Clinical Characteristics of Patients With Persistent Atrial Fibrillation Referred for Cardioversion: Spanish Cardioversion Registry (REVERSE)

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The objectives were to investigate the treatment and clinical characteristics of patients referred for cardioversion in Spain and to compare them with those reported in the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) and RACE (RAte Control versus Electrical cardioversion) studies. The prospective study involved 1515 consecutive patients with persistent atrial fibrillation who were referred for cardioversion at 96 Spanish hospitals. Half of the patients were being treated with Vaughan-Williams group I or III antiarrhythmic drugs. The most frequently used approach to anticoagulation was to administer dicoumarins 3-4 weeks before and after cardioversion. Our patients were younger than those in the AFFIRM and RACE studies. Compared with AFFIRM patients, our patients had a lower prevalence of previous embolism, ischemic heart disease, hypertension, diabetes, and systolic dysfunction. Compared with RACE patients, our patients had a lower prevalence of ischemic heart disease and previous embolism, but a slightly higher prevalence of hypertension and diabetes. We conclude that patients referred for cardioversion in Spain clearly had a lower cardiovascular risk profile than those in the AFFIRM study, and appeared to have a lower risk profile than those in the RACE study.

Key words: Atrial fibrillation. Cardioversion. Anticoagulation.

Perfil clínico de los pacientes con fibrilación auricular persistente remitidos a cardioversión: Registro sobre la cardioversión en España (REVERSE)

Los objetivos fueron conocer el manejo y las características clínicas de los pacientes remitidos a cardioversión en España y compararlos con los de los estudios AFFIRM y RACE. Se registró prospectiva y consecutivamente a 1.515 pacientes con fibrilación auricular persistente remitidos a cardioversión en 96 hospitales españoles. La mitad recibía tratamiento con antiarrítmicos de los grupos I o III de Vaughan-Williams. La estrategia de anticoagulación con dicumarínicos 3-4 semanas antes y después de la cardioversión fue la más utilizada. Nuestros pacientes eran más jóvenes que los de AFFIRM y RACE. Respecto al AFFIRM, tenían menor prevalencia de embolias previas, cardiopatía isquémica, hipertensión, diabetes y disfunción sistólica. Respecto al RACE, tenían menor prevalencia de cardiopatía isquémica y embolias previas, pero algo mayor de hipertensión y diabetes. Concluimos que los pacientes remitidos a cardioversión en España tienen un perfil de menor riesgo cardiovascular que los del AFFIRM y aparentemente menor que los del RACE.

Palabras clave: Fibrilación auricular. Cardioversión. Anticoagulación.

INTRODUCTION

The REVERSE (*REgistro sobre la cardioVERSión en España* [Spanish Cardioversion Registry]) study was undertaken with the aim of recording the clinical characteristics of patients with atrial fibrillation (AF) referred for cardioversion in Spain–no sufficiently large, specific, multi-center registries exist that describe the use of cardioversion in real life in this country.

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A full list of the researchers and hospitals involved in the REVERSE study is provided at the end of this paper.

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The AFFIRM[1,2] and RACE[3] studies concluded that the strategy of controlling the heart rhythm does not reduce mortality/morbidity more than the control of the heart rate. Knowing the characteristics of patients referred for cardioversion in Spain would be of great interest when extrapolating results of other studies to our population. The aim of the present analysis was therefore to describe the characteristics and clinical management of Spanish patients with AF referred for elective cardioversion, and to compare the findings with the results of the AFFIRM and RACE studies.

METHODS

In this study, patients with AF referred for elective cardioversion at 96 Spanish hospitals between 1 February and 30 June 2004 were prospectively and consecutively included in our registry. The requirements for inclusion demanded patients be >18 years of age, to have persistent AF (of at least seven days duration), to show no evidence of precipitating factors, and that they be considered candidates for pharmacological or electrical cardioversion (ECV). The results of an echocardiogram performed in the 6 months prior to cardioversion were requested. Patients with more than mild valve dysfunction or stenosis of any degree were considered to have valve disease. Isolated AF was defined as that seen in patients <60 years of age without high blood pressure or cardiopulmonary disease.[4] The REVERSE registry requires a follow-up of one year after ECV in patients without structural heart disease.

Statistical Analysis

Qualitative variables were expressed in terms of percentages; differences were analyzed using the χ^2 test. Quantitative variables were expressed as means (standard deviations); differences were analyzed using the Student *t* test. Patient clinical and echocardiographic information was compared with published data recorded by the AFFIRM and RACE studies.[1-3] Significance was set at $P<.05$. All calculations were made using SPSS 12.0 software.

RESULTS

The present study involved 1515 patients with persistent AF, all of whom were referred for cardioversion; Table 1 shows their clinical and echocardiographic characteristics. Some 20% had previously received ECV treatment. Some 51% had structural heart disease (including moderate or more severe left ventricular hypertrophy). Isolated AF was seen in 10% of patients.

Oral anticoagulation was the most common anticoagulation strategy used during the cardioversion period (employed in 55% of cases); this therapy was provided for at least three weeks prior to, and 1 month after, cardioversion. Some 31% of patients received chronic anticoagulation therapy. Transesophageal echocardiography (TEE) was rarely used (8%). Only 4% of patients received low molecular weight heparins, and only 2% were treated using other strategies.

A total of 752 (50%) patients received some type I or III Vaughan-Williams anti-arrhythmic drug prior to undergoing ECV; the most used was amiodarone (40%), followed by flecainide/propafenone (7%) and other drugs (3%). Among those patients who had undergone a previous ECV there was a tendency to more commonly prescribe anti-arrhythmic drugs (53% were thus treated compared to 48% of those who had undergone no prior ECV; $P=.10$). Some 53% received angiotensin converting enzyme inhibitors (ACEi) or angiotensin II receptor antagonists (ARA-II).

One hundred and sixty patients (21%) were pharmacologically reverted to sinus rhythm (SR); 1355 were therefore subjected to ECV. Among the latter, 87% were released with SR having been recovered. Taking into account both pharmacological and electrical cardioversions, stable SR was achieved in 88% of the present patients.

A comparison was made between the clinical and echocardiographic characteristics of the REVERSE, the AFFIRM, and the RACE study patients (Table 1). Compared to the AFFIRM study subjects, the present patients were younger (63[11] years compared to 69.7[9] years; $P<.0001$) and the prevalence of high blood pressure, diabetes, pulmonary disease, ischemic heart disease and previous embolisms among them was lower. In addition, conserved systolic function was more prevalent, the size of the left atrium was slightly greater, and the sample included patients with AF of longer duration. Compared to the RACE subjects, the present patients were younger (63[11] years compared to 68[8] years; $P<.0001$), and the prevalence of prior ischemic heart disease and embolisms among them was lower. However, high blood pressure and diabetes were somewhat more common. In addition, fewer of the REVERSE patients showed structural heart disease (51% compared to 79% in the RACE study); no statistical analysis was performed for this comparison since the criteria for reporting "heart disease" were not specified in the RACE study. The size of the left atrium was similar in both patient populations. The RACE study did not report left ventricular ejection fraction data, thus no comparisons can be made in this respect.

DISCUSSION

The present patients clearly had a less serious cardiovascular risk profile than the patients of the AFFIRM study, and an apparently less serious profile than the RACE patients. The AFFIRM study included patients with AF with a high risk of suffering embolism or death; it is therefore to be expected that their clinical

TABLE 1. **Clinical and Echocardiographic Characteristics of Patients in the REVERSE Registry and the AFFIRM and RACE Studies**

Characteristics	REVERSE, n (%)	AFFIRM, n (%)	*P*	RACE (%)	*P*
Age, mean (SD), y	63±11	69.7±9	<.0001	68±8	<.0001
Males	959 (63)	557 (61)	.12	(63)	.95
High blood pressure	837 (55)	2.876 (71)	<.0001	(49)	.02
Diabetes mellitus	223 (15)	813 (20)	<.0001	(11)	.006
Chronic lung disease	133 (9)	591 (15)	<.0001	(20)	<.0001
Cardiomyopathy	112 (7)	341 (8)	.22	(9)	.24
Valve disease	243 (16)	504 (12)	<.0001	(17)	.59
Ischemic cardiomyopathy	134 (9)	1.551 (38)	<.0001	(27)	<.0001
Previous embolism	73 (5)	542 (13)	<.0001	(14)	<.0001
No underlying cardiomyopathy	745 (49)			(21)	
Duration of problem >6 months	362 (24)	284 (7)	<.0001		
Functional class					
I	787 (52)			(50)	
II	624 (41)			(47)	.001
Size of left atrium, mm	44.6 (6.3)	43 (8)	<.0001	45 (7)	.25
Size of left atrium (qualitative)					
≤40 mm	373 (26)	1103 (35)	<.0001		
41-45 mm	515 (35)	919 (29)			
46-55 mm	495 (34)	955 (31)			
>55 mm	74 (5)	149 (5)			
LVEF, %	58.6 (11.6)				
LVEF (qualitative)					
EF≥50%	1215 (84)	2244 (74)	<.0001		
EF40%-49%	128 (9)	391 (13)			
EF30%-39%	75 (5)	242 (8)			
EF<30%	32 (2)	155 (5)			
Left ventricular hipertrophy	348 (23)				
Moderate-severe	222 (15)				

LEVF: left ventricular ejection fraction; SD: standard deviation.
In the REVERSE study no left atrial size was available for 58 patients, and no LEVF was available for 65.

profiles should be different to those of the present registry who were consecutive patients referred for cardioversion. The characteristics of the AFFIRM patients' AF were different since there was no requirement for treatment with ECV. In addition, 31% of the AFFIRM patients suffered paroxysmal AF (<48 h duration). From the point of view of clinical and AF characteristics, the former study is more comparable to the present since inclusion in the RACE study required ECV treatment and did not demand that patients were likely to suffer cardiovascular complications (the patients were therefore more representative of the cardioversion candidate population). Although the prevalence of high blood pressure and diabetes was greater among the RACE patients, given the significant differences in the prevalence of prior embolisms and their mean age (the two most important factors in embololic risk),[5] the REVERSE patients appear to be at lower risk of embolisms and other cardiovascular complications, bearing in mind the differences in the prevalence of ischemic heart disease and structural heart disease. We believe that the differences in clinical characteristics are in part due to these studies having influenced clinical practice in terms of a more strict selection of patients who are candidates for cardioversion. Hence, the extrapolation of their results to patients in the Spanish clinical setting should be performed with care.

The strategy of providing anticoagulation therapy for 3-4 weeks before and for at least 4 weeks after cardioversion, is preferred by Spanish cardiologists. The scant use of TEE is justified since, although it shortens the time between clinical decision-making and ECV, it provides little clinical benefit,[6] especially since nowadays anticoagulation treatment is maintained over a long period.

Half of the present patients referred for cardioversion were receiving anti-arrhythmic treatment with type I or III Vaughan-Williams drugs. This strategy can be useful for the prophylaxis of immediate recurrences and recurrences in the first days after cardioversion, and it can help in achieving SR before ECV (as seen in 21% of the present patients). The ESC/AHA/ACC[7] clinical practice guidelines on AF attach a grade IIa

recommendation (evidence level B) to anti-arrhythmia treatment prior to cardioversion. It may also be more justified in patients who have undergone previous ECV – a criterion that appears to be used in Spain.

The large number of patients involved in the present study, and the participation of hospitals providing different levels of assistance, suggest the REVERSE registry reliably reflects clinical practice surrounding cardioversion in Spain.

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