CME Information: A Multicenter Randomized Trial to Evaluate a Chemical-first or Electrical-first Cardioversion Strategy for Patients With Uncomplicated Acute Atrial Fibrillation

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CME

A Multicenter Randomized Trial to Evaluate a Chemical-first or Electrical-first Cardioversion Strategy for Patients With Uncomplicated Acute Atrial Fibrillation

Frank X. Scheuermeyer, MD, MHSc, Gary Andolfatto, MD, Jim Christenson, MD, Cristina Villa-Roel, PhD, and Brian Rowe, MD, MSc

ABSTRACT

Background: Emergency department (ED) patients with uncomplicated atrial fibrillation (AF) of less than 48 hours may be safely managed with rhythm control. Although both chemical-first and electrical-first strategies have been advocated, there are no comparative effectiveness data to guide clinicians.

Methods: At six urban Canadian centers, ED patients ages 18 to 75 with uncomplicated symptomatic AF of less than 48 hours and $CHADS_2$ score of 0 or 1 were randomized using concealed allocation in a 1:1 ratio to one of the following strategies: 1) chemical cardioversion with procainamide infusion, followed by electrical countershock if unsuccessful; or 2) electrical cardioversion, followed by procainamide infusion if unsuccessful. The primary outcome was the proportion of patients discharged within 4 hours of arrival. Secondary outcomes included ED length-of-stay (LOS); prespecified ED-based adverse events; and 30-day ED revisits, hospitalizations, strokes, deaths, and quality of life (QoL).

Results: Eighty-four patients were analyzed: 41 in the chemical-first group and 43 in the electrical-first group. Groups were balanced in terms of age, sex, vital signs, and $CHADS_2$ scores. All patients were discharged home, with 83 (99%) in sinus rhythm. In the chemical-first group, 13 of 41 patients (32%) were discharged within 4 hours compared to 29 of 43 patients (67%) in the electrical-first group ($p = 0.001$). In the chemical-first group, the median ED LOS was 5.1 hours (interquartile range [IQR] = 3.5 to 5.9 hours) compared to 3.5 hours (IQR = 2.4 to 4.6 hours) in the electrical-first group, for a median difference of 1.2 hours (95% confidence interval = 0.4 to 2.0

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The Providence Health Care research ethics board approved the study (reference number H12-0048), and this was approved at all sites via harmonized ethics review. Written informed consent was obtained from patients or a legal representative before enrollment.
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hours, p < 0.001). No patients experienced stroke or death. All other outcomes, including adverse events, ED revisits, and QoL, were similar.

Conclusion: In uncomplicated ED AF patients managed with rhythm control, chemical-first and electrical-first strategies both appear to be successful and well tolerated; however, an electrical-first strategy results in a significantly shorter ED LOS.

Atrial fibrillation (AF) is the most common significant dysrhythmia encountered in the emergency department (ED)[1] and in uncomplicated patients with symptoms less than 48 hours, the 2011 Canadian Cardiovascular Society (CCS) guidelines permit either rate or rhythm control.[2] In Canadian academic centers, the proportion of patients with acute AF who undergo rhythm control ranges from 42% to 85%[3] and emergency physicians typically employ one of two safe strategies.[4–8] Chemical cardioversion can be attempted first, typically with procainamide infusion; if this approach restores sinus rhythm, the patient is discharged. If unsuccessful, procedural sedation and electrical countershock are administered.[3–6,8] Alternatively, procedural sedation and electrical cardioversion may be attempted first; if successful, the patient is discharged home. If this fails to restore sinus rhythm, chemical conversion is attempted.[3,4,6–8] In both cases, if the patient converts to and maintains sinus rhythm, the patient is discharged home; otherwise the patient is typically consulted to cardiology.[3–8] Both strategies have been previously described and over a thousand patients have been collected for both electrical-first and chemical-first strategies with 30-day outcomes: no serious adverse events such as stroke, myocardial infarction, or death have been described to date.[3–8] Thus, although both strategies appear safe, comparative effectiveness data is lacking. As a result, Canadian management is variable: a chemical-first approach is used in 56% of patients and an electrical-first in 44%.[3] To date, there has been one randomized trial comparing to an electrical-only versus chemical-only strategies demonstrated a shorter ED length of stay (LOS) for the former, but nearly one-fifth of patients were discharged home in AF, and one-third was lost to follow-up.[9]

While both chemical-first and electrical-first cardioversion of uncomplicated AF appear very low risk,[3–8] we sought to determine if one strategy resulted in the achievement of sinus rhythm and resulting discharge more quickly. This could benefit patients by restoring normal physiology more quickly to minimize ED resource use. We conducted a randomized controlled trial focused on ED-based clinical outcomes and 30-day safety and patient-reported outcomes.

METHODS

Design and Oversight

This was a multicenter randomized study with concealed allocation involving ED patients with AF of less than 48 hours' duration. The study protocol was registered at ClinicalTrials.gov (NCT01994070).

Setting

This trial was conducted at six urban EDs in western Canada and was approved by the ethics boards at all sites. All are university-affiliated teaching centers staffed by board-certified emergency physicians who generally only work at one site. The EDs ranged from small community hospitals with no on-site cardiologists to provincial referral centers with electrophysiology labs, 24-hour catheterization capability, and cardiac surgery including transplants and varied substantially in annual census, patient flow, case distribution, and overall admission rate. Recruitment took place during time blocks when research assistants were available. (Please see Data Supplement S1, Appendix S1 [available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13669/full], for a detailed description of settings including ED and hospital resources and times of enrollment.) All sites have trainees, mostly family medicine residents, although attending physicians made nearly all care decisions, including study eligibility, and timing of rhythm control.

Patients

While research assistants were on duty, consecutive potentially eligible patients between 18 and 75 years of age with episode of AF less than 48 hours' duration as the primary diagnosis were screened by emergency physicians and referred for enrollment. Since > 90% of patients described in ED-based rhythm control studies[4–8] have a $CHADS_2$ score[10] less than 2 and little ED-based data on rhythm control in higher-risk patients exists, we stipulated that a $CHADS_2$ score of 0 or 1 was required. Patients were required to be taking appropriate anticoagulation as per the 2011 CCS guidelines.[2,11]

Patients who attended the ED for other reasons (for example, trauma or gout and were found to have incidental AF) were not included as the AF had likely been present for an unknown length of time. Hemodynamically unstable patients (those with altered mental status, acute chest pain or heart failure, or systolic blood pressure less than 90 mm Hg) were excluded as such patients are often treated with rapid electrical countershock.[2] Patients with atrial flutter were ineligible since this dysrhythmia does not readily convert with procainamide.[12] AF patients with an acute underlying medical illness were also excluded, since they respond poorly to rhythm control.[13] Patients could not have had a cardiac procedure such as coronary artery bypass grafting, percutaneous coronary intervention, electrophysiologic ablation, or pacemaker or defibrillation insertion within the prior 2 weeks, as such patients are typically managed by cardiologists or surgeons. Finally, patients who were acutely intoxicated or withdrawing from alcohol or illicit drugs were ineligible.

Ethics

Local research ethics boards approved the study at each site. Written informed consent was obtained from patients or a legal representative before enrollment.

Study Treatments

Prior to the study, and at regular intervals throughout the study, we informed all staff physicians regarding study protocol and patient eligibility. Approximately one-third of such patients may have an acute underlying illness, and this may be occult in many cases.[13] To ensure that we did not mistakenly enroll such a patient, we encouraged physicians to obtain an electrocardiogram, complete blood count, electrolytes, serum creatinine, thyroid-stimulating hormone, cardiac troponin, and a chest radiograph on all patients. Using the RedCap (Vanderbilt University, Nashville, TN, licensed to the Women's and Children's Research Institute, University of Alberta, Edmonton, AB) online algorithm, consenting eligible patients were block randomized in groups of four at each site in a 1:1 fashion using concealed allocation. Patients were randomly assigned to receive one of two treatments: 1) chemical cardioversion, followed by electrical cardioversion if unsuccessful; or 2) electrical cardioversion, followed by chemical cardioversion if unsuccessful. Failure to achieve and maintain normal sinus rhythm after both treatments were completed mandated cardiologist consultation (please see Figure 1 for study groups). As per the 2011 Canadian guidelines periprocedural anticoagulation was discouraged. 2) Research assistants prospectively recorded all data directly into the online RedCap system, including patient demographics, vital signs, results of investigations, times and doses of medications, potential adverse events, and times of consultation and discharge.

Chemical Cardioversion Rationale and Protocol

Chemical cardioversion was attempted with procainamide since this has been well studied in North America.[3–6,8] Although there are no specific ED-based guidelines, we recommended a dose of 17 mg/kg up to a maximum of 1500 mg infused over 1 hour. Furthermore, there is no current standardized time frame for chemical conversion, but prior research indicates that half of patients who convert do so within 1 hour and 90% convert within 2 hours.[8] This information was conveyed to all physicians at the start of the study, at regular intervals throughout the study, and by research assistants at the bedside via the following standardized script: "Fifty percent of patients who convert will do so within one hour and 90% of patients who convert will do so within two hours" and no additional information was given.

Electrical Conversion Rationale and Protocol

For procedural sedation and analgesia, all sites required the attendance of at least one emergency physician, and a trained nurse and respiratory therapist. Although physicians could manage patients at their discretion, comfort level, and ED policy, the following regimen was recommended by the study team: propofol was to be administered with an initial bolus of 0.50 mg/kg, with further slow boluses of 0.25 mg/kg every minute thereafter if sedation depth was deemed inadequate by the attending physician.[14] Electrical conversion was recommended as a synchronized biphasic waveform sequence of 100 to 150 to 200 J[9] and a maximum of three shocks were allowed. Procainamide was initiated immediately after failure of the third shock.

Outcomes

The primary outcome was the proportion of patients discharged within 4 hours of ED arrival, which was defined as the time the patient registered at triage. (Prior to study commencement, the NCT primary outcome was defined as ED LOS. However, to ensure a parametric result and straightforward sample size calculation, the primary outcome was clarified as the proportion of patients

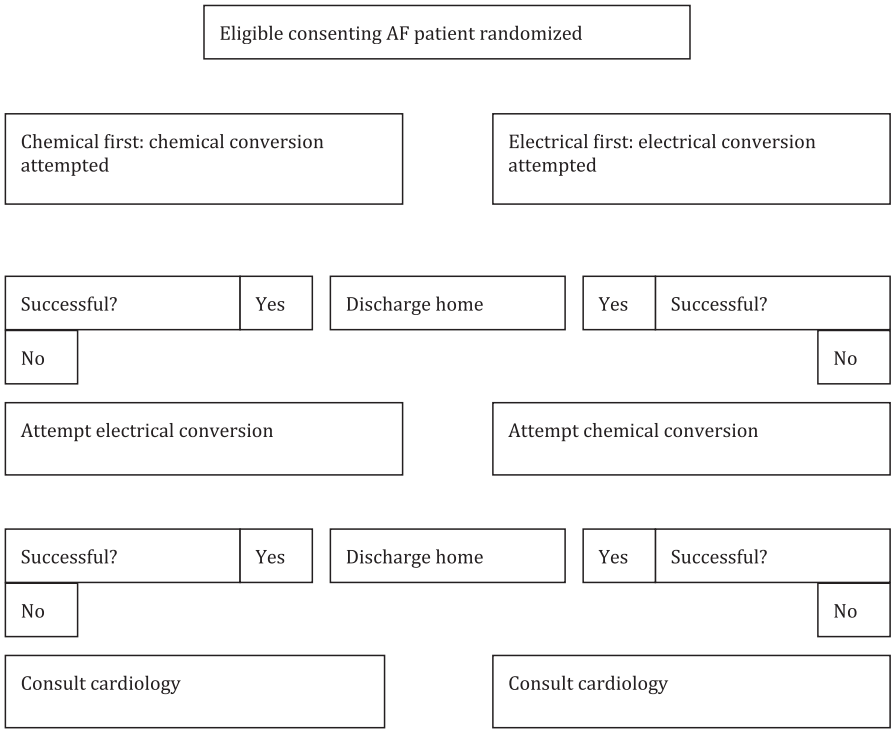

Figure 1. Study groups. AF = atrial fibrillation.

discharged within 4 hours.) Prior retrospective studies have demonstrated that a chemical-first approach appears to have a median 5-hour ED LOS,[3–6] while electrical-first approach appears to have a median 3-hour ED LOS.[7,8] Confirming this, a two-center study found that 80% of electrical-first patients were discharged at 4 hours, while 50% of chemical-first patients were discharged at 4 hours.[8] No attending physicians were aware of this outcome, since this could have biased the timing of any treatments. Instead, physicians were informed via standardized script that the study purpose "was to assess the safety and efficiency of both methods."

Secondary outcomes included additional median time intervals, ED-based adverse events (AEs), and 30-day patient-centered outcomes.[1] Regarding timing, the following patient care intervals were prespecified: registration to physician assessment, assessment to randomization, randomization to conversion, conversion to discharge, randomization to discharge, and registration to discharge.[2] Regardin gED-based adverse events, prespecified AEs were based on the World Society of Intravenous Anesthesia guidelines[15] (Table 1). Although these standards were developed for sedation, the main procainamide-related AEs—hypotension and arrhythmias—are also included. Research assistants familiar with these guidelines noted all potential AEs, and an independent safety committee of two emergency physicians blinded to allocation reviewed each to ascertain whether it was truly an AE.[3] Regarding 30-day outcomes, at 3 and 30 days, research assistants blinded to allocation telephoned patients and asked about further physician and hospital visits, as well as obtaining a quality-of-life (QoL) assessment based on the SF-8.[16] The full questionnaire can be seen in Data Supplement S1, Appendix S2. If a patient could not be contacted by telephone, the family physician was contacted; if that failed, the regional ED databases were assessed for further visits to ensure stroke-free survival.

Sample Size

Based on previous data (80% patients discharged in the electrical-first group at 4 hours and 50% in the chemical-first group),[3–8] 39 patients would be required in each group to have an 80% power to detect a difference of this magnitude or greater with a two-sided alpha of 0.05. An additional 10% enrollment was added to offset potential dropouts, resulting in a total sample size of 86 patients. No interim analysis was planned.

Data Analysis

The software package was STATA (StataCorp 2013, Stata Statistical Software, Release 13). Study variables are reported in terms of means with standard deviations (SDs) or medians with interquartile ranges (IQRs) where applicable. Patients with protocol violations were analyzed, but those who withdrew or were

Table 1
Description of Adverse Events, Interventions, and Outcomes[15]

1. Please note the adverse event. Check all that apply.
(a) Minimal risk
Vomiting/retching
Subclinical respiratory depression*
Muscle rigidity
Hypersalivation
Paradoxical response†
Recovery agitation‡
Prolonged recovery§
(b) Minor risk
Oxygen desaturation < 60 seconds
Apnea < 20 seconds
Airway obstruction
Failed sedation‖
Allergic reaction; no anaphylaxis
Bradycardia¶
Tachycardia¶
Hypotension¶
Hypertension¶
Ventricular arrhythmia
Seizure
Skin irritation/burn
(c) Sentinel risk
Oxygen desaturation > 60 seconds or < 75%
Apnea > 60 seconds
Shock**
Cardiac arrest
2. Please note the interventions. Check all that apply.
(a) Minimal risk
No intervention
Administration of additional sedative, antiemetic, or antihistamine
(b) Minor risk
Airway repositioning
Tactile stimulation
New or increased supplemental oxygen
(c) Moderate risk
Bag-valve-mask–assisted ventilation
Laryngeal mask airway
Oral/nasal airway
Positive pressure ventilation
Administration of reversal agents, IV fluids, or IV anticonvulsants
(d) Sentinel risk
Chest compressions
Administration of vasoactive agents
Neuromuscular blockade
Endotracheal intubation
Atropine for bradycardia
3. Please note the outcome of the adverse event. Check all that apply.
(a) Minimal risk
No adverse outcome
(b) Moderate risk
Unplanned hospitalization
(c) Sentinel risk
Death or permanent neurologic injury
Pulmonary aspiration††

*Subclinical respiratory depression is defined as capnographic abnormalities (pCO_2 > 50 or loss of waveform) without clinical evidence of respiratory depression.
†Paradoxical response is defined as unanticipated agitation in response to sedatives.
‡Recovery agitation is defined as crying, agitation, delirium, or hallucinations during the recovery phase.
§Prolonged recovery is failure to return to baseline within 2 hours.
‖Failed sedation is the inability to achieve a level of sedation adequate to perform the procedure.
¶Alteration in vital signs for brady-/tachycardia or hypo-/hypertension is defined as a > 25% change in baseline vitals.
**Shock is clinical evidence of inadequate perfusion.
††Pulmonary aspiration is defined as inhalation of gastric contents with worsening respiratory signs or a new infiltrate on chest radiograph.

withdrawn from the study were not. Parametric outcomes were analyzed by a chi-square test (or Fisher's exact test if there were five or less events per assessed outcome), while nonparametric outcomes were assessed by the Mann-Whitney U test. Significance was assumed at $p < 0.05$.

RESULTS

Consort Diagram and Study Flow

The consort diagram and study flow can be seen in Figure 2. From December 1, 2013, to March 1, 2015, six sites had varying enrollment times (Data Supplement S1, Appendix S1) for a total of 42 site-months. Overall, we screened 222 patients less 75 years of age with AF less than 48 hours. Of the 135 eligible patients (approximately 3.2 patients per month per site) 86 were enrolled and randomized. Nonenrolled patients had ages, sex distribution, $CHADS_2$ scores, and medication use similar to those of enrolled patients, but were more likely to have had prior AF, and nearly all had undergone prior cardioversion and already had a preferred method of management (Data Supplement S1, Appendix S3). Of the randomized patients, one patient withdrew from the chemical-first group prior to any treatment, and the investigators withdrew one patient from the electrical-first group for a troponin elevation prior to any treatment, leaving 84 subjects for analysis.

Baseline Characteristics

Baseline characteristics were balanced between the two groups, with 41 patients in the chemical-first group and 43 in the electrical-first group (Table 2). Four protocol violations occurred: A-77-year-old female with hypertension and 78- and 76-year-old males with hypertension were enrolled—all had a $CHADS_2$ score of 2. A 68-year-old male who failed to achieve normal sinus rhythm with electrical conversion was referred to cardiology, rather than administered procainamide.

Main Results

In the chemical-first group, 13 of 41 patients (32%) were discharged within 4 hours compared to 29 of 43 patients (67%) in the electrical-first group (difference 36% [95% confidence interval {CI} = 16%–56%], $p < 0.001$) for a number needed to treat of 3 (95% CI = 2–6). In the chemical-first group, the median ED LOS was 5.1 hours compared to 3.5 hours in the electrical-first group, for a difference of 1.2 hours (95% CI = 0.4–2.0 hours, $p < 0.001$). The median LOS from randomization to conversion was 2.3 hours for the chemical-first group, and 0.6 hours for the electrical-first group, for a difference of 1.4 hours (95% CI = 0.8–1.9 hours) a 74% time reduction (Table 3).

In the chemical-first group, 22 of 41 (54%) patients converted with procainamide while the remainder required electrical countershock to attain normal sinus rhythm; all were discharged home. For patients who had unsuccessful procainamide attempts, physicians waited a median of 110 minutes (IQR = 80 to 149 minutes) prior to starting sedation for electrical conversion. In the electrical-first group, 38 of 43 (88%) converted, and four of the five remaining patients who also received procainamide reverted back to normal rhythm. One patient in each group received a cardiology consult and all patients were discharged home (Table 3). Breakdowns by individual treatments are given in Data Supplement S1, Appendix S4.

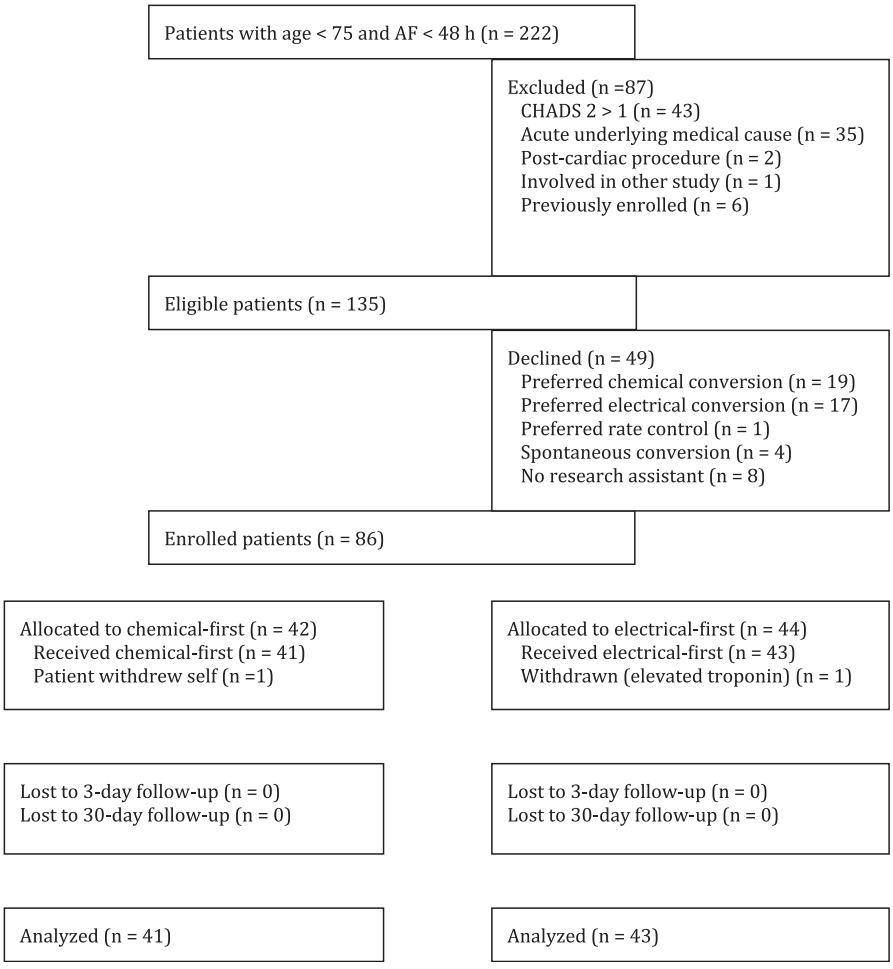

Figure 2. CONSORT diagram. *One patient declined to answer quality-of-life at 30 days, but the primary care confirmed that the patient was alive, not hospitalized, and stroke-free at 30 days. AF = atrial fibrillation.

Table 2
Baseline Characteristics

Variable	Chemical-first (n = 41)	Electrical-first (n = 43)
Demographics		
Female	15 (36.6)	17 (39.5)
Age (years)	58 (50–66)	60 (53–66)
Age range (range)	(21–77)	(28–78)
Canadian Triage and Acuity Score*		
Level 2	36 (87.8)	37 (86.0)
Level 3	5 (12.2)	6 (14.0)
AF history		
History of AF	29 (70.7)	34 (79.1)
Prior cardioversion of any type	21 (53.9)	22 (51.2)
Number of chemical conversions	1 (0–2)	1 (0–2)
Number of electrical conversions	2 (1–5)	1 (1–3)
Initial vital signs		
Pulse rate (beats/min)	117 (95–145)	116 (97–135)
Respiratory rate (breaths/min)	17 (16–20)	16 (16–18)
Systolic blood pressure (mm Hg)	131 (124–139)	128 (120–138)
Diastolic blood pressure (mm Hg)	80 (73–85)	80 (71–87)
Oxygen saturation on room air	99 (98–99)	98 (97–99)
Temperature in (°C)	36.6 (36.5–36.7)	36.6 (36.5–36.7)
Medical history		
Hypertension	10 (24.4)	14 (32.6)
Diabetes	1 (2.4)	2 (4.7)
Heart failure	0 (0.0)	0
Stroke	0 (0.0)	0
$CHADS_2$ score		
0	29 (70.7)	25 (58.1)
1	12 (29.3)	15 (34.9)
2	0 (0.0)	3 (7.0)
Medications		
ASA	18 (43.9)	19 (44.2)
Clopidogrel	0 (0.0)	0 (0.0)
Coumadin	2 (4.9)	1 (2.3)
Dabigatran	3 (7.3)	1 (2.3)
Apixaban	0 (0.0)	0 (0.0)
Rivaroxaban	2 (4.9)	5 (11.6)
Propafenone	3 (7.3)	1 (2.3)
Amiodarone	0 (0.0)	1 (2.3)
Sotalol	0 (0.0)	3 (7.0)
Digoxin	0 (0.0)	0 (0.0)
Metoprolol	3 (7.3)	2 (4.7)
Atenolol	0 (0.0)	1 (2.3)
Diltiazem	2 (4.9)	0 (0.0)

Data are reported as n (%) or median (IQR).
AF = atrial fibrillation; ASA = aspirin; $CHADS_2$ = stroke risk score composite of heart failure, hypertension, age > 75, diabetes (1 point each), stroke/TIA (2 points); IQR = interquartile range; TIA = transient ischemic attack.
*Canadian Triage and Acuity Score (CTAS) is a validated, reliable system used in Canada by triage nurses to determine in what time interval a patients should be seen. (The smaller the number the sicker the patients: CTAS 2 = 15 minutes to physician attendance; CTAS 3 = 30 minutes to physician attendance.)

Table 3
ED Outcomes

Variable	Chemical-first (n = 41)	Electrical-first (n = 43)	p-value	Test statistic
ED conversion				
Conversion with initial method	22 (53.7)	38 (88.4)	<0.001	12.4
Overall conversion	41 (100.0)	42 (97.7)	1.0	1
Times (hours)				
Registration to physician assessment	0.7 (0.5–0.9)	0.7 (0.5–1.1)	0.56	0.27
Physician assessment to randomization	1.2 (1.0–1.6)	1.2 (0.9–1.7)	0.59	0.29
Randomization to conversion	2.3 (1.3–3.4)	0.6 (0.4–0.9)	<0.001	43.5
Conversion to discharge	0.8 (0.6–1.2)	0.4 (0.3–1.0)	0.001	10.1
Randomization to discharge	3.1 (2.0–3.9)	1.0 (0.8–2.7)	<0.001	23.2
Registration to discharge (overall LOS)	5.1 (3.5–6.3)	3.5 (2.8–4.8)	0.005	11.1
Final disposition and timing				
Admitted to hospital	0 (0.0)	0 (0.0)	1.0	1
Discharged home	41 (100.0)	43 (100.0)	1.0	1
Discharged home in normal sinus	41 (100.0)	42 (97.7)	1.0	1
Overall LOS less than 4 hours*	13 (31.7)	29 (67.4)	0.001	10.7
Randomization to discharge < 4 hours	29 (70.7)	39 (90.7)	0.01	6.2

Data are reported as n (%) or median (IQR).
"Test statistic" is "chi-square statistic" (for parametric outcomes with more than 5 events), "Fisher exact test statistic" (for parametric outcomes with 5 or fewer events) and "H-statistic" for the Mann Whitney test (for nonparametric outcomes).
IQR = interquartile range; LOS = length of stay.
*Primary outcome.

Table 4
ED Adverse Events*

Adverse Events	Chemical-first (n = 41)	Electrical-first (n = 43)	p-value
Description			
Minimal risk	1 (2.4)	4 (9.3)	0.36
Minor risk	9 (22.0)	7 (16.3)	0.58
Sentinel risk	0 (0.0)	0 (0.0)	1.0
Intervention			
Minimal	6 (14.6)	6 (14.0)	1.0
Minor	2 (4.9)	5 (12.2)	0.16
Moderate	2 (4.9)	0 (0.0)	0.49
Sentinel risk	0 (0.0)	0 (0.0)	1.0
Outcome			
Minimal risk	10 (24.4)	11 (25.6)	1.0
Moderate risk	0 (0.0)	0 (0.0)	1.0
Sentinel risk	0 (0.0)	0 (0.0)	1.0

Data are reported as n (%).
*See Data Supplement S1, Appendix S4, for detailed vignettes.

Adverse Events

The chemical-first group had 10 adverse events (24%) while the electrical group had 11 (26%). All adverse events had minimal-risk outcomes (Table 4; please see Data Supplement S1, Appendix S5, for detailed vignettes, interventions, and outcomes).

Three- and Thirty-day Outcomes

Table 5 shows that all patients were contacted at 3 days, and 83 of 84 were contacted at 30 days. (One patient answered questions at 3 days, but when contacted at 30 days refused to answer; the primary care doctor was then contacted to confirm that this patient was alive and free from stroke or hospitalization.) At 30 days, there were no strokes or deaths in either group (95% CI = 0%–4.4%). All patients visited their family doctor; generally between 3 and 30 days after the ED visit. At 3 days, five of 41 chemical-first patients reattended the ED with one admission; one of 43 electrical-first patients reattended the ED with no admissions. At 30 days, nine of 41 chemical-first patients reattended the ED with two admission; three of 43 electrical-first patients reattended the ED with no admissions. All revisits were for recurrent AF and both admissions were for AF that was uncontrollable in the ED on the subsequent visit. QoL scores were similar for both groups across all domains.

DISCUSSION

In this multicenter randomized controlled clinical trial, a significantly greater proportion of ED patients with uncomplicated acute AF were discharged from the ED within 4 hours when managed with an electrical-first

Table 5
Three- and Thirty-day Outcomes

Outcome	Chemical-first (n = 41)	Electrical-first (n = 43)	p-value
Three-day outcomes			
Patients contacted	41 (100.0)	43 (100.0)	1.0
Saw a physician	8 (19.5)	5 (11.9)	0.381
ED revisit	5 (12.2)	1 (2.4)	0.109
Hospital admission	1 (2.4)	0 (0.0)	1.0
Stroke	0 (0.0)	0 (0.0)	1.0
Death	0 (0.0)	0 (0.0)	1.0
Quality of health rated "excellent"	25 (61.0)	21 (50.0)	0.380
No limitations to physical activity	29 (70.7)	30 (71.4)	1.0
No difficulties doing daily work	31 (75.6)	29 (69.0)	0.625
No bodily pain	27 (65.9)	26 (61.9)	0.820
"Very much" energy	26 (63.4)	23 (54.8)	0.505
No limitations to social activities	35 (85.4)	30 (71.4)	0.182
30-day outcomes			
Patients contacted	41 (100.0)	42* (97.7)	1.0
Saw a physician	27 (65.9)	23 (54.8)	0.372
ED revisit	9 (22.0)	3 (7.1)	0.067
Hospital admission	2 (4.9)	0 (0.0)	0.241
Stroke	0 (0.0)	0 (0.0)	1.0
Death	0 (0.0)	0 (0.0)	1.0
Quality of health rated "excellent"	21 (52.4)	21 (51.2)	1.0
No limitations to physical activity	29 (70.7)	31 (73.8)	0.810
No difficulties doing daily work	34 (82.9)	37 (88.1)	0.548
No bodily pain	32 (78.0)	36 (85.7)	0.405
"Very much" energy	28 (68.3)	23 (54.8)	0.261
No limitations to social activities	32 (78.0)	37 (88.1)	0.254

Data are reported as n (%).
*One patient in the electrical group declined to answer follow-up questions at 30 days, but was confirmed by his primary care physician to be alive, stroke-free, and not hospitalized at 30 days.

cardioversion strategy, compared to a chemical-first cardioversion strategy. In addition, the median LOS was shorter by 1.2 hours for the electrical-first group, a significant difference. This was likely driven by the 74% reduction in median time from randomization to conversion for the electrical-first group. This is noteworthy and clinically sensible since "randomization time" in our study likely corresponds to the time an emergency physician would make the decision to manage a non-study AF patient with either a chemical- or electrical-first approach. Adverse events were minor, and all patients were discharged home at the index ED visit, with no strokes or deaths at 30 days. QoL scores were similar at three and 30 days. This demonstrates that, although both methods appear safe and are well tolerated in acute AF, patients undergoing an electrical-first approach have a far shorter ED LOS.

Emergency department–specific CCS guidelines emphasize that uncomplicated AF patients with symptom duration of less than 48 hours may undergo rate or rhythm control[2] and ED-based rhythm control has been shown to be safe in thousands of patients over numerous retrospective and prospective analyses.[3–9,17,18] Our study showed that, similar to prior findings,[3–6,8] approximately half of patients undergoing chemical conversion alone converted to normal sinus rhythm. As a combination therapy, the Ottawa protocol (procainamide administration followed by electrical countershock if unsuccessful) has been well described and reports safe discharge of up to 97% of patients, with almost all in sinus rhythm.[5,6] Likewise, the success rate of electrical conversion alone was approximately 90%, also similar to prior studies.[3,4,6–8] In Canada, studies have shown that emergency physicians use each strategy approximately half the time,[3–8] and this study may assist clinicians by demonstrating that the electrical-first strategy may restore sinus rhythm more quickly.

In a single-center trial, Bellone and coworkers[9] randomized patients to a chemical-only versus an electrical-only strategy and found the latter had higher conversion rates (89% vs. 74%) and shorter LOS (3 hours vs. 7 hours). However, all patients required ED-based echocardiography, 19% of patients were discharged home while still in AF, and 33% were lost to follow-up. Furthermore, there was no reported ascertainment of clinically relevant outcomes such as strokes, deaths, ED revisits, or rehospitalizations. We extend these findings by employing a sequential approach to conversion, not mandating specialized imaging, and providing complete follow-up on our cohort.

Importantly, the rates of stroke and death post-rhythm control have been very low.[3–9] In a recent prospective Canadian six-ED study enrolling 1,091 patients with acute AF nearly exclusively managed with rhythm control, Stiell et al.[17] described no 30-day deaths and a single stroke—an 81-year-old on coumadin with an ED INR of 2.3 who spontaneously converted and had an ischemic stroke on Day 23. While Canadian academic emergency physicians may be comfortable managing patients with acute AF with rhythm control, this may not extend internationally. Physicians in Australasia and the United Kingdom employ rhythm control approximately half the time, while American physicians employ rhythm control one-quarter of the time.[19] However, there is evidence that emergency physicians might be able to facilitate safe early discharge, rather than admission, of AF patients: in a single center, Decker and coworkers[18] randomized 153 patients to either cardiology admission or an ED-based strategy of rate, then rhythm control, resulting in a decrease in LOS from 25 to 10 hours; nearly all patients were discharged in sinus rhythm. There may be increasing appeal for similar ED-based AF pathways that could incorporate rhythm control and safe discharge for low-risk patients.[20]

Of our patients receiving electrical countershock first, half were discharged within 1 hour of randomization, and some patients who received procainamide first were discharged in a similar time frame. The recent cohort of Stiell et al.[17] had a median ED LOS of 5 hours, but our data suggest that far shorter times—perhaps 1 to 2 hours—may be routinely possible. Some of our extreme LOS likely resulted from other factors including the presence of multiple critically ill patients in the department, the unavailability of trained nurses or respiratory therapists at a particular time, or single-physician coverage, when a hemodynamically stable AF patient might be a lower priority.

Although ED-based outcomes such as LOS and adverse events have been described, the QoL in ED AF patients has been minimally investigated.[21] Although AF in this group may not be "dangerous" in terms of death, stroke, or hospitalization,[3–8] symptoms can be profoundly unpleasant and interfere with daily activities and enjoyment of life for both patients and families. It is important to note that the proportion of patients in the chemical-first group reattending the ED was substantially (though not significantly) higher than in the electrical-first group. While the QoL scores may have been similar, this may indicate that the electrical-first approach provides a long-term benefit a greater proportion of patients. Importantly, our findings add to the literature by comparing two accepted treatments, measuring important outcomes—including patient-reported results—and demonstrating that these patients, irrespective of initial management strategy, are safe; have minimal discomfort after their ED visit; and have an acceptable QoL at 3 and 30 days.

LIMITATIONS

The study took place in six urban Canadian EDs, where all physicians were experienced at managing chemical conversion, electrical countershock, and procedural sedation and analgesia, and our results may not be generalizable to other EDs without such experience. At two of the six sites, research assistants were only available during daytime hours. Screening logs may be unreliable and some eligible patients missed. LOS can be driven by many variables including department crowding, the presence of other critically ill patients in the department, physician coverage, and nurse or respiratory therapist availability. Neither clinicians nor patients could realistically be blinded. Despite the standardized instructions and script, the timing of procainamide administration, tolerance for conversion, and departmental protocols for sedation may vary as physicians were allowed to exercise clinical judgment. While this introduces variability, it may also enhance external validity. Intravenous procainamide is the most commonly used chemical agent in Canadian EDs,[3–8] but is graded as level IIb evidence for rhythm control,[22] although it is important to note that these recommendations did not arise from ED-based studies. Anticoagulation was based on the 2011 Canadian ED guidelines[11] and we did not evaluate emergency

physicians' anticoagulation decisions. Furthermore, these guidelines were not congruent with American recommendations[22] and have been superseded several times in Canada.

Our study was not powered to assess such events, and given the very low rate of serious outcomes it would require a far larger trial to prove safety. Over one-third of eligible patients declined participation, and they were more likely have had prior AF with conversion attempts. This may bias results in favor of patients with infrequent or newly diagnosed AF. Our results cannot be extrapolated to patients with chronic AF, those at higher risk of stroke, those with acute underlying medical illnesses, or adults > 75 years of age, although such patients are not typically managed with rhythm control.[3–9,11,12] Finally, the SF-8 is a general health systems questionnaire and has not been validated in this cohort of patients, although AF-specific QoL measures have been recently developed.[21] Neither patient nor physician satisfaction was assessed, nor were costs. While Canada has universal health care, in different settings, it may potentially be less costly and provide better QoL to rapidly convert patients in the ED, rather administer than rate control and likely anticoagulation for eventual follow-up with a cardiologist.

CONCLUSION

In uncomplicated ED atrial fibrillation patients, chemical-first and electrical-first strategies both appear to be successful and well tolerated; however, an electrical-first strategy results in a significantly shorter ED length of stay. Our results should encourage clinicians to initially consider an electrical-first approach for such patients.

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Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13669/full

Data Supplement S1. Supplemental material.