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Characterization of the nonlinear content of the heart rate dynamics during myocardial ischemia

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ABSTRACT

We develop a method to quantify the changes in heart rate dynamics during local myocardial ischemia induced by a percutaneous transluminal coronary angioplasty procedure (PTCA). The method introduces an index measuring the nonlinear content of the beat-to-beat (RR) time series by using nonlinear time series techniques such as surrogate data analysis and average mutual information.

The index is applied to RR data from 67 subjects obtained before, during, and after the ischemic period and shows an increase in the nonlinearity of the cardiac control dynamics during ischemic and reperfusion stages. The nonlinear index is also used to characterize the effects of performing the coronary occlusion at different arteries and distances. We observe that the effect of ischemia becomes larger as the occlusion distance is reduced, and that most of the changes in the nonlinear content of the dynamics occur at long time scales typically related to sympathetic modulation of the cardiac rhythm (6–25 s).

1. Introduction

Cardiac ischemia occurs when the myocardium receives a reduced blood supply due to a partial or complete blockage of a coronary artery. During the ischemic period, the lack of oxygen in the tissue alters the electrical and mechanical properties of the beating heart. As a consequence, an abnormal firing pattern of the afferent fibers occurs, leading to dynamical changes in the autonomic heart regulation [1]. In a percutaneous transluminal coronary angioplasty (PTCA), a balloon is inflated inside a coronary artery inducing a localized heart ischemia during a short-time period [2,3]. PTCA provides an excellent experimental framework in order to study the dynamical changes in the cardiac control system in response to an ischemic process [4,5].

Cardiac rhythm dynamics reflects the coupling of the physiological mechanisms involved in the cardiac function at different timescales [6,7]. Indeed, heart rate variability (HRV) has already been established as a reliable clinical marker of the autonomic cardiac activity [6]. The high frequency (HF) band (0.16–0.4 Hz), for instance, is related to the vagal activity and contains the synchronization/coupling of the heart rate with the respiratory system. Similarly, the spectral content in the normalized low frequency band (LF) (0.04–0.15 Hz) is normally considered as an indicator of sympathetic modulation [8]. Several linear and nonlinear techniques have been developed to assess different heart dynamical regimes from HRV data. Some of these methods have been successfully applied to the detection, classification or risk estimation of different clinical conditions [6,9].

Monitoring of the heart rate before, during and after balloon occlusion may provide insight into the autonomic cardiac function in response to ischemia. Linear HRV methods have previously been used in short-time PTCA data, indicating an increase of the sympathetic activity during and in the few minutes immediately after the angioplasty [10]. However, linear techniques disregard the nonlinear couplings between the regulatory systems involved in ischemic and reperfusion stages. Thus, a specific method for quantifying the nonlinearity of short-time HRV series may improve the characterization of the autonomic response to ischemia.

Standard nonlinear time series techniques such as correlation dimension, phase reconstruction or detrended fluctuation analysis are based on measures of the complexity of the data [11,12]. These approaches typically require long time series containing a full exploration of the dynamical attractor of the system, making them unsuitable for the nonlinear analysis of short-time HRV series. As an alternative, information-theoretic measures can be an adequate approach for the analysis of short-time series since they do not necessarily require long data series. In particular, time-delayed

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average mutual information (AMI) has successfully been applied to HRV data analysis [9]. AMI characterizes the degree of correlation between two points of a time series separated by a certain time lag, thus defining an information flow within the evolution of the time series. This magnitude provides information about both linear and nonlinear correlations in the data, and it is specially suitable in physiological data processing [13,14] due to its robustness under the presence of noise [11]. When applied to RR data, it has been shown that AMI is capable to quantify temporal correlations in the feedback control loop of the heart control system at different time scales [15,16].

The main aim of the present study is to develop a method in order to assess the changes in the nonlinear content of short-term RR dynamics in response to short ischemic and reperfusion stages. The method is not intended to be used as a risk prediction procedure but rather as a technique to analyze the response of the autonomic control system to an ischemic process. To this end, we present a quantitative nonlinear index which combines surrogate data analysis and information-theoretic measures.

Surrogate data analysis allows performing a statistical hypothesis test under certain assumptions regarding the time series [17–19], and in particular its nonlinear content. Mutual information is used in order to determine the linear and nonlinear correlations of the data, whereas a linear surrogate set allows to define a net increment in nonlinearity with respect to the linear properties of the analyzed time series. We hypothesize that this intrinsic nonlinearity is a reliable indicator of the dynamical changes during ischemia and reperfusion.

Previous studies have already developed methods that combine mutual information and surrogate data in order to assess the nonlinear content of a time series [20–22]. The novelty of our approach is to provide a quantitative measure of the net nonlinear content of the system at different stages in the procedure. Specifically, the method presented here allows to compare HRV data obtained before, during and immediately after balloon inflation, thus detecting the effects of induced ischemia in the nonlinearity of the heart rhythm regulation.

The outline of the paper is as follows: in Section 2, we describe the RR data extraction, the different grouping of subjects and the time segments of data considered in the study. We also introduce in this section the nonlinearity index as a measure of the nonlinear content of a time series data segment. We report the main results of the study in Section 3, where we assess the changes in the nonlinear content of RR data under different conditions (occlusion arteries, occlusion distances, frequency bands). Final discussion about the main results of the study is given in Section 4, as well as a qualitative physiological interpretation in terms of dynamical changes in the heart rate control system.

2. Materials and methods

2.1. Database

RR sequences before, during and after the PTCA procedure were obtained from ECG recordings of the STAFF-III Study Database [23,24]. Among the 108 subjects included in the database, only 67 patients who met the following criteria were considered in the study: no history of coronary bypass surgery (without left or right ventricular hypertrophy), no evidence of right bundle branch block, QRS duration less than 120 ms measured on a previous control ECG, no clinical or ECG evidence of previous myocardial infarction and artery occlusion duration of at least 3 min. After the selection of the subjects, the mean duration of the artery occlusions was 4.5 min (4.5 ± 1.2 min). The ECG recordings were obtained within an interval of approximately 5 min before balloon inflation and 3 min after the PTCA procedure was finished. The ECG data was obtained from the six precordial monopolar leads (v1–v6) with a sampling frequency of 1 kHz. Signal-to-noise ratio (SNR) was calculated by estimating the noise in an isoelectric portion of the ECG using a 100 ms window from the ST segment. SNR was then calculated as the ratio between the RMS of one ECG beat (signal) and the RMS of the 100 ms window (noise). The lead which presented the largest signal-to-noise level was used for the extraction of the RR data analyzed in this study.

An adaptive filtering procedure based on LMS algorithm was used in order to remove the artifacts. For detection of normal sinus beats, artifacts and ectopic beats or premature ventricular contractions were removed from the RR signal using a 5-beat sliding window algorithm rejecting any beat with an interval difference higher than 15% of the window average. In order to obtain uniformly sampled data, the RR time series was interpolated using cubic splines and resampled at a frequency of 2 Hz.

2.2. Data, subjects and groups

We study whether there are significant changes in the nonlinear content in the RR time series for segments of data taken before, during, and after the PTCA surgical procedure (see Fig. 1). In particular, we consider the first and last 180 s of data within the regime previous to inflation (PRE1, PRE2), during inflation (PTCA1, PTCA2), and post balloon deflation (POST) as shown in Fig. 1. PRE, PTCA and POST segments correspond to normal, ischemic, and reperfusion regimes, respectively. We take two segments per regime in order to check whether the results are sensitive or not to the particular time segment considered for the analysis.

Each of the previous regimes are analyzed for a set of 67 patients. Among them, 63 subjects are classified depending on the occlusion

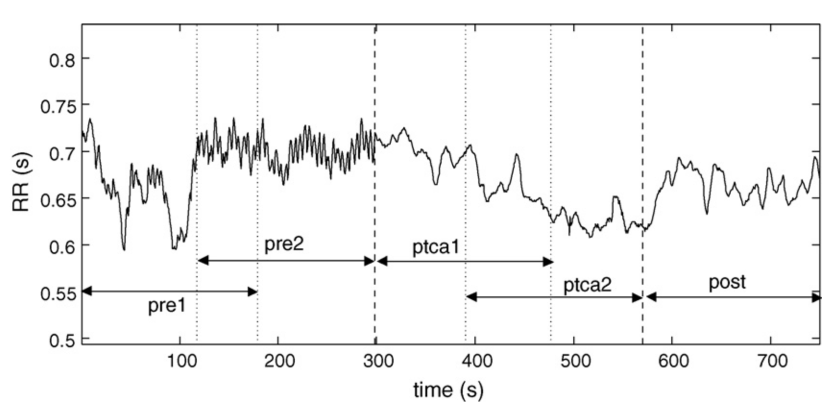

Fig. 1. Description of the segments being studied. PRE1 and PRE2 correspond to the period before inflation, PTCA1 and PTCA2 to the inflation interval (ischemia) and POST to the time after the balloon has been deflated (reperfusion).