

## Use of Oral Anticoagulants in Patients Discharged With Atrial Fibrillation in 2000

Pedro Blanch, Roman Freixa, Montserrat Ibernón, Javier Delso, Elena Salas, José L. Sobrepera, Jaume Padró, Laura Dos, and Pedro Codinach

Servicio de Cardiología, Hospital Dos de Maig, Consorci Sanitari Integral, Barcelona, Spain.

**Introduction and objectives.** Although there is consensus about the use of oral anticoagulants to prevent thrombi and embolisms in most patients with atrial fibrillation, this treatment is underused in actual practice. Our objective was to determine and analyze the use of acenocoumarol in patients diagnosed as having atrial fibrillation at discharge.

**Patients and method.** Between January and July 2000, we retrospectively studied 501 consecutive patients with a diagnosis of atrial fibrillation. We recorded whether they were discharged with or without oral anticoagulation treatment.

**Results.** We identified 482 patients with at least one associated thromboembolic risk factor, who comprised the study population. Mean age was 79.3 years, and 33.3% of the patients were men. Forty-six percent were discharged with acenocoumarol, and 36.3% with platelet antiaggregants. Twenty-three percent had a known contraindication for acenocoumarol. Nearly 62% of the patients without contraindications for anticoagulation received treatment with acenocoumarol. Multivariate analysis showed that rheumatic mitral valve disease, previous stroke or thromboembolism and dilated left atrium were associated with a higher probability of receiving anticoagulant treatment. Age over 75 years was associated with a lower likelihood of receiving acenocoumarol.

**Conclusions.** Oral anticoagulation was given in an inadequate proportion of patients who were discharged from a secondary-level hospital with atrial fibrillation and no contraindications. Rheumatic mitral valve disease, previous stroke or thromboembolism, and dilated left atrium were associated with a higher probability of anticoagulant treatment. Age over 75 years was related with less frequent use of this therapy.

**Key words:** Anticoagulants. Patients. Atrial fibrillation.

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Correspondence: Dr. P. Blanch Gracia.  
Servicio de Cardiología. Hospital Dos de Maig. Consorci Sanitari Integral.  
Dos de Maig, 301. 08025 Barcelona. España.  
E-mail [pere.blanch@consorciacreuroja.es](mailto:pere.blanch@consorciacreuroja.es)

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### Utilización de anticoagulantes orales en pacientes con fibrilación auricular al alta hospitalaria en el año 2000

**Introducción y objetivos.** Existe un amplio consenso sobre la utilización de dicumarínicos en pacientes con fibrilación auricular para prevenir eventos tromboembólicos, aunque su uso real es inadecuado. Nuestro objetivo es determinar y analizar su utilización en pacientes con fibrilación auricular al alta hospitalaria.

**Pacientes y método.** Entre enero y julio de 2000 se estudió retrospectivamente a 501 pacientes consecutivos con el diagnóstico de fibrilación auricular. Se evaluó si recibieron o no anticoagulación oral.

**Resultados.** Se identificó a 482 pacientes que tenían asociado al menos un factor de riesgo tromboembólico, los cuales constituyeron el grupo de pacientes a estudio. La edad media fue de 79,3 años y el 33,3% eran varones. El 46,5% de la muestra fue dada de alta con dicumarínicos y el 36,3% con antiagregantes. El 22,7% de la población presentaba contraindicación para recibir dicumarínicos. El 61,7% de los pacientes sin contraindicación para anticoagulación recibieron tratamiento con acenocoumarol. En el análisis multivariado, los factores predictores de mayor probabilidad de recibir tratamiento anticoagulante fueron: valvulopatía mitral reumática, accidente cerebrovascular, embolia periférica, aurícula izquierda dilatada. La edad superior a 75 años se relacionaba con una menor probabilidad de recibir tratamiento con dicumarínicos.

**Conclusiones.** El tratamiento anticoagulante oral se administró en una insuficiente proporción de pacientes con fibrilación auricular, sin contraindicaciones para recibir dicha terapia, que fueron dados de alta de un hospital de segundo nivel. La presencia de valvulopatía mitral reumática, accidente cerebrovascular, embolia periférica y aurícula izquierda dilatada es condición para un mayor uso de anticoagulación. La edad mayor de 75 años se relaciona con un menor uso.

**Palabras clave:** Anticoagulantes. Pacientes. Fibrilación auricular.

## INTRODUCTION

Clear recommendations currently exist for oral anticoagulant therapy in patients with atrial fibrillation

## ABBREVIATIONS

INR: international normalized ratio.  
OR: *odds ratio*.

who have risk factors for thromboembolism.<sup>1</sup> The main indication is prevention of systemic thromboembolism in arrhythmia patients with or without rheumatic valve disease and in patients with an artificial valve. Nevertheless, despite an increase in the percentage of the population receiving anticoagulation in recent years, this therapy is underused in actual practice.<sup>2</sup>

The factors leading to underuse of oral anticoagulation are related to both the patient and the physician. The physician is primarily concerned with bleeding accidents, particularly if there is some question about the patient's compliance with the prescribed doses and the laboratory tests. Patients receiving concomitant medications also represent a problem because there are many drug interactions that can alter the anticoagulation parameters. In fact, the physician's main challenge when prescribing the medication is to convey the benefits and risks of therapy to the patient, as well as the importance of strict compliance with the prescription guidelines in terms of dosage and monitoring. Various studies show that the risk of bleeding is acceptable<sup>3,4</sup> if this is achieved, and that the benefits clearly outweigh the risks.

The patient-dependent factors related to underuse of anticoagulant therapy include individual preference, an underprivileged social or intellectual background, and the obvious inconvenience of frequent hospital or outpatient visits.<sup>5</sup> In this regard, we feel that many of the patient-dependent factors are resolved when the patient wait is shorter, and particularly when home monitoring of the international normalized ratio (INR) becomes a habit.

There are few studies in Spain on oral anticoagulant prescription in patients with atrial fibrillation who have risk factors for thromboembolism,<sup>6-10</sup> none of them performed after 2000.

The objectives of our study were:

1. To determine the rate of prescription of coumarin derivatives in patients with atrial fibrillation at hospital discharge from a community center.
2. To analyze the factors that influence their use.

## PATIENTS AND METHODS

### Patients

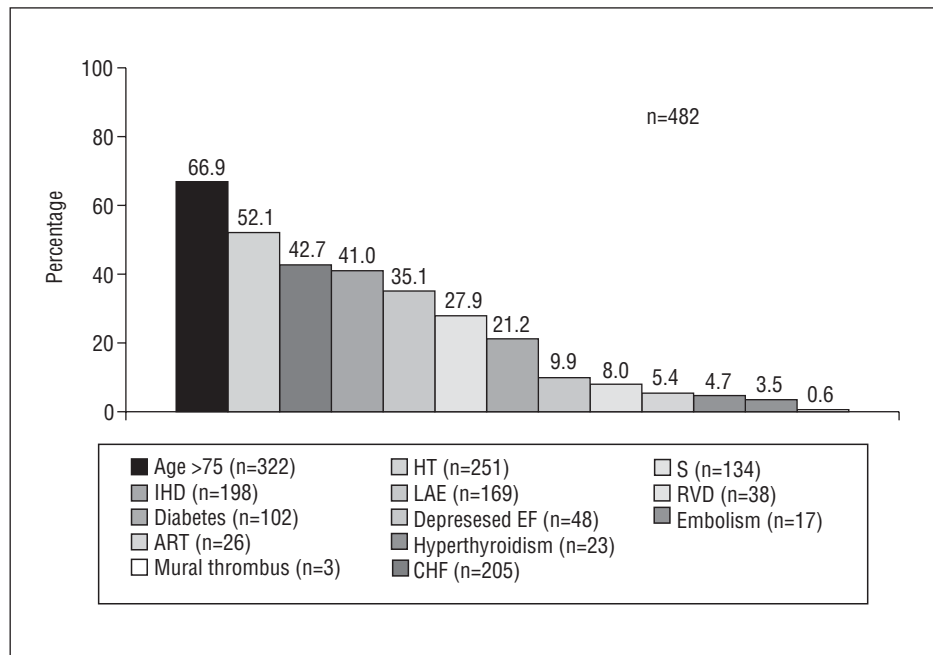
This cross-sectional, retrospective study was conducted between January and July 2000 by consulting

all hospital discharges during this period, identifying any discharge reports in which the coded diagnoses included atrial fibrillation or flutter (primary or secondary diagnosis) regardless of discharging department. The study identified 501 consecutive patients diagnosed as having atrial fibrillation or flutter. Among this initial population of 501 patients, 482 individuals with at least one thromboembolic risk factor were identified and included in the study population. Oral anticoagulation was indicated for these 482 patients unless contraindicated.

According to the clinical practice guidelines of the Sociedad Española de Cardiología (Spanish Society of Cardiology),<sup>1</sup> the following were considered risk factors for thromboembolism in the presence of atrial fibrillation: age above 75 years, heart failure, depressed ventricular function (ejection fraction <30%), medically uncontrolled hypertension, diabetes mellitus, intracardiac thrombus, history of embolism (stroke or peripheral embolism), ischemic heart disease, thyrotoxicosis, left atrial enlargement, rheumatic valve disease and artificial valves.

The absolute contraindications for oral anticoagulant therapy were considered to be: major bleeding in the previous six months, intracranial hemorrhage, recent major trauma, gastrointestinal bleeding, limited life expectancy, surgery performed or planned within one month, blood dyscrasia, severe hepatic impairment, cognitive impairment, failure to comply, severe uncontrolled hypertension, repeated falls, severe chronic alcoholism, pregnancy or lactation, allergy to acenocoumarol, prior withdrawal of treatment due to bleeding, and patient rejection. The following criteria defined impairment of cognitive function, and were considered contraindications for oral anticoagulation: diagnosis of severe dementia or psychiatric disease, or discharge report indicating the presence of a mental disability that would prevent the patient from using this type of medication.

The clinical history was reviewed and the following variables were included in the analysis of results: age, sex, anticoagulant therapy, antiplatelet therapy, risk factors for thromboembolism, contraindication for anticoagulation, and type of atrial fibrillation or flutter (chronic, paroxysmal, precardioversion). The term *precardioversion* refers to atrial fibrillation of recent onset in which anticoagulant therapy prior to electrical cardioversion was indicated. The variable *discharging department* was not assessed because the vast majority of patients with atrial fibrillation were seen by the Cardiology Department of our hospital at some point (whether in the outpatient clinic or during the hospital stay) and this department was responsible for the prescription and subsequent follow-up of oral anticoagulant therapy.



**Fig. 1.** Risk factors for thromboembolism. LAE indicates left atrial enlargement; S, stroke; IHD, ischemic heart disease; HT, hypertension; CHF, congestive heart failure; ART, artificial valve; RVD, rheumatic valve disease

## Statistical analysis

SPSS for Windows was used for the statistical analysis, with quantitative variables expressed as mean±standard deviation and qualitative variables as proportions (percentages). Pairs of mean values were compared with Student's *t* test, and proportions were compared with the  $\chi^2$  test. Significance was set at a *P* value of less than .05. Univariate analysis was carried out with the variables under consideration, and multivariate analysis was performed by logistic regression with variables included via a forward stepwise conditional method.

## RESULTS

Mean age was 79.3 years (range, 44-99 years) and 67% of the patients were women.

Among the 501 individuals initially included with the diagnosis of atrial fibrillation at hospital discharge, at least one associated risk factor for thromboembolism was found in 482 patients (96.2% of the initial population). According to current guidelines,<sup>1</sup> this patient group would benefit from oral anticoagulant therapy to prevent possible thromboembolic complications and should receive this therapy if there is no contraindication. These 482 patients comprised the study population.

The risk factors for thromboembolism in this population were the following: 322 (66.9%) >75 years, 251 (52.1%) hypertension, 205 (42.7%) heart failure, 198 (41%) ischemic heart disease, 169 (35.1%) left atrial enlargement, 134 (27.9%) stroke, 102 (21.2%) diabetes mellitus, 48 (9.9%) depressed ventricular function,

38 (8%) rheumatic valve disease, 26 (5.4%) artificial valve, 23 (4.7%) hyperthyroidism, 17 (3.5%) peripheral arterial embolism, and 3 (0.6%) mural thrombus (Figure 1). Some patients had more than one risk factor for thromboembolism.

Contraindications for oral anticoagulant therapy were found in 109 patients (22.7%). The most frequent contraindications were cognitive impairment in 47 patients (9.8%), uncertainty about proper compliance with treatment in 23 (4.8%), and a history of gastrointestinal bleeding in 17 (3.6%) (Figure 2). Other contraindications (frequency less than 1%) were limited life expectancy, blood dyscrasia, severe hepatic impairment, severe uncontrolled hypertension, repeated falls and recent trauma.

Chronic atrial fibrillation was observed in 386 patients (80%), paroxysmal atrial fibrillation in 75 (15.6%), atrial flutter in 15 (3.2%), and atrial fibrillation pending outpatient cardioversion in 6 patients (1.2%) who were discharged (Figure 3).

An analysis of the 482 patients in the study group revealed that 224 (46.5%) were discharged with oral anticoagulants, specifically Sintrom® (acenocoumarol) and 175 (36.3%) with platelet inhibitors. Once the patients with a contraindication for oral anticoagulation (109; 22.7%) had been excluded from the study, therapy was administered to only 61.7% of the patients. All patients with an artificial valve (5.4%) were discharged with acenocoumarol to maintain an international normalized ratio (INR) between 2.5 and 3.5.

Table 1 shows the results of the univariate analysis. Multivariate analysis identified the following predictive factors for greater probability of anticoagulation: rheumatic mitral valve disease (OR, 16.6 [5.06-54.8];

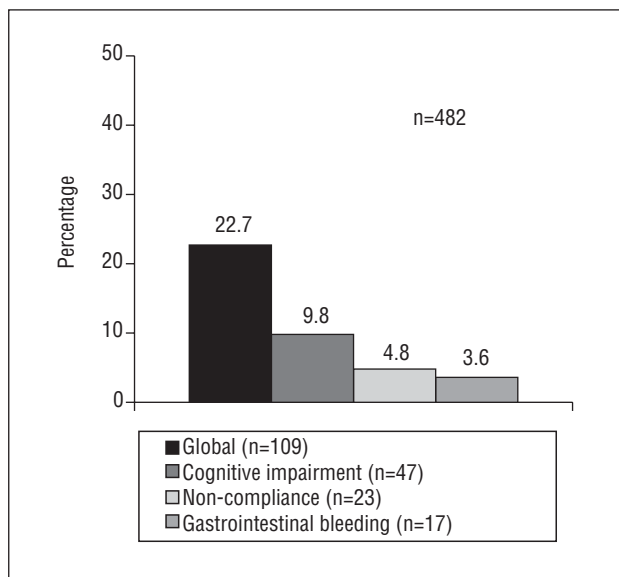


Fig. 2. Contraindications for oral anticoagulant therapy.

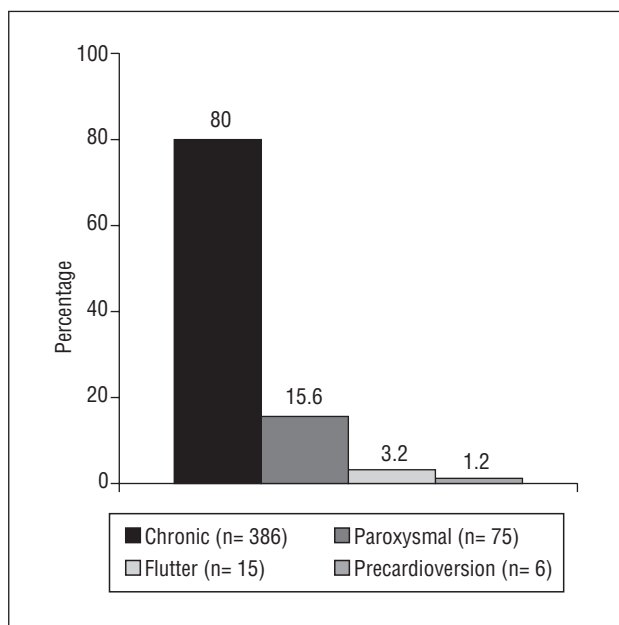


Fig. 3. Type of atrial fibrillation.

$P=.0001$ ), stroke (OR, 1.48 [1.02-2.19];  $P=.04$ ); peripheral embolism (OR, 5.6 [1.6-19.9];  $P=.002$ ), and left atrial enlargement (OR, 2.19 [1.5-3.1];  $P=.0001$ ). Age  $>75$  years was identified as a predictive factor for a lower probability of anticoagulation (OR, 0.32 [0.24-0.43];  $P=.0001$ ) (Table 2). In patients older than 75 years of age with no contraindication (249 patients), only 120 (48%) received treatment with Sintrom<sup>®</sup> at hospital discharge. The difference was statistically significant ( $P=.0001$ ) with respect to the 124 patients over

age  $<75$  years with no contraindication, among whom 78% (97) (Figure 4) received this therapy.

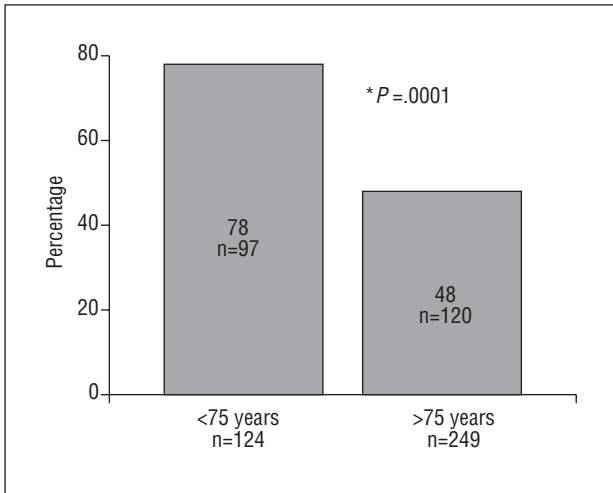
## DISCUSSION

Several studies published in recent years show that appropriate treatment with oral anticoagulants prevents stroke events in patients with atrial fibrillation.<sup>11-18</sup> In various studies, however, the percentage of patients receiving this treatment is very low and highly variable.<sup>2,5-10,19-32</sup> In our study, 61.7% of patients with atrial fibrillation, at least one associated risk factor for thromboembolism and no contraindications for this therapy received treatment with acenocoumarol at discharge. This shows a slight increase in the number of patients who receive the treatment, but also reveals that oral anticoagulants are still underused in these circumstances (Table 3). A recent meta-analysis<sup>5</sup> of patients with atrial fibrillation and no contraindications for warfarin reported that only 15% to 44% received anticoagulant therapy. Obstacles to anticoagulant prescription identified by this review included those related to the patient (refusal of or non-compliance with therapy), physician (improper assessment of the risk of stroke, prescription given by specialist versus general practitioner), and healthcare system (logistic difficulties for performing the analyses or difficulties with the dosing regimen the anticoagulant).

The mean age of patients in our study (79.3 years) was slightly higher than in most other studies and similar to another study conducted in Spain.<sup>6</sup> Advanced age is the single most important factor leading to underuse of oral anticoagulant therapy, a finding also reported in other publications.<sup>2,5-7,21,33</sup> This reduced use of therapy is related to poorer therapeutic compliance and greater potential risk of bleeding, an unsurprising association given the larger number of concomitant diseases in this population. In this regard, the SPAF II

TABLE 1. Oral anticoagulation

	Yes		No		P
	No.	%	No.	%	
Age $>75$ years	120	37	202	63	$<.0001$
Left atrial enlargement	100	59	69	41	$<.0001$
Stroke	72	54	62	46	.05
Depressed systolic function	29	60	19	40	.048
Diabetes mellitus	43	42	59	58	.3
Peripheral embolism	14	82	3	18	.005
Hypertension	100	40	151	60	.001
Heart failure	86	42	119	58	.06
Ischemic heart disease	90	45	108	55	.2
Mitral valve disease	35	92	3	8	$<.0001$
Intracardiac thrombus	3	100	0	0	.1
Artificial valve	26	100	0	0	$<.0001$
Hyperthyroidism	9	39	14	61	.5



**Fig. 4.** Prescription of oral anticoagulants according to age. Patients with no contraindications.

study<sup>14</sup> conducted in patients with non-rheumatic atrial fibrillation and receiving anticoagulation, found that patients over 75 years of age had a significantly higher rate of major bleeding per year than patients under 75 years (4.2% vs 1.7%, respectively). Nevertheless, this age-dependent bleeding complication has been questioned in more recent studies.<sup>34</sup> In our study only 48% of patients over 75 years of age with no contraindication for anticoagulant therapy were discharged on acenocoumarol. This percentage is lower than desired, in view of the fact that patients older than 75 years of age who have atrial fibrillation are precisely those who benefit most from treatment, as the decrease in the risk of stroke is greater<sup>3</sup> despite a higher incidence of bleeding episodes. Unquestionably, closer family supervision, a healthcare system that provides greater social support to these older patients, and resources that promote home-based testing would increase the use of the drug in these patients.

Almost the entire initial population (96.2%) presented with clinical or echocardiographic variables that predicted risk of thromboembolism. This figure is higher than the 70% to 80% reported in some earlier studies.<sup>6,19</sup> Therefore, most patients with atrial fibrillation discharged from our center met the criteria for oral anticoagulation.

An analysis of the literature shows that a number of studies did not assess the contraindications for anticoagulant therapy.<sup>6,8</sup> In these studies, the percentage of oral anticoagulation prescriptions in patients with atrial fibrillation is actually underestimated. In our study, 22.7% of patients had contraindication for coumarol derivatives. The presence or absence of contraindications is a decisive factor when initiating this therapy in actual clinical practice. As in our study, Cohen et al.<sup>20</sup> excluded patients with contraindications

**TABLE 2. Predictive factors of anticoagulation**

	OR	P
Rheumatic mitral valve disease	16.6 (5.06-54.8)	.0001
Stroke	1.48 (1.02-2.19)	.04
Peripheral embolism	5.6 (1.6-19.9)	.002
Left atrial enlargement	2.19 (1.5-3.1)	.0001
Age >75 years	0.32 (0.24-0.43)	.0001

**TABLE 3. Rate of oral anticoagulation in patients with atrial fibrillation**

Author, year and reference	No.	Patients treated with anticoagulation (%)
Weisbord SD, et al, 2001 <sup>30</sup>	1289	65%
Gaughan GL, et al, 2000 <sup>24</sup>	465	45%
Vázquez E, et al, 2000 <sup>6</sup>	302	29%
Falcó V, et al, 2000 <sup>10</sup>	17	39%
Bungard T, et al, 2000 <sup>5</sup>	(91-3575)	15%-44%
Cohen N, et al, 2000 <sup>20</sup>	510	59%
Pérez I, et al, 1999 <sup>25</sup>	11 082	55%
Callejas JL, et al, 1999 <sup>7</sup>	300	36%
Stafford R, et al, 1998 <sup>2</sup>	877	40%
Llop R, et al, 1997 <sup>8</sup>	375	14%

from his analysis. Of the 1027 patients in the initial study population, 14.8% had a high bleeding risk and 30.8% had a physical or mental disability.

In our study, the presence of rheumatic mitral valve disease, stroke, peripheral embolism and left atrial enlargement has been associated with greater use of acenocoumarol at hospital discharge. These findings are similar to those of other published series,<sup>6,8,35,36</sup> possibly because the physician is aware that these associated factors are clearly related to a greater risk of thromboembolic phenomena. Left atrial enlargement as a risk factor is not as well-defined. Although left atrial diameter was an independent predictive value in one study,<sup>37</sup> it was a less powerful predictor for these events in a meta-analysis.<sup>38</sup>

### Limitations of the study

The retrospective design of this study is one of its main limitations. Although the study revealed the actual extent to which oral anticoagulant therapy is used in patients with atrial fibrillation discharged from our center, it did not allow us to properly assess the incidence of contraindications and adverse effects resulting from treatment.

Because the data were obtained by reviewing clinical histories containing the diagnostic code for atrial fibrillation, one limitation may be missing atrial fibrillation cases caused by inaccurate coding, which would bias the estimated percentage of anticoagulation and the relationship with other factors studied here.

Another limitation is that the vast majority of patients were seen at some time by a cardiologist, a procedure that is frequent at our center, but not characteristic of most centers in Spain. As a result, we believe the percentage of patients treated with anticoagulants is slightly higher than in earlier studies because cardiologists are more aware of the benefit of this therapy than other specialists.

## CONCLUSIONS

Oral anticoagulant use at discharge for patients with atrial fibrillation in 2000 at a community hospital is still inadequate, despite the fact that most patients were seen by a cardiologist at some time. Therefore, the results of this study can only be extended to patients with atrial fibrillation treated by these specialists. The percentage of treated patients is, however, slightly higher than in previously published studies.

The presence of rheumatic mitral valve disease, stroke, peripheral embolism and left atrial enlargement is associated with greater use of oral anticoagulant therapy. Age over 75 years is a predictive factor of lower use of anticoagulation.

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