



Recurring patterns of atrial fibrillation in surface ECG predict restoration of sinus rhythm by catheter ablation



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ABSTRACT

Background: Non-invasive tools to help identify patients likely to benefit from catheter ablation (CA) of atrial fibrillation (AF) would facilitate personalised treatment planning.

Aim: To investigate atrial waveform organisation through recurrence plot indices (RPI) and their ability to predict CA outcome.

Methods: One minute 12-lead ECG was recorded before CA from 62 patients with AF (32 paroxysmal AF; 45 men; age 57 ± 10 years). Organisation of atrial waveforms from i) TQ intervals in V_1 and ii) QRST suppressed continuous AF waveforms (CAFW), were quantified using RPI: percentage recurrence (PR), percentage determinism (PD), entropy of recurrence (ER). Ability to predict acute (terminating vs. non-terminating AF), 3-month and 6-month postoperative outcome (AF vs. AF free) were assessed.

Results: RPI either by TQ or CAFW analysis did not change significantly with acute outcome. Patients arrhythmia-free at 6-month follow-up had higher organisation in TQ intervals by PD ($p < 0.05$) and ER ($p < 0.005$) and both were significant predictors of 6-month outcome (PD (AUC=0.67, $p < 0.05$) and ER (AUC=0.72, $p < 0.005$)). For paroxysmal AF cases, all RPI predicted 3-month (AUC(ER)=0.78, $p < 0.05$; AUC(PD)=0.79, $p < 0.05$; AUC(PR)=0.80, $p < 0.01$) and 6-month (AUC(ER)=0.81, $p < 0.005$; AUC(PD)=0.75, $p < 0.05$; AUC(PR)=0.71, $p < 0.05$) outcome. CAFW-derived RPIs did not predict acute or post-operative outcomes.

Higher values of any RPI from TQ (values greater than 25th percentile of preoperative distribution) were associated with decreased risk of AF relapse at follow-up (hazard ratio ≤ 0.52 , all $p < 0.05$).

Conclusions: Recurring patterns from preprocedural 1-minute recordings of ECG TQ intervals were significant predictors of CA 6-month outcome.

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1. Introduction

There is considerable interest in developing tools capable of identifying patients likely to benefit from catheter ablation (CA) of AF. Termination of AF during CA is associated with longer-term maintenance of sinus rhythm (SR) [1–3]. Pre-ablation factors, such as AF cycle length (AFCL), left atrial diameter or volume, and duration of AF have been shown to predict the likelihood of termination [2,4]. Motivated by the clinical interest in non-invasive predictors of outcome from CA and electrical cardioversion the surface electrocardiogram (ECG) has also been studied.

The f-wave, namely the atrial electrical signal (mainly observable in the TQ interval) has drawn considerable attention. Its amplitude and cycle length in preprocedural baseline recordings have been associated with acute [5–7] and intermediate [5,7] ablation outcomes. Techniques in the frequency or joint time-frequency domain, based on the spectral analysis of the estimated f-wave have also been applied to predict AF relapse following electrical cardioversion [8–10].

Recurrence quantification analysis, by Eckmann and colleagues [11] for the identification of dynamic patterns in time-series, has also been deployed in AF studies [12–15]. The method is based on a graphical representation, termed recurrence plot, of recurring patterns of sub-intervals of a given time-series. Indices can be calculated to quantify percentage, duration, and distribution of recurring patterns. The strength of this analysis is that it does not require modelling of the time-series, nor the removal of outliers [16].

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At present, a quantitative non-invasive assessment of f-wave temporal predictability based on recurring patterns in individual ECG signals (auto-recurrence) is lacking, and might make prediction of acute and longer-term outcome following AF-ablation possible. In a previous study [17] we have successfully explored the ability of recurrence plot indices (RPIs) to predict acute and 3-month ablation outcome from preprocedural recordings of invasive intracardiac electrograms of the coronary sinus and right atrial appendage.

The aim of this study was to investigate the ability of RPIs from surface ECG recordings to predict acute and postoperative (3-month and 6-month) ablation outcome.

2. Methods

2.1. Study population and data recording

62 consecutive patients with AF (32 paroxysmal AF, 30 persistent AF; 45 men; age 57 ± 10 years) undergoing catheter ablation for standard clinical indications at this hospital were enrolled in the study. The characteristics of the patient cohort are summarised

Table 1
Study Population.

	All	Acute outcome Sinus rhythm restored	
		Yes (T-AF)	No (NT-AF)
Patients	62	12 (19%)	50 (81%)
Women	17	4 (24%)	13 (76%)
Age [years] (mean \pm SD)	57 ± 10	61 ± 9	56 ± 10
AF history duration [years] (mean \pm SD)	5 ± 4	4 ± 3	5 ± 5
LV ejection fraction [%]	52 ± 6	54 ± 2	52 ± 7
LA volume [ml]	59 ± 18	59 ± 20	58 ± 18
Betablockers	51	9 (18%)	42 (82%)
Calcium antagonists (Diltiazem, Verapamil)	3	1 (33%)	2 (67%)
Antiarrhythmic (withdrawn 5 half lives pre-CA)			
Amiodarone ^a	2	0 (0%)	2 (100%)
Dronedarone	1	0 (0%)	1 (100%)
Flecainide	15	5 (33%)	10 (67%)
Propafenone	2	1 (50%)	1 (50%)
Sotalol	2	0 (0%)	2 (100%)
Anticoagulant			
Dabigatran	4	1 (25%)	3 (75%)
Warfarin	61	11 (18%)	50 (82%)
Further Ablation after PVI			
CFAE only	11	4 (36%)	7 (64%)
Linear only	13	1 (8%)	12 (92%)
CFAE+Linear	9	0 (0%)	9 (100%)

T-AF indicates “terminated” atrial fibrillation (AF); NT-AF, “non terminated” AF; LV, left ventricular; LA, left atrial; PVI, pulmonary vein isolation; CFAE, complex fractionated electrogram.

^a Not withdrawn pre-CA

Table 2
Study population: partition of sample size.

AF Substrate	Acute outcome		Postoperative outcome (3-month)		Postoperative outcome (6-month)		All
	T-AF	NT-AF	NSR	AF	NSR	AF	
Paroxysmal	11	21	23	9	20	12	32
Persistent	1	29	20	10	21	9	30
All	12	50	43	19	41	21	62

T-AF indicates “terminated” atrial fibrillation (AF); NT-AF, “non terminated” AF; NSR, normal sinus rhythm (at follow-up)

in Table 1; the sample partition with respect to AF classification (paroxysmal or persistent) and CA outcome are shown in Table 2.

Prior to any ablation, 12-lead ECG recordings of 1-minute duration were obtained (Labsystem Pro™ recording system (Bard EP, C. R. Bard, Inc.). The signal was digitised at a sample rate of 1000 samples/s and stored for offline processing.

2.2. Electrophysiology study

The study was conducted in compliance with the ethical principles of the Declaration of Helsinki. Patients gave informed consent. Class I and III antiarrhythmic drugs were discontinued five half-lives prior to ablation.

Ablation comprised the following stages.

1. PVI

All patients underwent PVI. Pulmonary veins were isolated electrically using one of three ablation technologies: (I) PVAC[®] multi-electrode circumferential ablation catheter (Medtronic Ablation Frontiers); (II) Arctic Front[®] cryo-balloon (Medtronic Cryocath); and (III) wide-area circumferential ablation using ThermoCool[®] SmartTouch™ catheter and CARTO[®]3 electro-anatomical mapping and navigation system (Biosense Webster). Electrical isolation was inferred by the absence of local electrograms distal to the sites of ablation or independent pulmonary vein activity and, in those patients in sinus rhythm, by demonstrating entrance and exit block between the pulmonary veins and left atrium using pacing manoeuvres.

2. LA substrate ablation

Patients who did not revert to sinus rhythm during pulmonary vein isolation received further left atrial ablation as follows:

a. CFAE ablation

A detailed analysis of the left atrium and inter-atrial septum was performed to identify CFAEs (focal sites exhibiting constant electrical activity, or multi-component electrograms with cycle length < 120 ms averaged over a 10-second period), which were then ablated. This process was completed when no residual CFAE sites could be identified in the body of the left atrium or inter-atrial septum or when sinus rhythm was restored by ablation.

b. Linear ablation

A combination of “roof line” (connecting right and left upper pulmonary vein ostia), “mitral line” (connecting left lower pulmonary vein ostium to mitral valve annulus) and “inferior line” (connecting right lower pulmonary vein to coronary sinus) was constructed depending on the degree of signal complexity at the various sites. Linear ablation was performed with the endpoint being the absence of electrograms and presence of double potentials along the length of each line. No differential pacing manoeuvres were performed.

Of 32 paroxysmal AF patients, 24 had PVI only; 7 had PVI and linear ablation; and one had PVI, CFAE and linear. Of 30 persistent AF patients, 5 had PVI only; 6 PVI and linear; 11 had PVI and CFAE; and 8 had PVI, CFAE and linear ablation. The mean procedure and fluoroscopy times for the 62 patients were 191 ± 36 and 33 ± 16 min, respectively.

All patients in AF at the end of the ablation procedure were labelled as “non-terminated” AF (NT-AF), the others as “terminated” AF (T-AF) and this defined the acute outcome. Patients with non-terminated AF subsequently received electrical cardioversion. Clinical outcome was further assessed three and six months after ablation (or electrical cardioversion if performed) by symptom review, 12-lead ECG and 72-hour Holter recordings. AF recurrence was defined as the presence of arrhythmia symptoms with documented AF on a 12-lead ECG and/or AF episodes lasting

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