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Prognostic impact of atrial fibrillation and flutter temporal pattern on anticoagulation and return visits to the emergency department: A historic cohort of 1112 patients

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ABSTRACT

Background: Emergency department (ED) visits due to atrial fibrillation and flutter (AFF) are common, and provide an opportunity to define stroke risk. The prognostic impact of AFF duration on return ED visits is unknown. We aimed to investigate both the prognostic impact of AFF classification on ED visits and the adherence to guideline recommendations on anticoagulation.

Methods: This single-center historic cohort of every patient treated for AFF in our ED during 2012. Follow-up data was obtained on May 2015 (median follow-up of 863 days).

Results: Among 1112 patients (495 Paroxysmal AF - parAF, 475 Persistent AF – persAF, and 142 flutter), those with parAF were less frequently under oral anticoagulation than persAF and flutter patients (15.8%, 39.4%, 40.1%, $p < 0.01$). Mean CHA2DS2-VASc scores of parAF were lower than persAF (2.2 vs. 3.12, $p < 0.01$), and did not differ from those with flutter. Return visits to the ED were highest among flutter patients and lowest among parAF (49.3% vs. 37.2%, $p < 0.01$). Heart failure, hypertension, female gender and atrial flutter were independent risk factors for repeated visits on multivariate regression.

Conclusions: AFF duration provide prognostic information in the ED. ED return visits were common and particularly incident among flutter patients. Furthermore, stroke risk was high and anticoagulation rates were low across all groups. Patients with paroxysmal AF were less commonly anticoagulated even though their mean CHA2DS2-VASc scores were 2.2. These results reveal that guideline adherence is still lacking and should raise awareness to a stricter patient follow-up after ED visits.

Introduction

Atrial Fibrillation and flutter (AFF) have similar pathophysiology and often cause symptoms such as fatigue, dyspnea, palpitations, lightheadedness and effort intolerance, which are common reasons for Emergency Department (ED) visits [1–3]. Even though American Heart Association (AHA) guidelines recommend that AFF patients presenting to the ED should have their stroke risk assessed and should be discharged on anticoagulation, few studies actually address this subject [4].

The usefulness of determining the duration of atrial fibrillation (paroxysmal, persistent or permanent) lies mostly on the choice between rate or rhythm control. However, the rhythm classification should not preclude anticoagulation [5,6]. The prognostic impact of this classification on return visits to the ED is unknown.

Aiming to investigate both the prognostic impact of AFF classification on ED visits and the adherence to guideline recommendations on anticoagulation, we studied a historical cohort of over 1000 patients admitted to our cardiology emergency unit.

Methods

Study design

We conducted a retrospective cohort study of patients that presented to our ED due to atrial fibrillation (AF) or flutter as a primary diagnosis. Our hospital is a tertiary care center specialized in cardiology that admits over 35,000 patients annually. Our ED unit medical staff is comprised of trained cardiologists, only. Our Ethics and Research Committee approved the study.

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Table 1
Clinical characteristics according to AFF subtypes ($n = 1112$).

Characteristic	Paroxysmal AF ($n = 495$)	Persistent AF ($n = 475$)	*Flutter* ($n = 142$)	*P*-Value
Age, years	63.4 ± 14	68.8 ± 12.9[a]	63.8 ± 14	<0.01
Male gender, n (%)	257 (52)	230 (48.4)	89 (63.6)[b,c]	<0.01
Anticoagulation, n (%)	78 (15.8)	187 (39.4)[a]	57 (40.1)[b]	<0.01
Comorbidities				
HF, n (%)	75 (15.2)	198 (41.7)[a]	46 (32.6)[b]	<0.01
SH, n (%)	284 (57.7)	331 (69.2)[a]	79 (56)	0.03
DM, n (%)	52 (10.6)	76 (16.7)	28 (19.9)	0.4
Stroke, n (%)	17 (3.5)	50 (10.5)[a]	8 (5.7)[b]	<0.01
CHADS2 score				<0.01
0	159 (32.1)[a]	53 (11.2)	43 (30.3)[c]	
1	183 (37)	161 (33.9)	40 (28.2)	
2	107 (21.6)	141 (29.7)	30 (21.1)	
3	31 (6.3)	78 (16.4)[a]	20 (14.1)	
4	11 (2.2)	27 (5.7)	6 (4.2)	
5	4 (0.8)	13 (2.7)	2 (1.4)	
6	0	2 (0.4)	1 (0.7)	
Mean CHA2DS2-VASc	2.2 ± 1.7	3.12 ± 1.6[a]	2.4 ± 1.8	<0.01

Data are expressed as mean ± standard deviation or number (%). AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LA: left atrium; HF: heart failure; SH: Systemic Hypertension; DM: Diabetes Mellitus.
[a] difference between Persistent AF and Paroxysmal AF.
[b] Difference between flutter and Paroxysmal AF.
[c] Difference between flutter and Persistent AF.

Inclusion criteria

All patients that presented to our ED from January 1st 2012 to December 31st 2012 and were discharged under an International Classification of Disease (ICD) of I48 (atrial fibrillation and atrial flutter).

Exclusion criteria

Patients with an alternate diagnosis other than AF or flutter as reported by the attending physician at the time of the ED visit.

Data collection and chart review

Trained medical students blinded to the study purpose reviewed data from our electronic medical records on March 2015, resulting in a median follow-up of 863 days. Our electronic medical charts integrates outpatient, inpatient and ED visit reports, as well as prescriptions, surgeries, coronary angiograms and procedures, electrocardiograms, echocardiograms, electrophysiology exams and procedures, laboratory exams, radiology and nuclear medicine exams. Data was collected simultaneously and reviewed for discrepancies. Trivial discrepancies in data input, such as typing mistakes, were closed as per self-evident correction method. Other discrepancies, such as AF type definition or the presence of clinical variables, were reviewed and closed by the corresponding author. The first author reviewed a random sample comprising 10% of the cohort to further assess for potential errors on data collection. No statistical analysis was performed for this purpose.

AF type was registered according to physician definition during the visit. Patients were divided in 3 groups, according to most recent AHA definition [5]: paroxysmal AF (parAF), persistent AF (persAF) and atrial flutter. Patients with persAF were not differentiated between persistent and permanent AF because these subtypes were often indistinguishable on medical records. When accurate date of arrhythmia onset was not reported and current AHA definitions were not used, terms such as "chronic AF", "longstanding AF" were deemed to be persistent/permanent AF.

The following clinical variables were evaluated on patient medical records: gender, age, hypertension, prior stroke or transient ischemic attack (TIA), diabetes mellitus, heart failure, prior myocardial infarction or known coronary artery disease, peripheral artery disease, presence of aortic plaque and use of anticoagulants. Any of these variables were considered present if reported either on ED visit or on outpatient visits and exams, when present. The stroke risk scores CHADS2 and CHA2DS2-VASc were determined based on these characteristics [7,8].

Medication use was also collected by reviewing ED reports, ED discharge prescriptions and outpatient visit reports (when available) up to 6 months previous to index ED visit. Patients were considered to be on anticoagulation if they were discharged with the therapy (either newly initiated or maintained). The following drug prescriptions were reviewed: acetylsalicylic acid, clopidogrel, prasugrel, ticlopidine, warfarin, phenprocoumon, dabigatran, rivaroxaban, amiodarone, sotalol, propafenone, beta-blockers, calcium channel blockers, digoxin, statins, diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blocker and antidiabetics. Medication dosage was not collected, as it was often not reported.

The following echocardiographic variables were collected if available on medical records: left atrial diameter (in milimeters, assessed using 2-dimentional mode) and left ventricular ejection fraction (in percentage, as determined by either Teicholtz's formula or Simpson's rule when suited). These variables were considered suitable for collection if the echocardiogram had been performed up to 1 year previous to index ED visits.

ED return visits to our institution for whichever reason were also collected, as was the date of its occurence (up until May 2015) in order to perform survival free from events analysis. We only evaluated for ED visits in our institution, as there is no integrated system to evaluate for visits and admissions to other hospitals.

Statistical analysis

Our database was stored in Microsoft Excel spreadsheets and analyzed using the Statistical Package for the Social Sciences software, version 20.0 (Armonk, NY, US: IBM Corp). Continuous variables were described as mean and standard deviation, or median and interquartile range, according to variable distribution. Variables were considered normal following observation of measurements of central tendency, kurtosis and asymmetry in frequency histograms. Categorical variables were summarized as frequencies and percentages. Group comparisons were made using the z test, with a Bonferroni post-hoc analysis to identify statistical difference between groups. We considered $p < 0.05$ as statistically significant. For the survival free from ED visits analysis, we used the Kaplan-Meier estimator. Differences between event frequencies over time were compared using the log-rank test. A logistic regression model was also performed using potential variables encountered on the univariate model. Variables entered the multivariate model if they had a p-value <0.20. Results were presented as Odds Ratio (OR) and 95% Confidence Intervals (CI). In order to reach a statistical power of 80% to detect a 10% difference in the incidence of ED visits between groups, we estimated that each group would require 376 patients. Our hypothesis was that paroxysmal AF would be less prone to ED visits when compared to both persistent AF and flutter.

Ethics

The study was conducted in accordance with the Declaration of Helsinki, and the Ethics and Research Committee of our Institution approved the research protocol.

Table 2
Echocardiogram according to AF and flutter subtypes ($n = 528$).

Echocardiogram	Paroxysmal AF ($n = 214$)	Persistent AF ($n = 232$)	*Flutter* ($n = 82$)	P-Value
LVEF, %	66 ± 12	57 ± 17[a]	57 ± 17[b]	<0.01
LA, mm	43 ± 7	49 ± 7[a]	48 ± 7[b]	<0.01

Data are expressed as mean ± standard deviation. AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LA: left atrium.
[a] difference between Persistent AF and Paroxysmal AF.
[b] Difference between flutter and Paroxysmal AF.

Table 3
Drug prescriptions according to AF and flutter subtypes (n = 1112).

Drug	Paroxysmal AF (n = 495)	Persistent AF (n = 475)	*Flutter* (n = 142)	*P*-Value
Vitamin K antagonist, n (%)	52 (10.5)	150 (31.6)[a]	47 (33.1)[b]	<0.01
NOAC, n (%)	16 (3.2)	17 (3.6)	5 (3.5)	NS
Amiodarone, n (%)	46 (9.3)	46 (9.7)	18 (12.8)	NS
Sotalol, n (%)	8 (1.6)	5 (1.1)	1 (0.7)	NS
Propafenone, n (%)	21 (4.2)	10 (2.1)	5 (3.5)	NS
Beta-blocker, n (%)	208 (42)	307 (64.9)[a,c]	71 (50.4)	<0.01
CCB, n (%)	47 (9.5)	76 (16.1)[a,c]	10 (7.1)	<0.01
Digoxin, n (%)	17 (3.4)	104 (22)[a,c]	16 (11.3)	<0.01
Antiplatelet, n (%)	131 (26.5)	172 (36.2)[a,c]	42 (29.6)[b]	<0.01

Data are expressed as number (%). AF: atrial fibrillation; NOAC: novel oral anticoagulant; CCB: calcium-channel blocker.
[a] Difference between Persistent AF and Paroxysmal AF.
[b] Difference between flutter and Paroxysmal AF.
[c] difference between flutter and Persistent AF.

Results

During 2012, 1112 patients were discharged from our ED with a primary diagnosis of AF and flutter (Table 1). Four hundred ninety five patients had parAF, and were on average 5.4 years younger than their persAF counterparts (63.4 vs. 68.8 years, $p < 0.01$). Those with flutter were on average 63.8 years old. Gender distribution was different among flutter patients when compared to parAF and persAF (males 63.8% vs. 52% vs 48.4%, $p < 0.01$). When compared to persAF, patients with parAF less frequently had comorbidities such as heart failure (15.2 vs. 41.7%, $p < 0.01$), hypertension (57.7 vs. 69.2%, $p < 0.01$) and prior stroke or TIA (3.5 vs. 10.5%, $p < 0.01$). ParAF patients also had less heart failure (15.2 vs. 32.6%, $p < 0.01$) and previous stroke (3.5 vs. 5.7%, $p < 0.01$) than flutter patients (Table 1).

Echocardiographic variables were present on 47.5% of cases. Left atrial diameters were lower in the parAF group when compared to both persAF and flutter (43 ± 7 mm vs. 49 ± 7 mm vs. 48 ± 7 mm, $p < 0.01$). ParAF patients also had higher mean left ventricular ejection fraction than persAF and flutter (66% vs. 57% vs. 57%, $p < 0.01$) (Table 2).

Mean CHA2DS2-VASc was lower among parAF patients when compared to those with persAF (2.2 vs. 3.12, $p < 0.01$). Those with flutter had a mean CHA2DS2-VASc score of 2.4, which did not statistically differ from the other groups. Those with parAF and flutter more frequently had a CHADS2 score of zero when compared to those with persAF (32.1% vs. 30.3% 11.2%, $p < 0.001$). Patients with parAF were less frequently on anticoagulation (15.8% vs. 39.4% persAF vs. 40.1% flutter, $p < 0.01$).

Patients with parAF and flutter were less frequently on calcium channel blockers (9.5% vs. 7.1% vs. 16.1%, $p < 0.01$), beta-blockers (42% vs. 50.4% vs. 64.9%, $p < 0.01$), digoxin (3.4% vs. 11.3% vs. 22%, $p < 0.01$) and antiplatelet agents (26.5% vs 29.6% vs. 36.2%, $p < 0.01$) than those with parAF and flutter (see Table 3). Those with parAF were also less frequently on antiplatelet agents than those with flutter. Non vitamin K oral anticoagulant prescription was low on our study population, and did not differ between groups.

When comparing patterns of anticoagulation, those with parAF and a CHA2DS2-VASc score of zero were less frequently on anticoagulation than those with persAF and flutter (2.4% vs. 40.9% vs. 29.2%, $P < 0.01$). Anticoagulation did not differ among persAF and flutter patients in this group (Fig. 1). Fig. 2 shows the proportion of patients with a CHA2DS2-VASc score of 2 or greater that were on anticoagulation upon ED discharge. Those with parAF were less frequently receiving anticoagulants than those with persAF and flutter (21.9% vs. 39.3% vs. 44.6%, $p < 0.01$). There were no statistical differences between persAF and flutter groups.

Given a median follow up of 863 days, the time to repeat ED visit was different between the three groups being higher among parAF patients, intermediate among persAF, and lowest among those with flutter (62.8% vs. 55.6% vs. 50.7%, $p < 0.01$), as shown on Fig. 3. The following variables met the inclusion criteria stated on Statistical Analysis for entering the multivariate logistic regression model: paroxysmal AF, persistent AF, atrial flutter, age, gender, previous stroke, hypertension, heart failure and diabetes. After multivariate adjustment, only atrial flutter (OR 1.46), heart failure (OR 1.94), female gender (OR 1.37) and systemic hypertension (OR 1.34) remained as statistically significant risk factors for ED visits (Table 4). Weighted Cohen's κ test for measurement of concordance between data collectors was 0.98 (95% CI 0.94–1.0).

Discussion

To our knowledge, this is the first study to prove that classifying AF and flutter patients into guideline-recommended temporal subtypes can provide additional prognostic information in the emergency department. As shown in Fig. 3, new visits due to these arrhythmias were less common among parAF patients and more common among flutter patients, but they were strikingly high across all sugroups. This should raise concern whether these patients are being provided adequate follow-up after their ED visit [4]. On multivariate logistic regression, as expected, hypertension and heart failure were found to be independent risk factors for return ED visits. Female gender was associated with a higher risk for new ED visit, which could be related to the fact that it is also a known risk factor for stroke [8]. The finding that flutter patients

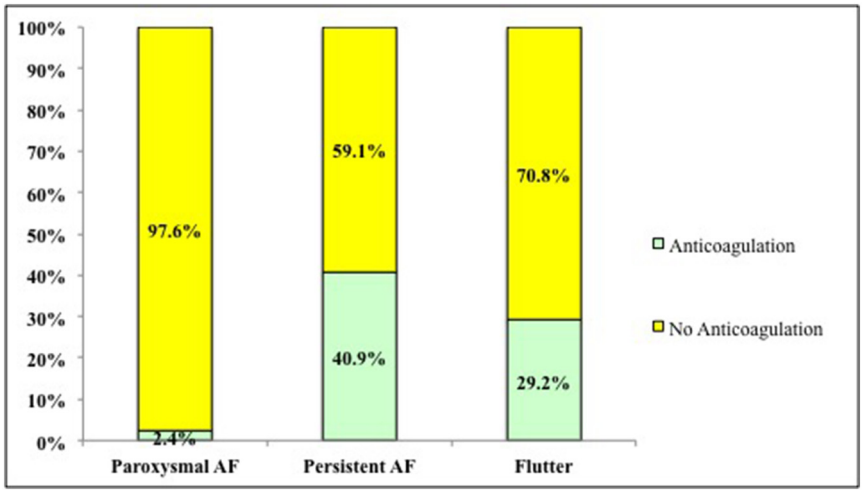

Fig. 1. Proportion of patients with a CHA2DS2-VASc score of zero with and without anticoagulation.

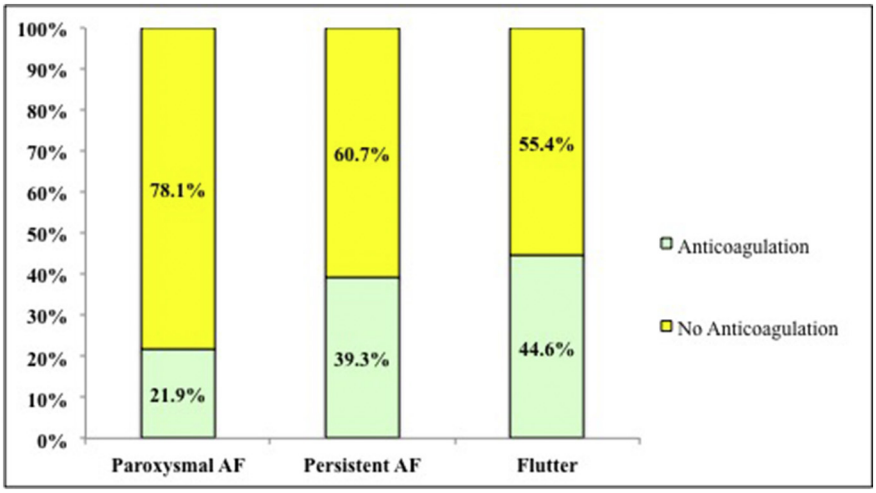

Fig. 2. Proportion of patients with a CHA2DS2-VASc score of 2 or greater with and without anticoagulation.

were more prone to new visits could be explained by the fact that they were given less rate-control drugs than persAF patients.

This historical cohort shows that anticoagulation is frequently overlooked in AF and flutter patients presenting to the ED. About 39.5% of patients with a CHA2DS2-VASc score of 2 or greater are prescribed anticoagulants when discharged home from the ED. Furthermore, patients with parAF were even less frequently prescribed such therapy, even though current guidelines recommend anticoagulation based on stroke-risk scores irrespective of AF type [5]. Previous studies have shown a reduction in mortality when patients are discharged from the ED with a warfarin prescription and a scheduled visit for prothrombin time evaluation [9,10]. These patients are also more likely to still be on anticoagulants after 1 year when compared to those that do not receive such prescription on ED discharge [11]. These studies have led to recent AHA recommendations, which state that high-risk patients should be started on anticoagulants upon ED discharge and provided a timely follow-up [4].

On the other hand, among patients with a low stroke risk, a high proportion were prescribed anticoagulants (i.e. were overtreated), particularly those with persAF and flutter, once again reflecting that anticoagulants prescription might still be influenced by AF type rather than stroke risk scores. This has also been shown in other registries, as depicted in Table 5 [12].

Our cohort shows that AF and flutter patients presenting to the ED are older than 60 years of age and usually present with other comorbidities, particularly hypertension. Patients were equally divided between genders, except for the flutter population, which was represented largely by male gender. Flutter patients presented with an intermediate risk profile between persAF and parAF, which is in accordance to findings that atrial fibrillation and atrial flutter share similar pathophysiology [2,3].

Those with perAF were more frequently on calcium-channel blockers, beta-blockers and digoxin, which can be explained by both the higher prevalence of heart failure and the fact that these are drugs

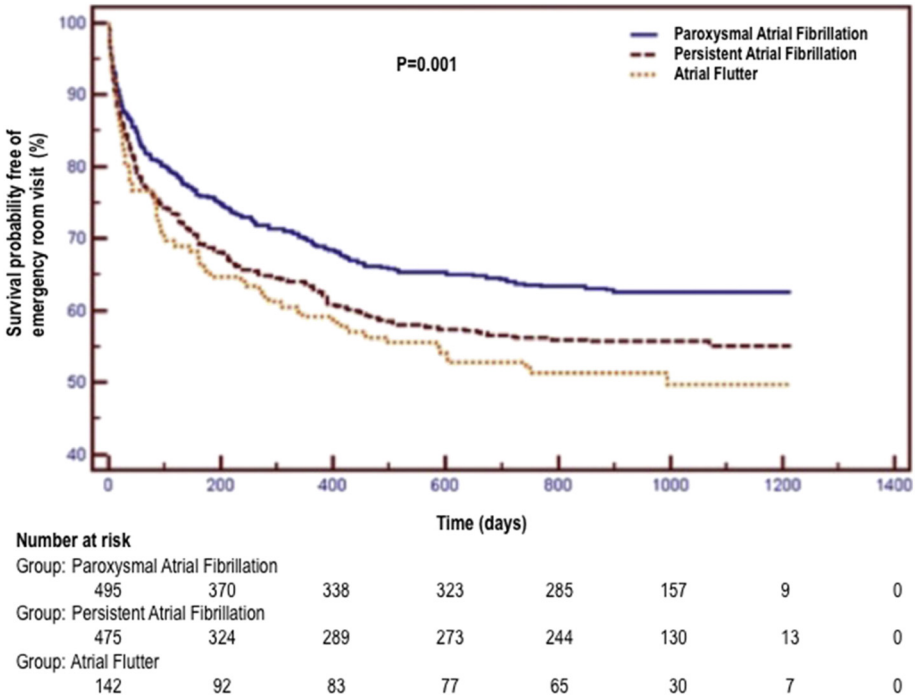

Fig. 3. Kaplan-Meier estimates for survival-free from Emergency department visits, according to arrhythmia subtype. The *p*-value is for the log rank test.

Table 4
Results of logistic regression analysis.

Variable	Odds Ratio	95% CI	P-value
Atrial flutter	1.46	1.01–2.11	0.04
Female gender	1.37	1.07–1.75	0.01
Previous stroke	1.42	0.87–2.31	0.16
Heart failure	1.94	1.49–2.56	< 0.01
Hypertension	1.34	1.04–1.75	0.02

Logistic regression using a Backward model including paroxysmal atrial fibrillation, persistent atrial fibrillation, atrial flutter, age, gender, previous stroke, hypertension, heart failure, diabetes.

used for rate-control, a strategy more frequently adopted with persistent and permanent AF [6]. Patients with flutter received vitamin K antagonists and antiplatelet agents more often than those with parAF.

Most of the reasons why patients with AF seek the ED are related to symptoms (fatigue, dyspnea, palpitations, lightheadedness and effort intolerance), stroke or bleeding. ACC/AHA Clinical Performance and Quality Measures suggests that AFF patients should be assessed for stroke risk, but it only recommends prescribing beta-blockers or not prescribing calcium channel-blockers for the purpose of concurrent HFrEF [4]. Our study has found a high recurrence of ED visits among AFF patients. Since most of these visits were not due to stroke risk or bleeding related to anticoagulation (usually classified under different ICD codes), our findings should also raise concern whether repeat ED visits are an epiphenomenon of the seriousness of the disease or if it they are avoidable through other means, such as systematic prescription or titration of rate and rhythm control drugs on discharge.

Study limitations

Our study has several limitations. We could not differentiate those with persistent AF from those with permanent AF on medical records, which could have provided further information as to which patients are at higher risk of ED visits. Furthermore, CHA2DS2-VASc variables could have been unreported, and as such, patients could have been incorrectly classified as having an incorrectly low stroke risk. However, this bias likely strenghtens the observation that anticoagulation rates are well below guideline recommendations.

The method used for data collection possibly undersized the magnitude of repeat ED visits, since AF and flutter patients might have been admitted to our ED under different ICD-10 codes (such as heart failure or stroke). We hypothesize that AF and flutter patients admitted under different ICD-10 codes would likely have more comorbidities and higher stroke risk, meaning that our results might not be applicable to these highest risk patients. We did not collect variables to define patient's bleeding risk. These variables include measurements of both liver and kidney function, often not performed during ED visits. However, bleeding risk assessment should not preclude anticoagulant prescription. We also did not collect information of readmissions in other institutions, so the rates encountered might be underestimated. Brazil does not yet have an integrated system to verify for admissions in multiple institutions. Even though it is most common for patients to remain in treatment with and return to the same institution, it is possible that they sought different hospitals for ED visits. Our area is responsible for about 2,000,000 people and there are 5 general hospitals that provide ED care as well. Nonetheless, our study still showed a high incidence of return ED visits, which strenghtens the observation that a stricter follow-up after a first ED visit is necessary.

The single center nature of our study also represents an important limitation. Provider behavior in the prescription of anticoagulants might limit the generalizability of our study. However, our center is the only one in our area in which all of the ED staff is comprised of trained Cardiologists, which also might have undersized the magnitude of the problem.

Our study also has several strenghts: sample size, as it represents a relatively large cohort of AF and flutter patients in the ED, still an understudied scenario for these arrhythmias; it represents a real-world, consecutive and unselected population that presents to a cardiology hospital, which strenghtens the external validity of this study for similar low-income populations, and it is one of few studies that it gives further insight about the characteristics of flutter patients presenting to the ED. It has become clearer in the past decades that flutter shares similar patophysiology with AF and that both arrhythmias can coexist in the same patient. However, data on flutter patients is lacking, and guideline recommendations on the management of this arrhythmia commonly use indirect evidence from AF trials and registries.

Table 5
Proportion of patients overtreated (CHA2DS2-VASc of zero on anticoagulants) and undertreated (CHA2DS2-VASc score ≥ 2 without anticoagulants) across different registries.

Registry	Overtreated	Undertreated
J-RHYTHM	–	12.7%
EORP-AF	21.7%	17%
GARFIELD	38.7%	40%
PINNACLE	26.6%	44.9%
Southern Brazil	**13.3%**	**66.7%**
China	–	80%

Data are expressed as number (%). The bold text highlights the patterns of anticoagulation use in our geographic region.

Conclusion

This retrospective cohort suggests that the time-based classification of AF and flutter adds prognostic information in the ED setting. New ED visits were common among all subgroups, but particularly high among flutter patients. Furthermore, stroke risk was high and anticoagulation rates were low across all groups. Even though the classification of AF should not interfere with the decision to start anticoagulation, we found that those with paroxysmal AF were less likely to receive such therapy. These results should raise awareness to a stricter patient follow-up after ED visits and to develop policies to improve adherence to guidelines.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Contributors

E.D.A. and T.L.L.L. participated in the study design. E.D.A. and T.L.L.L. performed the statistical analyses. All authors contributed to the interpretation of results, drafted the manuscript and approved the final manuscript.

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