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Use of Frequency Analysis on the ECG for the Prognosis of Low Energy Cardioversion Treatment of Atrial Fibrillation

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Abstract— **Electric cardioversion is the most effective therapy for restoring sinus rhythm in patient with atrial fibrillation (AF), however, there is not a guiding criteria for advising on when and in whom it will be successful. The objective of this study was to employ frequency analysis on the surface electrocardiogram (ECG) to predict the outcome of low energy internal cardioversion in patients with AF. Thirty nine patients with AF, for elective DC cardioversion were included in this study. One catheter was positioned in the right atrial appendage and another in the coronary sinus. A voltage step-up protocol (50-300 V) was used for patient cardioversion. Prior to shock delivery, residual atrial activity signal (RAAS) was derived from 60 seconds of surface ECG from defibrillator pads, by bandpass filtering and ventricular activity (QRST) cancellation. Dominant atrial fibrillatory frequency (DAFF) was estimated from the RAAS power spectrum as the dominant frequency within the 3-12 Hz band. DAFF was calculated from whole 60 seconds segment (DAFF_L) and from the finals 10 seconds segment (DAFF_S) of the RAAS. Lower DAFF_L and DAFF_S were found in successfully cardioverted patients than in those nonsuccessful ones, with energy ≤3 and ≤6 joules. Therapy result (employing 3J or less) was predicted in 35/39 (89.7%) patients with DAFF_L=5.40Hz, and DAFF_L was ≥5.75Hz in a 100% of noncardioverted patients. In conclusion, frequency analysis of the RAAS could be useful for predicting success of low energy internal cardioversion of patients with atrial fibrillation.**

I. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice, with a prevalence of approximately 5.5% in people more than 55 year of age [1]. AF accounts for 30-40% of all hospitalizations due to arrhythmias [2]. Although several studies have reported no advantages in a rhythm control strategy over rate control [3], restoration of sinus rhythm remains an important goal, particularly in younger and symptomatic patients [4].

AF can be terminated using antiarrhythmic drugs, and by application of external or internal electric shocks. Other techniques include maze procedures and radiofrequency ablation. The most commonly used and effective technique to terminate AF and thus restore sinus rhythm is electrical cardioversion [2], nevertheless, it is often difficult to predict when and in whom this will be successful.

Digital signal processing of the surface electrocardiogram (ECG) plays an important role in the quantification of patterns in AF and its properties. One example is the evaluation and quantification of the fibrillatory cycle length (FCL) [5], in the inverse way of dominant atrial fibrillatory frequency (DAFF), which previously have been used to predict spontaneous termination of paroxysmal AF [6] and pharmacological cardioversion of AF [7]. Even, it has been shown that DAFF has a close correlation with the success of electric cardioversion (internal and external) and the minimal energy necessary to achieve it [8, 9].

The aim of this work was to evaluate the usefulness of frequency analysis of the atrial activity in the prognosis of the response to therapy of intracardiac electric cardioversion in patients with atrial fibrillation.

II. Methods

A. Patient Population

Thirty nine patients with AF, referred for elective DC cardioversion at the Royal Victoria Hospital in Belfast, between August 2004 and September 2006, took part in our study. All patients provided written, informed consent before study participation.

All patients were treated with oral anticoagulation using warfarin to achieve an international normalized ratio (INR) of 2 to 3 for more than 3 weeks before the procedure.

B. Electrodes location

A venous sheath was located in the right femoral vein, and the jugular vein (in the cases which it was necessary for facilitating catheter positioning). Single use, commercially available defibrillation catheters, were positioned in the right atrial appendage and the distal coronary sinus, under fluoroscopic control.

C. Defibrillators and Waveforms

A passive implantable atrial defibrillator (PIAD) was employed in 22 patients. The device is radio-frequency powered and it can generate a rectangular waveform [10].

In 17 patients, a Ventritex HSVO2 defibrillator (which has a 150µF capacitor) was used. The patients were randomized

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to PIAD or Ventritex defibrillation. Figure 1 illustrates the asymmetric, rectangular, biphasic (6/6ms) waveform generated by PIAD defibrillator, and the capacitive discharge biphasic (6/6ms) waveform generated by the Ventritex.

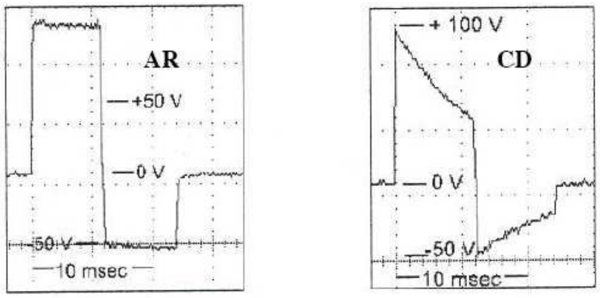

Fig. 1. At left, an asymmetric rectangular (AR), and at right, a capacitive discharge (CD) waveform is shown. For AR, negative phase has half amplitude than the positive phase, and for CD, negative phase starts with the same amplitude at the end voltage of the positive phase.

D. Defibrillation Protocol

Defibrillation was carried out using a step-up voltage protocol until sinus rhythm was achieved or until a maximum phase 1 (positive phase) leading edge voltage of 300 V was reached. Shocks were synchronized with the R-wave, and only delivered when the preceding R-R interval was greater than 400 ms.

The waveform voltages for PIAD were as follows: 50/-25 V, 100/-50 V, 150/-75 V, 200/-100 V, 240/-120 V, 280/-140 V, and 300/-150 V. Phase 1 for Ventritex defibrillator begins in 100 V (because the minimum phase 2 voltage produced by the Ventritex is 50 V) and follows with 150 V, 200 V, 240 V, 280 V until 300 V; the amplitude of negative phase depended on the capacitive discharge achieved on phase 1.

A minimum of 30 seconds was allowed between shocks. The success was determined as return to sinus rhythm for at least 30 seconds.

E. ECG recording and Signal Processing

The surface ECG from defibrillator pads in antero-apical position was continuously recorded and digitized at 170.667Hz sampling frequency, and 8 bit resolution. ECG processing was performed using Matlab® version 6.5 (The Mathworks Ins., Natick, MA, USA). The baseline ECG prior to the first cardioversion attempt was analyzed (60 seconds).

In order to reduce signal wandering due to respiratory activity and high frequency noise, a bidirectional high order filter, with pass band 0.5Hz-50Hz was used. Following this preprocessing step, atrial activity extraction from the ECG signal was performed. For this, the signal was first upsampled at 1024 Hz, to obtain a better definition. Once QRS detection was carried out, there was a chosen time period with a fixed numbered of data samples before and after the fiducial point, thus capturing the QRST complex. Thereafter the AF reduction process was performed [11].

The QRST complexes were classified according to their morphology, applying a cross correlation technique between an individual beat (QRST complex) and the average of all the complexes. Averaging takes place with beats of a same class. The adopted technique was very similar to that used by Cantini et al. [12], but they employed what they called a L1 distance with wiggling and vertical shifting, instead cross correlation technique for the QRST complexes classification and subtraction of the relative class in the ECG signal.

The next step was the creation of the template signal from the averaged complexes. Then an adaptive filter with full band cancellation configuration was employed. This was done with the objective of estimating the original filtered signal. Through this process we obtained a residual atrial activity signal (RAAS). The adaptive filter employed was of recursive least squared (RLS) type, order $M = 5$, and with a memory factor $\lambda = 0.99$. The method described by Haykin [13], for the weight adaptation of the RLS filter, was employed. This process has been before explained in [14].

R-R interval time series of 60 s segment were also analyzed, computing the mean (R-Rmean) and standard deviation (R-Rsd) of them.

F. Spectral analysis

RAAS was down-sampled to 256 Hz. The power spectrum of the residual signal was calculated by a 4096 point windowed FFT, a 1024 point Gaussian window and with a 768 point overlap. Peak frequency was determined in the 3.5-10 Hz range, and the dominant atrial fibrillatory frequency (DAFF) was estimated as the frequency component with maximum power amplitude. Spectral analysis of the atrial activity has been shown to have temporal variability [15].

DAFF was computed considering two time intervals, as DAFF_S (DAFF_Short) within a 10 second time segment and DAFF_L (DAFF_Long) within a 60 second time segment.

G. Statistical Analysis

Variables were presented as mean ± 1 SD. They were compared between patients successfully cardioverted and those who failed cardioversion following the protocol for energy ≤ 3 and ≤ 6 joules. Student-t test was applied to analyze differences between groups.

Receiver operating characteristic (ROC) curves were built. Sensitivities (Se) and specificities (Sp) were determined for specific DAFF values in order to obtain the best performance predicting the outcome of cardioversion for 2 energy ranges. Area under curve (AUC) was computed.

Spearman's technique was used in order to determine the relationship between fibrillatory frequency and the minimum defibrillation energy required in cardioverted patients.

A value of $p < 0.05$ was considered statistically significant.

III. Results

Twenty six patients were successfully cardioverted with a mean of 3.78 J (range 0.40–11.84 joules) and 3.27±1.73 shocks. Maximal energy for the Ventritex defibrillator was 6.02J. Almost a half (19) of the patients were cardioverted employing shocks ≤6 J, and more than a half of the non successful shocks delivered to the patients were ≤3 J. No significant differences were found between the means of DAFF_L (5.768±0.772 Hz) and DAFF_S (5.610±0.994 Hz) (P>0.05).

A strong positive correlation was found between DAFF_L and the minimal energy required for successful cardioversion (ρ= 0.715, P< 0.001). Similar result was found for DAFF_S (ρ= 0.708, P< 0.001). In figure 2 are plotted DAFF (Long and Short estimation) vs. the minimal energy necessary for patient cardioversion. The red line in fig. 2, corresponds to the best fitting of the data (in the least square sense).

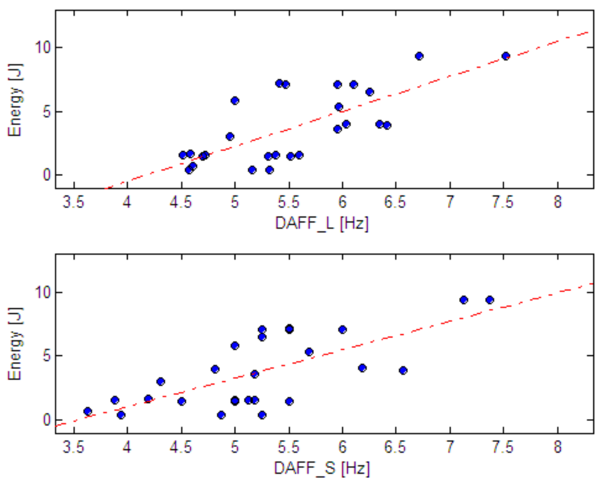

Fig. 2. Correlation between DAFF_L (top), DAFF_S (bottom) and energy threshold for successful cardioversion of the patients.

DAFF_L, DAFF_S, R-Rmean, were significantly lower for successfully cardioverted patients than in those nonsuccessful ones, with energy shocks ≤3 J (Table I).

TABLE I
DIFFERENCES BETWEEN VARIABLES FOR SHOCKS ≤3 J ACCORDING TO CARDIOVERSION SUCCESS OF THE PATIENTS.

Variables	Cardioverted N=13	Noncardioverted N=26	P-value
FFAD_L [Hz]	4.995 ± 0.399	6.154 ± 0.604	<0.001
FFAD_S [Hz]	4.644 ± 0.606	6.094 ± 0.774	<0.001
R-Rmean [s]	0.515 ± 0.115	0.642 ± 0.151	0.011
R-Rsd [s]	0.108 ± 0.048	0.132 ± 0.048	>0.05

ROC curve showed AUC=0.944 (P< 0.001) for DAFF_L, and AUC=0.942 (P<0.001) for DAFF_S, for AF cardioversion with ≤ 3J of energy. DAFF_L was >5.40Hz in 24/26 noncardioverted patients (Se=92%), and DAFF_L≤5.40Hz in 11/13 cardioverted patients (Sp=84.6%) at this energy range. It was obtained Sp=88% and Se=85.7% in the AF cardioversion prediction for DAFF_S=5.22Hz. Therapy outcomes (at this energy range) was predicted in 35/39 (89.7%) patients employing DAFF_L, and in 34/39 (87.2%) patients employing the DAFF_S, using these values as threshold. Cardioversion failed in all patients with DAFF_L≥5.75Hz (N=21), employing 3 J or less. Figure 3 shows ROC curves for the DAFF (Long and Short) according to the cardioversion success of the patient. Figure 4 shows the DAFF_L values for all the analyzed signals, for each group. Note DAFF_L threshold of 5.4 Hz for maximal classification exactitude.

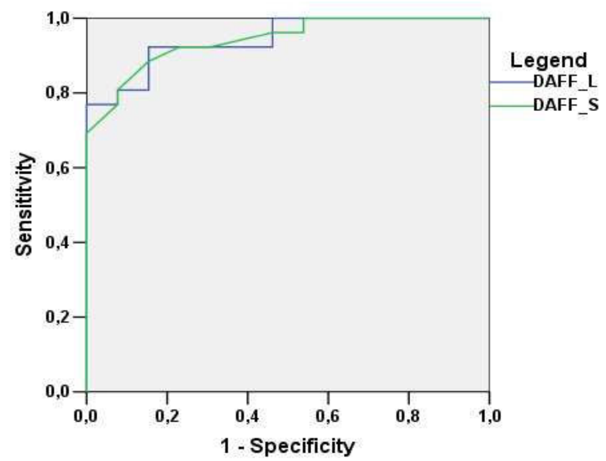

Fig. 3. ROC curves for DAFF_L and DAFF_S according to cardioversion success of the patients for energy ≤3 J.

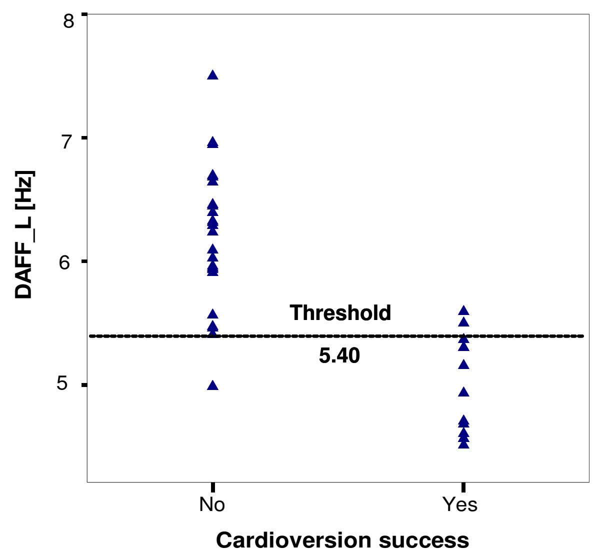

Fig. 4. Dispersion of DAAF_L values according to cardioversion success of the patients for energy ≤3 J.

Significant differences were also found for all variables, between cardioverted and noncardioverted patients with less and equal 6 J of energy (table II).

On the other hand, ROC curve analysis (AUC= 0.910, P< 0.001) revealed a maximal Se= 90% and Sp= 78.9% for a DAFF_S= 5.31Hz, for AF cardioversion with ≤6 J of energy. Cardioversion result was predicted in 33/39 patients (85.62%). All those patients (N=12) with DAFF_S<5.22Hz could be successfully cardioverted at 6 J or less.

TABLE II
DIFFERENCES BETWEEN VARIABLES FOR SHOCKS ≤6 J ACCORDING TO CARDIOVERSION SUCCESS OF THE PATIENTS.

Variables	Cardioverted N=19	Noncardioverted N=20	P-value
FFAD_L [Hz]	5.298 ± 0.623	6.214 ± 0.629	<0.001
FFAD_S [Hz]	4.938 ± 0.759	6.250 ± 0.740	<0.001
R-Rmean [s]	0.542 ± 0.129	0.654 ± 0.153	0.018
R-Rsd [s]	0.107 ± 0.046	0.140 ± 0.047	0.036

IV. DISCUSSION AND CONCLUSION

Although no significant differences were found between the DAFF_Long and DAFF_Short computations, we could note some slight differences of the performances in the therapy outcomes prediction for these variables. Such differences could be due to the interindividual variability of the spectral power in the time [11, 15], consequently producing dominant peak dispersion.

Fibrillatory cycle length (inverse of DAFF) has been considered as an useful index for assessment of electrical remodeling and estimation of organization in AF [16]. It has been probed that the number of propagating wavefronts is related to the organization of AF [17, 18], and higher level of organization has resulted in lower level of energy required for successful cardioversion [19]. Patients with persistent AF seem to exhibit higher fibrillatory frequency than patients with paroxysmal AF [20], which is in agreement with a progressive remodeling process from the paroxysmal to persistent form of AF. In concordance with a previous report [8], we have found a strong correlation between fibrillatory frequency and minimal energy for successful cardioversion of AF. Baseline atrial fibrillatory frequency (inverse form of FCL) has been found to predict paroxysmal AF spontaneous termination [21] and AF termination by antiarrhythmic drugs administration (class I) [20, 22], in which patients with lower DAFF have more probability of pharmacologic cardioversion. In a similar way, we found a threshold of DAFF_S<5.22Hz for successful electric cardioversion at 6 J or less, and DAFF_L≥5.75Hz for unsuccessful cardioversion at 3 J or less.

This study determined the usefulness of the frequency analysis over atrial activity of the surface ECG as a noninvasive technique for predicting therapy efficacy of low energy intracardiac cardioversion of atrial fibrillation in patients. Future works could be addressed to find more variables in addition to the fibrillatory frequency of the atrial signal in order to make a more robust the prediction.

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