Prediction of Successful Cardioversion in Atrial Fibrillation Using Wavelet Analysis Parameters and Sample Entropy

R Cervigón[1], R Alcaraz[1], C Vayá[1], C Heneghan[2], J Millet[3], C Sánchez[1]

[1]University of Castilla-La Mancha, Cuenca, Spain
[2]University College Dublin, Dublin, Ireland
[3]Technical University of Valencia, Valencia, Spain

Abstract

In a substantial number of patients atrial fibrillation (AF) recurs after successful electrical cardioversion, but at present there are no reliable clinical markers for confidently identifying the patients in which recurrence will occur within a short period of time. This study evaluates the predictive classification performance of some Discrete Wavelet Transform (DWT) indices in distinguishing recurrent and non-recurrent AF episodes. A validated database of 33 ECG recordings acquired from AF subjects undergoing cardioversion was used throughout the study, together with their known recurrence status at one month. The DWT was applied to these ECG recordings. Several parameters were extracted from the decomposition bands as potential features for predicting the recurrence of AF episodes. The estimated classification rate of the extracted features was evaluated using linear discriminant analysis (LDA). For a separate 11 registers training set and 22 registers testing set, the performance of the classifier testing set gave an estimated accuracy of 82%. We conclude that features extracted from sub-band decomposition of the ECG can provide some indicator of the likelihood of AF recurrence.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the general population, with significantly higher prevalence in the elderly (10% in people above 80 years)[1, 2].

The exact mechanisms that generate, perpetuate and terminate AF remain uncertain, and current preventative and curative therapies are not fully satisfactory yet. One of most useful therapies is electrical cardioversion (ECV), where external shocks are given in an attempt to convert AF to normal sinus rhythm (NSR). ECV based therapies are technically difficult and have some risk of complications. such as thrombo-embolism. However, following successful NSR restoration, the recurrence of AF after ECV is a major and largely unpredictable clinical problem, since only around 25% [3, 4] of the patients remain in sinus rhythm at one year post-cardioversion, with the proportion rising to approximately half of patients if antiarrhythmic treatment is employed. As a consequence, reliable predictors for NSR maintenance after successful ECV are required in order to avoid unnecessary ECVs and to search for more appropriate therapeutic alternatives.

The present study was conducted to analyze ECG signals from patients with persistent AF in order to extract reliable parameters to predict early AF recurrence after successful ECV. The technique used for ECG analysis was based on the wavelet transform (WT), which has been successfully employed to solve other ECG signal problems [5, 6, 7].

An important feature of the WT is its ability to localize simultaneously spectral and temporal information within a signal. In addition, the fact that the WT exhibits different window sizes depending on the frequency band, leads to a distinctive time-frequency resolution, with good frequency resolution at low frequencies, and good temporal resolution at high frequencies. The characterization of the WT coefficients at various subbands, (e.g., using Sample Entropy) has allowed us to extract a regularity measure at various frequency bands, which combined with other parameters and with appropriate statistical analysis tools provides a promising methodology for predicting the risk of AF recurrence after successful ECV.

2. Materials and methods

2.1. Materials

This study was carried out on a database of standard 12-lead ECG recordings obtained from 33 patients diagnosed with persistent AF. These recordings were obtained in the Electrophysiological Laboratory, Hospital Clínico Univer-

sitario de Valencia, during the ECV protocol. The signals provided a view of the ECG while in AF prior to cardioversion. All these signals were digitized at a sampling rate of 1KHz and 16-bit resolution. In order to process these signals, a 1 minute-length AF segment preceding the ECV procedure was extracted for each patient.

All patients with AF were monitored 4 weeks after cardioversion, and it was found that 14 out of 33 patients (42.4%) remained in NSR, whereas the rest of the patients reverted to AF.

2.2. Wavelet transform analysis

The ECG can be considered as a superposition of signals occurring at different frequencies and times. One purpose of wavelet analysis is to separate and sort these underlying structures into different time scales (frequency bands).

Wavelet analysis is the decomposition of a signal $x(t)$ into shifted and scaled versions of a reference wavelet. The reference function is called the mother wavelet $\psi(t)$, which is appropriately dilated with a factor a and shifted a certain time interval b (1). In the Continuous Wavelet Transform (CWT) the wavelet coefficients $C(a,b)$ are defined as the convolution of the signal with the mother wavelet:

$$\psi_{a,b}(t) = a^{-\frac{1}{2}}\psi(\frac{t-b}{a}) \ \forall a,b \in \Re^{+} \quad (1)$$

$$C(a,b) = \int_R x(t)\psi_{a,b}(t)dt \quad (2)$$

The Discrete-Time Wavelet Transform (DWT), according to Mallat's algorithm [8], is a sampled version of the CWT in a dyadic grid, where the wavelet coefficients are computed for discrete values of scale and translation factors, and the increments are in the dyadic scale.

In the so-called multiresolution algorithm (MRA), the original signal passes through two complementary digital filters and two downsamplers. The first one is a high-pass filter, which is characterized by the discrete mother wavelet $g[n]$ (3), whereas the second one is a low-pass filter, characterized by its mirror version $h[n]$ (4). The downsampled outputs of high-pass and low-pass filters provide the detail, and the approximation, respectively. The approximation is further decomposed into new detail and approximation coefficients, respectively. This process is repeated until all wavelet coefficients are determined. (The wavelet coefficients are the outputs observable from the detail/high pass branches of the decomposition). In this way, the DWT can be used to map a set of N raw signal samples to a new set of N wavelet coefficients, which represent the signal at various time scales/frequency bands.

$$y_{high}[k] = \sum x[n]g[2k-n] \quad (3)$$

$$y_{low}[k] = \sum x[n]h[2k-n] \quad (4)$$

2.3. Sample entropy

Entropy measures can be used to quantify the regularity (predictability) of time series. Algorithms developed for this purpose have potential applications in the analysis and understanding of complex physiological time sereis such as the ECG.

In this study, we have used sample entropy (SampEn) [9] as a useful measure of regularity. This is a similar, but less biased, measure than the approximate entropy (ApEn) family of parameters [10] introduced by Pincus to quantify the regularity of finite length time series.

The Sample Entropy can be calculated as follows. Consider the distance between two vectors as the maximum of the absolute differences between their components and fix a threshold value r for determining when these vectors are close to each other, ApEn reflects the likelihood that sequences that are close to each other, i.e., within r, for m consecutive data points remain close when one more data point is known. Mathematically, ApEn is computed as follows: Let $X_i = x_1;\ldots;x_i;\ldots;x_N$ represent a time series of length N. Consider the m-length vectors: $u_m(i) = x_i;x_{i+1};\ldots;x_{i+m-1}$. Let $n_{im}(r)$ represent the number of vectors $u_m(j)$ within r of $u_m(i)$. $C_i^m(r) = n_{im}(r) = (N-m+1)$ is the probability that any vector $u_m(j)$ is within r of $u_m(i)$. Define, $\phi^m(r) = 1/(N-m+1)\sum_{i=1}^{N-m+1} lnC_i^m(r)$. ApEn is defined as $ApEn(m,r) = \lim_{N\to\infty}\phi^m(r) - \phi^{m+1}(r)$. For finite N, it is estimated by the statistic, $ApEn(m,r,N) = \phi^m(r) - \phi^{m+1}(r)$.

SampEn has the advantage of being less dependent on the time series length, showing relative consistency over a broader range of possible r ,m, and N values. Starting from the definition of the entropy, it is defined:

$$SampEn(m,r,N) = -ln\frac{U^{m+1}(r)}{U^m(r)}$$

The differences between $U^{m+1}(r)$ and $C^{m+1}(r)$, $U^m(r)$ and $C^m(r)$ are the definition of the distance between two vectors as the maximum absolute difference between their components, the exclusion of self-matches, given a time series with N data points, only the first $N-m$ vectors of length m, $u_m(i)$, are considered, ensuring that, for $1 \le i \le llN-m$, the vector $u_{m+1}(i)$ of length $m+1$ is also defined.

SampEn is precisely equal to the negative of the natural logarithm of the conditional probability that sequences close to each other for m consecutive data points will also be close to each other when one more point is added to each sequence.

Larger SampEn values indicate greater independence, less predictability, hence greater complexity in the data. This, in turn, may imply that decreased complexity or

greater regularity in the time series is not associated with disease.

For the study discussed in this paper, SampEn is estimated using the widely established parameter values of $m = 2$, and $r = 0.25\%$, where σ represents the standard deviation of the original data sequence, as suggested by Pincus [10].

2.4. ECG signal analysis

The predictive capability of DWT coefficients to assess NSR maintenance after successful ECV was investigated. A biorthogonal family was applied to lead V1, which is the lead which typically shows the highest amplitude of the atrial fibrillatory signal, due to orthogonality properties, and a very high time resolution [8, 11].

The number of decomposition levels was chosen so that the DWT coefficients at each scale describe representative information of the atrial frequencies [11, 12]. In the present study, the number of decomposition levels was chosen to be 8. Therefore, the computed detail wavelet coefficients of the ECG signals were used as the feature vectors representing the signals at these 8 different subbands.

We can also apply spectral analysis to each sub-band decomposition. Frequency domain analysis consisted of obtaining the modified periodogram using the Welch-WOSA method [12] with a Hamming window of 4096 points length, an overlapping of 50% and 8192-point Fast Fourier Transform (FFT).

After observing the coefficients in both domains, the following parameters were considered:

- Average energy of the wavelet coefficients in each subband (E)
- Main peak frequency in each subband (F)
- Amplitude of the main peak frequency in each subband (A)
- Sample entropy in each subband (SE)

Several different combinations of features were used in the classifier in order to determine the utility of different feature subsets. Receiver Operating Characteristic (ROC) analysis was performed on individual features to quantify the ability of each feature to discriminate between recurrent and non-recurrent AF. The area under an ROC curve is equivalent to the Mann Whitney version of the two sample nonparametric Wilcoxon rank-sum statistic [13].

Linear discriminant analysis (LDA) was employed in this study as a classifier. (Other classifier models may provide better or worse performance, but typically an LDA classifier represents a robust first-order classifier approach). An LDA finds the linear combination of features that best discriminates among groups. Under certain assumptions, this method maximizes the ratio of between-class variance to the within-class variance in any particular data set thereby guaranteeing maximal separability. In an initial configuration, the classifier model was applied to all the data (i.e., the full set of 33 records was used as the training set).

Since classifier performance using trainig data only will be optimistically biased, a more realistic estimate of classifier perofrmance can be obtained using techniques such as cross fold validation. In this case, we used leave-one-out validation in which the classifier model was trained on $(m-1)$ of the m ECG records and using the m^{th} record to test the classifier performance.

3. Results

A statistical analysis to discriminate early AF recurrence from NSR maintenance after successful ECV was carried out.

The DWT was applied to the ECG from both groups using wavelets from a biorthogonal family, and the parameters described in previous section were extracted in order to proceed with the statistical analysis of the data.

The most significant results were obtained with the 'bior3.9' and 'bior3.1' wavelets. The energy (Ei), the SampEn (SEi) of the detail coefficients at different scales were evaluated, and the main peak frequency (Fi) and amplitude of the main peak frequency (Ai) at each scale were also calculated. As can be observed in Tables 1 and 2, several parameters provided statistically significant differences between the two groups. These tables also give the ROC values for a single-feature classifier based on that feature. The best-performing features are achieved with scale #7 of the 'bior3.1'and 'bior3.9' wavelets.

Table 1. Area under the ROC curves and the Wilcoxon rank-sum p-value obtained from DWT Bior3.1 analysis.

Parameters	Area	P
Bior3.1 Energy cd7 (E7)	0.761	0.010
Bior3.1 SampEn cd6 (SE6)	0.703	0.050
Bior3.1 SampEn cd7 (SE7)	0.707	0.046
Bior3.1 Amplitude cd7 (A7)	0.748	0.016

Multi-feature classification was evaluated using linear discriminant analysis (LDA). The stepwise procedure was used for feature selection. It starts with the best univariate parameter and looks only for these variables which improve classification in the training set. The procedure can also include a step to exclude previously included features, but this was not effective in our case.

A high-performing feature set was the linear combination of the parameters 'F7', 'E4', 'SE7', drawn from the bior3.9 analysis. Table 3 shows the the mean value and standard deviation of these variables for the two groups.

Table 2. Area under the ROC curves and the Wilcoxon rank-sum p-value obtained from DWT Bior3.9 analysis.

Parameters	Area	P
Bior3.9 Energy cd3 (E3)	0.759	0.011
Bior3.9 Energy cd4 (E4)	0.756	0.012
Bior3.9 SampEn cd6 (SE6)	0.703	0.050
Bior3.9 SampEn cd7 (SE7)	0.703	0.050
Bior3.9 Amplitude cd7 (A7)	0.752	0.014
Bior3.9 Frequency cd7 (F7)	0.703	0.050

Using this feature set on a separately training set of 11 subjects resulted in 81.8% (9/11) accuracy, with 80.0% sensitivity and 83.3% specificity. The performance of the classifier testing set obtained using the rest of the subjects, was an accuracy of 81.8% (18/22), with 85.7% sensitivity and 75.0% specificity.

Table 3. Parameters included in LDA.

Parameters	NSR	Recurrent AF	P
E4	0.12 ± 0.10	0.05 ± 0.02	0.012
SE7	0.09 ± 0.06	0.05 ± 0.04	0.050
F7	5.70 ± 0.69	6.12 ± 0.61	0.050

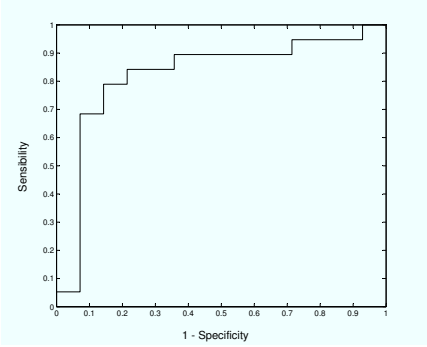

Figure 1. ROC Predictive Group LDA

4. Discussion and conclusions

In this study, the problem of selecting parameter sets which best characterize AF recurrence was investigated. Parameters extracted from surface ECG after wavelet processing were validated and shown to be statistically significant in their prediction of AF recurrence after a successful cardioversion. For the classification task a small manageable parameter subset was selected from the DWT decomposition. We showed that there is a potential for improving the performance of a classifier, by combining several individual parameters and classifying them by LDA.

These results suggest that the ECG signals contain information which provides clues as to the potential reoccurrence of AF. For example, the Sample Entropy is lower at certain time-scales in the recurrent AF cases. However, given the small sample size set, these initial results are only suggestive of a potentially useful clinical tool, with the requirement of collecting a significantly larger data set of ECV subjects in order to validate these initial findings.

Acknowledgements

This work was partly funded by several research grants from Junta de Comunidades de Castilla-La Mancha (Ref: PAC-05-008-1) and Conseller/ia de Empresa Universidad y Ciencia de la Generalitat Valenciana (Ref: GV06/299).

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