CME Safety and Efficiency of Calcium Channel Blockers Versus Beta-blockers for Rate Control in Patients With Atrial Fibrillation and No Acute Underlying Medical Illness

Frank Xavier Scheuermeyer, MD, MHSc, Eric Grafstein, MD, Rob Stenstrom, MD, PhD, Jim Christenson, MD, Claire Heslop, MD, PhD, Brett Heilbron, MD, Lorraine McGrath, and Grant Innes, MD

Abstract

Objectives: Many patients with atrial fibrillation (AF) are not candidates for rhythm control and may require rate control, typically with beta-blocking (BB) or calcium channel blocking (CCB) agents. Although these patients appear to have a low 30-day rate of stroke or death, it is unclear if one class of agent is safer or more effective. The objective was to determine whether BBs or CCBs would have a lower hospital admission rate and to measure 30-day safety outcomes including stroke, death, and emergency department (ED) revisits.

Methods: This retrospective cohort study used a database from two urban EDs to identify consecutive patients with ED discharge diagnoses of AF from April 1, 2006, to March 31, 2010. Comorbidities, rhythms, management, and immediate outcomes were obtained by manual chart review, and patients with acute underlying medical conditions were excluded by predefined criteria. Patients managed only with rate control agents were eligible for review, and patients receiving BB agents were compared to those receiving CCB agents. The primary outcome was the proportion of patients requiring hospital admission; secondary outcomes included the ED length of stay (LOS), the proportion of patients having adverse events, the proportion of patients returning within 7 or 30 days, and the number of patients having a stroke or dying within 30 days.

Results: A total of 259 consecutive patients were enrolled, with 100 receiving CCBs and 159 receiving BBs. Baseline demographics and comorbidities were similar. Twenty-seven percent of BB patients were admitted, and 31.0% of CCB patients were admitted (difference = 4.0%, 95% confidence interval [CI] = −7.7% to 16.1%), and there were no significant differences in ED LOS, adverse events, or 7- or 30-day ED revisits. One patient who received metoprolol had a stroke, and one patient who received diltiazem died within 30 days.

Conclusions: In this cohort of ED patients with AF and no acute underlying medical illness who underwent rate control only, patients receiving CCBs had similar hospital admission rates to those receiving BBs, while both classes of medications appeared equally safe at 30 days. Both CCBs and BBs are acceptable options for rate control.

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From the Department of Emergency Medicine (FS, RS, JC, CH), Division of Cardiology (BH, LM), St. Paul's Hospital and the University of British Columbia, Vancouver, BC, Canada; the Department of Emergency Medicine, Mount St. Joseph's Hospital and the University of British Columbia (EG), Vancouver, BC, Canada; and the Division of Emergency Medicine, Foothills Hospital and the University of Calgary (GI), Calgary, AB, Canada.

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Supervising Editor: Stephen W. Smith, MD.

Address for correspondence and reprints: Frank Scheuermeyer, MD, MHSc; e-mail: frank.scheuermeyer@gmail.com.

Atrial fibrillation (AF) is the most common dysrhythmia encountered in emergency department (ED) patients, and its management generates substantial controversy. There are over a half-million annual ED visits in the United States, with over 60% of patients admitted to hospital.[1]

Most ED-based studies have evaluated the safety of rhythm control,[2–10] or compared rate versus rhythm control,[11–13] in patients with AF of less than 48 hours' duration; however, many patients fall outside this time frame and are not eligible for rhythm control. The American Heart Association/American College of Cardiology 2006 guidelines describe six medications (esmolol, metoprolol, propanolol, diltiazem, verapamil, and

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digoxin) for acute rate control in these patients.[14] These medications have been infrequently compared in the ED setting for AF patients with rapid ventricular rates. Although two small randomized trials have shown that diltiazem appears to reduce heart rate more quickly than metoprolol,[15,16] minimal evidence exists to guide clinicians in which agents provide the best combination of safety and timely rate control.

With our aging population and growing numbers of patients with AF, it is increasingly important to optimize efficiency and control ED and hospital length of stay (LOS), especially in high-resource AF patients. While over 70% of AF patients receiving rate control may be safely discharged from the ED with very low 30-day rates of stroke or death,[17] it is still unclear which agent is associated with more successful ventricular rate control, denoted by discharge from the ED. Our objective was to determine whether beta-blockers (BBs) or calcium channel blockers (CCBs) would have a lower hospital admission rate and to measure 30-day safety outcomes including stroke, death, and ED revisits. Based on previous studies showing that diltiazem lowered ventricular rates significantly faster than metoprolol,[15,16] we hypothesized that admission rates would be lower with CCB agents.

METHODS

Study Design

This was a retrospective cohort study. The ethics review boards of Providence Health Care, which supervises both hospitals, and the University of British Columbia, approved this study.

Study Setting and Population

The study was conducted at two Canadian university-affiliated teaching EDs that share an ED database, and the methods have been summarized elsewhere.[17] St. Paul's Hospital is an inner-city referral center with 65,000 annual ED visits during the study period. It has comprehensive cardiology services with a coronary care unit, cardiology ward, and electrophysiology. Mount St. Joseph's Hospital is a community center with 25,000 yearly visits and a general internal medicine ward. Over 200 medical students and residents are trained at both sites annually.

From April 1, 2006, to March 31, 2010, consecutive patients residing in the health region with primary ED diagnoses of AF (ICD10 code I48.0) were identified in the ED database. At both sites, board-certified cardiologists verify each electrocardiogram (ECG) within 24 hours, and each patient required ECG confirmation of the diagnosis. As this was a secondary analysis of 1-year outcomes of ED patients, ED encounters occurring within 365 days of the index visit were considered outcome events, while those occurring more than 1 year post-index visit were treated as second index events. Patients treated only with CCBs or BBs were eligible for inclusion.

Patients who had cardiac procedures (pacemaker implantation, ablation, coronary artery bypass grafting, or percutaneous coronary intervention) within 7 days prior to the index ED visit were excluded, because management decisions are typically the responsibility of the surgeon or cardiologist. Similarly, patients who were referred to the ED for direct admission by cardiologists or internists were excluded because, in these cases, the admitting physician had decided on the treatment. Third, patients with AF who attended the ED only to monitor their anticoagulation were excluded as no arrhythmia-specific management took place. Fourth, patients with the following acute medical conditions were excluded, because they require hospitalization or specific therapy unrelated to AF: sepsis, shock, pneumonia, acute coronary syndrome, acute decompensated congestive heart failure, pulmonary embolism, chronic obstructive pulmonary disease, thyrotoxicosis, hypertensive emergency, drug overdose, acute valvular disease, or hypothermia.

Study Protocol

During the study period, physicians managed patients with AF in an individualized manner. Typically, patients who had clear arrhythmia onset times < 48 hours were treated with first-line electrical or chemical cardioversion. Patients who were not eligible for rhythm control were typically given rate control agents if the heart rate was greater than 100 beats/min. Generally, patients were admitted to the hospital if attempts at rate control were unable to lower the heart rate below 100 beats/min. This was a substudy of a larger review of 1-year outcomes of all AF patients.[17]

Rather than relying on emergency physician (EP) coding, we followed the prespecified criteria outlined in Data Supplement S1 (available as supporting information in the online version of this paper). A trained, blinded reviewer (CH or FS) assessed all charts of patients with such underlying illnesses to assure that exclusions were appropriate. A kappa value was obtained for eligibility decisions, and a board-certified cardiologist reviewed controversial cases.

The sites share an electronic ED database, which records patient demographics, arrival time, triage complaint,[18] acuity level,[19] and discharge times. The database is linked to the provincial Pharmanet database, which tracks all dispensed prescription medications. The sites also share a computerized physician order entry system that captures all ED investigations, medications, and consultations. For each patient, the EP completes an electronic discharge summary (also available on the ED database), which records all diagnoses, as well as investigations, medications, procedures, and discharge prescriptions. The nursing record provided all vital signs; these were typically recorded initially, then at least every hour until discharge and whenever the rhythm changed.

For the chart review we adhered to the criteria for medical record review described by Gilbert et al.[20] and Worster et al.[21] Two trained reviewers (one staff EP [FS] and a final-year medical student with a prior graduate degree [CH]), who were blinded to all patient outcomes, independently abstracted charts onto standardized electronic spreadsheets to document vital signs, comorbidities, and ED treatments. If AF duration differed between the nursing and physician notes, the longer time was recorded. The CHADS-2 score was derived from patient comorbidities and age.[22] To calculate stroke risk, one point is given for each of the

following: congestive heart failure, hypertension, age > 75 years, and diabetes, and two points are given for prior stroke or transient ischemic attack. While validated in hospitalized patients with chronic AF, this scheme has not been validated in an ED population.

Each patient's electronic chart was reviewed to the year 1999 to clarify missing or unclear information. For example, if a note from 1999 stated that a patient had a prior stroke, that information was included. Conflicting chart information (e.g., the nursing notes recorded a 3-day history of arrhythmia, and the physician noted a 2-hour history) resulted in the worst-case scenario being recorded (in the above case, the longer arrhythmia time would have been recorded). To ensure reliability, 10% of charts were independently assessed by the second reviewer (either CH or FS), and kappa values were determined for two key variables: history of prior AF and arrhythmia duration prior to ED arrival—the latter was recorded as either less than or greater than 48 hours.

Outcomes

In our institutions, patients who achieve adequate rate control are typically discharged, and therefore, a surrogate marker of unsuccessful rate control is hospital admission; this was chosen as the primary outcome. Secondary outcomes included ED LOS, which is another indicator of rapid rate control, as well as the proportion of patients who had adverse events. The latter are outlined in Table 1 and were predefined to reflect typical complications of AF management.

For longer-term outcomes, each patient's unique provincial health number was cross-referenced with the regional ED database to monitor regional follow-up visits and ascertain potential ED visits for stroke (see Data Supplement S2, available as supporting information in the online version of this paper, for details). Patients with ischemic or hemorrhagic stroke were included, because anticoagulation can lead to the latter.[23] To determine whether a patient died, the provincial vital statistics database was interrogated: patients who died had the cause of death recorded where available; otherwise the cause was listed as "unclear."

Data Analysis

Microsoft Excel 2008 (Microsoft Corp., Redmond, WA) was used for data entry and analysis. Discrete variables are reported as percentages. Continuous variables are presented as means with standard deviations (±SDs), if normally distributed, or medians with interquartile ranges (IQRs) if nonnormally distributed. The difference between medians was calculated in R version 2.1.1 (R Project, University of Wien, Wien, Austria). r × c chi-square testing was performed for normally distributed variables; Mann-Whitney U-tests or Kruskal-Wallis tests were used to compare nonnormally distributed variables.

Table 1
Index Visit ED Adverse Events

Respiratory distress requiring
Bag-valve mask
Oral airway
Noninvasive positive-pressure ventilation
Endotracheal intubation
Hypotension requiring IV fluid bolus (crystalloid) or colloid) or vasoactive agents
New bradycardia requiring pharmacologic intervention or pacing
Confirmed thromboembolic event
Chest compressions
Death

RESULTS

Figure 1 shows that, during the 4-year study period from April 1, 2006, to March 31, 2010, a total of 1,538 patients had primary ED diagnoses of AF. A total of 205 patients were excluded because of a prespecified underlying medical etiology for their AF. Inter-rater reliability for exclusion was 0.68 (95% confidence interval [CI] = 0.59 to 0.78), and 19 patients required cardiologist adjudication to determine whether the AF was primary or precipitated by an acute medical problem. Overall, 259 consecutive rate-controlled patients were

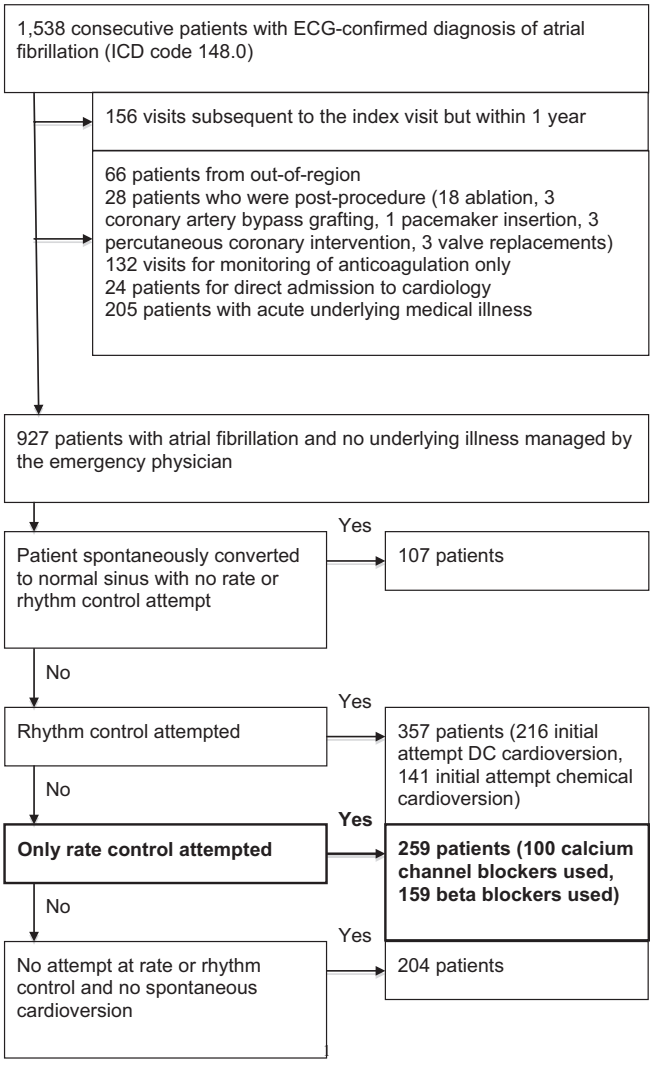

Figure 1. Study flow diagram. ECG = electrocardiogram.

analyzed. For comparison, during the same period, 216 patients were electrically cardioverted and 141 were administered chemical rhythm control at the two hospitals. Inter-rater agreements for the key chart-based data elements of AF duration and history of prior AF were substantial: $\kappa = 0.68$ (95% CI = 0.61 to 0.75) and 0.64 (95% CI = 0.59 to 0.72), respectively.

Table 2 shows that 159 patients received BBs and 100 CCBs; no patient received both. The two groups were similar in terms of age, sex, ambulance arrival, initial

Table 2
Baseline Characteristics Stratified According to Treatment Group

Characteristic	CCB	BB	Total	Difference (95% CI)
Number of patients	100	159	259	
Demographics				
Age (yr), mean (±SD)	66.8 (±14.7)	67.1 (±14.8)	67.0 (±12.8)	0.3 (−3.4 to 4.0)
Sex, male, *n* (% male)	55 (55.0)	90 (56.6)	145 (56.0)	1.6% (−11.1 to 14.4)
EMS arrival, *n* (%)	26 (26.0)	46 (28.9)	72 (27.8)	2.9% (−9.1 to 14.1)
Initial vitals on index ED visit, mean (±SD)				
Heart rate (beats/min)†	133.9 (±25.3)	126.8 (±24.1)	129.0 (±22.8)	−7.1 (−13.3 to −0.9)
Systolic BP (mm Hg)	137.0 (±24.6)	131.3 (±28.7)	133.7 (±23.7)	−5.7 (−12.5 to 1.1)
Diastolic BP (mm Hg)	83.4 (±12.6)	81.9 (±15.0)	82.5 (±12.0)	−1.5 (−5.1 to 2.1)
Respiratory rate (breaths/min)	19.3 (±2.2)	19.5 (±2.3)	19.4 (±1.8)	0.2 (−0.4 to 0.8)
SO_2	97.1 (±2.1)	97.2 (±2.2)	97.2 (±1.7)	0.1 (−0.4 to 0.6)
Temperature (°C)	36.7 (±0.3)	36.7 (±0.3)	36.7 (±0.2)	0.0 (−0.05 to 0.05)
Duration of atrial fibrillation episode prior to triage, *n* (%)				
Time of onset < 48 hr	25 (25.0)	44 (27.6)	69 (26.6)	2.6% (−9.2 to 13.7)
Time of onset < 48 hr, anticoagulated*	13 (13.0)	20 (12.6)	33 (12.8)	−0.4% (−10.1 to 8.1)
Onset > 48 hr, anticoagulated*	42 (42.0)	70 (44.0)	112 (43.2)	2.0% (−10.9 to 14.6)
Onset > 48 hr, not anticoagulated	33 (33.0)	45 (28.3)	78 (30.1)	−4.7% (−16.9 to 7.1)
Chief complaint, *n* (%)				
Palpitations	33 (33.0)	60 (37.7)	93 (35.9)	4.7% (−7.9 to 16.7)
Chest pain	29 (29.0)	43 (27.0)	72 (27.7)	−2.0% (−14.0 to 9.5)
Dyspnea	30 (30.0)	39 (24.5)	69 (26.6)	−5.5% (−17.4 to 6.0)
Weakness	8 (8.0)	15 (9.4)	23 (8.9)	1.4% (−7.1 to 8.7)
Acute focal neurologic symptom	0 (0.0)	1 (0.6)	1 (0.4)	0.6% (−4.0 to 4.0)
Other	0 (0.0)	1 (0.6)	1 (0.4)	0.6% (−4.0 to 4.0)
Prior arrhythmias, *n* (%)				
Atrial fibrillation	62 (62.0)	102 (64.1)	164 (63.3)	2.1% (−10.2 to 14.8)
DC cardioversion	6 (6.0)	11 (6.9)	17 (6.6)	0.9% (−6.9 to 7.4)
Ablation	1 (1.0)	3 (1.9)	4 (1.5)	
Risk factors, *n* (%)				
Hypertension	58 (58.0)	90 (56.6)	168 (64.9)	−1.4% (−14.0 to 11.5)
Coronary artery disease	16 (16.0)	27 (17.0)	43 (16.6)	1.0% (−9.5 to 10.4)
Valvular disease	10 (10.0)	15 (9.4)	25 (9.7)	−0.6% (−9.5 to 7.1)
Diabetes	14 (14.0)	22 (13.8)	36 (13.9)	−0.2% (−10.1 to 8.7)
Congestive heart failure	9 (9.0)	14 (8.8)	25 (9.7)	−0.2% (−8.8 to 7.2)
Prior stroke or TIA	8 (8.0)	11 (6.9)	19 (7.3)	−1.1% (−9.4 to 5.8)
CHADS 2 score, *n* (%)				
0	33 (33.0)	53 (33.3)	86 (33.2)	0.3% (−12.1 to 12.3)
1	29 (29.0)	47 (29.6)	76 (29.3)	0.6% (−11.6 to 12.1)
2	24 (24.0)	41 (25.7)	65 (25.1)	1.7% (−9.9 to 12.7)
3	8 (8.0)	9 (5.6)	17 (6.6)	−2.4% (−10.5 to 4.3)
4	2 (2.0)	6 (3.8)	8 (3.1)	1.8% (−4.4 to 6.7)
5	3 (3.0)	1 (0.6)	4 (1.5)	−2.4% (−8.6 to 1.7)
6	1 (1.0)	2 (1.3)	3 (1.2)	0.3% (−4.1 to 5.1)
Medications, *n* (%)				
Aspirin	26 (26.0)	49 (30.8)	75 (29.0)	4.8% (−7.3 to 16.1)
Clopidogrel	2 (2.0)	4 (2.5)	6 (2.3)	0.5% (−5.0 to 5.5)
Warfarin	21 (21.0)	38 (23.9)	57 (22.0)	2.9% (−8.5 to 13.4)
BB†	18 (18.0)	55 (34.6)	73 (28.1)	16.6% (4.9 to 27.0)
CCB†	22 (22.0)	16 (10.1)	38 (14.7)	−11.9% (−22.4 to −2.4)
Propafenone	1 (1.0)	1 (0.6)	2 (0.7)	−0.4% (−5.7 to 3.1)
Amiodarone	6 (6.0)	5 (3.1)	11 (4.2)	−2.9% (−10.2 to 2.8)
Sotalol	5 (5.0)	7 (4.4)	12 (4.6)	−0.6% (−7.9 to 5.2)
Digoxin	9 (9.0)	11 (6.9)	20 (7.7)	−2.1% (−10.6 to 5.0)
Flecainide	0 (0.0)	1 (0.6)	1 (0.4)	0.6% (−4.0 to 4.0)
Dronedarone	0 (0.0)	0 (0.0)	0 (0.0)	0.0% (−2.9 to 4.6)

*Appropriate anticoagulation: Using 2006–2010 Canadian Cardiovascular Society recommendations, for CHADS 2 = 0, no anticoagulation required; for CHADS 2 = 1, aspirin anticoagulation acceptable; for CHADS 2 > 1, coumadin anticoagulation required.
†Variables where there appears to be a significant difference between patients receiving CCBs and BBs.
BB = beta-blocker; BP = blood pressure; CCB = calcium channel blocker; EMS = emergency medical services; SO_2 = oxygen saturation; TIA = transient ischemic attack.

vital signs (except initial heart rate, which was a little higher in the CCB group), comorbidities, and arrhythmia onset times. More than three-quarters of patients had arrhythmia onset times of greater than 48 hours; patients who arrived within 48 hours typically had triage complaints such as acute chest pain or dyspnea rather than palpitations. Patients in the BB group were more likely to use BBs in the community, and patients in the CCB group were more likely to use CCBs; overall, 28.1% of patients took BBs in the community, and 14.7% took CCBs.

Emergency physician investigations are shown in Table 3. The rates of investigations, including 6-hour troponin testing, were similar in both groups. Although diastolic blood pressure decreased a bit more in patients given CCB than BB, there were no significant differences in final heart rates or blood pressures.

Table 4 illustrates the primary and secondary outcomes. Twenty-seven percent of BB patients were admitted and 31.0% of CCB patients were admitted (difference 4.0%, 95% CI = −7.7% to 16.1%). The final median heart rates of admitted patients were 110 beats/min (IQR = 95 to 123 beats/min) for BB and 113 beats/minute (IQR = 96 to 125 beats/min) for CCB; final median heart rates for discharged patients were 83 beats/min (IQR 70 to 96 beats/min) for BB and 81 beats/min (IQR = 69 to 95 beats/min) for CCB. Overall, for BB, the ratio of decrease in heart rate to the decrease in systolic blood pressure was 5.0 beats/min/mm Hg decrease; for CCB, the ratio was 3.39 beats/min/mm Hg decrease. In both groups, the EPs discharged approximately one-half of patients; in both groups, nearly one-quarter of patients were discharged from the ED after cardiology consultation. BB patients had a median LOS of 326

Table 3
ED Investigations and Final Vital Signs, Stratified by Treatment Group

Variable	CCB (n = 100)	BB (n = 159)	Total (N = 259)	Difference (95% CI)*
Investigations (n,%)				
Complete blood count	89 (89.0)	140 (88.1)	229 (88.4)	−0.9 (−9.1 to 8.4)
Blood chemistry	87 (87.0)	138 (86.8)	225 (86.9)	−0.2 (−8.8 to 9.5)
International normalized ratio	53 (53.0)	85 (54.7)	138 (53.3)	1.7 (−11.1 to 14.5)
Initial troponin	68 (68.0)	115 (72.3)	183 (70.7)	4.3 (−7.4 to 16.4)
Six-hour troponin	21 (21.0)	38 (23.9)	59 (22.8)	2.9 (−8.5 to 13.4)
Chest x-ray	42 (42.0)	60 (37.7)	102 (39.3)	−4.3 (−17.0 to 8.3)
Final vital signs, mean (±SD)†				
Heart rate (beats/min)	92.8 (±14.5)	89.8 (±16.6)	90.9 (±15.7)	−3.0 (−7.0 to 1.0)
Systolic BP (mm Hg)	124.9 (±19.5)	123.9 (±20.1)	124.3 (±19.6)	−1.0 (−6.0 to 4.0)
Diastolic BP (mm Hg)	73.7 (±11.3)	75.5 (±11.8)	74.8 (±11.4)	1.8 (−1.1 to 4.7)
Difference in initial and final vital signs, mean (±SD)				
Heart rate (beats/min)	−41.1 (±18.3)	−37.0 (±17.5)	−38.1 (±17.9)	4.1 (−0.9 to 8.0)
Systolic BP (mm Hg)	−12.1 (±15.8)	−7.4 (±17.2)	−9.4 (±18.5)	3.7 (−0.5 to 7.1)
Diastolic BP (mm Hg)‡	−9.7 (±12.0)	−6.4 (±13.5)	−7.7 (±12.7)	3.3 (0.6 to 6.9)

*BB minus CCB, with continuity correction.
†The final heart rate and blood pressures while in the ED, typically measured immediately prior to discharge or transfer to the ward.
‡variables where there appears to be a significant difference between patients receiving calcium channel blockers and beta-blockers.
BB = beta-blocker; CCB = calcium channel blocker.

Table 4
ED LOS, Overall and Stratified According to ED Disposition

Characteristic	CCB (n = 100)	BB (n = 159)	Total (N = 259)	Difference (95% CI)†
Consultation rates, n (%)				
Consulted	52 (52.0)	78 (49.1)	130 (50.2)	−2.9 (−15.8 to 10.0)
Not consulted	48 (48.0)	81 (50.9)	129 (49.8)	2.9 (−10.0 to 15.8)
Admission rates, n (%)*				
Admitted to cardiology	31 (31.0)	43 (27.0)	74 (28.6)	−4.0 (−16.1 to 7.7)
Discharged home	69 (69.0)	116 (78.0)	185 (71.4)	4.0 (−7.7 to 16.1)
Who performed discharge, n (%)				
Discharged by EP	48 (48.0)	78 (49.1)	126 (48.6)	1.1 (−11.9 to 13.9)
Discharged by cardiologist following consult	21 (21.0)	38 (23.9)	59 (22.8)	2.9 (−8.5 to 13.4)
ED LOS (minutes)				
Median (IQR)	302 (182 to 455)	326 (199 to 482)	316 (196 to 474)	24 (−11 to 62)
Range	64 to 1,230	45 to 1,274	45 to 1,274	Not applicable

*Primary outcome.
†BB minus CCB.
BB = beta-blocker; CCB = calcium channel blocker; IQR = interquartile range; LOS = length of stay.

minutes (IQR = 199–482 minutes), and CCB patients had a median LOS of 302 minutes (IQR = 182–455), median difference 24 minutes, and 95% CI = −11 to 62 minutes. There was no significant difference in either admission rate or LOS.

Table 5 shows the dosing, admission rates, and LOS of all agents. There was no significant difference in the admission rates for any of the medications. For oral formulations, patients receiving atenolol ($n = 10$) had a longer LOS than the three other agents. Intravenous (IV) formulations of metoprolol, diltiazem, and verapamil all had similar LOS.

Additional outcomes are outlined in Table 6, and there was no apparent difference between the two groups. Nine patients receiving CCB converted spontaneously, as did 12 receiving BB. There were 10 ED adverse events in the ED (six BB, four CCB); all involved patients who became hypotensive but responded to crystalloid boluses. There was no significant difference in 7- or 30-day ED revisits or hospital admissions. One patient who received metoprolol in the ED had a stroke within 30 days. He was a 59-year-old male with diabetes, hypertension, and severe reactive arthritis who was admitted to the hospital at the index ED visit for new-onset AF. Warfarin anticoagulation was initiated during this admission and he re-presented to the ED at 27 days with an international normalized ratio of 4.1 and a thalamic hemorrhage; he made an uneventful recovery. One patient who received diltiazem in the ED died within 30 days; he was a 56-year old male with metastatic pancreatic cancer and a do-not-attempt-resuscitation order in place at the index ED visit; he was admitted and died at 22 days. It is unlikely that ED management could be implicated in either outcome.

DISCUSSION

While most of the controversy regarding AF management has involved patients with arrhythmia durations of less than 48 hours,[2–13, 24–26] many patients arrive outside of this time and can only be managed by rate control. Rate control appears safe, as evidenced by the low rate of ED adverse events and strokes or deaths at 30 days, but clinicians have a variety of options and the relative effectiveness of CCB or BB is unclear. Our study expands on two randomized trials that compared diltiazem and metoprolol. Demircan and coworkers[16] found that 18 of 20 AF patients receiving diltiazem had a heart rate < 100 beats/min within 20 minutes, while 16 of 20 patients receiving metoprolol had this heart rate within 20 minutes. Similarly, Fromm and colleagues[15] compared 24 patients receiving diltiazem with 28 receiving metoprolol and concluded that the former group was more likely to achieve a heart rate < 100 beats/min within 30 minutes. Neither study reported any patients with hypotension. However, neither study reported important outcomes including consultations, admission rate, LOS, and out-of-hospital outcomes such as stroke or death. In a description of low-dose diltiazem for ventricular rate control, Lee and coworkers[27] documented that approximately one-third of patients had a 20% reduction in systolic blood pressure, but did not elaborate on subsequent ED treatments or other management decisions or patient outcomes.

Table 5
ED Outcomes Stratified by Rate Control Agent

Characteristic	Metoprolol	Atenolol	Diltiazem	Verapamil	p-value*
Number of patients	149	10	51	49	
Route of administration, *n* (%)					
Oral	28	10	11	8	
IV	121	0	40	41	
Dosing, oral					
Median dose (IQR) (mg)	50 (25–50)	50 (50–50)	60 (30–120)	100 (80–120)	
Range (mg)	(25–150)	(50–50)	(30–240)	(40–120)	
Dosing, IV					
Median dose (IQR) (mg)	10 (5–15)		20 (15–25)	5 (2.5–5)	
Range (mg)	(2.5–15)		(2.5–25)	(2.5–17.5)	
Disposition, oral agents, *n* (%)					
Admission	8 (28.6)	2 (20.0)	3 (27.3)	2 (25.0)	$\chi^2(6) = 1.42$, p = 0.96
Discharge	20 (71.4)	8 (80.0)	6 (54.5)	6 (75.0)	
Disposition, IV agents, *n* (%)					
Admission	33 (27.3)	0 (0.0)	12 (30.0)	14 (34.1)	$\chi^2((4) = 0.95$, p = 0.92
Discharge	88 (72.7)	0 (0.0)	30 (75.0)	27 (65.9)	
Disposition, overall, *n* (%)					
Admission	41 (27.5)	2 (20.0)	15 (29.4)	16 (32.7)	$\chi^2((6) = 1.19$, p = 0.98
Discharge	108 (72.5)	8 (80.0)	36 (70.6)	33 (67.3)	
LOS, hours:min (IQR)					
LOS, oral agents	5:43 (3:14–7:52)	9:04 (7:13–13:11)	4:15 (2:57–6:15)	3:41 (3:30–4:04)	H = 14.4, p = 0.002
LOS, IV agents	4:57 (3:19–7:29)		5:34 (3:35–8:02)	4:42 (2:56–8:32)	H = 0.10, p = 0.96
LOS, overall	5:19 (3:25–7:50)	9:04 (7:13–13:11)	5:28 (3:22–7:34)	4:34 (2:58–8:07)	H = 11.7, p = 0.008

For all analyses, $p \leq 0.05$ denotes statistical significance, with no adjustment for the multiple comparisons. p-values near 0.05 need to be interpreted cautiously. The family-wise error rate is $a_{fw} = 0.059$.
IQR = interquartile range; LOS = length of stay.
*r × c chi-square testing (with four or six degrees of freedom) for measuring difference in proportions between admission and discharge; Kruskal-Wallis test with two or three degrees of freedom for measuring difference in LOS.

Table 6
ED Outcomes and Disposition Stratified According to Treatment Group

Characteristic	CCB	BB	Total	Difference (95% CI)*
Number of patients	100	159	259	
ED adverse events, *n* (%)				
Respiratory distress	0 (0.0)	0 (0.0)	0 (0.0)	0 (−2.9 to 4.6)
Hypotension	4 (4.0)	6 (3.8)	10 (3.9)	−0.2 (−7.1 to 5.1)
Bradycardia	0 (0.0)	0 (0.0)	0 (0.0)	0 (−2.9 to 4.6)
Stroke/thromboembolism	0 (0.0)	0 (0.0)	0 (0.0)	0 (−2.9 to 4.6)
Chest compressions	0 (0.0)	0 (0.0)	0 (0.0)	0 (−2.9 to 4.6)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (−2.9 to 4.6)
Total adverse events	4 (4.0)	6 (3.8)	10 (4.1)	−0.2 (−7.1 to 5.1)
Revisit/admission data within 7 days†				
Patients revisiting ED, *n* (%)	7 (7.0)	10 (6.3)	17 (6.6)	−0.7 (−8.7 to 5.9)
Number of total revisits	16	13	29	Not applicable
ED visits per patient	0.16	0.08	−0.08	−0.08 (−17.4 to 0.01)
Number of hospital admissions	2	2	4	Not applicable
Hospital admissions per patient	0.02	0.01	0.02	−0.007 (−0.07 to 0.03)
Revisit/admission data within 30 days†				
Patients revisiting ED, *n* (%)	20 (20.0)	36 (22.6)	56 (21.6)	2.6 (−8.6 to 12.9)
Number of total revisits	47	79	126	Not applicable
ED visits per patient	0.47	0.50	0.49	0.03 (−0.10 to 0.15)
Number of hospital admissions	7	15	22	Not applicable
Hospital admissions per patient	0.07	0.09	0.08	0.02 (−0.06 to 0.09)
Strokes and deaths within 30 days, *n* (%)				
Deaths within 30 days	1 (1.0)	0 (0.0)	1 (0.6)	−1.0 (−5.2 to 2.1)
Strokes within 30 days	0 (0.0)	1 (0.6)	1 (0.6)	0.6 (−4.0 to 4.0)
Death and strokes within 30 days	1 (1.0)	1 (0.6)	2 (1.2)	−0.4 (−5.6 to 3.1)

BB = beta-blocker; CCB = calcium channel blocker.
*BB minus CCB; continuity correction employed.
†Related to atrial fibrillation but not including the index ED visit (please see Data Supplement S2 for details on follow-up visits). Patients could have more than one ED visit or admission in the following 30 days.

While diltiazem appears to reduce heart rate more quickly than metoprolol, prior ED-based studies have only typically reported data to 30 minutes.[15, 16] However, even if the ventricular rate has been slowed, such patients are unlikely candidates for discharge within this time. The high percentage of patients receiving investigations including blood tests and imaging implies that physicians were attempting to rule out serious acute underlying medical causes of the AF such as acute coronary syndrome or pulmonary embolism. In fact, it appears that approximately one-fifth of patients remained in the department for 6 hours or more primarily to obtain serial cardiac investigations to rule out acute coronary syndromes. It is feasible that the application of rapid acute coronary syndrome rule-out protocols such as those developed by Than and coworkers[28] may assist in much shorter LOS for such patients.

This study assists clinicians by demonstrating that, despite the more rapid decrease in heart rate observed with diltiazem, use of either CCB or BB agents is associated with similar ED resource use, hospital admission rate, adverse event profiles, and 30-day outcomes. Both agents may be considered acceptable in patients with acute AF who do not have underlying medical causes and are not candidates for rhythm control.

LIMITATIONS

This was a retrospective chart review with no sample size or power calculation. Although the patients were similar for 44 of the 47 measured baseline variables, as well as for six key investigations, for all disposition outcomes, and for the 30-day ED revisit and hospital admission rates, there are potentially unmeasured confounders that could affect the results. For example, there was no treatment protocol: individual physicians made decisions on rate control, timing, and dosing of medications, as well as referral and disposition, based on individual preference; patient preferences were not recorded. Although patients were generally admitted if the ventricular rate remained greater than 100 beats/min, EPs had no influence over consultant decisions regarding management. We investigated two agents from each class, rather than a single agent, as well as both oral and IV formulations, and this could have biased results toward nonsignificance. However, our medication-by-medication breakdown (Table 5) may help counter this argument. The study may not be adequately powered to capture adverse events; there have been insufficient patients to differentiate outcomes between the two groups or enough patients to produce a spurious difference among one or more variables or outcomes. An adequately powered randomized trial conducted with a single agent in each class would overcome most of these limitations.

Patients were included based on discharge diagnosis—if the coding was incorrect (for example "atrial flutter" [ICD I48.1]) or the discharge summary not completed, then patients would not have been captured. Patients with acute underlying medical conditions (for example, acute coronary syndrome or sepsis) were not included in this study, and it would be inappropriate to apply our

data and conclusions to such patients; the same caveat applies to patients with atrial flutter.

The results from our setting—where over 70% of patients were safely discharged home—may be difficult to apply to other environments, where the discharge rate is typically under 40% for all AF patients.[1] Furthermore, our physicians tended to employ rhythm control for patients with AF of less than 48 hours; in other centers, these patients might undergo rate control instead. However, patients who underwent rhythm control had very low rates of adverse events, stroke, or death at 30 days[9] and 1 year.[17] ED LOS is a meaningful outcome if the majority of patients are discharged, but may be of questionable importance in settings where AF patients are usually admitted. Our follow-up may have missed patients who moved outside the province and then suffered strokes within 30 days, although the yearly migration rate from the health region is less than 0.6%.[29] During the follow-up period, we did not record subsequent AF episodes that did not require hospitalization, nor did we have access to non-ED records to determine which patients might have had electrophysiologic procedures such as ablation.

CONCLUSIONS

In this cohort of ED patients with atrial fibrillation and no acute underlying medical illness who underwent rate control only, patients receiving calcium channel blockers had similar hospital admission rates to those receiving beta-blockers, while both classes of medications appeared equally safe at 30 days. Both calcium channel blockers and beta-blockers are acceptable options for rate control.

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Supporting Information

The following supporting information is available in the online version of this paper:

Data Supplement S1. Exclusion criteria for acute underlying medical causes of atrial fibrillation.

Data Supplement S2. Follow-up ED visits.

Abstracts en español!

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