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Original article

Prevalence of atrial fibrillation and stroke risk assessment based on telemedicine screening tools in a primary healthcare setting☆

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ABSTRACT

Background: Worldwide atrial fibrillation (AF) prevalence varies between 0.1% and 4.0%, and has been increasing. Little is known about the prevalence of AF in Brazil. Our objective was to estimate the prevalence of AF in several regions of Brazil using recordings of long-distance electrocardiogram (ECG) transmission.

Methods: Patients from 125 outpatient general practitioner units covered by the telemedicine service of the Federal University of São Paulo were included. Only one ECG was considered per patient. A scripted telephone interview was also performed. We analyzed the data to project the prevalence of AF in the Brazilian population and estimate it for the year 2025. The overall AF prevalence was calculated based on ECGs from primary care units where patients went for routine visits.

Results: Based on 676,621 ECG exams from January 2009 through April 2016, the mean age (±SD) of patients was 51.38 (±19.05) years, with 57.5% being female. The 7-year period prevalence of AF was 2.2% (n = 14,968). The prevalence of AF countrywide was projected to be 1.5% in 2016 and 1.7% in 2025. In the subset of patients with AF who were interviewed (n = 301), 91 (30.2%) were not receiving any type of treatment for rate or rhythm control. Among patients interviewed, 189 (62.8%) were at high risk for stroke; only 28 (14.8%) were regular oral anticoagulant users.

Conclusions: Our study highlights the importance of screening for AF in the primary care setting in Brazil and identifies important gaps in the treatment of AF in this population.

1. Introduction

Atrial fibrillation (AF) and its complications are a public healthcare problem worldwide. The global prevalence of AF in the adult population varies between 0.1% and 4.0%, and has been increasing in recent decades, especially in the elderly [1–4]. In Brazil, the estimated prevalence of AF in people over 40 years of age was 1.4% in 2010 [5].

Risk stratification for prevention of thromboembolism is still underused [6]. Telemedicine tools can improve AF screening and diagnosis by early electrocardiogram (ECG) detection and can be used to estimate the risk of thromboembolism. Data suggest that both rhythm and rate control strategies are associated with similar rates of morbidity and mortality, including the risk of thromboembolic events. However, there are several scenarios in which the rhythm control strategy would be preferred, including symptomatic younger patients and/or those without structural and electrical remodeling [7–10]. Oral anticoagulants are underused worldwide, including in Brazil, where direct oral anticoagulants (OACs) are still expensive and are not offered to the country's population by the public healthcare system.

Our aim was to estimate current prevalence of AF in Brazilian outpatient general practitioner units and to project prevalence for the year 2025. We also sought to assess the risk of thromboembolism and the use of antiarrhythmics and OACs.

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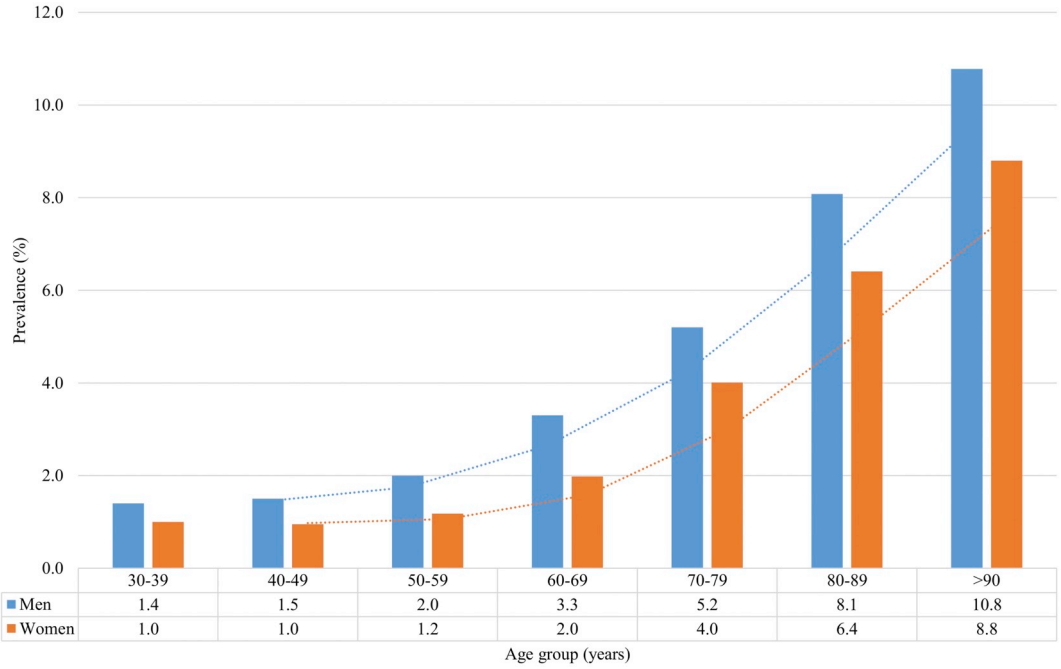

Fig. 1. Prevalence of atrial fibrillation by sex and age group.

2. Methods

2.1. Study design

This observational cross-sectional study was carried out in two phases by the telemedicine service of the Federal University of São Paulo (UNIFESP), which covers 125 outpatient general practitioner units from 9 states in four of the five geographic regions of Brazil (i.e., Southwest, comprising the states of São Paulo and Rio de Janeiro; Midwest, comprising Goiás, Mato Grosso, Federal District, and Mato Grosso do Sul; South, comprising Paraná and Rio Grande do Sul; and North, comprising Tocantins; see Supplementary Table 1). All patients included in the study received care by the Brazilian Public Healthcare System, which treats about 70% of the Brazilian population [11]. The study was assessed and approved by the local ethics committee. Informed consent was obtained for all interviewed patients.

In Phase A, our team of cardiologists analyzed ECG exams from an extensive database. We included all patients registered in the system with at least one valid ECG performed between January 2009 and April 2016, regardless of gender, age, symptom, or clinical conditions. We considered only the first ECG for each individual patient. ECG exams with technical problems, such as incomplete registration and those reported with artifacts or inverted cables, were excluded. Exams performed at ambulances and duplicates were excluded as well. With the data obtained on the prevalence of AF, the Brazilian Institute of Geography and Statistics (IBGE) method was used to project the prevalence of AF for the year 2025 in the Brazilian population. The IBGE method is based on observed trends for mortality, fertility, and migration over time [12]. The overall AF prevalence was calculated based on ECGs from primary care units where patients went for routine visits. The IBGE method was based on general population of the country.

Phase B was performed between February 2012 and January 2013. Using a nonprobabilistic sequential sample of Phase A, a random group of patients, selected for convenience, were interviewed via telephone using a closed-ended and structured questionnaire. The confirmatory diagnosis of AF on the ECG was performed by two independent electrophysiologists. We excluded patients with incomplete registration details and clinical data, and those who were difficult to contact, who refused to participate in the study, or who had died by the time the questionnaire was carried out. For reasons of scheduling and cost, we aimed to call 1000 patients. We estimated the risk of thromboembolism from the sample using variables already validated in classic risk scores, such as the $CHADS_2$ (congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke [double weight]) score [13–15]. Individuals aged >75 years, with history of hypertension or diabetes mellitus and/or those who had a history of stroke, were classified and scored. One point was given for each of the variables above, except for history of stroke, which was given two points. Data on the presence of heart failure were not reliably assessed over the telephone interview, so we decided to use a similar risk score to the $CHADS_2$ score, but without heart failure. All patients with two or more points were categorized as presumably at high risk.

2.2. Statistical analysis

The results of quantitative variables were expressed as mean (± SD) and categorical variables in absolute and percentage frequencies. Associations between numerical variables were determined by the Student *t*-test, according to data characteristics. Categorical variables were compared using Pearson's chi-square test. For variables related to the disease under study, a simple regression was used, according to population data, and a significance level of 5% was adopted. For the ECGs, EPACS Cardio® software was used, and statistical analyses were performed with Knime® version 3.0 and Dell Statistica® version 12.

There was no external funding for this UNIFESP study.

3. Results

3.1. Phase A

A total of 851,821 ECGs were performed between January 2009 and April 2016. Of these, 94,106 (11.0%) were excluded for being duplicate exams, 72,675 (8.5%) were excluded due to technical problems, and 8419 (1.0%) were excluded because they were performed in an ambulance. A total of 676,621 ECG exams were included and analyzed (Supplementary Fig. 1). The mean patient age was 51.38 (±19.05) years, with 389,187 (57.5%) patients being female.

The 7-year period prevalence of AF was 2.2% (14,968 of the

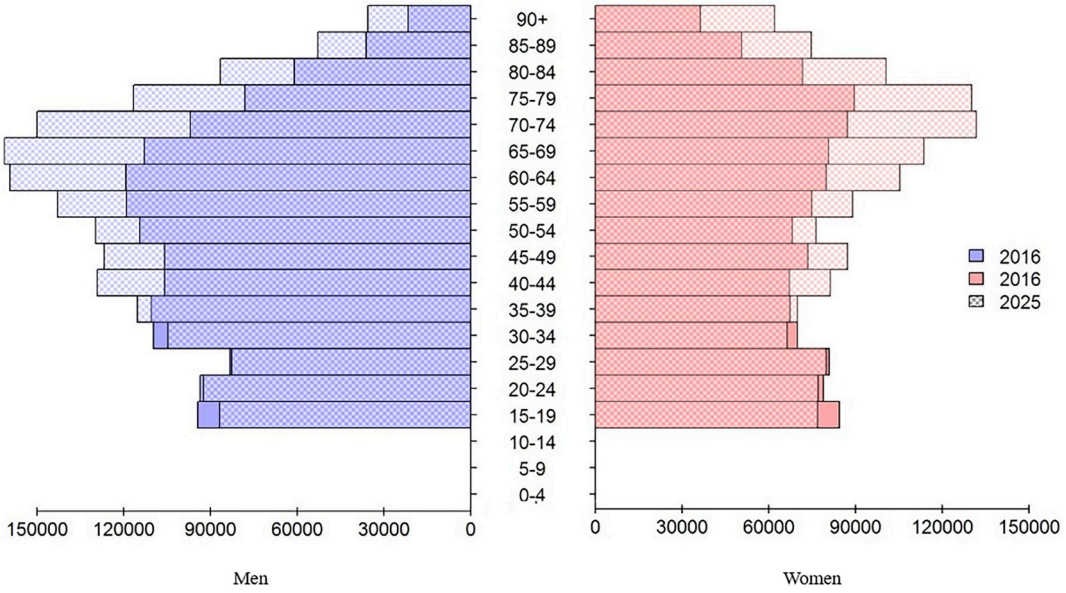

Fig. 2. Projected prevalence of atrial fibrillation in the Brazilian population in 2016 and 2025, by sex and age.

676,621 patients), with 7605 (50.8%) being male. Prevalence of AF increased with age, notably ≥70 years (Fig. 1). In all age groups ≥30 years, the disease was more prevalent among men ($p < .001$). In a comparison between the sample of patients with AF and without the disease, it was found that the mean age was 64.13 (±18.54) years in patients with AF and 51.09 (±18.98) years in those without AF ($p \leq .0001$). Additionally, male sex was more prevalent in those with AF than those without AF (50.84% vs 42.29%; $p \leq .0001$). Patients with AF had a mean heart rate of 102.40 (±34.01) beats/min, whereas mean heart rate was 73.72 (±16.53) beats/min in the group without AF ($p \leq .0001$).

Using the prevalence data obtained previously and the projections done according to IBGE [12], we estimated the current prevalence of AF in the adult Brazilian population (above 15 years of age) as 1.5%, or 2,421,688 of 159,321,555 people. We extrapolated the prevalence for the year 2025 as 1.7% (2,951,527 of 176,738,146 people). Maintaining future expectations on a constant basis, this would represent an increase in the prevalence of approximately 0.2% (500,000 new cases) over the next 10 years (Fig. 2).

3.2. Phase B

3.2.1. Interview respondents

At the beginning of Phase B, in February 2012, there were 4917 ECGs reported as AF in the database. Of these, 1196 (24.3%) exams were excluded because they had incomplete registration details and clinical data. For the remaining 3721 patients, we used non-probabilistic sequential sampling to create a random list of those with registered telephone numbers, to be called between February 2012 and January 2013. After making calls to 1080 patients, 336 (31.1%) contacts were successfully made. Of these, 32 (9.5%) patients had died and 3 (0.9%) patients refused to answer, and so Phase B was completed with 301 questionnaires. The mean duration of each interview was 90 s. The majority (165, 54.8%) of Phase B responders were female, with a mean age of 70.26 (±12.29) years. Of the 301 patients, 3 (1%) did not remember the date they went to the health unit and underwent an ECG. Of the 298 individuals who remembered the date of their ECG, 160 (53.7%) reported already having a diagnosis of AF at the time and 103 (34.6%) stated that AF was diagnosed on that day. Of the 263 respondents who were told or already knew about having AF, 233 (88.3%) stated that they were on treatment or were being referred for treatment, and 23 (9.9%) were still awaiting their first consultation with a cardiologist. The other 31 (11.7%) patients reported not having been referred for treatment and therefore were not being treated.

3.2.2. Hospitalizations and comorbidities

At the interview, 112 (37.6%) of the 298 patients who were contacted responded that they had already been hospitalized because of AF. A total of 28 (9.4%) reported having received at least one electrical cardioversion. Three (1%) patients knew of the possibility of radiofrequency ablation, but none had undergone it. Regarding associated diseases and symptoms, 252 (83.7%) reported having hypertension, 105 (34.9%) were diabetic, and 71 (23.6%) had a previous stroke or transient ischemic attack. Also, 39 (13%) patients reported previous syncope, and 2 (0.7%) had pacemakers.

3.2.3. Anti-arrhythmic or rate control treatments

Among the 301 respondents, a total of 91 (30.2%) patients were not treated. Of the remaining 210 patients on treatment, 147 (70%) used rate control agents (beta-blockers, digoxin, diltiazem or verapamil) and 25 (11.9%) used at least one antiarrhythmic drug (amiodarone or propafenone). The simultaneous use of antiarrhythmic drugs and beta-blockers was reported by 36 (17.1%) respondents. No patient reported the use of sotalol. A total of 36 (17.1%) individuals did not remember the medications in use, and 38 (18.1%) did not report use of any of these medications at that time (Fig. 3).

3.2.4. Treatments for stroke prevention

Regarding stroke prevention with the use of antiplatelet drugs or OACs, 136 (64.8%) of the patients being treated were using acetylsalicylic acid (ASA) alone, and 39 (18.6%) were using warfarin or phenprocoumon alone. In addition, 7 (3.3%) patients reported simultaneous use of ASA and OACs. Previous use of ASA with recent withdrawal due to adverse reaction was reported in 3 (1.4%) of the respondents, and previous use of OACs with recent withdrawal due to adverse reactions was reported in 5 (2.4%) patients. However, drug suspension due to bleeding was not reported by any of those who used ASA, and by just 3 (1.4%) patients using OACs. No patient reported the use of direct OACs, although dabigatran, apixaban, and rivaroxaban were available in Brazil. For the 46 (21.9%) respondents who reported using OACs, 38 (82.6%) individuals reported adequate and regular control of international normalized ratio.

Risk assessment of the 301 participants from the questionnaire found 189 (62.8%) patients at presumed high risk (Supplementary

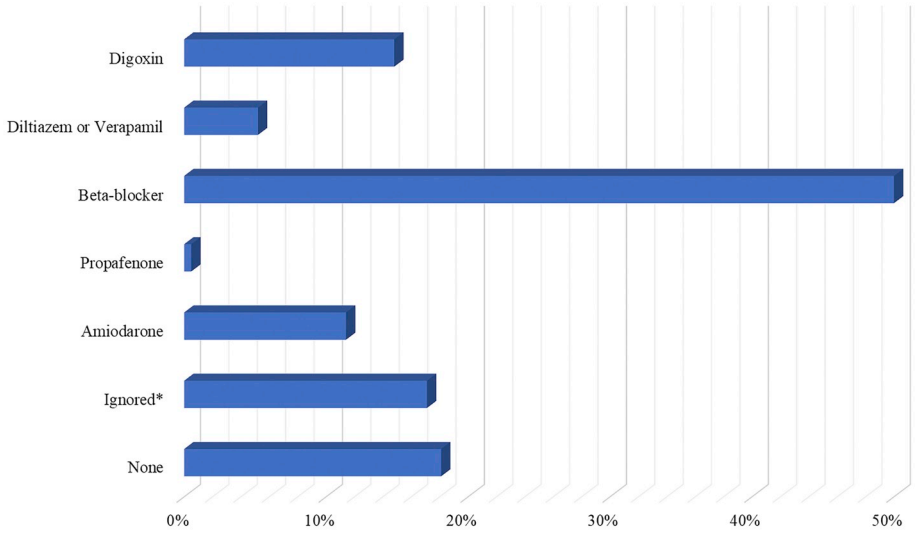

Fig. 3. Distribution of treatment by drug.
*Ignored = Could not remember.

Table 1
Distribution of acetylsalicylic acid and/or oral anticoagulant use for the estimated risk of thromboembolism.

Medication	Total (n, %)	Low Risk (n, %)	High Risk (n, %)
None[a]	119 (39.5)	55 (18.3)	64 (21.3)
ASA	136 (45.2)	39 (13.0)	97 (32.2)
OAC	39 (13.0)	16 (5.3)	23 (7.6)
ASA + OAC	7 (2.3)	2 (0.7)	5 (1.7)
Total	301 (100)	112 (37.2)	189 (62.8)

ASA, acetylsalicylic acid; OAC, oral anticoagulant.
[a] Patients who did not report the use of ASA, OAC or did not answer.

Table 2). For those with prior stroke, the mean risk score was 4. The number of high-risk patients taking OACs with or without ASA was 28 (9.3%) (Table 1).

4. Discussion

The prevalence of AF in the present study (2.2%) is consistent with the current literature. This is the first study to use a large amount of data from general practitioner units in more than one geographic region of Brazil. Although the prevalence we found was in line with that of other regions worldwide, we still need to know more about the prevalence of AF in this heterogeneous population. The prevalence of AF varies according to geographic regions, with studies showing rates of 0.2% in China [16], 3.0% in Israel [17], 4.4% in Spain [18], and 1.7% in the United States [19]. In our population, AF was more prevalent in men of all age groups and increased with age, which was consistent with other Brazilian studies [4,20,21]. The prevalence of AF in our study was likely underestimated because we used a single ECG per patient and because of the potential paroxysmal nature of the disease. We observed a technical problem rate of 10.6%, which reflects the lack of training of health professionals in the acquisition of ECGs, as was seen in another study with a similar population [21]. Regarding the projected prevalence of AF for 2025, a recent German study using a similar methodology showed a 0.5% increase in the prevalence of AF in 12 years (from 2009 to 2020), compared to the 0.2% increase over 10 years (from 2016 to 2025) projected in our study. One potential reason for this is that, unlike Brazil whose population is aging, Germany projects a decrease in the general population and minimal changes between the age groups over time [22].

Another interesting aspect of our study was that a third of the interview respondents discovered AF at the time of taking the ECG. A Spanish study with an adult population who underwent ECGs showed that 20.1% of patients with AF had not been previously diagnosed [23]. These data show the relevance of using ECGs as a tool for screening and diagnosing AF and other rhythm disturbances, as has already been shown in several studies, including in Brazil [24,25].

ECGs are cheap and easy to perform, and must be used early in all medical settings where arrhythmia is suspected, increasing the chance of an earlier diagnosis of AF. There are several screening tools available for AF; however, less is known about what to do with the results. Current European guidelines recommend opportunistic pulse-taking in all patients ≥65 years of age or in high-risk subgroups, and an ECG is always required to confirm AF diagnosis. A consensus document from major rhythm societies suggests that screening programs for AF can be beneficial if high positive predictive values are achieved at low cost using non-invasive tools. More data demonstrating that screening for AF improves clinical outcomes and is cost-effective are needed before it can be applied routinely in clinical practice [26,27].

Data collected continuously by telemedicine can generate a statistic of how many patients have been diagnosed and how the disease is being managed from its diagnosis. Our results also suggest that the establishment of adequate treatment for AF has been insufficient and inefficient in Brazil. Of those who already knew about the disease or who were diagnosed at that time, 8.7% had not had an appointment with a specialist and 11.7% said they were not even referred for treatment. Since health systems are very different across countries, there were no comparable data available to us on waiting time and referrals from other studies.

Clinical characteristics of the patients with AF who were interviewed are comparable to the results of population studies and multinational registries recently published [6,28,29]. However, the mean age in the present study is relatively lower than that of the other studies, which can be attributed to the Brazilian population having a life expectancy lower than that of other developed countries. The first Brazilian nationwide clinical registry of AF is ongoing [30].

In addition, there was a larger prevalence of diabetes and prior stroke in the present study compared to the registries. The Global Anticoagulant Registry in the Field (GARFIELD) showed interesting regional differences among patients from Asia, Europe, Latin America, North America, and other regions. When only Latin American patients in GARFIELD (n = 2503) are compared to ours, clinical characteristics are similar (Supplementary Table 3) [28].

Regarding treatments, only 8.4% of the subjects were on

amiodarone or propafenone, 9.4% had already received cardioversion, and no patient had undergone ablation in our study. A recent European registry reported higher rates of rhythm control, with 47.3% of patients receiving anti-arrhythmic drugs, 18.1% receiving electric cardioversion in the last 12 months, and 5% having undergone ablation [31]. In our study, 70% of the respondents on treatment were using rate control drugs (50% beta-blockers, 14.8% digoxin, and 5.2% diltiazem or verapamil).

The American Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) showed that 32% of patients with AF were on rhythm control strategies and 68% of them were on rate control agents (64% beta-blockers, 23% digoxin, and 17% diltiazem and verapamil) [32]. Thus, a longitudinal study with a larger number of participants is needed in this population to clarify the reasons for these findings and to propose measures to encourage the use of such strategies, especially non-drug related strategies. We believe that, in Brazil, general practitioners generally have little access and experience in conducting non-pharmacological strategies.

In relation to stroke prevention, our data showed an underuse of OACs, with only 21.9% of respondents on treatment confirmed using these agents. Despite methodological and regional differences, the findings of recently published registries corroborate this alarming finding, estimating the use of anticoagulants at around 30% on average [17,27,32–34]. The use of antiplatelet agents such as aspirin was frequent in our study, and the exact reason for its use is unknown. In our study, we showed that 68.1% of patients still used ASA alone and 3.3% used ASA and OACs simultaneously. These data differed from recently published registries, such as GARFIELD, which revealed the use of OACs by 45.2% of the participants, practically twice as much as in the present study. The use of ASA was found in 25.3% of the total, less than half the percentage reported in our study. Even when accessing risk, only 14.8% of the high-risk patients were using anticoagulants. These findings are a major concern since aspirin is not recommended for stroke prevention in patients with AF [26,35]. A subanalysis of the ARISTOTLE trial showed that 31% of participants were using ASA on randomization, and aspirin users had similar rates of stroke or systemic embolism, ischemic stroke, myocardial infarction, and death and higher rates of bleeding when compared with non-users [36].

In GARFIELD, for example, the number of patients with $CHADS_2 > 2$ on OACs was 72.2%. These findings illustrate important gaps in the care of patients with AF in Brazil that need to be addressed. Results from the IMProve treatment with AntiCoagulanTs in patients with Atrial Fibrillation (IMPACT-AF) trial, including Brazilian centers, showed an absolute difference in the change of oral anticoagulation use of 9.1% (95% CI 3.8–14.4), representing the proportional increase in anticoagulation use from baseline to 1 year in the intervention group (multifaceted educational program) compared with the control group [37]. Additional research is needed into the causes of underutilization of OACs in the Brazilian population. Some possible explanations for this lower use of OACs are the low income of the population, lack of information, fear (unwarranted generally) of the risk of bleeding, and the uneven distribution and routine use of OACs by public healthcare services [38,39]. Other known explanations are previous hemorrhage, the risk of falls, patient refusal, cognitive deficit, alcohol abuse, and the presence of severe and advanced disease [40]. Thus, regional implementation of quality improvement strategies like the one used in the IMPACT-AF study is urgently needed.

4.1. Limitations

Our findings should be interpreted in light of some limitations. The patients' answers in the questionnaire were voluntary and therefore susceptible to the limitations of the method. No stratification or comparison was made per service unit or geographic region because previous data showed similar findings among our different care units [41]. A diagnostic checking of the ECG traces reported as AF was only performed for the patients interviewed because the sample was very large and it would not be cost effective to evaluate all ECG traces. It was not possible to classify AF as paroxysmal, persistent, or permanent, as the ECG data were assessed only once. The medical reason why the ECGs were performed was not collected, and it is possible that some patients might have had symptoms that led physicians to perform an ECG. There were also no data available on the associated diseases (hypertension, diabetes, and stroke) and valve disease for the entire population, only for the sample selected for the interview. In fact, only a small proportion of the participants were interviewed. Since the study was conducted by analyzing an ECG database, it does not faithfully correspond to a random sample of the general population, which may be a selection bias. Regarding the projection of AF prevalence according to the population growth by 2025, there are variables relating to the improvement or worsening of conditions of health in general such as catastrophes, wars, epidemics, or natural disasters that could interfere with this projection. The stroke risk score that we used in our study was similar to the $CHADS_2$ score, but without heart failure, and therefore it might have underestimated the risk of the overall study population.

5. Conclusions

In this study, using telemetry as a screening tool, AF was found in 2.2% of Brazilian patients who had received an ECG. The projection of the prevalence of AF in our population for 2016 was 1.5%, and for 2025 it was 1.7%. Anticoagulant therapy was used in only 9.3% of patients at high risk for stroke. Our study highlights the importance of screening for AF in the primary care setting and identifies important gaps in the treatment of AF in this population.

Funding

None.

Declaration of Competing Interest

E.R.F.L.d.M. reports receiving speaker fees from Bayer, Pfizer, and Libbs. R.D.L. has disclosures available at https://dcri.org/about-us/conflict-of-interest/. A.A.V.d.P. reports receiving speaker fees from Boehringer Ingelheim.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejim.2019.04.024.

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