Higher Order Spectra for Heart Rate Variability and QT Interval Variability Analysis: A Comparison between Heart Failure and Normal Control Groups

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Abstract

Recent studies on heart rate variability (HRV) and QT interval variability (QTV) have shown that HRV and QTV might be related to some cardiac diseases. This study used higher order spectra (HOS) method and constructed a normalized bispectrum amplitude histogram, from which two quantitative indices: bispectrum amplitude entropy (BAEn) and high-low amplitude ratio (HLAr) were defined. A total of 49 subjects (29 heart failure subjects and 20 normal control subjects) were enrolled and the results showed that the histogram distributed differently in the two groups and both BAEn and HLAr for QTV in heart failure group were significantly lower than that in normal control group ($p<0.001$ for both of them), while all of them for HRV had no significant difference in the two groups. These findings pointed out that HOS analysis of QTV might give valuable information for the classification of heart failure and normal control groups.

1. Introduction

The previous studies have shown that heart failure is associated with several abnormalities in autonomic nervous system (ANS) function [1]. There is strong evidence shown that heart rate variability (HRV) signals, which is a simple, easier-to-use technique for the study of the dynamic interaction and balance between the sympathetic and parasympathetic nervous system, can reflect the autonomic control of cardiovascular system [2]. Recently, QT interval variability (QTV), follows HRV to some extent, is proved to be related to ANS function [3], and it appears to be an important and independent index of cardiac mortality and severity of illness in patients with heart disease [4]. QT interval measured on the surface electrocardiogram (ECG) reflects the time for repolarization. Thus, beat-to-beat QTV shows the lability in ventricular repolarization, which is mechanically related to the increased risk of malignant ventricular arrhythmias [5].

Several investigators have researched QTV in patients of different diseases, such as panic disorder, major depress [6], congestive cardiac failure [4] and dilated cardiomyopathy (DCM) [7]. QTV and HRV, which are the same to all other physiological signals, are nonlinear in nature and hence analysis using nonlinear methods might unveil the hidden but useful information. Yeragani et al. defined MEDqthr and LLEqthr which were calculated by the ratio of the minimum embedding dimension (MED) and the ratio of the largest Lyaponov exponent (LLE) of QTV and HRV respectively [6]. They used these indices in a comparison between anxiety and normal control groups and got a promising result.

Higher Order Spectra (HOS), which is spectra of representation of third order moment and cumulant, can be used for the detection of Gaussianity and nonlinearity [8]. It gives both the phase and the amplitude information of a signal unlike the power spectrum, which contains only the amplitude information. Chandran et al. defined invariants from HOS analysis for pattern recognition [9] and Chua et al. used these indices for cardiac health diagnosis using HRV signals and found the different behaviors of HOS among four classes of arrhythmias and normal HRV signals [2].

In this work, we studied the HOS of HRV and QTV in heart failure and normal control groups. We presented some general characteristics and extracted features from HOS analysis and gave a comparison among them in the two groups.

2. Method

2.1. Data acquisition

The experimental data for this work was obtained from a group of 29 patients with heart failure and a normal control group included 20 healthy volunteers. Surface ECG was recorded in lead II configuration using limb extremities with a sampling rate of 1000 Hz so as to preserve all the possible useful frequency components. Each record lasted for at least 5 min.

2.2. Preprocessing

The ECG data was firstly preprocessed through the following steps:

(1) The data was filtered using a low-pass filter with a cut-off frequency of 75 Hz to remove the noise. Then, a high-pass filter with a cut-off frequency of 0.3 Hz was applied to remove the baseline drift.
(2) A band-stop filter of 50 Hz was used to trap the power-line interference.
(3) R-wave positions for each ECG record were detected using a template matching procedure [10].

The fore-and-aft R-wave positions formed R-R interval and raw RR sequence was obtained from consecutive R-R intervals. Because that the raw RR sequence is an unevenly sampling signal, it was re-sampled at 4 Hz using the technique of Berger et al. [11]. The data was then detrended using a smoothness prior approach (SPA) according to Tarvainen et al. [12], which could take out the unstationary trend in the RR sequence.

The QT interval algorithm had been described by Berger et al. [7] in detail and was applied in this work. This algorithm found the QT interval for each beat using also a template matching procedure, wherein, the QT interval template should be chosen by the operator and one QT interval should be corresponded with one R-wave that detected in step (3). The consecutive QT intervals formed raw QT interval sequence and QTV signals were obtained by re-sampling the raw QT interval sequence and then detrending just the same as HRV signals.

All these series that we used were free of ventricular premature beats. Finally we truncated each series to 256s (1024 points after re-sampling) according to the previous studies [6].

2.3. Construction method of normalized bispectrum amplitude histogram

We used the bispectrum, which is the Fourier transform of the third order correlation of the signal to achieve the HOS analysis. Because of the symmetry of bispectrum, features extraction was all carried out in the non-redundant region as shown in Figure 1 [9].

Different HOS features had been already defined in some previous studies [2, 9], but these features did not have explicit sense for physiological signals usage. Because bispectrum amplitude reflects the phase coupling to some extent, it is easy to think that the phase coupling might be different in heart failure and normal control groups.

For an intuitionistic description of phase coupling from bispectrum, we defined a normalized bispectrum amplitude histogram as follows:

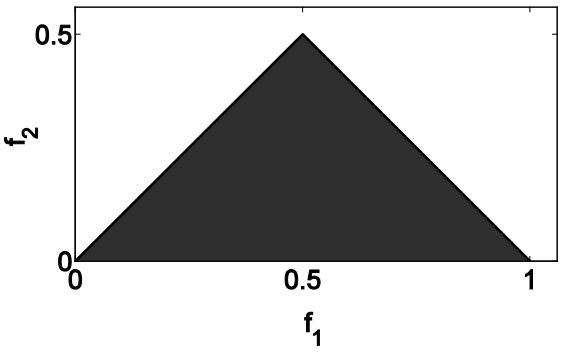

Figure 1. Features extraction was carried out in the non-redundant region, shown using the gray triangular region. Frequencies f_1 and f_2 here were normalized by the Nyquist frequency.

(1) The bispectrum amplitude in the non-redundant region was firstly arranged by sort ascending and then normalized using the maximum amplitude.
(2) The sorted data was then separated into 10 sections with the interval length of 0.1. Because most of them would be in the first section from 0 to 0.1, which was not sensitive to different features in our opinion, we abandoned it in the following steps. The 10 sections were described as follows:

$$\left\{ S_k \left| 0.1(k-1) < BA \le 0.1k, k = 1, 2, \cdots, 10 \right. \right\} \quad (1)$$

where BA stands for the bispectrum amplitude and S_k, k=1, 2, ..., 10 are the 10 sections. S_1 is just the first section that we abandoned.
(3) The sum of each section from k=2 to k=10 was calculated then and normalized each of them using the total sum of those sections reserved. Then a normalized bispectrum amplitude histogram was got.

2.4. Definitions of BAEn and HLAr

The normalized bispectrum amplitude histogram described the probability distribution of the bispectrum amplitude, which leaded us to the definition of information entropy proposed by Shannon [13]. The information entropy could describe quantitatively the uniformity of a certain distribution. The degree of phase coupling might be different between the two groups and this would lead to a different distribution of bispectrum amplitude.

Thus, we defined the following two indices: bispectrum amplitude entropy (BAEn) and high-low amplitude ratio (HLAr), to describe the distribution of normalized bispectrum amplitude histogram defined above.

$$BAE_n = -\sum_{k=2}^{10} p_k \log_2\left(p_k\right) \tag{2}$$

$$HLA_r = \frac{\sum_{k=6}^{10} p_k}{\sum_{k=2}^{5} p_k} \tag{3}$$

where

$$p_k = \frac{N\left(S_k\right)}{\sum_{i=2}^{10} N\left(S_i\right)} \tag{4}$$

and $N\left(S_k\right)$ is the number of points in the section S_k.

A QTV index (QTVi) was also calculated as suggested by Berger et al. [7] which could be defined by:

$$QTVi = \log_{10}\left(\frac{QT_v / QT_m^2}{HR_v / HR_m^2}\right) \tag{5}$$

where QT_v and HR_v are the variances, QT_m^2 and HR_m^2 are the squared mean of QTV and HRV respectively. The QTVi was proved to be elevated in patients with DCM [7] and congestive cardiac failure [4].

Finally, a student t-test was applied between heart failure and normal control groups.

3. Results

Higher HRV fluctuation but lower QTV fluctuation present in normal control group, whereas heart failure group had a mirror behavior (Figure 2). This is the same to some previous studies [4-7].

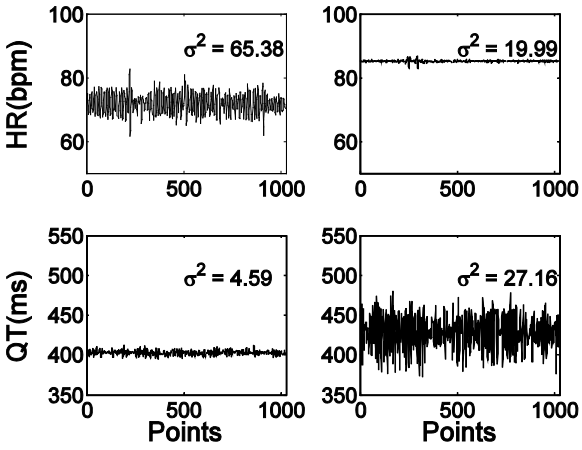

Figure 2. HRV and QTV signal in normal control group (left) and in heart failure group (right) with the signal length of 256s (1024 points) and sampling frequency of 4 Hz, each of which was detrended using SPA, shows a higher HR interval time series variance and a lower QT interval times series variance in normal control group, which has a mirror behavior in heart failure group.

Table 1. Results of t-test on various features.

	Features	Groups		p value
		Normal	Heart failure	
QTV	BAEn	1.842 ± 0.214	1.545 ± 0.263	<0.001
	HLAr	0.068 ± 0.028	0.040 ± 0.021	<0.001
HRV	BAEn	1.485 ± 0.348	1.603 ± 0.404	>0.1
	HLAr	0.064 ± 0.052	0.063 ± 0.037	>0.1
	QTVi	-1.296 ± 0.229	-0.684 ± 0.365	<0.001

Figure 3 shows the normalized bispectrum amplitude histograms in normal control and heart failure groups. A nearly evenly descendent distribution for QTV is present in normal control group, while in heart failure group it becomes an anomalistic left-skewed distribution. As to HRV, the two histograms are not so different to each other.

Table 1 shows the mean ± SD of BAEn and HLAr in normal control and heart failure groups for QTV and HRV and the mean ± SD of QTVi. The results show that HOS parameters BAEn and HLAr for QTV are all significantly lower in heart failure group compared to normal control group ($p<0.001$ for both of them); while the results are not so promising for HRV, where both BAEn and HLAr have no significant difference between the two groups.

The correlation results (Table 2) show that there is evident correlation between BAEn and HLAr, but no significant correlation between them and QTVi respectively.

4. Discussion

Previous researches have witnessed the recognition of a significant relationship between HRV and QTV signals and autonomic nervous activities [1-3, 5]. Because HRV and QTV signals are nonlinear in nature [2, 4, and 6], we used HOS as a nonlinear tool to analyze HRV and QTV signals and found the difference between heart failure group and normal control group, and also found the different behavior between QTV and HRV in the two

groups. HOS parameters BAEn and HLAr for QTV were all significantly lower in heart failure group than that in normal control group ($p<0.001$ fot both of them), while this was not the same to HRV, whose HOS parameters BAEn and HLAr had no significant difference. These results showed that the degree of phase coupling might distribute regularly in normal QTV signals; while with the diseases appearance, it came to an anomalistic left-skew distribution and appeared less phase coupling behavior. However, the phase coupling of HRV was not so different between heart failure and normal control groups. Thus HOS parameter BAEn and HLAr for HRV could not be used for the classification of the two groups.

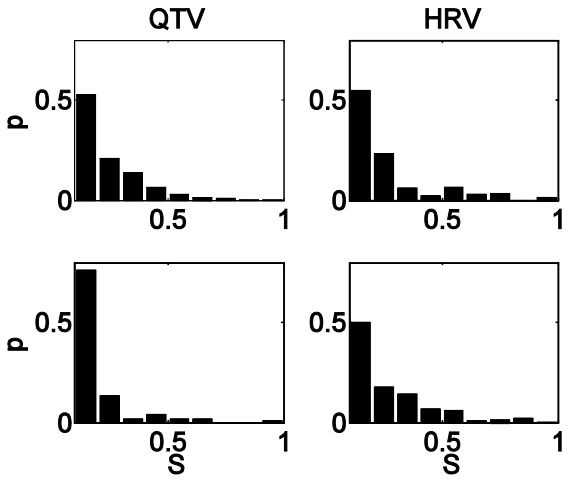

Figure 3. Normalized bispectrum amplitude histograms in normal control group (above) and in heart failure group (below) show that the height is nearly evenly descendent in normal control group and anomalistic left-skewed in heart failure group for QTV; while the histograms have no significant difference in HRV.

Table 2. The correlation results.

	BAEn	HLAr	QTVi
BAEn	1	0.80	-0.27
HLAr	0.80	1	-0.28
QTVi	-0.27	-0.28	1

There was evident correlation between BAEn and HLAr, but no significant correlation between them and QTVi respectively. It shows that BAEn and HLAr might reflect the same phase coupling behavior from different aspects. Thus, HOS analysis might give some valuable additional information about the cardiac state.

Future studies will be focus on the mechanism that leads to this different behavior between HRV and QTV, and the relationship between them. Besides, more different groups of patients will be selected in our future researches for much more precise index or cluster of indices that used for this classification.

Acknowledgements

We would like to thank Miss Xinning Liu for her careful correction of the words and grammatical mistakes regarding this paper.

This work is supported by the Hi-Tech Research and Development Program of China (863 Program, No. 2009AA02Z408).

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