Original Article

Lack of Anticoagulant Use in Patients with Atrial Fibrillation and Increased Risk of Thromboembolic Events According to Sex: Insights from a Multicentric Brazilian Study

Emiliano Medei,[1,2,3] Renata Moll-Bernardes,[1] Martha V. T. Pinheiro,[1,4] Andréa S. Sousa,[1,5] Barbara Abufaiad,[1,4] Andre Feldman,[1,4] Guilherme D'andrea Saba Arruda,[1,4] Thiago Libano Csernik Monteiro,[1,4] Fabio Augusto De Luca,[1,4] Benhur Davi Henz,[1,4] Denilson C. Albuquerque,[1,6] Antonio Aurelio P. Fagundes Junior,[1,4] Marcia M. Noya-Rabelo,[1,4,7] Angelina Silva Camiletti,[1] Rose Mary Frajtag,[1] Ronir R. Luiz,[1,8] Olga F. Souza[1,4]

Instituto D'Or de Pesquisa e Ensino,[1] Rio de Janeiro, RJ – Brasil

Centro Nacional de Biologia Estrutural e Bioimagem - Universidade Federal do Rio de Janeiro (UFRJ),[2] Rio de Janeiro, RJ – Brazil

Instituto de Biofísica Carlos Chagas Filho - Universidade Federal do Rio de Janeiro (UFRJ),[3] Rio de Janeiro, RJ – Brazil

Departamento de Cardiologia e Clínica Médica, Rede D'Or,[4] Rio de janeiro, RJ – Brazil

Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz,[5] Rio de Janeiro, RJ – Brazil

Departamento de Cardiologia, Universidade Estadual do Rio de Janeiro,[6] Rio de Janeiro, RJ – Brazil

Faculdade de Medicina e Saúde Pública da Bahia,[7] Salvador, BA – Brazil

Instituto de Estudos em Saúde Pública (IESC) Universidade Federal do Rio de Janeiro (UFRJ),[8] Rio de Janeiro, RJ – Brasil

Abstract

Background: **Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia, and its presentation differs according to age and sex. Recent studies have revealed differences in AF among various demographic groups, including the Latin American population.**

Objectives: **To better understand potential disparities in AF prevalence and treatment strategies in the Brazilian population through data from a large multicentric prospective registry.**

Methods: **The Rede D'Or AF registry is a multicenter prospective observational study including patients aged ≥ 18 years with AF who were seen in the emergency department of 32 tertiary hospitals in Brazil. Patients were characterized according to sex and other baseline characteristics and were classified according to previous anticoagulant use. The lack of anticoagulant use in patients with previous indications was analyzed. Statistical significance was set at 5%.**

Results: **The study data were from a total of 1955 patients enrolled. Male sex was more prevalent, and men were younger than the women. Due to an increased prevalence of previous AF episode and a higher CHA_2DS_2-VASc score, more women had indications for anticoagulant therapy; however, a significant proportion was not receiving this treatment. From 29 in-hospital deaths, 15 patients had previous indication for anticoagulation, but only 3 were using anticoagulants.**

Conclusion: **This study revealed sex-related differences in the Brazilian population of patients with AF that are consistent with trends in high-income countries. The promotion of better implementation of anticoagulant and antithrombotic therapies to reduce the risk of death and thromboembolic events among women with AF in Brazil is crucial.**

Keywords: **Atrial Fibrillation; Anticoagulants; Thromboembolism.**

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia worldwide, and its prevalence among adults in Brazil is 1.8% to 2.5%, representing about 1.5 million people.[1-3] The lifetime risk of AF is 25%, and it increases with age, with men being more commonly affected. Other known risk factors for the development and progression of the disease include hypertension, diabetes, heart failure, ischemic cardiomyopathy, chronic renal failure, chronic pulmonary disease, obesity, and obstructive sleep apnea.[4,5]

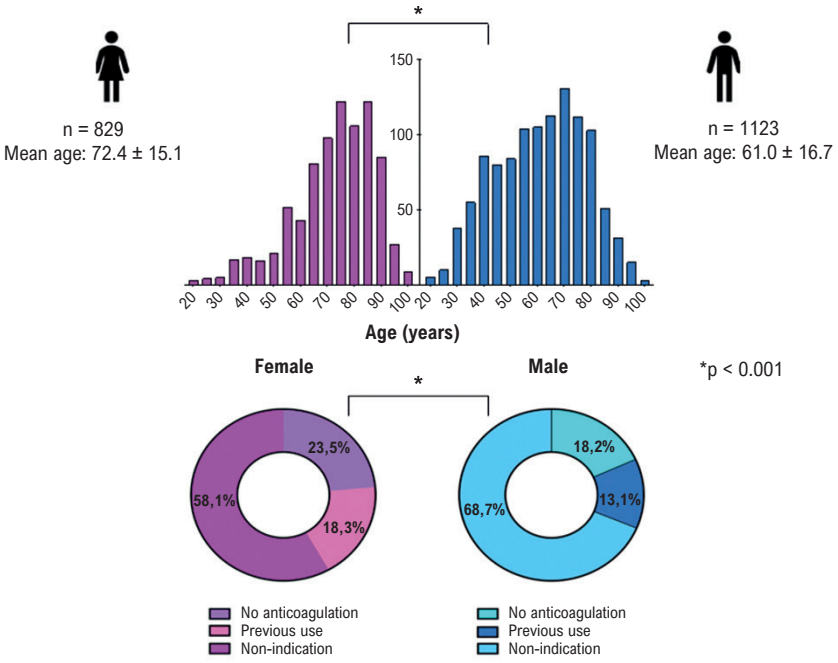
Thromboembolic complications, especially stroke, in association with AF have serious consequences, increasing morbidity and mortality.[6] Patients with AF have a 5-fold increased risk of stroke in the absence of anticoagulant treatment. The risk of stroke during AF doubles with each decade of life after the age of 55 years, and its incidence exceeds 25% in patients over 80 years of age. AF accounts for almost one third of all strokes and is the leading cause of cardioembolic stroke.[7,8]

Current guidelines recommend antithrombotic therapy for stroke prevention based on individual risk.[4,9,10] The CHA_2DS_2-

Mailing Address: Emiliano Medei •
Avenida Carlos Chagas Filho, 373 – CCS – Bloco G. CEP 21941-902, Rio de Janeiro, RJ – Brazil
E-mail: emedei70@biof.ufrj.br
Manuscript received December 11, 2023, revised manuscript June 10, 2024, accepted June 26, 2024
Editor responsible for the review: Mauricio Scanavacca

DOI: https://doi.org/10.36660/abc.20240310i

Central Illustration: Lack of Anticoagulant Use in Patients with Atrial Fibrillation and Increased Risk of Thromboembolic Events According to Sex: Insights from a Multicentric Brazilian Study



Arq Bras Cardiol. 2024; 121(9):e20240310

Age distribution and anticoagulant use of patients with atrial fibrillation according to sex.

VASc score is the most used in clinical practice to predict stroke risk, based on the increased risks conferred by heart failure, hypertension, age, diabetes, previous stroke, atherosclerotic disease, and female sex. Women with AF have greater stroke severity and permanent disability occurrence than do men. Still, they have been underrepresented in landmark randomized clinical trials of non–vitamin-K-antagonist oral anticoagulants (NOACs).[6,11] Relative to male patients, women with AF are less likely to undergo electrical cardioversion and are referred later for catheter ablation.[12]

The increasing prevalence and the complexity of AF pose significant clinical challenges.[13] Sex differences in AF could be attributed to variations in lifestyle, genetic and hormonal profiles, among other factors. To date, however, these differences have not been studied thoroughly in Latin American patients, including the Brazilian population. Thus, in the present study, we aimed to clarify the age and sex differences in the epidemiological aspects of AF and examine the underutilization of anticoagulants for patients with AF using data from a large-scale multicentric prospective Brazilian registry.

Methods

Study design

This is a multicenter prospective observational study called "Rede D'Or AF registry" of consecutive adults aged ≥ 18 years with symptomatic AF admitted to the emergency rooms of 32 tertiary hospitals in 6 Brazilian states (Table S1).

Participants

Patients with clinical suspicion and 12-lead electrocardiographic confirmation of AF or atrial flutter were eligible for inclusion in the registry. Those diagnosed with tachyarrhythmias related to other clinical conditions, such as sepsis and thyroid dysfunction, were excluded.

Data collection and management

Trained investigators collected demographic, clinical, and laboratory data from participants' electronic medical records and entered them into electronic case report forms using the Research Electronic Data Capture platform (Vanderbilt University, Nashville, TN, USA). Clinical data included previous history of AF, comorbidities, clinical presentation, cardioembolic risk factors, medical history, previous use of anticoagulants, diagnostic procedures, complications, and treatment during hospitalization. Laboratory data were from tests performed throughout participants' hospitalizations according to local clinical practice. The patients were followed prospectively until hospital discharge or in-hospital death.

For the present study, patients were characterized according to sex and other baseline characteristics and were classified according to previous anticoagulant use. The lack of anticoagulant use before hospital admission in patients with previous indications for such use (previous history of AF, CHA_2DS_2-VASc score ≥ 3 for women and ≥2 for men) was recorded and analyzed.

Statistical analysis

Categorical variables were characterized as proportions, and their frequencies were compared between groups using the chi-squared or Fisher test. The normal distribution of the data was calculated by the Kolmogorov-Smirnov test. As continuous variables were not normally distributed, they were described as medians and interquartile ranges and were compared using the Mann-Whitney test. Statistical significance was set at 5%. All analyses were performed using SPSS software (version 24.0; IBM Corporation, Armonk, NY, USA).

Ethical considerations

This study adheres to the principles of the Declaration of Helsinki. The protocol was approved by the institutional review boards and ethics committees at the participating sites (IRB#82452218.2.1001.5249). All patients provided written informed consent before enrollment. All patient-specific data were de-identified during analysis to ensure confidentiality.

Results

Between June 15, 2018, and February 17, 2023, data from a total of 1955 patients from the 32 participating sites were included in the registry. Among these patients, 707 presented paroxysmal AF; 369 had permanent AF, and in 879 the AF form was not determined. The median patient age was 68.0 years, and 57.5% of the patients were male. The age varied according to sex, with median ages of 61.0 years for men and 72.4 years for women (Central Illustration). More women than men had asthma and hyperthyroidism. More men than women had hypertension and coronary artery disease. The frequencies of renal failure, dilatation, and ischemic myocardiopathy did not differ between sexes (Table 1). Previous histories of AF were more prevalent among women than among men (49.6% versus 43.1%, $p < 0.01$), but this difference was not significant when the sample was stratified by age (Figure 1).

In-hospital mortality

A total of 29 (1.48%) patients died during hospitalization, and only 1 (0.05%) died in the emergency department. Mortality was associated with age, the presence of comorbidities ($p = 0.02$), dilated or ischemic myocardiopathy, and renal failure, but not sex, hypertension, or coronary artery disease (Table 2). The causes of death were cardiovascular in 9 patients (including 3 with heart failure, 1 with cardiogenic shock, 1 with cerebrovascular accident, and 4 with other cardiovascular causes). The cause of death was non-related to cardiovascular disease in 20 patients. It is important to remark that from 29 deaths, 15 (51.7%) patients had previous indication for anticoagulation, but only 3 were using anticoagulants. The mortality in the group lacking anticoagulation was 3.1%, compared with 1.1% in the group with previous anticoagulation ($p = 0.034$). There was no difference between sexes in this regard.

Table 1 – Baseline clinical characteristics of patients with atrial fibrillation according to sex

Caracteristics	Total		Sex				χ^2 Test p value
			Male		Female		
	n	(%)	n	(%)	n	(%)	
Age							
< 50 years	368	(18.9)	301	(26.8)	67	(8.1)	
50 to 69 years	667	(34.2)	434	(38.6)	233	(28.1)	<0.001
> 70 years	917	(47.0)	388	(34.6)	529	(63.8)	
Hypertension							
No	992	(55.6)	394	(51.8)	598	(58.5)	0.005
Yes	791	(44.4)	367	(48.2)	424	(41.5)	
Coronary artery disease							
No	1504	(84.4)	844	(82.6)	660	(87.0)	0.012
Yes	277	(15.6)	178	(17.4)	99	(13.0)	
Asthma							
No	1714	(96.2)	996	(97.5)	718	(94.5)	0.001
Yes	68	(3.8)	26	(2.5)	42	(5.5)	
Dilated/ischemic cardiomyopathy							
No	1677	(94.2)	962	(94.1)	715	(94.2)	1.000
Yes	104	(5.8)	60	(5.9)	44	(5.8)	
Renal failure							
No	1717	(96.3)	982	(96.1)	735	(96.6)	0.614
Yes	66	(3.7)	40	(3.9)	26	(3.4)	
Hyperthyroidism							
No	1751	(98.3)	1010	(98.8)	741	(97.5)	0.043
Yes	31	(1.7)	12	(1.2)	19	(2.5)	

Anticoagulant use

The median CHA_2DS_2-VASc score was 4 for women and 2 for men. In the study population, 25.6% of the women showed a CHA_2DS_2-VASc score ≥ 5; in men, this proportion was 5.5% (Table S2). Considering the previous history of AF and the CHA_2DS_2-VASc score, we estimated that 698 patients had previous indications for anticoagulant use. Among these patients, 299 (42.8%) reported anticoagulant use on hospital admission. From these, 236 (78.9%) were on a NOAC; 15 (5.0%) were

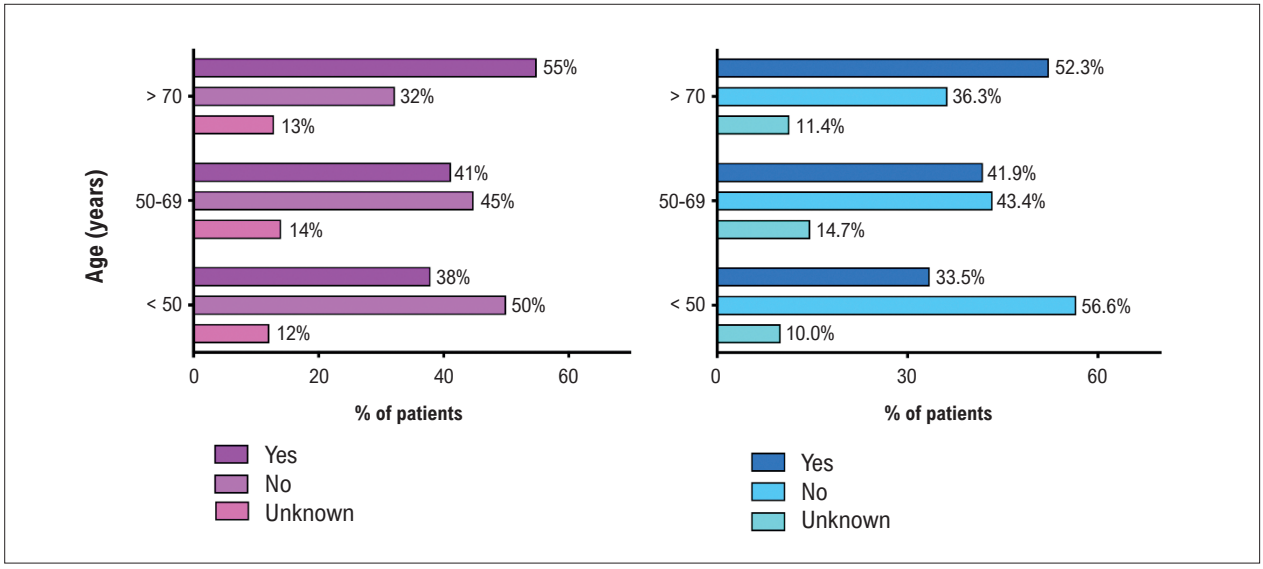


Figure 1 – *Previous history of atrial fibrillation among patients hospitalized for atrial fibrillation according to age and sex.*

on warfarin; 8 (2.6%) were taking low-molecular-weight heparin, and 40 (13.4%) were non-informed. There was no significant difference between sex regarding the type of anticoagulation (Table S3). More women than men had indications for anticoagulant use (41.8% versus 31.3%) and were not using anticoagulants (23.5% versus 18.2%; Central Illustration).

The 399 patients lacking anticoagulation were older, and more of them had hypertension, coronary artery disease, asthma, dilated or ischemic myocardiopathy, and renal failure than did those previously taking anticoagulants. The prevalence of hyperthyroidism did not differ according to anticoagulant use (Table 3). Among all hospital-admitted patients, 10 had some thromboembolic event; 31 had a hemorrhagic event, and 1 patient had a hemorrhagic cerebrovascular accident.

At hospital discharge, a total of 1196 patients were anticoagulated, 1161 (97.1%) with NOAC and 35 (2.9%) with warfarin. There was a higher percentage of women taking warfarin compared to men (4.5% versus 1.8%; $p = 0.007$), with no difference between sex regarding the use of NOAC. Also, at hospital discharge, 193 patients were receiving antiaggregant medications (Table S4).

Discussion

As AF is the most prevalent cardiac arrhythmia worldwide, new insights into its epidemiological characteristics, including age and sex disparities in specific geographic, racial, cultural, and economic environments, are needed.[14] This analysis of registry data from 32 sites over 5 years yielded interesting findings regarding demographic factors, sex specificities, and anticoagulant underutilization in the Brazilian population with AF.

This population had a preponderance of men, who were younger than the included women. This finding corroborates those from previous Brazilian registry studies, including the study published in 2015 by Marcolino et al.[3] and the recent RECALL study.[1] Additionally, we found that previous histories of AF were more prevalent among women than among men. Consistently, Tanaka et al.[15] reported sex-specific differences in AF recurrence after ablation suggesting that women are more resistant than men to this treatment.

In-hospital mortality was associated with age, but not sex, in our analysis. The in-hospital mortality rate in this study (1.48%) was higher than the one reported for a European population (0.6%),[16] but consistent with that observed in a previous Brazilian registry study.[3] We observed increased mortality in the group of patients who were lacking anticoagulation compared to those who were taking anticoagulants.

Appropriate thromboembolic risk assessment and anticoagulation strategy implementation are vital to prevent stroke and other associated complications in patients with AF.[17,18] Previous studies highlighted that racial, ethnic, sex, and socioeconomic disparities may affect treatment strategies.[19] In our population, women were more likely than men to require anticoagulant treatment. Therefore, a concerning 23.5% of women at high risk (i.e., with previous histories of AF) were not receiving appropriate anticoagulant therapy. This issue, although not unique to Brazil, appears to be particularly critical in the Brazilian population, as supported by previous findings.[3,20] Other works, including a multicentric study conducted in Japan[15] and another study conducted in Scotland,[21] have also revealed sex-based discrepancies in the prescription of oral anticoagulants to patients with AF, possibly conferring increased risk of stroke and hospitalization among undermedicated individuals, although associated with a lower risk of intracranial bleeding. Conversely, another registry of AF from China

Table 2 – In-hospital mortality of patients with atrial fibrillation according to baseline characteristics and comorbidities

Caracteristics	Total		Death				p value*
			No		Yes		
	n	(%)	n	(%)	n	(%)	
Age							
< 50 years	321	100.0	320	(99.7)	1	(0.3)	0.002
50 to 69 years	621	100.0	616	(99.2)	5	(0.8)	
> 70 years	838	100.0	815	(97.3)	23	(2.7)	
Sex							
Male	1032	100.0	1016	(98.4)	16	(1.6)	0.850
Female	748	100.0	735	(98.3)	13	(1.7)	
Hypertension							
No	906	100.0	890	(98.2)	16	(1.8)	0.852
Yes	731	100.0	719	(98.4)	12	(1.6)	
Coronary artery disease							
No	1376	100.0	1355	(98.5)	21	(1.5)	0.191
Yes	260	100.0	253	(97.3)	7	(2.7)	
Asthma							
No	1573	100.0	1548	(98.4)	25	(1.6)	0.090
Yes	63	100.0	60	(95.2)	3	(4.8)	
Dilated/ischemic cardiomyopathy							
No	1540	100.0	1517	(98.5)	23	(1.5)	0.021
Yes	96	100.0	91	(94.8)	5	(5.2)	
Renal failure							
No	1576	100.0	1554	(98.6)	22	(1.4)	<0.001
Yes	61	100.0	55	(90.2)	6	(9.8)	
Hyperthyroidism							
No	1609	100.0	1582	(98.3)	27	(1.7)	0.043
Yes	27	100.0	16	(59.3)	1	(3.7)	

**Fisher test.*

described no sex difference regarding the use of oral anticoagulants.[22]

Direct oral anticoagulants (DOACs) and warfarin are the most used anticoagulants in patients with AF.[23] Our results also presented a similar profile, and DOACs were more frequently indicated than warfarin. A large study in USA, which included more than 430,000 patients, reported that warfarin use declined from 52.4% to 17.7% from 2011 to 2020 among adults with AF.[24] The same study also remarked that 1 in 3 high-risk patients with AF was not on any anticoagulant. In a large Brazilian study (RECALL),[1] the authors found that, from all patients who were receiving anticoagulants, 62.6% were taking vitamin K antagonists and 37.4% were taking DOACs. These differences probably reflect the socio-economic status that precludes the widespread use of the more expensive DOACs. The practice in private Brazilian hospitals is similar to the one reported in high-income countries, contrasting to the predominant use of warfarin in public hospitals, as shown in the RECALL study.

The study has some limitations. It was not possible to estimate the HAS-BLED score, which prevented us from precisely determining the number of patients who should have received anticoagulants but did not. Since all patients enrolled were from private hospitals, the representativeness of the Brazilian population could be limited, even though Rede D'Or involves a large number of patients from different socioeconomic backgrounds and regions of Brazil. Future research should focus on the identification of strategies to optimize the management of patients with AF and reduce risks associated with the disease.

Conclusion

The findings from the present Brazilian study are in line with similar profiles of patients with AF in high-income countries, which reveal comparable sex-based differences. Although AF was more prevalent among men in our sample, our analyses showed that a significant number of high-risk patients, particularly women, had no previous anticoagulant use, resulting in an increased risk of thromboembolic complications associated with AF. Thus, intensive efforts must be made to promote the adoption of appropriate anticoagulant and antithrombotic therapies, particularly for women.

Acknowledgements

We are very grateful to the staff and research assistants at the D'Or Institute for Research and Education and Rede D'Or hospitals who dedicated their time to support this study.

Author Contributions

Conception and design of the research, Analysis and interpretation of the data and Writing of the manuscript: Medei E, Souza OF; Acquisition of data: Medei E, Moll-Bernardes R, Pinheiro MVT, Sousa AS, Abufaiad B, Feldman A, Arruda GDS, Monteiro TLC, De Luca FA, Henz BD, Albuquerque DC, Fagundes Junior AAP, Noya M, Camiletti AS, Frajtag RM, Souza OF; Statistical analysis: Luiz RR, Souza OF; Obtaining financing: Medei E; Critical revision of the manuscript for content: Medei E, Moll-Bernardes R, Pinheiro MVT, Sousa AS, Abufaiad B, Feldman A, Arruda GDS, Monteiro TLC, De Luca FA, Henz BD, Albuquerque DC, Fagundes Junior AAP, Noya M, Camiletti AS, Frajtag RM, Luiz RR, Souza OF.

Table 3 – Clinical characteristics of patients with atrial fibrillation according to previous anticoagulant use

Caracteristics	Total		Previous anticoagulation						χ^2 Test p value
			No indication		Previous use		Lacking anticoagulation		
	n	(%)	n	(%)	n	(%)	n	(%)	
No indication									
< 50 years	368	100.0	329	(89.4)	27.0	(7.3)	12.0	(3.3)	
50 to 69 years	669	100.0	490	(73.2)	82.0	(12.3)	97.0	(14.5)	<0.001
> 70 years	918	100.0	438	(47.7)	190.0	(20.7)	290.0	(31.6)	
Hypertension									
No	992	100.0	717	(72.3)	154	(15.5)	121	(12.2)	0.08
Yes	793	100.0	393	(49.6)	129	(16.3)	271	(34.2)	
Coronary artery disease									
No	1506	100.0	1000	(66.4)	220	(14.6)	286	(19.0)	<0.001
Yes	277	100.0	109	(39.4)	62	(22.4)	106	(38.3)	
Asthma									
No	1716	100.0	1077	(62.8)	269	(15.7)	370	(21.6)	0.029
Yes	68	100.0	32	(47.1)	14	(20.6)	22	(32.4)	
Dilated/ischemic cardiomyopathy									
No	1679	100.0	1067	(63.5)	254	(15.1)	358	(21.3)	<0.001
Yes	104	100.0	42	(40.4)	28	(26.9)	34	(32.7)	
Renal failure									
No	1719	100.0	1082	(62.9)	267	(15.5)	370	(21.5)	0.04
Yes	66	100.0	28	(42.4)	16	(24.2)	22	(33.3)	
Hyperthyroidism									
No	1753	100.0	1093	(62.4)	274	(15.6)	386	(22.0)	0.310
Yes	31	100.0	17	(54.8)	8	(25.8)	6	(19.4)	

Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

Sources of funding

The study was funded by Carlos Chagas Filho Foundation for Supporting Research in the State of Rio de Janeiro (FAPERJ), E.M. receives personal grant PQ CNPq, and grants E-26/210.155/2020, E-26/203.169/2017, E-26/210.191/2020, and E-26/210.253/2020; CNPq 310681/2018-9 (to EM). CNPq – INTERAS - 406761/2022-1.

Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the IDOR under the protocol number IRB#82452218.2.1001.5249. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Lopes RD, Silva PGMB, Hoffmann CR Filho, Cavalvante MA, Miranda CM, Esper RB, et al. The First Brazilian Cardiovascular Registry of Atrial Fibrillation: Primary Results of the RECALL Study. Am Heart J. 2023;264:97-105. doi: 10.1016/j.ahj.2023.06.007.
2. Santos IS, Lotufo PA, Brant L, Pinto MM Filho, Pereira ADC, Barreto SM, et al. Atrial Fibrillation Diagnosis using ECG Records and Self-Report in the Community: Cross-Sectional Analysis from ELSA-Brasil. Arq Bras Cardiol. 2021;117(3):426-34. doi: 10.36660/abc.20190873.

3. Marcolino MS, Palhares DM, Benjamin EJ, Ribeiro ALP. Atrial Fibrillation: Prevalence in a Large Database of Primary Care Patients in Brazil. Europace. 2015;17(12):1787-90. doi: 10.1093/europace/euv185.

4. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed in Collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC) Developed with the Special Contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42(5):373-498. doi: 10.1093/eurheartj/ehaa612.

5. Favarato D. Brazilian Population Presents Prevalence of Atrial Fibrillation Similar to Higher Income Countries, and a Low Use of Anticoagulation Therapy. Arq Bras Cardiol. 2021;117(3):435-36. doi: 10.36660/abc.20210562.

6. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, et al. Worldwide Epidemiology of Atrial Fibrillation: A Global Burden of Disease 2010 Study. Circulation. 2014;129(8):837-47. doi: 10.1161/CIRCULATIONAHA.113.005119.

7. D'Souza A, Butcher KS, Buck BH. The Multiple Causes of Stroke in Atrial Fibrillation: Thinking Broadly. Can J Cardiol. 2018;34(11):1503-11. doi: 10.1016/j.cjca.2018.08.036.

8. Reiffel JA. Atrial Fibrillation and Stroke: Epidemiology. Am J Med. 2014;127(4):15-6. doi: 10.1016/j.amjmed.2013.06.002.

9. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration with the Society of Thoracic Surgeons. Circulation. 2019;140(2):125-51. doi: 10.1161/CIR.0000000000000665.

10. Magalhães LP, Figueiredo MJO, Cintra FD, Saad EB, Kuniyoshi RR, Teixeira RA, et al. II Diretrizes Brasileiras de Fibrilação Atrial. Arq Bras Cardiol. 2016;106(4):1-35. doi: 10.5935/abc.20160055.

11. Lang C, Seyfang L, Ferrari J, Gattringer T, Greisenegger S, Willeit K, et al. Do Women with Atrial Fibrillation Experience More Severe Strokes? Results From the Austrian Stroke Unit Registry. Stroke. 2017;48(3):778-80. doi: 10.1161/STROKEAHA.116.015900.

12. Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, et al. Sex differences in Cardiac Arrhythmia: A Consensus Document of the European Heart Rhythm Association, Endorsed by the Heart Rhythm Society and Asia Pacific Heart Rhythm Society. Europace. 2018;20(10):1565. doi: 10.1093/europace/euy067.

13. Hsu JC, Reynolds MR, Song Y, Doros G, Lubitz SA, Gehi AK, et al. Outpatient Prescription Practices in Patients with Atrial Fibrillation (From the NCDR PINNACLE Registry). Am J Cardiol. 2021;155:32-9. doi: 10.1016/j.amjcard.2021.06.011.

14. Rodriguez CJ, Soliman EZ, Alonso A, Swett K, Okin PM, Goff DC Jr, et al. Atrial Fibrillation Incidence and Risk Factors in Relation to Race-ethnicity and the Population Attributable Fraction of Atrial Fibrillation Risk Factors: The Multi-Ethnic Study of Atherosclerosis. Ann Epidemiol. 2015;25(2):71-6. doi: 10.1016/j.annepidem.2014.11.024.

15. Tanaka N, Inoue K, Kobori A, Kaitani K, Morimoto T, Kurotobi T, et al. Sex Differences in Atrial Fibrillation Ablation Outcomes: Insights from a Large-scale Multicentre Registry. Europace. 2020;22(9):1345-57. doi: 10.1093/europace/euaa104.

16. König S, Ueberham L, Schuler E, Wiedemann M, Reithmann C, Seyfarth M, et al. In-hospital Mortality of Patients with Atrial Arrhythmias: Insights from the German-wide Helios Hospital Network of 161 502 Patients and 34 025 Arrhythmia-related Procedures. Eur Heart J. 2018;39(44):3947-57. doi: 10.1093/eurheartj/ehy528.

17. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: Antithrombotic Therapy to Prevent Stroke in Patients who have Nonvalvular Atrial Fibrillation. Ann Intern Med. 2007;146(12):857-67. doi: 10.7326/0003-4819-146-12-200706190-00007.

18. Goulart AC, Olmos RD, Santos IS, Tunes G, Alencar AP, Thomas N, et al. The Impact of Atrial Fibrillation and Long-term Oral Anticoagulant Use on All-cause and Cardiovascular Mortality: A 12-year Evaluation of the Prospective Brazilian Study of Stroke Mortality and Morbidity. Int J Stroke. 2022;17(1):48-58. doi: 10.1177/1747493021995592.

19. Daly DJ, Essien UR, Del Carmen MG, Scirica B, Berman AN, Como JS, et al. Race, Ethnicity, Sex, and Socioeconomic Disparities in Anticoagulation for Atrial Fibrillation: A Narrative Review of Contemporary Literature. J Natl Med Assoc. 2023;115(3):290-7. doi: 10.1016/j.jnma.2023.02.008.

20. Gabet A, Guenancia C, Duloquin G, Olié V, Béjot Y. Ischemic Stroke with Atrial Fibrillation: Characteristics and Time Trends 2006 to 2017 in the Dijon Stroke Registry. Stroke. 2021;52(6):2077-85. doi: 10.1161/STROKEAHA.120.030812.

21. Lee KK, Doudesis D, Bing R, Astengo F, Perez JR, Anand A, et al. Sex Differences in Oral Anticoagulation Therapy in Patients Hospitalized with Atrial Fibrillation: A Nationwide Cohort Study. J Am Heart Assoc. 2023;12(5):e027211. doi: 10.1161/JAHA.122.027211.

22. Li YM, Jiang C, He L, Li XX, Hou XX, Chang SS, et al. Sex Differences in Presentation, Quality of Life, and Treatment in Chinese Atrial Fibrillation Patients: Insights from the China Atrial Fibrillation Registry Study. Med Sci Monit. 2019;25:8011-8. doi: 10.12659/MSM.919366.

23. Navar AM, Kolkailah AA, Overton R, Shah NP, Rousseau JF, Flaker GC, et al. Trends in Oral Anticoagulant Use Among 436 864 Patients with Atrial Fibrillation in Community Practice, 2011 to 2020. J Am Heart Assoc. 2022;11(22):e026723. doi: 10.1161/JAHA.122.026723.

24. Bartholomay E, Polli I, Borges AP, Kalil C, Arroque A, Kohler I, et al. Prevalence of Oral Anticoagulation in Atrial Fibrillation. Clinics. 2014;69(9):615-20. doi: 10.6061/clinics/2014(09)07.

*Supplemental Materials

For additional information, please click here.