



## Emergency Physician Patterns Related to Anticoagulation of Patients with Recent-Onset Atrial Fibrillation and Flutter

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### Abstract

Guidelines strongly recommend long-term anticoagulation with warfarin for patients with newly recognized AF who have high embolic risk by virtue of a CHADS<sub>2</sub> (Congestive Heart Failure, Hypertension, Age >65, Diabetes, History of Stroke) score  $\geq 2$ . The goal of this study was to determine patterns of emergency department-initiated anticoagulation among eligible patients discharged from Canadian centers with an episode of recent-onset atrial fibrillation and flutter (RAFF) and determine if decision-making is driven by the CHADS<sub>2</sub> score or other factors. This was accomplished by examining health records using uniform case identification and data abstraction as well as centralized quality control; it was conducted in 8 Canadian university emergency departments over a 12-month period. Eligible patients for this analysis demonstrated RAFF requiring emergency management, were not already taking warfarin and were not admitted to hospital. Univariate analyses were conducted using T-test or Chi-square to select factors associated with anticoagulation initiation at a significance level of  $p < 0.15$  and multiple logistic regression was employed to evaluate independent predictors after adjustment for confounders. Among 633 eligible patients, only 21 out of 120 patients (18%) with a CHADS<sub>2</sub> score  $\geq 2$  received anticoagulation and among 70 patients who were given anticoagulation only 21 (30%) had a CHADS<sub>2</sub> score  $\geq 2$ . Independent predictors of anticoagulation included age by 10-year strata: (OR = 1.7; 95% CI 1.3 – 2.1), heparin use in the anticoagulation (OR = 9.6; 95% CI 4.9 – 18.9), a new prescription for metoprolol (OR = 9.6; 95% CI 4.9 – 18.9) and being referred to cardiology for follow-up (OR = 5.6; 95% CI 2.6 – 12.0). CHADS<sub>2</sub>  $\geq 2$  doubled the likelihood of being prescribed anticoagulation (OR = 2.0; 95% CI 1.5 – 3.5) but was not an independent predictor. It was thus determined that patients discharged from the emergency department in this study were not prescribed anticoagulation in keeping with current recommendations. This practice gap merits further investigation and may benefit from educational efforts or enhanced support for anticoagulation use from the emergency department.

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## Introduction

### Background

Atrial fibrillation (AF) is an important and common problem that is increasingly seen in emergency departments (ED). The major health burden associated with AF is the risk of thrombotic events, with at least a five-fold increase in the risk for stroke. AF has been found to be responsible for more than 15% of all ischemic strokes, as well as being associated with an increased severity of stroke.<sup>1,2</sup> While oral antithrombotic therapy remains the mainstay for stroke prophylaxis therapy, it nonetheless remains an ever-present challenge to distinguish those patients for whom anticoagulation with warfarin would be beneficial from those for whom less aggressive antithrombotics would be preferable.

### Importance

In 2004, Gage et al. devised a scoring system to assess the risk of stroke and thromboembolism in patients with AF, which has since come to be known as the "CHADS<sub>2</sub> score". Noted for its simplicity and ease of use in a busy clinical setting, CHADS<sub>2</sub> estimates risk of stroke in AF patients based on the presence of five established risk factors, after which patients with AF can then be stratified into 3 groups with separate recommendations for prophylactic therapy.<sup>3</sup> In particular, warfarin's superiority to antiplatelet therapy has been well established for all patients with CHADS<sub>2</sub> score greater than 2, and remains the oral antithrombotic therapy of choice in this category.<sup>4</sup> Recently, ambiguity over optimal therapy for patients with CHADS<sub>2</sub> score of 1 has led to the development of the CHADsvASC score to further clarify optimal oral antithrombotic therapy in these patients. Research to date has shown potential for this tool in clinical practice.<sup>5</sup>

Presently, despite the convenience of the CHADS<sub>2</sub> score, the majority of patients suffering from AF are still inadequately anticoagulated, many of them not being initiated on any antithrombotic therapy.<sup>6</sup> One study found similar rates of anticoagulation with warfarin across different CHADS<sub>2</sub> scores, reflecting lack of accurate risk stratification prior to therapy administration.<sup>2</sup> Another study found that only 40% of eligible patients received appropriate oral anticoagulation, an alarming situation given the significant increased incidence of stroke in AF

patients.<sup>6</sup> The under-coagulation of AF patients is thus a global theme and needs to be addressed.

### Goals

The ED provides an important setting for initiation of proper treatment for AF patients as it is often in this setting that they first present. Poor adherence to management guidelines in the ED could contribute to the overall under-coagulation of AF patients. To date, however, there is little literature documenting patterns of warfarin initiation in the ED. Our objective was to determine the extent to which warfarin for AF is being initiated in the ED and whether this decision is based on CHADS<sub>2</sub> score or other factors. Atrial flutter was included along with atrial fibrillation as there is evidence demonstrating little difference in stroke risk between these two entities, with over half of patients with atrial flutter converting to fibrillation within eight years.<sup>7</sup>

### Methods

#### Study Design and Setting

This study is a secondary analysis of the Recent Onset Atrial fibrillation and Flutter (RAFF) study, a cross-sectional study of an observational cohort of patients with recent onset atrial fibrillation and flutter throughout eight EDs in Canada. We reviewed health records of all patients presenting to the ED during the 12 months between January 1st and December 31st, 2008. The eight hospitals surveyed were all fully designated academic centres with both undergraduate and resident training programs, each associated with a different university. Each centre specifically had an emergency medicine residency program. The eight EDs involved were scattered across different geographic regions within Canada, with annual ED patient censuses ranging from 45,000 to 70,000. The populations of the respective cities ranged from 125,000 to 4 million inhabitants.

#### Study Subjects

Patients selected for this study all had a primary diagnosis of recent onset atrial fibrillation or flutter (and required urgent intervention). All patients were 18 years of age or older. Patients were included in this study if they had clear evidence of

onset of atrial flutter within 48 hours of presentation or within seven days if they were therapeutically anticoagulated (i.e. INR between 2 and 3). No distinction was made between patients with a first episode of atrial fibrillation or flutter and those with a recurrence of recent onset. Patients were excluded from this study if their arrhythmia was permanent, if atrial fibrillation or flutter was not their primary diagnosis, or if they had already been included in this study. This study has been approved by the research ethics board of all hospitals involved. In this sub-study of the Canadian RAFF project, we looked at those patients of the RAFF cohort that were not already on warfarin upon admission and were not subsequently admitted.

### Data Collection

Patients were found by searching through participating ED's electronic patient databases for specific keywords (atrial flutter, atrial fibrillation, arrhythmia, palpitations). A research nurse at each center, trained by the primary investigator through conference calls, was responsible for data abstraction, which was performed with a data extraction sheet. Quality assurance was provided by a single nurse at a central coordinating centre. The first 30 patients chosen were reviewed by the coordinating centre nurse to ensure accurate patient selection. Data on selected patients was then entered into an electronic database. Although

inter-rater reliability was not formally assessed, before a specific ED was included in the trial, data from the first 25 patients entered into the database from that centre was reviewed by the coordinating center nurse to ensure consistency and accuracy of data abstraction throughout the various centres included in the study. The coordinating center nurse was also regularly in contact with the individual research nurses through phone calls and emails to clear up any ambiguities in patient data. Unclear elements were resolved by the coordinating centre nurse in conjunction with the principal investigator, and missing elements were clearly identified as such. Finally, some pertinent information was included from those patients who had a primary diagnosis of recent onset atrial fibrillation or flutter but met exclusion criteria.

### Data Analysis

Patients were first stratified into whether or not they received warfarin upon discharge from the ED. CHADS<sub>2</sub> score was calculated for each patient. We then analyzed the compiled data with descriptive statistics with 95% confidence intervals. Univariate analyses were conducted using T-test or Chi-square to select factors, including CHADS<sub>2</sub> score, associated with anticoagulation initiation. Multiple logistic regression was employed to evaluate independent predictors of anticoagulation after adjustment for confounders. Only variables with p-values less than 0.05 were included in mul-

**Table 1** | **Characteristics for 633 Patients in the Study**

Characteristic	Patients not Administered Warfarin	Patients Administered Warfarin
Number of Patients (%)	563 (88.9)	70 (11.1%)
Age in years, mean (SD)	60.3 (16.1)	68.6 (11.7)
Range	18-93	41-94
Male patients, %	60.2	52.9
Systolic BP, mean (SD)	133.4 (24.8)	139.5 (23.4)
Hours since onset of AF at presentation, mean (SD)	7.4 (9.4)	13.1 (14.5)
Hours of stay in the ED, mean (SD)	5.7 (3.5)	7.3 (4.5)
Patients medically cardioverted (%)	260 (46.2)	45 (64.3)
Hours until first trial, mean (SD)	1.8 (2.6)	2.8 (3)
Patients electrically cardioverted (%)	271 (48.1)	18 (25.7)
Hours until first trial, mean (SD)	3.5 (2.8)	4.7 (4)
Patients with CHADS <sub>2</sub> >1 (%)	99 (17.6)	21 (30)

tivariate regression analysis. Data analyses were conducted with SAS statistical software. (version 9.2; SAS Institute, Inc.).

## Results

The initial RAFF study identified a total of 2,464 RAFF patients at the 8 involved ED centers over the 12 month period. Of these, 1,068 met the initial inclusion criteria. After exclusion of patients already receiving warfarin prior to presentation to the ED, a cohort of 633 patients remained. Table 1 describes the characteristics of this cohort. There were no significant differences between patients that received warfarin and those that did not.

Univariate analysis results are listed in table 2. Factors with the highest odds ratios were heparin administration in the ED (OR 10.14, 95% CI 5.77 – 17.83), cardiology follow-up organized in the ED (OR 5.66, 95% CI 2.91 – 11.00), having a new prescription of Metoprolol at discharge (OR 4.02, 95% CI 2.22 – 7.23), and having a new prescription of Diltiazem at discharge (OR 3.01, 95% CI 1.15 – 7.91). Notably, having a CHADS<sub>2</sub> score of 2 or higher, while doubling the odds of receiving warfarin at discharge (OR 2.01), was not significantly different from having a CHADS<sub>2</sub> score of 1 or higher (OR 2.07). Major factors associated with lack of warfarin administration included electrical (OR 0.37, 95% CI 0.21 – 0.65) and medical (OR 0.26, 95% CI 0.16 – 0.44) cardioversion, and having a history of AF (OR 0.50, 95% CI 0.30 – 0.83).

Multivariate analysis demonstrated significant predictors of warfarin administration at discharge to again include heparin administration (OR 9.59, 95% CI 4.88 – 18.87), Metoprolol prescription (OR 9.59, 95% CI 4.88 – 18.87), cardiology follow-up (OR 5.61, 95% CI 2.62 – 12.02), and age by 10 year increments (OR 1.69, 95% CI 1.34 – 2.14). Odds ratios and confidence intervals are shown in table 3. Interestingly, it was found that while patients with a CHADS<sub>2</sub> score of 1 or greater had double the likelihood of warfarin administration, it no longer became an independent predictor after regression analysis.

## Limitations

The major limitations of this study relate to the difficulties in elucidating the circumstances which influenced management decisions within the ED. Firstly, the overall management of each patient, including follow-up, was not standardized, which may have contributed quantitatively to the practice gap identified. Some patients may have been referred to cardiologists or family physicians for decisions regarding anticoagulation while others, inappropriately initiated on anticoagulation in the ED, may have been taken off warfarin on subsequent follow-up. While this may have yielded a better rate of adherence to guidelines in the long term, both situations suggest inadequate management within the ED. Second, contraindications to warfarin initiation were not systematically recorded in this retrospective study. In particular,

**Table 2 | Odds Ratios for Factors Predictive of Warfarin Administration at Discharge by Univariate Analysis**

Factor	Odds Ratio	95% Confidence Interval	P Value
ED Heparin administration	10.14	5.77 – 17.83	<0.0001
Cardiology follow-up arranged in ED	5.66	2.91 – 11.00	<0.0001
New Metoprolol prescription at DC	4.02	2.22 – 7.23	<0.0001
New Diltiazem prescription at DC	3.01	1.15 – 7.91	0.0192
Rate control in ED	2.33	1.38 – 3.94	0.0013
History of HTN	2.30	1.39 – 3.83	0.001
CHADS <sub>2</sub> score 1 or higher	2.07	1.22 – 3.49	0.006
CHADS <sub>2</sub> score 2 or higher	2.01	1.15 – 3.30	0.0124
History of AF	0.50	0.30 – 0.83	0.006
Rhythm control in ED	0.39	0.21 – 0.75	0.0035
Electrical cardioversion in ED	0.37	0.21 – 0.65	0.0003
Medical cardioversion in ED	0.26	0.16 – 0.44	<0.0001
Spontaneous conversion to sinus rhythm	0.17	0.10 – 0.28	<0.0001

risk of hemorrhage, which appears to be a major factor against anticoagulation, was not part of the exclusion criteria for subject selection. Canadian guidelines recommend the use of the HAS-BLED scoring system (1 point given for each Hypertension, Abnormal renal or hepatic function, history of Stroke or Bleed, Elderly above 65 years of age, and Drugs that can increase risk of bleeding and alcohol) for assessment of risk of bleeding. Including a high HAS-BLED score as exclusion criteria may have resulted in a greater rate of warfarin administration, although the CCA guidelines remain vague about specific cut-off levels for contraindication to oral anticoagulation.<sup>8</sup> Finally, the use of novel anticoagulants such as Dabigatran and Rivaroxaban was not yet approved at the time of data collection. The introduction of these agents may significantly alter management of atrial fibrillation in the ED.

## Discussion

### Summary and Interpretation of All Findings

To our knowledge, this is the first published manuscript describing the initiation of anticoagulation in RAFF patients presenting to the ED. Furthermore, it is the first to describe this trend among major Canadian centres. Overall, there was a discrepancy between CHADS<sub>2</sub> score and warfarin initiation in the ED. The major factors that influenced warfarin initiation were heparin use in the ED, having had a new Metoprolol prescription during that visit, having been referred to cardiology for follow-up, and increasing age. One possible explanation could be that emergency physicians may simply be incognizant of the CHADS<sub>2</sub> score itself, and base the decision to initiate warfarin at discharge on other factors, such as the management received throughout their stay. Specifically, while the commonly used

agents Metoprolol and Diltiazem were both associated with oral anticoagulation administration in the univariate analysis, only Metoprolol emerged as an independent predictor, likely due to the greater familiarity and use of Metoprolol in Canadian EDs. With greater sample size, Diltiazem may have also reached statistical significance as an independent predictor. To account for the increase in anticoagulation with both Diltiazem and Metoprolol, it is plausible that patients given rate control may be perceived to suffer from more severe disease, and thus be more prone to thromboembolic disease. Similarly, history of Atrial Fibrillation was another factor that was associated with anticoagulation administration in univariate but not multivariate regression analysis. This may be due to ED physicians relying on previous decision making not to administer oral anticoagulants to guide their current management, or perhaps the belief that a history of Atrial Fibrillation may be associated with a greater likelihood of spontaneous conversion, and thus a lower risk of stroke. The overall conclusion is that patients presenting with atrial fibrillation are grossly under-coagulated as per the Canadian Cardiovascular Association (CCA)'s guidelines, and this may reflect faulty decision making.

### Comparison to Prior Studies

The issue of oral anticoagulation and chronic atrial fibrillation has been fairly well researched. Studies are consistent in reporting a general trend of under-coagulation of atrial fibrillation patients. In general, it appears that rates of anticoagulation, when stratified by CHADS<sub>2</sub> score, are roughly equivalent, with rates varying from 40%<sup>2,6</sup> to 66%.<sup>9</sup> One Australian study remarked that although nearly 70% of atrial fibrillation patients on a stroke unit had been anticoagulated, only 6% were within the therapeutic range of INR.<sup>6</sup>

**Table 3** | Independent Predictors for Warfarin Administration at Discharge after Multivariate Regression Analysis

Factor	Odds Ratio	95% Confidence Interval
ED Heparin administration	9.59	4.88-18.87
New Metoprolol prescription at discharge	9.59	4.88-18.87
Cardiology follow-up arranged	5.61	2.62-12.02
Age (vs similar patient 10 years younger)	1.69	1.34-2.14

There is nonetheless a dearth of knowledge concerning trends in warfarin administration in the setting of atrial presentation of recent onset. This is the first study to our knowledge that comments on anticoagulation in atrial fibrillation of recent onset. The Euro Heart Study, an observational study performed on over 5,000 patients with atrial fibrillation, found that rates of warfarin administration in recently diagnosed atrial fibrillation were slightly lower than in patients with so-called permanent or long-standing atrial fibrillation,<sup>10</sup> although a more recent American study found an up to 10% increase in anticoagulation rates in this group.<sup>2</sup>

Of note, while previous studies on the topic typically included only atrial fibrillation, one Canadian study released in the American Journal of Cardiology stated that mortality and stroke risk were similar between atrial fibrillation and atrial flutter.<sup>11</sup> Furthermore, the CCA suggests that atrial flutter patients be treated as atrial fibrillation patients in regard to stroke risk and need of warfarin.<sup>8</sup> We were thus justified in our inclusion of atrial flutter along with atrial fibrillation.

### Summary of Study Strengths

While many studies have addressed the issue of anticoagulation initiation in atrial fibrillation, this is the first that studies this problem from a Canadian perspective, and moreover, within the ED. With a large sample size and a patient sample representative of trends across Canada, the study design allowed for strong external validity for Canadian centers managing RAFF.

### Research Implications

Future research should focus on determining the rate of anticoagulation (with both warfarin and direct thrombin inhibitors) in those patients for which it has not been contraindicated due to bleeding risk, and whether dedicated and consistent teaching on RAFF anticoagulation guidelines and bleeding risk assessment tools such as HAS-BLED will improve anticoagulation rates within the ED.

### Clinical Implications

The results of this study point to inadequate anti-

coagulation of RAFF patients in the ED. In order to improve compliance with guidelines, further training and reinforcement of anticoagulation recommendations should be provided in ED centers. Furthermore, hesitation for warfarin initiation should be eliminated by providing emergency physicians with a clear protocol for oral anticoagulation administration, ideally including factors like fall-risk and risk of hemorrhage on warfarin. Finally, although not a specific endpoint looked at in this study, evidence from the literature alludes to much discomfort in warfarin administration due to the risk of hemorrhage. It remains a challenge to concretely assess bleeding risk when it shares many of the same risk factors as risk of stroke such as age and high blood pressure. Use of assessment tools such as the HAS-BLED score, as per Canadian Guidelines, may empower decision making in the ED by providing physicians with a quick method of measuring and balancing bleeding risk against the risk of thromboembolic disease. Pisters et al., the designers of the HAS-BLED score, suggest that bleeding risk outweighs stroke risk when HAS-BLED is greater than 2 if CHADS<sub>2</sub> is 1, and otherwise when HAS-BLED score is greater than CHADS<sub>2</sub> score.<sup>13</sup>

An important point should be made on the use of new direct thrombin inhibitors. The CCA has recently approved the use of Dabigatran for anticoagulation in AF. The RE-LY trial established that Dabigatran is non-inferior for anticoagulation, with overall less bleeding risk, and no need for regular monitoring.<sup>1</sup> Major drawbacks to Dabigatran include the increased risk of dyspepsia and gastrointestinal hemorrhage, and the lack of effective anticoagulation reversal.<sup>1,8</sup> The 2010 CCA guidelines suggest that for patients with RAFF that require oral anticoagulation, Dabigatran is preferable to warfarin, and that in those patients with increased risk of bleeding, lower-dose regimens can be used with stroke prevention equivalent to warfarin but decreased bleeding risk. As use of Dabigatran becomes more widespread over the next few years, patterns of anticoagulation may improve.

Finally, the creation of the CHA<sub>2</sub>DS<sub>2</sub>-VASc risk assessment score may in the near future alter ED practice patterns with regards to anticoagulation. With this score, age greater than 75 is given an extra point, and three factors have been added, each being given a score of one: Vascular disease, Age

65-74 years, and female Sex. This has the advantage of classifying fewer patients into the ambiguous “indeterminate” category ( $\text{CHA}_2\text{DS}_2\text{-VASc} = 1$ ), and data suggests that the low-probability category ( $\text{CHA}_2\text{DS}_2\text{-VASc} = 0$ ) truly represents a low-risk group, with no reported thrombotic events.<sup>5</sup> There are currently too few studies validating the initial data for  $\text{CHA}_2\text{DS}_2\text{-VASc}$  to be used in clinical application, though it may prove to be more effective than  $\text{CHADS}_2$ , potentially improving physician compliance.<sup>12</sup>

## Conclusions

Patients that present to the ED with atrial fibrillation and flutter of recent onset are not appropriately anticoagulated in accordance to the  $\text{CHADS}_2$  risk score as per the 2010 CCA guidelines. ED physicians’ fear of bleeding risk may be alleviated through the use of effective hemorrhage predictor tools such as HAS-BLED. More education is required to inform ED physicians’ on concrete contraindications to oral anticoagulation and to reinforce guidelines. This paper presents a way that we can look at quality of care for patients in the ED. This exercise of determining whether RAFF are adequately treated with AC is a quality indicator that should be looked at a system-wide level.

## Disclosures

No disclosures relevant to this article were made by the authors.

## References

1. Siddiqi FM, Qureshi AL. Dabigatran Etxilate, a new oral direct thrombin inhibitor, for stroke prevention in patients with atrial fibrillation. *Expert opinion on pharmacotherapy*. 2010; 11(8): 1403-11
2. Zimetbaum PJ, Thosani A, Yu HT, Xiong Y, Kothawala P, Emons M. Are atrial fibrillation receiving warfarin in accordance with stroke risk? *American journal of medicine*. 2010; 123(5): 446-53
3. Gage BF, Waterman AD, Shannon William, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: Results from the national registry for atrial fibrillation. *JAMA*. 2001; 285(22): 2864-70
4. Bernstein RA, Passman R. Prevention of stroke in patients with high risk atrial fibrillation. *Current Neurology and Neuroscience Reports*. 2010; 10(1): 34-9

5. Pamukcu B, Lip GY, Lane DA. Simplifying stroke risk stratification in atrial fibrillation patients: implications of the  $\text{CHA}_2\text{DS}_2\text{-VASc}$  risk stratification scores. *Age and Aging*. 2010; 39(5): 533-535
6. Ahmad O, Ahmad KE, Dear KB, Harvey I, Hughes A, Lueck CJ. Atrial fibrillation and anticoagulation in a stroke unit population. *Internal medicine journal*. 2009; 39(11): 752-756
7. Biblo LA, Yuan Z, Quan KJ, Mackall JA, Rimm AA. Risk of stroke in patients with atrial flutter. *American Journal of Cardiology*. 2001; 87(3):346-9.
8. Cairns JA, Connolly S, McMurtry S, Stephenson M, Talajic M et al. Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Prevention of Stroke and Systemic Thromboembolism in Atrial Fibrillation and Flutter. *Canadian Journal of Cardiology*. 2011; 27(1): 74-90
9. Altmann DR, Kuhne M, Sticherling C, Osswald S, Schaer BA. Use of the  $\text{CHADS}_2$  risk score to guide antithrombotic treatment in patients with atrial fibrillation – room for improvement. *Swiss Medical Weekly*. 2010; 140(5-6):73-7
10. Nieuwlaat R, Capucci A, Lip GY, Olsson SB, Prins MH, Nieman FH, Lopez-Sendon J, Vardas PE, Aliot E, Santini M, Crijns HJ. Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation. *European Heart Journal*. 2006; 27(24):3018-26
11. Leloirier P, Humphries KH, Krahn A, Connolly SJ, Talajic M, Green M, Sheldon R, Dorian P, Newman D, Kerr CR, Yee R, Klein GJ. Prognostic Differences between atrial fibrillation and atrial flutter. *American Journal of Cardiology*. 2004; 93(5): 647-649
12. Singer DE, Fang MC, Go AS.  $\text{CHA}_2\text{DS}_2\text{-VASc}$  risk scheme: not ready for clinical use. *Chest*. 2010; 138(4): 1020
13. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation : the Euro Heart Survey. *Chest*. 2010; 138(5): 1093-1100