

Frequency Spectrum Correlation along Atria to Study Atrial Fibrillation Recurrence

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Abstract

Atrial fibrillation (AF) is an abnormal heart rhythm originated in the top chambers of the heart. The goal of pulmonary vein ablation for AF is regaining a normal heart rhythm; nevertheless restoration sinus rhythm is difficult to prognostic. Frequency spectrum was calculated from electrical activity registered along all the atria. We investigate whether there were differences between atrial electrical activity spectrum from both atria in recurrent and non-recurrent AF groups. The database includes intracardiac recordings from 43 paroxysmal and persistent AF patients submitted to an ablation procedure. All patients were monitored after ablation, and were divided in 2 groups according to AF recurrence outcome: 26 of them remained in sinus rhythm, whereas the other 17 turned back to AF. Results showed a stronger correlation between atrial activity frequency spectrum from dipoles located in the left atrium and in the right atrium in the non-recurrent group than in the recurrent AF group. In addition, statistical significant differences were found between atrial activity frequency spectrum correlation between dipoles located in the left and right atria in the non-recurrent and recurrent AF groups. These findings show the more regular atrial activity along the atria in the patients with non-recurrences in AF.

1. Introduction

Atrial fibrillation (AF) is the commonest sustained arrhythmia encountered in clinical practice [1]. AF management is one of the most difficult among cardiac arrhythmias [2]. The observation that ectopic beats originating from the pulmonary veins could act as triggers for the initiation of AF opened up the possibility of curative treatment by catheter ablation [3]. The potential

for curative treatment, with its association with significant morbidity and mortality, has generated much interest catheter ablation for AF [4]. Nevertheless, radiofrequency ablation has currently an important role for sinus rhythm restoration [5,6]. Pulmonary vein ablation procedure consists of generating electrical barriers in muscle fibers that extend from the left atrium into the pulmonary veins by altering the tissue properties in the vicinity of the ablating catheter tip [6]. Although, the energy is applied around the connections of the pulmonary veins to the left atrium, frequently, other areas involved in triggering or maintaining AF are also targeted [7]. As an alternative, studies published several years ago as it has been in recent prospective randomized trials and entailed a much lower risk of complications than what was seen in a similar meta-analysis of antiarrhythmic drug trials, according to researchers who ran the numbers on both treatment approaches [8].

Nevertheless, although success rates of sinus rhythm restoration after pulmonary vein ablation are promising, long-term results are not that satisfactory. In fact, AF recurrence rates after ablation procedure are with still high and underestimated [9-11].

Current AF guidelines recommend an initial 3-months follow-up [11]. During this time, in case of early AF recurrence, the initially paroxysmal AF may evolve towards persistent AF, as AF episodes may become more frequent and longer. Therefore, the identification of subjects at high risk of AF recurrence would have important clinical implications.

The main goal of this paper is to provide some parameters related to AF recurrence from the signal analysis of the electrograms in frequency domain. The main objective of spectral analysis is to provide an estimate of the distribution of atrial signal power at different frequencies. Spectral analysis and correlation techniques are an aid to the interpretation of signals and to the systems that generate them and this technique has applied to analyze AF previously [12].

This analysis has been applied to intracardiac AF recordings to assess if there is difference between atrial activity frequency spectrum correlation measurements of signals from both left and right atria (LA and RA, respectively) in recurrent and non-recurrent AF groups.

2. Materials

Intracardiac recordings during AF before ablation procedure and during the anaesthetic effect, were taken from 43 AF patients (9 paroxysmal AF and 13 persistent AF) submitted to an ablation procedure. The main age was 50 ± 14 years, 68% male, and mean left atrial size was 43.1 ± 7.4 mm. A 24-pole catheter (Orbiter, Bard Electrophysiology, 2-9-2 mm electrode spacing) was inserted through the femoral vein and positioned in the right atrium (RA) with the distal dipoles into the coronary sinus (CS) to record left atrial (LA) electrical activity as well. The medium and proximal group of electrodes were located spanning the RA free-wall peritricuspid area, from the coronary sinus ostium to the upper part of the interatrial region. Using this catheter, 12 bipolar intracardiac electrograms from the RA (dipoles from 14-15 to 23-24) and LA (dipoles 1-2, 3-4 and 5-6), were digitally recorded at 1 kHz sampling rate (16 bit A/D conversion; Polygraph Prucka Cardio-Lab, General Electric). Thirty to 60 seconds recordings from paroxysmal and persistent AF patients were analysed and compared. Four of these electrodes were located at the RA and 4 more at the LA were analyzed. All patients were monitored after ablation, and were divided in 2 groups according to AF recurrence outcome: 17 of them remained in sinus rhythm, whereas the other 26 turned back to AF.

3. Methods

The concept of the correlation coefficient, as a measure of the strength of linear relationship between two variables can be extended to signal analysis and in particular to signal spectrum analysis with the definition of the cross-correlation function (CCF). In this work spectrum correlation has been employed to measure the degree to which atrial activity in each chamber is related.

Initially, electrograms were preprocessed according to the steps proposed by Botteron, the properties of this preprocessing approach are described in [25]. After the preprocessing step, a modified periodogram introduced by Welch consisting of the multiplication of x_n by a window shape, before computing the individual spectral sample was applied. The application of a window justifies overlapping adjacent segments of data by as much as 50%. For a signal with a total duration of N samples, the combination of overlapping with segmentation can be lead to a further reduction of spectral variance. In this

case we applied a hamming window of 4096 samples with 50% of overlapping.

Cross spectrum of x_n and y_n can be defined as the product of the magnitude of the complex cross-power spectrum of signals registered from two close dipoles located in the LA or in the RA, $x(t)$ and $y(t)$ respectively, normalized to the product of the auto-power spectra of those two signals $X(f)$ and $Y(f)$, respectively. This can be expressed as: $C_{xy}(f) = X(f) \cdot Y(f)$

The cross-power spectrum ranges in value from 0, if the two signals are uncorrelated noise sources, to unity for two linearly-related signals. Thus it should be expected to have higher values in the coherence spectra of rhythms, which are well-organized than those which are relatively disorganized.

In addition, it is possible to extract another parameter from this analysis, it is the delay between maximum cross-correlation spectrum. The amplitude spectrum reflects the signal power at different frequencies. Then a cross-correlation value of approximately 1 corresponds to a time delay near zero, reflecting similar temporal patterns between the two measurements. Nevertheless, if the peak of the maximum cross-correlation has a delay, it reflects the different location in of these peaks.

4. Results

Results were inspected in both chambers to compare the patients that had recurrence in the arrhythmia with those that were in sinus rhythm.

4.1. Left atrium vs. right atrium results

Cross-correlation spectrum along dipoles located in the RA (dipole 21-22) and in the LA (dipole 5-6), with differences in maximum of cross-correlation of 0.91 ± 0.05 in the AF non-recurrent group vs. 0.87 ± 0.07 in the AF recurrent group, with a statistical difference ($p=0.04$) (Figure 1). These results were represented by a ROC curve (Figure 2), where cross-correlation showed an area under curve (AUC=0.69) with asymptotic signification ($p=0.04$) between both groups.

In addition, it was observed differences in the delays between maximum cross-correlation between both groups, whereas this frequency delay was 0.25 ± 0.22 Hz in the non-recurrent AF groups vs. 0.44 ± 0.37 Hz in the recurrent AF group with a statistical significant difference of 0.032.

4.2. Left atrium results

Results showed statistical significant differences in two leads located in the LA spectrum correlation between both groups.

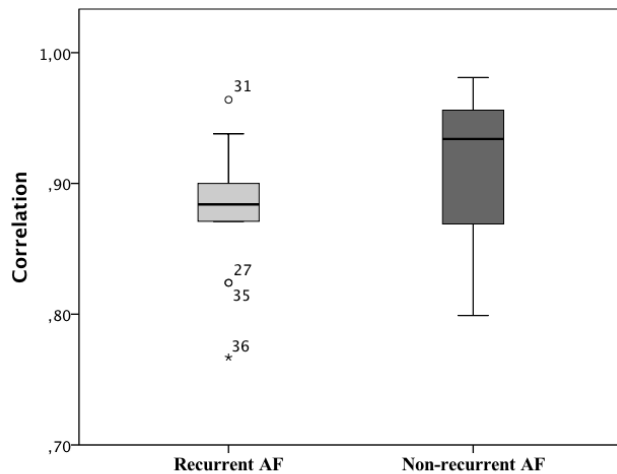


Figure 1. Cross-correlation spectrum from leads located in the RA and in the LA.

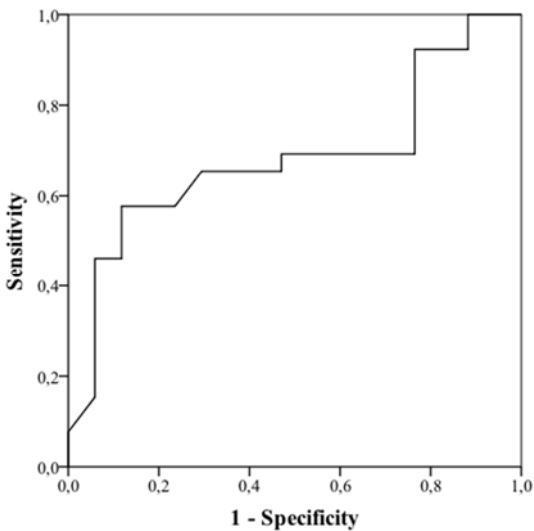


Figure 2. ROC in recurrent and non recurrent AF groups from the correlation of a dipole located in the LA with another located in the RA.

Indeed, both groups are statistically distinguishable, given that the statistic significance obtained by the t-student test of 0.016, with 0.96 ± 0.03 in the non-recurrent AF group vs. 0.92 ± 0.05 in the recurrent AF group. In addition it was (Figure 3).

4.3. Right atrium results

Results showed statistical significant differences in spectrum correlation between two leads located in the RA between both groups.

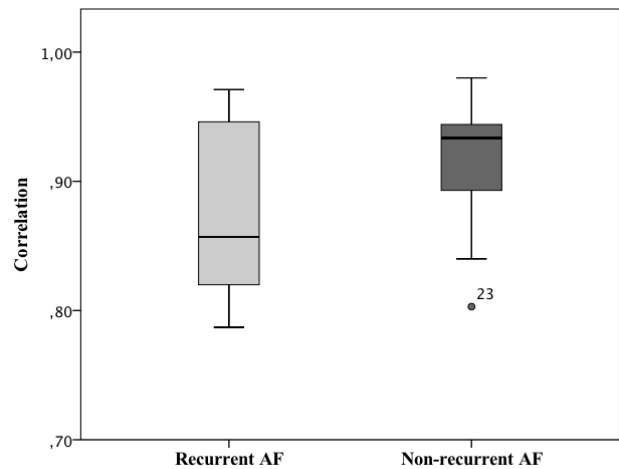


Figure 3. LA dipoles cross-correlation spectrum.

Cross correlation spectrum between two leads along RA was 0.96 ± 0.03 in the non-recurrent group vs. 0.92 ± 0.05 in the recurrent AF group, with a statistical significant difference of $p=0.016$. In Figure 4 is represented.

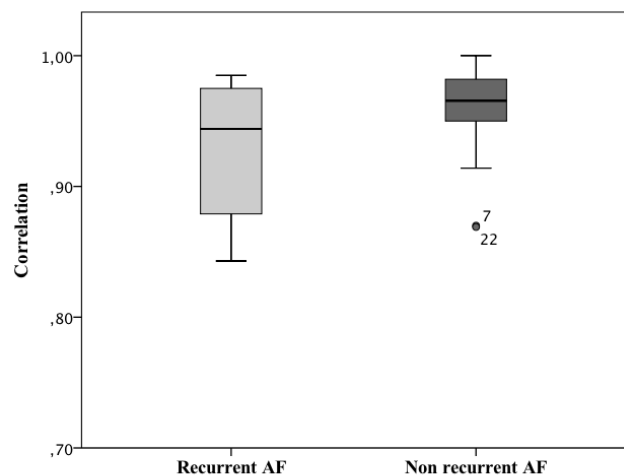


Figure 4. Cross-correlation spectrum from dipoles located in the RA.

4.4. Frequency results

Dominant frequencies from signals located in both atria were calculated.

The results obtained from signals power spectrum located in the RA showed differences not statistical significant ($p=0.09$) with 5.75 ± 0.78 Hz in the non-recurrent AF group compared with 6.23 ± 1.12 Hz in the patients with recurrences in the arrhythmia. In addition,

the differences obtained in the LA were not statistical significant ($p=0.56$) with very close values in both groups, 5.70 ± 0.73 Hz vs. 5.85 ± 0.95 Hz in the non-recurrent and recurrent AF groups, respectively.

5. Conclusions

Ablation is a curative treatment for AF, but has its limitations, including failure rates and recurrences [14].

The search for predictors of AF ablation success and AF recurrence is currently of high clinical interest. Just to mention few recent works, the dominant atrial frequency has been reported to play a role as a predictor of AF ablation outcome [15].

Results described provide some predictive information regarding the recurrence outcome after 3-months follow-up. Although these results are rather complex and not easy to interpret, it can be inferred that patients that remained in sinus rhythm presented different cross-correlation spectrum values than those who turned back to AF.

The amplitude spectra reflects the signal power at different frequencies, these spectral distribution was calculated from signals registered in dipoles located in the LA and RA. Indeed, patients within the recurrent AF group showed higher differences between signals spectrum from dipoles located in both atria, i.e. the atrial activation in this group was more disorganized than in the patients that maintenance sinus rhythm. This means, in turn, that patients with a more irregular frequency content of atrial activity have a higher risk to AF recurrence. These differences can be observed from the signals spectrum and the correlation between spectrums can be helpful to extract this information.

These findings show the more regular atrial activity along the atria in the patients with non recurrences in AF and lower main frequency in right atria compared with recurrent AF group.

References

- [1] Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. *N Engl J Med* 1982;306:1018–22.
- [2] Aliot E, Breithardt G, Brugada J, Camm J, Lip GYH, Vardas PE, Wagner M. Atrial Fibrillation Awareness and Risk Education group, Atrial Fibrillation Association, European Heart Rhythm Association, Stroke Alliance for Europe, and World Heart Federation. An international survey of physician 17 and patient understanding, perception, and attitudes to atrial fibrillation and its contribution to cardiovascular disease morbidity and mortality. *Europace* 2010;12:626–33.
- [3] Haissaguerre M, Jais P, Shah D. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659–66.
- [4] Pappone C, Rosanio S, Oreto G. Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000; 102:2619–28.
- [5] Combes S, Jacob S, Combes N, Karam N, Chaumeil A, Guy-Moyat B, Treguer F, Deplagne A, Boveda S, Marijon E and Albenque JP. Predicting favourable outcomes in the setting of radiofrequency catheter ablation of long-standing persistent atrial fibrillation: A pilot study assessing the value of left atrial appendage peak flow velocity. *Arch Cardiovasc Dis* 2013;106:36–43.
- [6] Callahan TD, Di Biase L, Horton R, Sanchez J, Gallinghouse JG, Natale A. Catheter ablation of atrial fibrillation. *Cardiol Clin* 2009; 27:163–78.
- [7] Calkins H, Reynolds MR, Spector P, Sondhi M, Xu Y, Martin A, Williams CJ, Sledge I. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. *Circ Arrhythm Electrophysiol* 2009;2:349–61.
- [8] Solheim E, Hoff PI, Off MK, Ohm OJ, Chen J. Significance of late recurrence of atrial fibrillation during long-term follow-up after pulmonary vein isolation. *Pacing Clin Electrophysiol* 2007; 30 Suppl 1:S108–11.
- [9] Hsieh MH, Tai CT, Tsai CF, Lin WS, Lin YK, Tsao HM, Huang JL, Ueng KG, Yu WC, Chan P, Ding YA, Chang MS, Chen SA. Clinical outcome of very late recurrence of atrial fibrillation after catheter ablation of paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2003;14:598–601.
- [10] Oral H, Knight BP, Ozaydin M, Tada H, Chugh A, Hassan S, Scharf C, Lai SWK, Greenstein R, Pelosi F, Strickberger SA, Morady F. Clinical significance of early recurrences of atrial fibrillation after pulmonary vein isolation. *J Am Coll Cardiol* 2002;40:100–4.
- [11] Camm J, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P. ESC Committee for Practice Guidelines-CPG, and Document Reviewers. 2012 focused update of the esc guidelines for the management of atrial fibrillation: an update of the 2010 esc guidelines for the management of atrial fibrillation. *Europace* 2012;14:1385–413.
- [12] Cervigón R, Moreno J, Castells F, Mateo J, Sánchez C, Pérez-Villacastín J, Millet J. Anesthesia with propofol slows atrial fibrillation dominant frequencies. *Computers in Biology and Medicine* 2008:792–798.
- [13] Castells F, Cervigón R and Millet J. On the preprocessing of atrial on electrograms in atrial fibrillation: Understanding botteron's approach. *Pacing Clin Electrophysiol* 2014;37:133-43.
- [14] Lubitz SA, Fischer A, and Fuster V. Catheter ablation for atrial fibrillation. *BMJ* 2008; 336(7648):819–26.
- [15] Okumura Y, Watanabe I, Kofune M, Nagashima K, Sonoda K, Mano H, Ohkubo K, Nakai T, Hirayama A. Characteristics and distribution of complex fractionated atrial electrograms and the dominant frequency during atrial fibrillation: relationship to the response and outcome of circumferential pulmonary vein isolation. *J Interv Card Electrophysiol* 2012;34:267–75.

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