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Comparison of time-domain, frequency-domain and non-linear analysis for distinguishing congestive heart failure patients from normal sinus rhythm subjects

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ABSTRACT

It is known that patients with congestive heart failure have reduced ability to modulate heart rate in comparison with normal subjects. However, the characteristics of these changes is not well understood. This study therefore investigated the characteristic features of heart rate changes to assess how they differed between both groups. Fifty-two normal sinus rhythm subjects and 18 congestive heart failure patients from the PhysioNet database were studied. Nine common heart rate indices were studied: three time-domain indices (MEAN RR interval, standard deviation of successive RR SDNN, and square root of mean squared differences of successive RR RMSSD), three frequency-domain indices (normalized low-frequency power LF_n, normalized high-frequency power HF_n, and their ratio LF/HF), and three non-linear indices (vector length index VLI, vector angle index VAI and sample entropy SampEn). Two 5-min segments from every subject, neither of which had any ectopic beat, were analyzed. The statistical differences between the two clinical groups for the first and second segments, and their average were determined for all nine indices. Results showed that there was no significant difference between the two 5-min RR interval segments for any technique. All frequency-domain and non-linear indices, but only one time-domain index (SDNN), were significantly different between subject groups. However, some indices were much more sensitive to the clinical differences than others; with the best performing techniques, one non-linear index VLI and one time domain index SDNN, followed by all three frequency indices of LF_n, HF_n and LF/HF, and finally two of the other non-linear indices VAI and SampEn. A simple RBF SVM-based classification algorithm gave a good performance for classifying the CHF and NSR subjects. And the mean *Se*, *Sp* and *Acc* of SVM classifier from 10 folds were 91.31%, 90.04% and 90.95% respectively. We have shown that there are characteristic differences in heart rate changes between congestive heart failure and normal sinus rhythm, suggesting characteristic rhythm differences.

1. Introduction

Heart rate variability (HRV) analysis is a non-invasive method for assessing the function of the cardiovascular autonomic nervous system (ANS) [1,2]. Depressed HRV has been used as a predictor of risk after acute myocardial infarction [3], and as an early warning sign of diabetic neuropathy [4]. In addition, low HRV has been observed in patients suffering from dilated cardiomyopathy [5], fetal distress conditions, and obstructive sleep apnea [6,7], as well as congestive heart failure (CHF) [8–11]. CHF is a typical degeneration of the heart function featured by the reduced ability for the heart to pump blood efficiently [7]. It is a difficult condition to manage in clinical practice, and the mortality from CHF is high [12–16].

For healthy subjects, it has been proven that the increased sympathetic and the decreased parasympathetic activity results in the decrease of mean RR interval, as well as the decrease of indices of the standard deviation of beat-to-beat intervals (SDNN), low frequency content (LF), and also non-linear indices VAI and VLI [17]. Moreover, the increased parasympathetic activity has been proven to be a the major contributor to the increase in the index for high frequency (HF) content [18]. HRV analysis has also given an insight

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into understanding the abnormalities of CHF, and can also be used to identify the higher-risk CHF patients. Depressed HRV has been used as a risk predictor in CHF [9,11,19,20]. CHF patients usually have a higher sympathetic and a lower parasympathetic activity [9,20]. Typical HRV analysis for CHF patients include the following publications: Nolan et al. performed a prospective study on recruited 433 CHF patients and found that SDNN was the most powerful predictor of the risk of death for CHF disease [13]. Binkley et al. studied 15 healthy subjects and 10 CHF patients, and reported that parasympathetic withdrawal, in addition to the augmentation of sympathetic drive, is an integral component of the autonomic imbalance characteristic for CHF patients and can be detected noninvasively by HRV spectral analysis [9]. Rovere et al. studied 202 CHF patients and reported that the LF component was a powerful predictor of sudden death in CHF patients [21]. Hadase et al. also confirmed that the very low frequency (VLF) content was a powerful predictor from a 54 CHF patient study [2]. Woo et al. studied 21 patients with heart failure and demonstrated that Poincare plot analysis is associated with marked sympathetic activation for heart failure patients and may provide additional prognostic information and an insight into autonomic alterations and sudden cardiac death [20]. Guzzetti et al. [22] studied 200 CHF patients and found significantly lower normalized LF power and lower $1/f$ slope in CHF patients compared with controls. Moreover, the patients who died during the follow-up period presented further reduced LF power and steeper $1/f$ slope than the survivors [23]. Makikallio et al. studied 499 CHF patients and showed that a short-term fractal scaling exponent was the strongest predictor of mortality of CHF [24]. Poon and Merrill studied 8 healthy subjects and 11 CHF patients, and found that the short-term variations of beat-to-beat interval exhibited strongly and consistently chaotic behaviour in all healthy subjects but were frequently interrupted by periods of seemingly non-chaotic fluctuations in patients with CHF [19]. Peng et al. used FDA analysis and confirmed a reduction in HR complexity in CHF patients [25]. Liu et al. studied 60 CHF patients and 60 healthy control subjects, and reported decrease of ApEn values in CHF group [26]. Costa et al. used the multiscale entropy method for classifying CHF patients and healthy subjects, and reported that the best discrimination between CHF and healthy HR signals with the scale 5 in the multiscale entropy calculation [27].

All those studies have verified that decreased HRV was associated with the increased mortality in CHF patients. However, detailed analysis of the power of the indices to distinguishing CHF from normal cardiac function is lacking. Existing studies included the work of Pecchia et al. that compared a limited number of time-domain and frequency-domain indices [28], the work from Mietus et al. comparing the performance of a family of pNNx indices, defined as the mean number of times per hour in which the change in consecutive normal sinus intervals exceeds x ms, [29], and the work from Isler et al. using a wavelet entropy method [7]. However, investigations comparing a wide range of indices is missing. Evaluating how well the common HRV indices can separate CHF patients from normal subjects could lead to an important clinical tool. This study therefore investigated the commonly used short-term HRV indices, subdivided into three groups: time-domain, frequency-domain and non-linear, to compare their abilities to differentiate normal sinus rhythm (NSR) subjects and CHF patients.

2. Method

2.1. Data

RR interval time series data were from a free-access, on-line archive database in http://www.physionet.org [30]. The original ECG signals were digitized at 128 Hz, and the beat annotations were obtained by automated analysis with manual review and correction. Fifty-two NSR subjects and 18 CHF patients were studied. Two 5-min RR segments from every subject/patient, neither of which had any ectopic beat, were analyzed. Fig. 1 shows the examples of 5-min RR segments from NSR subjects and CHF patients respectively.

2.2. HRV index calculations

2.2.1. Time-domain indices

The mean value (MEAN) of RR intervals, the standard deviation (SDNN) of RR intervals and the square root of mean squared differences of successive RR intervals (RMSSD) were used as time-domain indices [31,32], defined as:

$$\mathrm{MEAN} = \frac{\Sigma_{\mathrm{n}-1}^{\mathrm{N}} RR_n}{N} \tag{1}$$

$$\mathrm{SDNN} = \sqrt{E\left[(RR_n - E(RR_n))^2\right]} \tag{2}$$

$$\mathrm{RMSSD} = \sqrt{\mathrm{E}\left[(\mathrm{RR_n} - RR_{n+1})^2\right]} \tag{3}$$

where RR_n denotes the n^{th} RR interval.

2.2.2. Frequency-domain indices

The AR method can be used for the analysis of frequency domain. AR method of order p is expressed as the following equation [33]:

$$\mathrm{x[n]} = -\sum_{\mathrm{k}=1}^{\mathrm{p}} a(k)\,x[n-k] + w[n] \tag{4}$$

where $a(k)$ are the AR coefficients and $w[n]$ is white noise of variance equal to σ^2. The Burg method is used to get the AR model parameter. The power spectrum of a p^{th} order AR process is [33]:

$$\mathrm{P^{BU}}(f) = \frac{E_p}{\left|1 + \sum_{k=1}^{p} a_p(k)\,e^{-j2\pi fk}\right|^2} \tag{5}$$

where E_p is total least square error.

Burg's method with an order of 16 was used to produce the HRV frequency spectrum, which was integrated across the low-frequency power (0.04–0.15 Hz) and high-frequency power (0.15–0.40 Hz) spectra. The normalized low-frequency power ($\mathrm{LF_n}$) and normalized high-frequency power ($\mathrm{HF_n}$), and their ratio (LF/HF) were used as the frequency-domain indices [31].

2.2.3. Non-linear indices

The vector length index (VLI) and vector angle index (VAI) from Poincare scatter plots were studied as two non-linear indices. They are defined by [34]:

$$\mathrm{VLI} = \sqrt{\sum_{i=1}^{N} (l_i - L)^2 / N} \tag{6}$$

$$\mathrm{VAI} = \sum_{i=1}^{N} |\theta_i - 45| / N \tag{7}$$

where, l_i is the vector length of each point in the Poincare scatter plot of the RR interval time series, L is the mean vector length, θ_i is the angle of each point, and N is the point number of the Poincare scatter plot.

Sample entropy (SampEn) was also studied as a non-linear index. The detailed calculation can refer to [35]. Because SampEn values are influenced by the parameters of embedding dimension m and tolerance threshold r [36], we used the different parameter combinations as follows: m was set as 1, 2 and 3 and r set as 0.10,