

# Prevalence of oral anticoagulation in atrial fibrillation

Eduardo Bartholomay,<sup>1</sup> Ismael Polli,<sup>1</sup> Anibal Pires Borges,<sup>II</sup> Carlos Kalil,<sup>II</sup> André Arroque,<sup>1</sup> Ilmar Kohler,<sup>1</sup> Luiz Cláudio Danzmann<sup>1</sup>

<sup>1</sup>Universidade Luterana do Brasil, Cardiology, Porto Alegre/RS, Brazil. <sup>II</sup>Hospital São Lucas da Pontifícia Universidade Católica do Rio Grande do Sul, Cardiology, Porto Alegre/RS, Brazil.

**OBJECTIVES:** Atrial fibrillation is the most common sustained arrhythmia and is associated with poor outcomes, including stroke. The ability of anticoagulation therapy to reduce the risk of stroke has been well established; however, the prevalence of anticoagulation therapy use in the Public Health System is unknown. The aim of this study is to evaluate both the prevalence of anticoagulation therapy among patients with atrial fibrillation and the indications for the treatment.

**METHODS:** In this cross-sectional study, we included consecutive patients who had atrial fibrillation documented by an electrocardiogram performed between September 2011 and March 2012 at a university hospital of the Public Health System. The variables analyzed included the risk of a thromboembolic event and/or bleeding, the use of antiplatelet or anticoagulation therapy, the location where the electrocardiogram report was initially reviewed and the specialty of the physician who initially reviewed it.

**RESULTS:** We included 162 patients (mean age 68.9 years, 56% men). Hypertension (90.1%), heart failure (53.4%) and stroke (38.9%) were the most prevalent diseases found. Only 50.6% of the patients knew that they had atrial fibrillation. Regarding the use of therapy, only 37.6% of patients classified as high risk according to the CHADS2 scores and 35.5% according to the CHA2DS2VASc used oral anticoagulation. A presumptive diagnosis of heart failure and the fact that the electrocardiogram was evaluated by a cardiologist were the only independent predictors of the use of anticoagulants.

**CONCLUSIONS:** Our study found a low prevalence of oral anticoagulation therapy among patients with atrial fibrillation and an indication for stroke prophylaxis for the use of this therapy, including among those with high CHADS2 and CHA2DS2VASc scores.

**KEYWORDS:** Atrial Fibrillation; Stroke; Anticoagulation.

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E-mail: eduardo.bartholomay@gmail.com

## INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical medicine, affecting approximately 1.5-2% of the population in developed countries (1-5). In Brazil, it is estimated that approximately 1.5 million individuals have AF and that AF is responsible for 33% of all hospitalizations for arrhythmia. Moreover, AF is associated with the occurrence of stroke and heart failure and with an increase in total mortality (6). Although there has been a decrease in the death rate associated with cerebrovascular disease in Brazil over the past few decades, stroke has persisted as the leading cause of death (7). For the

prevention of stroke, anticoagulant therapy was established as the therapy of choice for the treatment of patients with AF (8-10).

Anticoagulation therapy using vitamin K inhibitors reduces the rate of stroke by 30% in high-risk patients, indicated by CHADS2 or CHA2DS2VASc risk scores  $\geq 2$  (11-12). Recently, new anticoagulants, such as dabigatran, rivaroxaban, apixaban and edoxaban have shown similar or superior results in the prevention of stroke in AF patients compared with warfarin (13-18). The consistent results of anticoagulants have led to the classification of these drugs as indication class I and evidence level A for the prevention of embolic events in AF patients with CHADS2 or CHA2DS2VASc scores  $\geq 2$ , according to major guidelines dedicated to this subject (4,6,14). However, despite recommendations, studies conducted in developed countries have shown that approximately 20-35% of AF patients with a formal indication for anticoagulation do not use this therapy (19-22). In Brazil in particular, so far, there are no data regarding the use of anticoagulants in AF patients in the Public Health System. Due to the high morbidity and

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mortality associated with stroke, it is crucial to determine the actual use of appropriate prophylactic therapy in this patient population.

The main objective of our study was to evaluate the prevalence of the use of anticoagulants among AF patients who had a formal indication for stroke prophylaxis.

## MATERIALS AND METHODS

### Population

The sample studied was provided by the University Hospital ULBRA/Hospital Mãe de Deus (HU-HMD) in Canoas, a city of 323,827 inhabitants located in the metropolitan region of Porto Alegre, Rio Grande do Sul, Brazil. The HU-HMD is a tertiary care institution responsible for servicing the entire municipality and for reviewing electrocardiograms (ECGs) from Basic Healthcare System units.

All ECG reports interpreted at the HU-HMD between September 1, 2011 and March 31, 2012, were initially analyzed. These reports were obtained from the computerized system of the institution. We included consecutive patients whose ECGs showed AF. These patients were identified using hospital registration forms and then contacted by telephone. Those who agreed to participate, completed a questionnaire about their medical condition. These data were used to classify the patients according to thromboembolic events (CHADS2 and CHA2DS2VASc) and bleeding (HAS-BLED) (23) risk scores, the site of care and the use of medications.

We excluded those individuals who did not respond to three calls at different times, those who refused to participate, those who did not clearly answer the questions and those who had died.

The study was approved by the Ethics Committee of the Lutheran University of Brazil and met the provisions of Resolution 196 of the National Health Council.

### Variables

Patients with CHADS2 or CHA2DS2VASc risk scores  $\geq 2$  were considered to have a formal indication for anticoagulant therapy in the absence of contraindications, such as a history of bleeding, blood dyscrasias or an allergy to anticoagulants. Patients with a HAS-BLED risk score  $\geq 3$  were considered to be at high risk for bleeding during anticoagulant therapy.

The specialty of the physician who requested and evaluated the ECG and the location where the patient performed clinical follow-up were determined.

### Statistical analysis

Continuous variables are expressed as the mean and standard deviation and Student's t-test was used to assess differences. Categorical variables are reported as percentages and the differences between these variables were evaluated by a chi-square or Fisher's exact test, when appropriate. The outcome-associated variables with a  $p$ -value  $< 0.10$  or with clinical relevance were selected for multivariate analysis. Logistic regression was then performed to identify independent determinants of outcomes. A  $p$ -value  $< 0.05$  was considered statistically significant. The results are expressed as odds ratios and 95% confidence intervals (CIs).

The analysis was performed with the Statistical Package for Social Sciences (SPSS), version 20.0.

## RESULTS

### Population characteristics

During the study period, 6,162 ECGs were interpreted, 295 of them (4.78%) showed AF. These ECGs belonged to 242 patients. Of the total sample, 52 patients (21.4%) could not be found, 23 (9.5%) had died and 5 (2.06%) refused to participate. Thus, 162 patients, representing 67.5% of the initial sample, were ultimately included.

The evaluated patients were predominantly hypertensive men aged  $> 65$  years. Nearly half of the patients already knew that they had arrhythmia. The main characteristics of the sample are described in Table 1.

### Therapy and the risk of bleeding and thromboembolic events

Table 2 illustrates the distribution of patients according to risk scores. An analysis of CHADS2 and CHA2DS2VASc scores showed that 87% and 95.7%, respectively, of patients had scores  $\geq 2$  points.

Only 37.6% of patients with a CHADS2 score  $\geq 2$  used anticoagulants. When stratified according to CHADS2 score, approximately half of the patients with a CHADS2 score of 3 or 4 used anticoagulants, whereas only 15% of patients with a CHADS2 score  $> 5$  used this therapy (Figure 1).

When the CHA2DS2VASc scores were analyzed, we observed similar results; of the patients with a CHA2DS2VASc

Table 1 - Baseline characteristics.

Characteristic	n = 162
Age (years)	68.94 $\pm$ 12
Gender (male)	92 (56.8)
Comorbidities	
Hypertension	146 (90.1)
DM	44 (27.2)
CHF	88 (54.3)
Stroke	63 (38.9)
ACS	31 (19.1)
Alcohol use	12 (7.4)
Extracardiac vasculopathy	58 (35.8)
Renal disease	4 (2.5)
Liver disease	3 (1.9)
Known to have arrhythmia	82 (50.6)
Medications	
ASA	80 (49.4)
Oral anticoagulant	55 (34)
First location where the ECG was reviewed	
Basic unit	57 (35.2)
Secondary hospital	9 (5.6)
Tertiary hospital	51 (31.5)
Private clinic	5 (3.1)
Emergency department	17 (10.5)
Outpatient clinic	20 (12.3)
ECG was not checked	3 (1.9)
First doctor who reviewed the ECG	
Generalist	56 (34.6)
Family physician	36 (22.2)
Cardiologist	40 (24.7)
Surgeon	5 (3.1)
Emergency physician	13 (8.0)
Neurologist	4 (2.5)
Other	5 (3.1)
ECG checked by a cardiologist at any time	84 (51.9)

The data are presented as the median  $\pm$  standard deviation or n (%). DM: diabetes mellitus; CHF: chronic heart failure; ACS: acute coronary syndrome; ASA: acetylsalicylic acid; ECG: electrocardiogram.



**Table 2** - Distribution of patients according to their CHADS2, CHA2DS2VASc and HAS-BLED scores.

Score	Score of risk (n (%))		
	CHADS2	CHA2DS2VASc	HAS-BLED
0	8 (4.9)	2 (1.2)	7 (4.3)
1	13 (8.0)	5 (3.1)	48 (29.6)
2	50 (30.9)	12 (7.4)	73 (45.1)
3	39 (24.1)	40 (24.7)	31 (19.1)
4	29 (17.9)	24 (14.8)	3 (1.9)
5	15 (9.3)	33 (20.4)	0 (0.0)
6	8 (4.9)	25 (15.4)	0 (0.0)
7	-	15 (9.3)	
8	-	6 (3.7)	

score  $\geq 2$ , only 35.5% had been adequately treated with anticoagulants (Figure 2).

When we compared the two score types, we realized that the CHA2DS2VASc score identified 3% of the patients as belonging to the high-risk group, which would be classified as moderate risk according to the CHADS2 score.

Regarding the use of antiplatelet agents, we observed that 25% of patients with a CHADS2 score of 0 and 61.5% of patients with a score of 1 used this medication. However, none of the patients with a CHA2DS2VASc score of 0 or 1 used antiplatelet therapy.

According to the HAS-BLED score, 34 patients (20.9%) had a score  $\geq 3$ , which suggested an increase in bleeding risk with the use of oral anticoagulants. Of these patients, 12 (35%) used anticoagulant therapy.

**Therapy recommendations based on the specialty of the attending physician**

Regarding the specialty of the physician who initially reviewed the ECG revealing the patient’s AF diagnosis, we

noticed large variation in the percentage of patients with a CHA2DS2VASc score  $\geq 2$  who were not using anticoagulant therapy, ranging from 20.6% among those whose ECGs were observed by cardiologists to 100% among those whose ECGs were observed by surgeons or neurologists ( $p < 0.01$ ) (Figure 3).

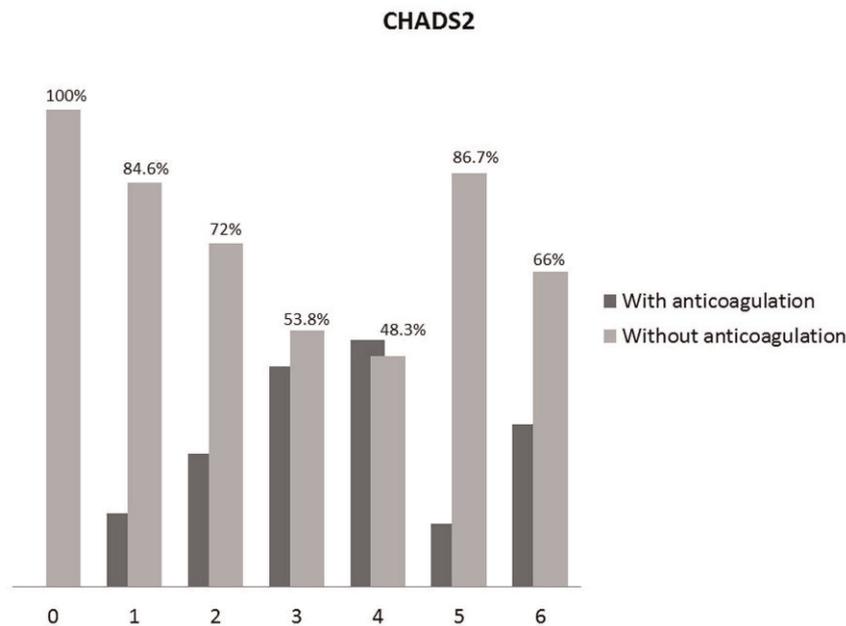
The location of the ECG review also showed large variation based on the use of anticoagulants ( $p < 0.01$ ) (Figure 4).

When we analyzed only patients with a history of previous ischemic stroke, we found that only 36.5% chronically used oral anticoagulants.

Heart failure, hypertension, advanced age, diabetes and prior stroke (CHADS2 factors), as well as the specialty of the doctor who initially reviewed the ECG and the location where the ECG was first reviewed, were used as variables in a multivariate analysis. In this analysis, heart failure (OR: 3.07, 95% CI: 1.35-7.00) and the fact the ECG was first reviewed by a cardiologist *versus* a non-cardiologist (OR: 12.14; 95% CI: 4.85-30.37) were independent predictors of anticoagulation.

**DISCUSSION**

Our study has shown a low prevalence of oral anticoagulation among patients with AF and an indication for the use of this therapy based on risk scores. An Italian study published in 2000 reported that anticoagulation rates were approximately 70% for moderate-risk patients and greater than 85% for high-risk patients (21). However, a study published in 2002 showed rates closer to 60% for therapy use in the U.S. population (22). The present study has revealed that only 35% of our patients were on anticoagulants, which is a much lower prevalence than values already reported for other countries. Furthermore, our findings highlight the low prevalence (36.5%) of anticoagulant use even in patients with a history of ischemic stroke.



**Figure 1** - Prevalence of the use of oral anticoagulants according to the CHADS2 score.



CHA2DS2VASc

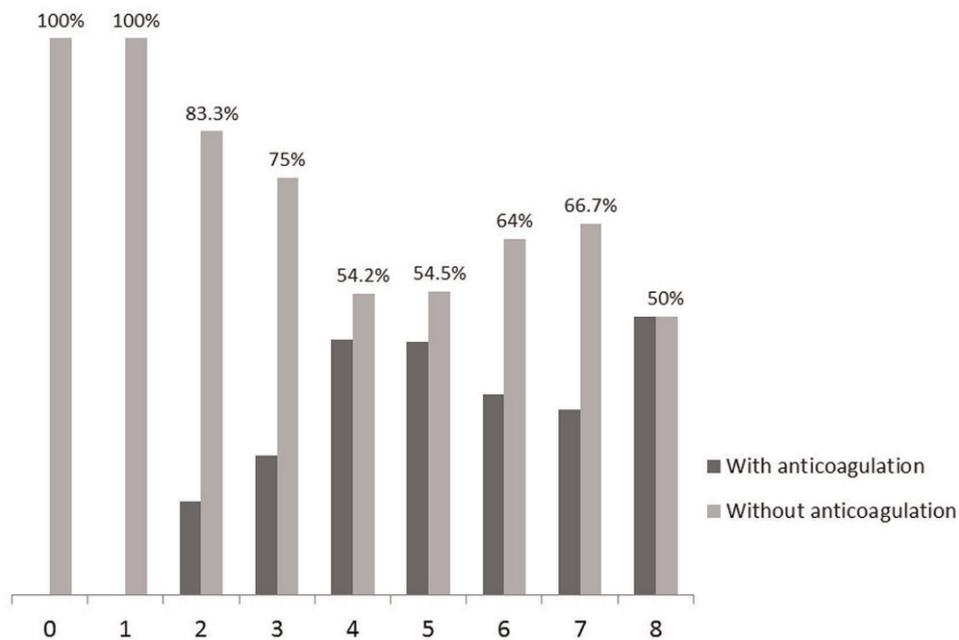


Figure 2 - Prevalence of the use of oral anticoagulants according to the CHA2DS2VASc score.

The risk scores used in our study have been widely studied and validated and are directly related to the occurrence of thromboembolic events. The CHADS2 score determines a cumulative risk of stroke of less than 2% per year for patients with a score of 0, of 4% per year for patients with a score of 2 and of up to 18.2% per year for patients with a score of 6 (11). The CHA2DS2VASc score, which was recently incorporated into standard guidelines to more accurately identify patients at moderate risk who would most benefit from the use of anticoagulants, directly correlates with the same outcomes. Additionally, the stroke rate per year varies: 0% for those with a score of 0, 2.2% for those with a score of 2, and 15.2% for those with a score of 9 (12).

The prevalence of AF in our study population was higher than that found in other population-based studies. Whereas the Anticoagulation and Risk Factors In Atrial Fibrillation (ATRIA) study (24) showed a prevalence of 0.95% in the general population and whereas other studies showed values up to 1.49%, our data revealed a 4.78% prevalence, possibly because our patients were selected solely based on the indication for performing an ECG.

Regarding AF prevalence by sex and age our data are similar to data found in the literature, with higher rates in men of all age groups and with a gradual and proportional increase with the aging of the population.

It is estimated that AF patients over 60 years old with no structural heart disease present a cumulative risk of stroke

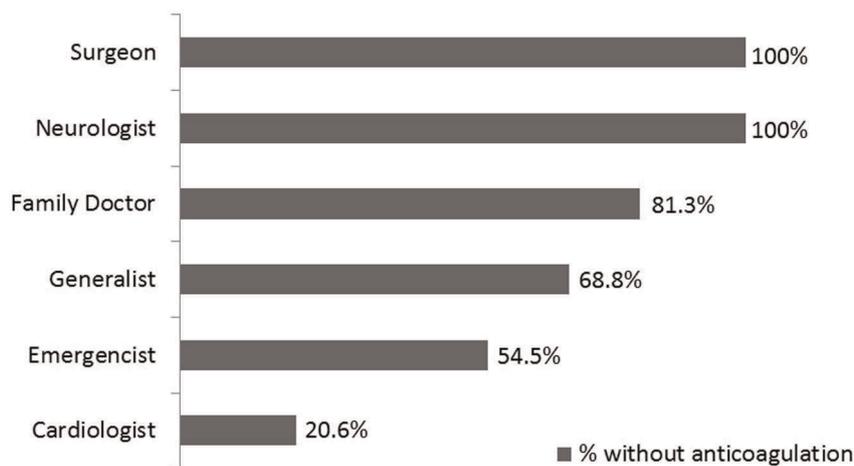
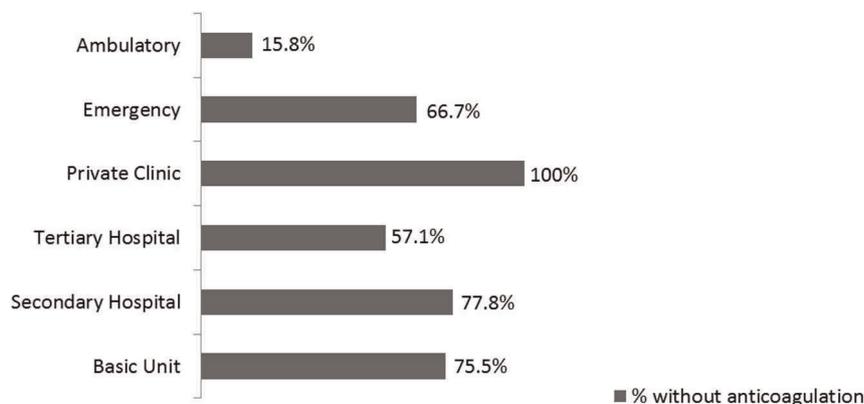


Figure 3 - Percentage of patients without anticoagulation therapy according to the specialty of the doctor who treated them.



**Figure 4** - Percentage of patients without anticoagulation therapy according to the location where the ECG was reviewed.

of 1.3% per year (6,25). This rate can be significantly reduced with the proper use of anticoagulant therapy (26,27). In fact, several studies published in recent decades have shown the benefits of anticoagulation in patients with AF, with even better results than those of antiplatelet agents (1-3). Based on current guidelines, the non-indication of anticoagulants in patients with AF and a high risk of thromboembolic events can only be justified by a high risk of bleeding. However, we found no relationship between HAS-BLED bleeding scores and misuse of anticoagulants in our entire study population.

In our study, the location where the patient was monitored seemed to be directly related to misuse of oral anticoagulants, with very low use in basic health units and in private clinics. In contrast, patients in outpatient clinics at a tertiary hospital (HU-HMD) showed a higher prevalence of anticoagulation use when indicated. Another relevant factor was the specialty of the attending physician, with frequent prescription by cardiologists and very infrequent or absent prescription by other specialties.

The most likely explanation for this difference in anticoagulant use based on the location of monitoring may be the difficulty of returning to the same health unit for a dose adjustment of vitamin K inhibitors according to the patient's prothrombin time, causing the doctor to choose not to prescribe anticoagulation therapy. This is especially an issue for elderly patients, who often present with other comorbidities, including a higher risk of falls (28), and reach optimal anticoagulation levels at lower doses of vitamin K inhibitors (29). Therefore, their care is more limited, which may contribute to their doctors not prescribing treatments that they cannot properly monitor.

The use of new anticoagulants that do not require monitoring may help to improve this scenario; however, these drugs are not yet available to the Public Health System. Another potentially much more important factor may be the unawareness of doctors about the importance of this therapeutic intervention to prevent the mortality and morbidity associated with stroke in AF patients.

## ■ STUDY LIMITATIONS

Our study has important limitations. For example, the prevalence of AF in the selected population may have been underestimated because the diagnosis was made based on an

ECG and not based on continuous monitoring (such as via a Holter monitor or loop recorder). Additionally, there were no data on patients with paroxysmal AF who presented with sinus rhythm on the ECG, for example. In particular, our population was selected because the patients were participating in the Public Health System. We believe that our data suggested a high prevalence of AF, chronic heart failure and stroke, among other conditions, compared with the prevalence in other populations because when the patients sought medical attention, they may have already been carriers of certain changes that could motivate an ECG request.

The data obtained in this study may not represent the whole of Brazil because the sample was limited to one hospital and one municipality, although it is important to note that the HU-HMD provides care to various levels of the Public Health System. However, our analysis may have incurred a measurement bias because the data were collected by telephone. In addition, we have no data regarding poor adherence. Thus, although anticoagulant therapy was prescribed, certain patients may not have used it. Considering the HAS-BLED score, it will be important to evaluate the use of anticoagulant therapy in patients with a high risk of bleeding, not only in the entire population but also in groups stratified by the specialty of the physician and the location where the ECG was first reviewed, given that the present analysis was hampered by the small number of patients within the groups.

Considering that AF is the most prevalent arrhythmia and given the high morbidity and mortality associated with stroke, it is possible that misuse of anticoagulants in this population is a major public health problem associated with the treatment of cardiac arrhythmias.

Our study found a low prevalence of oral anticoagulation therapy among patients with AF and an indication for stroke prophylaxis for the use of this therapy, including among those with high CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>VASc scores.

## ■ AUTHORS CONTRIBUTIONS

Bartholomay E, Polli I, Borges AP, Kalil C, Arroque A, Kohler I, Danzmann LC conceived and designed the study and were responsible for data acquisition, analysis and interpretation, drafting and critical review of the manuscript.



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