Early Risk of Stroke in Patients Undergoing Acute Versus Elective Cardioversion for Atrial Fibrillation

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BACKGROUND: Electrical cardioversion (ECV) is routinely used to restore sinus rhythm in patients with symptomatic atrial fibrillation. The European guidelines have been updated in recent years. Current information on differences in the risk for stroke after acute versus elective ECV is lacking.

METHODS AND RESULTS: All patients with a first-time acute or elective ECV in the Stockholm regional health care data warehouse from 2011 to 2018 were included. Cox regression analyses were performed evaluating ischemic or unspecified stroke within 30 days after ECV with adjustments for the CHA2DS2-VASc score, medical treatment, and year of inclusion. The study included 9139 patients, 3094 after acute and 6045 after elective ECV. The mean age was 65.9±11.3 years, 69.5% were men, and the mean CHA2DS2-VASc score was 2.4±1.7. Before the intervention, 49.6% of patients with an acute ECV and 96.4% of those with an elective ECV had claimed an oral anticoagulant prescription. Ischemic or unspecified stroke occurred in 26 (0.28%) patients within 30 days. The unadjusted risk was higher after acute compared with elective ECV (hazard ratio [HR], 2.29; 95% CI, 1.06–4.96), whereas there was no difference after multivariable adjustments (adjusted HR, 0.99; 95% CI, 0.36–2.72). Both non–vitamin K oral anticoagulants (adjusted HR, 0.28; 95% CI, 0.08–0.98) and warfarin (adjusted HR, 0.17; 95% CI, 0.05–0.53) were associated with a lower risk for stroke compared with no anticoagulation.

CONCLUSIONS: Acute ECV was associated with a higher unadjusted risk for stroke than elective ECV, but the risk was similar after adjustment for anticoagulant treatment. This study indicates the importance of anticoagulation before ECV according to recent European guidelines.

Key Words: anticoagulant ■ arrhythmia ■ atrial fibrillation ■ cardioversion ■ thromboembolism

Atrial fibrillation (AF) is the most common arrhythmia. Many patients with AF experience disabling symptoms and AF is associated with significant health care consumption including frequent emergency department (ED) visits.1 Rhythm control therapies like antiarrhythmic drugs and catheter ablation are associated with substantial recurrence rates and not suitable in all patients.2 Therefore, cardioversion remains an essential tool to restore sinus rhythm in routine AF management.

Electrical cardioversion (ECV) is known to be more effective than medical cardioversion for symptomatic AF. Irrespective of the mode, cardioversion is complicated by thromboembolic complications.3 Thromboembolic risk can be reduced by adequate anticoagulation treatment4 or transesophageal ultrasound guided exclusion of left atrial thrombus transesophageal echocardiogram before conversion and by continued anticoagulation 4 weeks afterwards.5 Non–vitamin K antagonist oral anticoagulants (NOACs) have replaced warfarin to a large extent in clinical practice.6 NOACs have a rapid onset of anticoagulation effect, fewer drug and food
interactions and facilitate shorter waiting times to cardioversion than warfarin.

In some situations, an emergency cardioversion must be performed in patients with AF who are hemodynamically unstable regardless of prior OAC treatment. However, in the past decade there has been a shift in the European guidelines on acute ECV for hemodynamically stable AF. In 2010, acute ECV for rhythm control was indicated without prior OAC even in the presence of risk factors for stroke if the onset was <48 hours or after a transesophageal echocardiography without a sign of thrombus in the patient with an onset of ≥48 hours. According to the more cautious current European Society of Cardiology guidelines, acute ECV can be considered in patients without prior OAC treatment in AF if the onset was <12 hours and the patient has no history of thromboembolism or within 48 hours if the patient has a low risk for stroke according to CHA₂DS₂-VASc (≤1 for men and ≤2 for women).

Interestingly, the risk of thromboembolic complications associated with acute versus elective conversion of AF has not been studied in greater detail and current data to inform decisions on acute or elective cardioversion from the NOAC era is lacking. We sought to investigate the incidence of ischemic or unspecified stroke and to compare the risk of stroke during the first 30 days in patients who underwent acute ECV compared with elective ECV.

**METHODS**

There was no direct patient or public involvement in the study, and patients were waived from informed consent. The study was approved by the Regional Ethical Review Board in Stockholm. The authors declare that all supporting data are available within the article.

**Study Population**

This population-based cohort study included all patients in the Stockholm Region with a first ECV of AF between January 1, 2011, and December 31, 2018. Individuals with mechanical heart valves or a mitral stenosis were excluded (Figure 1). Data were collected from the administrative health data register of the

**Figure 1.** Study inclusion flowchart of 9139 patients with nonvalvular atrial fibrillation with first-time acute or elective electrical cardioversion from 2011 to 2018 in the Stockholm Region. All instances of atrial fibrillation refer to nonvalvular atrial fibrillation.
was the first-line recommendation for thromboembolic
phylaxis recommended to exclude left atrial thrombus.
Cardioversion, then a transesophageal echocardiography
was included. The number of ECV was stable over
years (Table 1). The patients had a mean age
years (Table 2). The patients had a mean age
of 65.9±11.3 years and a mean CHA2DS2-VASc of
adjusted for known major confounders for stroke such
as age, sex, congestive heart failure, hypertension,
carbohydrate mellitus, previous transient ischemic attack/
stroke or thromboembolism, and previous history of
any vascular diseases. Adjustments were made for
the CHA2DS2-VASc score as a continuous variable,
anticoagulant treatment, and year of inclusion. As a
sensitivity analysis, we evaluated if adding the use of
antiarrhythmic agents would change the results of the
multivariable model. Patients were censored at the
primary end points, death, migration out of the region,
or at the end of follow-up. Furthermore, a sensitivity
analysis was performed investigating the risk for stroke
during the first 7 days after ECV.
All statistical analyses were performed using SAS
Enterprise Guide 8.2 (SAS Institute Inc., Cary, NC), and
the 5% level of significance was considered.

**RESULTS**
There were 9139 patients with a first-time ECV of
whom 3094 had an acute and 6045 an elective
ECV (Table 1). The number of ECV was stable over
the years (Table 2). The patients had a mean age of
65.9±11.3 years and a mean CHA2DS2-VASc of
2.4±1.7; 69.5% were men (Table 1). Hypertension was
the most common comorbidity followed by heart fail-
ure and vascular disease, whereas about 7% had a
history of ischemic or unspecified stroke. During the
6 preceding months, 49.6% of patients with an acute
ECV and 96.4% of those with an elective ECV had
claimed an OAC prescription; 9.2% and 5.7% had
claimed antiarrhythmic agents (Table 1). The propor-
tion of patients without OAC decreased from 22.8% to
14.4% during the study period in the whole cohort.
Although warfarin was the most common treatment in 2011 (77.2%) it had been replaced by apixaban in 2018 (68.2%) (Table 2).

In the main analysis, 68 patients were censored. There were 57 deaths (0.62%) and 11 patients who migrated out of the region (0.12%).

### Table 1. Baseline Table of 9139 Patients With Atrial Fibrillation With First-Time Acute or Elective Electrical Cardioversion From 2011 to 2018 in the Stockholm Region

|                         | Total          | Elective cardioversion | Acute cardioversion |
|-------------------------|----------------|------------------------|---------------------|
| **Number of patients**  | 9139           | 6045                   | 3094                |
| **Age, y**              | 65.9±11.3      | 67.0±10.0              | 63.7±13.1           |
| **CHA2DS2VASc**         | 2.4±1.7        | 2.5±1.8                | 2.2±1.8             |
| **Male sex**            | 6348 (69.5)    | 4319 (71.5)            | 2029 (65.6)         |
| **Age 0–64 y**          | 3459 (37.9)    | 2048 (33.9)            | 1413 (45.7)         |
| **Age 65–74 y**         | 3752 (41.1)    | 2682 (44.4)            | 1070 (34.6)         |
| **Age 75–79 y**         | 1215 (13.3)    | 874 (14.5)             | 341 (11.0)          |
| **Age ≥80 y**           | 713 (7.8)      | 443 (7.3)              | 270 (8.7)           |
| **Heart failure**       | 2108 (23.1)    | 1548 (25.6)            | 560 (18.1)          |
| **Hypertension**        | 5314 (58.2)    | 3636 (60.2)            | 1678 (54.2)         |
| **Diabetes mellitus**   | 1190 (13.0)    | 829 (13.7)             | 361 (11.7)          |
| **Ischemic stroke/TIA or peripheral embolus** | 638 (7.0) | 430 (7.1) | 208 (6.7) |
| **Vascular disease**    | 1481 (16.2)    | 913 (15.1)             | 568 (18.4)          |
| **Other comorbidity**   |                |                        |                     |
| **Cancer**              | 1181 (12.9)    | 781 (12.9)             | 400 (12.9)          |
| **Dementia**            | 42 (0.5)       | 21 (0.4)               | 21 (0.7)            |
| **Alcohol abuse**       | 314 (3.4)      | 220 (3.6)              | 94 (3.0)            |
| **Anemia**              | 576 (6.3)      | 356 (5.9)              | 220 (7.1)           |
| **Renal disease**       | 321 (3.5)      | 184 (3.0)              | 137 (4.4)           |
| **Liver disease**       | 110 (1.2)      | 65 (1.1)               | 45 (1.5)            |
| **Obesity**             | 677 (7.4)      | 482 (8.0)              | 195 (6.3)           |
| **COPD/emphysema**      | 538 (5.9)      | 375 (6.2)              | 163 (5.3)           |
| **Gastric/duodenal bleeding** | 25 (0.3) | 15 (0.3) | 10 (0.3) |
| **Intracranial bleed**  | 70 (0.8)       | 40 (0.7)               | 30 (1.0)            |
| **Any severe bleed**    | 299 (3.3)      | 193 (3.2)              | 106 (3.4)           |
| **Venous thromboembolism** | 419 (4.6) | 274 (4.5) | 145 (4.7) |
| **Frequent falls, ≥2 registrations** | 519 (5.7) | 332 (5.5) | 187 (6.0) |
| **Prior transesophageal echocardiography** | 59 (0.7) | 0 | 59 (1.9) |
| **Medication**          |                |                        |                     |
| **Apixaban**            | 2451 (26.8)    | 1991 (32.9)            | 460 (14.9)          |
| **Dabigatran**          | 1052 (11.5)    | 795 (13.2)             | 257 (8.3)           |
| **Edoxaban**            | 3 (0.0)        | 2 (0.0)                | 1 (0.0)             |
| **Rivaroxaban**         | 331 (3.6)      | 223 (3.7)              | 108 (3.5)           |
| **Warfarin**            | 3526 (38.6)    | 2816 (46.6)            | 710 (23.0)          |
| **No OAC**              | 1776 (19.4)    | 218 (3.6)              | 1558 (50.4)         |
| **LMWH**                | 376 (4.1)      | 241 (4.0)              | 135 (4.4)           |
| **Lipid-lowering treatments** | 2670 (29.2) | 1796 (29.7) | 874 (28.3) |
| **Antiarrhythmic agents** | 632 (6.9) | 346 (5.7) | 286 (9.2) |

Data are provided as mean±SD or number (percentage). COPD indicates chronic obstructive pulmonary disease; LMWH, low molecular weight heparin; OAC, oral anticoagulant; and TIA, transient ischemic attack.

### Stroke Risk

A total of 26 patients (0.28%; 95% CI, 0.18%–0.39%) experienced the primary outcome of ischemic or unspecified stroke within 30 days after ECV (Table 3). The absolute risk of stroke was 0.45% (95% CI, 0.22%–0.69%) in patients who underwent acute
ECV and 0.20% (95% CI, 0.09%–0.31%) in patients who underwent elective ECV. The unadjusted risk of stroke was higher in patients who underwent acute compared with elective ECV (HR, 2.29; 95% CI, 1.06–4.96). However, there was no increased risk after multivariable adjustment (adjusted HR, 0.99; 95% CI, 0.36–2.72). Overall, patients on NOAC (adjusted HR, 0.28; 95% CI, 0.08–0.98) and warfarin (adjusted HR, 0.17; 95% CI, 0.05–0.53) had a lower risk of stroke compared with those who were not on OAC. The risk of stroke after ECV decreased continuously from 2011 to 2018 (Table 4).

To confirm the role of oral anticoagulation, we separately analyzed patients who underwent acute ECV. Prior OAC treatment was associated with a lower risk of stroke compared with no treatment after adjustments for CHA2DS2-VASc and year of inclusion (adjusted HR, 0.12; 95% CI, 0.03–0.55). The absolute risk of stroke was low (0.21%; 95% CI, 0.00%–0.49%) after acute ECV without OAC at low risk according to CHA2DS2-VASc (≤1 for men and ≤2 for women) but increased at higher CHA2DS2-VASc scores (1.70%; 95% CI, 0.82–3.10). There were 59 transesophageal echocardiograms recorded, and none of these patients had a stroke in the following 30 days.

There were 195 (6.3%) patients who had a new cardioversion within 30 days after acute ECV while 342 (5.7%) patients had a new cardioversion within 30 days after elective ECV.

Most of the outcomes occurred during the first week after ECV (Figure 2). Visual examination of scatterplot smooths of scaled Schoenfeld residuals also indicated some risk of nonproportionality during the first 7 days after ECV. A sensitivity analysis investigating the risk for stroke during the first 7 days after ECV showed similar results as the main analysis (Table S3). Adding antiarrhythmic agents to the multivariable model did not change the associations of the main analysis (Table S4). In addition, to confirm the results, we performed a sensitivity analysis using logistic regression instead of Cox regression to evaluate stroke during the first 30 days after ECV, which showed almost identical associations as the main analysis (Table S5).

**DISCUSSION**

This population-based cohort study from the Stockholm Region indicates a low risk for stroke within 30 days. However, the risk for stroke was

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**Table 2. Treatment per Year of Inclusion in 9139 Patients With First-Time Electrical Cardioversion for Atrial Fibrillation From 2011 to 2018**

| Year | Warfarin | Apixaban | Dabigatran | Rivaroxaban | Edoxaban | No oral anticoagulant | Total |
|------|----------|----------|------------|-------------|----------|-----------------------|-------|
| 2011 | 807 (77.2) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 238 (22.8) | 1046 |
| 2012 | 750 (73.6) | 0 (0.0) | 55 (5.4) | 10 (1.0) | 0 (0.0) | 214 (21.0) | 1019 |
| 2013 | 601 (56.9) | 4 (0.4) | 208 (19.7) | 38 (3.3) | 0 (0.0) | 233 (22.1) | 1056 |
| 2014 | 571 (48.9) | 23 (2.0) | 287 (24.6) | 110 (8.3) | 0 (0.0) | 250 (21.4) | 1169 |
| 2015 | 435 (33.0) | 282 (21.4) | 234 (17.7) | 66 (5.0) | 0 (0.0) | 258 (19.6) | 1319 |
| 2016 | 176 (15.9) | 555 (50.1) | 103 (9.3) | 55 (4.6) | 0 (0.0) | 208 (16.8) | 1108 |
| 2017 | 117 (9.8) | 749 (62.8) | 74 (6.2) | 51 (4.2) | 0 (0.0) | 198 (16.6) | 1193 |
| 2018 | 69 (5.6) | 838 (68.2) | 91 (7.4) | 331 (28.0) | 3 (0.2) | 177 (14.4) | 1229 |
| Total | 3526 | 2451 | 1052 | 331 | 3 | 9139 |

Data are provided as number or number (percentage).

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**Table 3. Risk for Ischemic or Unspecified Stroke Within 30 Days After Electrical Cardioversion in 9139 Patients With Atrial Fibrillation**

| Type of cardioversion | CHA2DS2-VASc | Warfarin: number, percentage (95% CI), or 0/number of cardioversions | NOAC: number, percentage (95% CI), or 0/number of cardioversions | Apixaban: number, percentage (95% CI), or 0/number of cardioversions | Dabigatran: number, percentage (95% CI), or 0/number of cardioversions |
|-----------------------|--------------|------------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|
| Elective              | 0            | 3011 (20.9)                                                      | 2816 (19.9)                                                     | 0/51 (0.00–1.02)                                                | 0.21 (0.00–0.61)                                                |
|                       | 1            | 0.48 (0.00–1.02)                                                | 0.21 (0.00–0.61)                                               | 0.17 (0.00–0.37)                                                | 0.23 (0.00–0.48)                                               |
|                       | 2–4          | 0.88 (0.00–2.61)                                                | 0.17 (0.00–0.37)                                               | 0.23 (0.00–0.48)                                                | 0.23 (0.00–0.48)                                               |
|                       | 5–9          | 0.02                                                          | 0.23 (0.00–0.48)                                               | 2.86 (0.00–6.84)                                                | 1.48 (0.00–3.52)                                               |
| Acute                 | 1558         | 826                                                             | 710                                                            | 0.21 (0.00–0.61)                                                | 0.25 (0.00–0.75)                                                |
|                       | 0            | 0.00–1.02                                                       | 0.25 (0.00–0.75)                                               | 0.22 (0.03–2.11)                                                | 0.51 (0.00–1.02)                                               |
|                       | 2–4          | 0.00–1.02                                                       | 0.51 (0.00–1.02)                                               | 2.86 (0.00–6.84)                                                | 1.48 (0.00–3.52)                                               |
|                       | 5–9          | 0.00–1.02                                                       | 1.48 (0.00–3.52)                                               | 1.48 (0.00–3.52)                                                | 1.48 (0.00–3.52)                                               |

NOAC indicates non–vitamin K oral anticoagulant.
substantially higher after acute ECV than elective ECV, probably caused by a lack of protection with OACs. Acute ECV performed without anticoagulant treatment at low CHA2DS2-VASc scores according to recent guidelines was associated with a low risk for stroke.

The patients with a first-time ECV in the present study were substantially younger than both the total AF cohort in the region (65.9 versus 75.0) and patients with AF who initiated OAC treatment for the first time (65.9 versus 72.9–74.1).6,16 This may reflect clinical practice to use ECV preferably in the early course of disease and a preference to rhythm control over rate-control strategies in patients at younger ages. Still, 7.8% of the patients who underwent ECV were aged 80 years or older. From 2011 to 2018, there was an increasing proportion of patients treated with OACs before ECV, reflecting an increase in awareness and following the guideline recommendation. There was also a shift from warfarin to NOAC, which

**Table 4.** Univariate and Multivariable HRs for Ischemic or Unspecified Stroke Within 30 Days of First-Time Electrical Cardioversion in 9139 Patients With Atrial Fibrillation From 2011 to 2018

|                          | Univariate HR (95% CI) | Multivariable HR (95% CI) | Multivariable HR (95% CI) |
|--------------------------|------------------------|---------------------------|---------------------------|
| Acute vs elective cardioversion | 2.29 (1.06–4.96)       | 2.41 (1.11–5.21)          | 0.99 (0.36–2.72)          |
| CHA2DS2-VASc, per point  | 1.27 (1.03–1.57)       | 1.28 (1.04–1.57)          | 1.36 (1.12–1.65)          |
| Year of inclusion, per y | 0.83 (0.70–0.99)       | 0.82 (0.69–0.98)          | 0.81 (0.66–1.00)          |
| NOAC vs no oral anticoagulant | 0.21 (0.08–0.56)     | 0.28 (0.08–0.98)          | 0.17 (0.05–0.53)          |
| Warfarin vs no oral anticoagulant | 0.27 (0.11–0.67) | 0.28 (0.08–0.98) | 0.17 (0.05–0.53) |

HR indicates hazard ratio; and NOAC, non–vitamin K oral anticoagulant.

**Figure 2.** Kaplan–Meier diagram of ischemic or unspecified stroke in 9139 patients with atrial fibrillation with first-time acute or elective electrical cardioversion from 2011 to 2018.
is in line with treatment patterns in the total AF population. Both NOAC and warfarin were associated with a lower risk for stroke than no OAC treatment. The study was inadequately powered to investigate clinically relevant differences between the OACs, but a decreasing risk for stroke after ECV could be seen from 2011 to 2018.

The stroke rate in this study is similar to a previous report comparing ECV and pharmacological cardioversion. Moreover, in a large registry-based cohort study between 2000 and 2008, the incident rate for thromboembolism 30 days after ECV was 4.0 per 100-person years with warfarin and 10.33 without treatment, which corresponds to incidences of thromboembolism of 0.33% and 0.85%, respectively, during the first 30 days, as expected slightly higher than the incidence of ischemic or unspecified stroke in the present study. Similarly, in a Finish study on ECV, the risk for systemic embolism was 0.4% in patients with CHA2DS2-VASc scores 0 to 1 without any anticoagulant treatment, slightly higher than in the present study.

The CHA2DS2-VASc score and AF duration are known predictors of stroke after ECV. This may partly be linked to atrial stunning after ECV, facilitating the generation of micro thrombus in the atrium and atrial appendage. When atrial contractions restore after ECV, a thrombus may dislodge and thus explain why stroke incidence peaks several hours or days after ECV. Permanent AF is associated with decreased atrial contractile function and increased atrial volumes; 2 features that have been associated with increased risk for stroke. Even patients treated with OACs can have a stroke, but the risk is reduced. One way to minimize the stroke risk after ECV is to perform transesophageal echocardiography to exclude a thrombus in the left atrium and its appendage before ECV. Only a minority of the patients in our cohort had procedure codes for transesophageal echocardiography before ECV, and none of these patients suffered any type of stroke. There were not enough observations to draw any conclusions regarding this procedure in this study.

One important aspect after ECV is to maintain sinus rhythm to prevent the recurrence of AF. Appropriate investigation and management of underlying coronary heart disease, hypertension, and heart failure are of great importance to prevent stroke and death in many of the patients with AF. Antiarrhythmic drugs can help to prevent recurrence of AF and maintain sinus rhythm but have limitations in clinical use for many reasons. In our cohort, only about 7% of the patients had antiarrhythmic medications before the first-time ECV. Similarly, according to recent guidelines, ablation therapy is now an established treatment for rhythm control.

Limitations and Strengths of the Study
The main limitations of our study are, as for all registry-based observational studies, the possibility for misclassification as well as confounding by indication. To address these limitations, only specific procedure codes for AF related ECV were included, patients without an ICD-10 code for AF were excluded, and appropriate adjustments were made in multivariable models. The risk for residual confounding that we could not control for should be considered. Interpretations of the results must be made in the context of a publicly funded health care setting in a large region comprising both the capital and surrounding suburban and rural areas. Results from the multivariable adjustments should be interpreted cautiously because of the limited number of outcomes. Furthermore, the strength of association between acute versus elective cardioversion and stroke was reduced when considering only strokes within 7 days after ECV, and the reported difference may be attributed to chance alone (Table S3 primary outcome comparison of interest was 95% CI, 0.93–5.63). We do not have any data regarding the duration of AF before ECV. Some strokes that occurred during the first 30 days after ECV might be associated with other factors and thus not caused by the investigated procedure. Other possible ECV complications other than stroke were not investigated.

Nevertheless, the main strength of our study was the population-based large cohort of well-characterized patients with AF with minimal loss to follow-up. The administrative health data register of the Stockholm Region covers both primary and secondary care for the whole population and has been extensively used, notably for other studies of AF. Although the absolute number of ischemic stroke events in patients with acute ECV was small, we found a clear indication of higher event rates with acute compared with elective ECV, which could be plausibly explained in multivariable models by a lack of anticoagulant treatment and may also be attributed to underlying comorbidities.

In conclusion, this is so far the largest cohort study comparing acute and elective cardioversion. It indicates a low risk for stroke within 30 days after both acute and elective ECV with improvements during the study period. Acute ECV was associated with a higher unadjusted risk for stroke than elective ECV, but the risk was similar after adjustment for anticoagulant treatment. This study supports the importance of anticoagulation before ECV according to recent guidelines.

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Supplementary Material
Tables S1–S5

REFERENCES
1. Rozen G, Hosseini SM, Kaadan MI, Biton Y, Heist EK, Vangel M, Mansour MC, Ruscini NJ. Emergency department visits for atrial fibrillation in the United States: trends in admission rates and economic burden from 2007 to 2014. J Am Heart Assoc. 2018;7:e009024. DOI: 10.1161/JAHA.118.009024.
2. Piccioni JP, Fauchier L. Rhythm control in atrial fibrillation. Lancet. 2016;20:829–840. DOI: 10.1016/S0140-6736(16)31277-6.
3. Airaksinen KEJ, Grönberg T, Nuotio I, Miltanen M, Ylitalo A, Biancari F, Hartikainen JE. Thromboembolic complications after cardioversion of acute atrial fibrillation: the FinCV (Finnish Cardioversion) study. J Am Coll Cardiol. 2013;62:1187–1192. DOI: 10.1016/j.jacc.2013.04.089.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22:983–988. DOI: 10.1161/01.STR.22.6.983.
5. Prystowsky EN. Management of atrial fibrillation: therapeutic options and clinical decisions. Am J Cardiol. 2000;85:3–11. DOI: 10.1016/S0002-9149(00)00908-5.
6. Forslund T, Komen JJ, Andersen M, Wettermark B, von Euler M, Hasselström J. Oral anticoagulation in patients with atrial fibrillation: a population-based cohort study. Eur Heart J. 2018;40:420–428. DOI: 10.1093/eurheartj/ehy416.
7. Crijns HJGM, Weijis BJ, Fairley A-M, Lefever J, Maggioni AP, Martin A, Nikoukis P, Rosenqvist M, Sanders P, Scanavacca M, et al. Contemporary real life cardioversion of atrial fibrillation: results from the multinational RHYTHM-AF study. J Am Coll Cardiol. 2014;172:588–594. DOI: 10.1016/j.jacc.2014.01.099.
8. Hansen ML, Jepsen RMHG, Olesen JB, Ruwald MH, Karasoy D, Gisalson GH, Hansen J, Kaber L, Husted S, Torp-Pedersen C. Thromboembolic risk in 16 274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy. Europace. 2015;17:18–23. DOI: 10.1093/europace/euu189.
9. Grönberg T, Hartikainen J, Nuotio I, Biancari F, Ylitalo A, Airaksinen KE. Anticoagulation, CHA2DS2-VASc Score, and thromboembolic risk of cardioversion of acute atrial fibrillation (from the FinCV Study). Am J Cardiol. 2016;115:1294–1298. DOI: 10.1016/j.amjcard.2016.01.024.
10. Nuotio I, Hartikainen J, Grönberg T, Biancari F, Airaksinen KE. Time to cardioversion for acute atrial fibrillation and thromboembolic complications. JAMA. 2014;312:647–649. DOI: 10.1001/jama.2014.3824.
11. Leung M, Rosendaal PJ, Abou R, Marsan NA, Leung DY, Delgado V, Bax JJ. Left atrial function to identify patients with atrial fibrillation at high risk of stroke: new insights from a large registry. Eur Heart J. 2018;49:2122–2128. DOI: 10.1093/eurheartj/ehy243.
12. Niku AD, Shiota T, Siegel PJ, Rader F. Prevalence and resolution of left atrial thrombus in patients with non-valvular atrial fibrillation and flutter with oral anticoagulation. Am J Cardiol. 2019;123:63–68. DOI: 10.1016/j.amjcard.2018.09.027.
13. Lopes RD, Reper KS, Horton JR, Al-Khatib SM, Newby LK, Mehta RH, Van der Vel F, Armstrong PW, Mahaffey KW, Harrington RA, et al. Short- and long-term outcomes following atrial fibrillation in patients with acute coronary syndromes with or without ST-segment elevation. Heart. 2008;94:867–873. DOI: 10.1136/hrt.2007.134486.
14. Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. J Am Coll Cardiol. 2017;69:689–699. DOI: 10.1016/j.jacc.2017.08.001.
15. Cameron S, Ojeda FM, Niranjn T, Gianfagna F, Vishram-Nielsen JK, Costanzo S, Söderberg S, Vartainen E, Donati MB, Lechen ML, et al. Temporal relations between atrial fibrillation and ischaemic stroke and their prognostic impact on mortality. Europace. 2020;22:522–529. DOI: 10.1093/europace/euz312.
Supplemental Material
Table S1. Definitions of cardioversion and baseline co-morbidities by ICD-10, primary care codes and procedure codes.

| Diagnosis or procedure                        | ICD-code or procedure code beginning with |
|-----------------------------------------------|-------------------------------------------|
| Alcohol abuse                                 | E244, F10, G312, G621, G721, I426, K292, K70, K860, O354, P043, Q860, T51, Y90-91, Z502, Z714 |
| Anaemia                                       | D50-64                                    |
| Any severe bleeding                          | I60-62, I690-I692, S064-S066, I850, I983, K25-28 (sub codes 0-2 and 4-6 only), K625, K922, D500, D629, J942, I312, H431, H356 |
| Atrial fibrillation                          | I48                                       |
| Cancer                                        | entire C-series                           |
| Cardioversion of atrial fibrillation          | Elective: DF026                            |
|                                               | Acute: DF027                              |
| COPD/Emphysema                                | J43-44                                    |
| Dementia                                      | F00-F03                                   |
| Diabetes                                      | E10-E14                                   |
| Frequent falls (more than one registration)   | W00-19                                    |
| Gastric duodenal bleeding                     | K25-28 (sub codes 0-2 and 4-6 only)       |
| Heart failure                                 | I50                                       |
| Hypertension                                  | I10-I15                                   |
| Condition                                      | Codes                                                                 |
|------------------------------------------------|----------------------------------------------------------------------|
| Ischemic stroke, arterial embolism, and stroke, unspecified | I63, I64, I679, I693, I694, I698, I67-, I69-, Z866A, Z866B, Z867C, G450, G451, G452, G453, G458, G45.9, G45-, I74 |
| Intracranial bleeding                          | I60-I62, I690-I692, S064-S066                                          |
| Liver disease                                  | K70-77                                                                |
| Mechanical valve                               | Z952                                                                  |
| Procedure codes: FCA60, FDC10, FGE00, FGE96, FJF00, FJF96, FKD00, FKD96, FMD00, FMD96 |
| Mitral stenosis                                | I050, I052, I342                                                       |
| Obesity                                        | E65-66                                                                |
| Renal disease                                  | N17, N183, N184, N185, N189                                           |
| Transesophageal echocardiography               | AF064                                                                 |
| Vascular disease                               | I20-I25, I70, I739                                                    |
| Venous thromboembolism                         | I26, I80 (I80.0 excluded), I82 (I82.1 excluded), I27.82              |
Table S2. ATC-codes of the studied treatments.

| Treatment                     | ATC-code beginning with |
|-------------------------------|-------------------------|
| Antihypertensive treatments   | C03 C07 C08 C09         |
| Antiarrhythmic drugs          | C01B                    |
| Apixaban                      | B01AF02                 |
| Dabigatran                    | B01AE07                 |
| Dipyridamole                  | B01AC07                 |
| Edoxaban                      | B01AF03                 |
| Lipid lowering treatments     | C10                     |
| Low molecular weight heparin  | B01AB04 B01AB05 B01AB10 |
| Oral anticoagulant (OAC)      | B01AE07 B01AF01 B01AF02 B01AF03 B01AA |
| Rivaroxaban                   | B01AF01                 |
| Warfarin                      | B01AA                   |
Table S3. Univariate and multivariable hazard rates (HR) for ischemic or unspecified stroke within 7 days of first-time electric cardioversion in 9139 patients with atrial fibrillation 2011-2018.

|                                | Univariate HR (CI 95) | Multivariable HR (CI 95) | Multivariable HR (CI 95) |
|--------------------------------|-----------------------|--------------------------|--------------------------|
| Acute vs elective cardioversion| 2.18 (0.89-5.36)      | 2.29 (0.93-5.63)         | 1.02 (0.31-3.31)         |
| CHA2DS2-VASc (per point)       | 1.29 (1.01-1.64)      | 1.29 (1.02-1.64)         | 1.37 (1.09-1.73)         |
| Year of inclusion (per year)   | 0.81 (0.66-1.00)      | 0.80 (0.65-0.99)         | 0.76 (0.59-0.98)         |
| NOAC vs No oral anticoagulant  | 0.26 (0.09-0.76)      |                          | 0.39 (0.09-1.69)         |
| Warfarin vs No oral anticoagulant | 0.28 (0.09-0.83)    |                          | 0.17 (0.04-0.66)         |

NOAC: Non-vitamin K oral anticoagulants; CI: Confidence interval; HR: Hazard ratio
Table S4. Sensitivity analysis adding antiarrhythmic agents.

|                                      | Multivariable HR (CI 95) |
|--------------------------------------|--------------------------|
| Acute vs elective cardioversion      | 1.02 (0.37-2.87)         |
| CHA2DS2-VASc (per point)             | 1.35 (1.11-1.65)         |
| Year of inclusion (per year)         | 0.81 (0.66-1.00)         |
| NOAC vs No oral anticoagulant        | 0.29 (0.08-1.03)         |
| Warfarin vs No oral anticoagulant    | 0.18 (0.06-0.58)         |
| Antiarrythmic agents                 | 0                        |

Multivariable hazard rates (HR) for ischemic or unspecified stroke within 30 days of first-time electric cardioversion in 9 139 patients with atrial fibrillation 2011-2018.

NOAC: Non-vitamin K oral anticoagulants; CI: Confidence interval; HR: Hazard ratio
Table S5. Sensitivity analysis using logistic regression.

|                                      | Multivariable OR (CI95) |
|--------------------------------------|-------------------------|
| Acute vs elective cardioversion      | 0.98 (0.35-2.71)        |
| CHA2DS2-VASc (per point)             | 1.36 (1.11-1.65)        |
| Year of inclusion (per year)         | 0.81 (0.66-1.00)        |
| NOAC vs No oral anticoagulant        | 0.28 (0.08-0.99)        |
| Warfarin vs No oral anticoagulant    | 0.17 (0.05-0.53)        |

Multivariable odds ratios (OR) for ischemic or unspecified stroke within 30 days of first-time electric cardioversion in 9,139 patients with atrial fibrillation 2011-2018.

NOAC: Non-vitamin K oral anticoagulants; CI: Confidence interval; HR: Hazard ratio.