# A Clinical Prediction Model to Estimate Risk for 30-Day Adverse Events in Emergency Department Patients With Symptomatic Atrial Fibrillation

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**Study objective:** Atrial fibrillation affects more than 2 million people in the United States and accounts for nearly 1% of emergency department (ED) visits. Physicians have little information to guide risk stratification of patients with symptomatic atrial fibrillation and admit more than 65%. Our aim is to assess whether data available in the ED management of symptomatic atrial fibrillation can estimate a patient's risk of experiencing a 30-day adverse event.

**Methods:** We systematically reviewed the electronic medical records of all ED patients presenting with symptomatic atrial fibrillation between August 2005 and July 2008. Predefined adverse outcomes included 30-day ED return visit, unscheduled hospitalization, cardiovascular complication, or death. We performed multivariable logistic regression to identify predictors of 30-day adverse events. The model was validated with 300 bootstrap replications.

**Results:** During the 3-year study period, 914 patients accounted for 1,228 ED visits. Eighty patients were excluded for non–atrial-fibrillation-related complaints and 2 patients had no follow-up recorded. Of 832 eligible patients, 216 (25.9%) experienced at least 1 of the 30-day adverse events. Increasing age (odds ratio [OR] 1.20 per decade; 95% confidence interval [CI] 1.06 to 1.36 per decade), complaint of dyspnea (OR 1.57; 95% CI 1.12 to 2.20), smokers (OR 2.35; 95% CI 1.47 to 3.76), inadequate ventricular rate control (OR 1.58; 95% CI 1.13 to 2.21), and patients receiving $\beta$-blockers (OR 1.44; 95% CI 1.02 to 2.04) were independently associated with higher risk for adverse events. C-index was 0.67.

**Conclusion:** In ED patients with symptomatic atrial fibrillation, increased age, inadequate ED ventricular rate control, dyspnea, smoking, and $\beta$-blocker treatment were associated with an increased risk of a 30-day adverse event. [Ann Emerg Med. 2011;57:1-12.]

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## INTRODUCTION

### Background

Atrial fibrillation affects more than 2 million people in the United States, and the combination of increasing atrial fibrillation prevalence, high admission rate, and emergency department (ED) crowding will severely burden the health care system.[1,2] The atrial fibrillation prevalence is projected to double by 2020 and increase to 5.6 million by 2050.[2] Atrial fibrillation increases with age; 5.9% of individuals older than 65 years and 9% of those older than 80 years are diagnosed with the arrhythmia.[3] The proper management of patients with atrial fibrillation is critical because of the well-documented association with heart failure and stroke.[2,4-10]

The number of ED visits for complaints related to atrial fibrillation increased by 88% between 1993 and 2003 and now account for nearly 1% percent of all ED visits in the United States.[11,12] More than 65% of these atrial fibrillation visits result in hospital admission and more than $6.65 billion in expenditures.[11,13] During the past 20 years, hospital admissions for atrial fibrillation have increased by 66%.[14-16]

### Importance

Previous studies have suggested that incorporation of ED practice guidelines for atrial fibrillation management, the presence of observation units, and expedited cardioversion have been successful in reducing the atrial fibrillation admission rates

**Editor's Capsule Summary**

*What is already known on this topic*

Emergency department (ED) management of symptomatic atrial fibrillation varies greatly with respect to rate control, rhythm conversion, and disposition.

*What question this study addressed*

What clinical factors are associated with predefined 30-day adverse events after an ED visit for symptomatic atrial fibrillation?

*What this study adds to our knowledge*

Twenty-eight percent of the 638 admitted patients and 18% of the 192 patients discharged from the ED had a 30-day adverse outcome. Increased age, inadequate ventricular rate control at disposition, dyspnea, current smoking, and $\beta$-blocker treatment were associated with adverse events.

*How this is relevant to clinical practice*

The findings of this observational study will inform future efforts to define optimal management strategies for ED patients with symptomatic atrial fibrillation.

without compromising patient safety.[9,17-19] A strategy to better define the ED management of patients presenting with atrial fibrillation, especially one that categorizes patients in low and high risk, is required.[11] A recent study that reviewed 12 years of ED visits for atrial fibrillation from the National Hospital Ambulatory Medical Care Survey database found that patients hospitalized with symptomatic atrial fibrillation were similar to those discharged home from the ED with respect to age, sex, and whether ED rate control, cardioversion, or anticoagulation was attempted.[11] The development of a highly accurate prediction rule will assist emergency physicians in the risk stratification of patients with symptomatic atrial fibrillation.

### Goals of This Investigation

We developed our prediction rule through a systematic review of the electronic medical records of all patients treated for symptomatic atrial fibrillation at an urban, academic ED. This study's goal is to identify predictors of 30-day adverse events in ED patients evaluated for symptomatic atrial fibrillation. We hypothesize that data available in the ED management of symptomatic atrial fibrillation can estimate a patient's risk of experiencing a 30-day adverse event. The development of a highly accurate prediction rule may significantly advance the management of atrial fibrillation in the ED.

## MATERIALS AND METHODS

### Study Design and Setting

We performed a retrospective, observational cohort study, using a query of our electronic medical record archives and identified all patients aged 18 years or older and with a primary or supporting *International Classification of Diseases, Ninth Revision* (*ICD-9*) ED discharge diagnosis of atrial fibrillation or atrial flutter treated in the adult ED between August 1, 2005, and July 31, 2008. Our facility is an urban, academic, tertiary care referral center with an adult ED that treats 50,000 patients annually. The ED attending physician evaluates every patient in our ED, and the attending physician's dictated ED history and physical document are subsequently transcribed into the electronic medical record. The results of laboratory, radiographic, ECG and other diagnostic studies are also available in the electronic medical record. Our medical center's institutional review board approved this study.

Two investigators (T.W.B. and A.R.M.) systematically reviewed the electronic medical record for corresponding data, adhering to strict chart review methodology guidelines.[20] The study's principal investigator, an ED faculty physician, and a fourth-year medical student researcher were the 2 data abstractors. Both abstractors trained on a set of 10 records. Cases were selected according to the strict inclusion and exclusion criteria discussed below. We selected potentially important predictor variables a priori according to clinical expertise and a review of the related literature.[11,16,17,19,21-30] We recorded information on patient medical history, home medications, physical examination findings, and diagnostic test results. Our computer query system automatically populates some data (triage complaint, triage vital signs, and ED and hospital diagnostic [*ICD-9*] and current procedural terminology codes) into our database. We used a standardized electronic data abstraction form and entered data directly into a statistical database (SPSS, version 17.0; SPSS, Inc., Chicago, IL). We held twice-monthly meetings to review data collection and resolve any disputes. When there was a question about a record, the principal investigator reviewed the entire electronic medical record and often clarified the dispute. In rare instances, a question about data collection was discussed with the other study investigators for final determination. In an attempt to minimize missing data, we reviewed ED attending and resident history and physical examination documents, ED nursing notes, consultant notes, hospital records, outpatient clinic notes, diagnostic study reports, and electronic clinical communications. Reviewers were not blinded to the study's objective or the outcomes of interest. The reviewers, however, always entered the information on candidate predictors before recording whether the patient experienced a 30-day adverse event.

Both investigators independently reviewed a random sample of 46 (5%) records to measure interrater reliability for this structured medical record review. We calculated the interrater agreement with Cohen's $\kappa$ statistic.

**Selection of Participants**

All adult patients treated in our ED for atrial fibrillation or atrial flutter were eligible for inclusion in our cohort regardless of ED disposition (eg, discharge, hospitalization). We included patients with atrial flutter because it may degenerate into atrial fibrillation and atrial flutter commonly occurs together in patients with atrial fibrillation. The 2006 and 2008 American College of Cardiology/American Heart Association guidelines group the 2 arrhythmias together with regard to management and performance measures recommendations.[15,16] Previous landmark trials about treatment of atrial fibrillation have included patients with atrial flutter.[31-33] Inclusion criteria required documented evidence of atrial fibrillation or atrial flutter on an ED ECG or rhythm strip. The patient also must have signs (tachycardia, dyspnea) or symptoms (palpitations, chest pain, shortness of breath, weakness, lightheadedness, presyncope, or syncope) consistent with primary symptomatic atrial fibrillation documented in the electronic medical record. We also included patients whose initial presenting complaint was not directly related to their atrial fibrillation diagnosis (eg, evaluation for febrile illness, gastrointestinal complaint, injury) but had a secondary complaint consistent with symptomatic atrial fibrillation that required ED evaluation. We extensively reviewed the patient's entire electronic medical record related to that ED evaluation and determined whether the patient underwent an evaluation for atrial fibrillation in addition to the primary complaint. Patients with the following were included in the study: new atrial fibrillation diagnosis, atrial fibrillation associated with inadequate rate control (according to previous studies and our clinical experience, we defined adequate ventricular rate control as a resting pulse rate less than 100 beats/min),[31-33] atrial fibrillation associated with heart failure symptoms, atrial fibrillation in the setting of a cerebrovascular accident or transient ischemic attack, and atrial fibrillation associated with other thromboembolic complications. We excluded patients when our review of their electronic medical record determined that atrial fibrillation was unrelated to the ED complaints and did not require evaluation in the ED. When a patient had multiple ED visits during the study period, we included only their first visit to the ED in the analysis.

Candidate predictor variables were selected according to an extensive review of the medical literature and clinical expertise.[11,16,17,19,21-30] Candidate predictors need to be biologically plausible for the predictive rule to maintain face validity and be realistically available to most emergency physicians.[34] Invasive studies or laboratory results that are not returned within 2 hours will result in an ED rule rarely used. To that end, we recorded information on 50 variables that included patient history of present illness, medical history, home medications, physical examination findings, ED treatments, and diagnostic test results.

Given a set of candidate predictors, many published rules erroneously use a stepwise selection of predictors that is based on analyzing whether the association of each predictor with the outcome is statistically significant with bivariate analysis and *P* values. Stepwise methods may lead to instability of predictor selection, biased estimates of coefficients, exaggeration of *P* values, and worse predictive quality than using the full model without selection.[34,35] We selected 12 predictor variables for inclusion in our prediction rule from the larger set according to clinical relevance and the results of baseline descriptive statistics in our cohort of ED patients with symptomatic atrial fibrillation. Specifically, we reviewed the baseline characteristics of the patients who did and did not experience a 30-day adverse event and selected the 12 predictors for inclusion in the model from these 50 candidate predictors according to apparent differences in predictor representation between the 2 groups, clinical relevance, and sensibility. Colinearity of predictors can lead to inclusion of extraneous predictors and inflated standard errors for the regression coefficients.[36] Therefore, to limit colinearity and ensure a parsimonious model, Spearman's correlations were calculated between the clinically sensible associations within our 12 predictor variables. Specifically, Spearman's correlations were calculated between the following clinically sensible associations: (1) history of hypertension status and $\beta$-blocker and diuretic use, and (2) history of heart failure and $\beta$-blocker home use, diuretic home use, peripheral edema on physical examination, and dyspnea in the ED.

Adequate rate control in the ED was one of the predictors selected for consideration in the rule. For the purposes of analysis, we defined a priori that adequate rate control in the ED would be a ventricular rate less than 100 beats/min. The documented ventricular pulse rate at ED disposition determined whether patients were classified as having adequate ventricular rate control (pulse $<$100 beats/min) or not (pulse $\geq$100 beats/min). We obtained these data from reviewing the electronic and scanned nursing records for documentation of the patient's pulse rate at ED disposition. These included pulse rate at transfer to the floor or ICU and recorded pulse rate before discharge from ED. We did not continuously track ventricular rate but recorded the single measurement at ED disposition. Patients were subsequently classified as having adequate or inadequate rate control according to whether that data point was less than 100 beats/min.

**Outcome Measures**

The primary outcome measure was the occurrence of 1 or more adverse events within 30 days of the patient's ED visit. Predetermined adverse outcome measures were: 30-day ED return visit for an atrial fibrillation–related complaint, unscheduled hospital admission for an atrial fibrillation–related complaint, 30-day cardiovascular complication, and patient death as a result of an atrial fibrillation–related problem. We defined an atrial fibrillation–related complaint as one of the following: ED visit or hospitalization for signs (tachycardia, dyspnea) or symptoms (palpitations, chest pain, shortness of breath, weakness, lightheadedness, presyncope, or syncope) consistent with primary symptomatic atrial fibrillation, an atrial fibrillation–related medication adverse effect (eg, bradycardia

caused by excess β-blockade, supratherapeutic anticoagulation, or warfarin-associated bleeding), or an ED evaluation for a cardiovascular complication (eg, arrhythmia, acute heart failure exacerbation, acute coronary syndrome). We defined cardiovascular complications as the occurrence of one of the following: atrial fibrillation with rapid ventricular response, acute heart failure exacerbation, acute coronary syndrome, acute atrial or ventricular arrhythmia requiring evaluation, thromboembolic cerebrovascular accident, cardiogenic shock, or cardiac arrest. Cardiovascular complications that occurred during an admitted patient's index hospitalization were not counted as positive outcomes. When a patient died within the 30-day period, we reviewed the death summary and certificate (when available) to evaluate atrial fibrillation's role in causing the patient's death.

**Data Collection and Processing**

We reviewed patients' electronic medical records to record whether an adverse event occurred within 30 days of their ED visit. The observation period for patients discharged from the ED included the 30 days subsequent to the date of the initial ED visit. The observation period for admitted patients spanned the 30 days from the initial ED visit minus the days spent in the hospital. The only exception was that death related to atrial fibrillation during the first 30 days was considered an event even if the patient was in the hospital. The majority of our center's patients with atrial fibrillation follow up as outpatients in our cardiology or internal medicine clinics, resulting in excellent follow-up information on this patient cohort. When patients returned to the ED within 30 days of their initial visit, we reviewed the ED record and admission documentation (if applicable) to verify that the visit was atrial fibrillation related. In instances in which the visit or admission was for a non-atrial-fibrillation-related reason, this visit was not considered an adverse event. We specifically reviewed all cardiology and primary care clinic notes within 6 months of the patient's ED visit for mention of any adverse event, ED visit, or hospitalization that might have occurred at an outside hospital. Data were entered directly into a statistical database (SPSS, version 17.0).

**Primary Data Analysis**

To avoid overfitting and ensure a reliable prediction rule, we adhered to the accepted formula that there must be 15 events per predictor degree of freedom (ie, per regression coefficient estimated).[34,35,37] According to a query of our ED visit database, we anticipated approximately 300 individual patient visits for atrial fibrillation annually; therefore, we chose to review 3 years' worth of ED medical records to guarantee adequate sample size for formulating the model.

Descriptive statistics on baseline variables are presented as median (interquartile range [IQR]) or percentage (N) as appropriate. We analyzed the association of the a priori selected variables with 30-day adverse events with multivariable logistic regression, from which we derived the original model's β coefficients. Clinically meaningful interactions were included in the model. Their significance was tested as a group to avoid inflating type I error. All interaction terms were removed as a group, and the model was refit if results were nonsignificant. Specifically, interactions between home use of β-blockers and diuretics and between edema on physical examination and a history of heart failure were tested. The primary outcome was based on 30-day adverse event status. We assumed that missing values occurred at random and used multiple imputations to derive predictions for missing values of selected variables.[38-40] All analyses were done with the statistical programming language R, version 2.8.1 (R Development Core Team, Vienna, Austria).[40-42] Predictive discrimination was assessed with the C-statistic and a histogram of predicted probabilities.

Prediction models need to be validated and calibrated. Internal validation estimates the likely performance of the rule on a new sample of patients from the same patient stream. Calibration measures a rule's accuracy of the predicted probability of the outcome and the observed outcome frequency. This may be demonstrated with a smooth nonparametric calibration curve or scatterplot of predicted versus observed outcome, which illustrates the bias in predicted values. We internally validated and calibrated the model with 300 bootstrap resamples. Bootstrapping, a more efficient technique for model validation and calibration than data-splitting techniques, preserves the sample size, leading to more precision and power.[43] Each bootstrap resample involved randomly sampling a new set of patients from the original set, with replacement. Thus, in a given resample, some patients might be represented multiple times and others not at all. Each coefficient was averaged over the 300 bootstrap resamples to build the bootstrap model. The difference between the original and bootstrap model predictive probabilities provides a sense for how the original maximum likelihood model results would perform on future patient samples in our facility.

We performed 2 additional secondary analyses with our prediction model. We included patient disposition (eg, hospitalization, discharge) as an additional variable in the model to test for the potential confounding of hospitalization on the association between the predictors and adverse events. We compared the β coefficients and model's discrimination and calibration with and without inclusion of the disposition predictor variable to measure the effect of the hospitalization. We also performed a sensitivity analysis testing our original model on a more refined composite outcome that included only death, hospitalization, and cardiovascular complication within 30 days. This outcome focuses on the most severe adverse events and excludes patients with a return visit to the ED who do not require admission. Finally, agreement between electronic medical record reviewers was assessed on 30-day adverse events and model predictors with Cohen's κ statistic.

## RESULTS

During the 3-year study period, 914 patients accounted for 1,228 ED visits. Eighty patients were excluded for non-atrial-

**Table 1.** Subjects' characteristics.

| Variable | N | No. Missing (Total, %) | No 30-Day Adverse Event (N=616) | Experienced a 30-Day Adverse Event (N=216) |
|---|---|---|---|---|
| Age, y | 832 | 0 | 67 (55, 78) | 72 (61, 81) |
| Age at initial diagnosis of AF, y | 676 | 156 (19) | 62 (49, 73) | 68 (56, 79) |
| Sex: Female | 832 | 0 | 244 (40) | 98 (45) |
| Classification of AF | 810 | 22 (2.6) | | |
| New diagnosis | | | 222 (37) | 74 (35) |
| Paroxysmal/persistent | | | 265 (44) | 81 (38) |
| Permanent | | | 111 (19) | 57 (27) |
| Maximum pulse rate in ED, beats/min | 804 | 28 (3.4) | 123 (97, 144) | 130 (98, 148) |
| Adequate pulse rate control in ED, yes | 825 | 7 (0.8) | 386 (63) | 114 (53) |
| Body mass index, $m^2$/kg | 681 | 151 (18) | 27 (24, 31) | 25 (22, 30) |
| ≥2 home AV nodal blockers, yes | 832 | 0 | 90 (15) | 36 (17) |
| Home β-blocker use, yes | 832 | 0 | 254 (41) | 114 (53) |
| Home diltiazem/verapamil use, yes | 832 | 0 | 93 (15) | 37 (17) |
| Home digitalis use, yes | 832 | 0 | 101 (16) | 30 (14) |
| Home diuretic use, yes | 832 | 0 | 279 (45) | 114 (53) |
| Home amiodarone use, yes | 832 | 0 | 25 (4) | 14 (6) |
| Home sotalol use, yes | 832 | 0 | 42 (7) | 7 (3) |
| Home warfarin use, yes | 832 | 0 | 205 (33) | 78 (36) |
| Home statin use, yes | 832 | 0 | 200 (32) | 75 (35) |
| Home ACEI/ARB use, yes | 832 | 0 | 236 (38) | 90 (42) |
| Current smoker, yes | 830 | 2 (0.2) | 73 (12) | 42 (20) |
| Current alcohol drinker, yes | 830 | 2 (0.2) | 64 (10) | 23 (11) |
| Reported history of cocaine use, yes | 830 | 2 (0.2) | 14 (2) | 4 (2) |
| History of myocardial infarction | 828 | 4 (0.5) | 102 (17) | 33 (15) |
| History of coronary artery disease | 830 | 2 (0.2) | 197 (32) | 75 (35) |
| History of COPD | 829 | 3 (0.4) | 82 (13) | 44 (21) |
| History of hypertension | 832 | 0 | 401 (65) | 160 (74) |
| History of valvular heart disease | 831 | 1 (0.1) | 106 (17) | 56 (26) |
| History of heart failure | 832 | 0 | 140 (23) | 76 (35) |
| History of renal insufficiency | 831 | 1 (0.1) | 66 (11) | 40 (19) |
| History of insulin-dependent diabetes, yes | 830 | 0 | 42 (7) | 18 (8) |
| History of non-insulin-dependent diabetes, yes | 831 | 1 (0.1) | 98 (16) | 41 (19) |
| Pacemaker, yes | 830 | 2 (0.2) | 56 (9) | 27 (13) |
| Family history of AF, yes | 826 | 6 (0.7) | 37 (6) | 11 (5) |
| Family history of coronary artery disease, yes | 826 | 6 (0.7) | 255 (42) | 98 (46) |
| Family history of valvular heart disease, yes | 826 | 6 (0.7) | 11 (2) | 1 (0) |
| Complaint of palpitations in ED, yes | 830 | 2 (0.2) | 261 (42) | 75 (35) |
| Complaint of shortness of breath in ED, yes | 830 | 2 (0.2) | 261 (42) | 123 (57) |
| Complaint of neurologic deficit in ED, yes | 829 | 3 (0.4) | 51 (8) | 33 (15) |
| Presence of edema on physical examination in ED, yes | 832 | 0 | 154 (25) | 75 (35) |
| Presence of cardiac murmur on physical examination in ED, yes | 832 | 0 | 91 (15) | 40 (19) |
| Presence of pulmonary rales on physical examination in ED, yes | 832 | 0 | 122 (20) | 80 (37) |

*AF,* Atrial fibrillation; *AV,* atrioventricular; *ACEI,* angiotensin-converting enzyme inhibitor; *ARB,* angiotensin-receptor blocker; *COPD,* chronic obstructive pulmonary disease.

N equals total number of nonmissing responses for each variable. Categorical variables presented as number followed by percentage in parentheses. Continuous variables are represented as the median with IQR in parentheses.

fibrillation-related complaints, and 2 patients were excluded who had no follow-up recorded, resulting in a study population of 832 patients. The most common non-atrial-fibrillation-related complaints included trauma evaluations (n=26), dehydration/general malaise (n=13), infectious complaints (n=10), and abdominal/flank pain (n=10). The baseline characteristics for the subjects are presented in Table 1. Of the 832 patients, 717 (86%) had isolated atrial fibrillation, 95 (11%) had atrial flutter, and 20 (2.4%) had both atrial fibrillation and atrial flutter.

Two hundred sixteen patients (25.9%) had at least 1 of the following 30-day atrial fibrillation–related adverse events: ED return visit (124; 14.9%), unscheduled hospital admission (130; 15.6%), cardiovascular complication (128; 15.3%), or death (54; 6.5%). Of the 130 unscheduled hospitalizations, 98 (75.3%) were admitted through the ED. The most common cardiac complications and reasons for hospitalization were recurrent atrial fibrillation with rapid ventricular response and acute heart failure exacerbations. Heart failure and intracranial hemorrhage were the most common causes of death. All 7 of the

patients who died of an intracranial hemorrhage were receiving warfarin. A detailed listing of the outcome measurements is presented in Table 2. Adverse events occurred in 181 of the 638 (28.4%) admitted patients and 35 of the 192 (18.2%) patients discharged from the ED. Two patients died in the ED. The median hospital lengths of stay for admitted patients who did and did not experience an adverse event were 4 days (IQR 2 to 7.5 days) and 3 days (IQR 2 to 5.75 days), respectively. The median time to adverse event among discharged patients was 10 days (IQR 6 to 19 days).

Atrial fibrillation or atrial flutter was the primary reason for the ED visit in 651 (78%) of our cohort. Atrial fibrillation or atrial flutter was a complicating secondary diagnosis in the remainder. The most common triage complaints were chest pain (16.9%), shortness of breath (12.9%), and palpitations/arrhythmia (21.5%). More than half of the cohort, 494 patients (59.4%), achieved successful ventricular rate control at ED disposition. A continuous atrioventricular (AV) nodal-blocker infusion was administered in the ED to 144 (17.3%) patients. Among the 301 patients admitted who failed to achieve adequate rate control in the ED, 44 (14.6%) had a return visit to the ED within 30 days. Of these, 16 returned to the ED for atrial fibrillation with rapid ventricular response, and all but one were readmitted.

We selected 12 predictor variables for inclusion in the rule according to clinical relevance and a review of baseline descriptive statistics. No variables were removed from the a priori list because of overlapping information. Clinically meaningful interaction terms among these 12 predictor variables were tested as a group and failed to show significant contributions to the model. Therefore, they were not included in the final prediction rule. The odds ratios and 95% confidence intervals (CIs) for the selected predictors' influence on risk of 30-day adverse events in ED patients with symptomatic atrial fibrillation are presented in Table 3. Five of the 12 predictors met statistical significance at an $\alpha$ level of .05. Increased age, inadequate ED ventricular rate control, ED complaint of dyspnea, smoking, and $\beta$-blocker treatment were associated with an increased risk of a 30-day adverse event. Sex, diuretic use, heart failure, lower-extremity edema, chronic obstructive pulmonary disease, hypertension, and a complaint of palpitations were not found to be statistically significant. Figure 1 provides a nomogram of our rule's predicted probabilities for 30-day adverse events. Table 4 gives predicted probabilities for 30-day adverse events that can be computed from the nomogram for 5 hypothetical patient examples with various risk factors.

The atrial fibrillation rule's predictive discrimination was modest, with a C-statistic of 0.67 (95% CI 0.63 to 0.71). Figure 2 illustrates the histogram of predicted probabilities from the model. Figure 3 depicts the prediction rule's calibration curve.[41,43] The calibration accuracy for the original maximum likelihood model ("Apparent") and the bootstrap model ("Bias-corrected") would be perfect if both

**Table 2.** Description of specific 30-day adverse event outcomes.

| Adverse Event Category | N | Frequency, No. (%) |
|---|---|---|
| **Reason for return visit to ED** | 124 | |
| Shortness of breath | | 29 (23) |
| Chest pain | | 19 (15) |
| Palpitations | | 16 (13) |
| Weakness | | 15 (12) |
| Tachycardia | | 7 (6) |
| Altered mental status | | 6 (5) |
| Syncope | | 6 (5) |
| Extremity edema | | 5 (4) |
| CVA | | 4 (3) |
| Arrhythmia | | 4 (3) |
| Abdominal pain | | 3 (2) |
| Abnormal bleeding | | 3 (2) |
| Hypotension | | 2 (2) |
| Nausea | | 2 (2) |
| Other | | 3 (2) |
| **Hospital admission diagnosis** | 130 | |
| AF with rapid ventricular response | | 42 (32) |
| Heart failure | | 28 (22) |
| Chest pain/acute coronary syndrome | | 11 (7) |
| Symptomatic AF/atrial flutter | | 8 (6) |
| Shortness of breath/hypoxia | | 7 (5) |
| CVA/transient ischemic attack | | 6 (5) |
| Malaise | | 6 (5) |
| Hypotension/syncope | | 5 (4) |
| Tachycardia | | 8 (6) |
| Bradycardia | | 4 (3) |
| Palpitations | | 2 (2) |
| Acute limb ischemia | | 1 (1) |
| Other | | 2 (2) |
| **Cardiovascular complication** | 128 | |
| AF with rapid ventricular response | | 43 (34) |
| Heart failure | | 32 (25) |
| Embolic complications | | 10 (8) |
| AF with rapid ventricular response and heart failure | | 9 (7) |
| Acute coronary syndrome | | 7 (5) |
| Atrial flutter with rapid ventricular response | | 6 (5) |
| Syncope | | 5 (4) |
| Pacemaker dysfunction | | 4 (3) |
| Bradycardia | | 4 (3) |
| Adverse medication reaction | | 3 (3) |
| Cardiac arrest | | 3 (3) |
| Other | | 2 (2) |
| **Cause of death** | 54 | |
| Heart failure | | 9 (17) |
| Intracranial hemorrhage | | 7 (13) |
| Respiratory failure | | 7 (13) |
| Complications of metastatic cancer | | 7 (13) |
| Cardiac arrest | | 7 (13) |
| Sepsis | | 6 (11) |
| Ischemic stroke | | 4 (7) |
| Thoracic aortic disease | | 2 (4) |
| Pneumonia | | 2 (4) |
| Complications of renal failure | | 2 (4) |
| Myelodysplasia | | 1 (2) |

*CVA*, Cerebrovascular accident.

**Table 3.** Multivariate prediction models for 30-day adverse events.

| | Primary Model* | | Secondary Model† | | Secondary Model‡ | |
|---|---|---|---|---|---|---|
| **Predictor** | **Odds Ratio** | **95% CI** | **Odds Ratio** | **95% CI** | **Odds Ratio** | **95% CI** |
| Smoker | 2.35 | (1.47–3.76) | 2.23 | (1.34–3.70) | 2.35 | (1.47–3.76) |
| Age, y (10-y increment) | 1.20 | (1.06–1.36) | 1.27 | (1.11–1.46) | 1.19 | (1.05–1.35) |
| Inadequate ventricular rate control in ED | 1.58 | (1.13–2.21) | 1.88 | (1.32–2.67) | 1.55 | (1.10–2.20) |
| Complaint of dyspnea in ED | 1.57 | (1.12–2.20) | 1.63 | (1.14–2.33) | 1.55 | (1.10–2.19) |
| Home use of $\beta$-blockers | 1.44 | (1.02–2.04) | 1.37 | (0.95–1.96) | 1.44 | (1.02–2.03) |
| Heart failure history | 1.35 | (0.92–1.98) | 1.53 | (1.02–2.28) | 1.34 | (0.97–1.97) |
| Edema on physical examination | 1.28 | (0.89–1.85) | 1.46 | (1.00–2.14) | 1.27 | (0.88–1.84) |
| Hypertension history | 1.21 | (0.82–1.79) | 1.48 | (0.97–2.27) | 1.21 | (0.82–1.79) |
| Female | 1.11 | (0.79–1.56) | 1.02 | (0.71–1.46) | 1.11 | (0.79–1.56) |
| Palpitations in the ED | 0.90 | (0.63–1.30) | 0.94 | (0.64–1.38) | 0.91 | (0.63–1.31) |
| COPD history | 1.08 | (0.69–1.69) | 1.03 | (0.64–1.66) | 1.07 | (0.69–1.68) |
| Home use of diuretic | 1.00 | (0.69–1.44) | 0.91 | (0.62–1.33) | 1.00 | (0.69–1.43) |
| Admitted to hospital | | | | | 1.10 | (0.70–1.72) |

*Prediction model for 30-day adverse events in ED patients with symptomatic AF.
†Secondary model testing composite outcome that excluded 25 return visits to the ED that did not result in hospitalization or patient death.
‡Secondary model with hospital disposition included as additional covariate.

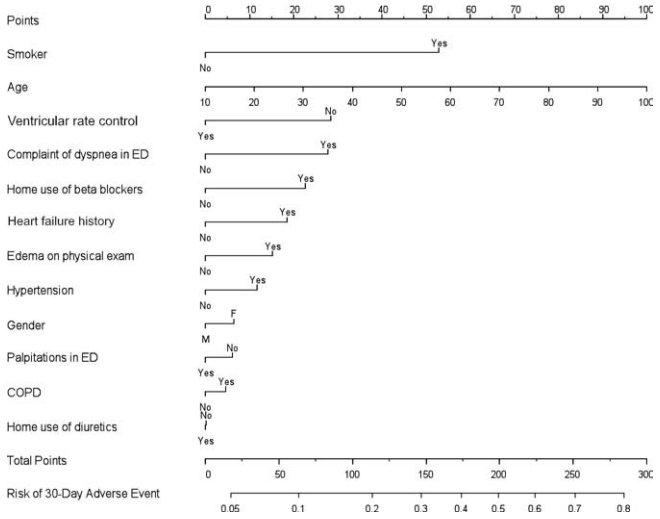


**Figure 1.** Thirty-day adverse event prediction rule nomogram. Points are assigned for each of the 12 predictors. The total points correspond to an absolute predicted risk for 30-day adverse events. This nomogram should not be used in clinical practice until an independent validation is completed.

**Table 4.** Hypothetical patient examples with the rule's calculated predicted probability of 30-day adverse events.

| | Case | | | | |
|---|---|---|---|---|---|
| **Predictor** | **1** | **2** | **3** | **4** | **5** |
| Age, y | 45 | 52 | 72 | 77 | 86 |
| Sex | F | M | F | M | M |
| Dyspnea in ED | No | Yes | Yes | No | Yes |
| Smoker | No | Yes | No | Yes | Yes |
| Use of $\beta$-blocker | No | No | Yes | No | Yes |
| Use of diuretic | No | No | Yes | Yes | Yes |
| Heart failure history | No | No | Yes | Yes | Yes |
| Peripheral edema on examination | No | No | Yes | No | Yes |
| Adequate rate control in ED | Yes | Yes | Yes | No | No |
| History of COPD | No | Yes | No | Yes | Yes |
| History of hypertension | No | No | Yes | Yes | Yes |
| Palpitations in ED | Yes | No | Yes | No | No |
| Calculated probability of 30-day adverse event | .08 | .27 | .39 | .49 | .77 |

*F,* Female; *M,* male.

lines fell along the "Ideal" line of unity for actual and predicted probabilities of having a 30-day adverse event. In Figure 3, we see that the "bias-corrected" estimate is slightly nonlinear but only slightly worse than the "apparent" calibration. The 0.9 quantile of absolute error in predicted probabilities between the "bias corrected" and "apparent" model is 0.03, suggesting only a small degree of bias from overfitting in the original model.

As a sensitivity analysis, we measured the prediction rule's performance on a more refined serious adverse event outcome that excluded the 25 return ED visits not requiring hospitalization. The model's adjusted odds ratios are presented in Table 3, and the rule's predictive discrimination C-statistic was 0.70. This revised model had similar odds ratios and 95% CIs for the predictors, with only patient history of heart failure replacing home use of $\beta$-blocker medication as the fifth significant predictor.

We further examined whether hospitalization affected an individual's odds of experiencing a 30-day adverse event. This secondary analysis showed no difference in model results or its predictive discrimination (Table 3). A description of the inpatient diagnostic and therapeutic procedures is listed in Table 5. Interrater agreement between electronic medical record reviewers ranged from moderate to perfect agreement (0.69 to 1.00). The interrater agreement for the composite outcomes was perfect for all ($\kappa$=1.0) except cardiovascular complication, with a $\kappa$ of 0.73.

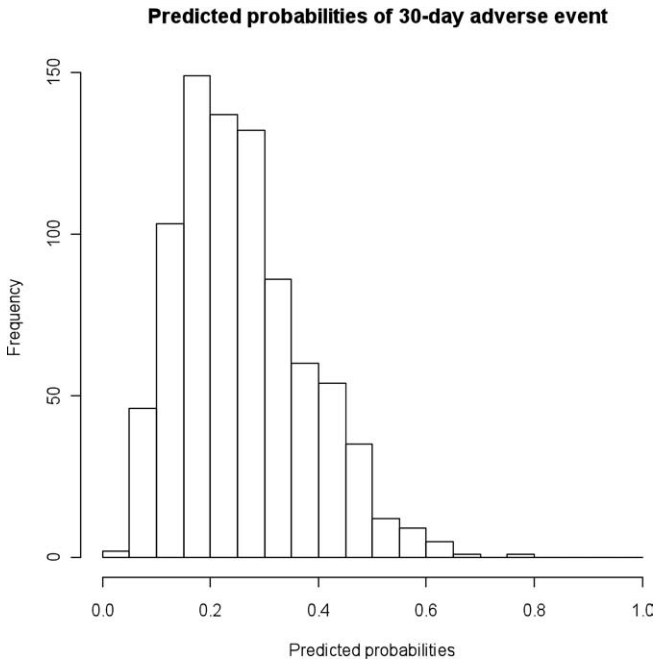


**Figure 2.** Histogram of predicted probabilities of 30-day adverse events. This figure illustrates the histogram of predicted probabilities from the model and shows that 3.4% of subjects had predicted probabilities greater than 0.50 and 5.8% had predicted probabilities less than 0.10.

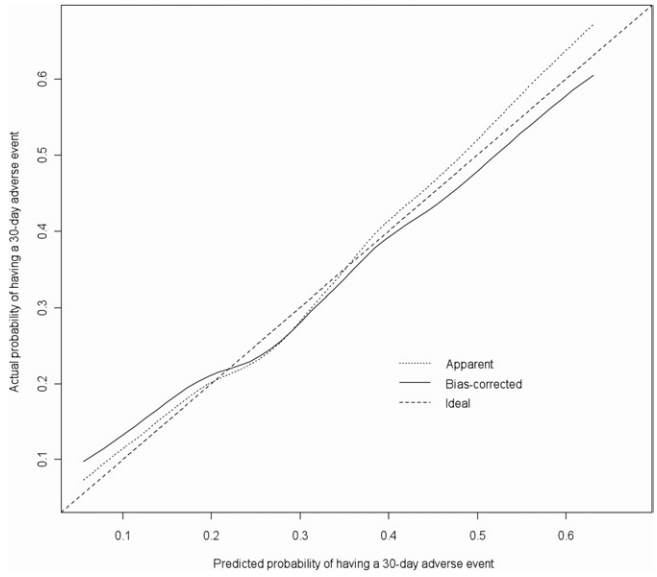


**Figure 3.** Calibration plot for atrial fibrillation clinical prediction model. This plot illustrates the calibration accuracy of the original model ("Apparent") and the bootstrap model ("Bias-corrected") for 30-day adverse events with locally weighted scatterplot smoothing used to model the relationship between actual and predicted probabilities. As can be seen, the model's calibration function estimate is slightly nonlinear, with the corrected calibration showing good agreement with the apparent calibration.

**Table 5.** Summary of inpatient procedures during initial hospitalization (total number of patients hospitalized=638).

| Inpatient Procedure | N (Total) | No 30-Day Adverse Event (N=457) | Experienced a 30-Day Adverse Event (N=181) |
|---|---|---|---|
| Thoracentesis | 9 | 3 | 6 |
| Insertion of coronary artery stent | 14 | 12 | 2 |
| Cardiac catheterization | 47 | 31 | 16 |
| Electrophysiologic study | 9 | 9 | 0 |
| Ablation | 11 | 9 | 2 |
| Pacemaker insertion | 26 | 20 | 6 |
| Pacemaker revision | 5 | 4 | 1 |
| Hemodialysis | 14 | 12 | 2 |
| Transthoracic echocardiogram | 60 | 44 | 16 |
| Transfusion of blood products | 51 | 31 | 20 |
| Atrial cardioversion | 18 | 15 | 3 |
| Other cardioversion | 31 | 25 | 6 |
| Intubation | 14 | 7 | 7 |
| Required continuous intravenous AV nodal blocking infusion in ED | 144 | 106 | 38 |

## LIMITATIONS

To our knowledge, this study is the first to develop a clinical prediction model for 30-day adverse events among ED patients evaluated for atrial fibrillation. The results of this study cannot be used to draw any conclusions about the safety of discharging patients with symptomatic atrial fibrillation from the ED. The study was a retrospective cohort analysis and therefore is subject to the inherent limitations of such studies. We did not prospectively collect data on predictors or the outcomes, and there is the potential that missing data might bias our results.

We limited our candidate predictors to data that are available to emergency physicians early in the patient evaluation. The prediction model did not include laboratory studies, such as troponin and brain natriuretic peptide, that were measured in only a minority of patients because there is likely selection bias in the physician ordering of these studies. Patients might have experienced additional events within the 30 days that were treated at other hospitals and not recorded in our database. We did examine follow-up clinic notes and electronic and telephone clinical communication reports, and searched for mention of any events since the original ED visit. Internists or cardiologists at Vanderbilt follow the majority of our patients closely. There were only 2 patients in the study who were out-of-state visitors and had no further records after their ED visit. The potential for undocumented adverse events might result in an underestimate of the actual incidence of 30-day adverse events. In addition, this study was conducted at a single tertiary referral center ED, which might introduce selection and referral bias and limit applicability to patients treated in other settings.

Our decision to include all ED patients treated for symptomatic atrial fibrillation might be criticized because clearly patients with an acute cerebrovascular accident will not be candidates for ED discharge. The majority (78%) of patients in our cohort visited the ED for primary atrial fibrillation–related

complaints. Our definition of adverse events that included an atrial fibrillation–related return visit to the ED or unscheduled hospitalization might be criticized as overly conservative. We chose these conservative outcome definitions so that our model would identify the lowest-risk patients. Given the significant practice variation in the management of atrial fibrillation, the high admission rate for atrial fibrillation, and that this is an initial study in the development of a novel ED-based atrial fibrillation prediction rule, we decided to measure all important predictors and potential serious outcomes in all eligible patients from our study cohort. We intend our clinical prediction model to assist, not replace, physician decisionmaking. We would expect physician gestalt to take precedence over the prediction model when patients are unstable and result in appropriate hospitalization. The results of this article cannot be used to determine appropriateness of discharge or to derive guidelines about appropriate utilization. All prediction rules, including this atrial fibrillation rule, must be prospectively validated in an independent diverse patient population before use in patient care. This rule, developed in a primarily inpatient cohort, if validated, will require further study to determine whether outpatient treatment is safe in the patients identified as low risk. Our hope is that this prediction rule will be validated and will assist emergency physicians with the disposition decisionmaking in stable patients.

Pulse rate fluctuation is the norm for atrial fibrillation, and there is the potential for misclassification bias with regard to adequate rate control. We recorded only the pulse rate at ED disposition and did not continuously record pulse rates throughout the ED stay. There is potential that patients were misclassified as having inadequate rate control according to a single falsely increased measurement. This might result in adequate rate control being a less reliable predictor in the model.

Patient disposition might have affected the primary outcome. The decision to hospitalize patients with atrial fibrillation is often subjective and multifactorial, according to the patient's acute and chronic conditions. The incidence of adverse events was 10% greater among admitted patients than those discharged from the ED, which might reflect that hospitalized patients represent a sicker cohort at higher risk for adverse events despite treatments initiated in the hospital. Furthermore, the inpatient hospital evaluation is not standardized and patients underwent various diagnostic and therapeutic interventions while hospitalized. An inpatient intervention, such as a pacemaker placement, might reduce the risk of a 30-day adverse event, whereas another intervention (ie, initiating a new antiarrhythmic medication) might increase the risk of an event. We examined the effect of hospitalization on our prediction rule's performance and found no difference in the model's performance. We also recorded the time to adverse events among the patients discharged from the ED to investigate whether hospitalization might have prevented the outcome or resulted in patient reclassification (ie, a cardiovascular complication that occurs during the initial hospitalization [not counted as positive outcome] rather than during outpatient status). The median time to adverse event was 1 week longer than the median hospital length of stay, demonstrating that these outcomes did not take place while the admitted patients were still hospitalized.

## DISCUSSION

We found 5 significant predictors of 30-day adverse events: age, smoking, complaint of dyspnea, inadequate ventricular rate control in the ED, and home $\beta$-blocker use. We limited predictors to those variables that would be readily available to treating physicians during their initial evaluation. The ultimate goal of our research is to accurately identify patients who are at low risk for adverse outcomes and can be safely discharged from the ED. This study is the initial step in the development of a prediction rule to achieve that goal. Our prediction rule should not be used to determine whether it is appropriate to discharge a patient from the ED until it is prospectively validated.

Presently, in the United States, more than 2 of every 3 patients presenting to an ED with symptomatic atrial fibrillation are hospitalized.[14-16] Significant practice variation occurs between US regions, with 76% admission rates in the Northeast versus 48% in the West.[11] Despite this regional variation, however, the admission rate is more than double the 29% admission rates reported in a large European study.[44] The American College of Cardiology/American Heart Association/European Society of Cardiology 2006 guidelines for the management of patients with atrial fibrillation state that management involves 3 objectives: rate control, prevention of thromboembolism, and correction of the rhythm disturbance.[16] According to the guidelines, a patient with a first-documented episode of atrial fibrillation, who achieves adequate rate control, does not need to be hospitalized.[16] In our study, 84% of patients with a new atrial fibrillation diagnosis were hospitalized despite nearly half (48%) of these patients achieving successful ventricular rate control in the ED.

Emergency physicians need to feel confident identifying stable, low-risk patients with atrial fibrillation. A highly accurate, easy-to-use prediction rule based on validated risk assessments is needed to accomplish this practice change. The incorporation of previous decision rules into emergency medicine practice has resulted in decreased admissions for low-risk patients with acute chest pain and community-acquired pneumonia.[45,46] Atrial fibrillation prediction rules have primarily focused on maintenance of sinus rhythm, reducing the risk of stroke and overall mortality.[22-25,29,47-56] One such example is the validated $CHADS_2$ score for predicting the stroke risk in atrial fibrillation patients.[22] Patients aged 75 years or older or with hypertension, diabetes, or previous stroke/transient ischemic attack are at moderate to high risk of subsequent stroke.[22] Similarly, a prospective analysis of the Framingham Heart Study found that advancing age, female sex, increasing systolic blood pressure, previous stroke or transient ischemic attack, and diabetes were also associated with an

increased risk of stroke in individuals with atrial fibrillation.[29] Although these outpatient studies provide excellent candidate predictors, they do not address the acutely symptomatic ED patient.

Determining severity of atrial fibrillation exacerbations in the ED is difficult and imprecise. Many patients have significant cardiac and noncardiac comorbidities serving as precipitants or contributors to patient instability.[11,44] For example, atrial fibrillation is known to occur with acute myocardial infarction; patients are frequently admitted to the hospital to exclude acute coronary syndrome as the cause of their atrial fibrillation.[19,30,57] Previous ED-based studies found that patients with atrial fibrillation and without evidence of significant ST-segment changes (ST-segment elevation or >2-mm ST-depression) are at very low risk for acute myocardial infarction and that atrial fibrillation did not change the relative risk of acute coronary syndrome in patients at an urban ED with chest pain syndromes.[30,57]

Physicians currently have no validated clinical prediction rules to assist with the decision to hospitalize an ED patient with symptomatic atrial fibrillation. The first branch point in this decision process often is whether a patient can achieve successful rate control in the ED. Inadequate ventricular rate control in the ED increases the risk for a 30-day adverse event in our prediction model. In this study, physicians hospitalized 20% fewer patients who achieved successful ventricular rate control in the ED, although the admission rate for these patients remained high, at 65%.

This prediction rule identified 5 variables that are associated with a patient's having an increased risk of experiencing an adverse event within 30 days of their ED visit. Previous studies have linked increasing age, smoking, and a complaint of dyspnea with atrial fibrillation–associated adverse events, including stroke and death.[22,23,29] Patients who were unable to achieve adequate rate control in the ED had increased risk of adverse events. This may be the result of associated illness (infections, dehydration) that triggered or exacerbated their atrial fibrillation, inadequate rate control with current AV nodal-blocking drugs, or suboptimal acute treatment of the atrial fibrillation in the ED. Patients receiving $\beta$-blockers were at increased risk for adverse events. This surprising result might reflect inadequate rate control with their current AV nodal-blocking drug regimen, associated heart failure or hypertension, or some other unmeasured predictor. We intend to further study these associations in a prospective study.

In summary, our study identified 5 important predictors for experiencing a 30-day adverse event among patients presenting to the ED with symptomatic atrial fibrillation. This study suggests that patients with increased age, smoking history, complaint of dyspnea, inadequate ventricular rate control in the ED, and home $\beta$-blocker therapy are more likely to experience an atrial fibrillation–related adverse event within 30 days.

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