Predicting Unsuccessful Electrical Cardioversion for Acute Atrial Fibrillation (from the AF-CVS Score)

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tähän varmaankin apurahat

Abstract

Objective: To derive and validate a clinical risk stratification tool for identifying patients at high risk for unsuccessful outcome following electrical cardioversion (ECV) for acute atrial fibrillation (AF).

Background: ECV is the standard treatment for acute AF, but identification of patients with increased risk of ECV failure or AF recurrence is of importance for easy clinical decision making.

Methods: Data on 2,868 patients undergoing 5,713 cardioversions of acute AF in three Finnish hospitals was included in the analysis. The composite of cardioversion failure and recurrence of AF within 30 days after ECV was recorded. Patients from western (n=3716 cardioversions) and eastern (n=1997 cardioversions) hospital regions were used as derivation and validation datasets, respectively. A clinical scoring system (AF-CVS score) was created using logistic regression analyses with a repeated measures model in the derivation dataset.

Results: A multivariable analysis for prediction of the composite end-point resulted in identification of five clinical variables for increased risk: **A**ge (OR 1.31, 1.13-1.52), not the **F**irst AF (OR 1.55, 1.19-2.02), **C**ardiac failure (OR 1.52, 1.08-2.13), **V**ascular disease (OR 1.38, 1.11-1.71), and **S**hort interval from previous AF episode (within one month before ECV, OR 2.31, 1.83-2.91). C-index for this score was 0.67 (95% CI, 0.65-0.69) with Hosmer-Lemeshow p-value 0.84. With high (>5) scores (i.e. 12-16% of the patients), the rate of composite end point was ~40% in both cohorts and amongst low risk patients (score <3), the composite end point rate was ~10%.

Conclusions: The risk of failure of ECV and early recurrence of AF can be predicted with simple clinical characteristics. The AF-CVS score is a simple clinical score to aid decision-making in predicting an unsuccessful ECV result.

Key words: atrial fibrillation, cardioversion, recurrence, failure, risk stratification, score.

Introduction

Electrical cardioversion (ECV) is the primary method for converting acute atrial fibrillation (AF) into sinus rhythm in the emergency department. Patients presenting with acute AF often experience marked discomfort and various symptoms due to the erratic and elevated heart rate. The good availability of ECV and the effectiveness of successful rhythm conversion in relieving symptoms make ECV an attractive treatment option from physician's and patient's perspective. However, almost 20% of ECVs are unsuccessful, i.e. the rhythm is not converted or AF recurs within 30 days [10]. In addition, cardioversion and rhythm control strategy increase the risk of thromboembolic complications in patients without adequate anticoagulation and do not offer prognostic advantage over rate control [6-8,11]. Since there is limited information on clinical factors contributing to the overall success of ECV our aim was to derive and validate a practical risk scoring system for ECV failure and early AF recurrence in the acute setting based on large multicenter FinCV study data.

Methods

This study is a part of the multicenter FinCV study (ClinicalTrials.gov Identifier: NCT01380574) assessing the thromboembolic and arrhythmic complications after cardioversion of acute (<48 hours) AF [11-13]. The study complies with Declaration of Helsinki and the study protocol was approved by the Medical Ethics Committee of the Hospital District of Southwest Finland and the ethics committee of the National Institute for Health and Welfare. Because of the register-based nature of the study, informed consent of patients was not required.

All patients (>18 years) with primary diagnosis of AF (ICD-10 code I48.0) admitted to the emergency departments of two university hospitals and one central hospital in western and eastern Finland during the study period were identified from the institutional discharge registers (11).

Databases and emergency clinic admission records were used to review all patients who underwent cardioversion of acute AF. Comprehensive data on type and duration of AF, relevant clinical characteristics, and cardioversion details were collected. Only patients living within the catchment area of the hospitals were selected in order to get adequate follow-up data. In patients with multiple cardioversions, only the first (<5) cardioversions were included in the current analysis, since repetitive cardioversions are redundant in current practice and predict early recurrence [10]. AF episodes lasting over 48 hours were excluded. Thus, there were originally 3,143 patients who underwent 7,660 cardioversions of acute AF. Of those, 5,713 cardioversions in 2,868 patients were qualified ECVs and included in the current analysis.

ECVs were performed according to the contemporary guidelines under general anesthesia [10]. A 12-lead ECG was recorded before and after the procedure. Patients were followed from the patient records for 30 days after the cardioversion to evaluate the recurrence of AF.

The short term failure of ECV was defined as the combination of initial failure of ECV or recurrence of AF within 30 days after ECV. For the purpose of the study, the population was divided in to the derivation (western region) and the validation (eastern region) cohorts according to the location of participating centers (Western Finland, Turku and Pori, n=3716, 65%; Eastern Finland, Kuopio, n=1997, 35%).

Statistical Analysis

Statistical analyses were performed using SAS 9.4 statistical software (SAS Institutute Inc; Cary; NC). Chi-square test and Wilcoxon nonparametric test were used for bivariable comparisons between groups. The score points were created employing logistic regression analyses with a repeated measures model from the derivation dataset. Covariates with known predictive value (age, gender, duration of the AF episode, AF episodes within 30 days before the index ECV, occurrence of previous AF episode, increasing number of ECV, atherosclerotic vascular disease, heart failure, diabetes, renal failure and history of stroke or TIA or peripheral embolism) [10,12] were initially included in the model and covariates with significance (<0.05) were included in the final model (Table 2). To create the score points the regression coefficients were divided by the smallest coefficient and rounded to the nearest integer [1]. Model calibration was consider acceptable at the Hosmer-Lemeshow goodness-of-fit test p>0.1 and model discrimination was evaluated with c-statistics. The predictive ability of the AF-CVS score was then tested in the validation dataset. All tests were two-sided with significance level at p<0.05.

Results

The characteristics of the derivation and validation datasets are presented in Table 1. The overall failure rate (unsuccessful ECV or early recurrence of AF) was higher (20.5% vs. 17.8 %, p<.001) in the derivation cohort. In addition, female gender, heart failure and AF within 30 days before the cardioversion were significantly more prevalent in the derivation dataset. In contrast, in the validation cohort there was significantly more hypertension, vascular disease, use of antiarrhythmic medication and first AF episodes.

The results of multivariable analysis in the derivation dataset (3716 events in 1830 patients) for the prediction of the overall failure of ECV (unsuccessful ECV or early recurrence of AF) are presented in Table 2. The most important score variable was another AF episode within 1 month before ECV (p < 0.001). Any prior AF episode (p<0.001), older age (p<0.001), congestive heart failure (p<0.001) and vascular disease (p<0.001) were the other significant predictors included in the developed AF-CVS score.

The c-statistics for the full score was 0.67 (95% CI, 0.65-0.69) with Hosmer-Lemeshow p-value 0.84. In both cohorts, the point scores < 3 show low failure rates (1.3-13.0%) and the point scores > 5 show high failure rates (34.4-66.7%) (Figure 1). The lowest short-term failure rates were seen in young males having the first AF episode (0% to 6% in the derivation and validation datasets). The predictive accuracy of AF-CVS score was independent of the use of antiarrhythmic drugs.

Discussion

To our knowledge this is the first attempt to develop a risk stratification tool for assessing the risk of unsuccessful ECV in the setting of acute AF. Our study shows that the risk of unsuccessful outcome of ECV can be predicted using five simple clinical variables. In patients classified as high-risk patients (cutoff score > 5) the rate of unsuccessful ECV outcome was around 40% in the derivation and validation cohorts. The c-statistics of the AF-CVS score was 0.67, which is at the same level as in the validation of CHADS- and CHA_2DS_2-VASc –scores [20,21].

The success rate of ECV for acute AF has been reported to vary from 86% to 96.5% [10,18,23- 25,],

but there is less information on early recurrence rate or predictors of early recurrence after

successful ECV [10]. Our present analysis shows that the AF disease "activity" reflected in recent

AF episode was the most potent predictor of unfavorable short-term outcome after ECV. Any

previous history of AF had additional, but milder negative effect on outcome. In this respect it is

noteworthy that the use of antiarrhythmic medication or beta-blockers and high number of earlier

ECVs, which reflect the severity of the disease, were also significant predictors for poor outcome

in the original population [10], but were not included in the model because of the lack of standard

indications for them.

Old age, heart failure and vascular disease were the patient characteristics included in the AF-CVS

-score. They are all included also in the CHA_2DS_2-VASc score and increase thromboembolic

complications if ECV is performed without effective anticoagulation. Female gender was of

borderline significance to predict the unsuccessful outcome of ECV. Importantly, female gender is,

however, a significant predictor of thromboembolic complications after ECV if no effective

anticoagulation is used and also increases the risk of bradyarrhythmic complications together with

old age [11-13].

Our findings suggest that the AF-CVS score can be used to identify a patient group with high short-

term failure risk of ECV already in the emergency room and the score may help the clinician to

decide the optimal treatment strategy for the patient. Repeated cardioversions may predispose

the patient to unnecessary thromboembolic complications, as we know that each cardioversion

promotes thrombus formation through atrial stunning [19]. For the high-risk patient group (score

>5), the treatment strategy of rate control may be more justified than rhythm control when more

definitive treatments (e.g. ablative therapy) are not suitable or available. Of note, the clinical features included in the score (old age, heart failure and vascular disease) are also problematic for antiarrhythmic medication of AF. At the other end of the spectrum, we can similarly identify patients at a low risk for AF recurrence or ECV failure.

As all retrospective studies, our retrospective multicenter analysis has its limitations. Even though the comprehensive electronic patient records have excellent coverage, we were reliant on the data documented by the physician who performed the cardioversion. Also, the recurrence rate of AF is likely to be an underestimation due to potential asymptomatic AF episodes. The AF-CVS score can be applied only for acute (<48h) AF, since the predictors of ECV failure and AF recurrence may differ in elective ECV of AF.

In conclusion, the AF-CVS score is a novel tool to help physicians in choosing the effective treatment strategy for acute AF.

Nämä siis järjestettävä ja luvut korjattava

Table 1. Demographic characteristics.

| Clinical variables	Derivation cohort (%)	Validation cohort (%)	p-value*
n	3716 (65.0)	1997 (34.0)	
Event rate	763 (20.5)	355 (17.8)	0.01
Age			0.9
<45 y.	522 (14.1)	278 (13.9)	0.09
50 to 65 y.	1442 (38.8)	832 (41.7)	
≥65 y.	1752 (47.2)	887 (44.4)	
Female gender	1423 (38.3)	626 (31.4)	<.001
Hypertension	1746 (47.0)	1067 (53.4)	<.001
Diabetes	372 (10.0)	181 (9.1)	0.2
Heart failure	217 (5.8)	63 (3.2)	<.001
Atherosclerotic disease	876 (23.6)	759 (38.1)	<.001
First AF episode	588 (15.8)	823 (41.2)	<.001
AF within last 30 days	555 (15.0)	237 (11.9)	0.001
Failure of CV	246 (6.6)	90 (4.5)	0.001
FA recurrence	556 (15.0)	286 (14.3)	0.5
Antiarrhythmic medication	477 (12.8)	356 (17.8)	<.001
Additive AF-CVS score	3.8±1.8	3.3±1.9	<.001

AF: atrial fibrillation; Atherosclerosis: coronary artery disease and/or peripheral arterial disease.

Table 2. Results of multivariable logistic regression analysis with repeated model for prediction of failure for or recurrence after electrical cardioversion. The derivation dataset included 3716 patients.

Clinical variables	B-coefficient	Multivariate analysis OR, 95%CI	Additive score points
Age group*	0.27	1.31, 1.13-1.52	1 to 2
Other than the **F**irst AF episode	0.44	1.55, 1.19-2.02	2
Congestive heart failure	0.42	1.52, 1.08-2.13	2
Vascular disease	0.32	1.38, 1.11-1.71	1
Short interval (<1 month) from previous AF episode	0.84	2.31, 1.83-2.91	3

AF: atrial fibrillation; OR: odds ratio; CI: confidence interval; *Age group 0 (<45 y.), 1 (45 to 65 y.), 2 (≥65 y.)

Figure 1. Incidence of ECV failure and AF recurrence in the derivation and validation datasets.
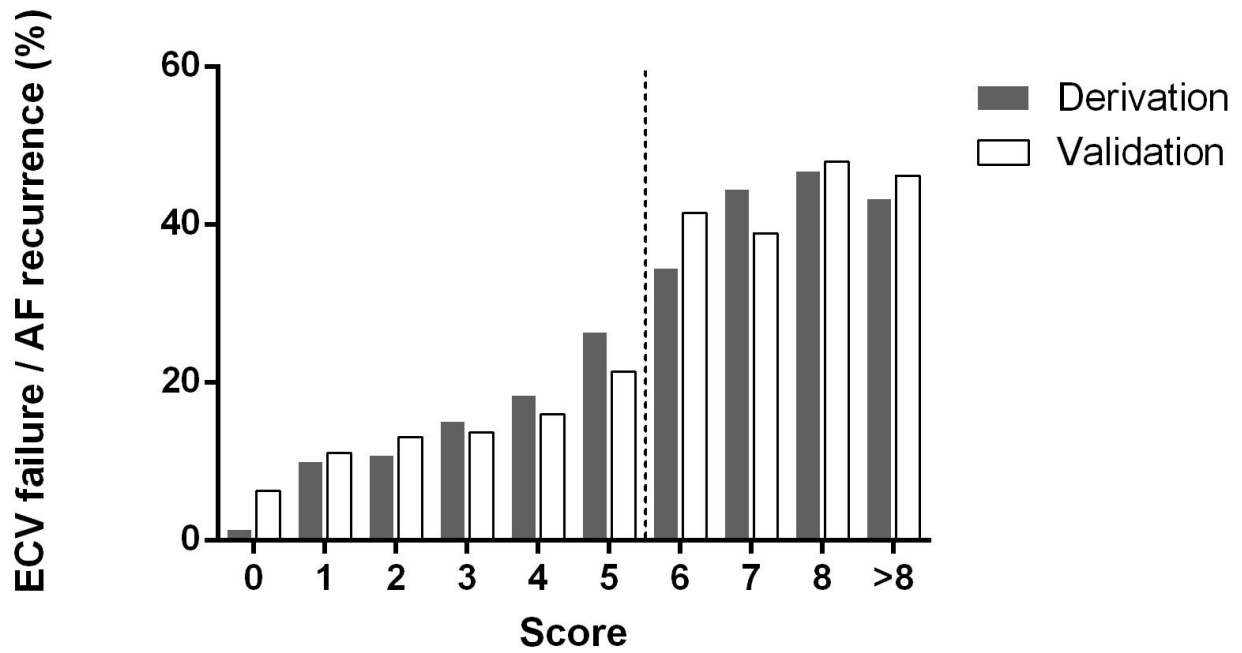
AF-CVS score points:
Age: <45 = 0 points; 45-65 = 1 point; >5 = 2 points. **F**irst AF episode? = 2 points if previous AF.
CHF = 2 points. **V**ascular disease = 1 point. **S**hort interval (AF within 1 month) = 3 points

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