computer methods and programs in biomedicine 92 (2008) 198–204

journal homepage: www.intl.elsevierhealth.com/journals/cmpb

Nonlinear dynamics analysis of electrocardiograms for detection of coronary artery disease

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ARTICLE INFO

Article history:
Received 11 April 2007
Received in revised form
12 June 2008
Accepted 4 July 2008

Keywords:
Rest ECG
Coronary artery disease
Computerized
Recurrences points
Mutual information
Fractal dimension

ABSTRACT

A computerized approach of nonlinear dynamics analysis of electrocardiogram (ECG) signals was applied for the detection of coronary artery disease (CAD). The proposed nonlinear dynamics descriptors were derived from 12-lead rest ECG data, and evaluated by originally developed computer software.

Fluctuations of potentials of ECG leads that occur during the period of 20 ms with a magnitude of 5–20 μV were significantly less beat-to-beat predictable in ischemic versus non-ischemic patients. The well-known nonlinear dynamics descriptors, recurrences percentage, mutual information, fractal dimension, and a new descriptor, next embedding dimension error, were good quantitative descriptors of fluctuations. They were significantly different ($<p = 0.00001$) in males with (108 patients) and without (54 patients) coronary artery lesions. The analysis of small fluctuations required a careful preprocessing technique based on knowledge of specifics of measurement errors and physiology of ECG signals. We considered finite differences of measured potentials with the time step of 20 ms as the initial source for nonlinear analysis. In nonlinear dynamics analysis, we also included such time moments that only belong to P- and T-waves or baseline drift with small positive slopes that allowed us to extract, under normal conditions, initial halves of P- and T-waves that displayed a better capacity to classify ischemic patients.

1. Introduction

Coronary artery disease (CAD) is the major cause of morbidity and mortality in adults. Several studies suggest that the prevalence of CAD in asymptomatic 50-year-old males is 15–20%, and some studies that include female data suggest a prevalence of about 5%. If these patients are not investigated or treated they are at high risk of first fatal myocardial infarction and sudden death [1]. According to several studies, 1–2 million middle-aged males in the USA with “silent” myocardial ischemia have false-negative exercise electrocardiogram (ECG) tests [2]. Recognition of coronary artery stenosis from the rest ECG in non-acute ischemia is limited. Modern computer-based tools of signal analysis (chaos theory, spectral, wavelet, nonlinear analyses) are being developed and can potentially improve diagnosis of non-acute ischemia. Even inaccurate detection of CAD based on rest ECG data can be combined with exercise ECG and myocardial scintigraphy to improve CAD recognition [3,4].

Despite the rise and spread of new diagnostic methods, non-invasive diagnostic methods are popular due to their low cost, safety, accessibility, and potential to detect CAD at

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0169-2607/$ – see front matter
doi:10.1016/j.cmpb.2008.07.002

early stages when visible luminal obstructions are not formed. Many researchers investigated the relationship between QT-interval variables and extent of coronary artery lesions [5,6]. Total cosine of R-to-T angle, T-wave morphology dispersion, T-wave loop dispersion, and normalized T-wave loop area have proven useful for identifying patients who would benefit from the implantable cardioverter-defibrillator [7–9]. Data regarding the relationship between the morphology and extent of the T-loop, and localization of coronary artery stenosis, is lacking. T-loop vector morphology seems to be more sensitive to coronary occlusion than QT dispersion measures [10]. Application of high-frequency components of the QRS complex for enhanced detection of myocardial ischemia has been studied [11].

In recent years, we have focused on recognizing coronary artery stenosis from the rest ECG. A multidipole heart electrical activity model has been developed to determine coronary artery lesions. The accuracy and value of the multidipole heart model was verified by coronary angiography results. The efficiency of this method was about 65% but over-diagnosis was about 30% [12]. The forms of P-, QRS-, and T- wave were coded using a singular value decomposition (SVD) approach, and rest ECG SVD parameters were used for the detection of coronary artery stenosis and its localization [13,14].

In this study, we applied the methodology of analysis of nonlinear dynamic systems and their descriptors (recurrences percentage, mutual information, and generalized fractional dimension) for classification of digital ECGs [15–17]. These descriptors were sensitive for the detection of small irregularities in T, P, QRS, and baseline ECG patterns that occur in a few minutes, and showed up well in the classification of CAD patients. We adapted traditional analysis of nonlinear dynamics specifically to ECG signals. To increase signal-to-noise ratio, the traditional lead potentials ECGs were replaced by finite difference consistent with the current period: 20 ms. Looking for small beat-to-beat irregular current flows (the frequency of which may be increased in ischemic tissues), we included in nonlinear analysis the time moments only at which lead potentials had positive slopes that corresponded to fluctuations of 5–20 μV magnitude. We carried out analysis for detection of optimal values for problem at hand of time delay, embedding dimension, and radius region that constitute three main free parameters in any nonlinear dynamics analysis [15–17].

Calculations were done by originally developed computer software written in Java language. Parameters were estimated for a set of 162 patients who had undergone coronary artery angiography. Calculations were done on a personal computer (2.8 GHz, 512 MB of memory). Estimation of nonlinear dynamics descriptors required about 10 s for each ECG of 5-min duration and 12 leads.

2. Methods

2.1. Initial data preprocessing

Twelve-lead rest ECGs of 5-min duration were recorded at a sampling rate of 2000 Hz with 1/3200 mV resolution. Outsets of R–R intervals were estimated by a computer program so that information about QRS complex and P- and T-waves could be included. Using the outsets $\{t_n\}_{n=1}^{N}$, a time moment t is considered as a *non-QRS-complex time point* if

$$\min_{t_n \le t}(t - t_n) > 0.1\,\text{s}.$$

If the opposite condition

$$\min_{t_n \le t}(t - t_n) \le 0.1\,\text{s}$$

holds true, then the time moment is considered as a *non-P- and non-T-wave time point*. Such a classification of time moments does not require exact knowledge of durations of QRS complex and P- and T-waves. To decrease baseline drift and current noise, measured ECG leads $U = U(t)$ were filtered by the following comb filter:

$$x(t) = U\left(t + \frac{0.5}{F_c}\right) - U\left(t - \frac{0.5}{F_c}\right), \tag{1}$$

where F_c denotes the current frequency ($F_c = 50$ Hz in our case). Such a simple approach removes slow components of the baseline drift of the ECG and reduces mains noise. Note that (1) filtration spreads QRS, P- and T-waves, and the resulting signal $x(t)$ is proportional to the current flow along a lead associated with potential $U = U(t)$. We will subsequently refer to lead potentials that were filtered by formula (1) as “filtered lead potentials”.

2.2. Nonlinear dynamics analysis and its adaptation to ECG signals

Let us consider $x(t)$ as a particular trajectory of a real-valued random process X. Eckmann et al. proposed a graphic method of visualization of recurrences [15]. Three years earlier, Takens [16] affirmed the possibility of reconstruction of original behavior of a multidimensional dynamic system by using a time series of one variable analyzed by the time-delay method. The approach proposed in [15,17] can be considered as a generalization of cross- and auto-correlation analysis of time series.

Let $x_i = x(i/FS)$, $i = 0, 1, \ldots, n-1$, be n samples of the trajectory $x(t)$ sampled with the sampling frequency FS. The approach consists in defining m-dimensional samples X_i build from the samples x_i and their $(m-1)$ delayed values:

$$X_i = (x_i, x_{i-\tau}, \ldots, x_{(m-1)\tau}).$$

Having n samples x_i, we can build $N = n - (m-1)\tau$ samples of x_i. Successions x_i define a trajectory of m-dimensional points and are used in evaluation of the recurrence matrix. Let a_{ij}, i, $j = 1, \ldots, N$, be the elements of the matrix. By definition a_{ij} can take only two values [15]:

$$a_{ij} = \begin{cases} 1 & \text{if } |X_i - X_j| \le r, \\ 0 & \text{otherwise}. \end{cases} \tag{2}$$

Here $|X_i - X_j|$ indicates a distance between samples X_i and X_j, and r is a positive threshold (parameter) called radius. If $a_{ij} = 1$, ij is referred as a recurrent point and, X_i and X_j are said to be recurrent. By construction, $a_{ij} = 1$ and $a_{ij} = a_{ji}$ for i, $j = 1, \ldots, N$. These symmetries influence definitions of quantitative descriptors of the matrix. A standard characteristic