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Adherence to guidelines and mortality in atrial fibrillation ☆,☆☆

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ABSTRACT

Objective: Determining the adherence to ACC/AHA/ESC 2006 guidelines and its influence on the survival of patients with atrial fibrillation.
Methods: Prospective observational study of patients discharged during 2007 from an Internal Medicine department with a main or secondary diagnose of atrial fibrillation. The stroke risk was estimated with the $CHADS_2$ score. The follow-up was carried out in outpatient medical office or via telephone.
Results: We included 259 patients (mean age 80.9 years); 73% of them had a high risk of stroke. Oral anticoagulants were administered to 134 (51.7%), and antiplatelet drugs to 71 (27%) patients. A rate control strategy was chosen for 155 (59.8%) patients and a rhythm control one for 28 (10.8%). In 100 (38.6%) patients, treatment was adherent to the guidelines. Adherence to the guidelines was associated with age (0.95 95%CI 0.92–0.99; $p = 0.03$), contraindication to the use of oral anticoagulants (0.38 95%CI 0.18–0.81; $p = 0.01$) and mitral valve heart disease/valvular prosthesis (2.10 95%CI 1.04–4.25; $p = 0.04$). The median follow-up was 727 days, and 191 patients died. Patients treated according to the guidelines had a higher rate of survival during the first three years (0.47 vs. 0.36; $p = 0.049$). The use of oral anticoagulants was associated with a higher probability of survival over a 5 year period (0.34 vs 0.21; $p = 0.001$) and the rate control strategy during the first year (0.69 vs 0.57; $p = 0.04$).
Conclusions: In the real world, the treatment of atrial fibrillation according to the guidelines is associated with improved survival for up to three years during follow-up.

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1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia among the population [1], and it has been associated with an increase in the occurrence of stroke [2]. The risk of AF-related stroke grows with age [3]. Other factors contributing to a higher risk are feminine gender, hypertension, valvular heart disease, impaired left ventricular function, previous myocardial infarct and previous thromboembolic events [4–6]. It has been shown that oral anticoagulants (OA) reduce the risk of AF-related stroke [7]. Despite that, they are still underused in real practice [8].

Several systems have been developed to stratify the risk of stroke in patients with AF. In a multivariate analysis from the Framingham Heart Study, age, feminine gender, history of stroke or transient ischemic attack (TIA) and diabetes were associated with the onset of stroke [9]. Another stratification system is $CHADS_2$, which assigns 2 points for previous stroke or TIA, and one point for each of the following factors: age over 75, hypertension, diabetes or heart failure [10]. Patients are considered low risk with zero points, moderate risk with one point and high risk with two or more points [10].

The American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology (ESC) 2006 guidelines for AF management recommended treating with aspirin those patients with no risk factors, with aspirin or OA those with moderate risk and with OA those with high risk [11]. Platelets under 100×10^9/L, alcoholism, recent (less than a month) surgery or trauma and major hemorrhage (that is, one that puts life at risk or causes hospitalization) during the previous month are considered contraindications (CI) for OA [12].

The meta-analysis of randomized clinical trials on AF patients comparing rate control and rhythm control strategies has shown no

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differences in mortality [13]. The drugs used for chronic rate control were beta blockers, non-dihydropyridine calcium antagonists and digoxin; for rhythm control, they were amiodarone, dofetilide, flecainide, ibutilide, propafenone and quinidine [11].

In the prevention of cardiovascular diseases, adherence to guidelines is associated with substantial benefits in terms of morbidity and mortality [14]. Patients admitted to Internal Medicine wards are different from those included in clinical trials; usually, they are older and have more comorbidity. Consequently, patterns of practice for these patients differ from those applied in clinical trials and guidelines.

This study aimed to determine whether treatment of AF at the time of hospital discharge is in agreement with the guidelines, and whether in the real world, adherence to the guideline recommendations is associated with longer patient survival.

2. Material and methods

A prospective observational study of patients admitted to an Internal Medicine unit during 2007 was carried out. All patients with paroxysmal, persistent or permanent AF as main or secondary diagnosis in their discharge report were included, so if they experienced one or more AF episodes, if that was the first detected AF, or if more than one AF episode had already been documented, and if they were in sinus rhythm or in AF at time of discharge. Patients who died during hospitalization were excluded. We define previous AF when this was not the first detected episode of AF.

2.1. Measurements

The following variables were gathered: age; sex; presence of hypertension; diabetes; heart failure; previous stroke or TIA; moderate or severe mitral valve heart disease; valve prosthesis; chronic kidney failure; chronic liver disease; antithrombotic treatment, rhythm at discharge, rate or rhythm control strategy at discharge; and hemoglobin, albumin, cholesterol and creatinine values. All data were collected at discharge. The stroke risk was estimated using the $CHADS_2$ score [10]. Risk was considered low for a $CHADS_2$ score of 0, intermediate for a score of 1 and high for a score ≥ 2. Even though the ATRIA score had not yet been developed at the time we began the study, we used this stratifying system in hindsight to assess the risk of OA-associated hemorrhage [15]. Three risk levels were considered: low (0–3 points), medium (4 points) and high (5–10 points).

2.2. Adherence to guidelines criteria

As a baseline, we took the ACC/AHA/ESC 2006 guidelines for the management of patients with (AF), current in 2007 [11]. Antithrombotic treatment was defined as adequate in the following circumstances: the use of OA in patients with mitral valve disease or valve prosthesis, the use of OA in patients with high risk of stroke but no CI for OA use, the use of antiplatelet agents (APA) in patients with high risk and CI for OA use, the use of OA or APA in patients with moderate risk but no CI for OA use, and the use of APA in patients with moderate risk and CI for OA use. Antithrombotic treatment was defined as inadequate in the following circumstances: the use of OA in patients with moderate or high risk and CI for it, the use of APA in patients with high risk and no CI for OA use, and the use of OA in patients with low risk. The strategy for rhythm control was deemed to be the use of amiodarone, dofetilide, flecainide, ibutilide, propafenone and quinidine, while for rate control it was the use of beta blockers, non-dihydropyridine calcium antagonists and digoxin [11]. Adherence to the guidelines was defined as the use of OA or APA following the previous criteria, along with a strategy for rhythm control, rate control or both.

2.2.1. Follow-up

The patients were followed up for 5 years. The follow-up was carried out in outpatient medical office or by telephone whenever the patient was unable to attend to consultation. The date of death was checked in the Spanish National Death Index (https://www.msssi.gob.es/estadEstudios/estadisticas/estadisticas/estMinisterio/IND_TipoDifusion.htm) and causes of death were ascertained in medical history.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Clinical Investigation Ethics Committee of Aragón. An informed consent was obtained from each patient (or from their caregivers, in case of cognitive impairment).

2.3. Statistical analysis

Assuming that patients without adherence to guidelines have a survival of 36% after three years, a 5% type I error and a difference > 10% in survival for adherence to guidelines, a sample size of 247 patients was calculated.

Qualitative variables are expressed as absolute frequencies and percentages, and quantitative ones as mean and standard deviation (SD). Comparisons between groups of patients were made by applying the chi-squared test for the former and the Student's *t*-test for independent samples for the latter. In the multivariate analysis, in order to determine which variables were associated with the different treatment strategies and with adherence to the guidelines, a logistic regression model was constructed using those variables associated with a $p < 0.1$ in the univariate analysis. To determine the variables associated with mortality, we used a Cox proportional regression model. The comparison of survival curves was carried out with the long-rank test. Statistical significance was established at $p < 0.05$.

3. Results

Fig. 1 shows the flowchart of included patients. In the end, 259 patients with a first admission with AF during 2007 were included. Their mean (SD) age was 80.9 (8.5) years.

3.1. Risk of stroke and bleeding

The risk of suffering a stroke applying the $CHADS_2$ score is presented in Fig. 2. Risk was high for 73% of the patients. The risk of OA-associated hemorrhage is presented in Fig. 2. The risk was low in 44.8% of the patients and high in 45.9% of them.

3.2. Treatment strategies

Baseline characteristics of patients and treatment strategies are presented in Table 1. OA were used on 134 (51.7%) patients, and APA on 71 (27%). A rate control strategy was used on 155 (59.8%) patients, and a rhythm control one on 28 (10.8%). In the multivariate analysis, older age (odds ratio [OR] 0.90 95% confidence interval [CI] 0.86–0.94; $p = 0.0007$), sinus rhythm at discharge (OR 0.24 95%CI 0.11–0.54; $p = 0.0005$) and the existence of CI for anticoagulant treatment (OR 0.27 95%CI 0.13–0.54; $p = 0.0003$) were associated with a lesser use of OA. Diabetes mellitus (OR 2.35 95%CI 1.19–4.62; $p = 0.01$) and the existence of a significant mitral valve disease or a valve prosthesis were associated with a greater use of OA (OR 4.84 95%CI 2.21–10.61; $p = 0.0008$). Rate control strategy was associated with the presence of heart failure (OR 2.02 95%CI 1.05–3.90; $p = 0.03$) and diabetes (OR 1.98 95%CI 1.03–3.81; $p = 0.04$) and with the absence of anemia (OR 0.50 95%CI 0.28–0.89; $p = 0.02$), and rhythm control strategy with a history of stroke/TIA (OR 3.84 95%CI 1.49–9.92; $p = 0.005$), and with sinus rhythm at discharge (OR 9.56 95%CI 3.91–23.39; $p = 0.0008$). Do not use neither rate nor control strategy was associated with the absence of heart failure (OR 2.08 95%CI 1.09–3.99; $p = 0.03$).

There was an obvious association between choosing a rate control strategy or a rhythm control one and the use of OA. OA were more

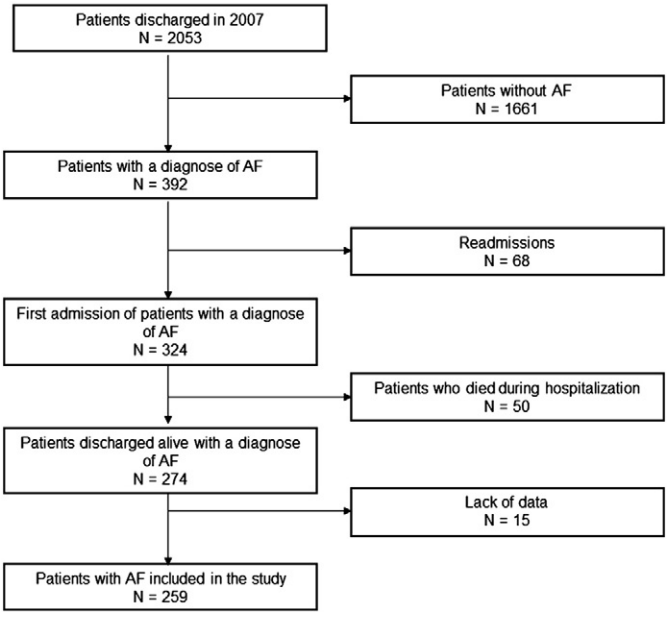

Fig. 1. Flow chart CONSORT of patients considered in the study. AF: atrial fibrillation.

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