Surface ECG Spectral Analysis to Predict Atrial Fibrillation Catheter Ablation Long-term Outcome

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Abstract

Catheter ablation (CA) has emerged recently as an effective tool to treat atrial fibrillation (AF), which is today the most common cardiac arrhythmia. However, the long-term AF recurrence rate is about 50% for patients in persistent AF. As a consequence the optimal selection of patients for the procedure remains as an interesting clinical challenge. To this respect, the dominant atrial frequency (DAF) analysis from the surface ECG has been widely studied in recent years, reporting promising results. In the present work two additional spectral metrics complementing the information provided by the DAF, such as its 3 dB bandwidth (BW) and the median frequency (MF), are for the first time studied. Results provided no statistically significant differences for the DAF as well as the BW between patients with and without freedom from AF after a mean follow-up of 12±7 months. In contrast, a statistically significant greater MF was observed in patients maintaining sinus rhythm (6.42±0.17 Hz) than for those who relapsed to AF during the folow-up (6.03±0.30 Hz). Moreover, the MF provided sensitivity, specificity and accuracy values of 83.33%, 100% and 91.67%, respectively. Hence, the MF could be considered as a more promising harbinger of long-term CA outcome than the DAF. Further studies in wider databases should validate this preliminar finding.

1. Introduction

Atrial fibrillation (AF) is a commonly encountered supra-ventricular arrhythmia, accounting for approximately one third of hospitalizations for cardiac rhythm disturbances [1]. Its prevalence also increases with age, such that about 4% of people aged 70 years and 15% of those older than 80 years suffer from this arrhythmia [2]. Although AF does not represent a life-threatening condition, it predisposes to thrombus formation within the atria. This increases mortality, stroke, and thromboembolism risks and reduces considerably the patients' quality of life [1]. As a consequence, this arrhythmia is currently a serious cardiovascular challenge in the developed world [3].

According to its natural progression, AF can be classified into different forms [4]. It often starts as paroxysmal (self-terminating) episodes and becomes persistent or permanent with time. Paroxysmal AF is defined as attacks of AF lasting from several seconds to less than 7 days, and spontaneously reverting to sinus rhythm (SR). Persistent AF lasts more than 7 days, but responds to external interventions and SR can be restored. Finally, permanent AF does not respond to therapy and both the clinician and the patient accept to make a joint decision to stop further attempts to revert AF. Thus, only interventions to control the heart rate are pursued. Approximately, between 15 and 31% of PAF patients progress to persistent AF during a time period between 4 and 8 years [5].

Regardless of its duration, when AF occurs the normal electrical impulse generated by the sinus node degenerates into a complex ever-changing pattern depolarizing randomly the atria [6]. Thus, the well-defined P-wave on the surface electrocardiogram (ECG) is replaced by rapid wavefronts varying shape and timing, which are named fibrillatory waves (f-waves) [7]. Today, the mechanisms generating this atrial behavior are not still completely known and several theories exist [6]. To this respect, some works support the idea that AF is triggered by one or multiple high-frequency fibrillatory reentrant sources, which are named ectopic foci. Other researchers however state the role of meandering activation waves propagating randomly throughout the atria, called reentries [6].

Within this context and despite some progress in the earlier decades, the current therapy of AF is still far from being satisfactory [3]. Catheter ablation (CA) has recently emerged as an effective tool to treat symptomatic patients

with drug-refractory AF [8]. However, although its long-term success in patients with paroxysmal AF is about 75%, approximately one half of persistent AF patients present arrhythmia recurrence [9]. Long-term CA success is normally defined as stability of SR in multiple Holter ECG recordings after an initial blanking period of 12 months [8]. Hence, the development of tools able to predict whether a persistent AF patient may benefit from CA is a highly interesting clinical challenge.

With the aim to anticipate CA outcome, numerous clinical factors have been recently studied. Aspects such as the conversion of AF into SR or atrial tachyarrhythmia during CA [10], left atrial diameter or volume or duration of AF [11] have been widely studied as predictors of CA outcome after a blanking period of 3, 6 and 12 months. However, they have provided conflicting results. In order to serve as a supplementary way of information, CA outcome predictors from signal processing tools have been explored. Indeed, spectral analysis of the f-waves has been widely used by numerous authors, mainly analyzing the dominant atrial frequency (DAF) [12]. Although, this metric has provided promising results, no much attention has been paid to other spectral features of the surface ECG. This work focuses on analyzing two additional spectral indices from the surface atrial activity (AA) signal to predict non-invasively long-term CA outcome from persistent AF patients.

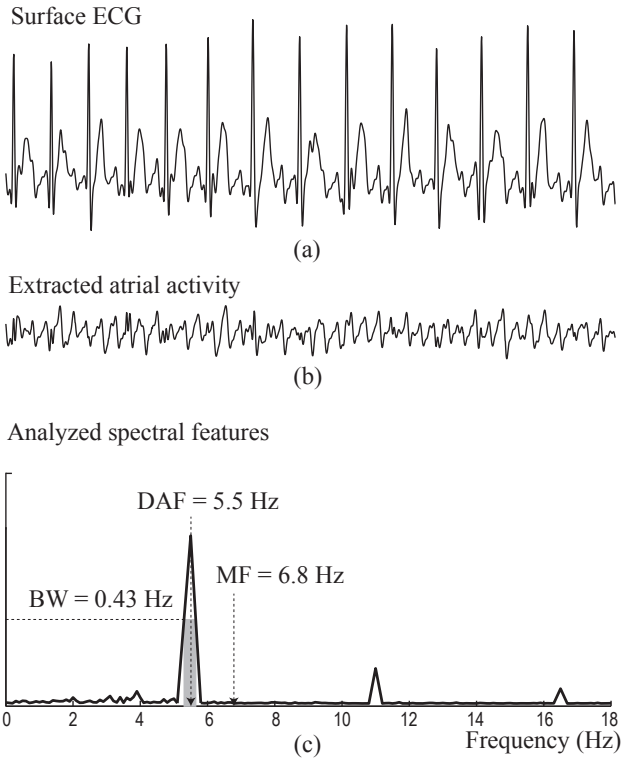

Figure 1. Example of an ECG interval (a) together with the extracted AA signal (b).The spectral content of this signal and the analyzed metrics are shown below (c).

2. Methods

2.1. Study population

The standard 12-lead ECG recording as well as other intracardiac recordings were obtained from 12 persistent AF patients immediately before CA. They were acquired during 10 seconds with a sampling rate of 977 Hz and 16 bits resolution. The used CA protocol was deeply described in [13]. Briefly, all antiarrhythmic drug therapy except amiodarone was withheld > 5 half lives before the study. The procedure started by isolating pulmonary veins. Next, the atrial point with the highest DAF was ablated by creating a circumferential set of lesions. The procedure continued by targeting the following highest DAF point. Finally, CA finished when AF was reverted to SR or all the points with a DAF greater than 1.2 times the basal frequency were ablated.

The patients were monitored after ablation during a mean period of 12 ± 7 months. Moreover, they were divided into two groups according to AF recurrence during the follow-up period. Note that one half of patients were free from AF at the end of follow-up.

2.2. Extraction of spectral features from the atrial activity

Lead V_1 was only analyzed in order to provide a non-invasive method able to reveal the CA success before the patient was exposed to any risk. This lead was selected because it reflects the largest f-waves compared with the ventricular activity [7]. For every patient the recorded 10 second-length ECG interval was firstly preprocessed. Thus, it was filtered by using a forward/backward high-pass filtering (0.5 Hz cut-off frequency) to remove baseline wander, a forward/backward low-pass filtering (70 Hz cut-off frequency) to reduce high frequency muscle noise and an adaptive notch filtering at 50 Hz to remove power-line interference [14]. Thereafter, the AA signal was extracted by using an adaptive QRST cancellation method [15] and, then, its power spectral density (PSD) was estimated by using the Welch Periodogram. A Hamming window of 4096 points in length, a 50% overlapping between adjacent windowed sections and a 10240-points Fast Fourier Transform (FFT) were used as computational parameters [16].

As for a variety of previos works [12], the frequency with the highest amplitude within the range of 3–9 Hz

Table 1. Mean and standard deviation values from the analyzed metrics for the patients with and without freedom from AF after CA. Statistical significance is also shown.

Metric	AF	AF-free	p-value
DAF	6.60 ± 0.46 Hz	6.20 ± 0.96 Hz	0.07
BW	0.47 ± 0.15 Hz	0.42 ± 0.12 Hz	0.18
MF	6.03 ± 0.30 Hz	6.42 ± 0.17 Hz	0.02

Table 2. Preoperative classification results for patients undergoing CA with and without freedom from AF at the follow-up end.

Metric	Sensitivity	Specificity	Accuracy
DAF	83.33%	83.33%	83.33%
BW	83.33%	66.67%	75.00%
MF	83.33%	100%	91.67%

was selected as the DAF. Additionally, its 3 dB bandwidth (BW) as well as the median frequency (MF) for the whole AA spectral content were also computed. This last metric was defined as the frequency containing 50% of the PSD power [17]. Figure 1 graphically shows a typical ECG interval in AF together with the extracted AA and its corresponding spectral features.

2.3. Performance assessment

Results were expressed as mean $\pm$ standard deviation for the spectral features identifying AF patients belonging to each group. Moreover, statistical differences between them were tested by a t-Student's test. A two-tailed value of $p < 0.05$ was considered as statistically significant.

On the other hand, the ability of each feature to discriminate between patients with and without freedom from AF after ablation was evaluated by means of a ROC curve. This plot is the result of plotting the fraction of true positives (TP) out of positives (sensitivity) against the fraction of false positives out of the negatives ($1-$specificity) at various threshold settings. Sensitivity was considered as the percentage of patients who relapsed to AF correctly classified. Similarly, the rate of patients maintaining SR was considered as the specificity. The optimal threshold was selected as those that provided the highest percentage of patients correctly classified, i.e. accuracy.

3. Results

Mean and standard deviation values of the analyzed spectral features are shown in Table 1. As can be observed, DAF and BW provided higher and lower values for patients in SR at the end of follow-up than for those who relapsed to AF, respectively. However, in any case statistical significances were relevant. Anyway, the p-value for DAF was near the set boundary of 0.05. On the contrary, MF revealed statistically significant differences between both groups, mean values being greater for patients with than without freedom from AF.

According to the aforesaid results, MF was the best predictor of CA outcome among the set of spectral features analyzed, such as Table 2 shows. It has to be highlighted that the three features provided the same sensitivity. However, DAF and BW presented significantly lower values of specificity than MF.

4. Discussion

Preoperative catheter ablation prediction is clinically useful for an improved selection of persistent AF patients who should be considered for the procedure [12]. Thus, the risks associated to CA could be avoided for those patients with low SR maintenance probability. Moreover, the clinical costs could be optimized because unproductive treatment time and bed usage could be reduced [8]. To the best of our knowledge, this work presents for the first time two novel metrics from the spectral characterization of the surface AA signal to address such a kind of prediction.

In contrast to previous works where the DAF reported very promising results [12], a less relevant CA outcome prediction was here obtained for this spectral feature. Thus, although its discriminant ability was greater than 80%, the DAF was unable to provide statistically significant differences between patients with and without freedom from AF. Nonetheless, it should be noted that this result could be affected by the limited number of patients considered in the present study. Moreover, a CA protocol notably different from the most used in previous works was considered. To this respect, note that Lemola et al [18] have proven significant differences in the relationship between DAF and the CA technique employed. In fact, circumferential pulmonary vein ablation was independent of changes in the DAF, whereas electrogram-guided ablation was associated to a decrease in the DAF [18].

On the other hand, the spectral power concentration around the DAF estimated by the feature BW did not provide differences between patients who relapsed to AF and those maintaining SR during the follow-up. To this respect, a similar result was also noticed when the BW was used to predict AF electrical cardioversion (ECV) outcome before it was attempted [16]. Hence, given that CA and ECV provokes different alterations on the AF substrate, it could be considered that this metric may also be poorly predictive of other AF therapeutical approaches, such as pharmacological cardioversion or MAZE surgery.

Finally, the MF provided to be a more promising harbinger of long-term CA outcome than the DAF. Moreover, it was a bit surprising that the mean values of this feature reported an opposite trend to that of the DAF. Indeed, patients with freedom from AF presented higher MF values than those who relapsed to AF after the follow-up, thus suggesting the presence of greater high-frequency energy in the first group of patients. The existence of higher DAF harmonics in patients who maintained SR could explain this result. In fact, given that more organized AA signals have been previously associated with stronger harmonics [19], this outcome is in agreement with the general observation that CA is more likely to be successful in patients with more organized AF [20]. Nonetheless, this is a preliminar finding obtained from a limited database, which requires to be validated by further studies analyzing wider databases.

5. Conclusions

The study of the preoperative surface ECG atrial activity spectral features has provided clinically useful information about the long-term outcome of persistent AF patients undergoing CA. The median frequency has provided to be a better outcome predictor of the procedure that the DAF and the BW. Further studies will deepen in the analysis of this feature as a potential and easy to interpret CA outcome predictor.

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