cardioversion and the difference is likely to depend on different baseline characteristics between the two groups (Table 5). It remains to be verified if the discriminating factor, left atrial appendage emptying velocity, also influences the maintenance of sinus rhythm, where a prevalence of 12–20% has been reported. One explanation for our lower prevalence could be the high prevalence of lone atrial fibrillation/flutter (46%) in our patients. In previous studies larger numbers of patients with structural heart disease were included and the prevalence of lone atrial arrhythmias varied between 4–25%.

The left atrial appendage is a muscular sac in which most thrombi of the left atrium reside. During atrial fibrillation two different types of flow are noted, one saw-tooth-like with regular and well-defined peaks of filling and emptying, the other irregular, with a lower velocity peak of emptying and filling. Low flow velocity is associated with thrombus formation and embolism. A possible explanation for thromboembolism at or after cardioversion is the de novo formation of thrombi in patients with inadequate anticoagulation at cardioversion. The mechanism seems to be a ‘stunning’ of the left atrial appendage in cardioversion first reported during direct current conversion where patients developed a new spontaneous echo contrast and impaired velocities in the left atrial appendage, which could predispose to thrombus formation. One embolic event has been described in a patient with a therapeutic anticoagulation level without thrombus formation but with a low flow velocity in the left atrial appendage and spontaneous echo contrast, after internal cardioversion with a lower energy than that needed for direct current cardioversion. A proposed mechanism has been administration of electrical energy. However, patients with sinus rhythm given shocks with an implantable defibrillator did not show any changes in left atrial appendage function or new development of spontaneous echo contrast. In patients with atrial fibrillation the decrease in left atrial appendage velocities did not differ between groups of patients who were cardioverted with different electrical energies. The stunning effect has also been noted both in pharmacological and spontaneous conversion. The explanation of left atrial appendage dysfunction could be the restoration of sinus rhythm itself, and not the method of achieving sinus rhythm.

Spontaneous echo contrast

Spontaneous echo contrast appears soon after stasis of the blood flow and is mediated by red blood cell aggregation with roleaux formation and simultaneous appearance of smoke-like echoes. In a low-flow experimental model, blood echogenicity could be increased by increasing the haematocrit and fibrinogen concentration and reduced by inhibition of red cell aggregation. The echogenicity was unaltered by heparin or warfarin. In patients with spontaneous echo contrast several haemodynamic changes are found; haematocrit and fibrinogen values are increased, and the viscosity of the blood at a low shear rate is raised. Patients with a marked spontaneous echo contrast have signs of a

Thrombi and velocities in the left atrial appendage

With transoesophageal echocardiography we have a safe and accurate method for detection of thrombi in the atria and their appendages. A sensitivity of 100% and a specificity of 93–99% compared to visual inspection during surgery has been reported. A pitfall is the presence of severe spontaneous echo contrast mimicking a thrombus, but the negative predictive value in both of the studies was 100%. In our study we found a prevalence of 6% which is lower than in previous studies.

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hypercoagulable state, with increased values of fibrinopeptid A, which is formed after cleavage of fibrinogen to fibrin[44]. In the left atrium, spontaneous echo contrast was first observed with transthoracic examination, occasionally together with mitral stenosis[55]. With transoesophageal echocardiography, spontaneous echo contrast is not an uncommon finding in atrial fibrillation patients, especially in those being evaluated for stroke. The presence of spontaneous echo contrast is a potent risk factor for stroke in patients with atrial fibrillation, either indicating previous stroke[50,21,46], or indicating an increased risk for future embolic events[47]. The presence of spontaneous echo contrast is not a static phenomenon. Follow-up of patients with non-rheumatic atrial fibrillation including serial transoesophageal echocardiography has shown that spontaneous echo contrast does not disappear during an observation time of 15 months, whereas during follow-up new spontaneous echo contrast occurred in 43% of patients without spontaneous echo contrast at the baseline examination[48]. Cardioversion not only induces impaired velocities in the left atrial appendage; the new development of spontaneous echo contrast or more severe spontaneous echo contrast in the post-cardioversion period has been described[12,34]. In one study a patient with moderate spontaneous echo contrast developed severe spontaneous echo contrast and a new thrombus after cardioversion, despite therapeutic anticoagulation at cardioversion[14]. In our patients spontaneous echo contrast was found in 78/262 (30%); however, in three patients the finding was intermittent. The number of patients with spontaneous echo contrast was lower than that reported in other studies with transoesophageal echocardiography-guided cardioversion, where patients with spontaneous echo contrast were found in 35–70% of cases[10–13]. This probably reflects the smaller number of patients with structural heart disease in our material.

Atrial flutter

The current recommendations for atrial flutter by American chest physicians suggest that anticoagulation is not required in the pre-cardioversion period unless the patient had a previous period of atrial fibrillation. Since the major trials of anticoagulation therapy for atrial fibrillation excluded patients with atrial flutter the risk for thromboembolism is unclear[1–5]. During the last year, two reports have addressed this issue, concluding that treatment with anticoagulation should be considered in patients with atrial flutter because of a substantial risk of thromboembolism[49,50]. Post-cardioversion thromboembolism has been described despite exclusion of thrombi in the left atrial appendage[27].

In atrial flutter, the risk of thromboembolism seems related to the same mechanism as in atrial fibrillation. A delay of several days before restoration of the atrial function has been described after cardioversion[51]. The stunning effect has also been noted after cardioversion in patients with atrial flutter[52]; however, the impairment in flow in the left atrial appendage is not so pronounced as in atrial fibrillation[53] which might suggest a lower thromboembolic risk compared to cardioversion of atrial fibrillation. We did not differentiate between atrial flutter or atrial fibrillation in our management of patients. The majority of patients with atrial flutter (34/40) were eligible for immediate cardioversion. However, three of 14 patients with thrombi had atrial flutter on ECG, which underlines the fact that atrial flutter should be treated in the same way as atrial fibrillation when cardioversion is considered.

Thrombus prophylaxis

To obtain an anticoagulated state at the time of cardioversion in the immediate group we chose to give dalteparin subcutaneously. Dalteparin was given after the transoesophageal echocardiography and before cardioversion and was continued until a therapeutic prothrombin level had been reached. The advantage of low molecular weight heparin is the long duration of inhibition of factor Xa; a single dose has a protective effect of 24 h[54].

The inhibition of factor Xa occurs 4 h after a subcutaneous injection at which time the patient is adequately anticoagulated. Subcutaneous dalteparin given as a single dose is practised in the treatment of deep venous thrombosis, instead of intravenous heparin[55,56]. With the use of dalteparin s.c. together with warfarin anticoagulant, treatment could be initiated on the day of the transoesophageal echocardiography, with the full effect by the time of cardioversion, thus reducing the time spent in hospital. No bleeding complications were reported by the patients given dalteparin together with warfarin.

This management differs from previous transoesophageal echocardiography-guided cardioversion studies in which patients were pre-treated with either heparin intravenously for 1 to 4 days or warfarin for up to a week before the transoesophageal echocardiography[9,13,15].

Clinical implications

At present, no randomized studies with transoesophageal echocardiography-guided cardioversion without previous treatment with anticoagulation have been published. While awaiting the results from the ongoing randomized ACUTE (Assessment of Cardioversion Using Transoesophageal Echocardiography) study, so far only observational studies have been published. Obviously our study is grossly underpowered to answer with statistical significance the hypothesis that transoesophageal echocardiography can safely select patients for immediate cardioversion. Nevertheless, it does indicate that this approach is a safe one.

To avoid the risk of cardioversion-related thromboembolism when we began using transoesophageal...
echocardiography-guided cardioversion we chose to define the low-risk group of patients for cardioversion more strictly than just by exclusion of thrombus formation. We also excluded patients with spontaneous echo contrast or with a low flow velocity in the left atrial appendage. With these exclusion criteria transoesophageal echocardiography-guided cardioversion could be applied in 162/242 cases and 145 patients were eventually cardioverted to sinus rhythm. The presence of atrial flutter was the only positive independent predictor for immediate cardioversion, while negative predictors for eligibility were the duration of arrhythmia, age and impaired left ventricular function.

In our opinion, only patients with a normal finding on transoesophageal echocardiography should be referred for immediate cardioversion. Patients with an abnormal finding on transoesophageal echocardiography need conventional anticoagulation therapy before cardioversion until a randomized study has shown that transoesophageal echocardiography-guided cardioversion is possible without embolic complications. Recommendations based on previous studies advocate exclusion of immediate cardioversion only in patients with severe spontaneous echo contrast and not in those with mild or moderate spontaneous echo contrast[23]. Based on the difficulty of distinguishing these differences, we decided to exclude all patients with any sign of spontaneous echo contrast in order to avoid any possible risk of embolization. In addition we excluded 5/262 patients with reduced flow velocities in the left atrial appendage for the reason that this represents stasis in the left atrial appendage, with an increased risk for thrombus formation.

Transoesophageal echocardiography examination can identify a group of patients with a markedly increased risk of embolic events. Patients who present with a thrombus in the left atrium have a poor prognosis. In previous studies, when patients were found to exhibit thrombi, an increased risk of embolism and death was noted. Manning et al. reported 31 patients with thrombi on transoesophageal echocardiography; three of these died shortly after examination despite anticoagulation therapy, presumably due to thromboembolism although autopsies were not performed[13]. Orselli et al. found eight patients with thrombi in the left atrium, one died after a stroke[11]. In our study group, 14 thrombi were found. All of these patients received anticoagulation therapy but despite this two died and one had a transient ischaemic attack, confirming the high risk involved.

In conclusion, using our transoesophageal echocardiography criteria, it seems possible to pursue immediate cardioversion without increased risk of thromboembolism in about 2/3 of patients with atrial fibrillation or atrial flutter lasting more than 48 h. The decreased time before reaching sinus rhythm is associated with increased maintenance of sinus rhythm, compared to patients whose transoesophageal echocardiography findings prompt oral anticoagulation before cardioversion. Finally, a left atrial thrombus seen at transoesophageal echocardiography is an alarming sign and the methods available today for dealing with this finding obviously need to be improved.

References


