Atrial Fibrillation Type Characterization and Catheter Ablation Acute Outcome Prediction: Comparative Analysis of Spectral and Nonlinear Indices from Right Atrium Electrograms

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Abstract

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. As catheter ablation (CA) is increasingly becoming the preferred treatment, identifying predictors of CA outcome is important to assist clinical decision making. Previous studies have explored spectral and nonlinear indices. However, a comparative analysis of indices from preprocedural intracardiac recordings is lacking.

The aim of this study was to present a comparative analysis of spectral and nonlinear indices derived from a simple threshold-based segmentation of intracardiac electrograms (EGM) to characterize AF type (paroxysmal vs. persistent) and predict AF termination by CA.

Preprocedural 1 minute recordings of right atrium EGM from 54 AF patients (age 58±9 years, 37 male; 27 paroxysmal AF, 27 persistent) were used. EGM were band-pass filtered (F-EGM). f-wave activation fiducial points were identified using a threshold-based segmentation. The AF cycle length (AFCL) time series was built calculating the distance between consecutive fiducial points. The instantaneous fibrillatory rate (IFR) time series was calculated as AFCL inverse. Nonlinear indices were calculated: i) median AFCL (MAFCL); ii) localization index (LI) (concentration of IFR histogram around the mode); iii) sample entropy (SampEn); iv) root mean square error (RMSE) of IFR vs. Gaussian distribution fit. Standard methods were used to calculate spectral indices: i) dominant frequency (f_P); ii) organization index (OI) (ratio of area under f_P and its harmonics to total power) of F-EGM.

Persistent AF was associated with higher f_P ($p<0.005$), lower MAFCL ($p<0.01$) and LI ($p<0.05$), higher SampEn ($p<0.05$) and RMSE ($p<0.01$). OI was not associated with AF type. Nonlinear indices: MAFCL($p<0.01$), LI ($p<0.05$), and RMSE ($p<0.005$) predicted AF termination by CA, whereas spectral indices (f_P, OI) did not.

Nonlinear indices outperform spectral ones in characterizing AF type and predicting AF termination by CA.

1. Introduction

Atrial fibrillation (AF) is the most common form of sustained arrhythmia observed in clinical practice, and a major cause of morbidity and mortality in the elderly population [1].

Although catheter ablation (CA) is increasingly becoming the preferred treatment for the middle-aged subjects, not all patients undergoing CA respond well. A substantial research effort has been devoted in recent years to identifying predictors of CA outcome, to assist clinical decision making.

Previous studies have shown that higher preprocedural AF cycle length (AFCL) is associated with increased likelihood of successful AF termination by CA [2,3]. Frequency domain techniques, based on spectral estimation of the dominant frequency (f_P) and organization index (OI) (i.e. the ratio of the area under f_P and its harmonics to the total power) [4] have also been explored [5]. A lower preprocedural right-atrium f_P was an independent predictor of AF termination by CA in [6]. Nonlinear indices, derived from the instantaneous fibrillatory rate (IFR) histogram [7] or the fractionation interval histogram [8] have also been explored with the goal of identifying predictors of CA outcome. Nonlinear indices such as *sample entropy* have also been used to assess the evolution over time of the degree of complexity of paroxysmal AF [9].

However, all studies suffer a major limitation in the identification of the actual fibrillatory wavefront, a necessary step in identifying the fiducial points of the atrial activity waveform.

The aim of this study was to present a comparative analysis of spectral and nonlinear indices derived from a simple threshold-based segmentation of intracardiac electrograms to characterize AF type (paroxysmal vs. persistent) and predict AF termination by CA.

2. Methods

2.1. Study population and data recording

This study included 54 patients (age 58±9 years, 37 male) who presented with AF for CA (27 paroxysmal AF, 27 persistent AF) at the Freeman Hospital, Newcastle upon Tyne, UK.

Preprocedural intracardiac recordings of 1 minute duration were obtained from the coronary sinus (CS) and right atrial appendage (HRA) using a decapolar (Livewire, St Jude Medical) and Josephson quadpolar catheter (St Jude Medical) respectively. The signals were recorded using a LabSystem™ PRO EP recording system (Bard Electrophysiology, Lowell, MA, USA) with sample rate F_S = 1000 samples/s. The HRA catheter was either positioned in the right atrial appendage or high lateral right atrium depending on catheter stability and ease of cannulation of the right atrial appendage. In order to minimize contamination by ventricular electrical activity, in this study only the distal HRA signal was considered in the analysis.

2.2. Electrophysiology study

A stepwise ablation approach was followed, which consisted of pulmonary veins isolation (PVI), followed by left atrium substrate ablation (complex fractionated electrogram ablation, linear ablation) for those who did not revert to sinus rhythm after PVI. All patients in AF at the end of the ablation procedure were labeled as "non-terminated" AF (NT-AF) (N=43), the others as "terminated" AF (T-AF) (N=11). Patients with non-terminated AF subsequently received electrical cardioversion.

2.3. Signal processing

2.3.1 Spectral indices

A filtered signal (Figure 1) was obtained from the raw HRA electrogram following the criterion proposed by [10]. Briefly, the raw signal was band-pass filtered (2nd order Butterworth, 3dB pass-band: 40-250 Hz). The absolute value of the filtered waveform was low-pass filtered (2nd order Butterworth, 3dB cut-off: 20 Hz) to obtain the filtered EGM (F-EGM) signal. The power spectral density (PSD) of F-EMG was calculated using the Welch periodogram (16 s sliding Hamming window, 50% overlap, frequency resolution ΔF = 62.5 mHz). f_P and OI were calculated as in [4].

2.3.2 Nonlinear indices

The peaks of F-EGM were assumed to represent the propagating fibrillatory wavefront [4, 10]. These peaks (fiducial points) were detected using a threshold method as below:

Detect all peaks of F-EGM
For each peak:
    if peak is not the highest in a ±50 ms window, then mark invalid
    if peak is lower than 30% of the highest peak in a ±300 ms window, then mark invalid
end

AFCL time series was calculated from the distance between consecutive fiducial points. The IFR time series was calculated as the inverse of AFCL. The nonlinear dynamics of AFCL were investigated calculating: *i)* the median AFCL (MAFCL); *ii)* the localization index (LI) [7] with histogram bin width of 0.1 Hz and ΔF = 0.5 Hz; *iii)* the sample entropy (SampEn) [9], with *embedding dimension* m = 4 and tolerance r = 0.20; i*v)* the *root mean square error* (RMSE) of the fit of IFR with a normal distribution whose expected value (μ) and standard deviation (σ) were estimated from the IFR histogram.

2.4. Statistical analysis

Group comparisons for AF type (paroxysmal vs. persistent) and acute outcome (T-AF vs. NT-AF) were calculated by the Mann-Whitney test, with significance level α = 0.05 (two-sided). To assess the ability of individual parameters to predict CA outcome the *Receiver Operating Characteristic* (ROC) curve was obtained for each parameter, and the area under the curve (AUC) was calculated. Statistical analysis was carried out using SPSS statistical software (IBM Corp., Armonk, NY).

3. Results

The fibrillatory rate (f_P) was lower in patients with paroxysmal compared with persistent AF (Table 1). MAFCL was consistently longer in paroxysmal AF. Paroxysmal AF also showed a higher histogram concentration around the dominant IFR (higher LI, $p<0.05$) which was not reflected by the organization index ($p=0.229$ for OI). Sample entropy was higher in persistent AF ($p<0.05$) denoting increased complexity. Furthermore, the deviation of IFR histogram from the normal distribution was higher in persistent AF (higher RMSE, $p<0.005$).

Spectral indices (f_P, OI) were not able to predict AF termination by CA (Table 2), although f_P nearly reached significance ($p=0.09$). On the other hand, nonlinear indices calculated from the IFR histogram (LI, RMSE) and AFCL histogram (MAFCL) were significant predictors of AF termination by CA.

The whole analysis was repeated for the proximal HRA bipolar signal, however the results (not shown) were nearly identical to those presented.

Table 1. AF type: group differences.

Parameter	Median(IQR)	
	Paroxysmal (N=27)	Persistent (N=27)
f_P [Hz]	5.44(1.19)	6.44(0.86)†
OI [%]	38(15)	34(9)
MAFCL [ms]	160(73)	129(40) ‡
LI [%]	42(39)	27(13)*
SampEn [d.u.]	1.27(0.34)	1.49(0.38)*
RMSE[(a)] [d.u.]	6.1(5.0)	4.8(0.5) ‡

[(a)]RMSE is expressed in units of probability density x100 (i.e. 0-100 range); †p<0.005; ‡p<0.01; *p<0.05

Table 2. Predictors of AF termination by CA.

Parameter	Median(IQR)		AUC (95% CI) x 100
	T-AF	NT-AF	
f_P [Hz]	5.6(1.7)	6.3(1.5)	67 (48, 85)
OI [%]	38(27)	36(11)	61 (38, 84)
MAFCL [ms]	181(55)	135(42)†	76 (58, 93)†
LI [%]	54(41)	29(19)‡	73 (54, 91)‡
SampEn [d.u.]	1.1(0.4)	1.4(0.4)	65 (47, 83)
RMSE[(a)] [d.u.]	8.2(13.8)	4.8(1.0)*	82 (70, 94)*

T-AF: Terminated AF (N=11); NT-AF: Non-terminated AF (N=43).
[(a)]RMSE is expressed in units of probability density x100 (i.e. 0-100 range); †p<0.01; ‡p<0.05; *p<0.005

4. Discussion

In this study, nonlinear indices derived from the AF cycle length and instantaneous frequency time series to predict AF termination by CA were presented and compared with established spectral indices. In a preliminary analysis of AF type (Table 1), the nonlinear indices consistently reflected increased complexity of AF substrate in persistent AF compared with paroxysmal AF (higher SampEn, lower LI, higher RMSE). All nonlinear indices except SampEn were significant predictors of AF termination by CA. Interestingly, the median value of the AF cycle length (MAFCL) was a significant predictor ($p<0.01$) whereas the dominant frequency f_P was not. Similarly, the IFR histogram concentration (LI) was a significant predictor whereas the spectral concentration (OI) was not.

In a previous study [5], preprocedural f_P was also not associated with CA outcome, unlike OI.

The present study was carried out using HRA electrograms to minimize the contamination by ventricular electrical activity. Replication on other intracardiac sites such as the coronary sinus or left atrium is needed to confirm the results presented.

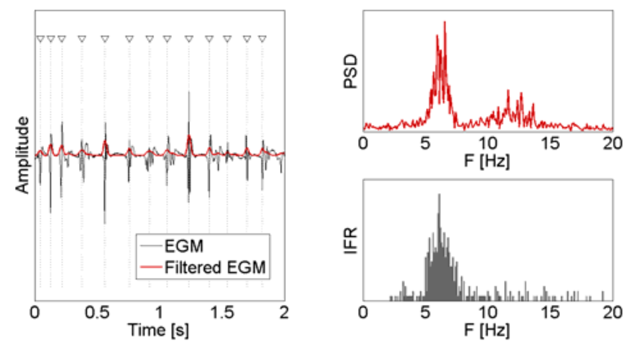

Figure 1. Raw HRA electrogram and filtered signal (left); power spectral density (PSD) of filtered signal (top right) and instantaneous frequency histogram (bottom right). Triangles with dotted vertical lines in left panel indicate fiducial points (peaks of filtered signal).

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