

Use of Anticoagulation at the Time of Discharge in Patients With Heart Failure and Atrial Fibrillation

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Introduction and objectives. To assess the degree of compliance with current guidelines for chronic anticoagulation in patients with heart failure and atrial fibrillation.

Patients and method. From the INCARGAL Study database, we analyzed data from 195 consecutive patients (88 men; mean age 76 ± 10 years) with both conditions, admitted to three Galician hospitals between January and March 1999. It was assumed that these patients should have received anticoagulant therapy at discharge, unless contraindicated. We studied the association of treatment at discharge (anticoagulation or not) with the presence or absence of contraindications.

Results. 152 patients (78%) had no contraindication for anticoagulation and 43 had at least one (absolute: 11, relative: 32). Only 50% of patients without contraindications received anticoagulation at the time of discharge. No patient with an absolute contraindication and 3 with a relative one received anticoagulation. Factors related with the less frequent prescription of anticoagulation therapy in patients without a formal contraindication were: age, a previous history of coronary heart disease, absence of valvular heart disease, prior myocardial infarction, treatment with beta-blocking agents, non performance of an echocardiogram, and admission to a department other than cardiology. On multivariate analysis, age, prior myocardial infarction, and non-valvular disease were found to be independent predictors of less use of anticoagulation.

Conclusions. Anticoagulant therapy is used less often than recommended at discharge in patients with heart failure and atrial fibrillation for whom there were no contraindications. Advanced age reduces its use. The presence of other indications for antiplatelet or anticoagulation therapy appears to determine the choice of one or the other. Noncompliance with the guidelines due to overprescription was not found.

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Uso de anticoagulación al alta hospitalaria en pacientes con insuficiencia cardíaca y fibrilación auricular

Introducción y objetivos. Evaluar el grado de cumplimiento de las guías sobre uso de anticoagulación crónica en pacientes con insuficiencia cardíaca y fibrilación auricular.

Pacientes y método. Se usó la base de datos del estudio INCARGAL, analizando datos de 195 pacientes consecutivos (88 varones, edad 76 ± 10 años) admitidos con ambos diagnósticos en tres hospitales gallegos entre enero y junio de 1999. Se asumió que todos deberían de haber recibido anticoagulación al alta hospitalaria en ausencia de contraindicaciones. Se comparó el tratamiento al alta (anticoagulación o no) con la presencia o ausencia de contraindicaciones.

Resultados. Un total de 152 pacientes (78%) no tenían contraindicaciones para la anticoagulación y 43 presentaban alguna (absoluta, 11; relativa, 32). De los pacientes sin contraindicación, sólo recibieron anticoagulación al alta el 50%. Ningún paciente con contraindicación absoluta y tres con contraindicación relativa recibieron anticoagulación. La prescripción de anticoagulación en los pacientes sin contraindicaciones fue menor en los que tenían una mayor edad, antecedente de cardiopatía isquémica, ausencia de valvulopatía, uso de bloqueadores beta, no realización de ecocardiograma e ingreso en un servicio diferente del de cardiología ($p < 0,05$). En el análisis multivariante, la edad, el infarto de miocardio previo y la ausencia de valvulopatía significativa permanecieron como predictores independientes de menor uso de anticoagulación.

Conclusiones. El empleo de anticoagulación al alta hospitalaria en pacientes sin contraindicación para su uso, con fibrilación auricular e insuficiencia cardíaca, es menor del recomendado. La edad avanzada disminuye su empleo. La presencia de otras indicaciones para la antiagregación o la anticoagulación parecen determinar la elección de una u otra terapia. No hubo mala adecuación por exceso de prescripción.

Palabras clave: Anticoagulantes. Fibrilación auricular. Insuficiencia cardíaca.

ABBREVIATIONS

ACE: angiotensin-converting enzyme.
 ARB: angiotensin II receptor antagonist.
 INR: international normalized ratio.
 NYHA: New York Heart Association.

INTRODUCTION

Atrial fibrillation and heart failure each affect 1%-2% of the general population, and the prevalence of both rapidly increases with age.^{1,2} They share some risk factors and frequently coexist. In fact, heart failure affects more than 50% of all patients with atrial fibrillation,³ whereas the prevalence of atrial fibrillation is linked with the severity of chronic heart failure (10% of New York Heart Association [NYHA] Class II-III patients,⁴ 48% of NYHA class IV patients⁵).

Nonrheumatic atrial fibrillation is associated with a fivefold increase in the number of strokes in comparison to patients without atrial fibrillation.⁶ The rate of stroke is between 1% and 8% per year depending on age and the presence of other stroke-related risk factors.⁷ These risk factors include heart failure and ventricular dysfunction, which triple the incidence of stroke.⁸ For this reason, the decreased incidence of stroke achieved with chronic anticoagulation in patients with nonrheumatic atrial fibrillation, as reported in various studies,⁷⁻¹⁷ is particularly important in the subset of patients with heart failure. The Sociedad Española de Cardiología [Spanish Society of Cardiology] guidelines for clinical practice in arrhythmias¹⁸ and for the use of antithrombotic therapy in cardiology,¹⁹ and the American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) Guidelines for the Management of Patients with Atrial Fibrillation,²⁰ consider chronic oral anticoagulation therapy a Class I indication in all patients with heart failure and atrial fibrillation. If this therapy is contraindicated, case aspirin at a dose of 325 mg daily is recommended.

The extent of compliance with these recommendations is unknown. Studies conducted in populations with all types of nonrheumatic atrial fibrillation (not specifically in patients with heart failure) in Spain^{21,22} indicate that anticoagulants are used in less than 50% of patients at high risk for stroke. A recent survey performed in Sweden²³ showed that 94% of physicians advocated chronic anticoagulation for patients with

atrial fibrillation and risk factors for stroke, but only 40% of such patients pertaining to a specific healthcare area were receiving warfarin. In general, these studies indicate that there is room for improvement in the use of these drugs, but they fail to take into account the potential contraindications for the therapy.

Because anticoagulation therapy is not frequently used for atrial fibrillation, the purpose of this study, conducted in Galicia, northwestern Spain, was to determine whether the use of anticoagulant drugs is appropriate in patients with nonrheumatic atrial fibrillation and heart failure, taking into account contraindications for these drugs. To our knowledge, there are no previous reports that address this specific application of anticoagulation therapy.

PATIENTS AND METHODS

Patients

The data used in this study were taken from the INCARGAL (Insuficiencia Cardíaca en Galicia, Heart Failure in Galicia) database.²⁴ Briefly, this hospital registry followed a previously defined protocol to compile cross-sectional information on consecutive hospital admissions for heart failure at participating departments in 14 Galician hospitals between January and June 1999. At the end of this period, the registry contained data on 951 hospitalizations for 837 patients, of which 435 (52%) had chronic or paroxysmal atrial fibrillation. For the present study, however, additional information on potential contraindications for chronic anticoagulation was required. Since these contraindications were not included on the INCARGAL case report form, the medical records of all patients included in this research were reviewed again. For the sake of convenience, the sample was reduced to three of the hospitals that had participated in the registry (Complejo Hospitalario Juan Canalejo de A Coruña, Complejo Hospitalario de Lugo and Complejo Hospitalario de Ourense), the first with a Catheterization Laboratory and Cardiac Surgery Department, and the other two with Cardiology and General Teaching Facilities, although not specific per se for Cardiology. The final sample included 214 patients with atrial fibrillation (49% of all atrial fibrillation patients in the original registry). There were no statistically significant differences between these patients and the entire series of patients from all the hospitals included in the INCARGAL registry (data not presented).

Definitions

In accordance with the current guidelines on atrial fibrillation management, all patients were considered to have a Class I indication for chronic anticoagula-

tion, provided there were no contraindications. Contraindications for chronic anticoagulation («contraindication» hereinafter) were defined as any contraindication included in the guidelines of the Sociedad Española de Cardiología for the use of antithrombotic therapy in cardiology (Table 1). Advanced age was not considered a relative contraindication, because it is not included in the current guidelines on atrial fibrillation, which merely state that older patients should have more frequent follow-up and less stringent anticoagulation regimens.

Anticoagulation was established when a patient was receiving oral anticoagulation and/or low-molecular-weight heparin (LMWH) at the time of discharge. In patients with no contraindications, compliance with the guidelines was defined as anticoagulation prescription at the time of discharge, and poor compliance was defined as the absence of this therapy at discharge, even though patients might be receiving antiplatelet therapy.

Endpoints

The endpoints directly related to the study objectives were the presence or absence of contraindications and the prescription or not of anticoagulant therapy at discharge. The study also collected information on the following variables: age, sex, place of residence (urban or rural), hospital, department (cardiology or other), type of heart disease, history of hypertension, history of stroke, ejection fraction, therapy at discharge with other drugs (antiplatelet agents, beta-blockers, angiotensin-converting enzyme [ACE] inhibitors, ARBs) and diagnostic tests (echocardiogram, cardiac catheterization). These drugs and tests were chosen as potential indicators of the patients' compliance with other recommendations and of the hospitals' facilities.

Statistical analysis

Quantitative data are expressed as the mean \pm standard deviation (SD) and qualitative data are expressed as an absolute number (percentage). The therapy received (anticoagulation or not) was compared to the presence or absence of contraindications. In patients with no contraindications, univariate analysis was performed using the χ^2 test to determine which variables were associated with proper compliance with the guidelines. Logistic regression analysis was then performed with anticoagulation as the dependent variable and significantly associated variables in the univariate analysis as the independent variables. Our results present only the variables definitively remaining in the model.

Significance was set at a *P* value of less than .05. SPSS for Windows, version 9.0, was used for the statistical analysis.

TABLE 1. Contraindications for chronic anticoagulation according to the guidelines of the Sociedad Española de Cardiología on the use of antithrombotic therapy in cardiology

Absolute
Propensity to bleed
Active bleeding processes
Severe, uncontrollable hypertension
Hemorrhagic retinopathy
Intracranial aneurysm or neoplasm
History of intracranial hemorrhage or severe liver or kidney disease
Relative
Chronic liver disease
Nonbleeding active gastroduodenal ulcer
Hiatal hernia
Steatorrhea
Chronic alcoholism
Pregnancy
Low cognitive status
Pericarditis with effusion
Mental disorder

RESULTS

Among the 214 patients, 201 were discharged and 13 died during hospitalization. There were no data on possible contraindications for six of the discharged patients. Therefore, further analysis was performed only with the 195 remaining patients (88 men and 107 women; age 76 ± 10 years; range, 44-92). In 95 patients (49%), this was their first hospitalization, whereas 100 (51%) had at least one previous hospitalization for heart failure (median: 2; range, 1-10). Data on systolic function were available for 119 patients (61%): ejection fraction was above 50% in 60% of patients, between 35% and 50% in 23% and below 35% in 17%.

A total of 43 patients (22.1%) had a contraindication (Table 2): absolute in 11 (5.7%) and relative in 32 (16.4%). No patient with an absolute contraindication and only three with a relative contraindication received anticoagulant therapy. In these three, one had hiatal hernia, one had mental alterations and one had chronic alcoholism.

There was no contraindication in 77.9% of the patients. Among these, 79 (50%) received anticoagulation therapy at discharge: 71 received oral anticoagulation alone, 4 were given low-molecular-weight heparin alone, and 4 were given both treatments. In the group with no contraindications, the variables associated with poorer compliance with the guidelines in the univariate analysis were older age, history of ischemic heart disease or previous myocardial infarction, absence of valve disease, absence of beta-blocker therapy, no echocardiogram and hospitalization in a department other than cardiology (Table 3).

TABLE 2. Antithrombotic therapy at discharge, according to contraindications for anticoagulation

	No contraindication (n=152)	Relative contraindication (n=32)	Absolute contraindication (n=11)	Total (n=195)
None	20 (13%)	11 (35%)	7 (64%)	38 (19.5%)
Antiplatelet agents	56 (37%)	18 (56%)	4 (36%)	78 (40%)
Anticoagulation	76 (50%)	3 (9%)	0	79 (40.5%)

The percentage represented by each column is expressed between parentheses.

TABLE 3. Demographic and clinical variables of patients without contraindications for anticoagulation, according to compliance with guidelines at discharge

	Anticoagulation	No anticoagulation/antiplatelet agents	P	Total
Age ≥75 years	34.2	77.0	<.001	55.3
Male sex	48.7	43.4	.515	46.1
Hospital	—	—	.840	—
Cardiology department	51.3	31.6	.014	41.4
Rural residence	56	62.2	.445	59.1
Previous hospitalizations for heart failure	53.9	47.4	.422	50.7
Ischemic heart disease	14.5	28.9	.033	21.7
Previous myocardial infarction	2.6	14.5	.009	8.6
Significant valve disease	42.1	21.1	.006	31.6
High blood pressure	51.3	65.8	.071	58.6
Diabetes	18.7	24	.430	21.3
Hypercholesterolemia	17.1	17.1	1.000	17.1
History of smoking	30.2	25	.582	29.2
COPD	28.9	36.8	.301	32.9
Previous stroke	15.8	11.8	.482	13.8
Peripheral artery disease	7.9	10.5	.578	9.2
Ejection fraction <50%	46.6	28.9	.087	39.6
Beta-blockers	13.2	2.6	.016	7.9
ACE inhibitors	63.2	65.8	.741	64.5
Echocardiography	72.4	44.7	.001	58.6
Catheterization	3.9	11.8	.085	7.9

All values are expressed as a percentage. No percentages for «hospital» are indicated, as this variable has more than two categories. COPD indicates chronic obstructive pulmonary disease; HT, hypertension; ACE inhibitors, angiotensin-converting enzyme inhibitors.

TABLE 4. Factors related to anticoagulation therapy at discharge in patients with no contraindication (multiple logistic regression analysis)

	Odds ratio	95% CI	P
Age ≥75 years	0.88	0.83-0.92	<.001
Previous myocardial infarction	0.16	0.03-0.77	.023
Valve disease	2.89	1.25-6.69	.013

These variables were included in a multivariate analysis, in which only age, history of myocardial infarction and the absence of significant valve disease were independently and inversely related to proper compliance with the guidelines (Table 4).

DISCUSSION

Chronic oral anticoagulation therapy in patients with nonrheumatic atrial fibrillation and associated thromboembolic risk factors had demonstrated a relative risk reduction in stroke and peripheral embolism rate of 64% per year, with an absolute decrease of 3.1%. Nevertheless, there is no significant increase in the rate of major bleeding versus aspirin in these patients when an international normalized ratio (INR) of 2-3 is maintained.^{7,8,25-29} Therefore, the main guidelines on the management of atrial fibrillation consider patients with atrial fibrillation and heart failure to have a Class I indication for oral anticoagulants. The use of anticoagulation below the recommended levels in the absence of contraindications leads to a loss of these benefits, particularly in terms of a higher number of cerebrovascular ischemic events

(50%-70% of them resulting in death or severe neurological deficit).³⁰

The main finding of our work was that three-fourths of the patients had no contraindication, although only half of them were discharged with anticoagulation therapy. In these patients there was an inverse, independent relationship between compliance with the guidelines and three variables: age, history of myocardial infarction and absence of significant valve disease.

The inverse relationship with age (Figure 1) is probably related to concern for increased bleeding risk in older individuals. However, in patients above 75 years of age with an associated risk factor for stroke, anticoagulation decreases the risk of stroke by 73% versus placebo and 40% versus aspirin, albeit with a slight increase in the risk of bleeding that does not cancel out the benefit observed.⁷ The only important clinical trial reporting an excess of bleeding events in older patients that was high enough to counterbalance the beneficial effect of anticoagulation therapy was the Stroke Prevention in Atrial Fibrillation II (SPAF-II) study.¹⁵ In this study, individuals over 75 years of age had a yearly incidence of 4.2% for bleeding and 1.8% for intracranial hemorrhage. In a later analysis²⁸ the same authors reported that the main factor related to the risk of bleeding was the intensity of anticoagulation. For this reason, anticoagulation therapy guidelines in atrial fibrillation merely specify that more frequent follow-up, less aggressive regimens, and a target INR near 2 should be used in patients over 75 years of age.

It is not clear whether the benefit of anticoagulation therapy outweighs the risk of bleeding in very elderly patients. The largest studies included a relatively young population, and therefore their conclusions cannot be applied to much older groups. In one study with 93 patients over 80 years of age, Fihn et al²⁷ reported a yearly incidence of serious and life-threatening or fatal bleeding of 4.4% and 3.4%, respectively. Even in this group of older individuals, the main risk factor for bleeding was the intensity of anticoagulation. Therefore, the authors concluded that it is not justified to withhold anticoagulant therapy on the basis of age alone.

The second factor leading to fewer anticoagulation prescriptions at discharge is a history of previous myocardial infarction. This may be related to the regular use of antiplatelet agents in patients with chronic ischemic heart disease. Although aspirin has been shown to reduce the number of events after a myocardial infarction by around 10%-20% versus placebo, chronic oral anticoagulation also reduces these events by the same proportion.^{31,32} In addition, the few studies directly comparing aspirin with oral anticoagulation have found no difference between them, either in the pre- and post-thrombolytic periods.^{33,34} Since aspirin is inexpensive and requires no monitoring, it is the most commonly used antithrombotic therapy following a myocardial infarction. If another

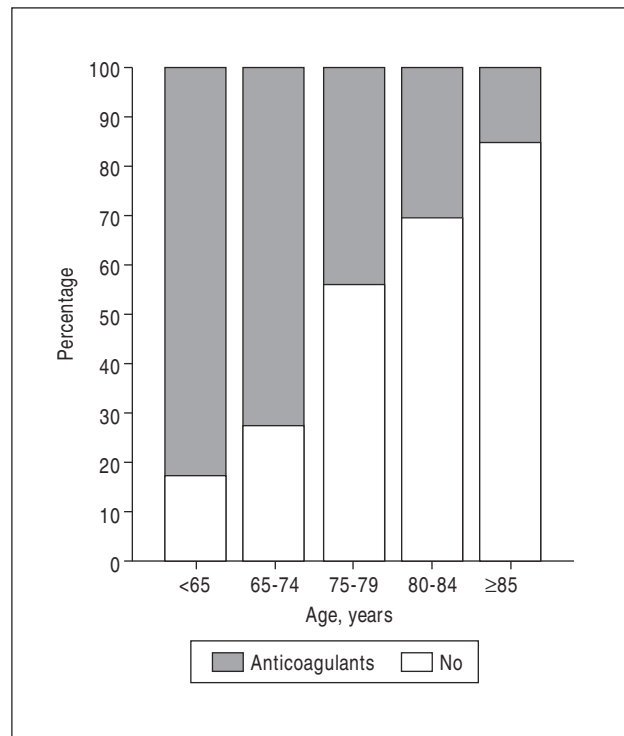


Fig. 1. Relationship between age and anticoagulation in patients with no contraindications.

indication for anticoagulant therapy exists, however, as in our patients, the latter appears to be the treatment of choice.^{35,36}

The positive relationship between anticoagulation at discharge and the presence of significant valve disease probably reflects the effect of cumulative indications for anticoagulation therapy in a specific patient, since significant mitral or aortic valve disease is an indication for anticoagulation in patients with atrial fibrillation.

No patients were discharged with both anticoagulation and antiplatelet therapy. Among patients with no contraindications, similar percentages were discharged with either of the two therapies. This probably reflects two tendencies: an inclination to avoid combining these drugs and, in many cases, a preference for antiplatelet therapy over anticoagulation therapy. It is still not clear whether combination therapy achieves greater benefit or whether it merely leads to an unacceptable risk of bleeding; the guidelines recommend it only when a stroke event occurs despite proper anticoagulation therapy. Nevertheless, the second tendency does appear to reflect poor compliance with the recommendations. Despite the superiority of aspirin versus placebo in preventing thromboembolism, its use in a patient eligible for anticoagulant therapy reduces the potential benefit. Although it is generally accepted that antiplatelet therapy has a lower risk of bleeding (particularly minor bleeding), the Copenhagen Atrial Fi-

brillation, Aspirin, and Anticoagulation Study (AFA-SAK-2)³⁷ reported a slightly higher annual rate of major bleeding events with aspirin than warfarin (1.4% vs 1.1%). Even though the difference was not statistically significant, the authors stressed that aspirin is not as harmless as is so often believed.

No differences were found in the use of anticoagulation therapy in relation to sex, place of residence, hospital, type of medical service, diagnostic tests, or concomitant therapy at discharge (except for antiplatelet agents).

Among the 43 patients with contraindications, only three with a relative contraindication were discharged with anticoagulation therapy. This suggests that physicians are conscious of the potential for contraindications and that there is no current problem of «excess» therapy. Only 45% of the remaining 40 patients with contraindications were discharged with antiplatelet therapy. Possible reasons for the low proportion of antiplatelet therapy in this subset of patients are: *a)* some of the contraindications for anticoagulation therapy are also contraindications for antiplatelets, and *b)* the older age of patients with contraindications (median, 83.3 years; range, 57-99 years) and the high comorbidity in some of them, which might discourage physicians from taking «non-essential» preventive measures.

Limitations

Because this was a cross-sectional study, determining the effect of anticoagulant therapy on future morbidity and mortality was beyond the scope of the research design we used.

Only patients admitted to three of the hospitals in the original registry were included. However, this did not affect the internal validity of the data, and is not relevant for the generalizability of our results: although these hospitals had the highest numbers of patients in the registry, no differences were found between these patients and the overall characteristics for all patients in the original registry.

The INCARGAL registry did not compile INR values in patients with anticoagulant therapy, and therefore it is impossible to determine how many patients received this therapy correctly. No data were collected on the presence or absence of valve replacement surgery with a mechanical valve prosthesis, although this information is essential to decide on the need for anticoagulation therapy.

Because of the cross-sectional study design, only therapy at discharge could be analyzed. There may be variations in the frequency of use of these drugs during outpatient follow-up, particularly in services that provide early follow-up after discharge.

CONCLUSIONS

Anticoagulant therapy at discharge in patients with heart failure and atrial fibrillation is prescribed less often than is recommended by current guidelines, particularly in older patients. In many cases, antiplatelet therapy as an alternative approach therapy is still preferred, with the resulting loss of potential benefits. Variables such as the patient's place of residence, admitting hospital or type of medical service do not appear to influence compliance with the guidelines.

We found no overprescription of anticoagulation therapy in patients with contraindications.

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