Surface ECG organization analysis to predict paroxysmal atrial fibrillation termination

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The aim of this work is to predict non-invasively if an AF episode terminates spontaneously or not by analyzing the increase of atrial activity organization prior to paroxysmal atrial fibrillation (PAF) termination. Sample entropy was selected as non-linear organization index. Synthetic PAF signals were used to evaluate the notable impact of noise in AA organization estimation. Three strategies to reduce noise, ventricular residues and enhance the atrial activity main features were proposed. The best prediction results were obtained through main atrial wave (MAW) organization estimation. The MAW can be considered as the fundamental waveform associated to the AA. The 92% of the terminating and non-terminating analyzed PAF episodes were correctly classified. Thereby, it can be concluded that the MAW non-linear analysis from the surface ECG is a reliable and useful tool to predict spontaneous PAF termination.

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1. Introduction

Atrial fibrillation (AF) is a supraventricular arrhythmia characterized by uncoordinated atrial activation. AF occurs when the electrical impulses in the atria degenerate from their usual organized pattern into a rapid chaotic pattern [1]. On the electrocardiogram (ECG), AF is described by the replacement of consistent P waves by rapid oscillations or fibrillatory waves (f waves) that vary in size, shape and timing, associated with an irregular ventricular response. Consequently, when AF occurs, a notably disorganized atrial activity (AA) can be observed on the ECG.

From an epidemiological point of view, AF is the most common cardiac arrhythmia, affecting 1% of the general population [3]. Considering its prevalence with age [4], this arrhythmia affects up to 15% of the population older than 80 and has an incidence that doubles with each advancing decade after 40/50 years. Paroxysmal (spontaneously terminated) AF (PAF) is, by evidence, antecedent to persistent AF, which requires a pharmacological or external electrical intervention (cardioversion) to allow its termination [1]. The associated risks of AF are quite serious because this arrhythmia predisposes to thrombus formation within the atria that can cause stroke or any other thromboembolic events [5]. Thus, PAF termination prediction, based on non-invasive techniques, can be of great clinical value in order to avoid useless therapeutic interventions and to minimize the associated risks for the patient.

The most widely accepted theory to explain AF mechanisms is based on the continuous propagation of multiple wavelets wandering throughout the atria [1]. The fractionation of the wave fronts as they propagate results in self-perpetuating independent wavelets called reentries. The number of simultaneous reentries depends on the refractory period, mass and conduction velocity along the atria, and these parameters present severe inhomogeneities in AF [1]. However, several invasive studies have demonstrated a decrease in the number of reentries prior to AF termination, thus producing simpler wavefronts into the atrial tissue [6–9] and f waves evolve to P waves [10]. Therefore, the recorded AA slightly evolves to a more organized pattern before AF termination [2]. This fact can be used to predict PAF termination when the proper organization analysis tools are used and could be helpful for a better understanding of AF termination mechanisms.

In the present work, a non-linear regularity estimator has been applied to study AA. In this sense, previous groups applied non-linear indexes to characterize AA organization from the surface ECG, but their results did not reveal significative differences between terminating and non-terminating PAF episodes. The low signal to noise ratio was believed to be the main reason to this result [11,12]. Thereby, in this work, the noise effect on AA regularity estimation was evaluated making use of synthetic AA signals generated following published models [13]. Obtained results, that will be next presented, showed that noise considerably degraded AA organization estimation. As a consequence, in order to reduce noise, ventricular residues and enhance the AA main features, three different digital signal processing

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processing strategies have been used. Finally, to discern between terminating and non-terminating episodes sample entropy (SampEn), which is a non-linear tool that quantifies the regularity of a time series [14,15], was selected as AA organization estimator.

The paper is structured as follows. Section 2 describes the used database and previous preprocessing applied to ECG recordings. Section 3 evaluates noise effect on the AA and develops three methods to reduce noise and ventricular residues and to enhance the AA main features. Section 4 summarizes the obtained results, which are discussed in Section 5. Finally, Section 6 presents the concluding remarks.

2. Materials

In this work two recording sets were used. Firstly, because AA with no noise or ventricular residues cannot be obtained from surface ECG recordings, 25 1 min synthetic AA signals were generated. Thus, noise effect on AA organization estimation could be evaluated. The synthetic AA signals were obtained making use of the model proposed by Stridh in [13]. In this model, a sinusoid and M − 1 harmonics are used to generate a sawtooth similar shape of AF. The non-stationary behavior is created by introducing a time-varying amplitude and cycle length of the sawtooth signal. In every lead the AA is modelled by

\[ y(n) = -\sum_{i=1}^{M} a_i(n) \sin(i\theta(n)), \quad n = 1, \ldots, N, \]  

where the term \( a_i(n) \) with the sawtooth amplitude, \( a \), the modulation peak amplitude, \( \Delta a \), and amplitude modulation frequency, \( f_a \), is given by

\[ a_i(n) = \frac{2}{\pi f_s} \left( a + \Delta a \sin\left(2\pi\frac{f_a n}{f_s}\right) \right), \]  

being \( f_s \) the sampling frequency. On the other hand, the fundamental frequency of the fibrillation waveform is assumed to vary around \( f_0 \) with a maximum frequency deviation of \( \Delta f \) and modulation frequency given by \( f_j \). The phase, \( \theta(n) \), is then given by

\[ \theta(n) = 2\pi \frac{f_0 n}{f_s} + \left(\frac{\Delta f}{f_j}\right) \sin\left(2\pi\frac{f_j n}{f_s}\right). \]

After several tests, the selected parameters were \( \Delta f = 3 \) Hz, \( f_j = 4 \) Hz, \( \Delta a = 10 \) µV, \( f_0 = 9 \) Hz and \( f_s = 128 \) Hz in order to synthesize a signal as close as possible to the real AA. Because of the typical AA frequency range is 3–9 Hz [16,17], a fundamental frequency \( f_0 \) equal to 6 Hz was selected. In order to obtain different regularities, the number of harmonics \( M \) and their amplitude \( a \) were varied, such that, a higher number of harmonics with lower amplitude will generate a more irregular AA. In this way, to generate AA signals representative of both terminating (i.e., more organized) and non-terminating (i.e., more disorganized) PAF episodes, \( M \) and \( a \) were randomly selected between 5 and 15 and between 6 and 18 µV, respectively. The generated signals were considered as realistic because their SampEn values were similar to those provided by the AA obtained from TQ segments, which will be presented in Section 4. In this respect, the AA extracted from TQ intervals can be considered as a real low noise signal because, on the one hand, the ECGs were preprocessed prior to AA extraction and, on the other, ventricular residues were avoided by selecting only AA segments. More details in this respect will be introduced in Section 3.4.1. Additionally, a notable similarity between real and synthesized recordings, both for terminating and non-terminating episodes, can be appreciated in Figs. 1 and 2, respectively. The signals with similar behavior to terminating episodes were synthesized with \( M \) between 5 and 10, and \( a \) between 12 and 18 µV. Similarly, signals representative of non-terminating episodes were created with \( M \) between 10 and 15 and \( a \) between 6 and 12 µV.

The obtained set of synthetic AA signals with different regularities were used to evaluate if noise effect was regularity-dependent. In this sense, available noise in Physionet [18] coming from real ECG recordings with different energy levels was added to the synthesized AA signals. Concretely, this noise was the recorded signal when the patient front-end is disconnected from the skin electrodes.

Secondly, the proposed methods performance was evaluated making use of 50 1 min and two leads (II and V1) real ECG recordings. They were extracted from 24-h Holter recordings available in Physionet [18] coming from 50 different patients digitized at a sampling frequency of 128 Hz. The database included non-terminating PAF episodes (group N), which were observed to continue in AF for, at least, 1 h following the end of the excerpts, and PAF episodes terminating immediately after the end of the excerpted segment (group T). Recordings were divided into a learning and a test set. Next, 10 labeled recordings from each group formed the learning set. Optimal thresholds, which should allow to discern between terminating and non-terminating PAF episodes, were defined making use of each proposed methodology together with the learning set. Finally, the test set was composed of the 30 remaining recordings.

These ECG recordings were preprocessed in order to improve later analysis. Firstly, baseline wander was removed making use of bidirectional high pass filtering with 0.5 Hz cut-off frequency [19,20]. Secondly, high frequency noise was reduced with an eight-order bidirectional IIR Chebyshev low pass filtering, whose cut-off frequency was 70 Hz [21,22]. Finally, powerline interference was
removed through adaptive filtering, which preserves the ECG spectral information [23]. All the signals were also upsampled to 1 kHz in order to get precise time alignment for R-peak detection and to improve the overall signal quality as suggested in [16]. Lead V1 was chosen because previous works have shown that AF is dominant in this lead [10].

3. Methods

3.1. Atrial activity organization relevance

Through invasive recordings, such as epicardial mapping and atrial electrograms, the mechanisms that provoke AF termination have been analyzed. In this respect, characterization of local AA with high degree of detail has been reached [24], and several observations with important clinical value, which are next discussed, have been obtained. The existence and localization of reentry-circuits can be obtained through the AA organization estimation [25]. AA organization increases when some reentries are more frequent than other ones [7]. In addition, AF activation with organized patterns is characterized by low fibrillatory frequencies [9,26]. Usually, the fibrillatory frequency suffers a decrease prior to AF termination, therefore, lower fibrillatory frequencies appear close to AF termination, as has been reported both by invasive [27] and surface studies [16,17,28–31].

Invasive recordings have also been used in order to evaluate Classes IA and III antiarrhythmic drug effect, with which 90% of AF episodes are reverted to sinus rhythm [32]. By providing these drugs to AF patients, atrial action potentials are modified enlarging atrial wavelength [8,6], that is, the product of refractory period and conduction velocity that represents the minimum path length for reentry. This determines the functional size of reentry circuits, so that the same tissue can support fewer reentrant circuits and, eventually, may cause fibrillation to self-terminate [6]. Clearly, a decrease in the number of reentries prior to AF termination produces simpler wavefronts into the atrial tissue [9] and, therefore, the AA becomes more organized before AF termination [2,6–8,16].

Therefore, the organization of AA plays a very important role in AF and its termination. In addition, the development of methods capable to estimate AA organization from non-invasive recordings is a valuable tool for a better understanding of AF termination mechanisms.

3.2. Sample entropy as regularity estimator

Sample entropy (SampEn) examines time series for similar epochs and assigns a non-negative number to the sequence, with larger values corresponding to more irregularity in the data [15]. Two input parameters, a run length m and a tolerance window r, must be specified for SampEn to be computed. SampEn(m, r, N), being N the length of the time series, is the negative logarithm of the conditional probability that two sequences similar for m points remain similar at the next point, where self-matches are not included in calculating the probability. Thus, a lower value of SampEn also indicates more self-similarity in the time series. SampEn is largely independent on record length [14,15].

Formally, given N data points from a time series \( x(n) \) = \( x(1), x(2), \ldots, x(N) \), SampEn can be defined as follows:

1. Form m vectors \( x_{m}(1), \ldots, x_{m}(N - m + 1) \) defined by \( x_{m}(i) = [x(i), x(i + 1), \ldots, x(i + m - 1)] \), for \( 1 \leq i \leq N - m + 1 \). These vectors represent m consequent x values, starting with the i th point.
2. Define the distance between vectors \( x_{m}(i) \) and \( x_{m}(j) \), \( d(x_{m}(i), x_{m}(j)) \), as the absolute maximum difference between their scalar components:

\[
d(x_{m}(i), x_{m}(j)) = \max_{k=0, \ldots, m-1} |x(i + k) - x(j + k)|.
\]

(4)

3. For a given \( x_{m}(i) \), count the number of \( j \) (\( 1 \leq j \leq N - m, j \neq i \)), denoted as \( B_{i} \), such that the distance between \( x_{m}(i) \) and \( x_{m}(j) \) is less than or equal to r. Then, for \( 1 \leq i \leq N - m \):

\[
B_{i}^{m}(r) = \frac{1}{N - m - 1} B_{i}.
\]

(5)

4. Define \( B^{m}(r) \) as

\[
B^{m}(r) = \frac{1}{N - m} \sum_{i=1}^{N-m} B_{i}^{m}(r).
\]

(6)

5. Increase the dimension to \( m + 1 \) and calculate \( B^{m+1}(r) \).

Thus, \( B^{m}(r) \) is the probability that two sequences will match for m points, whereas \( B^{m+1}(r) \) is the probability that two sequences will match for \( m + 1 \) points. Finally, sample entropy can be defined as

\[
\text{SampEn}(m, r, N) = \lim_{N \rightarrow \infty} - \ln \left( \frac{B^{m+1}(r)}{B^{m}(r)} \right),
\]

(7)

which is estimated by the statistic:

\[
\text{SampEn}(m, r, N) = - \ln \left( \frac{B^{m+1}(r)}{B^{m}(r)} \right).
\]

(8)

Although m and r are critical in determining the outcome of SampEn, no guidelines exist for optimizing their values. In principle, the accuracy and confidence of the entropy estimate improve as the number of length m matches increases. The number of matches can be increased by choosing small m (short templates) and large r (wide tolerance). However, probabilities appear when too relaxed criteria are used [14]. For smaller r values, poor conditional probability estimates are achieved, while for larger r values, too much detailed system information is lost and SampEn tends to 0 for all processes. To avoid a significant contribution of noise in SampEn calculation, one must choose r larger than most of the noise [33]. The m and r values suggested by Pincus are m = 1 or 2 and r between 0.1 and 0.25 times the standard deviation (SD) of the original time series \( x(n) \) [14]. In this study, the best results were obtained with \( m = 2 \) and \( r = 0.2 \) times the SD of \( x(n) \).

The SampEn application to AF is justified 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 in AF is a far-from-linear process [34]. This phenomenon is described as the progressive shortening of effective atrial refractory periods, thus increasing the number of simultaneous reentries and, as a consequence, the perpetuation of AF [1].

3.3. Noise effect on AA regularity estimation

The 25 synthetic signals were used in order to evaluate the noise effect on AA regularity estimation. The same noise signal was superimposed to all synthetic AA signals, which were synthesized with different regularity degrees. Firstly, SampEn values of the AA signals without noise were calculated. Next, the noise recording weighed by a gain factor \( k \) was added to these signals. In order to obtain a specific signal-noise ratio (SNR) for each signal, the \( k \) factor was chosen as

\[
k = \sqrt{\frac{1}{\text{SNR}} \frac{P_{s}}{P_{n}}},
\]

(9)
being \( P_s \) the considered AA signal power and \( P_n \) the noise recording power. Finally, SampEn values of the synthetic AA signals contaminated with noise were calculated. This methodology allowed to evaluate the evolution of AA regularity estimation in the presence of noise.

The SNR of an ECG recording is normally within the 14–24 dB range. However, because of the AA signal is obtained from ECG recordings using ventricular activity cancellation techniques, the SNR of an AA signal must be lower than the SNR of an ECG. Thereby, to obtain an approximation to the detection probability curve associated to PAF termination as a function of SNR, AA signals with various SNR, between 0 and 24 dB, were generated. Six synthetic AA signals were considered as representative of non-terminating AF episodes. This consideration was based on their SampEn values, computed without noise. Their values were higher than the discrimination threshold obtained from the application of SampEn to real AA extracted from TQ segments, which will be described in Section 4. The remaining 19 signals were considered as terminating episodes. For each specific SNR value, the optimum SampEn threshold was obtained making use of the receiver operating characteristic (ROC) curve, and the diagnostic accuracy, represented by the total number of synthetic signals properly identified, was computed. This accuracy was considered as the PAF termination detection probability for the analyzed SNR.

### 3.4. Atrial activity noise reduction strategies

The synthesized signals results, which will be shown in next section, revealed that noise degraded AA organization estimation. Thereby, three methods to reduce noise, ventricular residues and enhance the AA main features have been tested and are next proposed.

#### 3.4.1. TQ interval organization (TQO) analysis

In order to reduce ventricular residues in the AA, TQ segments, free of QRST complexes, were extracted from the surface ECG recordings. Organization analysis of these segments was performed with SampEn to predict PAF behavior (see Fig. 3). Firstly, all R waves were detected making use of the Pan-Tompkins technique [35]. Next, the Q wave onset was determined through an algorithm that exploits the relatively quiescent interval immediately before ventricular depolarization [36]. Within a 120 ms interval before the R peak, the point at which the amplitude range, within a 30 ms sliding window, fell to its minimum was selected as Q onset [37,38]. The computation of an indicator related to the area covered by the T wave was used to determine T wave ending. The maximum of the computed indicator inside each cardiac cycle was the T wave ending. The algorithm mainly consisted of an integration operator over a sliding window and was implemented as a simple finite impulse response (FIR) filter [39]. For each heartbeat, the segment between T wave ending and Q wave onset was extracted and its average value was removed. The elimination of sudden transitions between TQ segments is crucial. These transitions occur after the heartbeat and provoke artificial frequency components near to the original ventricular rate (see Fig. 4), thus degrading AA organization estimation. To avoid sudden transitions when the TQ segments were consecutively joined, these segments were multiplied by a softened extremes window, whose amplitude increases linearly from 0 to 1 during the first 10% of its length, is maintained to 1 during the next 80%, and finally decreases linearly from 1 to 0 during the last 10%. Finally, a 10% overlapping allowed us to obtain soft unions between consecutively joined segments. Thus, a continuous signal, which offers the main AA characteristics such as amplitude, regularity and time waveform, was obtained, such as Fig. 5(a) shows. The signal organization was estimated making use of SampEn and compared with a SampEn threshold to discern between terminating and non-terminating PAF episodes.

#### 3.4.2. Wavelet transformed organization (WTO) analysis

Wavelet analysis transforms the signal under investigation into another one including both frequency and time domain information. Hence, the wavelet transform (WT) allows to isolate certain time–frequency characteristics of a signal in limited decomposition coefficients [40]. This fact permits to observe regularity variations in the AA signal, that would be left masked in other cases [41]. Thereby, a new methodology based on WT to reduce noise and able to

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**Fig. 3.** Block diagram describing the methodology based on TQ intervals AA organization analysis. TQ segments are delimited using suitable algorithms. The average value of each TQ segment is removed. When these segments are consecutively joined to obtain a continuous signal, they are multiplied by a softened extremes window to avoid sudden transition. The signal organization is computed through SampEn and compared with a threshold to discern between terminating and non-terminating PAF episodes.

**Fig. 4.** Spectral information of the signal obtained with TQO when (a) concatenated TQ segments are not multiplied by a softened extremes window and (b) TQ segments are multiplied by this window. The elimination of sudden transition between TQ segments is crucial, because artificial frequency components appear producing unsuccessful prediction of PAF termination.
select the main features of the AA signal obtained from surface ECG recordings was proposed (see Fig. 6). Firstly, an acceptable approximation to the AA was obtained by cancelling QRST waves. Though a variety of QRST cancellation techniques exist, the average QRST template cancellation method was used, since only two leads were available [42]. Next, the residual signal power spectral density (PSD) was calculated using Welch Periodogram. A Hamming window of 4096 points in length, a 50% overlapping between adjacent windowed sections and a 8192-point fast Fourier transform (FFT) were used as computational parameters as suggested by previous works [43]. The largest amplitude frequency within the 3–9 Hz range was selected as the dominant atrial frequency. Next, AA was decomposed using WT in different detail and approximation coefficients, and only the frequency band containing the dominant atrial frequency was reconstructed back to the time domain. The reconstructed signal waveform can be visualized in Fig. 5(b). SampEn of this time reconstructed signal was calculated and compared with optimum SampEn threshold (Th), showing relevant differences between terminating and non-terminating AF episodes.

The wavelet scale containing the dominant atrial frequency was selected because this frequency band has proved to contain relevant information about the atrial fibrillation process [16]. In fact, the dominant atrial frequency study has revealed significative differences between terminating and non-terminating PAF episodes [29,28].

If six, seven or eight wavelet decomposition levels are used, approximation and low frequency detail scales can cover the typical AA frequency range, which is around 3–9 Hz [16,17]. Regarding the wavelet family selection, there are no established rules for the choice of wavelet functions. A cautious and still exploratory approach is to test different wavelet families and then to compare their efficiency in the specific problem [44]. However, successful results in ECG processing have been obtained making use of Morlet, Daubechies and Biortogonal wavelet filter families [45,46]. Thereby, all functions of these wavelet families were tested. In our experiments, the best results were obtained with a seven level wavelet decomposition and a fourth-order biorthogonal filter (‘bior4.4’) [41].

3.4.3. Selective filtering organization (SFO) analysis

The main goal of this third strategy was to obtain the main atrial wave (MAW) of the AA. This wave can be considered as the fundamental waveform associated to the AA, its wavelength being the inverse of the AA main frequency [26]. Fig. 7 shows the proposed methodology to obtain the MAW by selective filtering. Firstly, AA was extracted from surface ECG recordings as in the previous section, i.e. using the averaged QRST template cancellation method [42]. Next, the PSD was calculated using Welch Periodogram as described before with WTO. The dominant atrial frequency was detected and the MAW was obtained by applying a selective filtering to the AA signal centered around this frequency. Through these steps, noise was considerably reduced and the AA main features were selected. Finally, SampEn of the MAW, which is shown in Fig. 5(c), was computed and compared with a threshold (Th) to discriminate between terminating and non-terminating PAF episodes.

To prevent distortion, a linear phase FIR filter was used [47]. Chebyshev approximation was preferred because all the filter parameters can be suitably fitted and minimum ripple in the pass and stop bands was needed. Therefore, a high order filter should be used, such as the Kaiser approximation marks [48]:

$$L = \frac{-20 \log_{10}(\sqrt{\delta_1 \delta_2}) - 13}{14.6 \Delta f^2} + 1,$$  

where $L$ is the filter order, $\delta_1$ and $\delta_2$ are the pass and stop bands ripple, respectively, and $\Delta f$ is the transition bandwidth between bands. A selective filter must have $\delta_1$ and $\delta_2$ lower than 0.5% of the gain and $\Delta f$ lower than 0.01 Hz, thereby its order must be greater than 250.

The selected filter bandwidth should be lower than 6 Hz because the typical AA frequency range is around 3–9 Hz [16,17]. In our experiments, the best results were obtained with a 3 Hz bandwidth and 768 filter coefficients. The MAW organization results obtained through the application of SampEn to the learning set defined the optimum threshold (Th) that, later, will allow the test set classification into terminating and non-terminating PAF episodes.

![Fig. 5. Signals provided by each proposed methodology and whose organization has been estimated with SampEn. The TQO signal is the most irregular waveform, whereas those provided by WTO and SFO are much more regular.](image)

![Fig. 6. Block diagram describing the methodology based on WTO. Firstly, AA from TQ intervals of the ECG is extracted. Next, seven levels wavelet decomposition is applied to the AA using ‘bior4.4’ as wavelet family. The scale or frequency band containing the dominant atrial frequency is reconstructed back to time domain. The organization of this time reconstructed signal is estimated using SampEn to predict the PAF termination or maintenance.](image)
4. Results

The noise effect was evaluated making use of the aforementioned synthetic AA signals at different noise levels. The obtained results for four specific SNR values, such as 24, 15, 9 and 3 dB, are presented in Fig. 8. As can be seen, SampEn values for the 25 noise-free synthetic AA signals are stacked for comparison with their corresponding SampEn values computed with noise. It can be observed that SampEn, i.e., the AA irregularity, increases with noise, thus hiding the differences between organized and disorganized activities. In addition, Fig. 9 displays the total number of synthetic AA signals correctly classified for each SNR value between 0 and 24 dB. It can be appreciated that the diagnostic accuracy was 100% for SNR of 12 dB and above. Contrarily, for lower SNRs, the number of signals properly identified decreased notably, being lower than 85% for 5 dB and 75% for 3 dB. The same experiment was also tested by adding Gaussian noise instead of ECG noise to the synthesized AA signals and results were very similar, hence, they have been omitted. However, bearing this similar behavior in mind, any other kind of random and non-deterministic contaminating signal should provoke similar results of SampEn.

The optimum SampEn threshold for each proposed methodology to reduce noise in the AA was selected from the training set to improve the sensitivity/specificity pair according to the ROC plots [49].
Fig. 9. Representation of the diagnostic accuracy, i.e., the number of synthetic signals correctly classified, as a function of the SNR. This curve was considered as an approximation to the detection probability curve associated to PAF termination.

Different thresholds or cut-off points (SampEn values) were selected and the sensitivity/specificity pair for each one of them were calculated. Sensitivity (the true positive rate) is the non-terminating episode proportion correctly classified (SampEn value higher than the cut-off point), whereas specificity (the true negative rate) represents the terminating AF episode percentage correctly recognized (SampEn value lower than the cut-off point). The closest point to 100% sensitivity and specificity was selected as optimum SampEn threshold.

The three proposed methodologies were applied to the learning signals obtaining 80% sensitivity and 100% specificity for TQO, 80% sensitivity and 90% specificity for WTO, and 100% sensitivity and 90% specificity for SFO, respectively. For the three strategies, ROC curves obtained with learning sets provided 0.265, 0.089 and 0.085, respectively, as optimum SampEn discrimination thresholds between terminating and non-terminating PAF episodes. Fig. 10(a) shows SampEn values for the 20 learning signals together with the mean and standard deviation for each group obtained by applying TQO, WTO and SFO, respectively. Note that 90% (18 out of 20), 85% (17 out of 20) and 95% (19 out of 20), respectively, of the learning recordings were correctly discriminated.

Regarding the test set, the same three recordings were incorrectly classified by the three proposed strategies, thereby, the obtained results consistency was increased. Consequently, 90% (27 out of 30) of the test signals were correctly classified, obtaining 93.75% sensitivity and 85.71% specificity, see Fig. 10(b) for details. The SampEn mean value and standard deviation for test set together with the t-test statistic significance are shown in Table 1 for the three proposed methodologies. Note that the terminating episodes present lower SampEn values. Indeed, both PAF groups are statistically distinguishable, given that statistic significances are notably lower than 0.01.

Therefore, PAF behavior of 90% (45 out of 50), 88% (44 out of 50) and 92% (46 out of 50) of all analyzed PAF episodes was correctly predicted for TQO, WTO and SFO, respectively.

5. Discussion

As indicated in the results for synthetic AA signals, SampEn values increased with noise, thus reducing the differences between organized and disorganized activities. Thereby, if AA was contaminated by noise or any other undesired signal, the organization difference between terminating and non-terminating PAF episodes was considerably reduced and, consequently, successful prediction of PAF termination will be notably complicated. Indeed, according to the developed experiment with synthetic signals, the PAF termination probability successfully predicted is notably reduced (considerably lower than 85%) when SNR is below 5dB. Considering this fact, the application of techniques for noise reduction and AA main features enhancement is crucial.

In order to avoid the ventricular residues and noises present in the AA signal obtained from surface ECG recordings making use of QRST cancellation methods [10], the organization of AA segments free of QRST complexes was estimated with SampEn, and 90% of analyzed PAF episodes were correctly classified. However, two limitations associated to the TQO method should be considered. First, poorer outcomes could be obtained when TQ intervals are vanished at high heart rates. To this respect, it was corroborated that 4 out of 5 AF episodes incorrectly classified presented a heart rate above 120bpm, thus being the TQ segments duration lower than 50ms. In second place, the overlapping strategy used at TQ intervals borders, could provoke slight discontinuities in the resulting signal, which could disturb SampEn computation and locally modify its value.

To overcome the aforesaid limitations, WTO and SFO were proposed to reduce noise and ventricular residues in the AA signal obtained with ventricular cancellation methods. Although similar outcomes were provided by both techniques, WTO (88%) achieved a lower predictive ability than SFO (92%). In this case, the main limitation of WTO could be explained by considering that orthogonal wavelet filters, larger than two coefficients, must present asymmetrical impulse response. Therefore, linear phase behavior is impossible [50], such as Fig. 11 shows for the fourth-order biorthogonal function. In this figure it can be observed that both decomposition and reconstruction low-pass filters (LFP) introduce phase distortion in the highest frequencies of the sub-band (4–8 Hz frequency range). Thus, the incorrect classification of the three non-terminating AF episodes, which present dominant atrial frequency values higher than 7 Hz, could be caused by this high-frequency phase distortion. This observation is coherent with the fact that the best classification results were obtained with the biorthogonal family, since it reaches the best trade-off between asymmetrical impulse response and orthogonality [50] and, therefore, it introduces the lowest phase distortion.

Hence, the best predictive ability was obtained through the MAW organization analysis. Thereby, it could be considered that the MAW contains the most important information about spontaneous PAF termination and lower noise than the AA obtained directly from QRST cancellation. Thus, an in-deep MAW analysis should improve understanding of PAF termination mechanisms. Nevertheless, the similarity among the results obtained with the three methods increases their consistency, and corroborates that a suitable noise reduction in the AA signal prior to its organization estimation via non-linear regularity indexes is necessary to predict successfully PAF termination.

The signals provided by each proposed methodology are shown in Fig. 5. As can be seen, the TQO signal is the most irregular waveform and, therefore, SampEn values are higher. On the contrary, for WTO and SFO, regularity is computed over a concrete frequency band of the AA, thus giving lower SampEn values but better classification results. Hence, it could be considered that the MAW presents a higher SNR than that of the AA, because noise and nuisance signals outside the AA fundamental frequency band are removed.

In the three proposed strategies, terminating PAF episodes presented lower SampEn values and, consequently, higher organization than non-terminating episodes. This observation corroborates the AA organization increase prior to PAF termination reported through invasive atrial electrograms [7,8,51] that, at this moment, is clinically accepted [2]. Thereafter, the obtained results prove that this invasively observed increase in AA organization is reflected on the
Fig. 10. (a) Classification into terminating and non-terminating PAF episodes for the learning set recordings. Optimum thresholds are represented with a dashed line. (b) Classification into terminating and non-terminating PAF episodes for the test set recordings. Optimum thresholds are represented with a dashed line. Incorrectly classified recordings are surrounded with a dashed circle.
through selective filtering of the atrial activity, which was able to extract the main atrial wave. This study has shown that sample entropy of the main atrial wave predicts PAF spontaneous termination in the 92% of the analyzed episodes. Moreover, atrial activity organization increased in most part of the terminating PAF episodes but, on the contrary, organization decreased in three of them. Therefore, a variety of termination mechanisms should be considered.

Finally, as a consequence of the obtained results, the main atrial wave may involve the most relevant contribution regarding spontaneous PAF termination. Its in-depth analysis could improve effective therapeutic interventions and minimize the risk in AF patients.

7. Summary

The prediction of PAF termination or maintenance could avoid unnecessary therapy and contribute to take the appropriate decisions on its management. The aim of this work was to predict non-invasively if an AF episode terminates spontaneously or not by analyzing the increase of atrial activity organization prior to PAF termination. The organization varies as a consequence of the decrease in the number of reentries wandering the atrial tissue. The analysis was carried out through the use of surface ECG recordings and sample entropy was selected as non-linear organization index. Synthetic PAF signals were used in order to evaluate the notable impact of noise in AA organization estimation. Three strategies to reduce noise, ventricular residues and enhance the atrial activity main features were proposed. The first one was based on the analysis of AA organization obtained between TQ intervals. The second one made use of wavelet entropy analysis, and the last one was based on the MAW organization analysis. The MAW, that can be considered as the fundamental waveform associated to the AA, was derived by applying selective filtering. The best prediction results were obtained through MAW organization estimation, and 92% of the terminating and non-terminating analyzed PAF episodes were correctly classified. Thereby, it was concluded that the MAW non-linear analysis from the surface ECG is a reliable and useful tool to predict spontaneous PAF termination.

Conflict of interest statement

None declared.

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References


