Organization Tracking of Long-Term Atrial Fibrillation Recordings: Differences Between Paroxysmal and Persistent Episodes

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Abstract

In this work, a method for non-invasive assessment of AF organization has been applied to discriminating between paroxysmal and long-term persistent AF episodes. Following extraction of the atrial activity (AA) signal, the dominant atrial frequency (DAF) of the AA was computed based on a hidden Markov model. Finally, the main atrial wave (MAW) was obtained by bandpass filtering centered on the DAF, thus providing a time series suitable for AF organization estimation with sample entropy (SampEn). The performance of the method was evaluated on 24-h Holter recordings with long-term changes in AF organization. The results showed that episodes of paroxysmal AF (0.0693±0.0147) were consistently associated with lower SampEn than episodes with persistent AF (0.1056±0.0146). Moreover, 94.2% of 1-min segments with paroxysmal AF and 88.6% of 1-min segments with persistent AF could be correctly classified based on SampEn information, thus making it possible to classify long-term recordings of patients without AF history.

1. Introduction

Paroxysmal atrial fibrillation (AF) often progresses to sustained AF. About 18% of paroxysmal AF degenerates into persistent AF in less than 4 years [1]. The associated risks of persistent AF are quite serious because this arrhythmia predisposes to thrombus formation within the atria that can cause stroke or other thromboembolic events [2]. Additionally, AF of long duration is more resistant to treatment such as drug therapy or electrical cardioversion [3]. Hence, information about the AF chronification degree would be clinically very interesting for patients without AF history, because the presence of AF, even during periods as short as 24 hours, has been found to alter atrial electrophysiological properties to favor AF maintenance. Thus, early intervention could maximize the effectiveness of AF treatment [4].

Several authors have hypothesized that there is a relationship between AF organization, defined as how repetitive is the AF signal pattern, and the number of wavelets wandering the atrial tissue, such that fewer simultaneous wavelets imply more organized AF [3, 5–8]. In addition, one long-standing hypothesis of AF is that self-sustained AF would have more circulating wavelets than non-sustained AF [9, 10]. The present work investigates the value of a previously published method for estimating non-invasively AF organization, here used for discriminating between paroxysmal and persistent episodes. Long-term variations in AF organization were assessed in order to analyze whether organization differences between paroxysmal and persistent AF can be observed during the recorded time intervals.

2. Materials

A total of 24 patients without AF history undergoing 24-h Holter ECG recordings were enrolled in the study. Cardiologists diagnosed persistent AF in 13 of the selected patients and paroxysmal AF for the remaining 11. For patients with paroxysmal AF, the episode with the longest duration was selected from the 24-h recording. The selected episodes had a duration between 4 minutes and 4.5 hours. For patients with persistent AF, the whole 24-h recording was analyzed.

The recordings were acquired with a sampling rate of 125 Hz and 12-bit resolution. Next, the selected segments were upsampled to 1 kHz, as suggested in [11], in order to allow better alignment for QRST complex subtraction. This step is necessary to extract the AA from surface ECGs. On the other hand, although three leads (II, aV_F, and V_1) were recorded, only V_1 was considered for the study because previous work has shown that AA is dominant in this lead [12].

In order to improve subsequent analysis, the recordings were preprocessed before upsampling. First, baseline wander was removed making use of bidirectional high-pass filtering with 0.5 Hz cut-off frequency [13]. Second, high frequency noise and powerline interference were reduced with an 8th-order bidirectional IIR Chebyshev low-pass filtering whose cut-off frequency was 50 Hz [14].

3. Methods

The proposed method to assess AF organization is based on the non-linear regularity index sample entropy (SampEn), which is briefly described below. This method has been previously used in other AF-related applications, reporting successful results [15,16]. The results indicate that the approach provides a robust estimator of paroxysmal and persistent AF organization. Certain minor modifications are described below in order to ensure reliable assessment of long-term variations in AF organization.

3.1. Strategy to assess AF organization

The application of SampEn to estimate AF organization requires that the surface ECG is processed in several steps. First, ventricular activity is removed, because it presents much greater amplitude than atrial activity (AA) [12]. For this purpose, the spatiotemporal QRST cancellation technique is used, because three leads are available. This method produces an AA signal in which the influence of electrical axis alterations, provoked by the patient's respiratory activity, is reduced by combining mathematically the average beats of adjacent leads with the average beat of the analyzed lead [17].

Despite ventricular activity cancellation, QRST residua and noise are sometimes present in the extracted AA signal [12]. These disturbances degrade the characterization of AA organization using SampEn [18, 19]. To overcome this problem, the main atrial wave (MAW) is extracted which can be viewed as the fundamental waveform associated with the AA [19,20], its wavelength being the inverse of the AA main frequency [21].

From the AA, the MAW was obtained by applying a selective filter centered around the dominant atrial frequency (DAF) [19, 20]. The DAF is taken as the frequency of the largest spectral peak within the 3–9 Hz range [21] and was tracked by a recently published method based on a hidden Markov model (HMM), which is briefly described next. This technique provides a reliable long-term DAF trend with a temporal resolution of 2-s, even in noisy ECG recordings. Finally, SampEn was computed over each 2-s interval for which the DAF was estimated.

3.2. Dominant atrial frequency tracking

The HMM method produces an optimal DAF trend from a sequence of observed DAF estimates, using a priori knowledge about the likelihood of DAF changes and the frequency estimation method employed [22]. For each 2-s segment of AA, the observed DAF is chosen as the maximum peak of its Fourier-based periodogram, provided that the peak is contained in the interval 3–12 Hz and that its magnitude exceeds a predefined detection threshold. The HMM is characterized by a state transition matrix, defining the likelihood of DAF changes, and an observation matrix, defining the likelihood of estimating the correct frequency. Using the observed DAF estimates, a DAF trend optimized with respect to the a priori knowledge contained in the HMM matrices is created by the Viterbi algorithm.

3.3. Sample entropy

SampEn examines a time series for similar epochs and assigns a non-negative number to the sequence, with larger values corresponding to more irregularity in the data [23]. Two input parameters, a run length m and a tolerance window r, must be specified for SampEn to be computed. $SampEn(m, r)$ is the negative logarithm of the conditional probability that two sequences similar during m points remain similar at the next point, where self-matches are not included in calculating the probability. A detailed mathematic description can be found in [23].

Although m and r are critical in determining the outcome of SampEn, no guidelines exist for optimizing their values. Nevertheless, $m = 2$ and $r = 0.25$ were selected, because they showed successful results in previous works [15,16,19,20].

3.4. Statistical analysis

To develop a more reliable statistical study, SampEn values computed in 2-s segments were averaged in 1-min intervals. Moreover, each average value was independently considered in the statistical study. Both groups of paroxysmal and persistent AF 1-min segments had a normal and homoscedastic distribution as the Kolmogorov–Smirnov and Levene tests proved, respectively. Thereby, results are expressed as mean$\pm$standard deviation for all the segments belonging to the same group and a Student's t-test was used to determine whether there was any significant difference between the groups. A two-tailed value of statistical significance (p) lower than 0.05 was considered significant.

The SampEn threshold providing the best discrimination between the two groups was obtained by means of the receiver operating characteristic (ROC) curves [24]. Sensitivity was considered as the proportion of paroxysmal 1-min segments correctly classified, whereas specificity was the percentage of persistent 1-min intervals properly identified. The value providing the highest accuracy, i.e. the highest number of AF segments precisely discerned, was selected as optimum threshold.

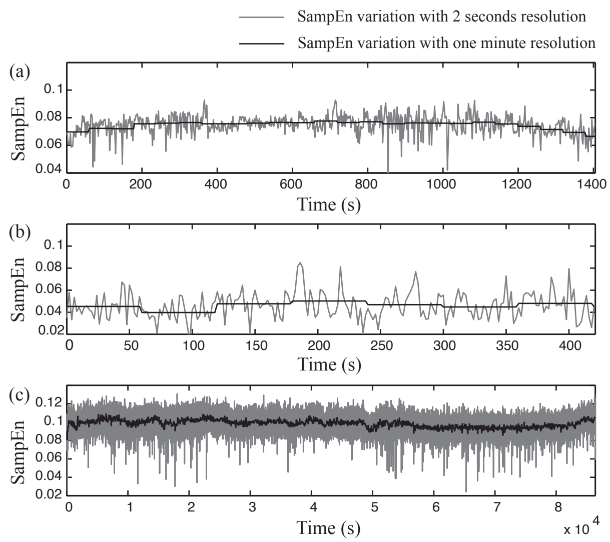

Figure 1. SampEn variation for a typical episode of (a) paroxysmal AF longer than 10 minutes, (b) paroxysmal AF shorter than 10 minutes and (c) persistent AF. Note that different scales on the vertical and horizontal axes are used.

4. Results

For paroxysmal episodes longer than 10 minutes (8 out of 11), SampEn increased during the first minutes after AF onset and decreased during the last minutes prior to AF termination. Within the central part of the episodes, SampEn was approximately stabilized and close to its mean value. To this respect, Fig. 1(a) shows the SampEn behaviour for a typical paroxysmal AF episode, having a duration of 24 minutes. On the contrary, the three paroxysmal episodes shorter than 10 minutes did not exhibit marked changes in SampEn, but the values were low in comparison with the longer episodes, see the 7-minute trend displayed in Fig. 1(b).

With regard to episodes with persistent AF, a very constant SampEn trend was observed during the analyzed 24-h interval. In this sense, Fig. 1(c) shows SampEn variation for a typical persistent AF Holter recording. Additionally, it is noteworthy that episodes of persistent AF (0.1056±0.0146) presented higher SampEn values than episodes with paroxysmal AF (0.0693±0.0147), the statistical significance being $p = 4.064 \times 10^{-6}$. As a consequence, a SampEn threshold of 0.087 could be established to discriminate between paroxysmal and persistent episodes. A minute-by-minute discrimination between paroxysmal and persistent AF through SampEn provided a sensitivity of 94.2%, a specificity of 88.6%, and an accuracy of 90.4%.

5. Discussion and conclusions

Non-invasive methods to analyze AA from the surface ECG have been advocated as being useful in AF treatment [25]. To this respect, this study is the first to apply organization analysis for discriminating between paroxysmal and persistent AF episodes from patients without AF history and Holter ECG recordings.

The results showed that persistent episodes presented higher SampEn values than paroxysmal ones, thus suggesting that AA is more disorganized in patients with persistent AF. This observation agrees with the results reported through invasive studies in humans [26, 27] and dogs [3], which showed that persistent AF exhibits a higher degree of disorganized activity in the atria than paroxysmal AF.

The relationship between AF organization and the number of reentries wandering throughout the atrial tissue [7, 8], together with the low probability of AF termination when a high number of reentries are present [7, 9], allow us to hypothesize that the different chronification stages of AF can be reflected by progressively higher SampEn values. Hence, the MAW-based SampEn analysis could be helpful in predicting the timing and progressive evolution that turns the arrhythmia from paroxysmal into persistent AF. This observation could have significant implications in AF management, thus allowing better selection of patients for the most suitable therapy.

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References

[1] Al-Khatib S, Wilkinson W, Sanders L, McCarthy E, Pritchett E. Observations on the transition from intermittent to permanent atrial fibrillation. Am Heart J 2000;147:142–145.

[2] Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et. al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association task force on practice guidelines and the european society of cardiology committee for practice guidelines (writing committee to revise the 2001 guidelines for the management of patients with atrial fibrillation): developed in collaboration with the european heart rhythm association and the heart rhythm society. Circulation Aug 2006; 114(7):e257–e354.

[3] Sih HJ, Zipes DP, Berbari EJ, Adams DE, Olgin JE. Differences in organization between acute and chronic atrial fib-

rillation in dogs. J Am Coll Cardiol 2000;36(3):924–931. ISSN 0735-1097 (Print).
[4] Bollmann A, Lombardi F. Electrocardiology of atrial fibrillation. current knowledge and future challenges. IEEE Eng Med Biol Mag 2006;25(6):15–23.
[5] Konings K, Kirchhof C, Smeets J, Wellens H, Penn O, Allessie M. High-density mapping of electrically induced atrial fibrillation in humans. Circulation 1994;89:1665–1680.
[6] Allessie MA, Konings K, Kirchhof CJ, Wijffels M. Electrophysiologic mechanisms of perpetuation of atrial fibrillation. Am J Cardiol Jan 1996;77(3):10A–23A.
[7] Sih HJ, Zipes DP, Berbari EJ, Olgin JE. A high-temporal resolution algorithm for quantifying organization during atrial fibrillation. IEEE Trans Biomed Eng Apr 1999; 46(4):440–450.
[8] Everett TH, Kok LC, Vaughn RH, Moorman JR, Haines DE. Frequency domain algorithm for quantifying atrial fibrillation organization to increase defibrillation efficacy. IEEE Trans Biomed Eng Sep 2001;48(9):969–978.
[9] Moe GK. On the multiple wavelet hypothesis of atrial fibrillation. Archives Internationales de Pharmacodynamie et de Therapie 1962;140:183–188.
[10] Allessie MA, Lammers WJEP, Bonke FIM, Hollen J. Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation. Cardiac Electrophysiology and Arrhythmias D P Zipes and J Jalife Eds Orlando FL Grune and Straton 1985;265–275.
[11] Bollmann A, Husser D, Mainardi L, Lombardi F, Langley P, Murray A, Rieta JJ, Millet J, Olsson SB, Stridh M, Sörnmo L. Analysis of surface electrocardiograms in atrial fibrillation: Techniques, research, and clinical applications. Europace Nov 2006;8(11):911–926.
[12] Petrutiu S, Ng J, Nijm GM, Al-Angari H, Swiryn S, Sahakian AV. Atrial fibrillation and waveform characterization. A time domain perspective in the surface ECG. IEEE Eng Med Biol Mag 2006;25(6):24–30.
[13] Dotsinsky I, Stoyanov T. Optimization of bi-directional digital filtering for drift suppression in electrocardiogram signals. J Med Eng Technol 2004;28(4):178–180.
[14] Sun Y, Chan K, Krishnan SM. ECG signal conditioning by morphological filtering. Comput Biol Med Nov 2002; 32(6):465–479.
[15] Alcaraz R, Rieta JJ. Wavelet bidomain sample entropy analysis to predict spontaneous termination of atrial fibrillation. Physiol Meas Jan 2008;29(1):65–80.
[16] Alcaraz R, Rieta JJ. A non-invasive method to predict electrical cardioversion outcome of persistent atrial fibrillation. Med Biol Eng Comput Jul 2008;46(7):625–635.
[17] Stridh M, Sörnmo L. Spatiotemporal QRST cancellation techniques for analysis of atrial fibrillation. IEEE Trans Biomed Eng Jan 2001;48(1):105–111.
[18] Nilsson F, Stridh M, Bollmann A, Sörnmo L. Predicting spontaneous termination of atrial fibrillation using the surface ECG. Med Eng Phys Oct 2006;28(8):802–808.
[19] Alcaraz R, Rieta JJ. Sample entropy of the main atrial wave predicts spontaneous termination of paroxysmal atrial fibrillation. Med Eng Phys Jun 2009;doi: 10.1016/j.medengphy.2009.05.002.
[20] Alcaraz R, Rieta JJ. Non-invasive organization variation assessment in the onset and termination of paroxysmal atrial fibrillation. Comput Methods Programs Biomed Feb 2009; 93(2):148–154.
[21] Holm M, Pehrson S, Ingemansson M, Sörnmo L, Johansson R, Sandhall L, Sunemark M, Smideberg B, Olsson C, Olsson SB. Non-invasive assessment of the atrial cycle length during atrial fibrillation in man: introducing, validating and illustrating a new ECG method. Cardiovasc Res Apr 1998; 38(1):69–81.
[22] Sandberg F, Stridh M, Sornmo L. Frequency tracking of atrial fibrillation using hidden Markov models. IEEE Trans Biomed Eng 2008;55(2 Pt 1):502–511.
[23] Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol Heart Circ Physiol Jun 2000;278(6):H2039–H2049.
[24] Bewick V, Cheek L, Ball J. Statistics review 13: receiver operating characteristic curves. Crit Care Dec 2004; 8(6):508–512.
[25] Chen SA, Tai CT. Is analysis of fibrillatory waves useful for treatment of atrial fibrillation? J Cardiovasc Electrophysiol 2004;15(8):918–919.
[26] Ndrepepa G, Karch MR, Schneider MAE, Weyerbrock S, Schreieck J, Deisenhofer I, Zrenner B, Schomig A, Schmitt C. Characterization of paroxysmal and persistent atrial fibrillation in the human left atrium during initiation and sustained episodes. J Cardiovasc Electrophysiol 2002; 13(6):525–532.
[27] Zrenner B, Ndrepepa G, Karch MR, Schneider MA, Schreieck J, Schomig A, Schmitt C. Electrophysiologic characteristics of paroxysmal and chronic atrial fibrillation in human right atrium. J Am Coll Cardiol 2001;38(4):1143–1149.

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