Beat-to-Beat Quantification and Analysis of ST Displacement from Holter ECGs: A New Approach to Ischemia Detection

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Abstract

The beat-to-beat analysis of the ST displacements in 24-hours digital Holter ECGs is not yet a common practice. Typical problems relate to the need for a robust baseline estimation and to difficulty in defining a threshold which could accurately discriminate between normal and ischemic ST segments. This study presents an algorithm which aims to a new definition of transient ischemia using variables extracted by the frequency distributions of ST segment displacements. A logistic regression, applied to the data extracted form 20 certified normal and 24 certified ischemic Holter ECGs, enhanced the classification performance of ST segment depression in identifying ischemic episodes. Sensitivity and specificity reached 95.8% and 90%, respectively.

1. Introduction

Ambulatory ECG recording was initially introduced to monitor arrhythmia, but it soon spread as a tool to evaluate ischemic changes as well. Classical myocardial ischemia studies involving Holter recordings can be found in [1-3]. The ST segment measurements calculated from Holter recordings are usually achieved with averaging techniques with a single observation involving several beats. However, the development of a beat-to-beat ST segment time series should provide more reliable analysis; besides, it would allow bivariate analysis with other well-known beat-to-beat signals, such as RR and RTm interval time series.

The classification of an episode of myocardial ischemia on a Holter recording is usually related to ST depression crossing depth and time thresholds. Typically, a time threshold of 1 minute and a depression amplitude threshold of 1 mm (0.1 mvolt) are used. The choice of these thresholds is somewhat arbitrary, leading to false-positive and false-negative classifications. In particular the amplitude of the ST segment displacement varies with the subject so that a more general approach is required.

In this paper we present an algorithm, developed in the last two years, which develops a set of beat-to-beat time series. The algorithm provides the support for a complete and operator-independent off-line analysis of ambulatory ECG recordings, spanning heart rate variability, repolarization duration variability, and detection of transient myocardial ischemia.

2. Methods

The algorithm, available in both FORTRAN and ANSI C languages, is applied on a beat-by-beat basis, according to the following steps:

QRS detection: the occurrence of a QRS complex is estimated by achieving a parabolic interpolation in correspondence of a portion of a signal where the first derivative overcomes a fixed threshold. The peak of the parabola is proved to estimate the QRS apex (R point), with high reliability [4]. In order to exclude artifacts and non ventricular events, a simple one-layer feed forward neural network (PERCEPTRON) has been developed. The NN has been trained to recognize sinus vs. non-sinus events on the basis of 100 sinus QRS (including examples with perturbing noise) and 100 non-sinus episodes (including different species of premature beats as well as various kind of artifacts). As far as the two-class problem sinus vs. non-sinus event is concerned, the perceptron was proven to be a robust classifier [5].

Fiducial Isoelectric Point: Once the R point has been detected a relative fiducial point is searched in a 90 msec window prior the R point by minimizing the first derivative of the signal and the absolute product between the derivative and the signal itself.

T wave detection: the peak of the T wave is detected, as for the R wave, using parabolic interpolation. This time, however, the parabola is fitted through a larger number of samples, due to the less enhanced sharpness of the T-wave peak. In addition, a

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second long portion of ECG signal following the R wave is low-passed filtered before fitting the parabola (Hamming window, 15 Hz cut-off).

Baseline Estimation: a beat specific isoelectric line (baseline) is calculated by interpolating with cubic splines six fiducial points, three prior and three following the beat under analysis. Several authors [6],[7] enhanced the advantages in using spline techniques rather than aggressive high-pass filters. Indeed, the cubic spline interpolation, not being a filter, avoids the problem of phase distortion of the ST segment which can be dramatic [8].

ST segment measurements: a heart rate dependent ST segment window is considered as the interval between two points RS1 and RS2 selected according to the following empirical formulae (which express msec from R point):

$$RS1 = 40 + k1\sqrt{RR} \quad (1)$$

$$RS2 = 40 + k2\sqrt{RR} \quad (2)$$

The constants k1 and k2 are set by forcing, at an heart rate of 60 bpm, RS1=70 msec and RS2=110 msec (k1=0.948 and k2=2.21).

The ST segment variables are then measured with respect to the estimated running baseline. These variables consist, at the window extremes, of the values of displacements and, within the window, of the averaged displacement, of the area between the baseline and the ECG signal, and of the ECG slope. The averaged displacement (AVD) is calculated as the mean value, in the ST segment window, of the regression line (least mean square) fitting the samples available in the same window. The slope of this line (in mm/msec), is considered to estimate the slope of the ST segment. The area is calculated, again in the ST window, with Simpson 1/3 rule and it is set to missing in the case of an ST segment crossing the baseline.

Noise exclusion. Different levels of perturbing noise can affect some ECG signal measures more than others. For instance, a low-frequency component oscillation due to breathing interference produces baseline drifts which generally do not compromise QRS detection while making ST segment displacement measures very difficult. For this reason the algorithm sets up a 3-digit code which takes into account various disturbances of the ECG signal. The first digit takes into account the nature of the identified QRS and it is set to values different than 0 by either the NN classifier or by short-long configuration of consecutive RR intervals. The second digit takes into account parameters derived by the estimated baseline and it set to values other than 0 in case of too wide oscillation of the baseline which would make ST segment measures not reliable, even with the cubic spline estimation. The last digit takes into account the noise level of the ST segment. A procedure counts the number of sign changes (strokes) during the ST segment with 4 different thresholds (0.02, 0.2, 0.3 and 0.5 mvolt); a ST segment is then considered reliable when all 4 stroke counts are smaller than relative thresholds. In order to determine the set of thresholds, a database of 2000 beats randomly collected from 10 normal and 10 ischemic tracings was created. The ST segment of the 2000 beats were then visually classified by two expert physicians and the best matching set of thresholds was calculated.

3. Population and Data Acquisition

The study population consisted of 44 ambulatory tracings acquired with three different recordings (Marquette analog 8500 series, Marquette Digital SEER, and ACS analog 8300 series). All the ECGs were played-back with a Marquette Laser Holter system at a sampling frequency of 128 Hz (120 Hz for the SEER recorder). The raw ECG tracings were then transferred to reel-to-reel 9-track magnetic tapes and finally loaded on a SUN Sparcserver 4/470 computer. All the positive tracings (n=24, ages from 39 to 85, 6 females) were chosen from a larger study involving subjects with coronary artery disease (all subjects had positive exercise-test, all but one positive thallium-201 test and half of them positive angiogram). The control tracings (n=20) consisted of 10 young healthy individuals (age ranging from 23 to 31, two females) and 10 older certified normal smokers extracted from another study (ages from 25 to 58, 4 females).

4. ST Segment Statistical Measurements and Analysis

Major hypothesis is that patiences with evidence of myocardial ischemia have significantly different ST segment frequency distributions than normals. In particular, episodes of ST displacement should cause large tails in the distributions, producing wider and more skewed profiles. The amount of distortion in the frequency distribution should depend upon the duration of ST depression. In Fig. 1 and 2 the histograms of a normal and of an ischemic subject are respectively reported with some of the statistical variables annotated. The histograms of the ST displacement time series were extracted, and spread and skewness coefficients were then calculated as function of the percentile positions (SAS software: statistical procedure Univariate). Six different spreads and three different skewness parameters were considered as follows:

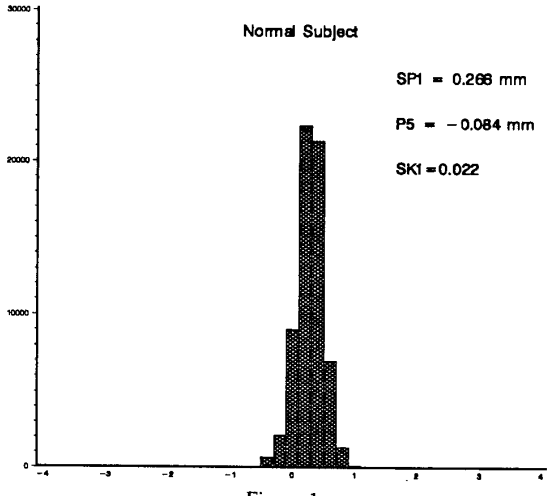

Figure 1

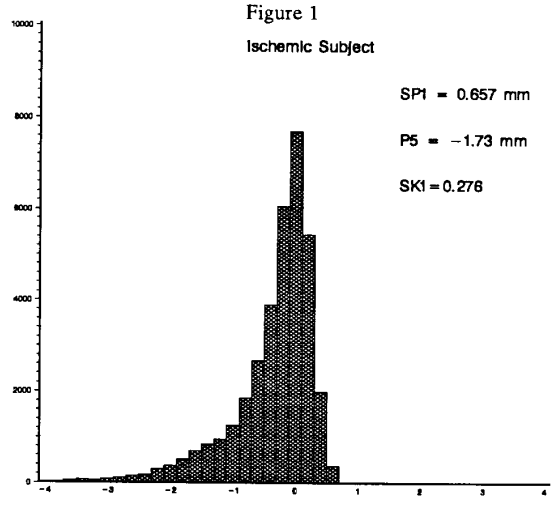

Figure 2

SP1=P75-P25 SP2=P90-P10 SP3=P95-P5

SP4=P50-P25 SP5=P50-P10 SP6=P50-P5

$$SK1 = \frac{2*P50-P25-P75}{P75-P25} \qquad SK2 = \frac{2*P50-P10-P90}{P90-P10}$$

$$SK3 = \frac{2*P50-P5-P95}{P95-P5}$$

where Pxx indicates the xx^{th} percentile location. SP1, SP2 and SP3 relate to symmetrical spread while SP4, SP5 and SP6 relate to left-side spreads by using as a reference the median of the distribution (P50).

The differences between the mean and the median values of the spreads, skewness and all the percentiles were tested respectively by a non-pooled Student's t-test and by a parametric Mann-Whitney test. Traditional statistics such as mean, standard deviation and third order central moment (skewness) were also analyzed. Logistic regression models were finally applied using the most significant variables as covariates and sensitivity-specificity figures were extracted.

5. Clustering

Quantification of ischemia is obtained by "clustering" back in time the beats in the frequency distribution tails, a tail being approximated by either the 5th or 10th percentile. A cluster is defined as a 20 second portion where at least 2/3 of the non-noisy ST segments are lower than either the 5th of 10th percentile. An episode of transient ischemia is finally defined as an ensemble of consecutive clusters. Myocardial ischemia can then be identified on the basis of RS1, RS2 and the averaged displacement AVD.

6. Results

Table I reports the results relative to the t-test applied on the quantitative measurements. The table refers to the t-test achieved on the average displacement variable (AVD). Similar results are obtained using RS1 and RS2. Parametric Mann-Whitney test enhanced the same characteristics in the three variables.

TABLE I

	Mn-N	Mn-I	SD-N	SD-I	p
MEAN	0.484	-0.572	0.421	0.603	<.0001
SD	0.413	0.510	0.114	0.134	0.013
SP1	0.469	0.599	0.155	0.183	0.0167
SP2	0.949	1.208	0.287	0.338	0.0088
SP3	1.314	1.640	0.377	0.430	0.011
SP4	0.252	0.331	0.089	0.113	0.014
SP5	0.563	0.726	0.208	0.234	0.019
SP6	0.809	1.025	0.302	0.312	0.025
SK1	0.085	0.098	0.087	0.084	0.61
SK2	0.172	0.193	0.129	0.099	0.56
SK3	0.210	0.240	0.141	0.105	0.44
P5	-0.275	-1.525	0.448	0.681	<.0001
P10	-0.029	-1.226	0.404	0.653	<.0001
P25	0.283	-0.831	0.402	0.624	<.0001
P50	0.535	-0.500	0.435	0.614	<.0001
P75	0.746	-0.232	0.454	0.594	<.0001
P90	0.920	-0.018	0.469	0.596	<.0001
P95	1.039	0.115	0.468	0.602	<.0001

Mn-N: Mean Normals, Mn-I : Mean Ischemics
SD-N: Standard Deviation Normals
SD-I: Standard Deviation Ischemics

Two findings are evident from Table I: the differences between the two populations in all the spreads and in all the percentile locations are significant, the differences between all the measures of skewness are never significant. We can conclude that the ST displacement frequency distributions of ischemic subjects are characterized by wider and left-shifted profiles. The failure in the detection of significant differences in the skewness parameters is mainly due to the occurrence, even in the normal subjects, of transient conditions such as small postural changes and (especially on young individuals) early repolarization phenomena that made the ditributions always asymmetric (normality tests were performed giving negative results 98% of the times).

The logistic regression analysis led to similar conclusions. When used as single explanatory variables in the logistic model, all the percentile parameters were highly significant ($p < 0.001$ with maximum likelihood parameter estimation); the spread were significant ($p < 0.01$) and the skewness never significant. Combination of any of the lower percentiles (P5, P10 or P25) with any of the spreads led to the best model fit. For instance, by using P5 and SP4 as explanatory variables, the logistic model was fitted with p=0.0001 and the predicted probabilities of the two groups could be separate with one false-negative (sensitivity=95.8%) and two false-positives (specificity=90%).

Episodes of ischemia identified with clustering technique showed high correlation with the ones visually extracted by physicians. In particular, by using P5 as threshold it was possible to find all the visually detected episodes (the use of P10 just added new beats to the already identified episodes).

7. Conclusions

The ability to discriminate between normal and ischemic ambulatory ECG recordings by means of ST segment frequency distribution predictors suggests a useful new approach for the detection of ischemia. The development of an algorithm for performing heart rate variability, repolarization variability and ST displacement analysis should provide insight into the pathophysiology of cardiac disorders.

The algorithm will be applied to the 1000 patients of the Multicenter Study of Silent Myocardial Ischemia (MSSMI) starting January 1993.

8. Acknowledgment

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9. References

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