Embolic Complications of Direct Current Cardioversion of Atrial Arrhythmias: Association With Low Intensity of Anticoagulation at the Time of Cardioversion

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OBJECTIVES
The goal of this study was to identify the factors responsible for embolic complications of direct current (DC) cardioversion of atrial arrhythmias.

BACKGROUND
Direct current cardioversion of atrial fibrillation (AF) carries a risk of thromboembolism, which is reduced, but not eliminated, by anticoagulation. The risk of embolism after conversion of atrial flutter is believed to be lower. No series to date has included enough patients receiving anticoagulants or enough patients with atrial flutter to estimate the risk in these groups.

METHODS
We reviewed the case records of 1,950 patients who underwent 2,639 attempts at DC cardioversion.

RESULTS
Cardioversion was performed within two days of the apparent onset of the arrhythmia in 443 episodes, 352 without subsequent prolonged anticoagulation with one embolic complication. Cardioversion was preceded by warfarin therapy for >3 weeks in 1,932 instances. No embolic complication occurred in 779 attempts performed with an international normalized ratio (INR) of ≥2.5 (95% confidence limits 0% to 0.48%). Of 756 cases in which the INR was =2.5 or was not measured before conversion, nine were complicated by thromboembolism. Embolism was significantly more common at an INR of 1.5 to 2.4 than at an INR ≥2.5 (0.93% vs. 0%, p = 0.012). The incidence of embolism after conversion of atrial flutter or tachycardia was similar to that after cardioversion of AF (0.72% vs. 0.46%, p = NS).

CONCLUSIONS
The INR should be ≥2.5 at the time of cardioversion if the duration of AF is uncertain or ≥2 days. Cardioversion of atrial flutter presents similar risks and requires similar anticoagulation. (J Am Coll Cardiol 2002;40:926–33) © 2002 by the American College of Cardiology Foundation

Pharmacologic or electrical conversion of atrial fibrillation (AF) to sinus rhythm is followed by thromboembolism in 1% to 5% of cases in patients not receiving anticoagulant therapy (1–8). In a nonrandomized retrospective series of 572 attempted direct current (DC) cardioversions, Bjerke-

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Abbreviations and Acronyms
AF = atrial fibrillation
DC = direct current
INR = international normalized ratio

METHODS
In 13 hospitals in three European countries, we used the hospital computer system, ward admission records, or an existing database to identify all patients who underwent DC cardioversion of atrial arrhythmias between January 1, 1990 and June 30, 1997. We retrieved and reviewed in detail the hospital notes of 87.2% of patients thus identified. In each case we determined the rhythm present immediately before each cardioversion, the apparent duration of that arrhythmia, the duration of anticoagulant therapy, the INR on the day of cardioversion, the energy of each shock administered, the duration of sinus rhythm after cardioversion, and the occurrence of complications within four weeks after cardioversion. If the case notes contained no record of a clinical assessment by a physician at four weeks or more after the cardioversion, we wrote to the physician in charge of the continuing care of that patient for information on outcome and complications. We collected details of the clinical course to at least four weeks for >90% and to at least three weeks for >97% of those whose case notes we reviewed.

Definitions. The rhythm for which cardioversion was performed was determined by review of the case notes and the precardioversion electrocardiogram. The duration of that arrhythmia was determined from the history recorded in the case notes. Patients were classified as having had a “definite” embolic event only if a stroke was documented clinically and shown by computerized tomography or magnetic resonance imaging to have been due to a cerebral infarction or if limb embolism was confirmed by angiography. “Probable” embolic complications included neurologic deficits reported by a physician but not confirmed by imaging or limb embolism suspected clinically but not tested by angiography. Confirmed myocardial infarction or pulmonary embolism was classified as a probable, rather than a definite, embolic complication because either of these events could represent a cause of AF or a consequence of cardioversion-related thromboembolism.

Any other condition that caused the patient to consult a physician within four weeks of cardioversion and any death in this period was recorded. Death was defined as “expected” if the patient was dependent on ventilatory or inotropic support at the time of cardioversion or if death was due to the progression of a neoplasm or infection present before cardioversion. Other deaths were described as “unexpected.” Bleeding was defined as “serious” if transfusion was required or if the hemorrhage was intracranial.

Anticoagulation practices. In all centers there was a policy of using anticoagulants for at least three weeks before cardioversion of AF if the arrhythmia was thought to be of >7 days duration. In cases of AF lasting <24 h, conversion was usually not followed by prolonged anticoagulation. For AF of one to seven days’ duration, policies varied. Control of anticoagulation before cardioversion varied between centers and evolved over the period of the study. In most of the hospitals in the study, control has become more strict over the past seven years, with a trend toward using anticoagulants in AF of shorter duration and an increased frequency of cancellation because of low INR values. In some cases flutter was treated in the same manner as AF, but in many cases anticoagulation was not used for atrial flutter, particularly in the earlier years of the study period.

Statistical analysis. Comparison of proportions was by chi-square test or Fisher exact test. Calculation of confidence intervals was based on the assumption of a Poisson distribution. Analysis of covariance was performed using SAS (SAS Institute, Cary, North Carolina).

RESULTS
Our search identified 2,754 patients as having had an attempted DC cardioversion (Fig. 1). We were able to obtain the hospital records of 2,401 (87.2%), with a retrieval rate of >97% in the largest center. In 451 cases there was no record of a DC cardioversion having been performed for an atrial arrhythmia, mostly in cases where conversion of a ventricular arrhythmia led to inappropriate coding in a computer database. We collected data pertaining to 2,639 cardioversion attempts in 1,950 patients. In 2,572 cases of cardioversion, we were able to collect data on the patients’ status at three to four weeks after cardioversion, the usual time for routine clinic review. Of the remainder we had data only to the time of hospital discharge 4 h to 8 h after cardioversion in 59, data to 5.1 ± 3.6 days in eight cases. Cardioversion was performed via intracardiac electrodes in 63 cases in 35 patients, including 14 using an implanted atrial defibrillator. Follow-up information to >4 weeks was available for all of these. In 34 cases transesophageal echocardiography was used to exclude atrial thrombus.

Anticoagulation was more rigorous in patients with AF than in those with other arrhythmias. Patients with AF for >2 days had coumadin anticoagulants before and after cardioversion in 1,551 of 1,682 cardioversions (92%) and an INR measured before cardioversion in 1,261 (81.3%) of these, compared with 56.9% and 75%, respectively, for other rhythms (p < 0.001 and p < 0.05, chi-square test). Only 21.6% of patients with atrial flutter or tachycardia for >2 days had a documented INR ≥2.5 at the time of cardioversion, compared with 38.3% of patients with AF for >2 days (p < 0.001, chi-square test). Patients with AF were cardioverted later than those with other rhythms (Table 1). Only 13.3% of cases of AF were converted within two days of the estimated time of onset, compared with 26.5% of other arrhythmias (p < 0.001, chi-square test).

The INR at the time of cardioversion was not related to
The INR was higher in patients with valvular AF than in others (2.80 ± 0.82 vs. 2.59 ± 0.73, p < 0.001, unpaired t test) and lower in those with lone AF, heart failure, or ethanol excess (2.53 ± 0.73, 2.51 ± 0.71 and 2.48 ± 0.85, all p < 0.05, unpaired t test) than in the remainder of the population.

**Complications.** Confirmed embolic events occurred after 14 cardioversion attempts in 14 patients, five after cardioversion of atrial flutter or atrial tachycardia, nine after conversion of AF (Fig. 1). None of those whose complication followed cardioversion from atrial flutter or atrial tachycardia had a previous history of AF. In all cases the

patient age. The INR was higher in patients with valvular AF than in others (2.80 ± 0.82 vs. 2.59 ± 0.73, p < 0.001, unpaired t test) and lower in those with lone AF, heart failure, or ethanol excess (2.53 ± 0.73, 2.51 ± 0.71 and 2.48 ± 0.85, all p < 0.05, unpaired t test) than in the remainder of the population.

**Figure 1.** Embolic and other complications within 28 days of direct current (DC) cardioversion. A small number of patients with recent-onset atrial fibrillation were receiving long-term warfarin therapy, most for paroxysmal arrhythmias or because of prosthetic valves. Arrhythmias of unknown duration were assumed to have a duration of >2 days.

**Table 1.** Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Atrial Fibrillation</th>
<th>Other Arrhythmias</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>Number of patients</td>
<td>1,438</td>
<td>512</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>62.9 ± 12.2</td>
<td>64.0 ± 14.5</td>
<td>NS</td>
</tr>
<tr>
<td>% Men</td>
<td>68.3</td>
<td>72.0</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of arrhythmia (days)</td>
<td>236 ± 565</td>
<td>97 ± 330</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Lone AF/flutter</td>
<td>319 (22.2%)</td>
<td>119 (23.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ischemic heart disease/CABG</td>
<td>289 (20.1%)</td>
<td>119 (23.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>287 (20.0%)</td>
<td>60 (11.7%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Valvar heart disease</td>
<td>222 (15.4%)</td>
<td>67 (13.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart failure/cardiomopathy/LV dysfunction</td>
<td>203 (14.1%)</td>
<td>69 (13.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ethanol excess</td>
<td>128 (8.9%)</td>
<td>14 (2.7%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>65 (4.5%)</td>
<td>38 (7.4%)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>14 (1%)</td>
<td>32 (6.3%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Thyrotoxicosis</td>
<td>32 (2.2%)</td>
<td>1 (0.2%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>SA node dysfunction</td>
<td>15 (1.0%)</td>
<td>4 (0.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Confirmed emboli</td>
<td>7 (0.46%)</td>
<td>7 (0.72%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; CABG = coronary artery bypass grafting; LV = left ventricular; SA = sinuatrial.
complication followed a successful transthoracic cardioversion. None of the patients had been screened by transesophageal echocardiography. The embolic events occurred between 6 h and 22 days after cardioversion (median 1.9 days, mean 5.1 days). In three cases the patient had undergone a previous DC cardioversion attempt without complication. Only one confirmed embolism occurred after conversion of an arrhythmia thought to have been present for 2 days.

Embolic complications occurred in association with long-term anticoagulation in nine patients, two of whom did not have an INR recorded at the time of cardioversion. In the remaining seven, the INR was between 1.4 and 2.2 (Fig. 2). The risk of embolism was significantly associated with lower INR at the time of cardioversion with no embolic events recorded in 779 attempts at cardioversion with an INR ≥2.5 compared with 7/754 (0.9%) in those with an INR <2.5 and 2/399 (0.5%) in those whose INR was not recorded (Fig. 3). The upper one-tailed 95% confidence limit for the incidence of embolism in this group is 0.48% from the Poisson distribution, significantly lower than the 1% risk that is commonly quoted for cardioversion in patients on anticoagulants.

Even if a composite end point of serious hemorrhage and systemic embolism is used, the incidence of complications was only 0.13% (95% confidence interval, 0.0024% to 0.72%) in those whose INR was ≥2.5 at the time of cardioversion. Among those in whom the INR was known at the time of cardioversion, the INR was significantly lower in cases where conversion was complicated by embolism. The INR was 0.77 lower in the embolic group (95% confidence limits, 0.17 to 1.37) after correction for age and underlying heart disease in analysis of covariance.

Of the cases of embolic complication in the presence of anticoagulation, all were associated with anticoagulation for over three weeks and two for over six months. All patients had continued their anticoagulant treatment up to the time of the complication. The INR at the time of the complication was known in five cases and ranged from 1.7 to 2.5 (mean = 2.1). All of the confirmed emboli occurred in patients with hypertension or some form of structural heart disease (Table 2), but this did not constitute a significant association.

Atrial flutter accounted for an unexpectedly high proportion of the embolic events with an overall rate similar to that for AF (Table 2). The five embolic events included three cases associated with warfarin use, one of which did not have an INR recorded before cardioversion. The others had an INR of 1.5 and 2.2, respectively (Fig. 2). The overall rate of embolism in those with atrial flutter receiving anticoagulants (3/323, 0.9%) was similar to that in patients not receiving anticoagulants (2/376, 0.5%). In the small proportion with an INR ≥2.5 at the time of cardioversion, there were no embolic complications (0/122, 0%), but the difference was not statistically significant.
Events defined as probable embolic complications occurred in seven cases in addition to the cases of confirmed embolism. Of these, three occurred in association with long-term anticoagulation. These events were transient focal neurologic deficits in four patients, pulmonary embolism diagnosed at postmortem, Q-wave myocardial infarction, and transient lower limb ischemia each in one patient. The INR at the time of conversion was not recorded in one of these patients who were anticoagulated at the time of cardioversion of AF. It was 1.7 and 2, respectively, in the others, both of whom had atrial flutter. The median time between cardioversion and a probable embolic event was 0.8 days.

Chest pain or dyspnea not attributable to pulmonary edema led to readmission to hospital or attendance at an emergency room within four weeks after cardioversion in 16 cases (Fig. 1). A pulmonary perfusion scan was performed in one case and was negative. In all other cases, the patient was discharged after exclusion of acute myocardial infarction. The median interval between cardioversion and the onset of

**Figure 3.** Relation between the international normalized ratio (INR) on the day of cardioversion and the risk of thromboembolism. Confidence intervals were calculated by assuming a Poisson distribution.

<table>
<thead>
<tr>
<th>Table 2. Characteristics of Patients With and Without Embolic Complications</th>
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<tbody>
<tr>
<td><strong>Confirmed Emboli</strong></td>
</tr>
<tr>
<td>Number of DC cardioversion attempts</td>
</tr>
<tr>
<td>Age (yrs)</td>
</tr>
<tr>
<td>% Men</td>
</tr>
<tr>
<td>Duration of arrhythmia (days)</td>
</tr>
<tr>
<td>Previous CVA/TIA</td>
</tr>
<tr>
<td>Lone AF/flutter</td>
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<tr>
<td>Ischemic heart disease/CABG</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Valvular heart disease</td>
</tr>
<tr>
<td>Including prosthetic valves</td>
</tr>
<tr>
<td>Ethanol excess</td>
</tr>
<tr>
<td>Heart failure/ cardiomyopathy/LV dysfunction</td>
</tr>
<tr>
<td>Respiratory disease</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; CABG = coronary artery bypass grafting; CVA = cerebrovascular accident; DC = direct current; LV = left ventricular; TIA = transient ischemic attack.
these symptoms was two days. There was an association with lower INR in the six cases associated with warfarin use (p < 0.05, two-tailed t test).

Two serious hemorrhages occurred within four weeks after cardioversion. A 64-year-old man with long-standing hypertension and two previous cerebral infarctions was found collapsed 14 days after successful cardioversion of AF (INR = 3.4 at the time of conversion). He was found to have a more severe hemiparesis, and computed tomography showed an intracerebral hemorrhage at the site of a previously documented cerebral infarction. He made a partial recovery with conservative management. A 60-year-old woman underwent cardioversion with heparin anticoagulation for recent-onset AF and was subsequently started on warfarin. She developed a large soft-tissue hematoma after minor trauma 23 days later associated with uncontrolled anticoagulation (INR = 6.5) but made a full recovery after transfusion and reversal of anticoagulation.

Only two fatalities can be attributed with reasonable certainty to DC cardioversion. In one, cardioversion of AF thought to be of short duration was followed by a fatal cerebral infarction. In the other, a failed attempt at internal cardioversion was followed by an unexplained out-of-hospital cardiac arrest 8 h later. This case has previously been reported (21) and was the only complication related to an internal cardioversion. The case of fatal pulmonary embolism may have been triggered by cardioversion. In nine other cases, death occurred unexpectedly within 28 days after cardioversion. In two of these, cardioversion without anticoagulation was followed by death, which was attributed on clinical grounds to pulmonary embolism, but autopsy was not performed. In the remaining seven, death was attributed to the underlying valvular or ischemic heart disease or to respiratory failure.

**DISCUSSION**

The relation between the intensity of anticoagulation and the risk of thromboembolism in chronic AF has been carefully documented (15). The risk of complications is substantially lower when the INR is >2 and very low at >2.5. Because the risk of hemorrhage increases sharply when the INR exceeds 4 to 5, it is recommended that the INR be maintained between 2 and 3 in chronic AF when anticoagulation is indicated. In practice, anticoagulation is usually adjusted to aim for a target INR of 2.5. In the absence of data specific to the period surrounding cardioversion, it has been assumed that the optimum intensity of anticoagulation is the same as in chronic AF. This assumption ignores the documented excess of thromboembolism within seven days after conversion. In the absence of anticoagulation, the incidence of systemic thromboembolism is 1% to 4% in this week, similar to the risk in a year of continuous AF. There is no evidence of any excess of hemorrhagic risk in this period, nor is there any theoretical reason to expect such an excess. The balance of these risks should, therefore, favor an INR higher than that that is optimal in chronic AF.

The relation between INR and risk of thromboembolism that we have observed is qualitatively similar to that documented in chronic AF. As in previous reports, the absolute risk of an event in the week after cardioversion was higher than in chronic AF. There was no apparent increase in the risk of serious hemorrhage after cardioversion. This suggests that cardioversion should not be attempted if the INR is near the lower end of the range considered acceptable for chronic AF. A lower limit of 2.4 to 2.5 seems reasonable on the basis of our data. The upper limit for the INR target range cannot be determined from the current set of data. International normalized ratio readings above 4 have been shown to increase the risk of hemorrhage (12) and should prompt a reduction in warfarin dosage, but an INR above the desired range should not delay cardioversion.

**Atrial flutter.** Previous reports have suggested that flutter carries a low risk of thromboembolism. In our series there was a nonsignificant excess of risk compared with AF. This probably occurred due to the documented acceptance of lower intensity anticoagulation for those with atrial flutter compared with AF. No series yet published has contained enough cases of atrial flutter to accurately define the risk of embolism in this group compared with AF, or to determine whether anticoagulation reduces the risk. Although our series did not answer either question conclusively, it shows that the risk of embolism is appreciable in the absence of adequate anticoagulation. The absence of embolic complications in the 122 patients with an INR ≥2.5 is encouraging but not conclusive.

**Lone AF.** There was a nonsignificant trend toward lower incidence of complications in patients without structural heart disease or hypertension. This finding should not be interpreted as an indication that anticoagulation can safely be omitted in such cases. Among those with emboli, one patient classified as having valvular AF had only mild mitral regurgitation with normal atrial dimensions, and one patient classified as hypertensive had well-controlled arterial pressure without ventricular hypertrophy. Our results suggest that those with lone AF represent a relatively low-risk subgroup in which a lower INR might be safe.

**Acute cardioversion.** In AF known to be of <2 days duration, cardioversion has been reported to be safe even without anticoagulation (22). We were unable to control the quality of the estimation of arrhythmia duration in our series, so we cannot quantify this risk with confidence. We recorded only one complication associated with an arrhythmia duration <2 days. The physician who performed that cardioversion later speculated that the estimated duration was incorrect. As the uncertainty was recorded after the complication and would probably not have occurred had the stroke not occurred, we have accepted the initial estimate of AF duration. This highlights the difficulty in pinpointing the onset of AF from the history alone. If the onset of AF has been observed on a cardiac monitor or recorded by an
implanted device, it may be safe to convert within 48 h without anticoagulation. In clinical practice the time of onset is seldom known for certain.

**Pathophysiology.** The mechanism of embolic complications is uncertain. They were once thought to occur when renewed atrial contraction displaced thrombi that had formed during AF. This theory implied that exclusion of atrial thrombus by transesophageal echocardiography should allow cardioversion without anticoagulation. Unfortunately, exclusion of thrombus appears to make no impact on the risk of embolism when anticoagulation is omitted (23). Restoration of sinus rhythm is followed by a fall in the velocity of blood flow in the left atrial appendage (24). It is now generally accepted that this accentuation of atrial stasis promotes new thrombus formation and embolization (25). Our data are in keeping with this hypothesis. We do not have sufficient data on patients screened by transesophageal echocardiography to comment on this strategy, except to state that safe cardioversion is achievable without it.

**Study limitations.** In a retrospective study, it is not possible to limit and characterize a cohort as accurately as in a well-executed prospective trial. We are dependent on the study limitations.


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