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Evaluation Method for Heart Failure Using RR Sequence Normalized Histogram

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Abstract

Histogram and scatter plot are important graphical indices for heart rate variability (HRV) analysis. However, they are difficult to quantify the complexity for time series and have little specificity to some cardiovascular diseases. This paper proposed a new graphical method for HRV analysis, which was named as RR sequence normalized histogram. Based on the analysis of RR sequence normalized histogram, three quantitative indices were defined: center-edge ratio (CER), cumulative energy (CE) and range information entropy (RIEn). To verify the validity of the new method, a total of 120 subjects (60 heart failure subjects and 60 healthy control subjects) were enrolled and the three indices were calculated respectively. A Wilcoxon rank sum test showed that: CER ($p = 0.232$) and CE ($p = 0.417$) had no statistical differences between heart failure and healthy control group while RIEn ($p = 0.027$) had. This indicated that the new method had a potential application in evaluating the heart failure and the index RIEn had a better effectiveness than the other two indices.

1. Introduction

As an early noninvasive detection method of studying the potential risk of cardiovascular diseases, heart rate variability (HRV), has been widely applied in clinical medicine, rehabilitation medicine, sports medicine, nerve medicine, and etc. (for a review, see [1-3]). Histogram and scatter plot analysis are two important methods for the analysis of HRV, which reflect directly the fluctuation of the RR sequence in morphological aspect and have an important reference value [1, 4]. However, they are difficult to quantify the complexity of the RR sequence. The existing quantitative indices of vector length index (VLI) and vector angle index (VAI) in scatter plot have little specificity to some cardiovascular diseases and the physical meaning of these indices is not clear enough. To solve the above problems, this paper proposed a new method for HRV analysis, named the RR sequence normalized histogram. Three quantitative indices were defined for the RR sequence normalized histogram: center-edge ratio (CER), cumulative energy (CE) and range information entropy (RIEn). At the same time, we designed the systemic clinical test to check the validity of the RR sequence normalized histogram and its quantitative indices.

2. Methods

2.1. Subjects

The subject enrolled in this study, either heart failure group or healthy control group, should primarily meet the following criteria:

- the age between 18 years and 75 years;
- agreed to sign the information consent form;
- not participated in other clinical trials within the past three months.

The individual criteria for heart failure group:

- accord with the class Ⅱ-Ⅲ of the New York Heart Association (NYHA) Functional Classification;
- LVEF<0.50 with ultrasonic cardiogram (UCG) detection.

The individual criteria for healthy control group:

- older than 50 years required to account for half;
- normal results with UCG, blood lipid and glucose checks and electrocardiogram (ECG).

Exclusion criteria were:

- subject with severe organ damage;
- subject with psychiatric disorders.

According to the above criteria, a total of 120 subjects were enrolled and they were divided into two groups, heart failure group (22 females and 38 males, median age 62.8 years; range, 38-75 years) and healthy control group (33 females and 27 males; median age, 51.2 years; range, 24-72 years). Each group included 60 subjects. The study had full approval from the Clinical Ethics Committee of the Qilu Hospitals of Shandong University. Data acquisition and processing use the CV FD - Ⅰ Cardiovascular Systerm State Detection Device produced by the Jinan HUIYIRONGGONG Technology Co., Ltd.

2.2. Data acquisition

All subjects were selected to ensure that they did not take medications or smoke cigarettes before the test. At the beginning, every subject was asked to lie on the bed and relax over a period of time. Subsequently, standard limb Ⅱ lead ECG data were recorded for about 10 minutes. The ECG data were sampled at 1000 Hz. Each subject was in the supine position during the recording. After the data acquisition, the ECG data were filtered through a band pass filter with its pass band frequency being set at 0.05–125 Hz. Then, the R-wave peaks of the ECG data were automatically detected by the Wavelet Transform Modulus Maxima (WTMM) method [5, 6], which was an important method for describing the characteristic elements of a complex quasi-periodic signal based on Wavelet Transform. The fore-and-aft R-wave peaks formed the R-R interval and the consecutive R-R intervals made up of the original RR sequence. The original RR sequence often contains some anomalies. The anomalies usually contain four kinds: a false negative (FN), a false positive (FP), supra-ventricular ectopic beats (sVEB) and ventricular ectopic beats (VEB) [7]. In this study, we used the method of impulse rejection filter (IRF) [8-9] to correct the anomalies. After correction, sharp transient in the original RR sequence has been removed. Figure 1 shows two demonstrations of correctional RR sequence respectively from healthy control group (a) and heart failure group (b).

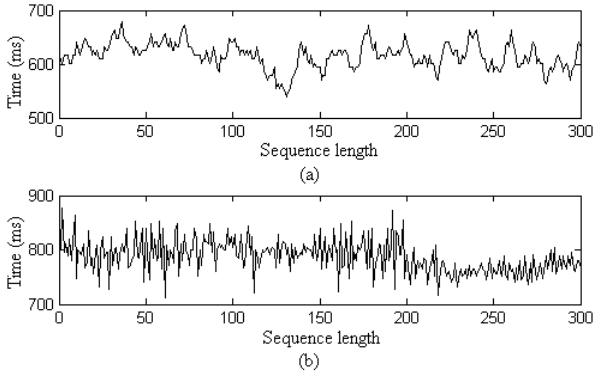

Figure 1. The demonstrations of RR sequence from two groups, (a) healthy control group, (b) heart failure group

2.3. Construction method for RR sequence normalized histogram

In this section, we outline the general construction procedure for RR sequence normalized histogram. Formally, given a RR sequence $\{RR_1, RR_2, \ldots, RR_N\}$, where N denotes the length of the RR sequence, the construction procedure can be summarized as follows：

1) The maximum and the minimum of the RR sequence are firstly found, respectively named as $RR_{\max}$ and $RR_{\min}$. Then the varying range of the RR sequence is calculated by the following formula:

$$RR_{\text{range}} = RR_{\max} - RR_{\min} \tag{1}$$

2) Set the threshold $\alpha=0.1\times RR_{\text{range}}$, then the left-step H_l and right-step H_r can be calculated

$$H_l = \frac{RR_{\text{mean}} - (RR_{\min} + \alpha)}{5} \tag{2}$$

$$H_r = \frac{(RR_{\max} - \alpha) - RR_{\text{mean}}}{5} \tag{3}$$

where RR_{mean} denotes the mean value of the RR sequence. The RR_i (i=1, 2, ⋯, N) is separated into seven kinds based on the value of the element.

a) Let L1 denotes the leftmost kind. Its element meets $RR_{\min}\le RR_i < RR_{\min}+\alpha$ and the number of elements in L1 kind is P_1.

b) Let L2 denotes the second kind of left. Its element meets $RR_{\min}+\alpha\le RR_i < RR_{\min}+\alpha+2\times H_l$ and the number of elements in L2 kind is P_2.

c) Let L3 denotes the third kind of left. Its element meets $RR_{\min}+\alpha+2\times H_l\le RR_i < RR_{\min}+\alpha+4\times H_l$ and the number of elements in L3 kind is P_3.

d) Let C denotes the middle kind. Its element meets $RR_{\text{mean}}-H_l\le RR_i < RR_{\text{mean}}+H_r$ and the number of elements in C kind is P_4.

e) Let R3 denotes the third kind of right. Its element meets $RR_{\text{mean}}+H_r\le RR_i < RR_{\text{mean}}+3\times H_r$ and the number of elements in R3 kind is P_5.

f) Let R2 denotes the second kind of right. Its element meets $RR_{\text{mean}}+3\times H_r\le RR_i < RR_{\max}-\alpha$ and the number of elements in R2 kind is P_6.

g) Let R1 denotes the leftmost kind. Its element meets $RR_{\max}-\alpha\le RR_i\le RR_{\max}$ and the number of elements in R1 kind is P_7.

3) The p_i of each kind is calculated as follows:

$$p_i = \frac{P_i}{N} \qquad i = 1, 2, \cdots, 7 \tag{4}$$

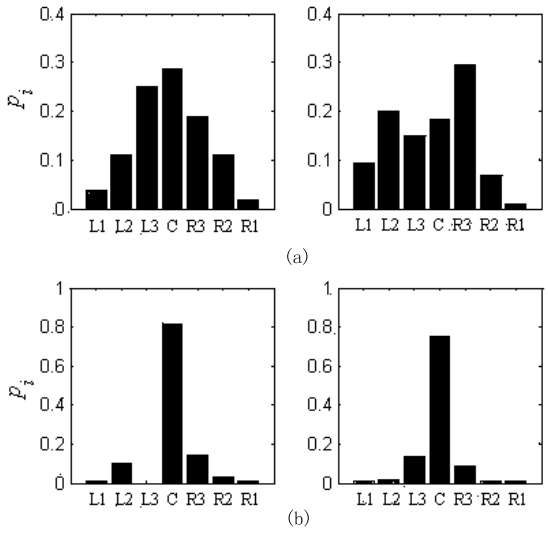

Figure 2. The demonstrations of the RR sequence normalized histogram from two groups, (a) healthy control group, (b) heart failure group

In a rectangular coordinate system, the p_i corresponding to the seven kinds (i.e. L1, L2, L3, C, R3, R2 and R1) of RR sequence is drawn to form the normalized histogram. Figure 2 gives a demonstration of four subjects from the healthy control and heart failure groups. Figure 2 (a) shows two subjects from the healthy control group and Figure 2 (b) shows two subjects from the heart failure group. It is clearly that RR interval has a more uniform distribution in healthy subjects but has a more concentrated in heart failure subjects. So the percentage p_i of each kind in the RR sequence normalized histogram exhibits a small difference in the healthy control group but has a significant difference in the heart failure group. This provides a possibility to explore the quantitative indices from the RR sequence normalized histogram to distinguish the heart failure subjects from the healthy subjects.

2.4. Quantitative indices

1) center-edge ratio and cumulative energy[10]: As shown in Figure 2, taking into account that the percentage p_i in the healthy control group distributes fairly evenly in all seven kinds, while the percentage p_i in the heart failure group has an uneven distribution, so two quantitative indices can be obtained from the analysis of the RR sequence normalized histogram. They are respectively named as center-edge ratio (CER) and cumulative energy (CE). They are calculated as follows:

$$\mathrm{CER} = \frac{p_4}{p_1 + p_2 + p_6 + p_7} \tag{5}$$

$$\mathrm{CE} = \sum_{i=1}^{7} p_i^2 \tag{6}$$

CER characterizes the fluctuation of the sequence element apart from the mean of RR sequence. CE indicates the equilibrium of the percentage p_i in all seven kinds.

2) range information entropy: The percentage p_i in the normalized histogram in fact describes the probability distribution of each kind elements of the RR sequence. It is easy to think that the probability distribution consist with the definition of information entropy by Shannon [11]. This paper proposes a new definition of entropy for the normalized histogram—range information entropy (RIEn) based on the definition of information entropy by Shannon. RIEn is calculated by the following formula:

$$\mathrm{RIEn} = -\sum_{i=1}^{7} p_i * \ln p_i \tag{7}$$

RIEn reflects the distribution of the elements in the RR sequence normalized histogram. If the elements distribution in the RR sequence is regard as the energy distribution, then the energy distribution exhibits more uniform in each kind, RIEn becomes larger. That means the RR sequence is more complex, the uncertainty of the sequence gets greater.

2.5. Statistical analysis

To compare different indices of the RR sequence normalized histogram between the heart failure and healthy control groups, we use the statistical analysis software of SPSS to analyze the results. First, we carried out the normal distribution and variance homogeneity test for the indices between two groups. If positive results were obtained in normal distribution and variance homogeneity test, we moved on to independent sample *t*-test. If the indices did not pass the tests, we turned to Wilcoxon rank sum test. $p = 0.05$ was took as the level of statistical significance for all tests.

3. Results and discussion

Three indices CER, CE and RIEn are analyzed and shown in Figure 3 and Table 1. Each index was separately calculated between the heart failure and healthy control groups. In Figure 3, we can clearly discern that the indices of CER and CE in the heart failure group are significantly higher than that in the healthy control group, while the index RIEn in the heart failure group is significantly lower than that in the healthy control group. After the normal distribution and variance homogeneity test, the resulting *p*-values of the Wilcoxon rank sum test are also reported in Table 1. A value of $p < 0.05$ is deemed statistically significant. The *p*-values of CER, CE and RIEn are 0.232, 0.417 and 0.027, respectively.

The explanation of this phenomenon is respectively expatiated as follows. Compared with the heart failure group, the healthy control group usually has a more uniform percentage p_i (in all seven kinds L1, L2, L3, C, R3, R2 and R1) in the normalized histograms. However, the percentage p_i of C kind in the heart failure group sometimes shows a distinct large, while sometimes has a similar results with the healthy control subjects. Therefore, CER in the heart failure group has a much larger change range than that in the healthy control group. Although CER exhibits a difference between the two groups, the statistical result p=0.232 shows that there is no statistical difference.

This phenomenon is also occurred in the index CE. CE is obtained by calculating the square sum of percentage p_i. The square operating restrains the phenomenon that the percentage p_i of C kind is particularly high in heart failure group. CE is less than 1 both in the heart failure and healthy control groups. Due to the larger percentage p_i of C kind, CE in the heart failure group is larger than that in the healthy control group. The statistical result p=0.417 shows that there is also no statistical difference between the two groups in CE.

The healthy control group has a more uniform percentage p_i in the normalized histograms shows that the RR sequence has a higher complexity and uncertainty. So the index RIEn in the healthy control group exhibits

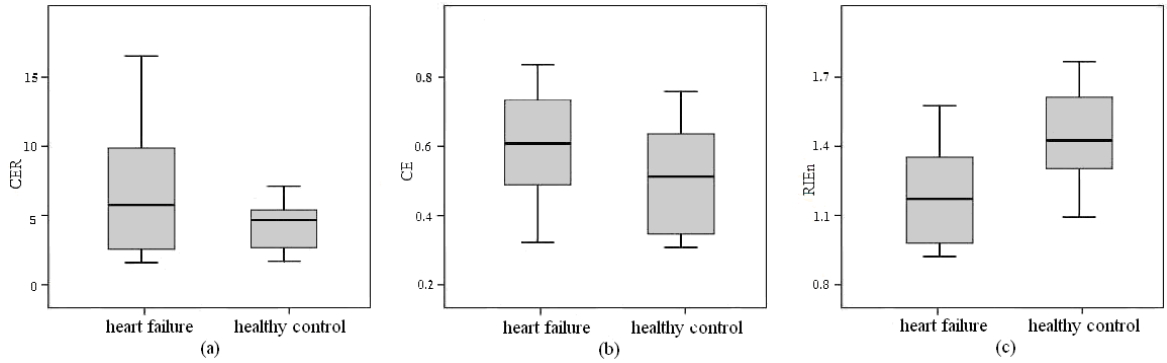

Figure 3. The boxplots of CER, CE and RIEn between heart failure and healthy control groups, (a) CER, (b) CE, (c) RIEn.

higher than that in the heart failure group. The statistical result p=0.027 shows that RIEn exhibits a significant difference between the two groups. Therefore, RIEn is a potential index to distinguish subject between the heart failure and healthy control groups.

Table 1. The analysis results of CER, CE and RIEn between heart failure and healthy control groups

Index	Heart failure	Healthy control	p-value
CER	5.76±4.84	4.18±2.51	0.232
CE	0.58±0.31	0.46± 0.33	0.417
RIEn	1.19± 0.35	1.43± 0.34	0.027

4. Conclusions

This paper proposed a new method to construct the RR sequence normalized histogram. Based on the analysis of the RR sequence normalized histogram, three quantitative indices CER, CE and RIEn were defined and calculated. A total of 120 subjects (60 heart failure subjects and 60 healthy control subjects) were enrolled and the results showed that: CER and CE had no significant statistical difference between two groups, while RIEn had. It indicated that RIEn was more likely to evaluate early heart failure and its clinical effectiveness was better than CER and CE. Furthermore, the construction method for the RR sequence normalized histogram and the definition of the three quantitative indices are also apply to other sequence analysis of physiological signals.

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References

[1] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Circulation 1996; 93: 1043–65.

[2] Perc M. Nonlinear time series analysis of the human electrocardiogram. Eur J Phys 2005; 26: 757-68.

[3] Michael S, Dejin Y, Jennifer S. Uncovering non-linear structure in human ECG recordings. Chaos, Solitons and Fractals 2002; 13, 1755-62.

[4] D'Addio G, Acanfora D, Pinna G, et al. Reproducibility of short- and long-term Poincare plot parameters compared with frequency-domain HRV indexes in congestive heart failure. Computers in Cardiology 1998; 24: 381–4.

[5] Cuiwei L, Chongxun Z, Changfei T. Detection of ECG characteristic points using wavelet transform. IEEE Trans. Biomed. Eng 1995; 42: 21–8.

[6] Martinez JP, Almeida R, Olmos S, et al. A wavelet-based ECG delineator: Evaluation on standard databases. IEEE Trans. Biomed. Eng 2004; 51: 570–81.

[7] Mateo J, Laguna P. Analysis of heart rate variability in the presence of ectopic beats using the heart timing signal. IEEE Trans. Biomed. Eng 2003; 50: 334–43.

[8] Mcnames J, Thong T, Aboy M. Impulse rejection filter for artifact removal in spectral analysis of biomedical signals. In: Proceedings of the 26th Annual International Conference of the IEEE EMBS. San Francisco, CA, USA, 2004: 145–48.

[9] Chengyu L, Changchun L, Peng S, et al. Comparison of different threshold values r for approximate entropy: Application to investigate the heart rate variability between heart failure and healthy control groups. Physiological Measurement 2011; 32: 167-80.

[10] Chengyu L, Changchun L, Qingguang Z, et al. Construction method for normalized histogram of RR sequence and its application for evaluation heart failure. Acta Biophysica sinica (in chinese) 2009; 25: 299–304.

[11] Shannon CE. A mathematical theory of communication. Bell System Technical Journal 1948; 1-54.

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