# The duration of atrial fibrillation influences the long-term efficacy of low-energy internal cardioversion

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*Key words:*
**Atrial fibrillation; Defibrillation.**

*Background.* **It is commonly held that long-lasting atrial fibrillation (AF), especially if associated with marked enlargement of the left atrium, is a negative predictive factor for both the recovery and the maintenance of sinus rhythm. The aim of the present study was to identify the clinical features of patients who have a greater likelihood of success both in the acute phase and, especially, in the medium-long term.**

*Methods.* **Since June 1997, we have performed low-energy internal cardioversion to 93 patients (66 males, 27 females, mean age 62 ± 9 years, range 26-80 years) with a mean duration of AF of 922 ± 1032 days. Seventy-four patients had heart disease and 19 isolated AF. External cardioversion had been previously performed in 79 patients to no avail. All patients underwent antiarrhythmic therapy and were followed for a period of 13 ± 7 months.**

*Results.* **Low-energy internal cardioversion proved efficacious, restoring sinus rhythm, in 92% of patients (86/93) and inefficacious in 8% (7/93). In 24% (21/86) the procedure, although efficacious, was followed by early recurrence of AF which proved to be intractable in 52% (11/21). At the end of the session, 81% (75/93) of the patients maintained sinus rhythm. At the end of follow-up, 40% (38/93) maintained sinus rhythm. Of all the parameters considered in the two groups, the duration of AF was the only one which differed significantly between the group in sinus rhythm and that in AF, with regard to both the efficacy of the procedure in the acute phase (755 ± 868 vs 1618 ± 1359 days, $p < 0.001$) and the long-term outcome (655 ± 5.8 vs 1107 ± 1098 days, $p < 0.05$).**

*Conclusions.* **AF lasting more than 2 years constitutes a negative predictive factor for both the recovery and the long-term maintenance of sinus rhythm.**

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## Introduction

Before the introduction of low-energy internal cardioversion, transthoracic electrical cardioversion was the most efficacious method available to the cardiologist for conversion of atrial fibrillation (AF) to sinus rhythm. However, transthoracic electrical cardioversion is of limited efficacy in obese patients with long-standing AF and/or atriomegaly[1-7]. The high percentage of sinus rhythm recovery that can be achieved by means of low-energy internal cardioversion even in these latter cases has led to the clinical adoption of this procedure. In spite of the high percentage of reversion observed in the acute phase (> 90%)[8-11] even among patients with AF that is long-standing and/or refractory to transthoracic electrical cardioversion[8,9], doubt has been cast on the clinical utility of low-energy internal cardioversion owing to the frequency of early recurrences and, especially, in view of the data from the first follow-up studies which revealed a high rate of permanent AF in the medium-long term[12-14]. These results, together with the high cost of catheters, have limited the indications for this procedure and suggest that accurate patient selection is necessary.

## Methods

Since June 1997, we have performed low-energy internal cardioversion in 93 patients divided into two groups: 1) 65 patients who had had AF for ≤ 3 years and in whom external cardioversion had proved ineffective; and 2) 28 patients who had had

AF for > 3 years and in 14 of whom transthoracic electrical cardioversion had proved ineffective. The study population consisted of 66 males and 27 females (mean age 62 ± 9 years, range 26-80 years) with a mean duration of AF of 922 ± 1032 days (range 30-4350 days); 74 had heart disease (17 dilated cardiomyopathy, 43 hypertensive heart disease, 8 non-rheumatic valvular disease, and 6 ischemic heart disease), and 19 had isolated AF. Before and after low-energy internal cardioversion, all patients underwent antiarrhythmic therapy: 79 with amiodarone (which had been administered for at least 1 month before low-energy internal cardioversion), 8 with sotalol, 5 with propafenone and 1 with carvedilol. Anticoagulation with dicumarols with INR > 2 was performed for at least 3 weeks in all patients. Before the procedure, all patients underwent complete hematochemical screening in order to evaluate blood counts, electrolyte balance, kidney and liver function, INR, and thyroid function. A baseline echocardiogram performed according to the guidelines of the American Society of Echocardiography[15] was carried out in all patients before the procedure and repeated within 24 hours of low-energy internal cardioversion in patients showing stable recovery of sinus rhythm. To avoid hemorrhagic complications due to anticoagulant therapy, access through the femoral or basilic vein was preferred, the jugular vein being used only as a second choice. The subclavian vein was not utilized.

Low-energy internal cardioversion was carried out by inserting the discharge dipole into the left branch of the pulmonary artery and the right atrium in 79 patients, and into the coronary sinus and right atrium in 14 patients. The mean energy delivered was 9.9 ± 5 J. A total of 242 shocks were administered, with a mean of 2.6 ± 1.6 shocks per patient. In 75 patients, we used the InControl system with a defibrillator capable of administering a biphasic shock synchronized on the R wave (Fig. 1), both for the two-catheter arrangement and for the single-catheter arrangement. In 18 patients, we used the Allert system with a single catheter and a defibrillator capable of delivering a biphasic shock up to 15 J. Before the procedure was started, mild sedation was induced by intravenous administration of one 10 mg phial of diazepam; further phials, up to a maximum of 3, were administered during the procedure according to the compliance of the individual patient. The mean duration of the procedures was 56 ± 21 min (range 45-120 min) and the mean length of the fluoroscopic time was 18 ± 9 min (range 3-42 min). Low-energy internal cardioversion was well tolerated by all patients and no complications were recorded. The clinical features of the patients are listed in table I. The patients were followed up for a period of 13 ± 7 months.

**Statistical analysis.** Continuous variables are expressed as means ± SD. With regard to intergroup comparison, the Student's t-test was used for values expressed as mean ± SD whereas for values expressed in percentages, the $\chi^2$ test and/or comparison between proportions were used. Values of $p < 0.05$ were regarded as statistically significant.

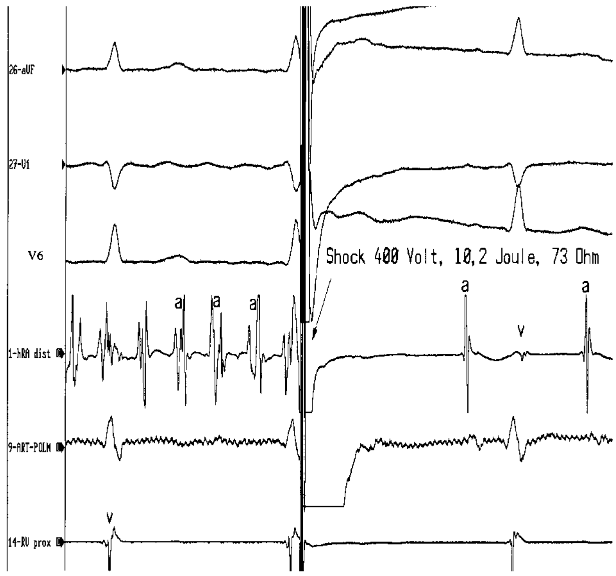


**Figure 1.** *Reversion to sinus rhythm by means of a 10-J shock. The figure shows three surface derivations (aVF, $V_1$ and $V_6$) and three endocavitary derivations (hRA = right atrium; ART-POLM = left branch of the pulmonary artery; RV prox = apex of the right ventricle). Note the atrial waves recorded in the right atrium (a) which is in fibrillation before the shock; subsequently, the restoration of sinus rhythm is accompanied by the appearance of a ventricular low potential (v). Note also that administration of the shock a few seconds after the R wave yields perfect synchronization with the QRS complex.*

**Table I.** Clinical features of the study population.

| | |
|---|---|
| No. patients | 93 |
| Age (years) | 62.4 ± 9.3 |
| Sex (M/F) | 66/27 |
| Duration of AF (days) | 922 ± 1032 |
| Amiodarone | 79 (85%) |
| Sotalol | 8 (8.6%) |
| Propafenone | 5 (5%) |
| Carvedilol | 1 (1%) |
| Left atrial AP diameter (mm) | 46.5 ± 5.7 |
| LVEDD (mm) | 52.9 ± 8.7 |
| LVEF (%) | 56.9 ± 11 |
| Heart disease | 74 (80%) |
| Previous DCS | 79 (85%) |

AF = atrial fibrillation; AP = antero-posterior; DCS = transthoracic electrical cardioversion; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction.

## Results

**Immediate results.** Low-energy internal cardioversion proved to be efficacious in 92% (86/93) of patients, and inefficacious in 8% (7/93). Among the 86 patients in whom sinus rhythm was restored, 24% (21/86) suffered a recurrence of AF during the procedure (Fig. 2). In 10 of these patients (48%), stable sinus rhythm was

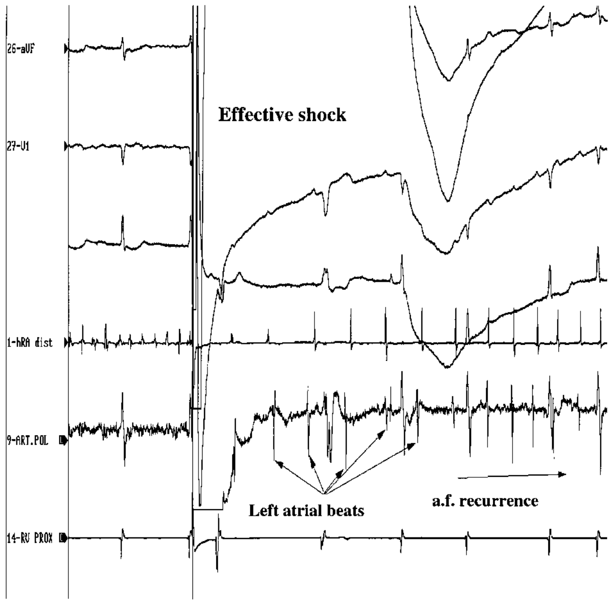


**Figure 2.** *The derivations are the same as in figure 1. After the shock, atrial fibrillation is interrupted and rapid atrial extrasystole appears. The latter begins in the left atrium (deducible from the earlier atrial deflection recorded on the dipole positioned in the left branch of the pulmonary artery than that recorded in the right atrium). This desynchronizes the electrical activity of the atrium and again triggers atrial fibrillation. Abbreviations as in figure 1.*

restored by means of a further shock following administration of IC drugs or by overdrive pacing of the interatrial septum. In 52% (11/21), the recurrence was intractable. At the end of the session, 81% (75/93) of the patients maintained sinus rhythm (group A), while 19% (18/93) had permanent AF (group B).

Comparison of the clinical features of the two groups (Table II) revealed that the two parameters which differed significantly were the duration of AF before low-energy internal cardioversion ($p < 0.001$) and age ($p < 0.005$).

**Follow-up.** During follow-up lasting 13 ± 7 months, 54/75 (72%) group A patients suffered recurrences of AF; one or more recurrences of paroxysmal AF followed by spontaneous recovery of sinus rhythm were recorded in 6/75 (8%), while persistent AF recurred in 48/75 (64%); 74% (40/54) of recurrences occurred within 1 month of low-energy internal cardioversion; 9% (5/54) between the first and sixth month, and 17% (9/54) after the sixth month (Fig. 3). In all 48 cases of persistent AF, further cardioversion was proposed. This was agreed to by 24/75 (32%, group A1) and refused by 24/75 (32%, group A2) patients. Among the 24 group A1 patients, transthoracic electrical cardioversion was performed in 22 and low-energy internal cardioversion in 2. In 7/24 patients (29%) cardioversion was unsuccessful, while sinus rhythm was restored in 17/24 (71%). During the subsequent follow-up, 9/17 patients had further recurrences; these were treated by means of transthoracic electrical cardioversion, which restored stable sinus rhythm in 2 (22%).

**Table II.** Clinical features of group A and group B patients.

| | Group A (n=75) | Group B (n=18) | p |
|---|---|---|---|
| Age (years) | 58.4 ± 10 | 63.3 ± 9 | < 0.005 |
| Sex (M/F) | 53/22 | 13/5 | NS |
| Duration of AF (days) | 755 ± 868 | 1618 ± 1359 | < 0.001 |
| Amiodarone | 64 (85%) | 15 (83%) | NS |
| Left atrial AP diameter (mm) | 46.4 ± 5.8 | 46.7 ± 5.4 | NS |
| LVEDD (mm) | 53.1 ± 6 | 52.2 ± 16 | NS |
| LVEF (%) | 57.5 ± 10 | 54 ± 15 | NS |
| Heart disease | 59 (79%) | 15 (83%) | NS |
| Previous DCS | 61 (81%) | 12 (66%) | NS |

Abbreviations as in table I.

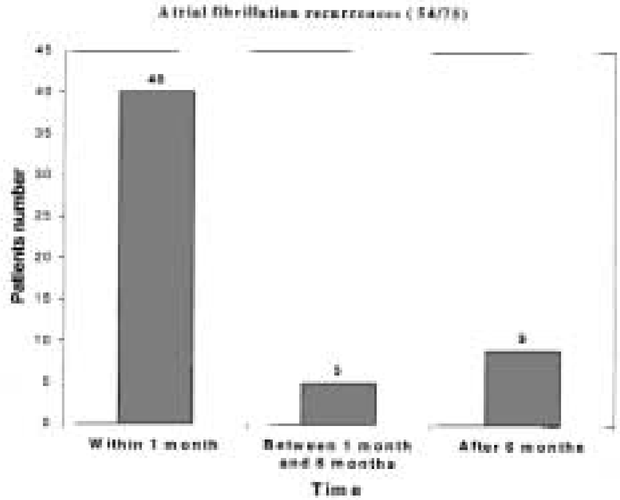


**Figure 3.** *Of the 54 group A patients who suffered from recurrences of atrial fibrillation, 74% (40/54) had the recurrence within 1 month of low-energy internal cardioversion, 9% (5/54) between 1 and 6 months, and 17% (9/54) after 6 months.*

At the end of follow-up, 41% (38/93) of the total population were in sinus rhythm; 49% (37/75) of these were group A patients and 6% (1/18) group B patients (1 patient recovered sinus rhythm spontaneously) (Fig. 4). Comparison between the clinical features of the patients in sinus rhythm at the end of follow-up (38/93, group C) and those of the patients in permanent AF (55/93, group D) revealed that the only parameter which significantly differed between the two groups was the duration of AF prior to the procedure ($p < 0.05$), while no significant difference emerged with regard to either age or left atrial size (Table III).

## Discussion

In agreement with the literature, our data confirm that low-energy internal cardioversion is able to restore si-

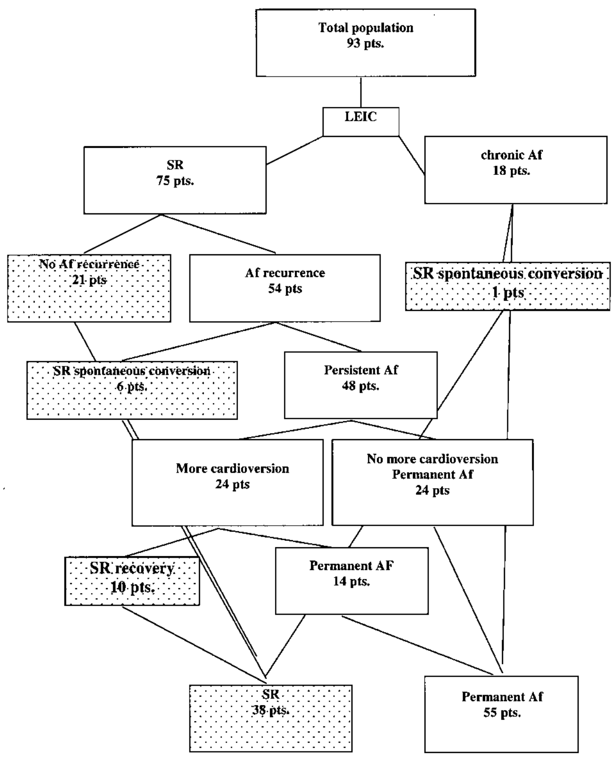


**Figure 4.** *Flow chart of the study. Af = atrial fibrillation; LEIC = low-energy internal cardioversion; SR= sinus rhythm.*

**Table III.** Clinical features of group C and group D patients.

| | Group C (n=38) | Group D (n=55) | p |
|---|---|---|---|
| Age (years) | 63 ± 10 | 62 ± 8 | NS |
| Sex (M/F) | 29/9 | 37/18 | NS |
| Duration of AF (days) | 655 ± 874 | 1107 ± 1098 | < 0.05 |
| Amiodarone | 30 (79%) | 49 (80%) | NS |
| Left atrial AP diameter (mm) | 46.1 ± 6.3 | 46.7 ± 5.4 | NS |
| LVEDD (mm) | 53 ± 5.8 | 53 ± 10 | NS |
| LVEF (%) | 56.8 ± 11 | 56.9 ± 11 | NS |
| Heart disease | 31 (81%) | 43 (78%) | NS |
| Previous DCS | 34 (89%) | 45 (81%) | NS |

Abbreviations as in table I.

nus rhythm in a high percentage of cases, even in patients with AF that is long-standing and/or refractory to external cardioversion[8,9]. Moreover, we have also confirmed the high percentage of arrhythmic recurrences in the short term and of permanent AF in the long term which have been reported by other authors[12,16]. It is important to emphasize that all our patients were treated with antiarrhythmic drugs before and after low-energy internal cardioversion and it is possible that the percentage of recurrences might have been higher if we had not treated them.

Neither the percentage of restoration in the acute phase nor the tendency to recur was correlated with the usual clinical variables or with the size of the left atrium. The influence of left ventricular function was not evaluated in our patient population, since the ejection fraction was generally within the normal range.

In contrast, both the probability of successful cardioversion in the acute phase and the tendency to recur were correlated with the duration of AF prior to low-energy internal cardioversion. Indeed, in those patients in whom low-energy internal cardioversion was able to restore sinus rhythm, the mean duration of AF prior to the procedure had been about 2 years, while it had been about 4 years in those patients in whom AF persisted in spite of the procedure. Similarly, in those patients who were in sinus rhythm at the end of the follow-up period, AF had lasted for about 2 years prior to the procedure, while it had lasted for about 3 years in those with permanent AF.

The fact that long-lasting AF tends to perpetuate itself and to render the atria more vulnerable to recurrences is well documented in the literature both in animals and in man[17-27]. In a study carried out on goats, Wijffels et al.[18] pointed out that the persistence of AF, even for a few days, can produce a so-called "electrical remodeling" in the atrial myocardium which shortens the refractory period of the cells, thus tending to maintain AF. Moreover, in short-duration AF, the same phenomenon of electrical remodeling seems to regress within a few days of the stable recovery of sinus rhythm. In addition to electrical remodeling, long-lasting AF also tends to produce anatomical remodeling. Ausma et al.[28] and Allessie[29], for example, have claimed that persistent AF can induce a sort of "cell hibernation" involving the loss of the sarcolemma, the accumulation of glycogen, perinuclear myolysis and nuclear alterations, and that when such alterations become irreversible, AF is no longer amenable to treatment. This notion has long been supported by published studies showing that the atria of patients with permanent AF are more dilated than those of patients with paroxysmal AF or in sinus rhythm. Furthermore, in tissue samples of dilated human atria, it has been observed that the myocardial cells, in addition to marked cellular degeneration, also present less negativity of the diastolic membrane potential, less overshoot and less depolarization velocity (dv/dt) than controls[30-33].

In view of these considerations, it seems clear that the longer AF is maintained, the greater will be the electrophysiological and structural modifications that take place in the atrial cells. At what point such modifications become irreversible, thus rendering AF intractable, remains to be established. Moreover, it has not yet been clearly established whether the speed and reversibility of cellular remodeling are influenced by other factors such as the presence of associated heart disease, arterial hypertension, left ventricular pump deficit, age, drugs, etc.

As already mentioned, among the several clinical variables evaluated in our study, the duration of AF was the only one that was able to predict the efficacy of low-energy internal cardioversion in the acute phase and patient progression during follow-up. The broad standard deviation encountered in the value of AF duration in group C (in sinus rhythm at the end of the follow-up period) and in group D (permanent AF at the end of follow-up) may well indicate the broad heterogeneity of the processes of electrophysiological and anatomical remodeling. That the duration of AF is an important parameter in predicting the outcome of low-energy internal cardioversion has already been observed by other authors, though in different case records. Levy et al.[34], for instance, examined the results of XAD, a multicenter study on low-energy intracardiac defibrillation, and found a significant difference in the percentage of reversion to sinus rhythm between patients with a duration of AF < 1 month (> 90%) and in those with a history of AF lasting > 1 month (70%). In a follow-up study, Alt et al.[35] found a significant difference at the end of the 12-month period between patients with AF lasting < 2 months and those with a duration of AF > 2 months ($p < 0.05$). It follows that AF should be treated as soon as possible.

With regard to age, our finding that low-energy internal cardioversion in the acute phase was more successful in older patients is difficult to explain and may be linked to the low number of patients involved. As far as the presence of heart disease, the type of antiarrhythmic therapy, the size of the left atrium, the end-diastolic diameter and the ejection fraction of the left ventricle and previous transthoracic electrical cardioversion were concerned, we found no significant differences neither between groups A and B nor between groups C and D.

With reference to the dimensions of the left atrium, Alt et al.[35] found a significant difference in the maintenance of sinus rhythm at the end of a 12-month follow-up period between patients with a left atrial antero-posterior diameter > 60 mm and those with a diameter < 60 mm ($p < 0.05$). This difference was not confirmed in our study, probably because, unlike Alt, we had few patients with marked atriomegaly (Table I).

Another noteworthy finding that emerged from our study is that by implementing an aggressive therapeutic strategy in patients with AF recurrence (resubmitting such patients to transthoracic electrical cardioversion or low-energy internal cardioversion), sinus rhythm can be maintained in almost half of the patients treated. Indeed, among the 24 patients who had suffered a recurrence of AF, this aggressive approach yielded, at the end of the follow-up period, stable sinus rhythm in 10 (42%). In theory, had such an approach been adopted in all cases, we would have been able to achieve stable sinus rhythm at the end of follow-up in 52% of the patients treated (48/93, 48 = 21 + 6 + 10 + 10 + 1) (Fig. 4).

Finally, it is worth noting that among patients with AF recurrence following low-energy internal cardioversion, transthoracic electrical cardioversion was able to restore sinus rhythm in 70% of cases, including those in which this procedure had previously been inefficacious. There is no simple explanation for this, though two hypotheses may be proposed. The first is that the successful outcome of treatment of the recurrence may have been favored by positive electrical remodeling resulting from the more or less long period of sinus rhythm. The second hypothesis is that the type of AF involved in the recurrence may have been different from that of the AF treated by means of low-energy internal cardioversion.

**Limitations of the study.** This study was begun before the clinical utilization of biphasic external cardioversion. Thus, the clinical indications to low-energy internal cardioversion were conditioned by the results of monophasic external cardioversion. Actually, since the introduction of biphasic external cardioversion, the percentage of non-responder patients is decreasing and consequently the indications to, and results of low-energy internal cardioversion might change in the future[36].

**Conclusions.** Low-energy internal cardioversion is a costly technique which does not always yield satisfactory long-term results. It therefore follows that candidates for this procedure should be accurately selected. On the basis of the data which emerge from the present study, low-energy internal cardioversion appears to be indicated in: 1) patients with AF that is refractory to transthoracic electrical cardioversion, and 2) patients in whom the duration of AF is not too long (< 2 years).

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