# The Canadian Community Utilization of Stroke Prevention Study in Atrial Fibrillation in the Emergency Department (C-CUSP ED)

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**Study objective:** Lack of oral anticoagulation prescription in the emergency department (ED) has been identified as a care gap in atrial fibrillation patients. This study seeks to determine whether the use of a tool kit for emergency physicians with a follow-up community-based atrial fibrillation clinic resulted in greater oral anticoagulation prescription at ED discharge than usual care.

**Methods:** This was a before-after study in 5 Canadian EDs in 3 cities. Patients who presented to the ED with atrial fibrillation were eligible for inclusion. The before phase (1) was retrospective; 2 after phases (2 and 3) were prospective: phase 2 used an oral anticoagulation prescription tool for emergency physicians and patient education materials, whereas phase 3 used the same prescription tool, patient materials, atrial fibrillation educational session, and follow-up in an atrial fibrillation clinic. Each phase was 1 year long. The primary outcome was the rate of new oral anticoagulation prescription at ED discharge for patients who were oral anticoagulation eligible and not receiving oral anticoagulation at presentation.

**Results:** A total of 631 patients were included. Mean age was 69 years (SD 14 years), 47.4% were women, and 69.6% of patients had a $CHADS_2$ score greater than or equal to 1. The rate of new oral anticoagulation prescription in phase 1 was 15.8% compared with 54.1% and 47.2%, in phases 2 and 3, respectively. After multivariable adjustment, the odds ratio for new oral anticoagulation prescription was 8.03 (95% confidence interval 3.52 to 18.29) for phase 3 versus 1. The 6-month rate of oral anticoagulation use was numerically but not significantly higher in phase 3 compared with phase 2 (71.6% versus 79.4%; adjusted odds ratio 2.30; 95% confidence interval 0.89 to 5.96). The rate of major bleeding at 6 months was 0%, 0.8%, and 1% in phases 1, 2, and 3, respectively.

**Conclusion:** An oral anticoagulation prescription tool was associated with an increase in new oral anticoagulation prescription in the ED, irrespective of whether an atrial fibrillation clinic follow-up was scheduled. The use of an atrial fibrillation clinic was associated with a trend to a higher rate of oral anticoagulation at 6-month follow-up. [Ann Emerg Med. 2019;73:382-392.]

Please see page 383 for the Editor's Capsule Summary of this article.



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## INTRODUCTION

Atrial fibrillation is the most common sustained cardiac dysrhythmia and has been targeted as becoming a worldwide epidemic in the upcoming decades.[1] It is associated with significant morbidity, mortality, and cost, including a 2-fold increase in mortality and a 6-fold increase in the risk of stroke.[2,3] The attributable stroke risk caused by atrial fibrillation is 15%, two thirds of which may be prevented with adequate oral anticoagulation.[4] Administrative data in Alberta demonstrated that the use of oral anticoagulation was associated with a significantly reduced risk of stroke and all-cause mortality in patients with incident atrial fibrillation.[5] The emergency department (ED) is often the location of the first diagnosis of atrial fibrillation.[6] The Randomized Evaluation of Long-Term Anticoagulation Therapy Atrial Fibrillation Registry is an ED-based registry of 15,400 patients with ECG-documented atrial fibrillation in 46 countries; the reported use of oral anticoagulation at discharge from an ED for patients with a $CHADS_2$ score of greater than or equal to 2 was found to be 65.7%.[7] Recognizing that this is a significant gap in care of patients with atrial fibrillation[8,9] and that addressing this gap could lead to reductions in stroke and death, we sought to determine whether a multidisciplinary ED-based intervention, with prompt follow-up by a community-based clinic dedicated

**Editor's Capsule Summary**

*What is already known on this topic*

Patients evaluated for atrial fibrillation in the emergency department (ED) often do not receive oral anticoagulation prescriptions despite increased thromboembolic risk.

*What question this study addressed*

The authors measured the rate of new oral anticoagulation prescriptions by emergency physicians for eligible atrial fibrillation patients before and after exposure to educational and atrial fibrillation specialty-clinic follow-up interventions during a 24-month period in 5 EDs in Canada.

*What this study adds to our knowledge*

New oral anticoagulation prescriptions increased from 15.8% to 54.1% after the educational tool was implemented. Additional telephone and atrial fibrillation clinic follow-ups did not improve oral anticoagulation prescribing (47.2%).

*How this is relevant to clinical practice*

Prescriber education improved oral anticoagulation initiation at ED discharge but without significant improvement at 1 and 6 months.

to the care of atrial fibrillation, would improve prescription of oral anticoagulation for patients presenting to the ED with atrial fibrillation.

## MATERIALS AND METHODS

### Study Design

This was a multicenter, pragmatic, 3-phase before-after study performed in 5 EDs in 3 urban communities in Canada (North Vancouver, British Columbia; Moncton, New Brunswick; Halifax, Nova Scotia; ED census 30,000 to 60,000), using the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting.[10] Further details on the sites is included in Appendix E1, Table 1, available online at http://www.annemergmed.com. All subjects in phases 2 and 3 provided informed consent before enrollment; a waiver of consent was obtained for patients included in phase 1. The study was conducted from June 2015 to May 2017.

### Selection of Participants

Patients were eligible for inclusion if they had ECG-documented atrial fibrillation on a 12-lead ECG and presented to the participating ED. Patients were excluded if they had a prosthetic or mechanical mitral or aortic valve, had known rheumatic heart disease, were unable to provide informed consent, were admitted to hospital at their index ED visit, had a known life expectancy of less than 6 months, or had metastatic malignancy. Patients who had recurrent ED visits during the study period were included only once in either phase 2 or 3 because their identity was known by the site. Patients transferred in from other institutions who were directed to a specialty service were not eligible for participation. Patients were approached for participation by the emergency physician, but provided consent after discharge to the research coordinator at each site.

### Interventions

The study consisted of 3 phases. Phase 1 (before) was a retrospective chart review performed on consecutive patients who presented to the ED with documented atrial fibrillation in each center in the year before the beginning of intervention phases 2 and 3. Each hospital and ED chart was abstracted by trained data abstractors to obtain demographic and clinical characteristics, including reason for ED visit (atrial fibrillation or other), stroke risk factors ($CHADS_2$65, consisting of congestive heart failure, hypertension, aged 65 to 74 years, aged ≥75 years, and diabetes, each giving 1 point and previous stroke or transient ischemic attack resulting in 2 points),[11] and status of oral anticoagulation at discharge. Each of the after phases 2 and 3 were conducted for 6 months, with a 1-month changeover permitted between each phase (Figure 1). Before initiation of phase 2, each emergency physician group underwent an educational session and introduction to the study in regard to atrial fibrillation management in the ED. These sessions were uniform between sites and based on the most recent Canadian Cardiovascular Society Guidelines for ED management of atrial fibrillation.[11,12] Phase 2 was a "low-intensity" intervention phase consisting of the following components: atrial fibrillation educational materials provided to the patient in the ED, a letter to the family physician outlining the visit to the ED, and a tool for emergency physicians to guide prescription of oral anticoagulation (Figure 2). The prescription of oral anticoagulation was left to the treating physician's discretion, according to the tool provided to him or her as part of the study; however, prescription of an oral anticoagulant for 2 weeks was strongly encouraged. Phase 3 was a "high-intensity" intervention phase that consisted of the same components as phase 2, but an additional telephone follow-up at 48 to 72 hours after discharge from the ED from a nurse specializing in atrial fibrillation, with a subsequent in-clinic visit with a cardiologist within 7 days of the index ED visit. This phase was specifically designed to better understand the

**Table 1.** Baseline characteristics: overall population.

| Characteristic | Phase 1 (N=360) | Phase 2 (N=145) | Phase 3 (N=126) |
|---|---|---|---|
| Age, mean (SD), y | 70.8 (15.1) | 66.5 (11.8) | 67.4 (12.6)* |
| Sex, male, No. (%) | 199 (55.3) | 64 (44.1) | 69 (54.8) |
| Primary diagnosis of AF, No. (%) | 236 (65.6) | 130 (89.7) | 113 (89.7)* |
| New-onset AF, No. (%) | 81 (22.5) | 69 (47.6) | 60 (47.6)* |
| Heart failure, No. (%) | 36 (10.0) | 8 (5.5) | 7 (5.6) |
| Hypertension, No. (%) | 168 (46.7) | 89 (61.4) | 79 (62.7)* |
| Diabetes mellitus, No. (%) | 46 (12.8) | 24 (16.6) | 18 (14.3) |
| Stroke/transient ischemic attack/systemic thromboembolism, No. (%) | 38 (10.6) | 14 (9.7) | 16 (12.7) |
| Vascular disease, No. (%) | 47 (13.1) | 7 (4.8) | 10 (7.9) |
| $CHADS_2$ score, median (IQR) | 1.0 (0.0–2.0) | 1.0 (0.0–2.0) | 1.0 (0.0–2.0) |
| $CHA_2DS_2$-VASc score, median (IQR) | 3.0 (1.0–4.0) | 2.0 (1.0–4.0) | 2.0 (1.0–4.0) |
| HAS-BLED score, median (IQR) | 1.0 (1.0–1.0) | 1.0 (0.0–1.0) | 1.0 (1.0–2.0) |
| Oral anticoagulation before ED visit, No. (%) | 167 (46.4) | 42 (29.0) | 36 (28.6) |

*AF*, Atrial fibrillation; *IQR*, interquartile range.
*$P<0.05$.

effect of early follow-up after ED discharge on ED prescription of oral anticoagulation. A single group educational session of 1 hour's duration was also offered to patients in phase 3 but was not mandatory as part of participation. These were performed by the atrial fibrillation clinic nurse at each site, at the hospital where the study took place. Patients were followed with 1-month and 6-month telephone calls to determine bleeding incidence, stroke, ED visits, hospitalizations, and status of oral anticoagulation.

The patients were grouped as follows: (1) efficacy analysis population: patients not previously receiving oral anticoagulation at the ED visit and who were oral anticoagulation eligible, defined as aged 65 years or older or $CHADS_2$ score greater than or equal to 1, according to the Canadian Cardiovascular Society atrial fibrillation guidelines[13]; (2) oral anticoagulation eligible population: defined as aged 65 years or older or $CHADS_2$ score greater than or equal to 1; and (3) the overall population. Patients were classified as having primary atrial fibrillation if this was the diagnosis most responsible for their ED visit. New-onset atrial fibrillation was defined as not having a diagnosis before the ED visit.

The tool kit was developed using an iterative process involving input from experts in knowledge translation

| Timeline | Phase | Study design | Intervention | Consent | Patient recruitment | Follow-up |
|---|---|---|---|---|---|---|
| 'Before' | Phase 1 N=360 | Retrospective chart review | none | Waiver of consent obtained | Consecutive patients | none |
| 'After' | | | | | | |
| 6 months | Phase 2 N=145 | Prospective recruitment of patients | a b c | Written consent | Consenting patients | 30 days and 6 months from ED visit by telephone |
| 6 months | Phase 3 N=126 | Prospective recruitment of patients | a b c d | Written consent | Consenting patients | 30 days and 6 months from ED visit by telephone |

a OAC tool used by emergency physician (Figure 2); OAC prescription given at physician discretion

b Package of written information about AF handed to patient at ED visit (based on Heart and Stroke Foundation of Canada)

c Letter sent from ED to family physician

d Telephone call within 48-72 hours of ED visit to review stroke risk followed by in-clinic visit with AF clinic nurse supervised by specialist within 7-10 days of ED visit; letter to family physician regarding treatment plan

**Figure 1.** Study description.

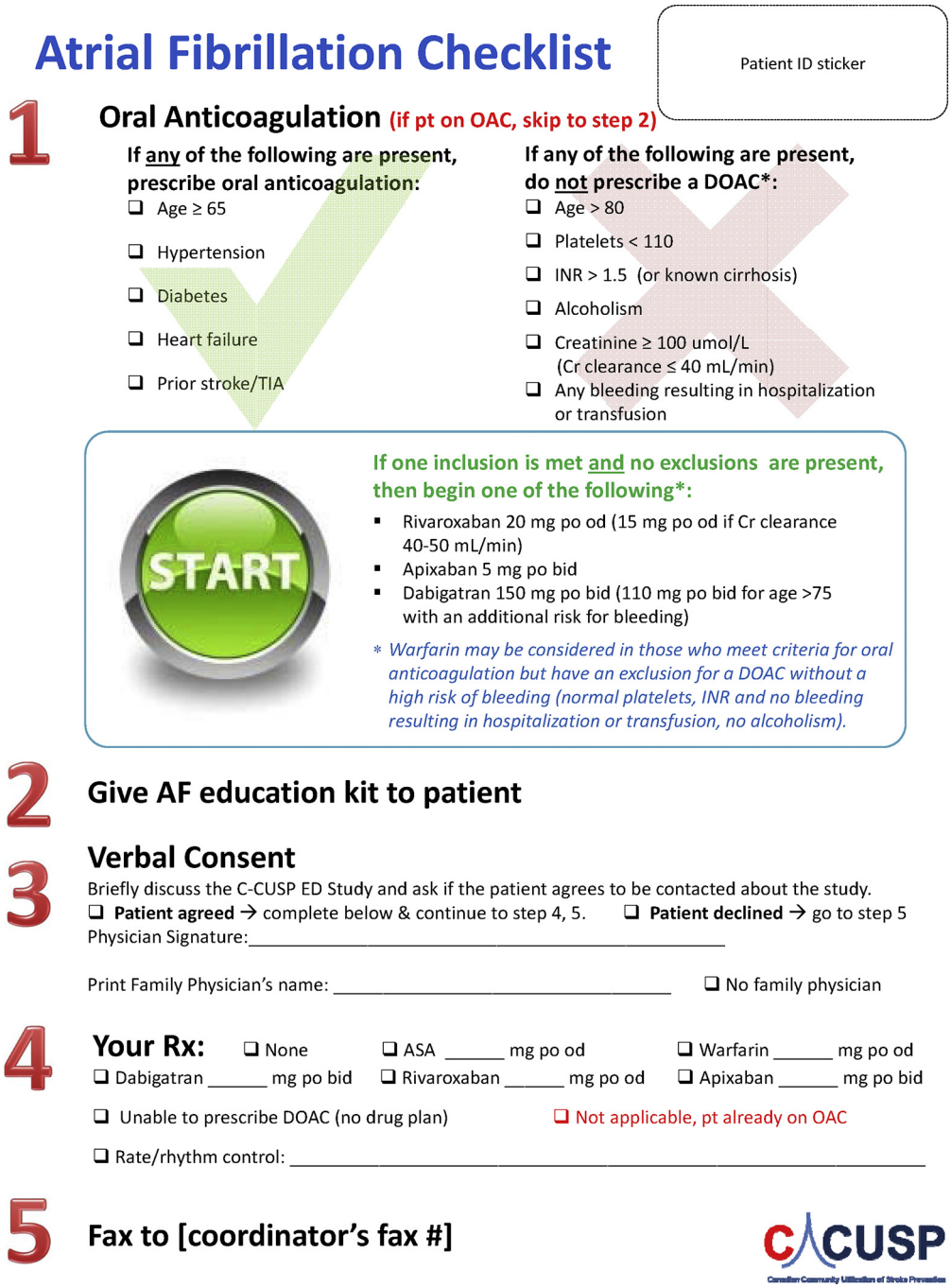


**Figure 2.** Tool used in the ED to guide oral anticoagulation prescription.

strategies (J.K., D.B., J.C., and I.D.G.), cardiac electrophysiologists (R.P., P.D., S.C., and J.H.), cardiologists (M.D. and T.H.), a family physician (N.I.), emergency physicians (K.M., M.M., M.C., G.A., B.R., and C.A.), epidemiologists and clinical trialists (R.P., L.T., R.N., S.C., and J.H.), and a pharmacist (L.D.). Input was obtained during several face-to-face meetings held by the Canadian Stroke Prevention Intervention Network, funded by the Canadian Institute of Health Research. The knowledge-to-action framework was used for development of the tools.[14] The following values for the atrial fibrillation prescription tool were derived from these meetings:

1) Safety to ensure that patients at high risk of bleeding were not provided with a prescription for oral anticoagulation. These safety measures were derived from the HAS-BLED score (hypertension, abnormal renal/liver function, stroke, bleeding predisposition, labile international normalized ratio [INR], age >65,

drugs [concomitant aspirin or non-steroidal anti-inflammatory or alcohol]) and included older than 80 years, platelet levels less than $110\times10^9$/L, INR greater than 1.5 or known cirrhosis, alcoholism, creatinine level greater than or equal to 100 μmol/L (or creatinine clearance ≤40 mL/min), and any bleeding resulting in hospitalization or transfusion.[15] The age cutoff of 80 years was derived from consensus as a guide to emergency physicians to ensure safe oral anticoagulation prescription for patients who had not previously been prescribed oral anticoagulation, but is not an exclusion to oral anticoagulation in the HAS-BLED score or other scores that profile risk of oral anticoagulation use. All educational sessions for the emergency physicians were funded by the Canadian Stroke Prevention Intervention Network and by the Heart and Stroke Foundation of Canada.

2) Short-term oral anticoagulation prescription for 2 weeks, followed by follow-up with general practitioner.
3) Prescription of oral anticoagulation according to the Canadian Cardiovascular Society atrial fibrillation guidelines.[13]

The checklist went through multiple iterations until consensus was achieved. The tool kit was available in print only for the study.

## Methods of Measurement

Each data abstractor at the sites was trained by the coordinating center to ensure homogeneity in data collection and was trained on a standardized data collection tool (see Appendix E1, available online at http://www.annemergmed.com, for details). The methods for chart reviews of ED records provided guidance for the data collection methods. Definitions for each field were provided (Appendix E1, available online at http://www.annemergmed.com) on the case report forms. Data abstractors collected patient demographics, including age at ED presentation, sex, date of ED visit, pulse rate, type of atrial fibrillation, primary diagnosis of ED visit, $CHADS_2$ score,[16] HAS-BLED score,[15,17] family physician, oral anticoagulation at the ED visit, and oral anticoagulation prescription at discharge. These were obtained from the ED visit. Further data on other cardiac history, sleep apnea, pulmonary disease, thyroid disease, medication history, bleeding, and laboratory investigations were obtained from the electronic medical record at the participating hospital. The telephone follow-up was performed by a single research assistant to ensure uniformity in data collection across sites. Data for bleeding events, repeated ED visits, and hospitalizations were obtained through review of the electronic medical record by each data abstractor at the participating site to ensure homogeneity of data collection between phases 1, 2, and 3. Data for oral anticoagulation prescription at follow-up were obtained through telephone follow-up only and hence were available for phases 2 and 3 only. Further details on data abstraction are presented in Appendix E1, available online at http://www.annemergmed.com.

## Outcome Measures

The primary outcome was the rate of new oral anticoagulation prescription at ED discharge for patients not previously receiving oral anticoagulation at the ED visit and who were oral anticoagulation eligible. New oral anticoagulation prescription was defined as a prescription for one of rivaroxaban, dabigatran, apixaban, or warfarin. This determination was made from the ED chart in all 3 phases. The primary analysis compared this outcome between phases 1 and 3. Secondary outcomes included the rate of new oral anticoagulation prescription in phase 2 compared with phase 1, as well as between phases 2 and 3; the oral anticoagulation prescription rate in oral-anticoagulation-eligible patients at 30 days and 6 months was compared between phases 2 and 3; major and minor bleeding, stroke, atrial fibrillation–related ED visits, and hospitalizations were compared between phases 2 and 3. Major bleeding was defined as bleeding that was not a hemorrhagic stroke but required hospitalization or caused a decrease in hemoglobin level of greater than 2 g/L or required a blood transfusion.[18] All other bleeding was classified as minor. A tertiary outcome was the uptake of the tool kit by the emergency physician; this was calculated as the rate of number of tool kits used compared with the overall number of patients with atrial fibrillation who presented during phases 2 and 3.

## Primary Data Analysis

The proposed sample size was based on the primary outcome examining the rate of new oral anticoagulation prescriptions given to the patient in the ED for those who were not receiving oral anticoagulation and were oral anticoagulation eligible. Using a weighted average from previous ED-based studies,[7-9] we estimated that the baseline new prescription rate for oral anticoagulation in the control group (phase 1) would be 22.4%. It was projected that the rate of new prescriptions would be 50% in phase 3 according to previous data.[19] With the above assumptions, a sample size of 47 patients who were not receiving oral anticoagulation and were oral anticoagulation eligible in each of phases 1 and 3 (ie, 94 patients in total) would be required to achieve 80% power at $\alpha=.05$ to detect a difference in rate of new oral anticoagulation

prescriptions between phases 1 and 3. Alternatively, if we assumed the analysis population in phase 1 was equal to that in phase 3 and the prescription rate in phase 1 remained the same (15.8%), then we would have 80% power to detect a difference of 6.1% between phases 1 and 3. The lowest prescription rate in phase 3 would be 21.9% to result in a detectable difference.

Patient characteristics were summarized as mean (SD) or median (interquartile range) for continuous variables, depending on the normality of distribution and frequency (percentage) for categorical variables. The normality of each continuous variable was examined with a combined approach, including visual inspection through histogram with fitted normal curve and Q-Q plot, and assessment using skewness and kurtosis. Pairwise difference between phases with corresponding 95% confidence interval (CI) were calculated with the Welch-Satterthwaite method for mean, Hodges-Lehmann method for median, and Wald method for proportion.

In this study, we implemented a logistic regression model with center treated as fixed effect to account for the underlying correlation of clustered observations because it was shown to perform better than multilevel model and generalized estimating equations when the number of clusters was extremely small ($N \leq 10$).[20,21] Considering the nonrandomized nature of this study, the models were adjusted for the following potential confounding factors: individual components of $CHA_2DS_2$-VASc scores (age, sex, heart failure, hypertension, previous thromboembolic event, diabetes, and vascular disease), previous risk of bleeding, and atrial fibrillation as the primary diagnosis in the ED. Hosmer-Lemeshow goodness-of-fit test was applied to evaluate the model fit. Results were expressed as odds ratios (ORs) with corresponding 2-sided 95% CIs and associated *P* values. Independent predictors of oral anticoagulation use at 6 months were identified with a logistic regression model. The initial model included all clinical variables suspected to be associated with oral anticoagulation use and those identified in univariate analysis with $P<.25$. A backward elimination approach was then applied to individually remove covariates with $P>0.10$ in the multivariable model, starting with those with the highest *P* value. Finally, to identify remaining potential confounders, all of the dropped variables were individually readded to the multivariable model and kept in it if the effect size of any other predictors changed by greater than 10%. Subgroups identified a priori were sex and $CHADS_2$ score greater than or equal to 2. All statistical analyses were performed with SAS (version 9.4; SAS Institute, Inc., Cary, NC). Unless otherwise stated, all hypothesis tests were conducted with 2-sided tests at the .05 level of significance. No adjustment for multiple testing was made because the secondary analyses were conducted for exploratory purposes.

## RESULTS

There were 631 patients included in the study in all 3 phases (phase 1 n=360; phase 2 n=145; and phase 3 n=126) (Table 1, Figure 3). In phases 2 and 3, there were 3,242 patients with a diagnosis of atrial fibrillation during these phases. Of these, 495 patients (15.2%) underwent use of the atrial fibrillation checklist. Compared with phase 3, which included the atrial fibrillation clinic in follow-up, patients in phase 1 were older (70.8 [SD 15.1] versus 67.4 [SD 12.6] years) and less likely to have a primary diagnosis of atrial fibrillation (65.6% versus 89.7%) or new-onset atrial fibrillation (22.5% versus 47.6%). For patients who were oral anticoagulation eligible and not receiving oral anticoagulation at the ED visit, those in phase 1 were older (74.7 [SD 12.4] versus 69.7 [SD 9.3] years), and fewer had a primary diagnosis of atrial fibrillation (73.3% versus 94.4%) or new-onset atrial fibrillation (46.7% versus 65.3%) than those in phase 3. There were no differences in the $CHADS_2$, $CHA_2DS_2$-VASc, or HAS-BLED scores (Table 2). There were no differences in baseline characteristics between phases 2 and 3. On implementation of the intervention, the checklist was used in 15.2% of ED visits for atrial fibrillation.

At ED presentation, there were 167 patients (46.4%) receiving oral anticoagulation in phase 1, 42 (29.0%) in phase 2, and 36 (28.6%) in phase 3. These patients were excluded from the primary analysis. For patients who were oral anticoagulation eligible and not receiving oral anticoagulation at the ED visit, the rate of oral anticoagulation at ED discharge increased from 15.8% in phase 1 to 54.1% in phase 2 and 47.2% in phase 3 (unadjusted OR 7.10, 95% CI 3.33 to 15.13 and adjusted OR 8.03, 95% CI 3.52 to 18.29 for phase 3 versus 1; unadjusted OR 8.64, 95% CI 4.13 to 18.04 and adjusted OR 10.01, 95% CI 4.38 to 22.86 for phase 2 versus 1) (Tables 3 and 4). The increase in rate of new oral anticoagulation prescription in phase 3 compared with phase 1 was 31.4% (95% CI 18.2% to 44.6%) (Table 3). Comparing phase 2 with phase 1 demonstrated a 38.2% increase (95% CI 25.1% to 51.3%) in rate of oral anticoagulation prescription. No statistically significant difference in oral anticoagulation prescription was observed when phase 3 was compared with phase 2 (adjusted OR 0.80; 95% CI 0.39 to 1.65). On subgroup analysis by sex and $CHADS_2$ score ($\geq 2$ versus $<2$), no significant interaction was observed (Table 4).

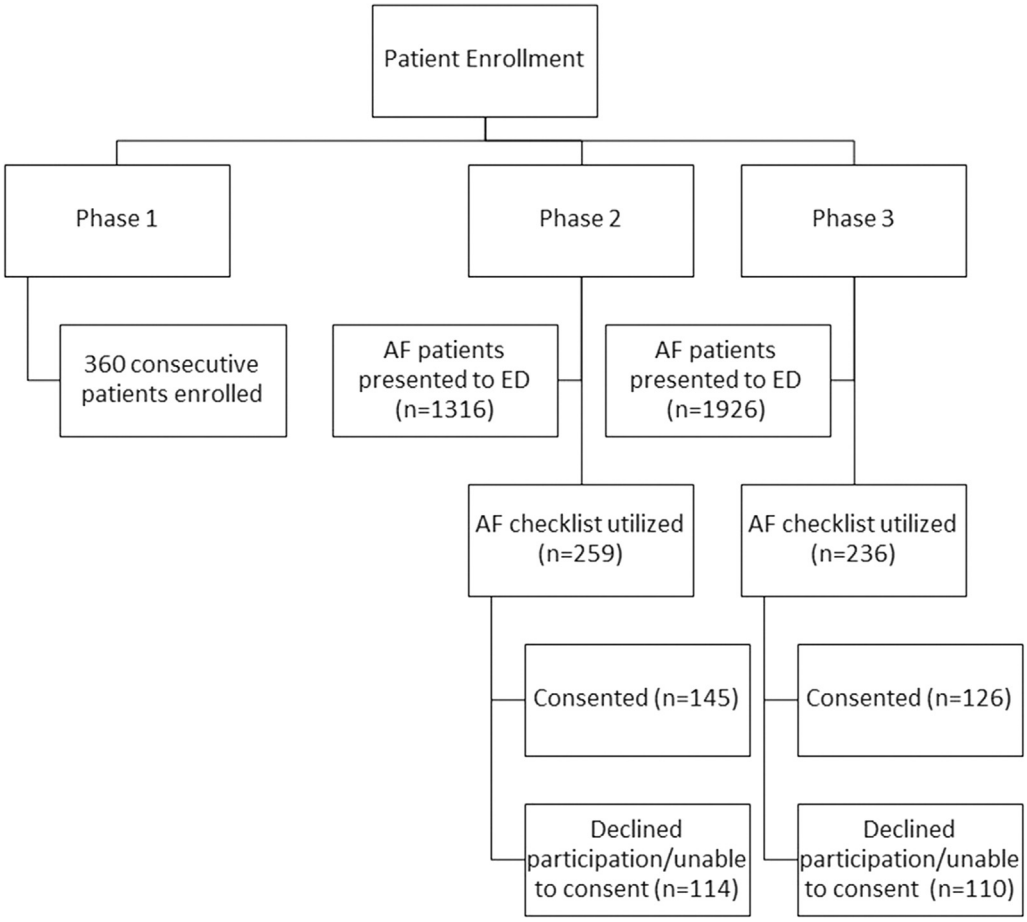


**Figure 3.** Patient enrollment by phase.

Follow-up data were available for 133 patients at 1 month and 127 at 6 months in phase 2, and 117 patients at 1 month and 107 at 6 months in phase 3. The reason for any patients lost to follow-up was inability to connect by telephone. At 30 days for the patients who were not receiving oral anticoagulation at the ED visit and were oral anticoagulation eligible, the oral anticoagulation rate was 63.2% in phase 2 and 72.1% in phase 3 (adjusted OR 1.51; 95% CI 0.66 to 3.44). At 6 months, oral anticoagulation use in this same group was numerically

**Table 2.** Baseline characteristics: efficacy analysis population (patients who are oral anticoagulation eligible and not receiving oral anticoagulation at presentation to the ED).

| Characteristic | Phase 1 (N=120) | Phase 2 (N=74) | Phase 3 (N=72) |
|---|---|---|---|
| Age, mean (SD), y | 74.7 (12.4) | 68.2 (10.7) | 69.7 (9.3) |
| Sex, male, No. (%) | 62 (51.7) | 29 (39.2) | 37 (51.4) |
| Primary diagnosis of AF, No. (%) | 88 (73.3) | 69 (93.2) | 68 (94.4) |
| New-onset AF, No. (%) | 56 (46.7) | 51 (68.9) | 47 (65.3) |
| Heart failure, No. (%) | 8 (6.7) | 3 (4.1) | 3 (4.2) |
| Hypertension, No. (%) | 64 (53.3) | 57 (77.0) | 52 (72.2) |
| Diabetes mellitus, No. (%) | 20 (16.7) | 15 (20.3) | 13 (18.1) |
| Stroke/transient ischemic attack/systemic thromboembolism, No. (%) | 14 (11.7) | 5 (6.8) | 7 (9.7) |
| Vascular disease, No. (%) | 9 (7.5) | 3 (4.1) | 6 (8.3) |
| $CHADS_2$ score, median (IQR) | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) |
| $CHA_2DS_2$-VASc score, median (IQR) | 3.0 (2.0–4.0) | 3.0 (2.0–4.0) | 2.0 (2.0–4.0) |
| HAS-BLED score, median (IQR) | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) |

**Table 3.** New oral anticoagulation prescription between 3 phases.

| Phase | Warfarin | Direct Oral Anticoagulant | Total |
|---|---|---|---|
| 1 | 5.0 | 10.8 | 15.8 |
| 2 | 10.8 | 43.3 | 54.1 |
| 3 | 8.3 | 38.9 | 47.2 |
| **Phase Comparison** | | **Rate Difference (95% CI)*** | |
| 3 vs 1 | | 31.4 (18.1 to ≈44.6) | |
| 2 vs 1 | | 38.2 (25.1 to ≈51.3) | |
| 3 vs 2 | | -6.8 (-23.0 to ≈9.4) | |

*Based on normal approximation to binomial distribution.

higher in phase 3 than in phase 2, although it did not reach statistical significance (71.6% versus 79.4%; adjusted OR 2.30; 95% CI 0.89 to 5.96). The predictors of oral anticoagulation use at 6 months in the oral-anticoagulation-eligible population on univariate analysis were older age, oral anticoagulation prescription before or at the ED visit, female sex, and specialist visit (Table 5). On multivariable analysis, oral anticoagulation before or at the ED visit and specialist visit remained the most important predictors of oral anticoagulation use at 6 months.

The rate of stroke at 6 months was 1.4% in phase 1, 1.6% in phase 2, and 1.9% in phase 3, with no significant difference between groups. Of the 9 patients who experienced a stroke, 3 were not receiving oral anticoagulation at their initial ED visit; it is unknown whether these patients were receiving therapeutic oral anticoagulation at the stroke. Major bleeding was observed in 0%, 0.8%, and 1.0% of patients in phases 1, 2, and 3, respectively. Minor bleeding was observed in 0.8%, 4.0%, and 1.0% of patients in phases 1, 2, and 3, respectively. There was no significant difference in any of these outcomes among the phases, except for minor bleeding, which was higher in phase 2.

Recurrent ED visits for atrial fibrillation–related reasons occurred for 37.6% of patients (221/588) at 6-month follow-up. There was no difference in the rate of atrial fibrillation–related ED visits between the 3 phases (37.5%, 37.9%, and 37.5%). There was a trend toward a reduction in atrial fibrillation–related hospitalizations in phases 2 and 3 (8.0% and 5.8%, respectively) compared with phase 1 (12.8%), but on multivariable analysis, no difference in atrial fibrillation–related hospitalizations or ED visits was found among the 3 phases.

## LIMITATIONS

There are some limitations to our study. It used a before-after design with a historical control, rather than a contemporaneous one. This design was chosen to permit the study intervention to result in minimal disruption in ED flow, which may have affected use of the tool. Alternatively, there may have been selection bias because recruitment of patients depended on their identification by the emergency physician in phases 2 and 3; the overall use of the tool was 15.2%. This may have resulted in an overestimate of the effect of the ED tool, but nevertheless, after multivariable adjustment of baseline characteristics, when the tool was not used it remained a significant predictor of increased oral anticoagulation prescription in patients for whom it was applied.

Limited data were available on the differences in baseline characteristics between patients who consented compared with those who did not. From the data available on these patients, there were no significant differences. We expect that if all patients presenting to the ED were included in phases 2 and 3, the population would be similar to what was observed in phase 1; however, the differences that were present provide some insight into which patients emergency physicians may be more likely to use such a tool for, such as those presenting with a primary diagnosis of atrial fibrillation, younger age, and new-onset atrial fibrillation.

The study had a short follow-up and was not powered to detect differences in ED visits or hospitalizations, so these outcomes should be interpreted with caution. In addition, the instructions given to patients in regard to when to return to the ED were not standardized among emergency physicians participating in the study, although the educational information provided to the patient was consistent.

**Table 4.** Oral anticoagulation prescription in oral-anticoagulation-eligible patients not receiving oral anticoagulation at presentation to the ED.

| OR | Phase 3 vs Phase 1 (95% CI) | Phase 2 vs Phase 1 (95% CI) | Phase 3 vs Phase 2 (95% CI) |
|---|---|---|---|
| Unadjusted | 7.10 (3.33–15.13)* | 8.64 (4.13–18.04) | 0.82 (0.41–1.64) |
| Adjusted† | 8.03 (3.52–18.29)* | 10.01 (4.38–22.86) | 0.80 (0.39–1.65) |

*$P<0.001$.

†Analysis was performed with a logistic model with the center treated as fixed effect, with or without adjustment of age, sex, individual components of $CHA_2DS_2$-VASc scores (hypertension, heart failure, previous thromboembolic event, diabetes, and vascular disease), history of bleeding, and AF as the primary diagnosis in the ED.

**Table 5.** Predictors of oral anticoagulation use at 6 months for patients who were oral anticoagulation eligible.

| | Univariate Analysis, OR (95% CI) | Final Model, OR (95% CI) |
|---|---|---|
| AF clinic (phase 3 vs 2) | 1.60 (0.76–3.39) | 2.18 (0.72–6.57) |
| OAC use before or at ED discharge | 9.54 (3.96–22.95) | 17.14 (4.79–61.35) |
| Age per 10-y increment | 1.66 (1.16–2.38) | 1.45 (0.85–2.47) |
| Sex, female | 2.22 (1.05–4.71) | 2.55 (0.86–7.54) |
| AF as primary diagnosis | 0.46 (0.10–2.11) | —* |
| Heart failure | 0.82 (0.21–3.13) | 0.19 (0.02–2.18) |
| Hypertension | 0.87 (0.35–2.17) | — |
| Diabetes | 1.61 (0.57–4.55) | — |
| Stroke/TIA/TE | 2.22 (0.62–7.98) | — |
| Vascular disease | 0.64 (0.16–2.55) | — |
| Previous bleeding | 1.53 (0.18–13.32) | — |
| Specialist† visit | 2.83 (1.02–7.80) | 4.83 (1.17–20.04) |

*OAC*, Oral anticoagulation; *TIA*, transient ischemic attack; *TE*, thromboembolism.
*Dashes indicate data not included in final model.
†Internal medicine specialist or cardiologist.

There are known limitations to retrospective data collection.[17,22] We made multiple efforts to limit the bias by predefinition of outcomes measures, periodic meetings with data abstractors, detailed protocol, and training of data abstractors. The data abstractors were not blinded to the phase of the study. This may have introduced some bias; however, the endpoint used was quantitative rather than qualitative, limiting the effect of lack of blinding.

Finally, residual confounding factors not adjusted for in the multivariable analysis could be another limitation.

## DISCUSSION

This study suggests that a simple intervention to guide oral anticoagulation prescription in the ED was associated with an increase in the rate of prescription of oral anticoagulation for patients who are at risk for stroke. We found that oral anticoagulation prescriptions increased by greater than 30% after the introduction of a simple ED oral anticoagulation prescription tool in combination with a patient educational pamphlet. The increased use of oral anticoagulation was sustained during 6 months of follow-up.

To our knowledge, this is the largest study to use an ED-based tool to increase oral anticoagulation prescription at discharge for patients who present to the ED with atrial fibrillation. The tool used in this study was designed to be scalable and easily implementable for broad use in the ED community. To ensure safety within our protocol, we designed our atrial fibrillation checklist with this in mind. One of the limitations we placed on oral anticoagulation prescription in the ED was for patients older than 80 years. The investigators thought that this population might be at increased risk of bleeding, according to previous studies,[15] and that these patients should undergo rigorous assessment by their family physician, with close observation, when oral anticoagulation is to be initiated. This was a safeguard in our study but may not necessarily be applied if this checklist were to be used in the future.

In our study, the addition of an atrial fibrillation clinic did not change ED prescribing behavior, refuting the hypothesis that early follow-up postdischarge will result in greater oral anticoagulation prescription from the emergency physician. Other studies have piloted using a rapid referral process (within 7 days) to an atrial fibrillation clinic and a toll-free hotline to evaluate outcomes in patients who present with recent-onset atrial fibrillation to an ED.[23] Similar programs with atrial fibrillation clinics have been established and have demonstrated reductions in ED visits and hospitalizations, and have shown increased rates of oral anticoagulation prescription over usual care, but the effect of these programs on ED management has not been previously evaluated, to our knowledge.[24-26] This study did demonstrate a trend toward increased oral anticoagulation use at 6 months with the addition of the atrial fibrillation clinic. A 79% rate of oral anticoagulation use for patients presenting to the ED, as observed in phase 3 at 6 months, is among the highest rates for ambulatory patients with atrial fibrillation.[7,27,28] A recent study demonstrated similar improvements during a short intervention period at 2 urban sites using an atrial fibrillation and atrial flutter pathway, with new oral anticoagulation increasing from 48.6% to 70.2% after implementation.[29]

Our findings suggest that the management decisions made during the encounter in the ED may be a critical point in the patient's care pathway for atrial fibrillation. Acute management of atrial fibrillation is the focus of an ED visit; whether oral anticoagulation prescription is part of acute management has been controversial. Similar findings were reported by a study using administrative data in Ontario, in which prescription of oral anticoagulation at the ED visit was associated with persistence at 6 months.[8] We found a high rate of return visits to the ED for atrial fibrillation–related reasons, reaching 37.6% at 6 months, with a trend toward reduction in hospitalization for atrial fibrillation–related causes in phases 2 and 3. This finding is in contrast to those of other studies that have demonstrated significant benefits with an atrial fibrillation clinic in these outcomes.[24,25] It is possible that the lack of ongoing follow-up with the atrial fibrillation clinic contributed to this finding because the clinic was available only in the context

of the research study. Patients were encouraged to make contact with the atrial fibrillation clinic for ongoing issues, but follow-up visits were not part of the protocol. This finding may be important in determining how resources should be allocated in the use of atrial fibrillation clinics, and that continuity of care with the atrial fibrillation clinic may be critical to providing a reduction in important atrial fibrillation–related outcomes, including recurrent ED visits and hospitalizations, as well as ensuring persistence of oral anticoagulation use.

There are important issues that need to be highlighted about the prescription of oral anticoagulation in the ED. Management of atrial fibrillation in the ED has primarily focused on restoring sinus rhythm and achieving adequate rate control, and less on preventing stroke. In a multicenter cohort study by Stiell et al[30] of atrial fibrillation patients presenting to the ED, 8.6% of patients received a prescription for oral anticoagulation at 30 days. A cohort study demonstrated a 0.7% risk of stroke at 30 days in patients who underwent cardioversion in the ED, without anticoagulation.[31] Barrett and Marill[32] proposed the notion that short-term prescription of oral anticoagulation, as was mandated in this study, is an appropriate option for emergency physicians, providing stroke prevention for patients and minimizing risks associated with long-term anticoagulation. Prescription of long-term oral anticoagulation has generally been performed by physicians who provide longitudinal care for the patient to ensure sufficient time for discussion of risks and benefits and provide adequate follow-up. The rate of bleeding associated with oral anticoagulation prescription in the ED in this study was low and was similar to the rate of stroke in the 6-month follow-up period. This study was not powered to detect differences in these outcomes, but it does suggest that there is no significant harm from increased oral anticoagulation prescription in the ED. Finally, the indications for oral anticoagulation use vary somewhat between guidelines; these variations are subtle and would need to be considered in the application of our intervention if used in jurisdictions aside from Canada.[33,34]

As the survival rate for patients older than 65 years continues to improve, the burden of atrial fibrillation worldwide will continue to increase. Atrial fibrillation–related stroke continues to be a source of significant morbidity and mortality. The ED is often the first point of diagnosis for this condition, for which appropriate management to reduce stroke, as well as recurrent ED visits and hospitalizations, is required. Further work to implement this intervention widely to assist in addressing the gap in atrial fibrillation–related stroke prevention should be performed.

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## REFERENCES

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 study. *Circulation*. 2014;129:837-847.

2. Wolf PA, Dawber TR, Thomas HE Jr, et al. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. *Neurology*. 1978;28:973-977.
3. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation: a major contributor to stroke in the elderly. The Framingham study. *Arch Intern Med*. 1987;147:1561-1564.
4. Gladstone DJ, Bui E, Fang J, et al. Potentially preventable strokes in high-risk patients with atrial fibrillation who are not adequately anticoagulated. *Stroke*. 2009;40:235-240.
5. Yu AY, Malo S, Wilton S, et al. Anticoagulation and population risk of stroke and death in incident atrial fibrillation: a population-based cohort study. *CMAJ Open*. 2016;4:E1-E6.
6. Lip GY, Tse HF. Management of atrial fibrillation. *Lancet*. 2007;370: 604-618.
7. Oldgren J, Healey JS, Ezekowitz M, et al. Variations in cause and management of atrial fibrillation in a prospective registry of 15,400 emergency department patients in 46 countries: the RE-LY Atrial Fibrillation Registry. *Circulation*. 2014;129:1568-1576.
8. Atzema CL, Austin PC, Chong AS, et al. The long-term use of warfarin among atrial fibrillation patients discharged from an emergency department with a warfarin prescription. *Ann Emerg Med*. 2015.
9. Scheuermeyer FX, Innes G, Pourvali R, et al. Missed opportunities for appropriate anticoagulation among emergency department patients with uncomplicated atrial fibrillation or flutter. *Ann Emerg Med*. 2013;62:557-565.
10. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370:1453-1457.
11. Verma A, Cairns JA, Mitchell LB, et al. 2014 Focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. *Can J Cardiol*. 2014;30:1114-1130.
12. Stiell IG, Birnie D. Managing recent-onset atrial fibrillation in the emergency department. *Ann Emerg Med*. 2011;57:31-32.
13. Skanes AC, Healey JS, Cairns JA, et al. Focused 2012 update of the Canadian Cardiovascular Society atrial fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. *Can J Cardiol*. 2012;28:125-136.
14. Graham ID, Logan J, Harrison MB, et al. Lost in knowledge translation: time for a map? *J Contin Educ Health Prof*. 2006;26:13-24.
15. Pisters R, Lane DA, Nieuwlaat R, et al. 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;138:1093-1100.
16. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285:2864-2870.
17. Gilbert EH, Lowenstein SR, Koziol-McLain J, et al. Chart reviews in emergency medicine research: where are the methods? *Ann Emerg Med*. 1996;27:305-308.
18. Schulman S, Kearon C. Subcommittee on Control of Anticoagulation of the Scientific Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *J Thromb Haemost*. 2005;3:692-694.
19. Elmouchi DA, VanOosterhout S, Muthusamy P, et al. Impact of an emergency department–initiated clinical protocol for the evaluation and treatment of atrial fibrillation. *Crit Pathw Cardiol*. 2014;13:43-48.
20. McNeish D, Stapleton LM. Modeling clustered data with very few clusters. *Multivariate Behav Res*. 2016;51:495-518.
21. Kahan BC. Accounting for centre-effects in multicentre trials with a binary outcome—when, why, and how? *BMC Med Res Methodol*. 2014;14:20.
22. Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. *Ann Emerg Med*. 2014;64:292-298.
23. Angaran P, Mariano Z, Dragan V, et al. The Atrial Fibrillation Therapies After ER Visit: outpatient care for patients with acute AF—the AFTER3 study. *J Atr Fibrillation*. 2015;7:1187.
24. Carter L, Gardner M, Magee K, et al. An integrated management approach to atrial fibrillation. *J Am Heart Assoc*. 2016;5:1-10.
25. Gillis AM, Burland L, Arnburg B, et al. Treating the right patient at the right time: an innovative approach to the management of atrial fibrillation. *Can J Cardiol*. 2008;24:195-198.
26. Hendriks JM, de Wit WR, Crijns HJ, et al. Nurse-led care vs usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs routine clinical care in ambulatory patients with atrial fibrillation. *Eur Heart J*. 2012;33:2692-2699.
27. Fauchier L, Lecoq C, Clementy N, et al. Oral anticoagulation and the risk of stroke or death in patients with atrial fibrillation and one additional stroke risk factor: the Loire Valley Atrial Fibrillation Project. *Chest*. 2016;149:960-968.
28. Cullen MW, Kim S, Piccini JP Sr, et al. Risks and benefits of anticoagulation in atrial fibrillation: insights from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry. *Circ Cardiovasc Qual Outcomes*. 2013;6:461-469.
29. Barbic D, DeWitt C, Harris D, et al. Implementation of an emergency department atrial fibrillation and flutter pathway improves rates of appropriate anticoagulation, reduces length of stay and thirty-day revisit rates for congestive heart failure. *CJEM*. 2018;20:392-400.
30. Stiell IG, Clement CM, Rowe BH, et al. Outcomes for emergency department patients with recent-onset atrial fibrillation and flutter treated in Canadian hospitals. *Ann Emerg Med*. 2017;69:562-571.e2.
31. Nuotio I, Hartikainen JE, Gronberg T, et al. Time to cardioversion for acute atrial fibrillation and thromboembolic complications. *JAMA*. 2014;312:647-649.
32. Barrett TW, Marill KA. Anticoagulation for emergency department patients with atrial fibrillation: is our duty to inform or prescribe? *Ann Emerg Med*. 2013;62:566-568.
33. Camm AJ, Lip GY, De Caterina R, et al. 2012 Focused update of the ESC guidelines for the management of atrial fibrillation: an update of the 2010 ESC guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J*. 2012;33:2719-2747.
34. January CT, Wann LS, Alpert JS, et al. 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 Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2014;130:e199-e267.