ORIGINAL ARTICLE

Safety of emergency-department electric cardioversion for recent-onset atrial fibrillation

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Objective. To analyze the safety of electric cardioversion performed for recent-onset atrial fibrillation in a hospital emergency department.

Methods. Observational retrospective analysis of consecutive emergency department cases of atrial fibrillation of less than 48 hours' duration in hemodynamically stable patients. All included cases were either treated with emergency electric cardioversion or referred for evaluation and scheduling of outpatient cardioversion. The outcome variable was the occurrence of a thromboembolic or hemorrhagic event within 90 days.

Results. A total of 718 cardioversions in 570 patients were analyzed. The mean (SD) age of the patients was 64 (13.5) years. Four hundred seventy-nine emergency cardioversions (66.7%) and 239 (33.3%) scheduled cardioversions were performed. Eleven adverse events (1.5% of the cohort) occurred: 2 were thromboembolic events (0.3%) and 9 were hemorrhagic (1.3%). All bleeds were minor. There were no statistically significant differences in the rate of adverse events between the emergency and scheduled cardioversion groups.

Conclusion. Emergency cardioversion for recent-onset atrial fibrillation is safe.

Keywords: Atrial fibrillation. Electric countershock. Emergency department.

Seguridad de la cardioversión de la fibrilación auricular de reciente comienzo en urgencias

Objetivo. Analizar la seguridad de la cardioversión de la fibrilación auricular (FA) de reciente comienzo realizada en un servicio de urgencias hospitalario (SUH).

Método. Estudio observacional, retrospectivo y analítico en un SUH. Se recogieron de forma consecutiva los episodios de FA de menos de 48 horas de evolución y hemodinámicamente estables, en los que se realizó una cardioversión urgente (CVU) y los episodios derivados para valorar cardioversión programada ambulatoria (CVP). La variable de resultado fue la presencia de eventos embólicos (EE) o hemorrágicos (EH) a los 90 días.

Resultados. Se analizaron 718 cardioversiones en 570 pacientes. La edad media fue de 64 años (DE 13,5). Se realizaron 479 (66,7%) CVU y 239 (33,3%) CVP. Se recogieron un total de 11 (1,5%) eventos: dos EE (0,3%) y 9 EH (1,3%). Todos los EH fueron hemorragias menores. No se encontraron diferencias estadísticamente significativas entre ambos grupos.

Conclusión. La CVU de la FA de reciente comienzo en los SUH es una estrategia segura.

Palabras clave: Fibrilación auricular. Cardioversión. Urgencias.

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Introduction

Atrial fibrillation (AF) is the most frequently treated arrhythmia in hospital emergency departments (EDs) and accounts for 3-4% of all consultations[1,2]. EDs play a very important role in the management of episodes of AF of recent onset - less than 48 hours from the start of the episode - subsidiary to a rhythm control strategy[3]. The incidence of embolic events (EE) in the cardioversion of AF of recent onset varies according to studies between 0-0.9%[4-6] and is considered an acceptable percentage that allows recommending restoration at sinus rhythm in this period of time[7]. However, a study conducted in Finland[8] questioned this time margin as it found an excess of EE in patients with AF lasting less than 48 hours, even 24 hours if accompanied by certain risk factors[9]. Given that early restoration of sinus rhythm in the ED is associated with benefits for patients[10], it is important to know the safety of cardioversion in the ED (CVE) and compare it with a more controlled environment, where correct anticoagulation is ensured, such as patients who undergo scheduled cardioversion (SCV).

In order to do this, the following study was conduc-

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ted comparing the occurrence of EE and haemorrhagic events (HE) in two groups of patients. One group were patients with newly diagnosed AF of less than 48 hours undergoing CVE and the other group were patients with AF referred for SCV to the cardiology department.

Method

An observational, retrospective and analytical study was performed in the emergency department of a tertiary hospital. The recruitment period was from January 2009 to April 2017. Episodes of AF or atrial flutter with an evolution of less than 48 hours were collected consecutively and presented in hemodynamically stable patients undergoing effective CVE in the emergency department - patients were in sinus rhythm at discharge. Episodes of AF that were referred to the cardiology department were also collected to assess the performance of an electric SCV. Our service does not require the presence of another specialist to perform a CVE, but they are available if required. The independent variables collected were: demographics (sex and age), personal history (arterial hypertension, dyslipemia, diabetes and chronic renal failure), antiarrhythmic, anticoagulant and antiaggregant base treatment, characteristics of AF, analytical data (creatinine, estimated glomerular filtrate, troponin T), thrombotic and haemorrhagic risk (CHADS2, CHA2DS2-VASc, CHADSVASC # 3 points, HAS BLED) and anticoagulant treatment at discharge.

The outcome variable was the combined variable presence of EE or HE after 90 days of cardioversion. The EE collected were: ischemic stroke, nonspecific stroke, transient ischemic attack and systemic arterial embolism. Any bleeding recorded in the follow-up period was defined as HE. Greater HE were defined as those requiring hospital admission. Those that did not require admission were classified as minor HE. Follow-up at 90 days was performed by consulting the computerized clinical history of the hospital and primary care.

The study was approved by the Clinical Research Ethics Committee of the General University Hospital of Alicante and was carried out following the guidelines of the Declaration of Helsinki on ethical principles for medical research.

Qualitative variables were defined as absolute and relative frequencies; quantitative variables were expressed as mean and standard deviation. For the comparisons, the chi-square test was used for the former (or in the tables 2 × 2 Fisher's exact test when the expected values were below 5) and the Student's t test for independent measures for the latter. Differences between the CVE and SCV groups were analyzed using a logistic regression model and input method, including variables whose differences showed a value of $p < 0.05$. Differences were considered statistically significant when the p-value was below 0.05 or when the 95% confidence interval (95% CI) of the OR excluded value 1. The statistical program used was SPSS 24.0 (SPSS Inc., Chicago, USA).

Results

A total of 718 cardioversion procedures were analyzed in a total of 570 patients (Figure 1). The general characteristics of the studied cohort are shown in Table 1. The mean age was 64 years (SD 13.5) and 51.5% were women. There were 479 CVE (66.7%) and 239 SCV (33.3%). In the episodes in which pharmacological CVE were performed, the antiarrhythmics used were: amiodarone in 71 episodes (22.5%), Ic group in 113 (35.9%, 112 flecainide and 1 propafenone); beta-blockers in 63 (20.0%) and vernakalant in 52 (16.5%). Table 1 shows the differences between these two groups, highlighting that patients admitted to CVE were in a higher percentage women and young, received more basic antiarrhythmics, especially from group Ic, and anticoagulant treatment. The prevalence of newly diagnosed AF was lower in this group, with a higher proportion of paroxysmal AF. When multivariate analysis adjusted by logistic regression was performed, being a woman with an OR of 1.79 (95% CI 1.13-2.86), receiving basic treatment with an OCP with an OR of 3.76 (95% CI 2.10-6.72) and receiving an OCP with an OR of 0.16 (95% CI 0.09-0.29) remained statistically significant for the CVE.

No differences were found in thrombotic risk, but differences were found in haemorrhagic risk, which was higher in the SCV group. At discharge, the CVE group received less de novo anticoagulation. Table 1 shows the comparative study of the characteristics of patients

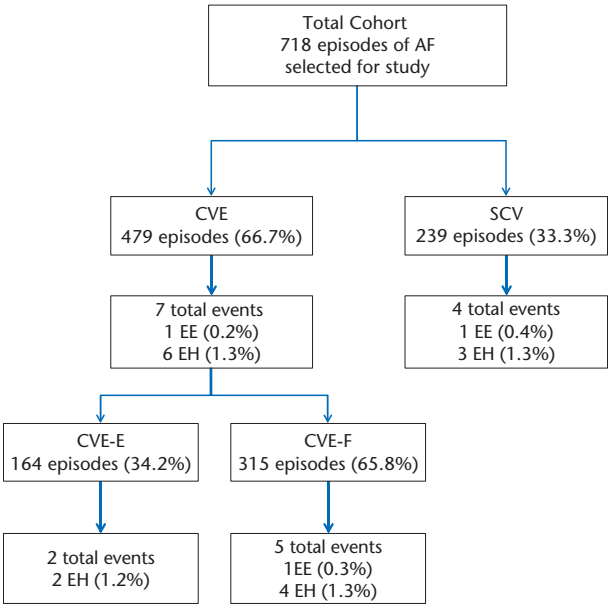

Figure 1. Flowchart of patient inclusion and security events.
SCV: Scheduled cardioversion performed in the cardiology department; CVE: cardioversion performed in the emergency department; CVE-E: electrical cardioversion performed in the emergency department; CVE-P: cardioversion performed in the pharmacological emergency department; EE: embolic events; HE: hemorrhagic events; AF: atrial fibrillation.

Table 1. Univariate and bivariate study according to the cardioversion scenario and according to the type of cardioversion performed in the emergency department

	Total N = 718 n (%)	CVE N = 479 n (%)	SCV N = 239 n (%)	p	CVU-E N = 164 n (%)	CVE-E N = 315 n (%)	p
Demographic data							
Age (years) [average (SD)]	64.0 (13.5)	62.7 (14.1)	66.6 (11.9)	< 0.001	59.7 (13.2)	64.2 (14.3)	0.001
Women	370 (51.5)	263 (54.9)	107 (44.8)	0.010	72 (43.9)	191 (60.6)	< 0.001
Personal history							
High blood pressure	426 (59.3)	274 (57.2)	152 (63.6)	0.100	86 (52.4)	188 (59.7)	0.128
Dyslipemia	277 (38.6)	185 (38.6)	92 (38.5)	0.973	59 (36.0)	126 (40.0)	0.391
Diabetes mellitus	83 (11.6)	50 (10.4)	33 (13.8)	0.183	7 (4.3)	43 (13.7)	0.001
Chronic renal failure	26 (3.6)	16 (3.3)	10 (4.2)	0.568	5 (3.0)	11 (3.5)	0.798
Base-treatment							
Antiarrhythmic treatment	113 (15.8)	88 (18.4)	25 (10.5)	0.006	35 (21.3)	53 (16.9)	0.232
Amiodarone	35 (4.9)	23 (4.8)	12 (5.0)	0.902	9 (5.5)	14 (4.5)	0.618
Group Ic[1]	57 (7.9)	50 (10.4)	7 (2.9)	< 0.001	20 (12.2)	30 (9.5)	0.364
Dronedarone	21 (2.9)	15 (3.1)	6 (2.5)	0.642	6 (3.7)	9 (2.9)	0.633
Previous anticoagulant treatment	214 (29.8)	174 (36.3)	40 (16.7)	< 0.001	65 (39.6)	109 (34.6)	0.277
Antivitamin K	137 (19.1)	109 (22.8)	28 (11.7)	< 0.001	41 (25.2)	68 (21.6)	0.378
LMWH	7 (1.0)	6 (1.3)	1 (0.4)	0.434	3 (1.8)	3 (1.0)	0.415
Direct anticoagulants	72 (10.0)	61 (12.8)	11 (4.6)	< 0.001	23 (14.1)	38 (12.1)	0.525
Anti-aggregate treatment	136 (18.9)	80 (16.7)	56 (23.4)	0.030	27 (16.5)	53 (16.8)	0.920
Acute episode data							
Characteristics of AF							
AF for new diagnosis	251 (35.0)	120 (25.1)	131 (54.8)	< 0.001	49 (29.9)	71 (22.5)	0.079
Permanent FA	22 (3.1)	13 (2.7)	9 (3.8)	0.441	6 (3.7)	7 (2.2)	0.383
Persistent AF	24 (3.3)	14 (2.9)	10 (4.2)	0.376	6 (3.7)	8 (2.5)	0.570
Paroxysmal AF	412 (57.4)	324 (67.6)	88 (36.8)	< 0.001	98 (59.8)	226 (71.7)	0.008
Flutter headset	9 (1.3)	8 (1.7)	1 (0.4)	0.285	5 (3.0)	3 (1.0)	0.130
Analytical data							
Creatinine (mg/dl) [mean (SD)]	0.99 (0.47)	0.97 (0.49)	1.01 (0.42)	0.263	0.95 (0.42)	0.98 (0.53)	0.472
eGF	76.4 (21.7)	77.8 (22.1)	73.8 (20.7)	0.028	81.5 (22.0)	75.7 (22.0)	0.010
Troponin (ng/l) [medium (SD)]	13.2 (15.7)	12.3 (13.5)	15.1 (19.5)	0.046	11.7 (10.5)	12.7 (14.8)	0.481
Thrombotic and haemorrhagic risk							
CHADS2 (points) [mean (SD)]	1.0 (0.9)	1.0 (0.9)	1.1 (0.9)	0.096	0.8 (0.7)	1.1 (1.0)	< 0.001
CHA2DS2-VASc (points) [mean (SD)]	2.2 (1.6)	2.2 (1.6)	2.3 (1.4)	0.131	1.7 (1.4)	2.4 (1.7)	< 0.001
CHA2DS2-VASc # 3 points	552 (76.9)	367 (76.6)	185 (77.4)	0.813	141 (86.0)	226 (71.7)	< 0.001
HAS BLED (points) [mean (SD)]	1.3 (1.0)	1.2 (1.0)	1.4 (1.0)	0.001	1.0 (0.8)	1.3 (1.0)	< 0.001
Treatment at discharge							
Anticoagulant treatment	488 (70.0)	289 (61.4)	199 (88.1)	<0.001	113 (71.1)	176 (60.9)	0.002
Antivitamin K	257 (36.9)	163 (34.6)	94 (41.6)	0.074	66 (41.5)	97 (31.1)	0.025
Direct anticoagulants	194 (27.8)	101 (21.4)	93 (41.2)	< 0.001	43 (27.0)	58 (18.6)	0.035
LMWH	87 (12.5)	42 (8.9)	45 (19.9)	<0.001	13 (8.2)	29 (9.3)	0.687
Evolutionary data after 3 months							
Global ED Revisit	229 (31.9)	163 (34.0)	66 (27.6)	0.082	50 (30.5)	113 (35.9)	0.238
ED Revisit for AF	191 (26.6)	134 (28.0)	57 (23.8)	0.238	45 (27.4)	89 (28.3)	0.850
Global Mortality	1 (0.1)	1 (0.2)	0 (0.0)	1.000	0 (0.0)	1 (0.3)	1.000

SCV: Scheduled cardioversion performed in the cardiology department; CVE: cardioversion performed in the emergency department; CVE-E: electrical cardioversion performed in the emergency department; CVE-P: cardioversion performed in the pharmacological emergency department CVE-P; AF: atrial fibrillation; eGF: estimated glomerular filtrate; LMWH: low molecular weight heparin.
[1]Base group Ic: 56 cases of flecainide and one case of propafenone.

in which CVE was performed according to the method used and where the differences found were small.

Table 2 shows the results of the 90-day follow-up of cardioversion. A total of 11 (1.5%) events were collected: two EE (0.3%) and 9 HE (1.3%). All HE were minor haemorrhages. No statistically significant differences were found between the two groups. The characteristics of all the events collected are shown in Table 3. Both EE were ictus and occurred in patients receiving antivitamin K anticoagulants (AVK). No systemic EE arterial or major HE were recorded. In the CVE group there was one EE (0.21%), who died from this cause, and 6 lower HE (1.25%). Five patients were treated with AVK (bleeding rate 3%) and one with rivaroxaban (bleeding rate 1.4%). In the SCV group an EE (0.41%) and 3 minor HE (1.25%) were observed. Two patients (2.1%) were treated with AVK and one (0.7%) with rivaroxaban. The median number of days to perform SCV in patients with AVK was 63 (95% CI 33-96), and 41 (95% CI 31-73) in patients with direct-acting oral anticoagulants (DAOA), with no significant difference between the two (p = 0.32).

Table 2. Embolic and haemorrhagic events after 90 days following cardioversion depending on the cardioversion scenario

Characteristic	Total N = 718 n (%)	CVEN = 479 n (%)	SCVN = 239 n (%)	p
Total Events	11 (1.5)	7 (1.5)	4 (1.7)	1.000
Total embolic events	2 (0.3)	1 (0.2)	1 (0.4)	1.000
Total bleeding events	9 (1.3)	6 (1.3)	3 (1.3)	1.000
Major bleeding	0 (0)	-	-	
Minor bleeding	9 (1.3)	6 (1.3)	3 (1.3)	1.000
Global Mortality	1 (0.1)	1 (0.2)	0 (0.0)	1.000

SCV: scheduled cardioversion performed in the cardiology department; CVE: cardioversion performed in the emergency department.

Discussion

The present study includes a large number of patients with AF of recent onset who underwent CVE, and who had few pericardial ischemic or haemorrhagic complications. CVE was a safe technique, with a very low number of thromboembolic events and as safe as SCV with well-established prophylactic anticoagulation. This result confirms the recommendation of the current clinical practice guidelines on the convenience of controlling the rhythm of AF in the ED[7].

Patients with AF lasting less than 48 hours are considered to be at low embolic risk, as this is the time required for thrombus formation[11]. However, there is evidence that thrombus may form in patients within hours of onset of symptoms[12]. In addition, there is the fact that, as we see in our daily clinical practice, AF often occurs asymptomatically and, therefore, the clinic expressed by the patient does not always coincide with the actual onset of the arrhythmia. Grond et al.[13] conducted a study in patients with an ischemic stroke without prior known AF who had a 72-hour Holter implanted. An episode of AF was reported in 49 of the 1,135 patients. The existence of AF was related to advanced age or a history of previous stroke. In this sense, transesophageal ultrasound (TEU) performed before cardioversion has been shown to be useful for the detection of atrial thrombus[11,12], but it is not a 24-hour technique available in EDs. In our study the prevalence of EE after performing a CVE was 0.21%, even below the 0.7% published in other studies[6]. This may indicate that a duration of less than 48 hours is a sufficient safety limit, but it may also be influenced by the fact that the risk of thromboembolism in the patients included in our work has not been high - with a mean CHA2DS2-VASc of 2.2 points - and that a third of them were already receiving anticoagulant treatment at the time of cardioversion. According to the literature, in most cases EEs occur in the first 72 hours after cardioversion, and is attributed to the previous presence of atrial thrombus[14]. In our case, the only two EEs reported were much later (days 34 and 61), in patients receiving AVK and with an INR limit or below that recommended at the time of the event. In this sense, the pharmacokinetic characteristics of the DAOAs are an obvious advantage as long as a correct compliance is assured. The low thromboembolic risk of one of these patients, with a CHA2DS2-VASc of 0 points, is striking.

There are no clinical trials comparing CVE versus SCV. Case series have been published in which atrial thrombus was detected in 14% of patients with AF of less than 48 hours, so the administration of anticoagulant treatment prior to cardioversion is recommended in all cases[15]. Our data show a very similar complication rate in both groups, and given that the effect of cardioversion decreases with the duration of the arrhythmia[16], they support the implementation of acute rhythm control in patients with AF of recent onset treated in the ED. However, in patients with episodes of more than 48 hours or of unknown duration, safety should be paramount; therefore, cardioversion should be performed after 3 weeks of effective anticoagulation or by ruling out a thrombus through TEU. In these cases, as already mentioned, DAOAs have advantages over other anti-

Table 3. Characteristics of embolic and haemorrhagic events collected after 90 days following cardioversion

Embolic events						
Strategy	**Method**	**Days**	**CHA2DS2-VASc**	**OAC**	**Hemorrhagic event**	**INR[1]**
Cardioversion in the ED	Pharmacological (amiodarone)	34	6	Warfarin	Ictus[2]	2.0
Scheduled Cardioversion	Electric	61	0	Acenocumarol	TIA	1.4
Hemorrhagic events						
Estrategia	**Method**	**Days**	**HAS BLED**	**OAC**	**Hemorrhagic event**	**INR[1]**
Cardioversion in the ED	Electric	67	2	Acenocumarol	Hematuria	1.59
	Electric	18	2	Acenocumarol	HGI	5.50
	Pharmacological	57	4	Acenocumarol	Gingivorragia	5.7
	Pharmacological	72	2	Rivaroxaban	Hematuria	–
	Pharmacological	17	3	Acenocumarol	Hematuria	5.52
	Pharmacological	42	2	Acenocumarol	Intramuscular	ND
Scheduled Cardioversion	Electric	77	2	Rivaroxaban	Epistaxis	–
	Electric	29	1	Acenocumarol	Hematuria	1.24
	Electric	32	2	Acenocumarol	Hematuria	2.46

OAC: oral anticoagulant; TIA: transient ischemic attack; HGB: high gastrointestinal bleeding; NA: not available.
[1]INR at date of EE or HE.
[2]Death.

coagulants, since their effect is more stable and predictable, allowing earlier cardioversion, and therefore effective, with levels of safety and effectiveness comparable to the AVK[17,18]. In addition, in the case of patients with high thrombotic risk, their rapid onset of action allows effective anticoagulation in the first hours, and provide adequate protection in the first days, in which the thrombotic risk is greater[8]. In our study, SCV in patients receiving DAOA was earlier compared to those receiving AVK, even though it did not reach statistical significance, probably because of an insufficient sample. To date, the efficacy and safety of these drugs in the CVE of recent onset AF, performed according to usual clinical practice in EDs in patients who do not receive anticoagulant treatment, has not yet been evaluated prospectively.

We have detected a difference in anticoagulation at discharge between CVE (61.4%) and SCV (88.1%) that could be attributed to a lower recommendation of anticoagulation from the ED after CVE in patients with recent onset AF and CHA2DS2-VASc 0 (or 1 in women).

Our studio has a number of limitations. First, it is a retrospective observational study conducted in a single center, so the results may not be reproducible in other EDs. However, both patient characteristics and treatment results are similar to other studies published in our setting[1,10]. Secondly, the time that AF evolved was calculated by interviewing the patient, so it can sometimes be imprecise, but it faithfully represents what happens in normal clinical practice. Thirdly, the number of EE and HE has been very low, so the study is not powerful enough to find significant differences between the two rhythm control management strategies. Fourth, SCV was not performed on all referred patients; however, this fact does not influence the results, as the study assesses the strategy and not the cardioversion itself. Fifth, there are differences in the clinical characteristics of patients in the CVE group and the SCV group. This reflects that these are different populations and therefore the occurrence of EE and HE may be different. Finally, EE and HE are to a large extent related to the quality of anticoagulant treatment and not only to the safety of the procedure itself. Our study is not designed to identify the influence of this factor, and should therefore be taken into consideration in the interpretation of the results, particularly in the SCV group.

In conclusion, in our study, CVE of AF of recent onset in its acute phase is shown as a safe strategy, without differences with SCV. Prospective and randomized studies should be conducted to increase knowledge about post-cardioversion EE and HE.

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