



BRIEF REPORT

Cardiology



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Cardioversion and the Risk of Subsequent Stroke or Systemic Embolism and Death in Emergency Department Patients With Acute Atrial Fibrillation or Flutter

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Abstract

Objectives: Guideline recommendations for the emergency department cardioversion of patients with acute atrial fibrillation/flutter have recently changed. This was related to several studies that found a higher-than-expected risk of subsequent stroke or systemic embolism in cardioverted atrial fibrillation/flutter patients. We sought to confirm an elevated rate of stroke, systemic embolism, or death following emergency department cardioversion to normal sinus rhythm compared with similar patients who were not converted.

Methods: This retrospective cohort study combined 4 datasets of atrial fibrillation/flutter patients seen at 25 emergency departments in Ontario, Canada, 2000-2012, who were all eligible for cardioversion. We linked patients to province-wide datasets to determine the primary outcome, a composite of stroke, systemic embolism, or all-cause death. To adjust for baseline differences between patients who cardioverted vs those who did not, we used overlap weights based on the propensity score. The latter included 28 variables, including oral anticoagulant prescriptions.

Results: Of 2521 patients, 2060 (81.7%) converted to sinus rhythm in the emergency department, and 1055 (41.8%) left on anticoagulation. Twelve (0.48%) patients met the primary outcome at 30 days and ≤ 5 ($\leq 0.2\%$) at 7 days. In the weighted sample, at 30 days, the primary outcome occurred in 0.37% (95% CI, 0.04%-0.78%) of cardioverted patients vs 0.23% (95% CI, 0.00%-

abstract continues

Abstract (continued)

0.60%) in those not cardioverted; the absolute risk increase was 0.13% (95% CI, -0.36% to 0.69%; $P = .61$), and the number needed to harm was 747.

Conclusion: In atrial fibrillation/flutter patients eligible for cardioversion at 25 emergency departments, the rate of subsequent stroke or systemic embolism and death was very low. After adjusting for risk factors and post-conversion oral anticoagulant use, the rate of subsequent stroke and systemic embolism and death was not significantly higher in patients who cardioverted vs those who did not.

Keywords: atrial fibrillation, cardioversion, stroke, emergency department

1 INTRODUCTION

1.1 Background

Worldwide, >33 million persons have atrial fibrillation/flutter (AFF).¹ Many AFF patients are seen in the emergency department (ED),² where they seek care when they experience potentially serious symptoms such as palpitations or chest pain.³ Over 10% of the ED visits that are made for atrial fibrillation (AF) in Ontario, Canada, and >5% in the United States include cardioversion.⁴

1.2 Importance

For over 20 years, cardioversion was generally considered safe without pretreatment with anticoagulation if the duration of AFF was <48 hours⁵; however, several large studies from a European dataset of cardioversions reported higher-than-expected rates of stroke or systemic embolism (SSE) at 30 days.^{6,7} Conversely, 15 observational studies (11 performed in the ED, 9 in North America) totaling 4380 cardioverted acute AFF patients found only 12 (0.27%) SSE at 30 days,⁸ about a third of the rate reported in the Finnish CardioVersion (FinCV) studies. None of the studies included a control group. Nonetheless, recent national guideline recommendations around acute cardioversion without prior anticoagulation have been changed to become more restrictive.^{9,10}

1.3 Goals of This Investigation

We sought to assess the risk of SSE and mortality following ED cardioversion in a multicenter sample of North American ED AFF patients, comparing them with eligible patients who were not cardioverted while adjusting for risk factors and oral anticoagulant (OAC) prescriptions.

2 METHODS

2.1 Study Design, Setting, and Selection of Participants

We combined 4 existing clinical datasets on adult ED AFF patients seen at 25 EDs in Ontario, Canada, who were eligible for cardioversion and did not have a different primary ED diagnosis (eg, pneumonia). Briefly, 3 datasets from the Ottawa

Hospital sites included (1) a health records review of all patients receiving intravenous procainamide at the Ottawa Civic Hospital between 2000 and 2005 (which should be followed by electrical cardioversion if procainamide is not successful, as per the Ottawa Aggressive Protocol),¹¹ (2) a health records review at the same site of all AFF patients eligible for cardioversion in 2008, and (3) a prospective cohort study of eligible AFF patients performed at The Ottawa Hospital's Civic and General sites, 2010-2012 (97.4% of eligible patients enrolled).¹² With the exception of the 2000-2005 cohort, only the first presentation during the study period was included.

In the fourth dataset, patients with a main diagnosis of AF (*International Classification of Diseases, Version 10* [ICD-10], code I480) between 2008 and 2009 were identified retrospectively from the other 23 hospital sites using the National Ambulatory Care Reporting System database (Table S1). Trained abstractors went to each hospital and abstracted each of the identified charts for the required detailed clinical information, if AF was confirmed as the main ED diagnosis (flutter was excluded).³ See individual study publications for further details.^{3,11,12}

We specifically collected chart documentation of whether warfarin or dabigatran prescriptions were provided in the ED (dabigatran was the only direct OAC [DOAC] available in Canada during the study period). If the patient came in on either and did not have chart documentation that it was discontinued, this was also counted as leaving the ED on OAC. As a confirmatory step, we also linked patients aged > 65 years to the Ontario Drug Benefit Program to confirm an ongoing prescription (based on quantity dispensed) or new prescription fill for either medication.

Eligibility for cardioversion was defined similarly in all 4 datasets. It was originally defined at the time of data collection for the first dataset as either AFF duration < 48 hours, or if it was <7 days but they were appropriately anticoagulated (ie, OAC ≥ 3 weeks).^{3,11,12} This was consistent with published guidelines at the time.^{5,13}

Data in these 4 clinical datasets were then linked to province-wide health datasets held at our research institute (ICES) in order to assess the study outcomes. We also used these health datasets to confirm the OAC prescription, as described above. Linkage occurred using unique encoded identifiers, and the resulting data were analyzed at ICES (see Table S1 for database details).

The Bottom Line

Studies on stroke or systemic embolism following emergency department cardioversion of patients with atrial fibrillation/flutter of less than 48 hours duration have had conflicting results, and none have included a control group. In this study of 2521 such patients from 25 Canadian emergency departments, the rate of subsequent 30-day stroke, systemic embolism, or all-cause death was not significantly different from matched patients who were not cardioverted (absolute risk increase of 0.13%, and the number needed to harm 747). Although there were limitations to this retrospective study, the data appear reassuring, with a very low rate of adverse events postcardioversion. In addition, at the time of the data collection, less patients were given anticoagulation following cardioversion, a practice that is now recommended by many guidelines.

2.2 Exposure

The exposure group was those who successfully cardioverted in the ED, whereas the nonexposed group did not cardiovert. Success was defined as a reversion to normal sinus rhythm (NSR) at any time and by any means (ie, spontaneous, pharmacological, or electrical cardioversion).

2.3 Outcomes

The primary outcome measure was a composite outcome of all-cause death or hospital presentation for SSE within 30 days. We also assessed the primary outcome within 7 days. SSE was defined as hospitalization for ischemic stroke, pulmonary embolism, or systemic embolism (see Table S2 for ICD-10 codes).

2.4 Data Analyses

We estimated a propensity score for ED cardioversion by regressing ED cardioversion to NSR on 28 *a priori* selected variables, including whether the patient was discharged on OAC.^{3,14} The use of propensity score methods allows

accounting for a larger number of variables than conventional regression adjustment. We used the propensity score to compute overlap weights for each subject, which are similar to inverse probability of treatment weights, but they assign greater weight to subjects whose propensity score is closer to 0.5 (ie, those for whom there is greater equipoise about treatment selection).¹⁵ The balance between groups was assessed using weighted standardized differences.¹⁶ We computed the adjusted risk increase (ARI), or the difference in the weighted proportion of the primary outcome, between the 2 exposure groups. We computed 95% CIs using nonparametric bootstrap percentile intervals using 2000 bootstrap samples. We used the complement of the weighted Kaplan-Meier (KM) curves (ie, the cumulative incidence function) to compare the incidence of the primary endpoint over time between the 2 exposure groups. The statistical significance of between-group differences in the cumulative incidence function was determined using permutation tests.

We performed 2 sensitivity analyses: (1) we repeated the main analysis after excluding patients who converted spontaneously, and (2) we removed patients who were admitted to the hospital. Analyses were performed with SAS software (version 9.3, SAS Institute Inc). Research Ethics Board approval was obtained from each of the sites.

3 RESULTS

Of 2521 eligible patients, 2060 (81.7%) cardioverted to NSR in the ED (Table 1). The median age was 66.0 years, and 48.2% were female. Two-thirds had a history of AFF, and the CHA₂DS₂-VASc score was 0 to 1 for 40.5%. Thirty-four percent presented on OACs, and 42% left the ED on OACs. Prior to the application of overlap weights, the cohort that did not convert was older and had higher CHA₂DS₂-VASc scores than the group that did convert.

Overall, there were 12 (0.48%; 95% CI, 0.25%-0.83%) occurrences of the primary outcome in the study cohort at 30 days, and ≤ 5 ($\leq 0.2\%$) were SSEs. Events by group cannot be reported due to the small cell size (ie, ≤ 5) in the non-cardioverted group (small cell sizes cannot be reported when using province-wide datasets due to the risk of identification and privacy protections). Of the 12 patients who met the primary outcome, ≤ 5 ($\leq 0.2\%$) patients were on OACs when they left the ED. At 7 days, the primary outcome occurred in ≤ 5 ($\leq 0.2\%$) patients.

After overlap weights were applied, the groups were well balanced on the 28 *a priori* selected variables (Table 2).¹⁶ The estimated risk of the primary outcome at 30 days in patients who converted was 0.37% (95% CI, 0.04%-0.78%) vs 0.23% (95% CI, 0.00%-0.60%) in those who did not convert; ARI was 0.13% (95% CI, -0.36% to 0.69%; $P = .61$), and the number needed to harm was 747 (Table 3). The cumulative incidence function curve is shown in the Figure. At 7 days, the estimated risk of SSE or death was 0.00% (95% CI, 0.00%-0.00%) in patients who converted vs 0.00% (95% CI, 0.00%-

TABLE 1. Descriptive characteristics of patients who cardioverted to normal sinus rhythm in an emergency department vs those who did not.

Characteristic		All (%) N = 2521	Cardioverted (%) n = 2060 (81.7%)	Not cardioverted (%) n = 461 (18.3%)	P
Patient demographics					
Age, y	Median (IQR)	66.0 (55.0-76.0)	65.0 (54.0-75.0)	71.0 (61.0-79.0)	<.001
	Mean (SD)	64.6 (14.8)	63.7 (4.9)	68.9 (13.2)	<.001
Female sex		1215 (48.2)	989 (48.0)	226 (49.0)	.69
Rural residence		66 (2.6)	53 (2.6)	13 (2.8)	.44
Income quintile (5: highest)	1	344 (13.6)	259 (12.6)	85 (18.4)	<.001
	2	410 (16.3)	331 (16.1)	79 (17.1)	.57
	3	467 (18.5)	393 (19.1)	74 (16.1)	.13
	4	573 (22.7)	467 (22.7)	106 (23.0)	.88
	5	727 (28.8)	610 (29.6)	117 (25.4)	.08
Past medical history					
Atrial fibrillation		1670 (66.2)	1329 (64.5)	341 (74.0)	<.001
Heart failure		121 (4.8)	86 (4.2)	35 (7.6)	.002
Hypertension		1149 (45.6)	921 (44.7)	228 (49.5)	.06
Diabetes mellitus		311 (12.3)	238 (11.6)	73 (15.8)	.01
Stroke or TIA		142 (5.6)	107 (5.2)	35 (7.6)	.04
Coronary artery disease		417 (16.5)	352 (17.1)	65 (14.1)	.12
Valvular disease		165 (6.5)	112 (5.4)	53 (11.5)	<.001
Chronic obstructive pulmonary disease		133 (5.3)	110 (5.3)	23 (5.0)	.76
Chronic renal failure		63 (2.5)	51 (2.5)	12 (2.6)	.87
Chronic liver failure		^a	^a	^a	.21
Gastrointestinal bleed		19 (0.8)	11 (0.5)	8 (1.7)	.007
CHA ₂ DS ₂ -VASc score	0	485 (19.2)	416 (20.2)	69 (15.0)	.01
	1	536 (21.3)	460 (22.3)	76 (16.5)	.006
	2	441 (17.5)	359 (17.4)	82 (17.8)	.85
	3	447 (17.7)	356 (17.3)	91 (19.7)	.21
	4+	612 (24.3)	469 (22.8)	143 (31.0)	<.001
HAS-BLED score	0	612 (24.3)	529 (25.7)	83 (18.0)	<.001
	1	759 (30.1)	634 (30.8)	125 (27.1)	.12
	2	751 (29.8)	600 (29.1)	151 (32.8)	.12
	3	356 (14.1)	271 (13.2)	85 (18.4)	.003
	4+	43 (1.7)	26 (1.3)	17 (3.7)	<.001
Pre-ED medications					
Warfarin		852 (33.8)	601 (29.2)	251 (54.4)	<.001
Dabigatran		13 (0.5)	^a	^a	.06
Clopidogrel		80 (3.2)	60 (2.9)	20 (4.3)	.11
Aspirin		584 (23.2)	494 (24.0)	90 (19.5)	.04
Antiarrhythmic ^b		505 (20.0)	410 (19.9)	95 (20.6)	.73
ED arrival and care					
Triage score ^c	1/2	1817 (72.1)	1468 (71.3)	349 (75.7)	.06
	3/4/5	485 (19.2)	373 (18.1)	112 (24.3)	.002
	Missing	219 (8.7)	219 (10.6)	0 (0.0)	<.001

(Continues)

TABLE 1. (Continued)

Characteristic		All (%) N = 2521	Cardioverted (%) n = 2060 (81.7%)	Not cardioverted (%) n = 461 (18.3%)	P
Presenting heart rate (beats per minute)	Median (IQR)	118 (91-140)	120 (91-140)	110 (89-130)	<.001
Presenting systolic blood pressure, mm Hg	Median (IQR)	133 (118-149)	133 (117-149)	136 (121-151)	.02
Chest x-ray	Pulmonary edema	49 (1.9)	35 (1.7)	14 (3.0)	.06
	No pulmonary edema	2115 (83.9)	1170 (83.0)	405 (87.9)	.01
	Not done	357 (14.2)	315 (15.3)	42 (9.1)	<.001
Converted in ED	Did not convert	461 (18.3)	0 (0.0)	461 (100.0)	
	Spontaneous	435 (17.3)	435 (21.1)	0 (0.0)	
	Pharmacological	673 (26.7)	673 (32.7)	0 (0.0)	
	Electrical	739 (29.3)	739 (35.9)	0 (0.0)	
INR	<2.0	1216 (48.2)	1001 (48.6)	215 (46.6)	.45
	2.0-3.0	428 (17.0)	287 (13.9)	141 (30.6)	<.001
	>3.0	126 (5.0)	71 (3.4)	55 (11.9)	<.001
	Not done	751 (29.8)	701 (34.0)	50 (10.8)	<.001
Post-ED					
Admitted to hospital		302 (12.0)	296 (14.4)	6 (1.3)	<.001
On OAC post-ED visit		1055 (41.8)	741 (36.0)	314 (68.1)	<.001

CHA₂DS₂-VASc, congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes mellitus, and prior stroke, transient ischemic attack or thromboembolism (doubled), vascular disease, age 65 to 74, sex category (female); ED, emergency department; HAS-BLED, Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile International Normalized Ratio, Elderly, Drugs/Alcohol; INR, international normalized ratio; OAC, oral anticoagulation; TIA, transient ischemic attack. The bold font indicates the results are statistically significant.

^a Numbers cannot be shown if there are small cells (≤ 5 patients) as per the privacy agreement between the Canadian Institute for Health Information and ICES.

^b Vaughan Williams classes I and III, not including digoxin.

^c Using the Canadian Triage and Acuity Score.

0.00%) in those who did not; ARI was 0.00%. In the sensitivity analyses, the results were not meaningfully different (specifically in the cohort *without* patients who spontaneously converted, the direction of ARI changed but was still not significant; among patients who converted: 0.20% [95% CI, 0.00%-0.65%] vs 0.25% [95% CI, 0.005%-0.69%] with an ARI of -0.05 [95% CI, -0.56 to 0.57; $P = .85$]).

4 LIMITATIONS

We accounted for differences in 28 baseline covariates, but residual confounding due to unmeasured confounders may persist. The data are old, and a major practice change in that time is that DOACs are now used instead of warfarin for most AFF patients, and initiation is now recommended with cardioversion. Based on the time of onset of both drugs (hours for DOACs and longer for warfarin), as well as an unstable international normalized ratio (INR) in the initial few days after warfarin initiation (ie, not in therapeutic range), it is likely that the current use of DOACs instead of warfarin postcardioversion has made the difference in outcomes between groups smaller, not larger; this is reassuring to physicians who provide ED cardioversion. Nonetheless, a very large study (ie, >50,000 cardioversion-eligible ED AFF patients)

using current data would be needed to confirm this. The sample size is another limitation. The results suggest a future study would need to use a very large number of sites that have standardized ED data collection (eg, use the same electronic health record [EHR]), which is programmed to reliably record not only the presence of cardioversion (spontaneous or otherwise) but also the duration of AFF prior to cardioversion and whether the patient was unstable, as well as risk factors for SSE and the use of DOACs. If designed to reliably capture this information, EHRs may offer the opportunity for more definitive (although not randomized) results in the next decade. Our brief report is the best that can be done currently, given the very low event rate; however, this work is still needed to provide information for guidelines and ED practice *now*.

5 DISCUSSION

In this study of 2521 acute AFF patients seen at 25 EDs in Ontario, Canada, who were eligible for cardioversion, we found that SSE *and/or* death occurred in 12 (0.48%) patients within 30 days. The rate of solely SSE within 30 days was too low to be reported (≤ 5 or $\leq 0.2\%$), as was the composite outcome at 7 days. Few of the 12 patients in question were on

TABLE 2. Balance between groups after application of overlap weights.

		Cardioverted (%)	Not cardioverted (%)	SD
Patient demographics				
Age, y, median (IQR)		68 (58-78)	68 (58-77)	0.01
Female sex		47.5	47.6	0.00
Rural residence		2.2	2.3	0.00
Income quintile	1	15.9	15.9	0.00
(5: highest)	2	16.2	16.1	0.00
	3	16.7	16.7	0.00
	4	23.0	23.0	0.00
	5	28.2	28.3	0.00
Past medical history				
Atrial fibrillation		70.8	70.5	0.01
Heart failure		4.4	4.3	0.00
Hypertension		47.2	47.1	0.00
Diabetes mellitus		13.8	13.7	0.00
Stroke or TIA		6.4	6.4	0.00
Coronary artery disease		14.1	14.0	0.00
Valvular disease		9.5	9.5	0.00
Chronic obstructive pulmonary disease		4.6	4.6	0.00
Chronic renal failure		2.3	2.3	0.00
Chronic liver failure		0.13	0.15	0.01
Gastrointestinal bleed		1.0	1.0	0.00
CHA ₂ DS ₂ -VASc score	0	18.0	18.1	0.00
	1	18.6	18.6	0.00
	2	18.9	18.9	0.00
	3	18.8	18.8	0.00
	4+	25.7	25.7	0.00
HAS-BLED score	0	21.0	21.2	0.01
	1	28.6	28.6	0.00
	2	31.1	31.0	0.00
	3	16.4	16.3	0.00
	4+	2.9	2.8	0.00
Pre-ED medications				
OAC (warfarin or dabigatran)		45.7	45.3	0.01
Clopidogrel		4.9	4.9	0.00
Aspirin		24.0	24.1	0.00
Antiarrhythmic ^a		21.0	21.0	0.00
ED arrival and care				
Triage score	1/2	80.6	80.7	0.00
	3/4/5	19.3	19.4	0.00
	Missing	0.1	0.0	0.05
Presenting heart rate (beats per minute)	Median (IQR)	114 (88-136)	113 (92-135)	0.00
Presenting systolic blood pressure, mm Hg	Median (IQR)	134 (120-150)	135 (120-150)	0.00
Chest x-ray	Pulmonary edema	2.2	2.2	0.00
	No pulmonary edema	84.2	84.3	0.00
	Not done	13.6	13.6	0.00

(Continues)

TABLE 2. (Continued)

		Cardioverted (%)	Not cardioverted (%)	SD
INR	<2.0	51.5	51.7	0.00
	2.0-3.0	26.5	26.3	0.00
	>3.0	8.0	7.9	0.00
	Not done	14.0	14.1	0.00
Post-ED				
Admitted to hospital		2.2	2.3	0.01
Post-ED OAC prescription		56.0	55.4	0.01

ED, emergency department; INR, international normalized ratio; SD, standardized difference; TIA, transient ischemic attack.

^a Vaughn Williams classes I and III, not including digoxin.

OACs after they left the ED. After adjusting for 28 potential confounders, including OAC use and CHA₂DS₂-VASC score, we found an ARI of 0.13% for 30-day SSE or death in patients who cardioverted, which was not statistically different from patients who did not.

With an event rate this low, at well under 1%, it has been estimated that the sample size required to detect a difference between groups is well over 50,000 cardioversion-eligible ED AFF patients.¹⁷ A prospective study of that size is impractical; therefore, in this brief report, we collaborated to combine multiple clinical datasets and used an innovative approach with propensity scores and a control group to try to answer this question. However, although the results demonstrate an event rate that is reassuringly very low, this same low event rate still limits firm conclusions due to being underpowered.

Large studies on this topic have been performed primarily in Europe. The 2013 FinCV study of 5116 cardioversions performed within 48 hours and without anticoagulation reported a 30-day SSE rate of 0.7%⁶; however, there was no comparison group of eligible patients who did not receive an attempted cardioversion, and how similar these emergency clinics are to an ED (vs a cardiology clinic) is uncertain. A Danish database study of 5084 hospitalized cardioverted AFF patients who did not receive anticoagulation reported a rate of 1.1%,¹⁸ and a Swedish database study of 12,152 such patients (also hospitalized) reported a rate of 0.9%.¹⁹ Hospitalized patients are sicker than ED patients (88% of our cohort were discharged home from the ED), with more comorbidities, so a higher rate might be expected. Perhaps most importantly, using solely population-based administrative data makes it impossible to remove *patients who have AFF > 48 hours without anticoagulation* but still receive immediate cardioversion because they are unstable (as

per guideline recommendations); this small but important group of patients may have contributed to an elevated 30-day rate of SSE in those studies. Studies performed in the ED by primarily emergency physicians who have excluded AFF > 48 hours have reported a 30-day rate of SSE of ~0.2% following cardioversion of acute AFF,⁸ which is similar to our 30-day SSE rate of ≤0.2%.

Although not significantly different, in our cohort, the adjusted difference in outcomes between groups appeared to *increase* over time from the ED visit: 0.0% at 7 days and 0.13% (higher in the cardioverted group) at 30 days. The increased risk associated with cardioversion happens early in the period following conversion to sinus rhythm (ie, it is front-loaded).^{7,18,20,21} Our finding of lower SSE within 7 days than between days 8 and 30 has several possible explanations: (1) chance, (2) the converted cohort is a higher risk due to unmeasured confounders (and this is their baseline risk of stroke, unrelated to cardioversion), (3) events in the month *following* ED cardioversion may contribute to outcomes (eg, repeated cardioversion), or (4) cardioversion in this cohort of patients with an AFF duration < 48 hours does not increase the risk of SSE.

In this brief report of acute AFF patients seen between 2000 and 2012 who were eligible for ED cardioversion according to guidelines at that time, early SSE and death were very low following cardioversion and were not statistically different from eligible ED AFF patients who did not cardiovert. EHRs that serve a very large number of EDs and are appropriately designed to reliably collect key data points may provide a means to power a study with such a low event rate in the future, which could further inform future guideline recommendations.

TABLE 3. Primary outcome (stroke, systemic embolism, or mortality) after the application of overlap weights.

Timing of outcome	Cardioverted, %	Not cardioverted, %	ARI, %	95% CI	P	NNH
7 d post-ED visit	0.00	0.00	0.00	0.0-0.0	.16	857,087
30 d post-ED visit	0.37	0.23	0.13	-0.36 to 0.69	.61	747

ARI, absolute risk increase; ED, emergency department; NNH, number needed to harm.

SSE or mortality, after application of overlap weights

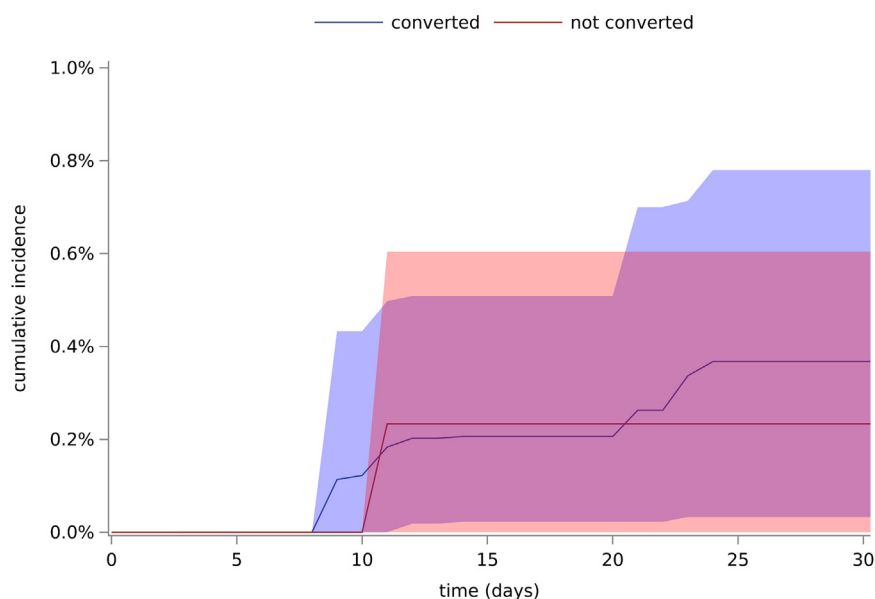


FIGURE. Cumulative incidence of all-cause mortality and stroke or systemic embolism in those who cardioverted vs not cardioverted in the weighted sample, with 95% CIs around each curve.

AUTHOR CONTRIBUTIONS

Study concept and design: all.

Acquisition of data: Atzema, Chong.

Analysis and interpretation of data: all.

Drafting of the manuscript: Atzema.

Critical revision of the manuscript for important intellectual content: all.

Statistical Analysis: Atzema, Austin, Chong.

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CONFLICT OF INTEREST

All authors have affirmed they have no conflicts of interest to declare.

DATA AVAILABILITY

Dr Atzema had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.




The dataset from this study is held securely in coded form at ICES. Although legal data sharing agreements between ICES and data providers (eg, health care organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors on request, understanding that the computer programs may rely on coding

templates or macros that are unique to ICES and are, therefore, either inaccessible or may require modification.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.acepjo.2025.100072>

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