HRV Spectral and Fractal Analysis in Heart Failure Patients with Different Aetiologies

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Abstract

Heart Rate Variability (HRV) has been widely studied both in healthy subjects and congestive heart failure (CHF) patients. Significant variations in the HRV patterns have been reported in cardiac patients and quantified both in time and spectral domain by various linear and nonlinear parameters which may be useful not only for the characterization of the autonomous nervous system but also for patients risk stratification. Nevertheless, the relationship between HRV measures and CHF aetiologies has not been completely investigated yet.

The purpose of this work was to evaluate the spectral and fractal properties of HRV in patients with CHF caused by either dilated cardiomyopathy or ischemic heart disease, and to compare the results with those coming from normal subjects. Results revealed that changes in some of the examined parameters may lead to a possible separation of the CHF aetiologies.

1. Introduction

Heart Rate Variability (HRV) has been widely investigated both in health and disease and a large number of HRV measures have been proposed in order to quantify this variability [1]. In particular, the study of HRV in patients affected by congestive heart failure (CHF) revealed that CHF may lead to impaired HRV patterns, due to abnormalities in both the sympathetic and parasympathetic control mechanism [2].

Previous studies also showed the potential of the nonlinear methods based on chaos theory and fractal analysis to study the complex mechanisms involved in HRV and demonstrated that nonlinear measures may better differentiate between healthy and unhealthy heart rhythm [3]. Fractal behaviour has been reported in the RR time series, because of the irregular fluctuations across multiple time scales of the RR time series [4], and Higuchi's fractal dimension (FD) has been successfully applied to quantify the complexity of RR time series in a variety of clinical situations [5-7].

The aim of this study was to assess the spectral and fractal properties of HRV in patients with dilated cardiomyopathy (DCM) and ischemic heart disease and to investigate whether classical linear measures of HRV (in particular the power spectral analysis in very low, low and high frequency bands and the LF/HF ratio) and Higuchi's FD could discriminate different CHF aetiologies.

2. Material and methods

2.1. Population and data acquisition

The study population consisted of 40 patients with CHF (30 men, mean age 61 ± 18 years). Patients were divided into two equal groups considering CHF aetiology: (1) dilated cardiomyopathy and (2) ischemic heart failure. The two groups with CHF were compared to 20 healthy control subjects (15 men, mean age 56 ± 18 years).

All subjects completed 24-hours Holter monitoring using a 3 channel recorder with sampling frequency of 200 Hz. RR intervals were automatically identified from ECG records using SyneScope® (Sorin Group, Italy) Holter analysis software, which also labelled each QRS complex as normal or artefact. Moreover, since recordings were started at different times, the RR series of the different subjects were aligned using a common start and stop time.

2.2. Data pre-processing and analysis

In order to minimize the effect of artefacts and to obtain a reliable estimation of the HRV parameters, RR raw data were adequately pre-processed. RR time series were divided into intervals of 15 min length and, for each interval, the percentage of artefacts (based on time, not on number of beats) and the duration of each set of subsequent artefacts were considered. Data were excluded from analysis whether the artefact percentage was over 5% [8] or the duration of a sequence of artefacts was over 10 seconds [9], because the correction of large amounts of

RR interval data may cause significant errors in the measurement of HRV indices. In this work, we decided to include ectopic beats in the HRV analysis, because they represent the real RR time series and they may have an important role in the discrimination of the CHF aetiology [10-12]. Cubic spline interpolation and resampling at 2 Hz were applied on the original RR sequences in order to obtain a constant sampling time.

Power spectral density was computed by periodogram method after Hamming windowing. Three main spectral components were distinguished [13]: Very Low Frequency (VLF) < 0.04Hz, Low Frequency (LF) 0.041-0.15Hz, High Frequency (HF) 0.151-0.4 Hz. All the values were expressed in normalized units (n.u.). In addition, the ratio between LF power and HF power (LF/HF), frequently used in literature [14], was calculated. Finally, fractal dimension, which quantifies the fractal-like behaviour of a time series, was estimated with Higuchi's algorithm [15].

In the first part of the work, for each patient, the entire time series were analysed; successively, being HRV influenced by circadian variations [16], two time epochs, day-time and night-time, lasting six hours each were selected for analysis. Day-time was defined from 3 pm to 9 pm and night-time from 12 pm to 6 am. For each subject, the parameters calculated on 15min were then averaged distinguishing the two epochs.

2.3.   Statistical analysis

The nonparametric Kruskal-Wallis test was used to compare three groups (normal, ischemic and DCM), while the Wilcoxon rank sum test was used to compare each pair of groups, followed by Bonferroni's correction due to multiple testing. Differences were considered significant for a p-value < 0.05. In addition, based on descriptive statistics, medians with 25th and 75th percentile were calculated for each parameter.

3.   Results

Table 1 summarizes the median values of the various parameters calculated for the three groups. Changes in the parameters, associated with the three groups, were statistically significant for HF, LF/HF and FD calculated during the day-time.

Because of the inclusion in the HRV analysis of ectopic beats, HF and FD were lower in normal subjects with respect to DCM and ischemic patients. On the other hand, the LF/HF ratio was lower in the ischemic group than in the normal one, while also in this case the DCM had intermediate values with respect to the other two groups. Such changes in the HF, LF/HF and FD values are displayed in Figure 1.

Moreover, also the other proposed parameters calculated in the day-time epoch had significantly different values for normal and ischemic and VLF also showed significant different values in DCM and ischemic patients.

LF, LF/HF and FD effectively distinguish the normal from the ischemic group also in the night-time, but none of the proposed parameters had significant differences for the DCM group with respect to the other two groups. The DCM group showed intermediate values with respect to normal and ischemic also for the parameters calculated in the night-time epoch, but the differences were not significant mainly because of the great variability within the subjects of the DCM group.

Table 1. Median (25th-75th percentile) of the different parameters for the three groups and respective p-values of the nonparametric Wilcoxon rank sum test followed by Bonferroni's correction.

| Parameter	Median (25th-75th percentile) Normal	Median (25th-75th percentile) DCM	Median (25th-75th percentile) Ischemic	p-value Normal vs. DCM	p-value Normal vs. Ischemic	p-value DCM vs. Ischemic
VLF day-time	0.64 (0.53-0.71)	0.54 (0.41-0.66)	0.31 (0.21-0.46)	n.s.	<0.003	<0.03
VLF night-time	0.55 (0.30-0.67)	0.46 (0.29-0.62)	0.33 (0.24-0.65)	n.s.	n.s.	n.s.
LF day-time	0.25 (0.15-0.32)	0.18 (0.13-0.24)	0.13 (0.10-0.19)	n.s.	<0.009	n.s.
LF night-time	0.22 (0.17-0.29)	0.18 (0.14-0.23)	0.16 (0.11-0.21)	n.s.	<0.04	n.s.
HF day-time	0.08 (0.06-0.18)	0.24 (0.14-0.39)	0.52 (0.36-0.58)	<0.02	<0.0001	<0.01
HF night-time	0.16 (0.11-0.46)	0.24 (0.16-0.47)	0.45 (0.18-0.58)	n.s.	n.s.	n.s.
LF/HF day-time	2.03 (1.03-4.21)	0.77 (0.41-1.62)	0.35 (0.17-0.57)	<0.02	<0.0001	<0.02
LF/HF night-time	1.17 (0.58-2.36)	0.80 (0.39-1.38)	0.36 (0.30-0.95)	n.s.	<0.006	n.s.
FD day-time	1.45 (1.31-1.52)	1.60 (1.45-1.70)	1.74 (1.65-1.79)	<0.008	<0.0001	<0.02
FD night-time	1.43 (1.38-1.55)	1.50 (1.38-1.69)	1.59 (1.54-1.71)	n.s.	<0.004	n.s.
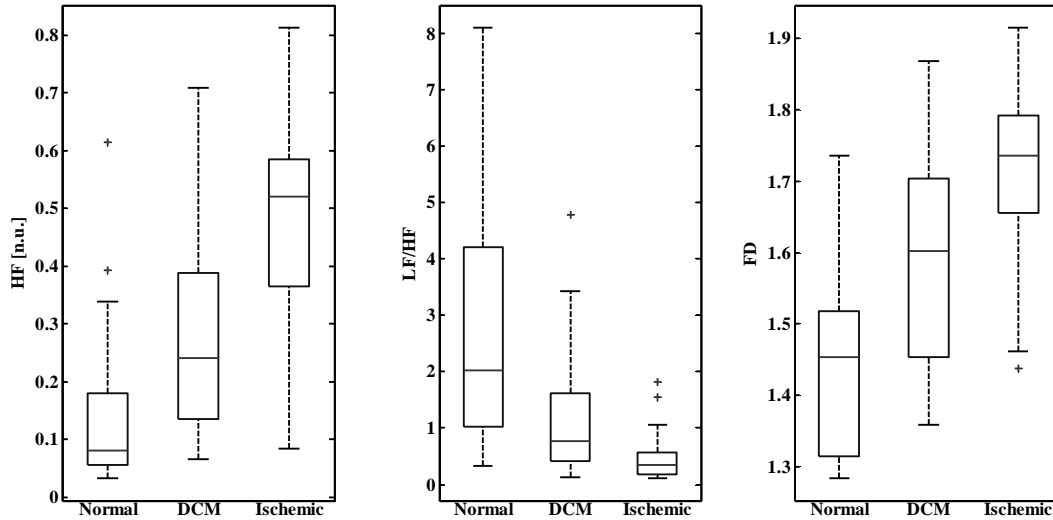
Figure 1. Box plot comparison of (A) high frequency, (B) LF/HF ratio and (C) Higuchi's fractal dimension in the three groups of subjects calculated for the day-time epoch. Tops and bottoms of each box are the 25th and 75th percentiles, respectively, and the line in the middle of each box is the median value. Whiskers extend to the most extreme data points not considered outliers. Outliers are plotted with a + sign.

4.   Discussion

The present study was designed to assess if it was possible to discriminate between DCM and ischemic heart disease, in comparison to normal subjects, analysing spectral and fractal behaviour of RR time series. For this purpose, the replacement of ectopic beats, which is traditionally applied in order to evaluate the autonomic nervous system activity from various HRV parameters, was avoided.

The analysis of these RR time series including premature beats showed significant differences in most of the proposed measures between the normal and the ischemic group, with the latter group having HRV properties highly altered due to impaired beat-to-beat dynamics [17].

On the contrary, the changes in the parameters were reduced for the DCM group in respect of both normal and ischemic group. The intermediate values of the DCM group for all the parameters as well as the great variability within the subjects of the DCM group may suggest to further refine the analysis of this group, individuating the clinical characteristics which determine some subjects to be assimilated to those of the normal group and some other to those of the ischemic group.

HF, LF/HF and FD calculated during the day-time seemed to be the most useful parameters in the discrimination of the groups, but probably the optimal characterization of the HRV is based on a combination of the different parameters rather than on a single one.

It is to note that the present results cannot be compared to other studies in which ectopic beats were excluded from the RR time series as well as the physiological interpretation of the spectral components and of the LF/HF cannot be easily associated to the sympathetic and parasympathetic activity of the autonomous nervous system. In fact, it is known that ectopy introduces a bias into HRV measures and thus represents a significant problem in the interpretation of these results [18].

The higher irregularities of the RR series of ischemic and DCM groups in comparison to the normal one were revealed by both HF and FD higher values for CHF patients. The changes of the LF/HF ratio between the three groups, even if statistically significant, may confound the problem because both LF and HF capture abnormally organized HRV patterns [19].

5.   Conclusion

Even if this study is limited to a reduced number of subjects, it demonstrated that spectral and fractal HRV measures could be profitably used in the HRV feature identification of ischemic and DCM patients. The DCM group showed intermediate characteristics between the normal and the ischemic ones, thus suggesting further investigation to better understand the clinical characteristics determining this result.

Further studies are needed also to clarify the role and the importance of the inclusion of ectopic beats in the HRV analysis for the differentiation of the three groups and of the CHF aetiologies.

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