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Utility of amiodarone pre-treatment as a facilitator of the acute success of electrical cardioversion in persistent atrial fibrillation

--Manuscript Draft--

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Abstract:	Purpose: The usefulness and mechanisms of antiarrhythmic drug (AAD) pre-treatment as a facilitator of the acute success of electrical cardioversion (ECV) in atrial fibrillation (AF) remain controversial. We sought to analyze the role of AADs treatment with this purpose, differentiating its possible utility either facilitating the restoration of sinus rhythm (SR) or reducing immediate AF recurrences (IAFR). Methods: We analyzed 2962 consecutive patients with persistent AF undergoing ECV prospectively included in 3 national registries. The acute success of ECV was indicated by the reversion to SR without presenting an IAFR (<2h). Results: A total of 1410 patients (48%) received AAD treatment prior to ECV (80% amiodarone, 15% class Ic AAD, 2% other AAD). The rate of restoration SR was similar between the patients treated with amiodarone (92%), class Ic AAD (91%) and who did not receive AAD pre-treatment (91%) (p=0.92). However, those treated with amiodarone had fewer IAFR than those in the other two groups (amiodarone 3% vs class Ic 7% vs without treatment 6%; p=0.002) so the ECV success rate was higher in the amiodarone group than in the other groups (amiodarone 89% vs Ic 84% vs without treatment 86%; p=0.04). After adjusting for multiple variables, amiodarone remained as an independent predictor of a lower occurrence of IAFR (OR=0.57; p=0.01) and of a successful ECV (OR 1.37; p=0.01). Conclusions: For patients with persistent AF undergoing ECV, AAD has a neutral effect on the restoration of SR but amiodarone increases its effectiveness due to a lower incidence of IAFR.

Reus, 19 th December 2019

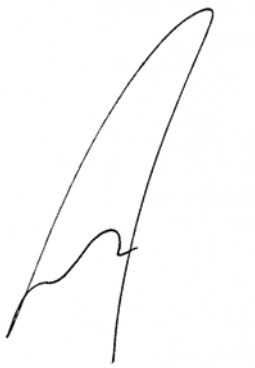
To Prof. Willem J. Remme, Editor-in-Chief,
Cardiovascular Drugs and Therapy:

Enclosed is the revised version of our manuscript entitled **"Utility of amiodarone pre-treatment as a facilitator of the acute success of electrical cardioversion in persistent atrial fibrillation**" to be considered for publication in *Cardiovascular Drugs and Therapy*. We have included a Conflict of Interest statement (page 11, lines 19-21). Previously this declaration was included in the *Funding* declaration.

All authors have participated in the work and have reviewed and agree with the content of the article. We would release the copyright to your journal if the manuscript is accepted. No conflict of interest exists in relation to this manuscript.

We hope this new version meet the conditions to be published in your journal.

Sincerely,



Josep M. Alegret

Reviewer #5: Dr. Alegret et al presented an interesting report on the effects of antiarrhythmic agents, mainly, amiodarone, on the acute success of electrical cardioversion (ECV) in patients with persistent atrial fibrillation.

This Reviewer found the manuscript was well written and the data were well presented. The large number of patients involved certainly lends strength to the report. However, there are several issues that this Reviewer feels necessary to be clarified and such clarification could further strengthen the manuscript.

1. The nature of the study: it is indicated that the data were drawn from a registry that was the data base for three previously reported studies with different objectives. it is not clear if the objective of the current study and the definitions of clinical outcomes (restoration of sinus rhythm and acute success of ECV) were determined prior to the formation of registry. If not, the study is best classified as a retrospective study and the limitation of retrospective data analysis needs to be discussed.

Thank you for this comment, that help us to better describe the nature of the study. The three studies that constitute the basis of this registry were aimed at knowing the practice of electrical cardioversion in real life in Spain. Their main objectives were to know the acute success of cardioversion, the maintenance of sinus rhythm, the effect of anti-arrhythmic drugs and the management of anticoagulation. For this, multiple clinical, echocardiographic and procedure-related variables were collected prospectively. It is true that, although the success of cardioversion and the incidence of immediate AF recurrences were pre-defined objectives, the analysis of the factors involved in immediate recurrences was not pre-defined, so it should be strictly defined that this is a retrospective analysis. We have introduced specific comments in the Methods and Limitations sections (Page 5, lines 15-17 and 21-22; page 11, lines 5-6).

2. The selection bias among anti-arrhythmic drugs (ADDs) is evident and comparisons among ADDs are not feasible based on the data presented, which the authors are likely aware of. Therefore the conclusion the authors had made (page 12 last paragraph) regarding the superiority of amiodarone over other ADDs are suggestive to the most and definitively not conclusive. This Reviewer is not disputing the effectiveness of amiodarone as it is the most potent agent we have but merely stating that the study itself with its weakness from selection bias did not provide "solid information ... on the superiority of amiodarone ..."

Thank for this comment. We have modified the text following the instructions of this reviewer.

We have deleted in this paragraph the comments related to the superiority of amiodarone over the Ic class AAD based in our data: "**Our study adds new information from a large sample of patients on the usefulness of amiodarone in the improvement of ECV success and specifies its benefit in the reduction of IAFR, while it shows a neutral effect in the restoration of SR. Such effect** of amiodarone may be explained by several cellular electrophysiological aspects [5, 16, 17]." (Page 9, lines 22-24).

3. Are data available regarding the length and/or dosage of amiodarone pre-treatment before ECV? If so, would a low dose and short duration of pre-treatment be negative factors in amiodarone effect on sinus restoration and acute success of ECV? This could provide practical guide to the readers in optimally preparing patients for ECV

Thank you for this comment, that allow us to better define this point. Treatment with amiodarone was a dichotomic variable: "Treatment with amiodarone was considered when amiodarone was initiated at least 3 weeks before ECV **at a dose of at least 1000 mg/week".** (page 5, lines 21-22). We have completed this description in the new version. We hope this specification could be useful for the readers. We cannot assess the effect of other doses or treatment periods.

4. It is not clear the rationale(s) for the authors to have chosen 2 hours as the cut-off to define acute success. Clinically, does it make much difference if it recurs in 1, 2 or 3 hours?

There is no consensus on which cut-off point should be taken as a reference to define an immediate AF recurrence. Different cut-offs have been used in the literature. We decided to define immediate AF recurrence when SR was achieved but AF recurred in the first 2 h. This definition was a priori and was defined as a dichotomic variable, so we have no information on what would have happened with other cut-offs.

We thanks the comments of this reviewer, that help us to improve the manuscript.

Utility of amiodarone pre-treatment as a facilitator of the acute success of electrical cardioversion in persistent atrial fibrillation

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Abstract

Purpose: The usefulness and mechanisms of antiarrhythmic drug (AAD) pre-treatment as a facilitator of the acute success of electrical cardioversion (ECV) in atrial fibrillation (AF) remain controversial. We sought to analyze the role of AADs treatment with this purpose, differentiating its possible utility either facilitating the restoration of sinus rhythm (SR) or reducing immediate AF recurrences (IAFR).

Methods: We analyzed 2962 consecutive patients with persistent AF undergoing ECV prospectively included in 3 national registries. The acute success of ECV was indicated by the reversion to SR without presenting an IAFR (<2h).

Results: A total of 1410 patients (48%) received AAD treatment prior to ECV (80% amiodarone, 15% class Ic AAD, 2% other AAD). The rate of restoration SR was similar between the patients treated with amiodarone (92%), class Ic AAD (91%) and who did not receive AAD pre-treatment (91%) (p=0.92). However, those treated with amiodarone had fewer IAFR than those in the other two groups (amiodarone 3% vs class Ic 7% vs without treatment 6%; p=0.002) so the ECV success rate was higher in the amiodarone group than in the other groups (amiodarone 89% vs Ic 84% vs without treatment 86%; p=0.04). After adjusting for multiple variables, amiodarone remained as an independent predictor of a lower occurrence of IAFR (OR=0.57; p=0.01) and of a successful ECV (OR 1.37; p=0.01).

Conclusions: For patients with persistent AF undergoing ECV, AAD has a neutral effect on the restoration of SR but amiodarone increases its effectiveness due to a lower incidence of IAFR.

Keywords: antiarrhythmic drugs, amiodarone, class Ic, atrial fibrillation, electrical cardioversion

1. Introduction

Electrical cardioversion (ECV) is a routine technique used for the management of persistent atrial fibrillation (AF) and is complementary to ablation within the therapeutic scenario of an AF rhythm control strategy. The use of antiarrhythmic drugs (AAD) has been shown to be valuable in reducing AF recurrences after successful ECV [1-3]. However, the usefulness of AAD pre-treatment with the intent to facilitate successful ECV is controversial. Although the results are discordant, some previous studies with relatively low ECV success rates and a small number of patients have suggested the usefulness of AAD pre-treatment (mainly amiodarone) for this purpose [4-9]. These studies did not clarify whether the possible benefits came from facilitating the reversion to sinus rhythm (SR) or by reducing the immediate AF recurrence (IAFR).

Contemporary series describe a higher success rate of ECV than older series, perhaps due to a more accurate selection of patients and a more extended use of biphasic energy [10]. Due to the current high success rate of ECV, a very large number of cases are required to demonstrate the usefulness of AAD with this purpose.

The objective of this study was to analyze, in a current, large and prospective population of patients treated with ECV, the role of AADs in facilitating the success of ECV, differentiating its possible utility either facilitating the restoration of SR, reducing IAFR or both.

2. Methods

The REVERSE [11], CARDIOVERSE [12] and REVERCAT [10] studies featured surveys that prospectively recorded all patients with persistent AF who were considered candidates for ECV in 99 Spanish hospitals. These surveys sought to monitor the clinical practice of ECV in Spain and were conducted by the same steering committee between 2003 and 2012 using common guidelines. The characteristics of the surveys have been described previously in detail [11]. The inclusion criteria were consistent between the three studies: ≥18 years of age, an AF duration ≥7 days, and no precipitating conditions such as hyperthyroidism, fever, recent thoracic surgery and pericarditis. The data recorded included the clinical characteristics, treatment details, echocardiography results, ECV procedure variables.

Out of a total number of 3263 candidates to ECV included in all 3 surveys, the present analysis included those 2962 finally undergoing ECV. A maximum energy shock for the device was required to consider a failed procedure. No other instructions for the conduct of ECV had been recommended. **Restoration of sinus rhythm (SR), IAFR and the acute success of ECV were pre-defined objectives. In this retrospective analysis we assessed the factors involved in each of them.** We considered SR to be restored when at least 3 consecutive beats in SR were achieved after ECV. IAFR was considered when SR was achieved but AF recurred in the first 2 h. An acute success of ECV was considered when SR was achieved, and the patient did not present IAFR. Treatment with amiodarone was considered when amiodarone was initiated at least 3 weeks **at a dosis of at least 1000 mg/week** before ECV. Structural heart disease was considered in the presence of any of the following anomalies: moderate or severe valvular heart disease;

mitral stenosis of any grade; previous myocardial infarction; systolic dysfunction (EF <50%); or any cardiomyopathy. Because of the date of the studies, the CHA_2DS_2VASC score was recorded only in the CARDIOVERSE study. Patients could only be included once. In case of recurrence during the follow-up that required a new cardioversion, it was not considered as a new case.

Statistical analysis

Qualitative variables are expressed as percentages, and the differences were assessed using chi square tests. Quantitative variables are presented as the mean+standard deviation (SD), and the differences were evaluated using Student's t-tests. A logistic multivariate regression analysis was performed to identify the independent variables related to the success of ECV and to the incidence of early IAFR. The variables included in the multivariate analysis were those that had a significance of $p < 0.15$ in the univariate analysis. Statistical significance was indicated by $p<0.05$. All analyses were performed with the IBM SPSS software (version 22).

3. Results

3.1 Patients population

Of the 2962 patients considered, 1410 patients (48%) received AAD prior to ECV. Of these patients, 1130 (80%) received amiodarone, 217 (15%) class Ic drugs (flecainide or propafenone), and 63 (2%) patients other AAD (this last group was not considered in the analysis due to the small number of patients). The remaining 1552 patients (52%) did not receive any AAD before undergoing ECV. Table 1 summarizes the

characteristics of the patients. Patients treated with amiodarone were older, had a lower left ventricular ejection fraction, a larger left atrial size and a lower use of biphasic energy than patients who did not receive AAD. Patients treated with class Ic drugs had a higher prevalence of AF that lasted for a duration of more than one year and a lower cardiovascular disease burden (LV hypertrophy, LV dysfunction, NYHA ≥2, structural heart disease and CHADS score) than patients who did not receive AAD. Patients who did not receive any antiarrhythmic drugs had a lower prevalence of previous ECV than patients who received AAD.

3.2 Sinus rhythm restoration and immediate AF recurrence rates

The restoration of SR was similar in the groups treated with amiodarone, treated with class Ic drugs and received no AAD treatment (amiodarone 92% vs Ic 91% vs without AAD 91%; p=0.92). When we considered the type of energy used, the results did not differ for biphasic (amiodarone 94% vs Ic 93% vs without antiarrhythmic treatment 93%; p=0.96) or monophasic energy (amiodarone 90% vs Ic 87% vs without antiarrhythmic treatment 88%; p=0.59). Among the patients for whom SR was restored (n=2708), 133 (5%) patients presented IAFR. However, the patients treated with amiodarone had fewer IAFRs than the patients in the other two groups (amiodarone 3% vs Ic 7% vs without treatment 6%; p=0.002). Therefore, considering the incidence of IAFR, the success rate of the ECV was higher in the amiodarone group than in the other two groups (amiodarone 89% vs Ic 84% vs without treatment 86%; p=0.04).

3.3 Predictors of ECV success: Uni and multivariate analysis

We analysed the parameters related to SR restoration, the occurrence of IAFR and the success of ECV (including IAFR) by means of uni- and multivariate analysis (Table 2). In these analyses, we considered a new dichotomic variable defined as the use of amiodarone vs the use of other AAD or no antiarrhythmic treatment, due to the similar results of these last two groups in the rates of restoration of SR and IAFR. Treatment with amiodarone before ECV was independently related to a lower occurrence of IAFR (OR=0.57; p=0.01) and with a higher success rate for ECV (OR 1.37; p=0.01), but it had a neutral effect on SR restoration. BSA and biphasic energy were independently related to SR restoration and the success of ECV. Chronic obstructive pulmonary disease and the number of shocks were other independent variables related to a higher occurrence of IAFR (Table 2).

4. Discussion

In the present study, we observed that in patients with persistent AF, oral treatment with AAD prior to ECV has a neutral effect on the restoration of SR. However, treatment with amiodarone led to a lower incidence of IAFR, which resulted in an increase in the efficacy of ECV.

ECV may be unsuccessful either because of the inability to convert AF to SR or because of IAFR. Several studies have studied the capacity of AAD (such as amiodarone [5, 7-9], sotalol [8], flecainide [6], ibutilide [4], vernakalant [13] and ranolazine [14]) to facilitate ECV. However, inconclusive data about the usefulness of these drugs were obtained for different reasons. Most of the studies were small studies, had a relatively low ECV

success rates, and had methodological limitations that did not allow conclusive data to be obtained about the effectiveness of the drugs or assess whether the facilitation of the successful ECV was due to a higher reversion rate to SR or to a lower incidence of IAFR. Amiodarone is the most studied antiarrhythmic drug for this purpose. In a small randomized study, Capucci et al [5] compared amiodarone and diltiazem (± potassium plus insulin) for their effectiveness on the success of ECV and maintenance of SR at one month post-ECV in patients with persistent AF. Finally, 81 patients were treated with ECV. SR was restored only in 69% of the patients, with a higher rate in the group treated with amiodarone (87% vs 58%). The small number of patients did not allow a reliable comparison between groups for early AF relapse. In the SAFE-T trial [8], 504 patients with persistent AF were randomized for amiodarone, sotalol or placebo treatments prior to ECV. The rate of successful ECV (72%) was relatively low, and amiodarone (OR=2.16) and sotalol (OR=1.92) facilitated successful ECV. There was no analysis of IAFR, so the authors could not distinguish if the success was due to the facilitation of SR restoration or to the prevention of IAFR. In the RHYTHM-AF study [9], which focused on the first AF episode and paroxysmal AF, amiodarone pre-treatment was associated with successful ECV (OR=1.56), but again information about its effect distinguishing between facilitated SR restoration versus lower incidence of IAFR was lacking. Finally, a very recent meta-analysis [15] that has analysed the effects of pre- and post-treatment with amiodarone for elective ECV has shown that pre-treatment with amiodarone was associated with higher rates of acute restoration of SR (relative risk 1.22).

Our study adds new information from a large sample of patients on the usefulness of amiodarone in the improvement of ECV success and specifies its benefit in the reduction of IAFR, while it shows a neutral effect in the restoration of SR. Such effect of amiodarone may

be explained by several cellular electrophysiological aspects [5, 16, 17]. First, a widely spread and multi-compartmental distribution of the drug (as compared to other AADs) within the atrial tissue, the pulmonary veins and the atrio-ventricular node. Second, a more pronounced effect on the atrial refractory period and action potential duration. Third, a more favorable profile of beta-adrenergic and calcium channels blockades parallel to the specific anti-arrhythmic effect. Finally, parallel to the electrophysiological effect of amiodarone over the atrial tissue, other mechanisms that may help reducing the incidence of IRAF include the suppression of premature atrial contractions and of atrial or pulmonary vein tachycardia. Altogether, it appears reasonable that amiodarone surpasses the effect of other AAD agents by helping to stabilize SR during the vulnerable period immediately after ECV. Oral amiodarone impregnation several weeks prior to the ECV rather than amiodarone intravenous infusion immediately before the ECV should be preferred due to a cumulative effect on reducing the vulnerability to arrhythmias of the atrial tissue [9, 13, 18, 19].

Amiodarone pre-treatment before ECV in patients with persistent AF leads to an approximately 25% increase in the rate of pharmacological and protects against AF recurrences in follow-ups cardioversion [2, 3, 5]. Our study adds evidence about the effectiveness of amiodarone in facilitating ECV by reducing IAFR. Although antiarrhythmic class Ic drugs may also be useful in other aspects, our data support the specific benefit of facilitating ECV with amiodarone by protecting against IAFR. The current ESC AF guidelines [20] suggests pre-treatment with amiodarone, flecainide, ibutilide, or propafenone to enhance the success rate of ECV. Our results add evidence that supports the use of amiodarone as an elective antiarrhythmic drug with this

purpose. On the other hand, the role of amiodarone seems limited in enhancing the results of patients who previously underwent ECV with failed SR restoration.

5. Study limitations

This study has the inherent limitations **of a retrospective analysis of an observational study.** Consequently, the patients were not randomized to specific drugs or placebo. However, the large number of patients included in this study allowed for the formation of subgroups and multivariate analyses that, to the best of our knowledge, had reliable results.

6. Conclusions

AAD had a neutral effect on the restoration of SR in patients with persistent AF treated with ECV. However, treatment with amiodarone led to a lower incidence of IAFR, which resulted in an increase in the acute efficacy of ECV. Our results support/emphasize the usefulness of initiating pre-treatment with oral amiodarone to improve the acute success rate of ECV.

Funding

None.

Conflict of interest

No author has any competing financial or non-financial interest related to the content of this manuscript.

Compliance with Ethical Standards

This study was performed according to the Declaration of Helsinki and approved by the Ethics Committee of Institut d'Investigació Sanitària Pere Virgili (IISPV). The surveys from which the data were obtained were approved by the Institutional Review Boards (Clinical Ethics Committee) of each participating hospital. Written informed consent was obtained from all the patients who participated in these surveys.

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Table 1. Baseline Characteristics of the Patients.

Characteristics	Total (n=2962)	Amiodarone (n=1130)	Class Ic agents (n=217)	None AADs (n=1552)	P value
Age; years	64±11	64±11	61±10	63±11	0.001
Male gender	2048 (69)	788 (70)	142 (65)	1077 (69)	0.45
Weight; kg	81.3±14.5	81.4±14.6	80.5±14.6	81.1±14.4	0.72
Height; cm	168±9	168±9	168±9	168±9	0.59
BSA; m^2	1.90±0.19	1.90±0.19	1.90±0.19	1.91±0.19	0.77
Hypertension	1668 (56)	637 (57)	108 (50)	886 (57)	0.11
Diabetes Mellitus	493 (17)	170 (15)	34 (16)	281 (18)	0.11
COPD	227 (8)	75 (9)	13 (7)	136 (9)	0.54
CHADS ≥ 2	1189 (40)	461 (42)	67 (32)	639 (42)	0.01
Previous Embolism	188 (6)	76 (7)	17 (8)	90 (6)	0.40
NYHA Class ≥ II	1078 (36)	435 (46)	47 (32)	578 (52)	0.0001
LA size (mm) (n= 2327)	44.8±6.2	45.2±6.5	44.1±5.6	44.5±6.1	0.008
LA enlargement (>50mm)	497 (17)	204 (21)	27 (15)	256 (19)	0.10
LVH (n= 2549)	933 (32)	374 (35)	45 (22)	496 (34)	0.001
LVEF (%) (n= 2399)	58±12	57±13	61±9	58±12	0.0001
LVEF <40%	302 (10)	139 (14)	6 (3)	151 (11)	0.0001
Structural Heart Disease	1355 (46)	570 (51)	61 (28)	694 (45)	0.0001
Previous ECV	434 (15)	201 (22)	35 (24)	186 (18)	0.04
AF duration >1 year	399 (14)	135 (12)	42 (19)	218 (14)	0.01
Biphasic energy	1776 (59)	589 (53)	140 (67)	1014 (67)	0.0001

AADs, antiarrhythmic drugs; BSA, body surface area; COPD, chronic obstructive pulmonary disease; LA, left atrium; LVH, left ventricle hypertrophy; LVEF, left ventricle ejection fraction; ECV, electric cardioversion; AF, atrial fibrillation. Notes to Table 1: Values are n (%) or mean ± SD. Patients treated with other anti-arrhythmic drugs (n=63) are not presented.

Table 2. Parameters associated with sinus rhythm restoration, immediate atrial fibrillation recurrence and successful electrical cardioversion in uni- and multivariate analysis.

	SR Restoration				IAFR				Successful ECV			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p
Age (year)	1.02 (1.01-1.03)	0.004			0.99 (0.97-1.003)	0.13			1.02 (1.01-1.03)	0.001		
Male gender	0.66 (0.49-0.89	0.006			1.69(1.11-2.58)	0.01			0.62 (0.49-0.80)	0.0001		
BSA (m2)	0.25 (0.13-0.50)	0.0001	0.18 (0.09-0.39)	0.0001	3.17 (1.26-7.97)	0.01			0.26 (0.15-0.46)	0.0001	0.22 (0.12-0.40)	0.0001
Diabetes	1.19 (0.82-1.70)	0.36			0.92 (0.57-1.48)	0.73			1.15 (0.86-1.56)	0.35		
COPD	1.19 (0.69-2.06)	0.53			1.86 (1.13-3.06)	0.01	1.88 (1.07-3.31)	0.03	0.80 (0.54-1.17)	0.24		
Hypertension	1.07 (0.83-1.39)	0.60			1.08 (0.64-1.31)	0.63			1.01 (0.82-1.26)	0.91		
LV hypertrophy	1.25 (0.94-1.67)	0.13			1.25 (0.87-1.80)	0.22			1.06 (0.84-1.33)	0.65		
Structural heart disease	1.02 (0.79-1.32)	0.87			1.38 (0.97-1.98)	0.08			1.14 (0.92-1.42)	0.22		
ACEI or ARB	1.00 (0.78-1.30)	0.99			1.01 (0.72-1.42)	0.95			1.00 (0.81-1.24)	0.98		
Amiodarone pre-ECV	1.04 (0.79-1.35)	0.80			0.50 (0.33-0.75)	0.001	0.57 (0.36-0.90)	0.01	1.31 (1.04-1.64)	0.02	1.37 (1.07-1.75)	0.01
NYHA ≥ II	1.08 (0.80-1.45)	0.63			1.18 (0.78-1.80)	0.43			0.99 (0.77-1.27)	0.93		
LVEF (%)	1.00 (0.99-1.01)	0.58			1.00 (0.99-1.02)	0.75			1.00 (0.99-1.01)	0.81		
LVEF <40%	1.24 (0.78-1.95)	0.36			1.03 (0.58-1.82)	0.92			1.16 (0.80-1.67)	0.43		
LA size (mm)	1.00 (0.98-1.02)	0.82			0.99 (0.96-1.02)	0.38			1.00 (0.99-1.02)	0.72		
LA size >50mm	0.87 (0.62-1.21)	0.40			1.60 (0.94-2.74)	0.09			1.07 (0.80-1.43)	0.67		
Previous ECV	1.10 (0.76-1.61)	0.61			0.95 (0.51-1.70)	0.86			1.09 (0.79-1.50)	0.61		
AF duration > 1 year	0.87 (0.61-1.26)	0.47			1.16 (0.71-1.89)	0.55			0.87 (0.64-1.17)	0.35		
Biphasic energy	1.84 (1.41-2.40)	0.0001	1.84 (1.34-2.45)	0.0001	1.37 (0.93-1.99)	0.11			1.34 (1.07-1.67)	0.01	1.44 (1.13-1.82)	0.003
Anteroposterior patchs	0.91 (0.69-1.20)	0.50			1.23 (0.85-1.77)	0.28			0.87 (0.69-1.09)	0.23		
Successful energy (J)					1003 (1001-1005)	0.005						
Number of shocks					2.36 (2.00-2.78)	0.0001	2.34 (1.94-2.81)	0.0001				

SR, sinus rhythm; IAFR, immediate atrial fibrillation recurrence; ECV, electric cardioversion; BSA, body surface area; COPD, chronic obstructive pulmonary disease; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; LVEF, left ventricular ejection fraction; LA, left atrium.