Original articles

A new therapeutic strategy for electrical cardioversion of atrial fibrillation

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Key words:
Atrial fibrillation; Electrical cardioversion; Low-molecular-weight heparins; Transesophageal echocardiography.

Background. **The conventional approach to cardioversion of atrial fibrillation includes a period of anticoagulation with oral anticoagulant therapy (OAT) extending from 3 weeks precardioversion to 4 weeks postcardioversion. The protocol of rapid anticoagulation (such as that of the ACUTE study) consists of a precardioversion transesophageal echocardiography (TEE) followed by OAT for 4 weeks. In the last few years low-molecular-weight heparins have established themselves as a safe and efficacious alternative to traditional antithrombotic therapies. The aim of this study was to demonstrate that the exclusion of thrombi by precardioversion TEE together with the exclusion of atrial stunning by a second TEE performed after 1 week, to date not suggested in the literature, could reduce to 7 days the period of pericardioversion anticoagulation. This therapy would be carried out using low-molecular-weight heparins with no need for biological monitoring and with the possibility of self-administration.**

Methods. **We have studied 57 consecutive patients who had atrial fibrillation or flutter with a history of atrial fibrillation lasting > 48 hours. All patients received enoxaparin at a dosage of 100 IU antiXa/kg twice daily before undergoing multiplane TEE. Previous informed consent and ethical committee authorization had been obtained. Twenty-four hours following TEE, in the absence of thrombi and/or spontaneous moderate/severe echocontrast in the atrial chambers, the patients underwent electrical cardioversion and were discharged within 24 hours of sinus rhythm restoration. These patients were prescribed enoxaparin at the indicated dosage twice daily until TEE, performed in an outpatients setting 7 days following cardioversion. In the absence of thrombi and/or atrial and/or left atrial appendage stunning, OAT was terminated. Enoxaparin was associated with OAT for the following 3 weeks if any of the following signs of stunning were present: A wave inferior to the normal value for age at transmitral Doppler; a left atrial appendage emptying velocity < 40 cm/s; the appearance or increase in the severity of spontaneous echocontrast. For all patients, clinical and electrocardiographic follow-up was carried out at 1 month.**

Results. **In one patient TEE was not tolerated and one refused it. In 7 patients cardioversion was not performed: 4 because of the presence of thrombi, 1 because of moderate/severe spontaneous echocontrast and 2 owing to spontaneous cardioversion. Of the remaining 48 patients, cardioversion proved to be efficacious in 38, with sustained sinus rhythm at 1 week in 33 patients. One of these refused the second TEE and of the remaining 32 patients, 24 (75%) showed no signs of stunning at the second TEE and so anticoagulation was terminated. Thus, after 1 week, 75% (24/33) of patients in sinus rhythm could benefit from a shortened anticoagulation therapy which lasted for a mean of only 8.5 days. No patients showed signs of a thromboembolic accident at 1 and 2 months of follow-up.**

Conclusions. **Most patients undergoing electrical cardioversion for atrial fibrillation could benefit from a shorter period of anticoagulation with low-molecular-weight heparins for 1 week if TEE precardioversion and 7 days postcardioversion excludes thrombi and atrial stunning. The management of patients with atrial fibrillation would be greatly simplified.**

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Atrial fibrillation is regarded as the most common symptomatic cardiac arrhythmia and is associated with an increased risk of thromboembolism, heart failure, and death[1,2].

Since 1962, electrical cardioversion has been utilized in order to restore sinus rhythm in patients with atrial fibrillation. However, the sudden conversion to sinus rhythm – an expression of the efficaciousness of electrical cardioversion – is associated with an increased risk of embolization of thrombi from the left atrium, mainly from the left atrial appendage[3,4]. Anticoagulant treatment for 3-4 weeks significantly reduces the incidence of the thromboembolic complications of cardioversion[5-7].

Since 1992, the American College of Chest Physicians has recommended 1 month of anticoagulant prophylaxis, on the basis of previous non-randomized, non-controlled trials. This approach also includes 4 weeks of anticoagulant treatment following cardioversion, due to potential thromboembolic sequelae[8].

The time and limitation this approach entails[9] has led many researchers to pursue new strategies in order to guarantee a quicker, easier and safer management (in terms of embolic event prevention) of patients suffering from atrial fibrillation.

In the protocol of rapid anticoagulation performed in the ACUTE study[9], transesophageal echocardiography (TEE) is recommended to rule out the presence of cardiac thrombi before cardioversion, allowing patients not presenting with atrial thrombi to undergo cardioversion within 24 hours[10,11]. However, negative TEE does not exclude thromboembolism after cardioversion[12]. Consequently, to date, 4 weeks of anticoagulant treatment following cardioversion has been mandatory.

The occurrence of thromboembolic events in the postcardioversion period is most likely associated with a lack of recovery of atrial contractility, a condition known as atrial "stunning" which, as documented by TEE, usually lasts for about 1 week following electrical cardioversion[13-15].

On the basis of the above-mentioned considerations, we decided upon a second TEE-guided postcardioversion approach to screen patients who are found not to present with thrombi and stunning of the atrium and left atrial appendage as evaluated by TEE performed at 1 week after cardioversion[16,17]. In this case anticoagulant treatment can be shortened and even terminated.

Anticoagulant treatment is usually performed by continuous adjusted-dose intravenous infusion of unfractionated heparin and subsequent oral anticoagulation. Recently, low-molecular-weight heparins (LMWH) have shown to be safe and efficacious in antithrombotic prevention and treatment in both venous and arterial thromboembolism[18-23]; several randomized clinical trials have shown LMWH therapy to be just as efficacious as unfractionated heparin with the advantage that it is not at a fixed dosage, does not need monitoring and can be self-administered.

The aim of this study was to assess the feasibility and the safety of a TEE-guided pericardioversion anticoagulant therapeutic approach (POSTEC study: POStcardioversion Transoesophageal EChocardiography), according to which, in case of a normal mechanical function of the atrium and auricula at a second TEE performed 1 week after cardioversion, therapy using LMWH in alternative to oral anticoagulants may be significantly reduced. The management of the electrical cardioversion of atrial fibrillation would thus be greatly simplified.

Methods

Study population. From October 1st, 1999 through October 30th, 2000, 57 consecutive patients (46 males, 11 females) with atrial fibrillation and recommended for electrical cardioversion were admitted to our division. The patients' age ranged from 60 to 76 years. All patients were examined by a cardiologist who determined whether cardioversion was indicated or not before enrolling the patients into this prospective study.

Patients were eligible for inclusion if they had atrial fibrillation for at least 48 hours and/or atrial flutter associated with a history of atrial fibrillation. Exclusion criteria were the following: 1) moderate-severe mitral stenosis; 2) chronic oral anticoagulant therapy; 3) contraindications to TEE, to heparin or oral anticoagulants; 4) urgent cardioversion due to hemodynamic instability; 5) women in whom pregnancy could not be excluded; 6) a cardioembolic event within the previous month.

Study protocol (Fig. 1). Having verified the criteria for inclusion and having obtained informed consent, the LMWH antithrombotic drug enoxaparin was subcutaneously administered at doses of 100 IU antiXa (1 mg)/kg every 12 hours. All patients underwent clinical evaluation and routine laboratory examinations. All patients were first submitted to a thorough transthoracic echocardiography (TTE). In the absence of thrombi evidenced by TTE examination, a TEE was performed as soon as possible and no later than 24 hours following enrollment (after 2-3 administrations of enoxaparin).

The patients with thrombi and/or spontaneous echocontrast of a moderate to severe degree at TTE or TEE began therapy with oral anticoagulants for 4 weeks (INR 2-3) and, in the absence of thrombi at second TEE, were submitted to cardioversion. The patients who, on the other hand, following an efficacious cardioversion, had restored sinus rhythm were given proper training and discharged as early as possible. Prior to discharge these patients were submitted to a transthoracic ultrasound check-up (24-48 hours after cardioversion), with particular attention being paid to the mitral Doppler pattern. These patients continued to take enoxaparin at the indicated dosage at home. After 1 week they returned to the hospital as outpatients and their condition evaluated at ECG, TTE and a second TEE. In the presence of stable sinus rhythm and in the absence of thrombi or signs of atrial and/or left atrial appendage "stunning", heparin therapy was discontinued. If there were signs of atrial and/or left atrial appendage stunning, the patients began a 3-week oral anticoagulant therapy, initially associated with enoxaparin until, on the basis of the prothrombin time, the therapeutic range was reached (INR 2-3).

The protocol was approved by the ethical committee of our hospital and written informed consent was obtained from all participants.

The patients underwent clinical check-ups, ECG and TTE 4 weeks after cardioversion.

Echocardiographic examination. A complete TTE was initially performed in all patients using the commonly available equipment (Sequoia, Acuson XP/10, Mountain View, CA; Sonos 5500, Hewlett Packard, Andover, MA, USA). Particular attention was paid to

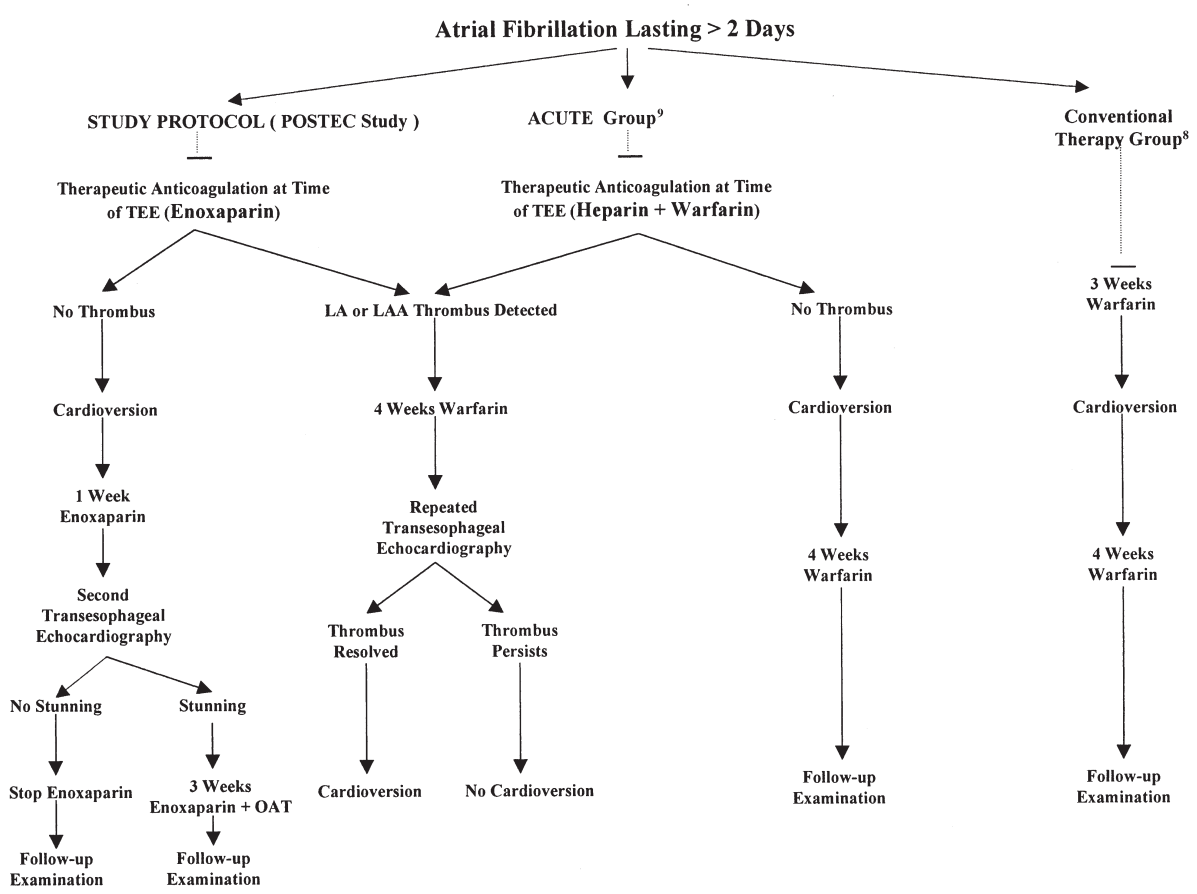

Figure 1. *Flow-chart of our study protocol (POSTEC study) compared with the transesophageal (TEE)-guided study (ACUTE group) and the conventional therapy group. LA = left atrial; LAA = left atrial appendage; OAT = oral anticoagulant therapy.*

the left atrial systolic dimensions as evaluated in the long parasternal view in accordance with standardized methods, to the evaluation of the left ventricular function, defined as abnormal in the presence of global or regional hypokinesia and to the calculation of the ejection fraction according to standardized methods. With regard to those patients in sinus rhythm, particular attention was paid to the recording of the velocities of the pulsed Doppler transmitral flow in the 4-chamber view positioning sample volume at the tip of the mitral valve. We measured the peak E and A wave velocities, and the E/A ratio, their velocity/time integral and the E and A filling fractions. A wave inferior to the normal values for a given age[24] was considered as indicative of a lack of recovery of atrial mechanical function (atrial stunning).

A complete multiplane TEE was performed with the patient in pharyngeal anesthesia achieved using a 10% lidocaine solution and in conditions of mild sedation with diazepam before proceeding to cardioversion. Particular care was paid to the achievement of an optimal visualization of the atria and of the left atrial appendage in order to determine the presence or absence of thrombi and/or spontaneous echocontrast. The presence of a thrombus was diagnosed when TEE was suggestive of the presence, within the atrial body or left atrial appendage, of a clearly defined, echoreflecting mass which was distinct from the underlying endocardium, observable in more than one section and not related to the pectinate muscles. Spontaneous echocontrast was defined as a pattern of dynamic intracavitary echoes with a typical swirling movement, not clearly distinguishable from artifacts and classifiable as mild, moderate or severe. The left atrial appendage was evaluated using pulsed Doppler and a sample volume positioned into the outlet of the left atrial appendage cavity ≥ 1 cm away from the left atrial cavity. In atrial fibrillation, a repetitive biphasic pattern was recorded and the peak velocity of the emptying and filling waves calculated as the average of 5 cardiac cycles. The following were considered as signs of left atrial appendage stunning as evidenced by TEE[25,26]: 1) the appearance or the intensification of the spontaneous echocontrast, 2) peak emptying and filling velocities < 50 cm/s.

Results

The clinical characteristics of this group of patients are reported in table I: 39 had hypertension, 8 coronary artery disease, 2 cardiomyopathy and 5 valvulopathy. The ejection fraction was < 50% in 13 patients. Among those enrolled, 42 patients (73.6%) had atrial fibrilla-

Table I. Clinical, demographic and echocardiographic characteristics of the 57 patients.

Male sex	46 (80%)
Mean age (years)	69 (60-76)
Atrial fibrillation	42 (73.6%)
Recurrent arrhythmia	29
Hypertension	39
Coronary artery disease	8
Valvulopathy	5
Cardiomyopathy	2
Lone atrial fibrillation	3
Left atrial appendage dimensions (mm)	43.2 ± 5.0
Ejection fraction < 50%	13

tion lasting > 2 days and 15 patients had atrial flutter and a documented history of atrial fibrillation. Twenty-nine of these patients had a history of recurrent arrhythmia.

TEE was not tolerated by one and was refused by another of the 57 studied patients (Fig. 2). Among the remaining 55 patients, 7 were not submitted to cardioversion due to the presence of thrombi in 4, spontaneous severe echocontrast in 1, and the onset of spontaneous cardioversion in another 2. With regard to the remaining patients, cardioversion successfully achieved a sinus rhythm in 38 patients and in 33 of these this rhythm was still present at 1 week of follow-up. Thirty-two of these patients were submitted to a second TEE after 1 week. Evidence of stunning was found in 8 patients who were then placed on oral anticoagulant therapy including enoxaparin for a further 3 weeks. In 24 of 32 patients (75%) there were no signs of stunning and so their anticoagulant therapy was terminated. No embolic events were recorded in either of these two groups at 1 month of follow-up. Sinus rhythm was present in 21 patients who had no atrial stunning and in 5 patients who had presented with signs of stunning (Fig. 2).

Figure 3 refers to a patient who, at check-up, did not present with any signs of stunning. It may be seen that a high velocity profile was already observable at basal conditions. The normal velocity profile was maintained after electrical cardioversion and sinus rhythm restored after 1 week of anticoagulant therapy. There is also a high-amplitude, high-velocity transmitral A wave.

Figure 4, on the other hand, refers to a case of atrial stunning. It may be seen that there is a low velocity profile at basal conditions and that 1 week following

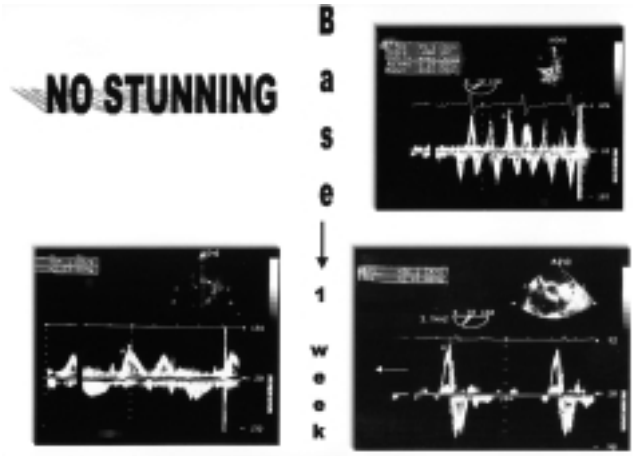

Figure 3. *A patient with no signs of stunning. It may be seen that a high-velocity profile is already present at basal conditions. The normal velocity profile is kept after electrical cardioversion and restoration of sinus rhythm after 1 week of anticoagulant therapy. There is also a high transmitral A wave with an elevated amplitude and velocity.*

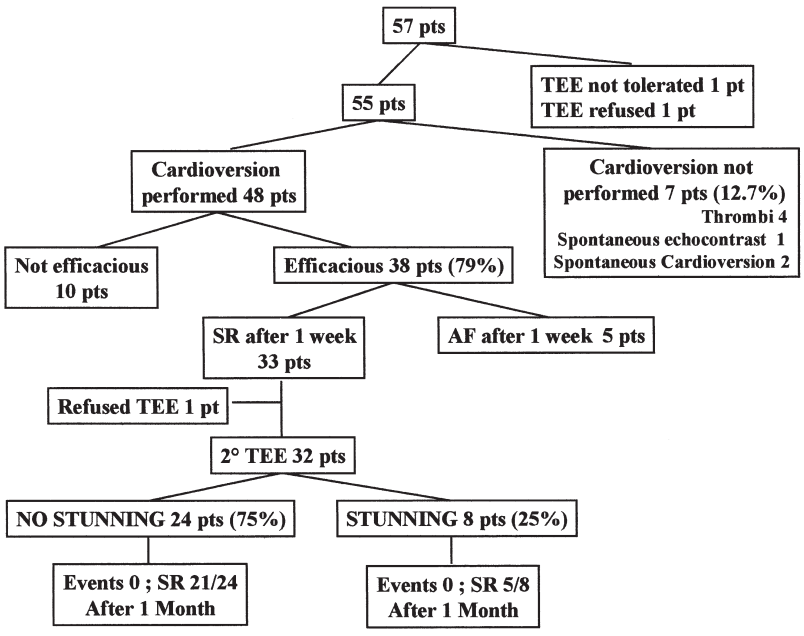

Figure 2. *Flow-chart of 57 patients undergoing electrical cardioversion. SR = sinus rhythm; TEE = transesophageal echocardiography.*

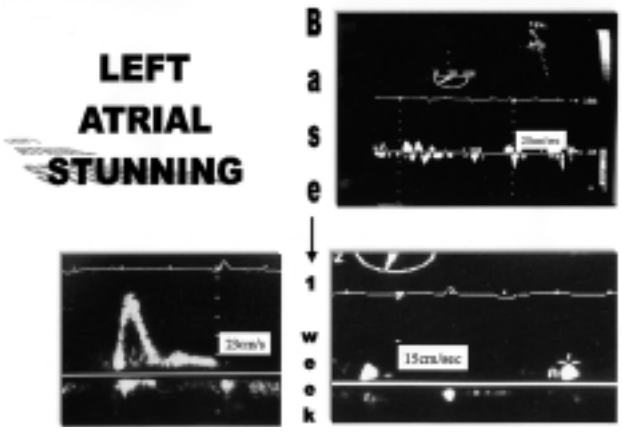

Figure 4. *A case of atrial stunning. It may be seen that at basal conditions there is a low-velocity profile which persists to the level of the left atrial appendage 1 week following sinus rhythm restoration. A low-amplitude and velocity A wave on the transmitral pattern may also be seen.*

sinus rhythm restoration, it persists to the level of that of the left atrial appendage. One may also detect a low-amplitude and velocity A wave at the transmitral pattern.

Table II shows the general characteristics and p values of the patients with and without stunning; unfortunately, the sample is too small to have a significant statistical power.

Table II. General characteristics of the patients with and without stunning.

	No stunning (n=24)	Stunning (n=8)	p
Age (years)	69 ± 80	71.3 ± 7.6	NS
Left atrial dimensions (mm)	40.9 ± 3.07	45.3 ± 5.6	0.004
Energy (J)	243 ± 137.77	300 ± 198	NS
Shocks (n=)	1.16 ± 0.38	1.32 ± 33	NS
Duration of AF	22.7 ± 39.4	32.2 ± 34.6	NS

Values are expressed as mean ± SD. AF = atrial fibrillation.

All the 8 patients showing atrial stunning after 1 week had signs of spontaneous echocontrast which was mild in 4 cases and moderate in the other 4. All but one had a precardioversion emptying velocity < 50 cm/s (Table III). The group of 24 patients showing no signs of stunning, instead, presented a left atrial appendage emptying velocity generally > 50 cm/s; in only 1 patient was this velocity equal to 25 cm/s whereas in 5 it was approximately 40 cm/s (Table IV).

In 4 patients, all hypertensive and 3 diabetic, echocardiography revealed the presence of a thrombus in the left atrial appendage; in 1 of these patients the thrombus appeared pedunculated and mobile while in the other 3 the thrombus appeared only slightly mobile and attached to the left atrial appendage wall.

In all the patients studied, 4 hours following the administration of the second dose of enoxaparin, the activated factor X activity was evaluated. The activated factor X activity is a marker of the biological activity of heparin and in all cases the administered dose was found to be within the therapeutic range.

Table V is a synthesis of the data concerning the feasibility and safety of this therapeutic regimen. These data have been compared with the data observed for a conventional therapeutic regimen and with those reported by the authors of the ACUTE pilot study[9]. No substantial differences between the number of successful cardioversions in the three groups (48/57 vs 37/64 in the group undergoing conventional anticoagulant therapy and 47/62 in the ACUTE group) was found. However, there was a reduction in the time delay from enrollment to cardioversion (1.4 vs 33 days for the conventional group and 4.2 days for the ACUTE group). The difference is clearly significant when the comparison is made with the conventional group but is still noteworthy when made with the group undergoing shortened TEE-guided anticoagulation of the ACUTE type. With regard to the data relative to the safety of the three approaches, no embolic or hemorrhagic event or death occurred in our group or

Table III. Echocardiographic parameters of the 8 patients with stunning.

Patient	A wave	E/A ratio	SEC		EV-AA (ms)	
	(ms)		Before	After	Before	After
1	128	1.2	2	2	27	40
2	50	1.2	0	1	80	25
3	45	1.9	2	2	32	36
4	33	3.6	2	2	48	43
5	71	0.9	2	2	35	18
6	40	2.8	2	1	38	25
7	32	3	1	1	30	38
8	40	1.9	1	1	25	28
Mean ± SD	54.9 ± 32.01	2.07 ± 0.98	1.5 ± 0.7	1.5 ± 0.53	39.4 ± 18	31.6 ± 8.8

EV-AA = emptying velocity of the left atrial appendage before and after 1 week; SEC = spontaneous echocontrast before and after 1 week (1 = mild, 2 = moderate).

Table IV. Echocardiographic parameters of the 24 patients without stunning.

Patient	A wave (ms)	E/A ratio	SEC		EV-AA (ms)	
			Before	After	Before	After
1	32	1.3	0	1	70	50
2	80	0.9	0	0	52	60
3	70	1	0	0	40	70
4	105	0.8	2	0	40	72
5	112	0.8	1	1	53	51
6	60	1.4	0	0	40	50
7	52	1	0	0	50	51
8	98	1.4	2	1	25	60
9	85	0.6	0	0	74	89
10	73	1.2	0	0	80	59
11	64	1.2	0	0	60	101
12	107	0.7	0	0	60	70
13	95	0.7	1	1	45	65
14	88	0.7	0	0	80	108
15	73	1.3	0	0	60	60
16	97	0.9	0	0	80	67
17	62	1.2	0	0	75	52
18	52	1.3	0	0	50	52
19	100	1.6	0	0	85	68
20	84	1	0	0	72	80
21	83	1.08	0	0	42	42
22	79	1.6	0	0	31	50
23	68	0.88	0	0	69	78
24	70	0.8	0	0	71	70
Mean ± SD	78.7 ± 19.8	1.06 ± 0.3	0.25 ± 0.6	0.17 ± 0.4	58.5 ± 17.2	65.6 ± 16.5

Abbreviations as in table III.

Table V. Summary of the data concerning the feasibility and safety of the group under study compared with the data of a conventional group treated in accordance with the American recommendations and those of the ACUTE group.

	Study protocol	ACUTE pilot study	
		Conventional therapy group	TEE-guided group
Feasibility outcomes			
Cardioversion	48/57 (84%)	37/64 (58%)	47/62 (76%)
Time from enrollment to cardioversion (days)	1.4 (1.1 to 2.8)	33 (26 to 40)	4.2 (2.1 to 5.6)
Safety outcomes			
Embolic event	0/57	1/64	0/62
Death related to cardioversion	0/57	0/64	0/62
Bleeding	0/57	5/64	0/62
Other outcomes			
RA or LA thrombi at TEE	4/57 (7%)	–	7/56 (13%)
SR after cardioversion	38/48 (79%)	28/37 (76%)	40/47 (85%)
SR at 4 weeks	33/57 (58%)	37/64 (56%)	34/62 (55%)
SR at 4 weeks in patients with successful cardioversion	27/38 (66%)	–	–

LA = left atrial; RA = right atrial; SR = sinus rhythm; TEE = transesophageal echocardiography.

in the ACUTE group, but one peripheral embolic and 5 hemorrhagic events were recorded in the conventional group. Evaluating other data (Table V), the percentage of thrombi as diagnosed at TEE turned out to be 7% (4/57) compared to 13% in the ACUTE group. Other results, which were similar to those of the ACUTE group, regarded the percentage of patients in whom cardioversion was successful in restoring sinus rhythm (79 vs 76% and 85%) and the percentage of those who maintained sinus rhythm after 4 weeks (58 vs 56% and 55%). We would like to point out that in our group, after 1 week, 75% (24/33) of patients in sinus rhythm were able to take advantage of a shortened anticoagulation therapy which lasted for a mean of only 8.5 days.

Discussion

The global incidence of atrial fibrillation for adults is 0.4% and it increases to 7.9% for subjects > 75 years. If feasible, cardioversion is attempted in order to decrease symptoms and improve cardiac function. Yet, efficacious electrical cardioversion, with the abrupt conversion to sinus rhythm, is itself associated with an increased risk of embolism following the dislocation of the thrombi from the atrial chambers, especially from the left atrial appendage[3,4]. Embolic stroke is a serious complication of cardioversion with a reported prevalence ranging between 0.6 and 5.6%. Three to 4 weeks of anticoagulant therapy significantly decrease the incidence of thromboembolic manifestations[5-7]. This explains the wide use of the therapeutic scheme proposed in 1992 by the American College of Chest Physicians for patients with atrial fibrillation lasting > 2 days[8]. The main limits of the conventional approach are: 1) a delayed cardioversion for a great number of the patients who do not have thrombi and who could consequently benefit from an early and safe cardioversion; 2) an increased risk of hemorrhage due to the prolonged anticoagulant therapy; 3) the need for hospitalization; 4) the absence of controlled studies that could demonstrate its efficacy. In the light of these considerations, research aimed at finding new strategies that would allow a more rapid and simple management of the patients with atrial fibrillation without any drawbacks in terms of the prevention of thromboembolic phenomena was started. Thus the protocol of rapid anticoagulation or of TEE-guided cardioversion, in which TEE, thanks to its accuracy in the diagnosis of atrial thrombi, is the tool to be used for the selection of those patients who may benefit from early cardioversion[10,11]. The exclusion of atrial thrombi at the time of TEE, however, does not preclude the possibility of embolic events after cardioversion since thrombi could still be formed during the interval between TEE and cardioversion and during the postcardioversion period[12]. This explains the need, confirmed by retrospective studies, of an anticoagulation therapy during the pericardioversion period. At least 4 prospective trials have examined the safety of the TEE-guided approach to early cardioversion[9,27-29] and the results published to date are promising. At present, this protocol may be considered to have a high safety profile similar to that of the conventional one. The initial results reported for the ACUTE study, a multicenter trial which was intended to include more than 3000 randomized patients undergoing the two treatments but precociously interrupted because of the difficulty in recruiting patients and owing to the lack of funds, confirm the previous results[30]. The observed occurrence, during the period following cardioversion, of thromboembolic phenomena even in patients with a negative precardioversion TEE, probably related to the formation of new thrombi between TEE and cardioversion or after cardioversion itself, imply that, during the pericardioversion period, anticoagulant treatment is mandatory[12]. In the absence of controlled studies and on the basis of the recommendations of the American College of Chest Physicians, the postcardioversion period of anticoagulant therapy should last for 4 weeks. The persistence of reduced mechanical atrial and left atrial appendage functions, the so-called "stunning", even after the sinus rhythm has been re-acquired for days or even weeks, has provided the pathophysiological explanation of the clinically evidenced atrial stasis and consequently thrombus formation[13-16]. Ultrasound is the tool for the identification of the condition of "stunning". This condition can be explored by means of TTE through the transmitral flow and the evidence of a lack of or a reduced amplitude and velocity of the A wave[26]. Yet, the demonstrated possible mechanical dissociation between the atrium and left atrial appendage calls for TEE, with its recognized capacity to provide an optimal functional and anatomical profile not only of the atrium but also of the left atrial appendage. A reduced velocity of left atrial appendage emptying and filling, a reduced left atrial appendage "change", the appearance or intensification of spontaneous echocontrast in the atrium or left atrial appendage, may all be considered as expressions of stunning. An interesting datum is that the duration of stunning correlates to the duration of precardioversion atrial fibrillation. As observed by Manning et al.[31], patients with non-valvular atrial fibrillation lasting < 6 weeks have a more or less complete recovery of the atrial mechanical functions within 1 week of cardioversion. There are numerous other reports which confirm Manning's findings[32-36]. A recent large-scale study including 4621 patients was carried out to define the timing of the postcardioversion thromboembolic events and showed that in 98% of the cases these take place within the first 7 days of sinus rhythm recovery[37]. For these reasons we decided to resort to an approach including a second TEE performed 1 week after cardioversion. To date, such an approach has not been suggested in the literature. This approach was employed with the aim of identifying those patients who, in the absence of thrombi or atrial and/or left atrial appendage stunning and so in the presence of normal atrial and left atrial appendage mechanical functions, may benefit from a shortened period of anticoagulant therapy. At present, anticoagulant treatment consists of continuous adjusted-dose intravenous infusion of unfractionated heparin and subsequent oral anticoagulation. Yet, therapy with dicoumarols, though it reduces the risk of cardioversion-correlated thromboembolism, is unfortunately associated with a greater risk of hemorrhagic complications. This occurs in 1-2% of patients and these may require hospitalization, blood transfusion and emergency surgery and obviously have to suspend therapy. Minor complications (nosebleeds, hematuria, menorrhagia) have been reported in 6-8% of patients and for these it was decided to reduce the dosage of anticoagulant therapy to subtherapeutic

values. Even in the absence of hemorrhagic complications subtherapeutic prothrombin levels are frequent. Italian and international reviews agree that anticoagulant treatment, with cardioversion performed along the American College of Chest Physicians' guidelines, is often underused, particularly in elderly patients[38-40]. On the other hand, the efficacy of LMWH[18], both for arterial and venous thromboembolism, has now been demonstrated by numerous randomized clinical studies which have compared unfractionated heparin with fractionated heparin in various clinical conditions. All the studies have shown that the two drugs have an equivalent therapeutic effect. Therefore, LMWH can be the drug of choice for almost all the arterial and venous conditions in which it is necessary to administer heparin, for example in the treatment of a non-Q wave myocardial infarction and in unstable angina[19-21] and in the treatment and the prophylaxis of venous thrombi and deep venous thrombosis[22,23]. Moreover, LMWH have substantial advantages: 1) administration at fixed dosages, which do not need to be adjusted unless in exceptional circumstances, with a greater reliability in terms of outcome, 2) it is not necessary to carry out coagulation analysis to monitor the activity of the drug (administering LMWH, in fact, does not necessitate repeated measurements of the parameters of coagulation which, on the other hand, would be necessary to avoid the administration of insufficient or excessive dosages in case of other therapeutic approaches), 3) the possibility of self-administration, 4) thanks to its longer half-life it necessitates less frequent administrations, 5) the risk of osteoporosis and the incidence of thrombocytopenia are decreased, 6) the risk of hemorrhagic complications is decreased. The aim of this study was to evaluate the feasibility and safety profile of a new TEE-guided strategy compared with the TEE-guided approach (ACUTE study), in the management of patients with atrial fibrillation lasting > 48 hours and for whom electrical cardioversion is recommended (Fig. 1). The new strategy of a second TEE carried out 1 week after cardioversion means that patients who show no signs of atrial and/or left atrial appendage "stunning" can benefit from a shortened anticoagulation therapy. This therapy, which begins within 24 hours prior to cardioversion, includes the administration of LMWH and may be employed as an alternative to oral anticoagulation. It may be suspended 1 week after cardioversion. In this study, the rationale behind the use of anticoagulation is based on three assumptions: 1) the reliability of pre-cardioversion TEE in excluding atrial thrombosis; 2) the reliability of a second TEE performed 1 week after cardioversion in excluding the presence of thromboembolic risk factors, including the condition of atrial "stunning"; 3) the reliability of LMWH therapy in the prevention of thrombus formation between the first TEE and cardioversion and in the postcardioversion period. In the absence of the risk factors for thromboembolic events as determined by TEE performed 1 week after cardioversion, LMWH therapy may be suspended. In our opinion, TEE is the ideal instrument for excluding the potential thromboembolic indicators and for the selection of a low-risk group of patients who may be submitted to this new brief anticoagulation strategy. Indeed, the results of the ACUTE I study demonstrate that all those patients with embolic events had echocardiographic risk factors such as spontaneous echocontrast or aortic plaques. Our preliminary results are very encouraging. Overall, we were able to reduce the time of pre and postcardioversion anticoagulant therapy from the 2 months for the conventional group and the 1 month in TEE-guided ACUTE study group to about 1 week in our study (Fig. 5). Moreover, the use of LMWH seems to have practical advantages since there is no need to monitor the patient during therapy using these drugs. Our results also show that LMWH are safe and efficacious, perhaps even more so than conventional drugs. Indeed, being short in time and at fixed

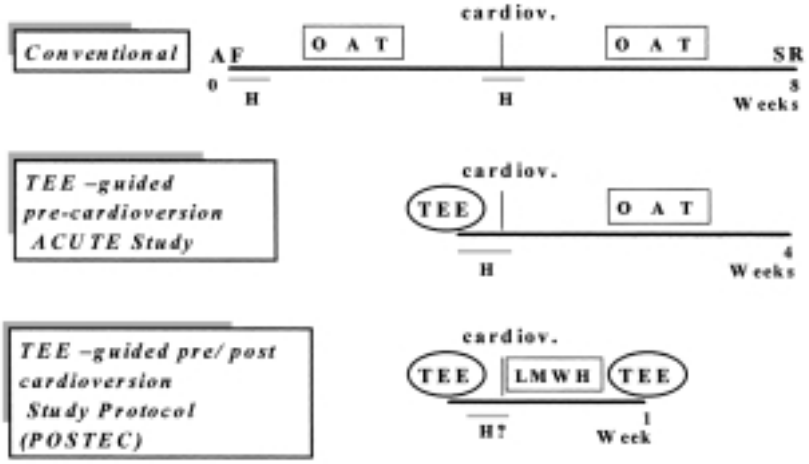

Figure 5. *Three different strategies in the electrical cardioversion of atrial fibrillation (AF). LMWH = low-molecular-weight heparins; OAT = oral anticoagulant treatment. Other abbreviations as in figure 2.*

dosages, such a therapeutic approach avoids the risk of complications caused by inadequate doses which are quite frequent in case of conventional therapy. The cardioversion approach for atrial fibrillation we propose may, therefore, constitute a feasible and safe therapeutic alternative with undoubted clinical advantages. The latter include a reduced duration of the arrhythmia, a reduced time of anticoagulation therapy and a reduced hospitalization. Potential advantages, which need to be studied further and in studies including larger numbers of patients, are those related to the embolic risk. Analysis of the costs may also well demonstrate another advantage. The fundamental disadvantage is represented by the semi-invasive nature of the TEE method, though, in our experience, this is well tolerated and has not led to any drop-outs.

In conclusion, the pre and postcardioversion TEE approach with brief anticoagulation therapy using LMWH for electrical cardioversion of atrial fibrillation may be a feasible and safe alternative to the conventional and TEE-guided precardioversion strategies. It is obvious that this study does not have sufficient statistical power and that consequently the real significance of our results remains to be determined. However, it does indicate that the approach is a safe one. A new simple management of a patient recommended for electrical cardioversion of atrial fibrillation will be possible if our data are confirmed by the prospective, multicenter, randomized trial (POSTEC) promoted by the Italian Society of Cardiovascular Echography which we are coordinating on a national scale and which will include a larger population.

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