The Analysis of Heart Rate Fragmentation for Congestive Heart Failure

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Abstract

Background: Congestive heart failure (CHF), also known as chronic heart failure, is the end stage of all kinds of cardiovascular diseases with high mortality. Heart rate fragmentation (HRF) indices may be a potentially valid approach to diagnose CHF.

Objective: The aims of this study were to: (1) find out the differences of HRF indices between healthy subjects and patients with CHF; (2) explore whether HRF indices can be applied to diagnose CHF.

Methods: Open-access cardiac interbeat (RR) interval databases (Physiobank) were introduced here. Twenty subjects were selected from CHF RR interval database and normal sinus rhythm RR interval database, and included into CHF group and healthy group respectively. Then the values of PIP, IALS, PSS, and PAS were calculated and compared according to these 40 subjects. Statistic difference between two groups on same indice was computed.

Results: PIP (Healthy vs CHF, 0.72 VS 0.77, P=0.006), IALS (0.72 VS 0.78, P=0.0036), PSS (0.86 VS 0.95, P=0.0008), and PAS (0.11 VS 0.12, P=0.8392) of CHF group are significantly higher than that in healthy group.

Conclusion: HRF indices could be used as an efficient and easy tool to diagnose CHF. What’s more, HRF indices are a valuable approach to analyse heart rate.

1. INTRODUCTION

Congestive heart failure, also known as chronic heart failure, would result in decreased cardiac output and increased left ventricular terminal diastolic pressure, mainly because of the impairment of the myocardial systolic function [1]. Clinically, pulmonary congestion and insufficient peripheral circulatory perfusion were always observed among patients with CHF, as well as the combination of the two symptoms on different degree [2]. ECG (electrocardiogram) is the major source for the diagnosis of CHF. Patients with CHF have morphological changes in ECG, such as moderate changes in the height of RS wave and QR wave [3]. Poincare map measures can be derived from ECG data and have been applied to the diagnosis of CHF [4]. At present, ECG and X-ray examination are common diagnostic methods. However, these kinds of methods need much professional medical knowledge and have a drawback that has difficulty to operate [5].

Detecting CHF in time is particularly important, because sudden heart failure is often associated with a high mortality rate. ECG signal may provide some omens [6]. As long as doctors have an effective and immediate way to detect CHF, the death rate would reduce. Quantity assessment is the most intuitive and rapid method of judging a disease.
Costa et al. [7] coined the new term “heart rate fragmentation indices” to refer to anomalous short-term HRV with apparent dynamical signature of frequent changes in heart rate acceleration sign. These indices were derived from ECG data and were used to the analysis of cardiac interbeat interval dynamics and test of coronary artery disease (CAD). Such a new CAD detection method performed better than time and frequency domain measures of heart rate variability, and was also superior to non-linear measures according to previous research [7]. Accordingly, this paper wants to study whether doctors can apply HRF indices to the analysis of CHF. These indices have a feature that the more fragmented a time series is, the higher the PIP, IALS, PSS, and PAS indices will be. Thus, these indices are useful tools to doctors for rapid response to acute heart failure.

Thus, this study aimed to explore whether the HRF indices method was useful to diagnose CHF and quantize a subject’s physical condition.

2. METHODS

2.1 Databases

Databases come from Physiobank. The specific databases employed are Congestive Heart Failure RR Interval Database (https://www.physionet.org/physiobank/database/chf2db/), and Normal Sinus Rhythm RR Interval Database (https://www.physionet.org/physiobank/database/nhr2db/).

2.1.1 Normal Sinus Rhythm RR Interval Database [8]. The database includes 54 normal sinus rhythm subjects’ long-term ECG recordings. Subjects included in this database were found to have no significant arrhythmias. The former 20 subjects were employed in this paper, including 5 males aged 64 to 76, and 15 females aged 58 to 74. The original ECG recordings were digitized at 128 samples per second, and the beat annotations were obtained by automated analysis with manual review and correction.

2.1.2 Congestive Heart Failure RR Interval Database [9]. The database includes 29 congestive heart failure (NYHA classes I, II, and III) subjects’ long-term ECG recordings. The former 20 subjects were employed in this paper. They included 8 males aged 39 to 68, 2 females aged 38 and 59, 10 subjects aged 34 to 79 whose gender is undefined. The sample rate of original ECG recordings and the beat annotations followed the same standard above.

2.2 HRV Analysis: Heart Rate Fragmentation indices

According to the ECG recording of each subject, \( t_{Ni} \) is used to represent the time of \( i_{th} \) normal sinus beat, \( \{NN_i\} = \{t_{Ni} - t_{Ni-1}\} \) is the time series of NN (normal-normal) intervals, the difference (or increment) between consecutive NN intervals can be represented as \( \Delta NN_i = \{NN_i - NN_{i-1}\} \). Defining the length of a segment is how many NN intervals belong to that segment.

Four HRF indices can be computed using the time series mentioned above:

- The percentage of zero-crossing points in the increment time series, or equivalently, the percentage of inflection points (PIP). In the NN interval time series, if \( \Delta NN_i \times \Delta NN_{i+1} \leq 0 \), \( t_{Ni} \) then was defined as an inflection point. This point means that heart rate acceleration changes sign or changes to or from zero. Under the circumstance that heart rate acceleration changes from zero to zero, the point can’t be regard as an inflection point. PIP can be calculated through the number of inflection points divided by the number of all sinus rhythm beat points.

- The inverse of the average length of the acceleration/deceleration segments (IALS). For a segment between consecutive inflection points, it is acceleration, deceleration segment if \( \Delta NN < 0 \) and \( >0 \), respectively. The length of a segment is how many NN intervals belong to the segment. IALS can be calculated through the total number of acceleration and deceleration segments divided by the total length of acceleration and deceleration segments.

- The complement of the percentage of the NN intervals in acceleration and deceleration segments with three or more NN intervals (PSS). PSS can be calculated through the total length of
acceleration and deceleration segments with three or more NN intervals divided by the total number of NN intervals between inflection points.

bol The percentage of NN intervals in alternation segments (PAS). While ΔNN changes sign every beat, this type of segment called alternation segment, such as a sequence of four NN intervals at where the heart rate acceleration changes sign every beat. PAS can be calculated through total length of alternation segments (with four NN intervals) divided by total number of four-consecutive NN intervals.

With higher PIP, IALS, PSS, and PAS indices, the time series should be more fragmented. Figure 1 shows a schematic representation of all the definitions introduced above.

Figure 1 | Schematic diagram of NN intervals in an ECG segment. There are 25 sinus rhythm beat points, including 12 inflection points; 10 acceleration intervals (light green, located in 6 acceleration segments); 9 deceleration intervals (dark green, located in 5 deceleration segments); 3 segments (length =4) with three or more NN intervals; 4 4-base alternation segments. Overall this ECG segment has a length (number of NN interval in a segment) of 24.

2.3 Statistical analysis
Wilcoxon rank-sum test is a kind of non-parametric statistical hypothesis test. This test was employed here to test whether PIP, IALS, PSS and PAS of healthy group and CHF group have a statistical difference. In this paper, MATLAB R2017a was used to calculate value of P.

That P < 0.05 is for statistical difference, that P < 0.01 is for a statistically significant difference, that P < 0.001 is extremely significant statistical differences.

3. RESULTS
3.1 Data Result
According to the algorithms presented in the methods, four HRF indices for normal sinus rhythm RR Interval database (healthy subjects) and congestive heart failure RR Interval database (CHF subjects) are shown in the Table 1 below. After analysing four indices of healthy subjects and CHF subjects, the minimum, maximum, average, median, and quartiles were found and presented in Table 2. According to Table 2, for the four HRF indices, CHF subjects has a higher value. We also calculated the percentages under certain condition that healthy subject has higher value than CHF subject with same age, which were shown in the following Table 3. The unnormal percentage of two groups is not considerably small and inconsistent with overall result.

Table 1 HRF indices of Healthy(N=20) and CHF groups(N=20)

|        | Healthy | CHF |
|--------|---------|-----|
| PIP (%)|         |     |
| IALS   |         |     |
| PSS    |         |     |
| PAS    |         |     |
| PIP (%)|         |     |
| IALS   |         |     |
| PSS    |         |     |
| PAS    |         |     |
Table 2 Minimum, maximum, average, median, and quartiles values of HRF indices of Healthy(N=20) and CHF groups(N=20)

|        | Healthy (N=20) |           |           |        | CHF (N=20) |           |           |
|--------|----------------|-----------|-----------|--------|------------|-----------|-----------|
|        | PIP  | IALS     | PSS      | PAS    | PIP  | IALS     | PSS      | PAS    |
| Minimum | 58   | 0.58     | 0.69     | 0.61   | 58   | 0.58     | 0.69     | 0.61   |
| Maximum | 78   | 0.79     | 0.94     | 0.95   | 78   | 0.79     | 0.94     | 0.95   |
| Average | 70   | 0.70     | 0.86     | 0.84   | 70   | 0.70     | 0.86     | 0.84   |
| 1/4Quartile | 68   | 0.67     | 0.83     | 0.82   | 68   | 0.67     | 0.83     | 0.82   |
| Median  | 72   | 0.72     | 0.86     | 0.86   | 72   | 0.72     | 0.86     | 0.86   |
| 3/4Quartile | 73   | 0.73     | 0.90     | 0.91   | 73   | 0.73     | 0.90     | 0.91   |

4.2 Statistical Analysis Result

From four HRF indices mentioned above, rank-sum test was used to test their difference. And the p-values are shown in Table 4. Accordingly, for healthy group and CHF group, PIP, IALS, and PSS have significant statistical difference. While PAS has no statistical difference.
Table 4 P-value of HRF indices between Healthy(N=20) and CHF groups(N=20)

| PIP | IALS | PSS | PAS |
|-----|------|-----|-----|
| P-value | 0.0060 | 0.0036 | 0.0008 | 0.8392 |

HRF indices were plotted on histograms. As presented in Figure 2, the four parameters of patients with CHF are universally higher than that of healthy group.

![Histograms of PIP, IALS, PSS and PAS between Healthy(N=20) and CHF groups(N=20)](image)

4. Discussion

This study presented a new method to diagnose and analyze cardiac state of CHF. Four HRF indices, PIP, IALS, PSS and PAS, were introduced as the diagnostic markers of CHF. Comparative analysis of the indices, I finally found that patients with CHF generally had higher degree of fragmentation or higher indices. This result may prove that the patient's heart system function has become worse, which may be caused by the disease. Therefore, measurement and analysis of HRF indices may can be used as a clinical synergic diagnosis and beneficial to the clinical study of CHF. No one else have ever applied fragmentation indices to detect CHF, so this study would be the first report.

HRF indices had been used as a new way to detect CAD. Such a new CAD detection method performed better than traditional heart rate variability measures within previous research [7]. This paper explored potential link between HRF indices and CHF, whether HRF indices were also better method for diagnosis of CHF. Based on previous research, SDNN, SDANN, SDNNIndex and other time domain indexes were less than 50ms, which meant heart rate variability is significantly reduced and case fatality could be greatly increased [10]. Compare this study of heart rate variability to our research, low level of heart rate variability generally accompanied high level of HRF indices, which demonstrated the impairment of cardiac function. Thus, HRF method indeed was an effective way to examine CHF.

Recent years, there were also many new methods which were put forward to diagnosis of CHF. Detecting CHF by using Renyi Entropy is a relatively simple way [11]. This special approach under a situation that heart rate is easy to get for everyone. Nowadays, enough accuracy of ECG signals was beneficial for layperson to detect CHF. Using microwave techniques as a tool of the diagnosis of CHF was reported in a recent research [12]. This study developed a portable microwave imaging system provided an entire new stratagem to detect CHF. However, this detection technology was still immature due to the hardware difficulties.
It seems to be a novel approach to use HRF indices to explore abnormal performance of heart rate and sequentially diagnose CHF. At present, observing the external signs of patients, such as paroxysmal dyspnea, visceral stasis symptoms and so on, are the main diagnosis method of patients with CHF [13]. Such diagnoses are not very accurate or convenient and cannot determine incubation period of the disease. By introducing HRF indices, detection of CHF can be visualized, automatically, repeatable and especially analysis quantitative. PIP, IALS, PSS and PAS are also data that can be measured easily. Thus, the diagnosis of CHF is simplified. Furthermore, according to the visualized data, even layperson can understand his physical situation and then find this disease in an early stage, which may be seen as prevention methods for keeping the disease from getting worse.

However, there are also some limitations to this paper. For instance, some physical conditions which may confuse the results of HRF indices were not considered in this paper [14]. Besides, although these indices may can detect disease, there is no quantitative analysis of the severity of the disease. More samples need to be included. Research of the mechanism of using HRF indices derived from ECG data to detect CHF also need deeper work. Further work could be done to explore other application for these indices.

5. Conclusion
In the paper, CHF patients have significantly higher value of HRF indices than healthy subjects on the analysis of their long-term ECG recording. CHF patients may have more fragmented feature on their ECG signal and reduced cardiac function. Thus, HRF method may be a novel and better approach to measure cardiac state and diagnose CHF problem.

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