

Assessment of the Value of Wavelet Analysis of Holter Recordings for the Prediction of Sudden Cardiac Death

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Abstract

The aim of this paper is to validate wavelet analysis of Holter recordings as a tool for the detection of risk of sudden cardiac death for patients surviving an acute myocardial infarction. The study uses time-averaged HR-ECGs from the European Myocardial Infarct Amiodarone Trial (EMIAT). Each HR-ECG is transformed into 511 orthogonal Meyer wavelet coefficients, extending from 128 ms before to 384 ms after QRS onset, and their value is assessed by means of the CARTEF Time-Frequency Abnormalities Stratification method. We then perform a linear discriminant analysis to assess the discriminant power of all wavelet coefficients with a significant p -value ($p < 0.0001$), and we compare them to the clinical parameters and also to a combination of them.

1. Introduction

Cardiac disease is the most frequent cause of death in the western world. The number of cardiac patients is steadily increasing, and in many European countries this trend is counter-balancing the benefit of the improvement of the quality of care and preventive actions. Sudden cardiac death is dramatic. It may be caused by arrhythmias (90%) or by irreversible heart failure (the remaining 10%) [1]. Due to arrhythmia, sudden death is characterized by loss of consciousness and absence of an arterial pulse, without prior circulatory collapse, whereas sudden death due to heart failure involves progressive failure and leads to circulatory collapse before cardiac arrest occurs.

The identification of patients at high risk of sudden cardiac death is of prime interest for clinicians who search for procedures to reduce post infarction death rate at short, medium and long terms. Present prognostic indices for sudden death mainly are the left ventricular ejection fraction (LVEF) and electrocardiography indices. A LVEF $\leq 40\%$ is considered as a prognostic factor for

heart failure and arrhythmic events [2]. Electrocardiography indices are computed from ECGs at rest, with high amplification and 24H Holter recordings. The measured variables are: presence, number and type of ventricular extrasystoles, late potentials and sinus variability [2][3]. However, these prognostic indices usually lack in sensitivity [4].

The objective of our study is to validate wavelet analysis (time-frequency analysis) as a tool to detect the patients at risk of sudden cardiac death after an acute Myocardial Infarction (MI). Our goal is to find a new marker more efficient than the classical ones (such as clinical markers).

In the following, we first describe the data extracted from the EMIAT database, and then we present the principle of the CARTEF Time-Frequency Abnormalities Stratification method used to assess the value of wavelet analysis for the prediction of sudden cardiac death. After that, we briefly describe the approach adopted to test the discriminant power of the wavelet coefficients. Finally, we present and discuss some of the results respectively provided by the CARTEF method and by discriminant analysis; they both show the efficiency of wavelet markers.

2 Materials and methods

2.1. Study populations

EMIAT (European Myocardial Infarct Amiodarone Trial) [5] is a database that was initially set up in order to evaluate the effect of amiodarone against Placebo for a population of patients surviving a recent Myocardial Infarction, with a left ventricular ejection fraction LVEF $\leq 40\%$ and age < 75 years. EMIAT enrolled 1486 patients who were followed for a mean of 21 months. 24-H Holter tapes were recorded during three visits. The tapes have been digitized at 1000 Hz, and for each 24 hour record six High Resolution ECGs (HR-ECG) have been computed, corresponding to six time sequences equally spaced over the 24 hour period. The EMIAT

database contains not only the ECG-HR signal of each patient but also clinical parameters like LVEF, age and sex, blood pressure, etc.

We extracted different groups from the EMIAT population. In a first step we constituted two patient groups: the "Control" group (154 patients) containing all clinical free patients (e.g. without angor, CABG, etc.) for whom Holter records (numbered 0,1,3) were available for all visits, with 6 noiseless sequences (3 during the night and 3 during the day), and another group, called "Sudden", containing 55 patients with a sudden cardiac death.

In a second step, we selected the patients with other, non sudden cardiac death causes (77 patients) that we called "Other Death" group and we merged the "Sudden Death" and the "Other Death" groups to form a new group that we called the "All Death" group.

2.2. Discrete wavelet transform

The orthogonal wavelet transform (Meyer transform) has the advantage to decompose the whole HR-ECG signal into a finite number of coefficients. We applied this transformation on $512=2^9$ points, extending from 128 ms before the beginning of the QRS complex up to 384 ms after QRS onset. The decomposition was performed for 9 different scales and four different leads (X, Y, Z and module). We thus obtained 511 coefficients for each lead.

2.3. Significant abnormality mapping of the HR-ECG

The CARTEF Time-Frequency stratification method [7] compares the time-scale representations of the HR-ECGs obtained for the population under study g_2 to a reference population g_1 . The significance of each abnormality is assessed by comparing the mean value of each of the wavelet transforms of the two studied populations by means of a one-way analysis of variance technique [6], using the F test to test for the null hypothesis that means are equal. For each patient, the wavelet transform coefficient $C_p(s,t)$ is computed at the time localization t for the scale s . We obtain the classic probability value $P_{s,t}(g_1, g_2)$ that the wavelet coefficients means are equal at scale s and time location t for populations g_1 and g_2 . Figure 1 shows the different processing steps involved in this method [7]. The p-values are computed for all s and t , thus providing a direct mapping of any abnormality of the time-scale components of the HR-ECG into a p-value axis. A three-dimensional representation of the mapping results, giving the p-value as a function of the wavelet location in the time-frequency plane, is shown in figure 2.

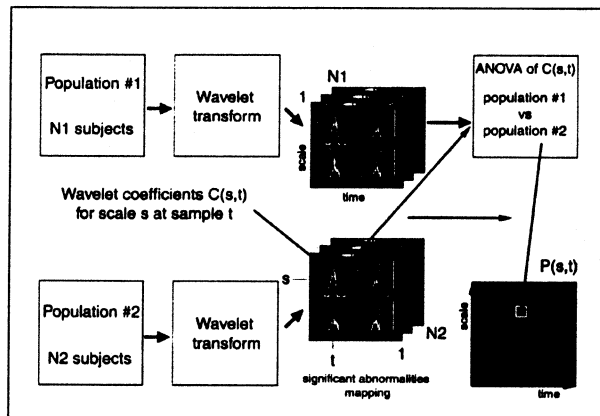


Figure 1. Schematic representation of the CARTEF time-frequency stratification method (reproduced with permission from [7])

2.4 Decision method

To assess the discriminating power of the wavelet coefficients, we selected all wavelets with a p-value <0.001 and combined them with the following clinical parameters: Left ventricular ejection fraction (LVEF), QRS duration at visit V0 (QRSV0), QT at V0 (QTV0), Heart rate at rest (HRRest), Heart Rate at V0 (HRV0), systolic (SBP) and diastolic (DBP) blood pressure. The decision method used for the assessment of the prediction power of the different descriptors was stepwise linear discriminant analysis.

3. Results

To test the repeatability of the stratification method, we randomly subdivided the "Control" group into two subgroups of 77 patients each and we compared one subgroup versus the other for all 6x3 time sequences. The mapping results of the wavelet coefficients of the HR-ECGs corresponding to the same time sequences of the two "Control" subgroups (figure 2) show that there are

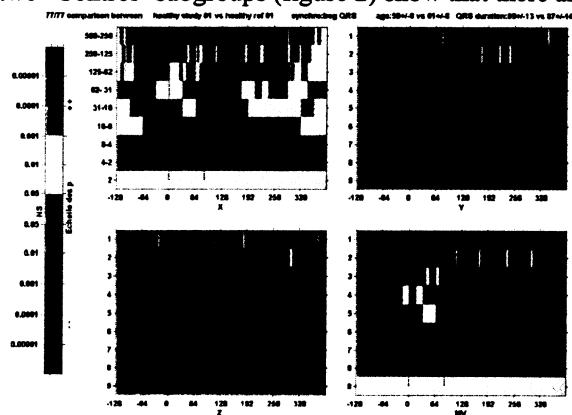


Figure 2. Comparison of the second "Control" subgroup of 77 patients versus the first "Control" subgroup at sequence 1 and visit 0. The vertical lines indicate the onset of QRS and the mean QRS end.

only minor differences within the QRS and the ST segment (p-values > 0.01).

We also studied the intra sequence, intra day variability of the Control group by comparing all sequences for each visit with the first sequence chosen as a reference. The mappings show that there are significant intra day differences, between sequences 4, 5 and 1 (figure 3), especially in the 31-500 Hz frequency range at the signal extremities.

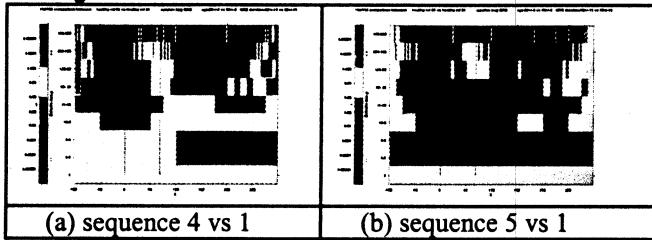


Figure 3. Comparison of different sequences of the "Control" group patients (N=154) for visit 0.

When comparing the "Sudden" group with the "Control" one for the same time sequences, we observed very significant differences ($10^{-5} < p\text{-value} < 0.001$) for different time-frequency locations (figure 4): intra QRS, at the end of QRS, and also in the ST segment, especially in the 8-32 Hz and 62-125 Hz frequency ranges.

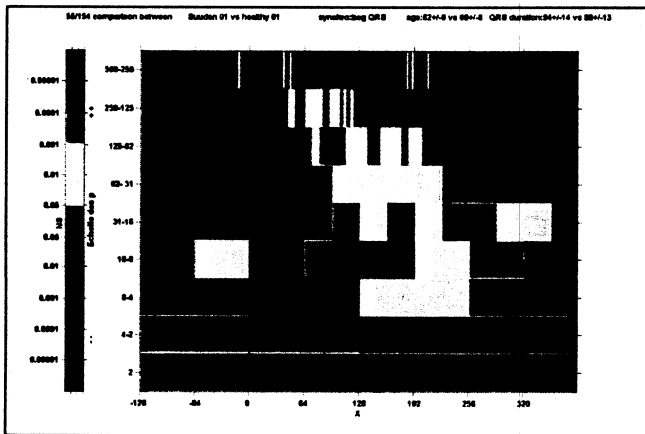


Figure 4. Comparison of the "Sudden" group versus the "Control" group.

Figure 5 shows the comparison between the "Sudden" group and the "Other Death" one. There is no difference on the CARTEF representation. So we decided to merge these two groups into the "All Death" group, and we compared it to the "Control" one. Figure 6 confirms that the significant differences are in the same time-frequency locations.

In a second step, we performed a discriminant analysis based on the wavelet coefficients corresponding to the areas in which the p-value is less than 10^{-3} . Five variables (w#3, w#5, w#12, w#25, w#91, w#92) fulfilled this

criteria. We also performed a discriminant analysis based on the clinical parameters provided by the EMIAT database. Seven clinical parameters have been used for this test: LVEF, QRSV0, QTV0, HRRest, HRV0, SBP and DBP.

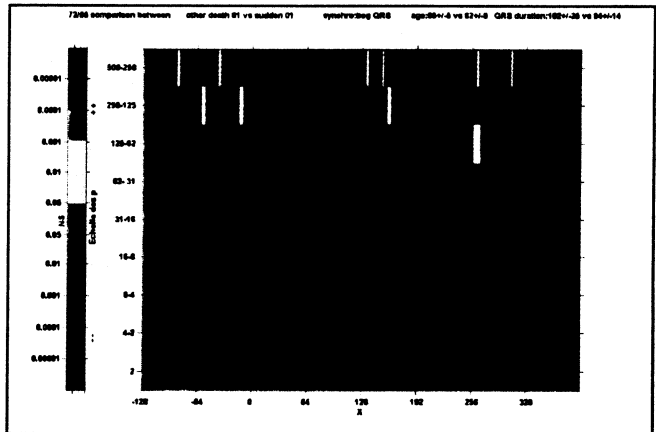


Figure 5. Comparison between the "other deaths" versus the "sudden" deaths groups.

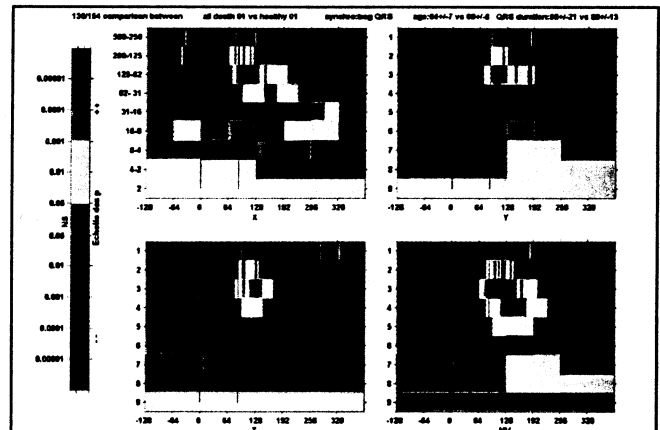


Figure 6. Result of the comparison of the "all death" versus the "Control" groups.

Table 1 summarizes the sensitivity and the specificity values of the classification results. It shows that the detection rate of patients at risk of sudden death is slightly better with the wavelet coefficients than the rate obtained with the clinical parameters (75.1% vs 73.2%). However, the combination of the two types of parameters (wavelet and clinical) provide a very substantial increase of the detection rate. Table 1 also indicates the descriptors that have been taken into account by the stepwise linear discriminant analysis with their order of entry in the calculation process. In all cases the first entered variable is wavelet coefficient w#12 (frequency range: 8-16Hz) located in the ST segment between 128 and 192 msec after QRS onset.

Table 1. The most relevant wavelet coefficients and clinical parameters selected by step-by-step linear discriminant analysis.

Descriptors	Sensitivity	Specificity	Total accuracy
w#12, w#91	52.7%	83.1%	75.1%
3 Clinical parameters*	65.5%	76.0%	73.2%
w#12, w#91 +3 clinical parameters**	70.9%	85.7%	81.8%

* entry order: HRV0, LVEF, QRSV0

** entry order: w#12, HRV0, LVEF, QRSV0, w#91

4. Discussion

The CARTEF representation showed a very good inter-visit stability for all chronologically equivalent sequences, both in the "Control" group and in the "Sudden" or "Other Death" groups. It also showed a very large variation between sequences 4, 5 and 1 for the same group of patients (see figure 3). These variations might be explained by circadian variations or by changes in the heart position related to changes of the patient activity, and for the variations at the beginning and the end of the analyzed signal, by cardiac frequency variations.

Discriminant analysis indicated that the discrimination power of the selected wavelet coefficients was quite satisfactory since the total accuracy obtained by using these coefficients was higher than the one obtained with clinical parameters, even if the sensitivity is slightly lower with wavelet coefficients. Another important result is that the overall accuracy is distinctly better when the two types of parameters are jointly used. Moreover, it's always the same wavelet coefficient, named w#12, that enters in the first step of the discriminant analysis calculation. This confirms that essential information is brought by wavelet coefficients for the prediction of patients at risk of sudden cardiac death.

We used the discriminant analysis as a method to highlight the advantage of the wavelet coefficients as markers of the patients at risk of sudden death. However, because of the statistical properties of the distributions of the wavelet coefficients, this analysis may not be efficient enough, and one could achieve even better results by using more efficient classification methods.

5. Conclusions

In this paper we have highlighted the importance of using wavelet coefficients. Indeed, wavelet decomposition results in a lot of information compared to the classical markers such as LVEF and cardiac frequency, but the diagnostic information contained in these wavelet coefficients is still limited and is only interesting if used jointly with the clinical markers. The

EMIAT database contains also patients with different other clinical problems (angor, CABG, etc.). The next step would be to study these additional clinical populations and to compare them with the "sudden" and the "other cardiac death" populations, and to imagine another diagnostic process to improve the sensitivity and the specificity of decision making by:

- choosing a more efficient decision method adapted to the EMIAT data base
- trying to understand the circadian variations
- and maybe, by using digital Holter recorders instead of the analog ones used in the EMIAT study.

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