Clinical determinants of early spontaneous conversion to sinus rhythm in patients with atrial fibrillation

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Abstract

Background The current standard of care for acute atrial fibrillation (AF) focuses primarily on immediate restoration of sinus rhythm by cardioversion, although AF often terminates spontaneously.

Objective To identify determinants of early spontaneous conversion (SCV) in patients presenting at the emergency department (ED) because of AF.

Methods An observational study was performed of patients who visited the ED with documented AF between July 2014 and December 2016. The clinical characteristics and demographics of patients with and without SCV were compared.

Results We enrolled 943 patients (age 69 ± 12 years, 47% female). SCV occurred within 3h of presentation in 158 patients (16.8%). Logistic regression analysis showed that duration of AF <24 h [odds ratio (OR) 7.7, 95% confidence interval (CI) 3.5–17.2, \( p<0.001 \)], left atrial volume index <42 ml/m² (OR 1.8, 95% CI 1.2–2.8, \( p=0.010 \)), symptoms of near-collapse at presentation (OR 2.4, 95% CI 1.2–5.1, \( p=0.018 \)), a lower body mass index (BMI) (OR 0.9, 95% CI 0.91–0.99, \( p=0.028 \)), a longer QTc time during AF (OR 1.01, 95% CI 1.0–1.02, \( p=0.002 \)) and first-detected AF (OR 2.5, 95% CI 1.6–3.9, \( p<0.001 \)) were independent determinants of early SCV.

Conclusion Early spontaneous conversion of acute AF occurs in almost one-sixth of admitted patients during a short initial observation in the ED. Spontaneous conversion is most likely to occur in patients with first-onset, short-duration AF episodes, lower BMI, and normal left atrial size.

Keywords Acute atrial fibrillation · Spontaneous conversion · Determinants · Treatment · Cardioversion · Wait-and-see approach

Introduction

Atrial fibrillation (AF) is a commonly encountered arrhythmia and causes a significant health care burden [1, 2]. The prevalence of AF and thereby the economic costs (mainly for hospitalisation and treatment), continues to increase [3, 4]. Current treatment is focused primarily on appropriate anticoagulation, rate

What’s new?

- Spontaneous conversion is most likely to occur in patients with first-onset, short-duration episodes of atrial fibrillation (<24h), lower body mass index, and normal left atrial size.
- The results of the current study facilitate the identification of patients with a high likelihood of spontaneous conversion to sinus rhythm and the implementation of a wait-and-see approach.
Original Article

or rhythm control strategy, and the assessment of underly-
ing conditions that predispose to AF. In patients
with acute symptomatic AF, the primary aim of treat-
ment is early restoration of sinus rhythm (SR) by phar-
macological cardioversion (PCV), electrical cardiover-
sion (ECV) or a combination of both [4]. However, it
could be questioned whether immediate restoration
by means of cardioversion is necessary, since several
previous studies have reported that spontaneous con-
version (SCV) of AF to SR occurs in up to 70% of acute
AF cases [1, 5–9], making prompt ECV or PCV un-
necessary. Appropriate identification of patients with
a high likelihood of SCV of AF is needed. The aim of
this study is to determine the clinical characteristics
associated with early SCV in patients presenting with
AF at the emergency department (ED).

Methods

Setting

We conducted an observational study of 943 adult
patients who visited the ED with AF between July
2014 and December 2016. Patients were included at
the Maastricht University Medical Centre+ (MUMC+).
The study was approved by the Institutional Review
Board of the MUMC+.

Study population

All patients were aged over 18 years. The patients ei-
ther had electrocardiographic documentation of AF at
presentation or were patients with pre-hospital con-
version if they had previous electrocardiographically
documented AF with a verified symptom-rhythm cor-
relation or if the current episode was electrocardio-
graphically documented by the general practitioner
and patients converted on their way to the hospi-
tal. For the purpose of this study the following ex-
clusion criteria were applied: a history of persistent
or permanent AF, defined as a previous episode of AF lasting longer than >48 h, were excluded. The duration of the current episode was not an ex-
clusion criterion; therefore episodes longer than 48 h
were also included if the patient had no history of persistent or permanent AF. Conversion was defined
as spontaneous if the patient converted to SR without
active cardioversion, either ECV or PCV, before pre-
sentation at the ED or within 3 h after ED presentation,
which was the time interval allowing proper work-up
towards active cardioversion and during which spon-
taneous cardioversion could happen.

Data collection

Baseline characteristics were collected, including age,
sex, duration of AF, current symptoms, medical his-
tory, and (prior) echocardiographic data. Patients un-
derwent a full physical examination, a 12-lead elec-
trocardiogram analysed with software from the MUSE
system (GE Medical Systems, Milwaukee, WI, USA),
and laboratory investigation at the ED. Information
regarding therapeutic strategy including rate versus
rhythm control was noted. We compared characteris-
tics between patients with SCV and non-spontaneous
conversion (non-SCV).

Definitions

For the purpose of this study patients with a history
of persistent or permanent AF, defined as a previous
episode of AF lasting longer than >48 h, were excluded.
The duration of the current episode was not an ex-
clusion criterion; therefore episodes longer than 48 h
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taneous cardioversion could happen.

Statistical analysis

Data management and analysis were performed using
IBM SPSS version 25 (Armonk, NY, USA). Results
were reported as mean ± standard deviation or me-
dian with interquartile range (IQR). A chi-square or
Fisher’s exact test was used to compare categorical
variables. Normally distributed continuous covariates
were compared using the Student’s t-test. For com-
parison of skewed continuous covariates the Mann-
Whitney U test was used. A binary logistic regres-
sion was performed, using backward selection until
all variables in the model reached a p-value <0.05, to
identify possible determinants for SCV. All variables

Fig. 1 Study flow chart. Exclusion criteria were a history of persistent or permanent atrial fibrillation (AF), haemodynamic instability, or signs of acute coronary syndrome (ACS) or heart failure at presentation. Persistent AF was defined for this trial as a previous episode lasting longer than 48 h. Haemodynamic instability was defined as a heart rate above 170 bpm or a systolic blood pressure below 100 mmHg. ED emergency department, SCV spontaneous conversion
# Table 1  Baseline characteristics according to spontaneous cardioversion

| Total, n=943 | Non-SCV n=785 (83.2%) | SCV n=158 (16.8%) | p-value (non-SCV vs SCV) |
|-------------|-----------------------|-------------------|-------------------------|
| **Demographics** | | | |
| Age, years (±SD) | 68.5 (±12.6) | 69.7 (±11.3) | 0.257 |
| Female, n (%) | 361 (46.0%) | 85 (53.8%) | 0.073 |
| BMI, kg/m² (±SD) | 28.5 (±6.5) | 27.0 (±4.6) | 0.001 |
| **History** | | | |
| Hypertension, n (%) | 475 (60.5%) | 107 (67.7%) | 0.089 |
| Diabetes mellitus, n (%) | 101 (12.9%) | 23 (14.6%) | 0.566 |
| Hypercholesterolaemia, n (%) | 285 (36.3%) | 41 (25.9%) | 0.013 |
| Smoking: | | | |
| – Current, n (%) | 87 (11.1%) | 16 (10.1%) | 0.725 |
| – Past, n (%) | 69 (8.8%) | 12 (7.6%) | 0.625 |
| Myocardial infarction, n (%) | 90 (11.5%) | 18 (11.4%) | 0.979 |
| Coronary artery disease, n (%) | 140 (17.8%) | 27 (17.1%) | 0.823 |
| Percutaneous coronary intervention, n (%) | 81 (10.3%) | 16 (10.2%) | 0.962 |
| Coronary artery bypass graft, n (%) | 59 (7.5%) | 3 (1.9%) | 0.009 |
| Valve surgery, n (%) | 42 (5.6%) | 4 (1.3%) | 0.021 |
| **Stroke** | | | |
| – Ischaemic, n (%) | 36 (4.6%) | 3 (1.9%) | 0.122 |
| – Haemorrhagic, n (%) | 0 (0%) | 1 (0.6%) | 0.188 |
| Transient ischaemic attack, n (%) | 31 (3.9%) | 9 (5.7%) | 0.320 |
| Pulmonary embolism, n (%) | 8 (1.0%) | 1 (0.6%) | >0.999 |
| Deep venous thrombosis, n (%) | 2 (0.2%) | 3 (1.9%) | 0.036 |
| Congenital heart disease, n (%) | 10 (1.3%) | 2 (1.3%) | >0.999 |
| Hyperthyroidism, n (%) | 18 (2.3%) | 7 (4.4%) | 0.168 |
| Hypothyroidism, n (%) | 19 (2.4%) | 5 (3.2%) | 0.588 |
| Chronic obstructive pulmonary disease, n (%) | 30 (3.8%) | 1 (0.6%) | 0.040 |
| Peripheral artery disease, n (%) | 26 (3.3%) | 7 (4.4%) | 0.485 |
| Obstructive sleep apnoea syndrome, n (%) | 18 (2.3%) | 5 (3.2%) | 0.569 |
| Atrial flutter, n (%) | 89 (11.3%) | 23 (14.6%) | 0.254 |
| ICD, n (%) | 29 (3.7%) | 2 (1.2%) | 0.118 |
| PM, n (%) | 20 (2.5%) | 4 (2.5%) | >0.999 |
| Ablation therapy for AF, n (%) | 87 (11.1%) | 12 (7.6%) | 0.192 |
| CHA2DS2-VASc (±SD) | 2.6 (±1.6) | 2.7 (±1.5) | 0.370 |
| **Medication at baseline** | | | |
| Vitamin K antagonist, n (%) | 281 (35.8%) | 41 (25.9%) | 0.017 |
| Direct oral coagulants, n (%) | 144 (18.3%) | 32 (20.3%) | 0.574 |
| **Other medication** | | | |
| Acetylsalicylic acid, n (%) | 88 (11.2%) | 23 (14.6%) | 0.234 |
| ACE inhibitors, n (%) | 142 (18.1%) | 27 (17.1%) | 0.765 |
| ARB, n (%) | 246 (31.3%) | 50 (31.8%) | 0.900 |
| Spironolactone, n (%) | 19 (2.4%) | 2 (1.3%) | 0.556 |
| Beta-blocker, n (%) | 353 (45.0%) | 68 (43.0%) | 0.656 |
| Digoxin, n (%) | 37 (4.7%) | 5 (3.2%) | 0.388 |
| AAD use, n (%) | 231 (29.4%) | 39 (24.7%) | 0.229 |
| Statin, n (%) | 303 (38.6%) | 56 (35.4%) | 0.449 |
| **Echocardiography** | | | |
| LAV index <42 ml/m², n (%) | 317 (47.8%) | 84 (61.3%) | 0.004 |
| Normal RAV index ml/m², n (%) | 258 (32.9%) | 66 (41.8%) | 0.031 |
| LHV, n (%) | 248 (31.6%) | 47 (29.7%) | 0.648 |
| LVEF (±SD) | 59.5 (±7.5) | 61.6 (±5.0) | 0.002 |
showing a significant ($p<0.05$) univariable relationship for SCV were included in the regression analysis. A $p$-value of $<0.05$ was considered statistically significant.

**Results**

We enrolled 943 consecutive patients (Fig. 1) with a mean age of 69±12 years, 47% females. Expressed symptoms at presentation were palpitations in 74% of patients, dyspnoea in 28%, chest pain in 20%, dizziness in 16%, fatigue in 8%, near-collapse in 7%, and 10% experienced other symptoms of AF. An overview of the baseline characteristics of SCV and non-SCV patients is presented in Table 1.

**Spontaneous conversion**

The median duration from onset of symptoms until the end of the observation period was 4.0 h (IQR 7, range 0–86 h) in patients with SCV, and 11.0 h (IQR 19, range 3–1355 h) in patients without SCV. The median observation time at the ED pending SCV was 32 min (IQR 81, range 0–165 min). The number of patients in SC after 1 h was 100 (10.6%), and after 2 h 138 (14.6%). The mean age of the SCV and non-SCV groups was comparable (70±11 vs 69±13 years, $p=0.257$, respectively). There was a trend towards more spontaneous cardioversions in female patients (53.8 vs 46.0%, $p=0.073$). Patients with SCV less frequently had a history of hypercholesterolaemia (25.9 vs 36.3%, $p=0.013$), coronary artery bypass grafting (1.9 vs 7.5%, $p=0.009$), chronic obstructive pulmonary disease (0.6 vs 3.8%, $p=0.040$), and less frequently had a history of valve surgery (1.3 vs 5.6%, $p=0.021$). Mean body mass index (BMI) was lower in patients with SCV.
(27.0 vs 28.5 kg/m², \( p = 0.001 \)). First-detected AF was more common in patients with SCV than in non-SCV patients (41.8 vs 32.0%, \( p = 0.017 \), respectively). In addition, patients with SCV had a shorter median duration of symptoms (3.0 h; IQR 5 vs 8.0; IQR 19, \( p < 0.001 \)) and more often suffered symptoms of near-collapse (11.4 vs 6.1%, \( p = 0.018 \)), palpitations (81.6 vs 72.0%, \( p = 0.012 \)), chest pain (27.8 vs 18.6%, \( p = 0.008 \)), and dizziness (20.3 vs 14.9%, \( p = 0.093 \)). Patients complaining of near-collapse more often had first-detected AF (58% vs 42%, \( p < 0.001 \)). Patients with SCV more often had a higher ventricular rate (125 vs 118 bpm, \( p = 0.004 \)), longer QTc time during AF (460 ms ± 34 vs 452 ms ± 34, \( p = 0.035 \)) and more often had a lower left atrial volume index (LAVI) (<42 ml/m²) (61.3 vs 47.8%, \( p = 0.004 \)). A longer QTc was observed in patients who had a breakthrough arrhythmia (460 ± 40 ms in patients with antiarrhythmic drugs (AAD) vs 450 ± 40 ms in patients without AAD, \( p < 0.001 \)).

Logistic regression analysis showed that duration of AF <24 h (OR 7.7, 95% CI 3.5–17.2, \( p < 0.001 \)), LAVI <42 ml/m² (OR 1.8, 95% CI 1.2–2.8, \( p = 0.010 \)), symptoms of near-collapse at presentation (OR 2.4, 95% CI 1.2–5.1, \( p = 0.018 \)), a lower BMI (OR 0.9, 95% CI 0.91–0.99, \( p = 0.028 \)), a longer QTc time during AF (OR 1.01, 95% CI 1.0–1.02, \( p = 0.002 \)) and first-detected AF (OR 2.5, 95% CI 1.6–3.9, \( p < 0.001 \)) were independent determinants of early SCV (Tab. 2).

In patients with a duration of AF <24 h, first-detected AF, and smaller LAVI, the SCV rate was high: 38% (38 of 99 patients).

**Discussion**

The present study showed that early SCV to SR occurred in 16.8% of patients presenting with AF at the ED within a median time at the ED of 32 min. Duration of symptoms <24 h, first-detected AF, LAVI

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**Table 2** Univariable and multivariable regression analyses for predictors of spontaneous conversion to sinus rhythm. This model is based on \( n = 759 \) due to missing data on left atrial volume index

| Demographics | Univariable | Multivariable | p-value | OR | 95% CI | p-value |
|--------------|-------------|---------------|---------|----|--------|---------|
| BMI          | Non-SCV, \( n = 785 \) | SCV, \( n = 158 \) |         |    |        |         |
|              | 28.5 (±6.5) | 27.0 (±4.6)   | 0.001   | 0.9 | 0.91–0.99 | 0.028  |
| Presentation characteristics | | | | | | |
| Duration <24 h | 534 (68.0%) | 143 (90.5%) | <0.001 | 7.7 | 3.5–17.2 | <0.001 |
| First-detected AF | 251 (32.0%) | 66 (41.8%) | 0.017 | 2.5 | 1.6–3.9 | <0.001 |
| Near-collapse | 48 (6.1%) | 18 (11.4%) | 0.018 | 2.4 | 1.2–5.1 | 0.018 |
| Echo- and electrocardiography | | | | | | |
| QTc (ms) | 452 (±34) | 460 (±34) | 0.035 | 1.01 | 1.00–1.02 | 0.002 |
| LAVI index <42 ml/m² | 317 (47.8%) | 84 (61.3%) | 0.004 | 1.8 | 1.2–2.8 | 0.010 |

AF: atrial fibrillation, BMI: body mass index, CI: confidence interval, LA: left atrial, OR: odds ratio, SCV: spontaneous conversion
of acute AF ranging from 26 to 71% [1, 5–11], mostly depending on differences in study design, observation period and patient selection criteria. Danias et al. included 356 in-hospital patients with symptomatic AF <72 h and observed a SCV rate of 68%. In the absence of initial AAD therapy, these investigators found that the best predictor of SCV was a duration of symptoms <24 h [1]. This was confirmed by Lindberg et al. [6], who reported a SCV rate of 54% in patients in hospital with first-onset AF (n=374). In 153 patients with paroxysmal AF and a symptom duration <24 h and without structural heart disease, heart failure or hyperthyroidism, Geleris and co-workers observed a SCV rate of 71.2%. In this homogeneous group, small left atrial size was the only predictor for SCV [7]. Boriani et al. performed a randomised controlled trial of propafenone versus placebo for recent-onset AF (<7 days) and observed a SCV rate in the placebo group of 37% after 8 h of observation [11]. Sub-analyses of this study showed a higher likelihood of SCV in patients without underlying heart disease [11] and those aged <60 years [12].

The lower rate of SCV observed in our cohort is likely the result of shorter observation periods (censored at 3 h maximum) at the ED. The SCV rate we found is comparable to that in other reports of recent-onset AF by Vinson et al. (28.6%) [13] and Stiell et al. (26.5%) [10]. Vinson et al. investigated the management of recent-onset AF or atrial flutter at the ED. A total of 206 patients were included with a duration of symptoms <48 h. They found a SCV rate of 28.6% [13]. A similar SCV rate was reported by Stiell et al., who included 1068 patients with recent-onset AF (<48 h) at the ED. During a median observation period of 6.7 h, 26.5% of patients had SCV [10]. Sub-analyses of the ENSURE-AF trial, which included patients with non-valvular atrial fibrillation with a duration >48 h and who were scheduled for ECV on anticoagulation therapy, have demonstrated SCV rates of 7.6%. In the sub-analysis of Cohen et al., a history of paroxysmal AF was the only predictor for SCV [14].

To the best of our knowledge, our study is the largest concerning determinants of early SCV and enables clinicians to identify patients who are most likely to convert spontaneously to SR. In our cohort, the following characteristics appeared to be determinants of early SCV at the ED: AF duration <24 h, first-detected AF, a lower LAVI, a lower BMI, a longer QTc time during AF and symptoms of near-collapse at presentation. These parameters are most likely indicative of early phases of AF evolution. A lower LAVI suggests that macroscopic electrical and structural remodelling of the atrium has not been evident yet or is at an early stage. It is well known that this is related to higher conversion rates [15, 16]. Obesity is a well-known risk factor for developing AF [17] and a higher BMI is independently associated with progression from paroxysmal to permanent AF [18]; this could explain the higher SCV rate in patients with a lower BMI. Patients presenting with near-collapse during AF more often had first-detected AF, which may be related to the higher SCV rates seen in those patients.

‘Wait-and-see approach’ in acute AF

The substantial rates of SCV of acute AF in this and other reports [1, 5–8, 10], combined with the rising prevalence of AF, cost aspects and the possible complications associated with acute cardioversion may justify less aggressive arrhythmia management. A wait-and-see strategy for patients with stable AF with onset of symptoms <48 h encompasses standard rate control measures, adequate initiation of anti-coagulation and delayed cardioversion within 48 h if necessary. In a small study investigating this wait-and-see approach, two-thirds of 35 patients had converted spontaneously within 48 h [5]. This finding was recently confirmed by the RACE 7 ACWAS trial, a multicentre randomised controlled trial which compared a wait-and-see approach (symptom alleviation and delayed cardioversion when necessary) with immediate cardioversion in patients with recent-onset AF [9, 19]. This study showed that a wait-and-see approach is non-inferior with respect to the presence of SR at 4 weeks when compared to immediate cardioversion; almost 70% of the patients in the wait-and-see group had SCV to SR within 48 h. Those results support the opinion that a wait-and-see approach is a worthy alternative to discuss with patients but will not replace early cardioversion completely. Early cardioversion could be beneficial, since it shortens the time until conversion, which might eliminate symptoms earlier. However, in the above-mentioned study symptom control was similar in both groups [9]. Another advantage of early pharmacological conversion is the observation of the antiarrhythmic response, which tests the safety of a pill-in-the-pocket approach [20]. Therefore, patients with stable recent-onset AF and their physicians might choose between the two approaches in a shared decision-making process.

The results of the current study facilitate the identification of patients with a high likelihood of SCV to SR and the implementation of a wait-and-see approach. Identification of acute AF patients susceptible to spontaneous restoration of SR may reduce the number of emergency visits (especially in stable patients with recurrent episodes and a known symptom-rhythm correlation), costs and unnecessary and potentially harmful treatment.

Limitations

Since this study was not designed to evaluate SCV rates, our results are probably an underestimation
of the true SCV rate: patients who received active cardioversion might have converted spontaneously if a wait-and-see approach had been adopted. Due to the observational study design we could not adjust for this possible bias. Patients with pre-hospital SCV were included in the analysis. Even if the likelihood of those patients having AF was extremely high, one cannot be completely certain that those patients had an actual episode of AF which could have led to an overestimation of the SCV rate.

**Conclusion**

Early SCV of acute AF occurs in almost one-sixth of admitted patients during a short initial observation in the ED. Spontaneous conversion is most likely to occur in patients with first-onset, short-duration AF episodes, lower BMI, and normal left atrial size.

**Conflict of interest** J.G.L.M. Luermans reports a consultancy agreement with Medtronic, outside the scope of the submitted work. K. Vernooij reports grants from Medtronic, Abbott, and Biotronik, outside the scope of the submitted work. H.J.G.M. Crijns reports financial support from the Netherlands Cardiovascular Research Initiative: an initiative with support of the Dutch Heart Foundation, CVON 2014-9: Reappraisal of Atrial Fibrillation: interaction between hyperCoagulability, Electrical remodeling, and Vascular destabilisation in the progression of AF (RACE V). N.A.H.A. Pluymaekers, E.A.M.P. Dudink, B. Wejs, D.E.J. Hartgerink, J.S. Jacobs, Ö. Erküner, N.G.H.M. Marcks, Y.J.M. van Cauteren, T. Dinh, R.M.A. ter Bekke, J.E.M.W. Sels, T.S.R. Delnoij, Z. Geyik, R.G.H. Driessen, D.K. Linz and D.W. den Uijl declare that they have no competing interests.

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