Left atrial and appendage mechanical function after pharmacological or electrical cardioversion in patients with chronic atrial fibrillation: a multicenter, randomized study

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Atrial fibrillation; Cardioversion; Echocardiography.

Background. **Transient atrial and appendage dysfunction occurs after cardioversion of atrial fibrillation. It has been suggested that one component of early dysfunction is related to the method of restoration of sinus rhythm and it is less severe in patients undergoing pharmacological than electrical cardioversion. The aim of this study was to compare left atrial chamber and left atrial appendage mechanical function before and after 48 hours from electrical or pharmacological cardioversion in patients with chronic atrial fibrillation.**

Methods. **We studied the effects of the mode of cardioversion on Doppler left atrial and appendage function in 19 patients with persistent atrial fibrillation (4 weeks), who were randomized to pharmacological (quinidine) or electrical cardioversion (protocol: 200, 300, 360 J) after pre-treatment with verapamil. Transthoracic and transesophageal echocardiography were performed before and 48 hours after the restoration of sinus rhythm. To determine left atrial and appendage mechanical dysfunction, the peak A wave velocities were obtained from transmitral flow velocity profiles recorded in the apical 4-chamber view, and peak emptying and filling appendage velocities were measured by the transesophageal approach with the sample volume placed at the orifice of the left atrial appendage. All the patients were pre-treated with verapamil before cardioversion in order to achieve a satisfactory control of heart rate.**

Results. **Mean peak A wave velocities were 0.52 – 0.12 m/s in the patients treated electrically and 0.54 – 0.08 m/s in those treated pharmacologically (p = NS). Before and after electrical cardioversion, the peak filling velocities of the left atrial appendage were 0.42 – 0.17 and 0.43 – 0.17 m/s respectively, and the peak emptying velocities 0.30 – 0.14 and 0.36 – 0.17 m/s respectively; before and after pharmacological treatment, the peak filling velocities were 0.38 – 0.1 and 0.43 – 0.1 m/s respectively, and the peak emptying velocities were 0.30 – 0.13 and 0.43 – 0.24 m/s respectively (p = 0.08).**

Conclusions. **Even a long period of atrial fibrillation does not lead to a marked depression of global left atrial and left atrial appendage function 48 hours after the restoration of sinus rhythm by means of electrical or pharmacological cardioversion. There is no evidence that electrical cardioversion causes greater post-cardioversion atrial and/or appendage dysfunction than pharmacological treatment after 48 hours. Pre-treatment with verapamil may have reduced the dysfunction (probably because of a reduction in mechanical remodeling during atrial fibrillation).**

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Introduction

Transesophageal echocardiography provides a clinically applicable tool for evaluating left atrial function and defining the conditions predisposing to thrombus formation during and after atrial fibrillation (AF) cardioversion[1-13], and the identification of decreased left atrial appendage emptying velocities (< 15-25 cm/s) during AF may predict thrombus formation[3,4].

Transthoracic and transesophageal echocardiographic studies of patients immediately after the electrical reversion of AF have shown an initial impairment of overall atrial contraction[3,12,13], the depression of left atrial appendage velocities to values below those measured during the arrhythmia[5], and a worsening or *de novo* development of left atrial spontaneous echocardiographic contrast reflecting stagnant blood flow[3,5].

In patients with AF chemically converted to sinus rhythm, the restoration of atrial and appendage contraction is similarly slow and gradual[6].

In an observational study, Manning et al.[12] found a greater and more prolonged depression of atrial function in the patients undergoing electrical instead of chemical cardioversion, whereas Grimm et al.[7] reported that the worsening of left atrial appendage function, in a non-randomized study, occurred after AF cardioversion regardless of electrical or pharmacological therapeutic interventions.

Therefore, it seems that cardioversion to sinus rhythm is itself sufficient to predispose to atrial appendage dysfunction. However only a randomized study is capable of showing whether the mode of cardioversion (spontaneous, pharmacological or electrical) affects the duration of post-cardioversion atrial or appendage "stunning"[8,12], which is another important factor that may influence the risk of post-cardioversion thrombus formation and the consequent duration of anticoagulant therapy.

To the best of our knowledge, there is only one published randomized study[10] in which atrial function was evaluated after electrical or pharmacological cardioversion, but left atrial appendage was not considered.

The aim of this study was to assess the magnitude of left atrial and appendage "stunning" in patients with persistent AF (• 4 weeks) randomized to chemical or electrical cardioversion.

Methods

Study patients. Between January 1996 and July 1998, 30 subjects were selected from a group of 79 consecutive patients with sustained AF. All the patients underwent ECG, chest X-ray, transthoracic and transesophageal echocardiography. The onset of AF was determined on the basis of the onset of symptoms.

Forty-nine patients were excluded for one or more of the following reasons: refusal to give consent, esophageal disease, intolerance to antiarrhythmic therapy (verapamil, quinidine, propafenone), heart rate < 60 b/min, bundle branch block, left atrial diameter • 5 cm in M-mode or left atrial area • 30 cm^2, mitral regurgitation with a jet • 30% of atrial area or a jet area • 6 cm^2, or atrial or appendicular thrombosis revealed during the baseline examination.

Study protocol. All the patients received oral verapamil (from 40 mg bid up to 80 mg tid) before cardioversion starting from enrollment in order to achieve satisfactory heart rate control and if this was not achieved, oral digoxin was associated.

Warfarin (INR 2-3) was administered for at least 3 weeks before cardioversion. Oral digoxin was withdrawn 48 hours before cardioversion and oral verapamil was continued until restoration of sinus rhythm.

After a complete transthoracic and transesophageal examination, patients were randomized to receive an increasing dosage of oral quinidine sulfate (200 mg at the beginning and 400 mg every 2 hours until cardioversion to sinus rhythm, onset of side effects or cumulative dose of 1800 mg) or a direct current (DC) shock (protocol: 200, 300, 360 J).

After restoration of sinus rhythm, warfarin therapy was given for 4 weeks. A further transthoracic and transesophageal echocardiographic examination was performed 48 hours after cardioversion in all the patients; transthoracic echocardiography was also performed 12-24 hours after cardioversion in 10 cases.

After discharge, all the patients were followed at monthly intervals for a mean of 12 months.

In order to maintain sinus rhythm, every case received pharmacological therapy with slow release quinidine or propafenone.

Echocardiographic evaluation. Transthoracic two-dimensional and pulsed-wave Doppler echocardiographic studies were performed, using commercially available equipment (Hewlett-Packard Sonos 1500, St. Louis, MO, USA) with 2.5 and 3.5 MHz phased-array transducers.

A one-lead electrocardiogram was continuously recorded. The M-mode left atrial dimension was measured at end-systole in the parasternal long-axis view, left ventricular shortening fraction and the evaluation of left ventricular function were estimated from the parasternal long- and short-axis views and apical 4- and 2-chamber views according to the recommendations of the American Society of Echocardiography[14].

Transmitral inflow velocities were recorded from the apical 4-chamber view, with the sample volume positioned between the tips of the mitral valve leaflets. To ensure standardization, all the studies were performed in the morning, with the patients lying in a left lateral supine position after 10 min of rest.

Studies were recorded on S-VHS videotape for later review by one of the investigators who were unaware of the patients' clinical background. An average of 5 to 7 beats were studied with pulsed-wave Doppler recording of the transmitral flow velocities. Maximal and integrated velocities of early (E) and atrial (A) transmitral diastolic flow waves were determined at each study.

Effective mechanical atrial function was assessed by means of transthoracic Doppler echocardiography in accordance with Manning et al.[12] and defined as the presence of atrial waves with a peak velocity □ 0.5 m/s.

Transesophageal echocardiography was performed with commercially available equipment with a 5 MHz phased-array omniplane transducer. The left atrial cavity and appendage anatomy and function were evaluated before and 48 hours after cardioversion, with special care being taken to identify spontaneous echocontrast and thrombi. Left atrial appendage function was assessed using pulsed Doppler echocardiography with the sample

volume being placed 1.5 cm into the atrial appendage orifice in the basal transverse plane at the level of the aortic valve. Peak flow velocities at end-diastole were measured and averaged over 6 cardiac cycles for patients in AF before cardioversion and over 3 cardiac cycles for all the patients in sinus rhythm after cardioversion. Left atrial appendage systolic and diastolic areas were measured in the basal transverse plane by means of off-line planimetry and the atrial appendage shortening fractions were calculated as (left atrial appendage max - left atrial appendage min)/left atrial appendage max u 100[13].

Spontaneous echocontrast was defined as dynamic intracavitary echoes with a characteristic swirling pattern distinct from white noise artifacts. The degree of spontaneous echocontrast was categorized as absent, mild or severe on the basis of a previously described system[3].

Written informed consent was obtained from all the patients.

Statistical analysis. The results are expressed as mean ± SD. The continuous variables were analyzed by Student's t-test. c^2 was used to compare dichotomous variables. Fisher's exact test was used when appropriate. A p value of □ 0.05 was considered statistically significant. The SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) release 5.0 program for Windows 3.1 was used for statistical analyses.

Results

Patients. We enrolled 30 patients. One, after the first transesophageal echocardiogram, refused to continue the protocol and so only 29 patients were randomized to electrical (Group I, n = 13) or pharmacological cardioversion (Group II, n = 16). Sinus rhythm was obtained in 22 (75.8%) (11 in both groups), but only 19 (86.5%) were still in sinus rhythm after 48 hours (10 in Group I and 9 in Group II). So the comparison of left atrial and appendage function before and after cardioversion was possible in 19 patients (12 females and 7 males, mean age 65 ± 10 years) with a long-lasting AF (83 ± 46 days), with an underlying heart disease in 13 and lone AF in 6 (Table I).

None of the patients took antiarrhythmic drugs except verapamil, which is known not to affect atrial and/or appendage mechanical function. Twelve patients took digoxin until 48 hours before cardioversion.

Demographic, clinical and echocardiographic characteristics resulted homogeneous in the two randomized groups at enrollment (Table II). No statistically significant between-group differences were found at univariate analysis. There was a slight increase in left atrial diameter and area in both groups and a slight spontaneous echocontrast in 3/10 patients in Group I (30%) and in 2/9 patients in Group II (22%). None had atrial or appendicular thrombosis. The patients with echocontrast at the first transesophageal echocardiogram (5 vs 14) frequently maintained smoke after the restoration of sinus rhythm: 3 maintained echocontrast against only one who acquired a new echocontrast.

Electrical cardioversion was performed by an averaged 290 ± 145 J administration (range 200-500 J), without any side effects. Chemical cardioversion required a mean quinidine dose of 1100 ± 264 mg. On treatment 5 patients complained of diarrhea and one

Table I. Individual patient characteristics.

Patient	Age (years)	Sex	AF duration (days)	Underly ing heart disease	Type of intervention
1	61	M	67	Hypertensive	DC
2	59	F	94	Hypertensive	DC
3	50	F	85	Lone AF	DC
4	74	F	112	Hypertensive	DC
5	70	F	162	Hypertensive	DC
6	69	F	149	Hypertensive	DC
7	68	F	49	Degenerative	DC
8	66	F	110	Hypertensive	DC
9	49	M	45	Lone AF	DC
10	73	M	52	Ischemic	DC
11	74	F	102	Hypertensive	Pharmacological
12	40	M	61	Lone AF	Pharmacological
13	56	M	28	Lone AF	Pharmacological
14	67	M	180	Lone AF	Pharmacological
15	76	M	52	Lone AF	Pharmacological
16	70	F	69	Ischemic	Pharmacological
17	69	F	70	Hypertensive	Pharmacological
18	65	F	30	Hypertensive	Pharmacological
19	79	F	77	Degenerative	Pharmacological
Total	65 – 10	7 M/12F	83 – 46	6 lone AF/13 heart disease	10 DC/9 pharmacological

AF = atrial fibrillation; DC= electrical cardioversion.

Table II. Enrollment demographic, clinical and echocardiographic characteristics of patients returned to sinus rhythm by means of electrical (Group I) or pharmacological cardioversion (Group II).

	Group I (n=10)	Group II (n=9)	p
Sex (M/F)	3/7	4/5	NS
Age (years)	64 – 9	66 – 12	NS
AF duration (days)	92.5 – 41	74 – 46	NS
Underly ing heart disease	8	5	NS
Lone AF	2	4	NS
Hypertension	7	6	NS
Left atrial diameter (cm)	4.4 – 0.4	4.2 – 0.7	NS
Left atrial area (cm^2)	23.7 – 3.8	24.1 – 4.3	NS
E wave (m/s)	0.85 – 0.15	0.79 – 0.09	NS
LVEDD (cm)	4.93 – 0.5	4.76 – 0.6	NS
LVESD (cm)	3 – 0.4	2.97 – 0.5	NS
LVSF (%)	39.5 – 4.8	36.8 – 11.6	NS
Echocontrast	3	2	NS
LAA-DA (cm^2)	4.58 – 1.6	3.81 – 1	NS
LAA-SA (cm^2)	3.03 – 1	2.5 – 0.8	NS
LAA-SF (%)	31 – 18	34 – 12	NS
LAA absent-low flow	3	3	NS

AF = atrial fibrillation; LAA-DA = left atrial appendage diastolic area; LAA-SA = left atrial appendage systolic area; LVEDD = left ventricular end -diastolic diameter; LVESD = left ventricular end -systolic diameter; LVSF = left ventricular shortening fraction; SF = shortening fraction.

had an episode of marked hypotension, rapidly solved.

After sinus rhythm restoration, 18 patients received chronic prophylaxis with quinidine and one with propafenone; all of them continued anticoagulant prophylaxis for at least 4 weeks.

In all the patients the A wave of transmitral flow appeared 48 hours after pharmacological or electrical cardioversion of AF to sinus rhythm, evidence of a recovery of left atrial contractile function.

It is of value that, in patients who underwent pharmacological cardioversion, A wave velocity was, although not statistically significant, slightly increased (0.54 ± 0.08 m/s) in comparison with electrically treated (0.52 ± 0.12 m/s). The same was found in the subgroup of 10 patients (5 pharmacological and 5 electrical group) who underwent transthoracic echocardiogram 12-24 hours after reversion. In this subgroup A wave velocity increased in 2/5 patients at 48 vs 24 hours after electrical cardioversion, while in pharmacologically treated patients A wave increased in 3/5 at 48 vs 24 hours after cardioversion.

Forty-eight hours after restoration of sinus rhythm, 8/10 Group I and 8/9 Group II patients had an A wave • 0.5 m/s.

Moreover, in a subgroup of 10 patients, we compared the maximal velocity of early left ventricular diastolic filling (E wave) occurred at 12-24 and 48 hours after sinus rhythm recovery and we found an increase of E wave in 6/10, while it decreased or remained unchanged in the remaining 4. The patients with an increased E wave were equally distributed between the groups (Tables III and IV).

We did not find any statistical differences between the mean E wave velocities before and after sinus rhythm recovery in either the electrically treated (0.85 ± 0.15 vs 0.84 ± 0.21 m/s) or pharmacologically treated patients (0.79 ± 0.09 vs 0.83 ± 0.26 m/s).

The ratio of maximal E and A wave velocities slightly increased in 5 patients and did not change or decreased in the other 5. The values and ratio of the integrated velocities of the A and E waves followed a similar pattern.

The integrated velocities of total transmitral flow changed in 60% of patients, thus suggesting an increasing flow pattern of left ventricular diastolic filling early after sinus rhythm restoration. However, the atrial contribution to total transmitral flow increased from 28% 12-24 hours after cardioversion to 34% after 48 hours, thus confirming that atrial mechanical function improves early and that sinus rhythm offers a rapid hemodynamic benefit (Tables III and IV).

Table III. Doppler transmitral flow velocity variables 24 and 48 hours after electrical cardioversion to sinus rhythm (Group I).

No. patient	Peak E wave (m/s)	Peak A wave (m/s)	E-ITV	A-ITV	A-ITV/ ITV-total %	E/A	E-ITV/A-ITV	ITV-total
24 hours post-cardioversion								
6	0.6	0.7	14	10.9	44	0.9	1.3	24.9
7	0.8	0.5	NR	NR	NR	1.6	NR	NR
8	1.1	0.7	21.1	7.29	26	1.6	2.9	28.39
9	0.6	0.3	9.3	3.7	28	2.0	2.5	13
10	1	0.4	16.4	6.94	30	2.5	2.4	23.34
48 hours post-cardioversion								
6	0.7	0.7	10.7	9.04	46	1	1.2	19.74
7	1.1	0.5	NR	NR	NR	2.2	NR	NR
8	1	0.7	17.2	11	39	1.4	1.6	28.2
9	0.6	0.5	15.9	10.4	40	1.2	1.5	26.3
10	1.1	0.6	19.5	9.7	33	1.8	2.0	29.2

ITV = integrated transmitral velocity; ITV-total = integrated velocity of total transmitral flow; NR = not recorded.

Table IV. Doppler transmitral flow velocity variables 24 and 48 hours after electrical cardioversion to sinus rhythm (Group I).

No. patient	Peak E wave (m/s)	Peak A wave (m/s)	E-ITV	A-ITV	A-ITV/ ITV-total %	E/A	E-ITV/A-ITV	ITV-total
24 hours post-cardioversion								
15	0.6	0.7	11.7	6.71	36	0.9	1.7	18.41
16	1	0.4	17.7	4.9	22	2.5	3.6	22.6
17	0.8	0.5	NR	NR	NR	1.6	NR	NR
18	0.6	0.2	13.4	3.8	22	3.0	3.5	17.2
19	1.1	0.5	21.45	4.7	18	2.3	4.5	26.2
48 hours post-cardioversion								
15	0.6	0.5	9.9	5.6	36	1.2	1.7	15.5
16	1.0	0.4	18.5	5.5	23	2.5	3.3	24.03
17	1.0	0.6	NR	NR	NR	1.7	NR	NR
18	0.8	0.6	13.3	6.8	34	1.3	2.0	20.1
19	1.2	0.5	22.3	6.92	24	2.4	3.2	29.22

Abbreviations as in table III.

Left atrial size and spontaneous echocontrast. Left atrial size did not change during serial evaluation (4.4 ± 0.4 cm before vs 4.24 ± 0.5 cm, p = NS, after atrial defibrillation), either in the patients who underwent electrical cardioversion (4.2 ± 0.7 vs 4.17 ± 0.54 cm, p = NS) or in those treated with pharmacological therapy.

Spontaneous echocontrast was detected in the left atrium in 5 patients (3 in Group I and 2 in Group II) before cardioversion and in 4 patients (3 in Group I and 1 in Group II) after cardioversion (Table V).

Ventricular size. No substantial changes were recorded in ventricular size during the observation period. Left ventricular end-diastolic diameter was 4.93 ± 0.5 cm at enrollment and 5 ± 0.4 cm 48 hours after restoration of sinus rhythm in Group I (p = NS) and 4.76 ± 0.6 and 4.7 ± 0.8 cm in Group II (p = NS); left ventricular end-systolic diameter was 3 ± 0.4 and 3.2 ± 0.4 cm in Group I (p = NS) and 2.97 ± 0.5 and 2.8 ± 0.7 cm in Group II (p = 0.09) (Table V).

Left atrial appendage flow velocity profile. Before atrial defibrillation, the profile of the velocities of left atrial appendage demonstrated a fibrillatory pattern in all the patients (Fig. 1).

The peak filling and emptying velocities are shown in tables VI and VII[15]. They were not significantly different 48 hours after cardioversion compared to the peak fibrillatory velocities before cardioversion, but they were clearly faster in comparison with those obtained before atrial defibrillation.

Age, left ventricular function, left atrial appendage area, AF duration before atrial defibrillation and the total energy required for atrial defibrillation did not significantly correlate with the peak velocities of left atrial appendage 48 hours after atrial defibrillation.

In Group I, peak filling velocity increased from 0.42 ± 0.17 m/s before to 0.43 ± 0.17 m/s after cardioversion (p = NS); in Group II, it increased from 0.38 ± 0.1 to 0.43 ± 0.1 m/s (p = NS). Left atrial appendage peak emptying velocity increased from 0.30 ± 0.14 to 0.36 ± 0.17 m/s (p = NS) in Group I and from 0.30 ± 0.13 to 0.43 ± 0.24 m/s (p = 0.08) in Group II. Left atrial appendage mean peak velocities undoubtedly showed a better mechanical function in the pharmacological group than in the electrically treated one, although not statistically significant (Table V).

After pharmacological cardioversion left atrial appendage peak filling velocity increased in 7/9 and impaired only in 2, whereas this parameter increased in 5/10 and decreased in 5 of the electrically treated patients.

Similarly, left atrial appendage peak emptying velocity enhanced in 7/9 and impaired in 2 (the same patients with left atrial appendage peak filling velocity impairment) in Group II and it increased in 6/10 but impaired in 4/10 in Group I (Tables VI and VII)[15].

Follow-up. All the patients were followed up for an average of 12 ± 5 months.

We have analyzed and recorded every document and all the data concerning arrhythmic recurrencies and hospital admissions, occurred after the enrollment. Seven patients (37%) experienced documented recurrencies of AF, while the other 12 remained in sinus rhythm. None of the patients experienced embolic events during follow-up.

Discussion

The present study is a unique randomized and multicenter trial designed to compare left atrial and appendage function before and 48 hours after electrical or chemical cardioversion in patients with persistent AF and it offers some meaningful answers to the question as to whether the atrium really cares how sinus rhythm is restored.

Table V. Echocardiographic variables at enrollment and 48 hours after sinus rhythm restoration by electrical (Group I) or pharmacological treatment (Group II).

	Group I (n=10)			Group II (n=9)		
	Baseline	Sinus rhythm	p	Baseline	Sinus rhythm	p
Left atrial diameter (cm)	4.4 – 0.4	4.24 – 0.5	NS	4.2 – 0.7	4.17 – 0.54	NS
Left atrial area (cm^2)	23.7 – 3.8	23 – 4	NS	24.1 – 4.3	25 – 4	NS
LVEDD (cm)	4.93 – 0.5	5 – 0.4	NS	4.76 – 0.6	4.7 – 0.8	NS
LVESD (cm)	3 – 0.4	3.2 – 0.4	NS	2.97 – 0.5	2.8 – 0.7	0.09
LVSF (%)	39.5 – 4.8	36 – 7	NS	36.8 – 11.6	42 – 7	NS
A wave (m/s)		0.52 – 0.12			0.54 – 0.08	
E wave (m/s)	0.85 – 0.15	0.84 – 0.21	NS	0.79 – 0.09	0.83 – 0.26	NS
PFV (m/s)	0.42 – 0.17	0.43 – 0.17	NS	0.38 – 0.1	0.43 – 0.1	NS
PEV (m/s)	0.30 – 0.14	0.36 – 0.17	NS	0.30 – 0.13	0.43 – 0.24	0.08
LAA-DA (cm^2)	4.58 – 1.6	4.74 – 1.1	NS	3.81 – 1	3.6 – 0.6	NS
LAA-SA (cm^2)	2.97 – 0.9	2.91 – 1	NS	2.34 – 0.6	2.4 – 0.7	NS
LAA-SF (%)	31.5 – 18	37 – 12	NS	34 – 12	30 – 14	NS
Echocontrast +	3 (30%)	3 (30%)	NS	1 (11%)	1 (11%)	NS
Echocontrast ++	0	0		1 (11%)	0	
LAA absent-low flow	3 (30%)	2 (20%)	NS	3 (30%)	1 (11%)	NS

PEV = peak empty ing velocity; PFV = peak filling velocity. + = mild echocontrast; ++ = mild to moderate echocontrast. Other abbreviations as in table II.

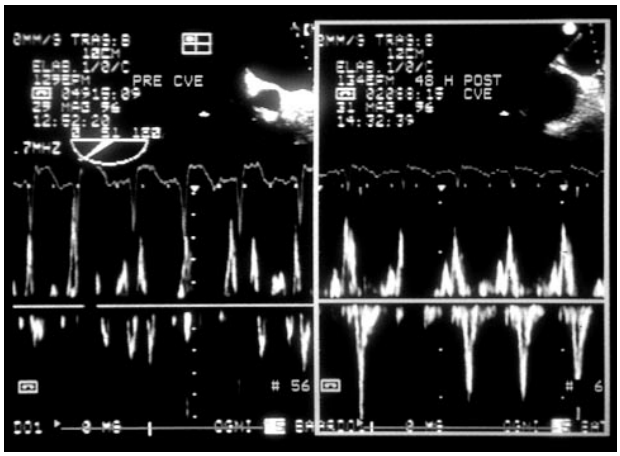

Figure 1. Left panel: *left atrial appendage flow pattern before cardioversion during transesophageal echocardiography. Note the typical irregular waves corresponding to the atrial activity during atrial fibrillation.* Right panel: *the left atrial appendage flow of the same patient 48 hours after successful cardioversion. Note the typical quadriphasic appendage flow pattern with regular and coordinate waves.*

Previous studies. In a normal canine model, Louie et al.[16] demonstrated that even brief (60 min) periods of AF result in a marked depression of global left atrial and appendage systolic function upon restoration of sinus rhythm. The mechanical stunning appears to be more profound and of longer duration for the appendage compared with the atrium as a whole, a condition which may predispose the appendage to blood stasis and thrombus formation.

Previous clinical investigations[1,5-7,11-13] demonstrated the phenomenon of left atrial and appendage stunning immediately after successful electrical cardioversion in humans.

However, a definitive answer to the question regarding the potential role of the mode of cardioversion in the development of atrial and appendage stunning needs further studies.

The few published studies[11,17-19] comparing atrial and appendage mechanical function before and after electrical or chemical cardioversion are limited by the fact that they were not randomized (except the study by Mattioli et al.[10]), they usually used transthoracic echocardiography (only Falcone et al.[18] performed Doppler evaluation of left appendage with transesophageal echocardiography); furthermore the patients were studied immediately after DC shock therapy.

In all the studies, many of the patients who subsequently underwent electrical cardioversion were treated with antiarrhythmic agents (with potential action on appendage, atrial and ventricular function), in an attempt to convert the arrhythmia or maintain sinus rhythm[8,20].

These studies showed that electrical cardioversion determined a greater degree and longer duration of atrial mechanical dysfunction than chemical or spontaneous cardioversion.

On the contrary Abascal et al.[21] found no significant difference in atrial velocities between electrically and chemically cardioverted patients assessed 24 hours after restoration of sinus rhythm.

Moreover, those studies compared patients responsive to pharmacological cardioversion with those unresponsive to this treatment: in our opinion, this kind of comparison is misleading in order to reveal a difference between the modes of reversion to sinus rhythm of AF; in fact in each of these studies, the causal relation of electric or chemical cardioversion to impaired atrial and

Table VI. Pharmacologically treated patients with sinus rhythm after 48 hours.

No. patient	PFV during AF (m/s)	PFV after 48 hours of sinus rhythm (m/s)	Δ%	PFV (normal values*) (m/s)	PEV during AF (m/s)	PEV after 48 hours of sinus rhythm (m/s)	Δ%	PEV (normal values*) (m/s)
11	0.46	0.49	6	0.57 – 0.18	0.55	0.87	37	0.71 – 0.24
12	0.36	0.40	10		0.32	0.35	9	
13	0.28	0.62	55	0.54 – 0.16	0.23	0.77	70	0.77 – 0.22
14	0.32	0.37	14	0.57 – 0.18	0.19	0.30	37	0.71 – 0.24
15	0.55	0.56	2	0.53 – 0.14	0.39	0.57	32	0.74 – 0.27
16	0.29	0.36	19	0.57 – 0.18	0.16	0.19	16	0.71 – 0.24
17	0.52	0.38	-37	0.57 – 0.18	0.39	0.32	-22	0.71 – 0.24
18	0.41	0.30	-37	0.57 – 0.18	0.34	0.24	-42	0.71 – 0.24
19	0.23	0.36	36	0.53 – 0.14	0.16	0.31	48	0.74 – 0.27
Mean – SD	0.38 – 0.1	0.43 – 0.1	+8		0.30 – 0.13	0.43 – 0.24	+20	

Δ% = percentage difference between values. Other abbreviations as in tables II and V. * age-associated normal values of left atrial appendage function from the SPAF population[15]. There was no statistical difference between PFV and PEV before or after restoration of sinus rhythm.

Table VII. Electrically treated patients with sinus rhythm after 48 hours.

No. patient	PFV during AF (m/s)	PFV after 48 hours of sinus rhythm (m/s)	Δ%	PFV (normal values*) (m/s)	PEV during AF (m/s)	PEV after 48 hours of sinus rhythm (m/s)	Δ%	PEV (normal values*) (m/s)
1	0.25	0.67	63	0.54 – 0.16	0.28	0.63	56	0.77 – 0.22
2	0.32	0.27	-19	0.54 – 0.16	0.30	0.22	-36	0.77 – 0.22
3	0.63	0.75	16	0.59 – 0.19	0.32	0.65	51	0.80 – 0.22
4	0.16	0.39	59	0.57 – 0.18	0.14	0.32	56	0.71 – 0.24
5	0.56	0.35	-60	0.57 – 0.18	0.35	0.32	-9	0.71 – 0.24
6	0.39	0.52	25	0.57 – 0.18	0.21	0.32	34	0.71 – 0.24
7	0.48	0.31	-55	0.57 – 0.18	0.28	0.32	13	0.71 – 0.24
8	0.30	0.24	-25	0.57 – 0.18	0.27	0.12	-125	0.71 – 0.24
9	0.69	0.37	-86	0.59 – 0.19	0.68	0.27	-152	0.80 – 0.22
10	0.42	0.44	5	0.57 – 0.18	0.22	0.46	52	0.71 – 0.24
Mean – SD	0.42 – 0.17	0.43 – 0.17	-8		0.30 – 0.14	0.36 – 0.17	-6	

Abbreviations as in tables II, V and VI. * age-associated normal values of left atrial appendage function from the SPAF population[15]. There was no statistical difference between PFV and PEV before or after restoration of sinus rhythm.

appendage function after the procedures was largely circumstantial. Finally, about patient selection, the lack of a randomized list had the consequence that some authors[18] included just a few patients in the pharmacological group and others used electrical cardioversion only in subjects unresponsive to a previous pharmacological cardioversion[11].

Present study. In the present study, patients after a first (pre-cardioversion) transesophageal echocardiography, were randomized to chemical or electrical cardioversion. We evaluated left atrial and appendage function before and 48 hours after cardioversion to sinus rhythm. We chose the 48 hour cut-off period because previous studies[10,13,17,18] have demonstrated that mechanical dysfunction recovers early and because, in our clinical practice, patients are discharged within 48 hours of a successful cardioversion.

The two groups of patients had a similar distribution in terms of age, sex, AF duration before cardioversion and heart rate during the post-cardioversion echocardiographic studies.

It is interesting to note that in a large proportion of quinidine randomized patients we obtained sinus rhythm despite the long duration of AF (• 4 weeks).

Atrial and ventricular size. No statistically significant between or within-group differences were found in atrial or ventricular diameters comparing the variables during AF with those observed after restoration of sinus rhythm.

Mechanical dysfunction of the left atrium seemed to recover rapidly after both electrical and chemical cardioversion, normalizing within 48 hours in the majority of patients. In fact in all the patients the A wave of transmitral flow appeared 48 hours after pharmacological or electrical reversion and this finding is consistent

with a recovery of left atrial contractile function. The absence of the A wave (a sign of atrial stunning), which is sometimes seen immediately after DC electrical cardioversion, was not recorded in any of our patients (Table VIII).

The degree of mechanical recovery of atrial and appendage function did not show any significant differences between chemical and electrical cardioversion even after adjusting for patient age (our subjects had similar ages), underlying cardiovascular disease, left ventricular ejection fraction, left atrial diameter, left appendage area or AF duration[11,22].

In all the patients with AF verapamil (with or without digoxin) is widely used to control the ventricular rate, however, this drug has no major electrophysiological effects on the atrial myocardium[23]. We excluded from our study any antiarrhythmic agents that could influence left atrial chamber or appendage function before cardioversion.

Table VIII. Echocardiographic variables 48 hours after restoration of sinus rhythm in electrically (Group I) vs pharmacologically treated patients (Group II).

	Group I (n=10)	Group II (n=9)	p
Left atrial diameter (cm)	4.24 – 0.5	4.17 – 0.54	NS
Left atrial area (cm^2)	23 – 4	25 – 4	NS
E wave (m/s)	0.84 – 0.21	0.83 – 0.26	NS
A wave (m/s)	0.52 – 0.12	0.54 – 0.08	NS
LVEDD (cm)	5 – 0.4	4.7 – 0.8	NS
LVESD (cm)	3.2 – 0.4	2.8 – 0.7	NS
LV-SF (%)	36 – 7	42 – 7	NS
Echocontrast	3	1	NS
PFV (m/s)	0.43 – 0.17	0.43 – 0.1	NS
PEV (m/s)	0.36 – 0.17	0.43 – 0.24	NS
LAA-DA (cm^2)	4.74 – 1.1	3.6 – 0.6	0.02
LAA-SA (cm^2)	2.91 – 1	2.4 – 0.7	NS
LAA-SF (%)	37 – 12	30 – 14	NS
LAA absent-low flow	2 (20%)	1 (11%)	NS

Abbreviations as in tables II and V.

Mechanisms of atrial and appendage dysfunction and possible role of calcium channel blockers. The underlying mechanisms that cause the electrical and functional remodeling of the atria and appendage after cardioversion are not yet completely understood. However, there are some indications that intracellular calcium overload plays an important role[24]. During AF there is a calcium overload in the atrial myocardium, leading to desensitization or down-regulation of calcium receptors. Restoration of sinus rhythm and the consequent elimination of the overload may then result in a state of relative calcium deficiency and an associated impairment in mechanical function. This situation would expect to be normalized as calcium receptors return to their baseline state.

Leistad et al.[25] have suggested that the increased intracellular calcium may be responsible for the atrial systolic dysfunction after electrical or chemical cardioversion and they have shown that the infusion of verapamil during episodes of AF significantly reduces the duration of the dysfunction.

In the study of Tielman et al.[24] the extent of atrial remodeling appeared to be significantly limited by verapamil, although not completely prevented, suggesting that other mechanisms may be involved in the process of electrical remodeling.

Daoud et al.[26] have recently confirmed the attenuation of post-cardioversion atrial dysfunction in patients with AF pre-treated with verapamil.

In the present study pre-treatment with verapamil was performed in order to control ventricular rate during AF. The drug probably may have contributed to the attenuation of electrical atrial and appendage remodeling by reducing the degree and duration of post-cardioversion dysfunction.

The routine use of the drug represents an attractive additional therapy to the electrical or pharmacological cardioversion of AF, but its clinical relevance needs further randomized studies.

Study limitations. One limitation of this study is the small sample size; although 79 patients were screened, the protocol was performed in only 25%. This percentage largely reflects the reluctance of patients to consent to transesophageal echocardiography when it is not clinically indicated.

A second limitation is that pre-treatment with verapamil was not randomized.

A third limitation is the lack of a transesophageal echocardiogram 7-30 days after the restoration of sinus rhythm to investigate any further recovery of atrial and/or appendage mechanical function at a later time[27].

Clinical implications. The results of this study have potential clinical implications concerning the duration of anticoagulant therapy after defibrillation[8,28]. After 48 hours, the majority of our patients with chronic AF who underwent chemical or electrical cardioversion recovered fairly effective mechanical atrial and appendage function. None of the demographic, clinical or echocardiographic variables had any impact on the degree of recovery of atrial and appendage function.

The pooled data from 32 studies[29] have been reviewed to assess the timing of thromboembolic complications after electrical cardioversion of AF and it was found that 98% of the embolic episodes occurred within 10 days of cardioversion particularly in the 3 days post-cardioversion interval. Prospective randomized studies should be conducted to demonstrate whether anticoagulant therapy can be discontinued as early as 1 week after intervention without an increase in embolic complications[30].

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