Organization Deterioration Assessment from the Surface ECG in the Onset and Termination of Paroxysmal Atrial Fibrillation

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Abstract

Recently, it has been suggested that many episodes of Atrial Fibrillation (AF) may be partially organized at the onset. Moreover, several clinical studies have demonstrated that an AF organization increase occurs prior to its spontaneous termination (paroxysmal AF), which could be used to predict the paroxysmal AF termination. However, although severals AF organization estimators based on invasive and non-invasive analysis have been proposed, the time course of organization in the first and last minutes of AF has not been quantified yet. Thereby, the aim of this work was to study the organization variations within the first and last minutes of paroxysmal AF episodes from surface ECG recordings making use of sample entropy. An organization decrease in the first minutes after AF onset and an increase within the last minute before spontaneos AF termination were obtained, these results were coincident with the conclusions presented in previous clinical works. Thus, it can be concluded that paroxysmal AF organization variations can be assessed from surface recordings without the need of invasive measurements.

1. Introduction

Atrial Fibrillation (AF) is a common arrhythmia and is a significant public health problem worldwide, affecting up to 1% of the general population and nearly 1 in 10 people over 80 years [1]. Thus, the AF prevalence increases with advancing age [2]. Data from the Framingham heart study show that AF is associated with a 1.5- to 1.9-fold higher risk of death, which may be due to thromboembolic stroke [3]. While patients can be asymptomatic, many experience a wide variety of symptoms, including palpitations, dyspnea, fatigue, dizziness, angina, and congestive heart failure. In addition, the arrhythmia can be associated with hemodynamic dysfunction, tachycardia-induced cardiomyopathy, and systemic embolism

During the first minutes following the AF onset, profound changes occur in atrial metabolism, provoking a progressive alteration of electrophysiological properties [4]. Thus, several instants after AF onset, a progressive variation in atrial refractory period, conduction velocity and ion concentrations is started. Changes in these electrophysiological parameters cause variations in the number of simultaneous reentries into the atrial tissue and thus in the atrial activity (AA) organization degree. Thus, it has been recently suggested that at the beginning many AF episodes may be partially organized and thus more suitable for antiarrhythmia pacing therapy [5].

To date, the time course of organization in the first minutes after AF onset has been very recently studied from invasive recordings by means of a beat-to-beat analysis of cycle length and wave similarity [6], obtaining a progressive organization deterioration within the first 3 minutes. However, this temporal evolution of the AA organization has not been quantified yet from surface ECG recordings, which can be easily and cheaply obtained and could avoid the risks associated to the invasive electrodes placing.

On the other hand, several studies have demonstrated a decrease in the number of reentries prior to spontaneous AF termination (paroxysmal AF), thus producing simpler wavefronts [7, 8] and f waves to evolve to P waves [9]. In other words, the atrial activity slightly evolves to a more organized pattern before AF termination [8, 10]. This AA organization increase could be used to predict the spontaneous AF termination, and thus unncesary therapy could be avoided, the associated clinical costs could be reduced and the patient's quality of life could be improved.

Several indixes of AF organization based on invasive and non-invasive analysis have been proposed by different research groups. However, no index has been used yet to evaluate the time course of AA organization wihtin the last minutes before spontaneous AF termination. Hence, the aim of this work is to study the possibility to evaluate the organization variations within the first minutes after AF onset and the last minutes prior to its spontaneous termination from surface ECG recordings. A non-linear regularity index, such as Sample Entropy (SampEn), will be used to estimate the AA organization because it has been recently

demonstrated that this index can robustly evaluate the organization degree of the AA obtained from surface ECG recordings [11, 12].

2. Materials

In order to analyze the initial progressive deteroration of AA organization, 25 ECG recordings continuously registered during the first five minutes following paroxysmal AF onset were used. On the other hand, to evaluate the increase of AA organization prior to AF termination, 20 ECGs registered two minutes before spontaneous AF termination were used. All signals were extracted from 24-hour Holter recordings with two leads (II and V1) from 45 different patients and were available in Physionet [13]. They were digitized at 128 Hz with 16 bits/sample and 5 μV resolution.

The ECG recordings were preprocessed in order to reduce noise, nuisance interferences and improve later analysis. Firstly, baseline wander was removed making use of bidirectional high pass filtering with 0.5 Hz cut-off frequency [14]. Secondly, high frequency noise was reduced with an eight order bidirectional IIR Chebyshev low pass filtering, whose cut-off frequency was 70 Hz [15]. Finally, powerline interference was removed through adaptive notch filtering, which preserves the ECG spectral information [16].

The recordings were upsampled to 1024 Hz. This preprocessing step was mainly useful in order to allow better alignment for QRST complex averaging and subtraction, which is necessary to extract the atrial activity from surface ECGs, see section 3. Lead V1 was chosen for the analysis because previous works have shown that AF is dominant in this lead [9].

3. Method

The AA analysis in the surface ECG is complicated by the simultaneous presence of ventricular activity, which is typically of much greater amplitude. Whereby, cancellation of QRST waves from the ECG signals was firstly performed, obtaining an acceptable approximation to the AA. Though a variety of QRST cancellation techniques exist, the average QRST template cancellation method was used, since only two leads were available [17].

Bearing in mind that the median beat cannot represent each individual beat accurately, since QRST morphology is affected by respiration, patient movement, etc., QRST residuals and noise are often present in the AA [9]. These nuisance signals can degrade AA organization estimation using non-linear regularity indexes and, consequently, unsuccessful results could be obtained [18, 11]. Hence, in order to reduce the presence of noise, ventricular residues and any other nuisance signal in the AA, the main atrial wave (MAW), which can be considered as the fundamental atrial waveform, was analyzed. The MAW was obtained through selective filtering of the AA by tracking the its dominant frequency. The dominant atrial frequency was defined as the largest amplitude frequency within the 3-9 Hz range, that is the typical AA frequency range [19].

To prevent distortion, a linear phase FIR filter was used. Chebyshev approximation was preferred because all the filter parameters can be suitably fitted and minimum ripple in the pass and stop bands was needed. Because of the typical AA frequency range is around 3-9 Hz [19], the selected filter bandwidth should be lower than 6 Hz. In our experiments, the best results were obtained with a 3 Hz bandwidth and 768 filter coefficients.

In order to obtain a robust tracking of the dominant atrial frequency, the AA power spectral density in non-overlapping segments of 10 seconds was calculated making use of Welch Periodogram. A Hamming window of 2048 points in length, a 50% overlapping between adjacent windowed sections and a 4096-points Fast Fourier Transform (FFT) were used as computational parameters.

Finally, the MAW organization was estimated in non-overlapping segments of different time lengths through the application of SampEn, that is a non linear regularity index that examines time series for similar epochs and assigns a non-negative number to the sequence, with larger values corresponding to more complexity or irregularity in the data [20]. Overlapping segments were not tested in order to not favor the organization assessment, obtain more consistent results and increase the proposed strategy reliability. The best results were obtained analyzing segments of 2 seconds in length.

The SampEn application is justified in this work because (i) the non-linearity, as necessary condition for a chaotic behavior, is present in the diseased heart with AF at cellular level and (ii) the electrical remodelling starting after AF onset is a far-from-linear process [21]. Moreover, in previous works it has been shown that Sample Entropy is a robust estimator of organization degree of the AA obtained from surface ECG recordings [11, 12].

4. Results

The AA organization temporal evolution averaged over all patients is shown in Figure 1. SampEn average values of the first five minutes after AF onset, calculated over one minute windows, are presented in Table 1. Note that the SampEn mean value after AF onset was progressively increasing from 0.0660 ± 0.0027 to 0.0703 ± 0.0016 ($p < 0.00001$). However, the largest variation (97.5%) ocurred within the first 180 seconds, since next the SampEn mean value was stabilized around 0.07 and non-significative differences between the fourth and fifth minute after AF onset were obtained ($p = 0.3231$).

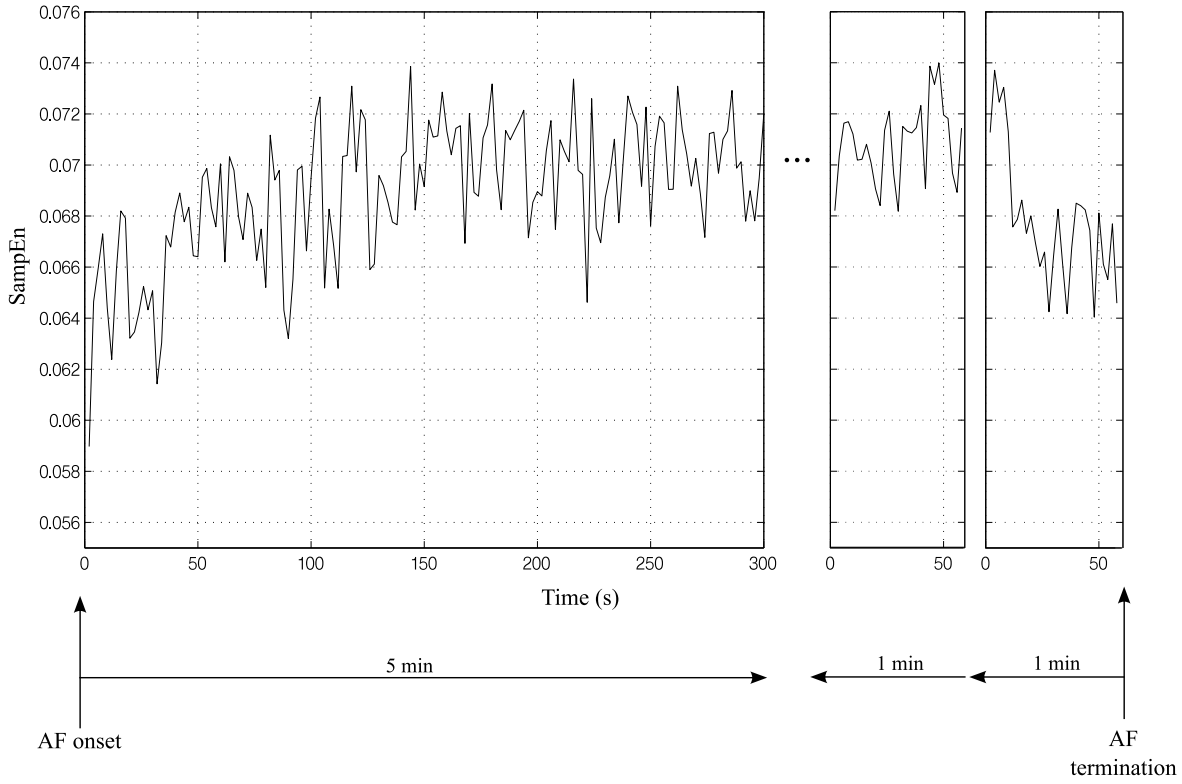

Figure 1. AA organization time course averaged over all analyzed ECG recordings.

Table 1. SampEn average values of the first five minutes after AF onset.

Minute	First	Second	Third	Fourth	Fifth
Mean	0.066	0.068	0.070	0.070	0.071
Std	0.003	0.0023	0.002	0.002	0.002

Regarding the last 2 minutes before AF termination, the SampEn mean values of each minute were 0.0705 ± 0.0016 and 0.0679 ± 0.0025 respectively. Notice that non-significative differences between the fifth minute after AF onset and the last but one minute before its termination were obtained ($p = 0.1012$). Moreover, SampEn values were progressively decreasing within the last 60 seconds, obtaining a high statistical difference with the previous minute ($p < 0.001$).

5. Discussion and conclusions

The obtained results demonstrated the existence of a certain AA organization degree in the first instants and a subsequent progressive deterioration of organization within the first 3 minutes following the AF onset. This finding is in agreement with the conclusion obtained by Ravelli et. al. [6], who performed a beat-to-beat analysis of cycle length and wave similarity using atrial electrograms. The authors obtained an electrical activity organization decay within less than 3 minutes. The presence of instances of organized activity in the first instants of AF is consistent with the results of Israel et. al. [5], who showed in a large database of patients with implanted devices for antitachycardia therapy that a large proportion of spontaneous episodes displayed a considerable degree of organization, at least for the first minute after AF onset.

On the other hand, the results also showed a progressive increase of AA organization during the last minute prior to AF termination. In other studies, where the AF termination was provoked using different treatments, similar outcomes were reported. Thus, Takahashi et. al. [8] obtained that a higher organization index (the ratio of the area under the dominant atrial frequency and its harmonics to the total power) of atrial electrograms is associated with termination of AF during limited ablation. In Hoekstra et. al. [22] the nonlinear analysis of unipolar epicardial electrograms revealed that cibenzoline produces a slowing down of the atrial activation and increases global organization of the atrial activation pattern during pharmacological cardioversion.

Moreover, the outcomes obtained in the study show that MAW organization analysis can robustly and relia-

bility estimate the temporal variation of electrical activity organization during paroxysmal AF episodes. They also demonstrate that sample entropy is a suitable estimator of organization degree of the AA obtained from surface ECG recordings, such as other previous works had obtained [11, 12]. In addition, it can be considered that the main atrial wave contain relevant information regarding paroxysmal AF onset and termination. Thus, it can be concluded that paroxysmal AF organization variations can be assessed from surface recordings without the need of invasive measurements.

Acknowledgements

This work was partly supported by the projects 20070086 from the R+D+i Vice-rectorate of the Valencia University of Technology, GV06/299 from Consellería de Empresa, Universidad y Ciencia de la Generalitat Valenciana and TEC2007–64884 from the Spanish Ministry of Education and Science.

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