A New Method to Assess Sinus Rhythm Maintenance Likelihood Before Electrical Cardioversion of Persistent Atrial Fibrillation

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Abstract

For many patients in persistent Atrial Fibrillation (AF), normal sinus rhythm (NSR) restoration use to be required to reduce the risk of stroke and improve cardiac output. Electrical cardioversion (ECV) is the most effective alternative to revert AF to sinus rhythm. However, because of the high risk of AF recurrence (especially during the first 2 weeks following the procedure) and because of potential collateral effects of ECV, it is clinically important to predict NSR maintenance after ECV before it is attempted. Thereby, the aim of this work is to obtain a robust and non-invasive predictor of NSR maintenance after ECV. The organization degree of the atrial activity (AA) obtained from surface electrocardiographic (ECG) recordings was estimated using a non-linear regularity index because it can be hypothesized that AF recurrence can be greater in those patients who present a highly disorganized AA. With the proposed strategy, 90.24% sensitivity and 78.57% specificity were obtained. Therefore, therapeutic interventions for the treatment of persistent AF could be improved, since unsuccessful electrical cardioversion and the consequent risks for the AF patients could be avoided.

1. Introduction

Atrial Fibrillation (AF) is the most commonly sustained cardiac arrhythmia in clinical practice, with a prevalence of 0.5% in the adult population [1], rising to 10% or more in those over 75 years [2, 3]. This disease can be divided into different forms, namely paroxysmal AF (self-terminating within 7 days), persistent AF (interventions are required for its termination), and permanent AF (sinus rhythm cannot be restored) [2]. For many patients in persistent AF, restoration and maintenance of normal sinus rhythm (NSR) is the main therapeutic goal because symptoms, cardiac output, and exercise tolerance are improved whereas the risk of stroke is reduced [2]. Thus, the first step in the rhythm control strategy is generally cardioversion. While chemical-induced cardioversion is sometimes possible, particularly with amiodarone [4, 5], it is generally more unsuccessful than electrical cardioversion (ECV), specially if the arrhythmia has been present for more than 24 hours [6]. However, because of the high AF risk of recurrence, especially during the first 2 weeks following the procedure [7] and because of the potential secondary effects of ECV [8, 9], it would be clinically useful to predict NSR maintenance after electrical cardioversion before it is attempted. In this way, the risks of cardioversion could be avoided for those patients with low NSR maintenance probability, and for the health care provider, the clinical cost could be optimized because unproductive treatment time and bed usage could be reduced.

To date, numerous studies have attempted to find invasive and non-invasive parameters (clinical, electrophysiological, demographic, etc.) for the prediction of electrical cardioversion outcome for AF. However, very different and, consequently, inconclusive results have been obtained [10]. Thereby, the aim of this work is to obtain a new robust and non-invasive predictor of NSR maintenance after ECV before it is attempted. In this respect, the atrial activity (AA) organization was estimated noninvasively, because it can be hypothesized that NSR maintenance would be more likelihood in patients who present a highly organized AA. This hypothesis is based on the observation that the more disorganized the AA, the higher the number of propagating wavelets [11], and the larger the atrial volume that could support reentries propagation after the shock [12].

In order to estimate the AA organization obtained from surface electrocardiographic (ECG) recordings, Sample Entropy (SampEn), which is a non-linear index for quantifying time series regularity [13], was selected because nonlinearity, as necessary condition for a chaotic behavior, is present in the diseased heart with AF at cellular level, and the electrical remodeling in AF is a far-from-linear process [14]. This phenomenon can be 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 [2]. Moreover,

in previous works it has been shown that Sample Entropy is a robust organization estimator of the AA obtained from surface ECG recordings [15, 16].

2. Materials

Forty patients (15 men and 25 women) with persistent AF lasting more than 30 days, undergoing the first attempt of electrical cardioversion were followed during four weeks. A standard 12-lead ECG was acquired prior to cardioversion. All signals were digitized at a sampling rate of 1024 Hz and 16-bit resolution by means of Cardiolab System in the electrophysiology laboratory during ECV protocol. In order to process these signals, a 30 seconds-length AF segment preceding the ECV was extracted for each patient. After the ECV, NSR was not restored in 5 patients (12.5%) whereas in 21 (52.5%) NSR duration was below one month. In the remaining 14 patients (35%) NSR was maintained. All patients were in drug treatment with amiodarone.

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 cutt-off frequency [17]. Secondly, high frequency noise was reduced with an eight order bidirectional IIR Chebyshev low pass filtering, whose cut-off frequency was 70 Hz [18]. Finally, powerline interference was removed through adaptive notch filtering, which preserves the ECG spectral information [19].

3. Methods

3.1. Strategy to predict NSR maintenance

The analysis of the AA obtained from the surface ECG is complicated by the simultaneous presence of ventricular activity, which is of much greater amplitude. Whereby, the AA signal of lead V_1 was firstly extracted using the average QRST template cancellation method [20]. Previous works have shown that AF is dominant in this lead, whereby it was chosen for the analysis [21].

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 remainder ECG [21]. These nuisance signals can degrade AA organization estimation using non-linear regularity indexes, which could provoke unsuccessful results. Hence, in order to reduce the presence of noise, ventricular residues and any other nuisance signal in the AA, a wavelet decomposition analysis of AA is proposed. Seven levels wavelet decomposition was applied to AA signals because the seventh discrete scale (sub-band corresponding to 4-8 Hz) covers most typical AA frequency range, that is around 3-9 Hz [22]. This scale was reconstructed back to the time-domain and its organization was estimated making use of Sample Entropy (SampEn), which is notably independent on record length and obtains coherent results when short and noisy data sets are analyzed [13]. A more detailed mathematic description of SampEn can be found in [13].

Because of there are not established rules for the choice of a wavelet family, several orthogonal families were tested. The best results were obtained with Biorthogonal wavelet family (order 4.4). A wide description of Wavelet Transform and wavelet families can be found in [23].

3.2. Statistical analysis

Results were expressed as mean $\pm$ standard deviation, unless otherwise specified. In order to evaluate the organization analysis predictive cability for the NSR maintenance, receiver operating characteristic (ROC) curves were constructed. Different thresholds or cutoff points (SampEn values) were selected and the sensitivity/specificity pair for each one of them was calculated. Sensitivity (the true positive rate) is the ECVs relapsing to AF proportion correctly classified (SampEn value higher than the cutoff point), whereas specificity (the true negative rate) represents the ECVs resulting in NSR percentage correctly recognized (SampEn value lower than the cutoff point). The closest point to 100% sensitivity and specificity was selected as optimum SampEn threshold. The t-student test was used to determine whether there was any significant difference between the groups. A two-tailed value of $p < 0.05$ was considered statistically significant.

4. Results

With the proposed methodology, 90.47% sensitivity and 78.57% specificity were obtained, see Fig. 1(a). The ROC curve provided 0.0990 as optimum SampEn discrimination threshold between recordings relapsing to AF and resulting in NSR after one month. Fig. 1(b) shows the SampEn values for the all analyzed signals together with the mean and standard deviation values for each group. Note that the patients who resulted in NSR presented lower SampEn values (0.0930 ± 0.0150) than those who relapsed to AF (0.1136 ± 0.0151). Indeed, both groups were statistically distinguishable, given that statistic significance was lower than 0.0001. In addition, the five patients who relapsed to AF immediately after the ECV were also studied separately and they presented the lowest AA organization (0.1255 ± 0.0165), thus reinforcing the robustness of the presented approach.

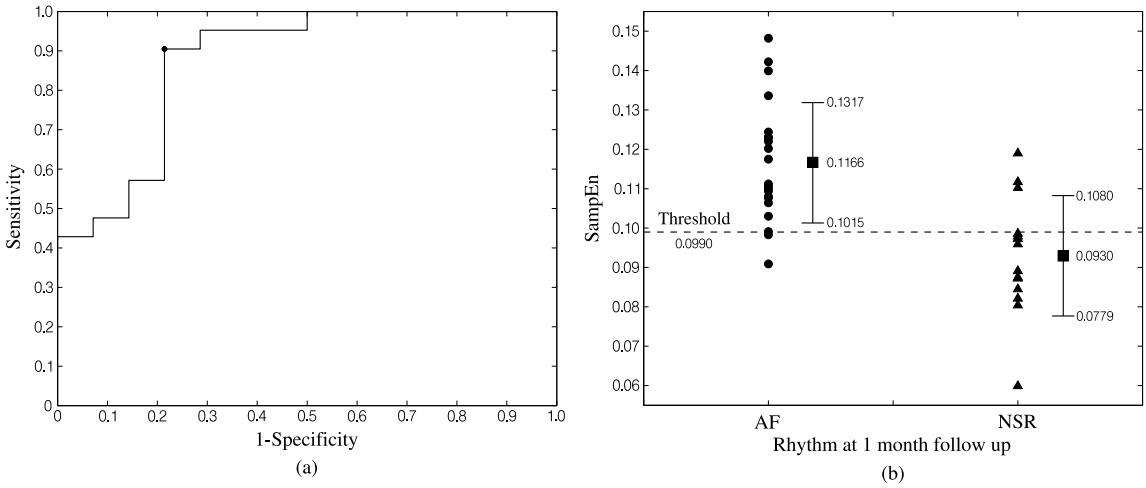

Figure 1. (a) Receiver Operating Characteristic (ROC) curve calculated with the obtained organization values. (b) Classification into ECVs resulting in NSR and relapsing to AF after 4 weeks following ECV.

5. Discussion and conclusions

The organization analysis results show that recordings relapsing to AF present higher AA disorganization than those resulting in NSR after 4 weeks. This observation agrees with findings reported in other works, such as: (i) the higher the AA organization, the higher the success rates in AF cardioversion [24, 11], (ii) the higher the level of AA organization, the lower the energy required for successful cardioversion [12] and (iii) paroxysmal AF requires less energy for cardioversion than persistent AF [25]. These previous observations highlight the fact that, when a higher number of reentries are wandering throughout the atrial tissue, a lower probability of successful electrical cardioversion is obtained. One possible explanation could be that a low degree of AA organization might result in an increased mass of atrial myocardium that is not fully excitable [24]. Moreover, the necessity of a lower refractory period prolongation into a lower volume of atrial tissue, when the AA is highly organized, could also justify the obtained results.

The five patients in which NSR was not immediately restored after ECV presented the lowest AA organization. This observation also agrees with the outcomes reported with invasive recordings [24, 11] and, thereby, the obtained results consistency is increased.

Other authors have also tried to estimate AF organization for predicting NSR maintenance after ECV. Holmqvist et. al. [26] evaluated a parameter obtained from time-frequency analysis of the atrial signals, such as harmonic decay [22]. This parameter was designed to be an index of the waveform shape (and indirectly organization) of the atrial component of the ECG, but a low number of recordings relapsing to AF were correctly identified (47%). In [27], ventricular rhythm was analyzed using three-dimensional RR intervals plots, quantifying clustering of RR intervals. The authors speculated that RR intervals clustering represents a relatively high organization degree of atrial fibrillatory activity, and hypothesized that ECV would be more effective in patients with clustering. However, only 53.8% of patients who relapsed to AF (during the first 4 hours following ECV) were correctly discerned. These results also motivated the use of non-linear regularity indexes for estimating the AA organization.

Hence, the obtained results presented in this work prove that the noninvasive and non-linear assessment of AA organization is a reliable and robust method to determine the individual risk for early AF relapse, thereby avoiding unnecessary cardioversion attempts.

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