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<td>Tse, HF; Lau, CP; Ayers, GM</td>
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Incidence and modes of onset of early reinitiation of atrial fibrillation after successful internal cardioversion, and its prevention by intravenous sotalol

H-F Tse, C-P Lau and G M Ayers

Heart 1999;82;319-324

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Incidence and modes of onset of early reinitiation of atrial fibrillation after successful internal cardioversion, and its prevention by intravenous sotalol

H-F Tse, C-P Lau, G M Ayers

Abstract

Objective—To study the incidence and mode of onset of early reinitiation of atrial fibrillation (ERAF) following successful internal cardioversion of chronic atrial fibrillation, and to determine the effects of sotalol in the prevention of ERAF.

Design—The incidence and modes of onset of ERAF and the acute effects of intravenous sotalol in the prevention of ERAF were studied retrospectively.

Setting—Electrophysiology laboratory at a university teaching hospital.

Patients—64 patients, mean (SD) age 62 (10) years, who underwent internal cardioversion of chronic atrial fibrillation (mean duration of atrial fibrillation 31 (39) months).

Main outcome measures—ECGs and intracardiac electrograms recorded during the internal cardioversion of atrial fibrillation using 3/3 ms biphasic, R wave synchronised shocks.

Results—52 patients (81%) had successful electrical cardioversion, and 20 (31%) of these had ERAF during the procedure. There was no clinical predictor for the occurrence of ERAF. Fifty eight episodes of ERAF were observed. Five ERAF episodes (9%) had preceding bradycardia and 53 (91%) of these were triggered by atrial premature beats with normal preceding heart rate. Atrial premature beats that reinitiated atrial fibrillation had a shorter coupling interval (333 (43) ms v 396 (100), p < 0.001) and a lower prematurity index (0.44 (0.11) v 0.55 (0.14), p < 0.001) than those that did not reinitiate atrial fibrillation. Repeated shock delivery and increasing the defibrillation energy did not prevent ERAF. Intravenous sotalol infusion decreased the numbers of atrial premature beats and prolonged their coupling interval, and prevented ERAF after repeated defibrillation in 83% of patients with ERAF.

Conclusions—ERAF is a significant clinical problem after successful internal cardioversion of chronic atrial fibrillation, and was observed in up to 31% of patients. In most episodes, ERAF was triggered by short coupling atrial premature beats with preceding normal heart rate. Intravenous sotalol was effective in preventing ERAF in most cases. (Heart 1999;82:319–324)

Keywords: atrial fibrillation; low energy cardioversion; sotalol

Low energy internal cardioversion has been shown to be very effective in converting atrial fibrillation.7–9 This procedure requires only mild sedation and is more effective than external cardioversion.7–8 Thus the use of low energy internal cardioversion may result in restoration of sinus rhythm in a greater number of patients. However, unstable sinus rhythm followed by early reinitiation of atrial fibrillation (ERAF) shortly after successful electrical cardioversion was observed in up to 13–36% of patients.9–11 It could significantly limit the number of patients with successful clinical termination of atrial fibrillation. A rational approach to preventing ERAF may depend on a better understanding of its incidence and modes of onset. Furthermore, the role of class III antiarrhythmic agents in preventing the spontaneous reinitiation of atrial fibrillation after successful cardioversion remains largely unknown. The purpose of the present study was to investigate the incidence and clinical variables that predict the occurrence of ERAF shortly after successful internal cardioversion of chronic atrial fibrillation, the modes of onset of ERAF, and the efficacy of a class III agent, sotalol, in the prevention of ERAF.

Methods

Patients

We carried out a retrospective study of 64 consecutive patients with chronic atrial fibrillation of at least one month’s duration who underwent internal cardioversion. A detailed clinical examination was performed and a complete medical history was taken. Routine 12 lead ECG, 24 hour Holter monitoring, chest x ray, routine laboratory and thyroid tests, and transthoracic and transoesophageal echocardiography were assessed in all patients. Patients with the following conditions were excluded from study: reversible causes of atrial fibrillation, moderate to severe valvar heart disease, unstable angina or recent myocardial infarction, class III or IV heart failure, contraindication to sotalol (asthma, chronic obstructive pulmonary disease, significant sinus nodal or conduction system dysfunction, or a previous adverse reaction to a β blocker), or evidence of left atrial thrombus. No study patient had been receiving any class I, III, or IV antiarrhythmic drugs for more than five half lives, or amiodarone for longer than three months.

All patients gave written informed consent before the procedure, and the protocol was approved by the ethics committee of the University of Hong Kong.
ANTICOAGULATION PROTOCOL

All patients were treated with oral anticoagulants, using warfarin to achieve an international normalised ratio (INR) of 2–3 for at least three weeks before the procedure. Warfarin was discontinued two days before the procedure and was replaced with an intravenous heparin infusion. The heparin infusion was stopped four hours before and restarted after the procedure.

The INR was checked daily and immediately before the procedure, and the minimum INR value considered safe for venous puncture was less than 1.5. Warfarin was restarted after the procedure and heparin infusion was discontinued when the therapeutic INR of 2–3 was achieved.

STUDY PROTOCOL

Details of the internal cardioversion procedure in our laboratory have been described previously. In brief, low energy biatrial shocks were delivered through two transvenously introduced defibrillation catheters. One of these catheters was positioned in the coronary sinus and one in the anterolateral right atrium. In 36 patients, a pair of temporary 6F decapolar catheters (Elecath, New Jersey, USA) was used. In the remaining 28 patients, two custom built spring coil electrodes were used (Perimeter 7107 and 7023, InControl Inc, Redmond, Washington, USA). The right atrial catheter served as the cathode and the coronary sinus catheter as the anode. Two additional 6F catheters were positioned, one in the right ventricular apex (for shock synchronisation and post-shock pacing) and one in high right atrium (for recording the atrial electrogram and pacing); both were advanced from the right femoral vein. The defibrillation catheters were connected to a custom made external atrial defibrillator (XAD, InControl Inc) capable of delivering an R wave synchronised biphasic shock waveform (3/3 ms) with a leading edge voltage that could be programmed between 10 and 400 V.

Patients were sedated with intravenous midazolam (0.05 mg/kg) and pethidine (0.5 mg/kg), and additional doses were given as required. Starting with a 20 V test shock, R wave synchronised shocks were delivered starting at 180 V and increasing in steps of 40 V until sinus rhythm was restored, or the until two at the highest output of 400 V had been delivered. Between unsuccessful defibrillation attempts, at least two minutes were allowed to elapse before the next shock was applied.

During the study, two surface ECGs (lead II and V6), a bipolar high right atrium and ventricular electrogram, and arterial blood pressure were recorded simultaneously. ERAF were defined as the occurrence of spontaneous reinitiation of a sustained atrial fibrillation episode after successful internal cardioversion. Following successful internal cardioversion, the rhythm was monitored for up to five minutes to look for any episodes of ERAF and their mode of onset. Where ERAF were triggered by atrial premature beats, their characteristics were studied and compared with those not triggered by atrial premature beats. We determined the following:

- Coupling interval of atrial premature beats (atrial to atrial premature beat)
- Mean atrial cycle length of three to five consecutive preceding beats
- The prematurity index (atrial premature beat cycle length/preceding rhythm cycle length) using a high right atrium endocardial electrogram
- The density of atrial premature beats (number of atrial premature beats/min).

In those patients with ERAF, a repeat defibrillation shock at the initially successful energy was given. If the atrial fibrillation still recurred, up to two high energy shocks at the maximum voltage of 400 V were tested in some patients. For patients who still had ERAF, an intravenous infusion of sotalol (1.5 mg/kg) over 30 minutes was given, and defibrillation shocks were repeated using the same step up protocol, starting at 180 V. In those patients who failed cardioversion at baseline, intravenous sotalol was also given to determine whether it could reduce the atrial defibrillation requirement. The effect of sotalol on the atrial defibrillation threshold has been reported before. Oral sotalol 160–320 mg/day was given to those patients who had successful cardioversion and were maintained in sinus rhythm after the procedure.

STATISTICAL METHODS

Continuous data are presented as mean (SD). Statistical analysis was performed by analysis of variance, Mann–Whitney U test, or Fisher exact test, as appropriate, and between group comparisons were performed by a multiple Bonferroni test. A probability (p) value of < 0.05 was considered statistically significant.

Results

PATIENT CHARACTERISTICS

The 64 patients included 45 men and 19 women, aged 36 to 80 years, mean 62 (10) years. The duration of atrial fibrillation ranged from 1 to 192 months, mean 31 (39). Mean left ventricular ejection fraction was 58 (10)% (range 35% to 75%) and mean left atrial diameter was 4.4 (0.6) cm (range 3.1 to 5.5 cm). Underlying heart disease was present in 36 patients (56%), including hypertension (23), treated thyroid heart disease (5), mild valvar heart disease (4), dilated cardiomyopathy (3), and congenital heart disease (1).

EFFICACY OF INTERNAL CARDIOVERSION AND INCIDENCE OF ERAF

These results are summarised in fig 1. Before sotalol, successful internal cardioversion of atrial fibrillation was achieved in 52 patients (81%) at a mean threshold of 325 (60) V and a mean energy of 3.92 (1.4) J. However, 20 patients (31%) had ERAF shortly after successful cardioversion and failed to maintain stable sinus rhythm. Two patients had only one
Table 1 Clinical characteristics of study patients according to the result of internal cardioversion

<table>
<thead>
<tr>
<th></th>
<th>Successful cardioversion</th>
<th>Early reinitiation of atrial fibrillation</th>
<th>Failed cardioversion</th>
</tr>
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<tbody>
<tr>
<td>Number (%)</td>
<td>32 (50)</td>
<td>20 (31)</td>
<td>12 (19)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61 (11)</td>
<td>64 (9)</td>
<td>65 (9)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>20:12</td>
<td>15:5</td>
<td>10:2</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>44 (6)</td>
<td>43 (7)</td>
<td>44 (7)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>59 (12)</td>
<td>58 (8)</td>
<td>57 (12)</td>
</tr>
<tr>
<td>Threshold (V)</td>
<td>324 (56)</td>
<td>326 (54)</td>
<td>–</td>
</tr>
<tr>
<td>Energy (J)</td>
<td>3.95 (1.24)</td>
<td>4.06 (1.45)</td>
<td>–</td>
</tr>
<tr>
<td>Drug treatment (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β Blocker</td>
<td>12</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Digitalis</td>
<td>7</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>13</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>No heart disease (n)</td>
<td>14</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Duration of atrial fibrillation (months)</td>
<td>25 (37)*</td>
<td>28 (44)*</td>
<td>51 (31)</td>
</tr>
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Values are mean (SD).

*p < 0.05 vs failed cardioversion.

Table 1 Clinical characteristics of study patients according to the result of internal cardioversion.

Figure 1  Flow chart showing the outcome of patients after low energy internal cardioversion of atrial fibrillation (AF) and the results of treatment for spontaneous reinitiation of atrial fibrillation by repeated defibrillation, intravenous sotalol and atropine, and atrial pacing. SR, sinus rhythm.

Reinitiation of AF after internal cardioversion

Internal cardioversion

Spontaneous AF reinitiation n = 20 (31%)

AF n = 12 (19%)  n = 6 (9%)

Reinitiation of AF after internal cardioversion

AF n = 64

SR n = 32 (50%)  n = 30

Spontaneous AF reinitiation n = 20 (31%)

AF n = 12 (19%)

Repeated cardioversion n = 20

High energy cardioversion n = 14

Intravenous sotalol and repeated cardioversion n = 30

Atrial pacing (n = 1) or Atropine (n = 1) n = 15

n = 15

n = 2

n = 2

n = 5*

n = 7*

n = 1

n = 2

n = 4

n = 14

n = 34

n = 2

n = 2

n = 58 (91%)

n = 6 (9%)

n = 20 (31%)

n = 2

n = 14

n = 2

n = 2

n = 2

n = 12*  n = 30

n = 12*  n = 2

n = 2

n = 2

n = 12 (19%)

n = 6 (9%)

n = 20 (31%)

n = 2

n = 2

n = 5*

n = 7*

n = 1

n = 2

n = 4

n = 14

n = 34

n = 2

n = 2

n = 58 (91%)

n = 6 (9%)

n = 20 (31%)

n = 2

n = 2

n = 5*

n = 7*

n = 1

n = 2

n = 4

n = 14

n = 34

n = 2

n = 2

n = 58 (91%)

n = 6 (9%)

n = 20 (31%)

n = 2

n = 2

n = 5*

n = 7*

n = 1

n = 2

n = 4

n = 14

n = 34

n = 2

n = 2

n = 58 (91%)

n = 6 (9%)

n = 20 (31%)

n = 2

n = 2

n = 5*

n = 7*

n = 1

n = 2

n = 4

n = 14

n = 34

n = 2

n = 2

n = 58 (91%)

n = 6 (9%)

n = 20 (31%)

n = 2

n = 2

n = 5*

n = 7*

n = 1
seven of 12 had successful cardioversion after sotalol infusion and none of these had ERAF. In the two patients with ERAF associated with bradycardia, sotalol alone was not effective in preventing recurrence of atrial fibrillation but worsened the bradycardia, with long sinus pauses after cardioversion. Elimination of this bradycardia after cardioversion seemed to be effective in preventing further ERAF. Thus the administration of intravenous atropine before repeated defibrillation resulted in sinus rhythm without sinus pauses or ERAF in one of the patients. In the other patient, atrial pacing at a cycle length of 500 ms was started immediately after defibrillation and was effective in preventing recurrence of further atrial fibrillation. Both of these patients remained in stable sinus rhythm thereafter. One patient failed to maintain in sinus rhythm owing to persistent ERAF, despite administration of sotalol and repeated defibrillation (fig 1).

COMPLICATIONS
Overall, 1402 R wave synchronised shocks were delivered to the 64 patients without ventricular proarrhythmia or acute complication. Cardiac enzymes including creatine kinase and its isoenzyme CK-MB measured before and after defibrillation did not show any significant change. One patient developed symptomatic persistent junctional bradycardia after sotalol which required temporary pacing for two days. Two patients experienced heart failure with oral sotalol and required drug termination.

Discussion
EFFICACY OF INTERNAL CARDIOVERSION AND INCIDENCE OF ERAF
Restoration of sinus rhythm is the preferred goal of treatment in patients with persistent atrial fibrillation, as it should eliminate symptoms, improve exercise capacity, and reduce thromboembolic complications, and as it might improve survival. However, for patients with atrial fibrillation of prolonged duration, electrical cardioversion with external shocks requires higher energies and has a low success rate.13 Recently, internal cardioversion has been shown to be highly effective in conversion of atrial fibrillation, even where external cardioversion has failed.1–8 The results of our study have confirmed the efficacy and safety of low energy internal cardioversion in restoring sinus rhythm, with a success rate of 81% in patients with prolonged atrial fibrillation before cardioversion (mean duration 31 (39) months).

Recurrences of atrial fibrillation are commonly observed after successful cardioversion. In previous studies, unstable sinus rhythm followed by ERAF recurrence occurred in 13–36% of patients within minutes after successful electrical cardioversion, either external or internal.9–11 In the present study we showed that up to 31% of patients with chronic atrial fibrillation without pretreatment with antiarrhythmic agents had spontaneous ERAF shortly after cardioversion. We found that the occurrence of ERAF was not related to the previous arrhythmia duration or to any of the clinical variables (age, sex ratio, left atrial size, left ventricular ejection fraction, defibrillation energy and voltage, use of β blockers and digoxin, or the type of heart disease). Repeated cardioversion was only effective at preventing ERAF in 10% of patients, and ERAF could not

Figure 2. Different modes of onset of early reinitiation of atrial fibrillation (AF). (A) AF reinitiation preceding by bradycardia (mean atrial cycle length = 1240 ms). (B) AF was reinitiated an atrial premature beat (APB) after a short period of organised electrical activity. Note the normal heart rate preceding the onset of APB. (C) AF was reinitiated by APB with preceding long/short cycles. HRA, high right atrium.
be prevented by increasing the energy of the defibrillation shock.

MODES OF ONSET OF ERAF
It is well known that a spontaneous atrial fibrillation episode is usually initiated by atrial premature beats."17 18 Previous studies using Holter recording have shown that atrial premature beats that initiated atrial fibrillation had a shorter coupling interval and greater prematurity than isolated atrial premature beats that did not initiate atrial fibrillation."16–18 Consistent with these findings, recent studies"19 21 have demonstrated that ERAF following internal cardioversion was usually preceded by an atrial premature beat with a short coupling interval, and occurred within the first minutes after cardioversion. However, the characteristics of cardiac rhythm preceding the onset of ERAF remain unclear. Observations on the heart rate, initiation sequence, and coupling interval of the initiating atrial premature beats may allow treatment strategies to be tailored appropriately. Suppression of ERAF has important implications for the use of temporary low energy internal cardioversion and may require more frequent treatment with an implantable atrial defibrillator."19

In the present study, the onset of ERAF episodes and the characteristics of the atrial premature beats were recorded using a surface ECG and an intra-atrial electrogram. In about 10% of patients, the ERAF episodes were preceded by a long sinus pause. The cause of the bradycardia may be underlying sinoatrial disease or electrical remodelling of the sinus node by atrial fibrillation."20 It may be further aggravated by shock induced sinus node suppression. During bradycardia, the escape atrial ectopic activity, together with the pause dependent conduction abnormalities, may trigger the onset of atrial fibrillation."15 However, in the majority of episodes (90%), atrial fibrillation was reinitiated by atrial premature beats with a short coupling interval which were not preceded by bradycardia or tachycardia. Consistent with previous studies,"10 11 16–18 atrial premature beats that reinitiated atrial fibrillation had a significantly shorter cycle length and greater prematurity than those that did not. We observed that in up to 30% of patients the onset of atrial fibrillation was preceded by a long–short atrial sequence. A recent study has shown the occurrence of a preceding long–short atrial sequence was strongly associated with development of atrial fibrillation even in patients without a history of this arrhythmia."21 It has been postulated that long–short cardiac sequences increase the dispersion of myocardial refractoriness and their vulnerability for reentrant arrhythmias."22 23 Furthermore, in one third of our patients, the atrial premature beats that initiated atrial fibrillation had a very similar P wave morphology and consistent cycle length, suggesting the presence of a similar or focal origin. These patients might have a focal source of atrial fibrillation, and more detailed endocardial mapping may be useful to identify the origin of these atrial premature beats."23
detailed mapping of the onset of atrial fibrillation and the origin of the atrial premature beats, using multiple endocardial catheters or new mapping techniques, might provide a better understanding of the mechanisms of ERAF. Although our observations suggested that sotalol might be effective in preventing ERAF, it is impossible to draw firm conclusions because the study was not randomised. Nevertheless, before sotalol infusion all patients with ERAF underwent repeated cardioversions that were followed by reinitiation of atrial fibrillation. This suggests that the observed effect after sotalol administration was attributable to its use. Furthermore, our observations that sotalol suppressed atrial premature beats and that none of the patients in whom cardioversion was successful only after sotalol infusion had ERAF provide further indirect evidence to support the efficacy of sotalol in preventing ERAF.

CONCLUSIONS

We have shown that ERAF occurred in up to 31% of patients with chronic atrial fibrillation after successful internal cardioversion. This is a significant clinical problem which limits the number of patients having successful clinical termination of sustained atrial fibrillation. It has implications for the use of both temporary and permanent transvenous defibrillation in treating atrial fibrillation. ERAF is usually preceded by the occurrence of atrial premature beats, although the cardiac sequences preceding their onset seem to be heterogeneous. Intravenous sotalol effectively suppressed ERAF in the majority of patients. The use of other antiarrhythmic agents and the role of non-pharmacological treatment for the prevention of ERAF after internal cardioversion require further investigation.

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