Prediction of Atrial Fibrillation Recurrence by Pulmonary Vein Electrogram Correlation

Raquel Cervigón[1], Javier Moreno [2], José Millet[3] and Francisco Castells[3]

[1]Escuela Politécnica de Cuenca, UCLM, Spain
[2] Unidad de Arritmias, Hospital Ramón y Cajal, Madrid, Spain
[3] ITACA, Universidad Politécnica de Valencia, Valencia, Spain

Abstract

Time and frequency domain analysis has been applied to atrial electrograms to quantify the temporal and spatial organization during atrial fibrillation (AF). Intracardiac recordings obtained before AF ablation procedure were analyzed in order to predict the recurrence outcome of AF after an ablation intervention. Such analysis may be used to quantify both temporal/ frequency and spatial organization during AF. Pulmonary vein electrogram recordings from ten AF patients were analyzed. Results showed changes in spectral characteristics with higher dispersion in spatial organization along the pulmonary veins in patients that had recurrence in the arrhythmia 0.14±0.01 vs. 0.07±0.02 in patients that maintained sinus rhythm (p<0.001). Moreover, similar results were obtained by frequency and temporal domain analysis. The proposed analysis could be useful for a better understanding of electrophysiological mechanisms during AF in both groups of patients, where the electrical activity is collected from electrodes located in the pulmonary veins area before the isolation procedure.

1. Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder in the world, and it is an important cause of health care expenditure in developed regions [1, 2]. AF is characterized by an uncoordinated atrial electrical activation, whose foci in most cases are found in the pulmonary veins. Moreover, the prevalence of AF is expected to increase significantly in the next decades as the population ages, therefore it is crucial to have a better understanding of AF mechanism to plan appropriate interventions.

Antiarrhythmic drugs have long been the main therapeutic approach, although almost two decades ago, therapeutic pulmonary catheter-based radiofrequency ablation was introduced into the AF treatment and nowadays is applied to the patients that are resistant to drug therapy [3]. It requires a change in strategy, since recovering the therapeutic ideal of cure a disease that until recently was considered incurable, resulting in improved quality of life. Radiofrequency energy is applied to destroy this small area of tissue [4] to isolate pulmonary veins. The resulting tissue blocks the extra electrical signals from the pulmonary veins reaching the left atrium, so the area can no longer generate or conduct the fast, irregular impulses. This process is repeated around the opening of each of the four pulmonary veins. However, the long-term goal of this procedure is to eliminate the need for medications to prevent AF.

Nevertheless, the predictors of recurrent AF after a successful AF ablation procedures are not known exactly. Recent studies claim that predictors of AF recurrence after pulmonary vein (PV) isolation, include non-paroxysmal AF or arterial hypertension [5, 6]. Also, the history of failure to antiarrhythmic drugs was a predictor for AF recurrence after ablation, while age was not a predictor of AF recurrence [7–9]. Nevertheless, many aspects of the therapy are still controversial and at the moment it is difficult to predict when AF will be cured.

The decision for catheter ablation, therefore, should be based on a decision explaining the benefits and potential risks and alternatives such as antiarrhythmic drugs or the acceptance of the therapy of rhythm control.

In this study we proposes the use of time and frequency domain features from pulmonary vein electrogram recordings during the arrhytmia, in order to analyze the recurrence outcome of AF patients according to long-term ablation success.

2. Materials

AF intracardiac recordings were registered in 10 patients submitted to an AF ablation procedure immediately before the intervention.

Lasso catheter, a 10-pole pulmonary vein sized loop-shaped, was introduced via a trans-atrial septal long sheath, 5 bipolar intracardiac electrograms from each PV was digitally recorded at 1 kHz sampling rate (16 bit A/D conversion; Polygraph Prucka Cardio-Lab, General Electric). In

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all patients, 4 dipoles of the Lasso catheter were situated along the circumference of each PV. Lasso catheter was changing from the right superior pulmonary vein (RSPV), the right inferior pulmonary vein (RIPV), the left inferior pulmonary vein (LIPV), to the left superior pulmonary vein (LSPV) and as result we had recordings from the four PVs before the procedure. Fifty to 60 seconds Lasso from AF patients were registered before the ablation.

All patients were monitored after the procedure and divided into two groups, five patients with recurrences in the arrhythmia and five patients that maintenanced sinus rhythm according to long-term ablation success, defined as the absence of arrhythmia 12 months after the ablation.

3. Methods

An accurate quantification of AF organization in a straightforward way is crucial in determining the current progression of AF in every single patient. New insights in organization quantification can be useful to clinical diagnostic techniques. In the following paragraphs time and frequency organization proposed methods will be presented.

3.1. Cross-Correlation coefficient

To quantify the relationship between two time series, it is possible to use parametric methods such as the linear correlation coefficient of Pearson's

The statistical technique of cross-correlation is applied to the series and it is possible to stand out very clear associations between the series. To quantify the degree of interdependence between two processes or the similarity between two signals, calculated by cross-correlation. The correlation is also used to detect displacement between signals. Let two real functions of integer variable x and y be both of length N, the correlation of both functions is defined as:

$$r_{xy} = \frac{1}{N-1} \sum_{i=1}^{n} (\frac{x_i - \overline{x}}{s_x})(\frac{y_i - \overline{y}}{s_y}) \quad (1)$$

where s_x and s_y are the sample standard deviation for x and y, and $\overline{x}$ and $\overline{y}$ are the mean for x and y, respectively.

Previous studies have reported that AF organization, which can be defined as the level of repetitiveness of the atrial activity patterns, and it correlates with the arrhythmia status as well as with the therapy outcome. In this study, correlation along the different dipoles in each pulmonar vein (PV) was calculated. Result are represented as correlation matrices for the different dipoles in each PV with the mean and the dispersion of the correlation along the four veins.

3.2. Spectral Coherence

Coherence can be defined as the density spectral cross-power of two signals recorded simultaneously. The main interest of the coherence is its use as a measure of the synchronization between two signals to allow a study of the connections between them. We apply the non-parametric methods based on the Fourier Transform (FT) of a sampled function x, whose power spectral density (PSD) is given by: $S_x(\omega) = |X(\omega)|^2$

Wiener-Khinchin Theorem relates the spectrum of a signal with the FT of its autocorrelation function. When, it is applied to the case of two signals, x and y, the spectral coherence function is obtained, which is defined as the FT of the cross correlation function. The spectral coherence allows a study in the frequency domain equivalent to the time domain analysis by the function of cross correlation:

$$C_{xy}(\omega) = \frac{S_{xy(\omega)}}{\sqrt{S_y(\omega) S_y(\omega)}} \leq 1 \quad (2)$$

where S_x and S_y correspond to the PSD of the signals x and y, $S_x(\omega) = |X(\omega)|^2$ and $S_y(\omega) = |Y(\omega)|^2$ corresponds to the cross-power spectral density of the signals x and y and $S_{xy}(\omega) = TF(r_{xy})$.

This function has been applied to the analysis of electrograms registered simultaneously in positions different around the PVs, or from the atrium for the analysis of atrial relationships before AF ablation procedure. For its calculation, it was considered segments of 4096 samples sampled at 977 Hz with an overlap of 2048, with 4096 points of the FFT.

3.3. Statistical Analysis

As a final step statistical techniques were applied to the extracted parameters. The parameters are expressed in terms of mean and standard deviation values. Independent t-student test was used for comparison between both groups. Results were considered to be statistically significant at $p < 0.05$.

4. Results

4.1. Cross-Correlation coefficient

Correlation between different waveform recorded from dipoles located in each PV were analyzed such as a type of atrial activity organization indicator.

The results showed differences between the patients that had recurrence in the arrhythmia and those patients who did not. The correlation mean coefficient along each of the PVs did not show statistical significant differences. Moreover, it was observed that in patients with recurrences in the arrhythmia the dispersion of correlation coefficient was smaller, with a standard deviation of the cross-correlation of 0.25±0.02 in the group of AF recurrent patients and 0.17±0.03 in the patients that maintain sinus rhythm ($p < 0.001$). It was possible to observe these values between the four dipoles located in PVs in patients that maintain sinus rhythm (Figure 1) and patients that have recurrences in the arrhythmia (Figure 2).

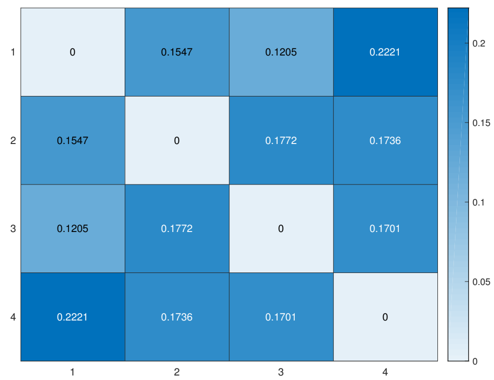

Figure 1. PVs Std Cross-Correlation in non-recurrent AF patients.

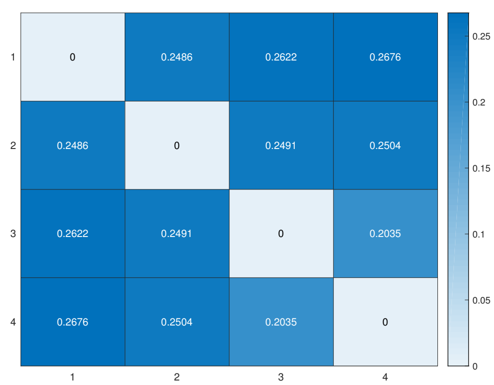

Figure 2. PVs Std Cross-Correlation in recurrent AF patients.

4.2. Spectral Coherence

Spectral coherence analysis of electrogram recordings was applied to the four dipoles located in each of the 4 PVs before starting the ablation procedure. These signals were recorded simultaneously sequentially along the four veins, changing the position of the catheter. Spectral coherence showed differences between recurrent patients in arrhythmia and non-recurrent in the arrhythmia.The standard deviation also showed differences between both groups ($p<0.001$), with 0.07±0.02 in the AF non-recurrent group and 0.14±0.01 in the group that recurred in the arrhythmia (Figure 3), moreover the mean spectral coherence showed the same trend with statistical significant differences between both groups ($p = 0.003$).

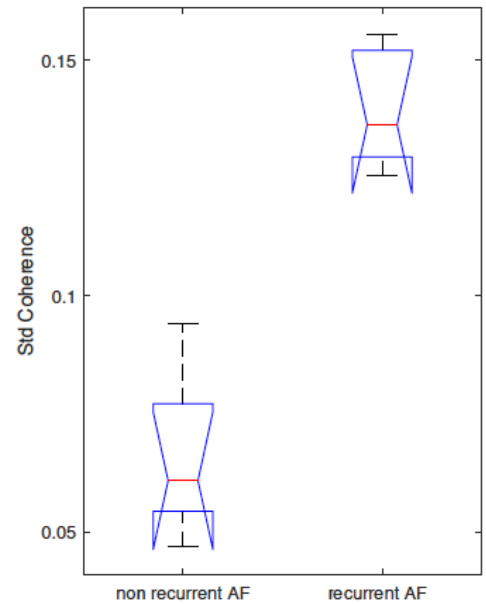

Figure 3. Spectral coherence standard deviation in PVs.

5. Conclusions

Catheter ablation is a procedure widely used for rhythm control in patients with AF [10]. Pulmonary vein isolation is an intervention that produces a frequent need for re-ablations and has limited overall success rates. This is caused by limitations in our current understanding of the pathophysiology of the arrhythmia. Nevertheless, previous studies have described numerous clinical variables that were identified as independent predictors of recurrence of AF: non-paroxysmal AF, aging, left ventricular systolic and diastolic dysfunction, LA enlargement, the presence of non-PV triggers, obesity, hypertension [8, 9].

Moreover, high dominant atrial frequency sites are reported to be related to the center of a focal-firing rotor or local reentry circuit, producing a favourable condition for maintenance of AF [11]. Based on mechanistic studies, rotor sites are expected to exhibit greater electrical periodicity, unique spectral characteristics such as higher dominant frequency [12], and higher entropy [13] and lower causality from the PV to the atria [14].

In this study we analyze ten patients before AF procedure. We registered bipolar electrograms from PVs electrical activity because their abnormal electrical activation can be responsible for the generation of AF in many patients [15]. Considering that during AF, atria is a complex system which consist of many parts or subsystems that interact in a complex way, our goal is to estimate whether there exists differences in correlation along each PV in patients that have recurrences in the arrhythmia and those patients that maintenance sinus rhythm.

Results showed a higher dispersion along PVs in the recurrent AF group than in the patients that maintenance sinus rhythm, it shows higher differences between pulmonary electrical activity in patients that will returned to AF. Nevertheless, mean cross-correlation coefficient did not show statistical differences between both groups. Moreover, spectral coherence showed a higher mean spectral coherence in patients with recurrences. This results are consistent with previous studies, where a significantly lower prevalence of AF foci in PVs and recurrence after PV isolation was related with higher prevalence of AF foci in other atrial areasI [16]. Therefore, experimental studies suggest that focal drivers of AF or stable or unstable reentry circuits may reside in different critical regions of the atria [17].

Organization indexes, such as correlation or spectrum coherence along the PVs before the ablation procedure can be helpful to understand the pathophysiological mechanisms behaviour of the atrial interactions across different patients.

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Address for correspondence:

Raquel Cervigón Abad

Escuela Polictécnica. Camino del Pozuelo sn. Cuenca 16071.

raquel.cervigon@uclm.es