

Heart Rate Variability Analysis—An Overview

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ABSTRACT

It has been found that the Heart Rate of a human being is not constant but fluctuates constantly. Various factors are attributed to this fluctuation. The Heart Rate Variability Analysis concerns with the systematic and quantitative study of these fluctuations. This paper presents the different methods and applications of Heart Rate Variability Analysis.

Introduction

Quite contrary to our expectation, a healthy heart does not beat at a regular, constant rate. In fact, one can almost say that perfectly rhythmic activity occurs only in disease. In normal individuals, the Heart Rate (HR) fluctuates constantly, reflecting the modulation of the sinus node activity by autonomic and other homeostatic mechanisms. Some of the factors which affect HR are breathing [1], posture [2], physical activity [3], mental stress [4], different stages of sleep and circadian rhythm [5]. The determinants of the respiratory fluctuations in heart rate include a stretch reflex from the lungs and thoracic wall, changes in cardiac filling, arterial baroreceptor responses to blood pressure changes, changes in baroreflex sensitivity with respiratory phase and respiratory center activity overflow to medullary vasomotor neurons [6]. The pattern of these changes are modified in pathological conditions such as post-myocardial infarction, diabetes and psychiatric disorders such as alcoholism and depression. HRV analysis concerns with the systematic, quantitative study of the fluctuations in the heart rate. The time and frequency domain parameters that are usually measured from this HRV signal are indirect indicators of the integrity of the control mechanisms that cause the variability. Thus, the HRV investigations provide a useful non-invasive window to measure neurocardiac control. This article presents a general overview of the methodology and applications of HRV analysis.

Methodology

A noise-free record of ECG is obtained lasting several minutes. In most studies, ECG is recorded twice from the subject, first in supine position and then, immediately after standing. This enables one to study the changes, mediated through the baroreceptors, resulting from the orthostatic stress. The ECG is sampled at a sufficiently high rate (usually 500 Hz) to

determine the time locations of the R waves at the accuracies needed for the analysis. The R waves are detected using a suitable algorithm and from the resulting R-R interval series, several time domain descriptors of the variability are computed. Alternatively, the instantaneous heart rate series is first obtained from the R-R intervals. Fig. 1 shows a typical HR time series plotted against the time of occurrence of R waves, with the subject in supine position. Fig. 2 shows the HR values obtained for the same subject immediately after standing. The sudden increase in HR due to orthostatic stress is clearly seen. The HR signals shown in Figs. 1 and 2 are discrete-time signals, with unequal time intervals (corresponding to individual R-R intervals) between the individual values. This data is suitably interpolated to obtain evenly spaced (in time, usually 0.25 sec.) heart rate samples. From this time series, the mean is removed to obtain the Heart Rate Variability point series. Various spectral parameters are then computed from this signal.

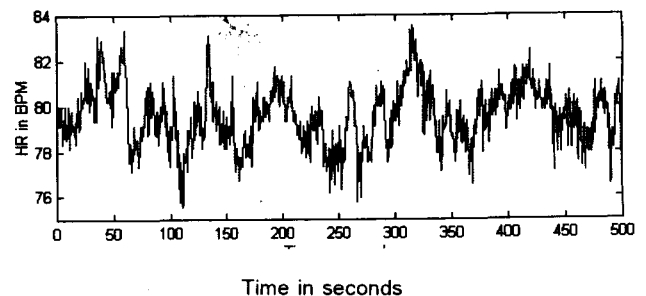


FIG. 1: A Typical HR Time Series (Subject in supine position)

A. Time Domain Analysis

From the original R-R intervals, a number of parameters are calculated: The mean R-R interval (MRI), the standard deviation of the mean R-R intervals of consecutive short periods (SD), mean of the absolute differences between consecutive R-R intervals (MAD), the Root Mean Square Successive Difference (RMSSD)

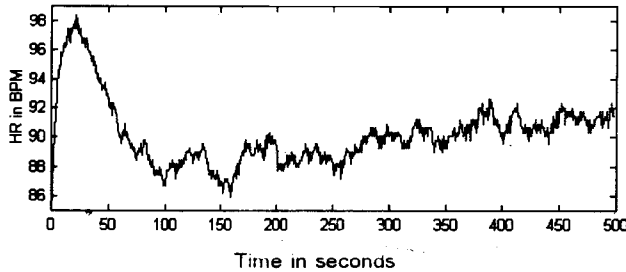


FIG. 2: HR Time Series (Immediately after the subject stood)

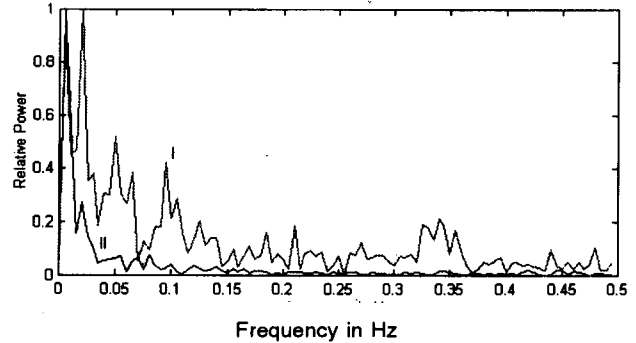


FIG. 3: Power Spectrum of HRV (I - Supine; II - Standing)

of intervals, the number of successive R-R intervals which differ by more than 50 msec. (pNN50) as a percentage of the total number of ECG cycles analyzed, the ratio (E/I) as well as the difference (E-I) between the maximum (E) and minimum (I) heart periods (E and I typically occur during some Expiratory and Inspiratory phases respectively of the breathing cycle). Also computed is the Coefficient of Variation, CV_{R-R} , defined as the ratio of the standard deviation of the R-R intervals to their average value.

B. Spectral Domain Analysis

In order to obtain the power spectrum, we need to have uniform time interval samples of the HR. Since HR values are available only at the R occurrence instants, we need some interpolation technique. Berger's algorithm [7] is accepted as one of the standard techniques in the literature but, in the author's experience, a simple linear interpolation gives results as good. From this uniform interval HR series, the mean is then removed. Either FFT or a Linear Prediction model (usually, Autoregressive) spectrum of this HRV signal is then obtained. Fig. 3 shows sample HRV spectra for supine and standing postures of a subject. The absolute power in the very low frequency band (VLF, frequency range 0.01 - 0.05 Hz), the low frequency band (LF, 0.05 - 0.15 Hz) and high frequency band (HF, 0.16 - 0.35 Hz) and ratios of HF and LF to total HRV power are calculated. The HF peak is correlated to the respiratory driven vagal (parasympathetic) efferent input to the sinus node. The LF band probably represents both sympathetic and vagal drive and the VLF band is supposed to be linked to the thermoregulatory system. A ratio of the energies in the LF and HF bands is currently being accepted as representing sympathovagal balance.

Though most studies have analyzed the HRV samples, a few investigators have directly obtained the power spectrum of the R-R interval series, ignoring the fact that the latter is a non-uniformly sampled data. These results are not always directly comparable to

those obtained from the HRV series. A recent article by Castiglioni [8] discusses in detail the advantages, disadvantages and the relationship between these two methods of analysis. Another problem in comparing results of different groups using LP spectrum is that the model order is rarely specified.

Clinical Applications

The anatomic location of the Autonomic Nervous System (ANS) renders it inaccessible to direct physiological testing. The study of HRV Power Spectra is gaining acceptance as a non-invasive method for identifying the role of the ANS in regulating cardiac function. HRV decreases with age and this factor must be kept in mind while interpreting the results of any study. It may be possible to roughly normalize the data with respect to age. HRV analysis being a field of current research, the possible clinical applications are increasing. The following are some of the potential clinical uses already identified:

Risk Stratification of Post-Myocardial Infarction Patients

Decreased heart rate variability is a strong and independent predictor of adverse outcome after acute Myocardial Infarction (MI). Either time or frequency domain measures are excellent predictors of death or arrhythmic events after MI and they are equivalent for this purpose. Post-infarction patients with low HRV exhibit a profound autonomic imbalance that results in an increased incidence of sudden death [9]. The presumed pathologic mechanism for the sudden death is the excessive autonomic discharge, especially norepinephrine and epinephrine. The relative risk of patients with a R-R interval variance of $< 1000 \text{ msec}^2$ has been found to be 3.8. HRV index is equivalent to Left Ventricular Ejection Fraction (LVEF) for predicting all-cause mortality, but is better than LVEF or Signal Averaged ECG for predicting arrhythmic events.

Similarly, power spectral analysis of HRV could also be used to categorize patients according to risk of sudden cardiac death.

Psychiatry

The significance of HRV analysis in psychiatric disorders arises from the fact that one can easily detect a sympatho-vagal imbalance (relative cholinergic and adrenergic modulation of HRV), if it exists in such pathologies. It has also been applied to identify possible autonomic dysfunction resulting from the side effects of pharmacological treatment. In situations such as this, one needs to eliminate subjects known to have cardiovascular diseases.

HRV Analysis of Holter Data

The power in the Very Low Frequency (VLF) band (from DC to about 0.03 Hz) of the HRV spectrum is probably due to slow mechanisms of regulation such as humoral and thermoregulatory factors. Obtaining a single power spectrum over a long period can help investigate the long-term regulatory mechanisms involved in the VLF component. However, the sampling frequency in current Holter systems is 125 Hz, thus limiting the resolution of measurement of R-R intervals. The interpretation of results is also obscured by the fact that the patient's dynamic state keeps varying during the recording.

Sleep Research

To study the autonomic mechanisms in sleep, HRV may serve as one of the techniques. HR is significantly reduced during all stages of non-REM sleep. Normal healthy individuals studied during sleep using the above techniques show an elevated vagal modulation during stages 1, 2, 3 and 4, whereas REM sleep is characterized by decreased respiratory sinus arrhythmia (i.e., reduced HF power in HRV spectrum).

Heart Transplantation

Following transplantation, the heart rhythm is completely controlled by the donor sinoatrial node with no neurally mediated influence from the recipient. The power spectra of HRV of such a donor organ, devoid of autonomic innervation, has been observed to resemble a white noise power spectrum. However, in only one isolated case, all parameters of HRV were indistinguishable from normal subjects, including responses to respiration, orthostatic stress, etc. [10]. This suggests possible functional reinnervation in the human heart allograft. Thus, HRV analysis offers a unique method of establishing reinnervation of human transplanted hearts.

Other Applications

This provides another sensitive non-invasive method of detecting autonomic neuropathy in diabetes. Spectral studies in diabetics have shown lower LF/HF ratio during tilting as compared to normal subjects, whereas no significant difference was observed in supine state. In addition to the above mentioned applications, changes due to exercise, relation between autonomic cardiac function and the clinical and angiographic features of myocardial ischemia and autonomic imbalance in patients with congestive heart failure [11] have been studied exploiting the advantages of the above techniques.

References

1. A. G. Ramakrishnan and T. M. Srinivasan, *Significance of Breathing Pattern Variability in HRV Studies*, in *Abst. of 2nd Far Eastern Conf. on Med. and Biol. Engg.*, Beijing, China, pp. 335, August 1993.
2. Pomeranz, et al, *Assessment of Autonomic Functions in Humans by Heart Rate Spectral Analysis*, *Am J. Physiol.*, H15. pp. 248, 1985.
3. M. V. Kamath, E. L. Fallen, and Mckelvie R., *Effects of Steady State Exercise on the Power Spectrum of Heart Rate Variability*, *Med. Sci. Sports Exerc.* Vol. 23(4), pp. 428 – 434, 1991.
4. D. N. Nandagopal, E. L. Fallen, D. N. Ghista, and S. Connally, *Reproducibility of Resting HRV Spectrum and its Changes following Physiological Perturbations*, *Automedica*, Vol. 6, pp. 235, 1985.
5. M. V. Kamath and E. L. Fallen, *Diurnal Variations of Neurocardiac Rhythms in Acute Myocardial Infarction*, *Am J. Cardiol* Vol. 68, pp. 155 – 160, 1991.
6. J. P. Saul and R. J. Cohen, *Respiratory Sinus Arrhythmia, in Vagal Control of the Heart: Experimental Basis and Clinical Implications*, M. N. Levy and P. J. Schwartz, Eds. New York: Futura Publishing Co. Inc., 1994, pp. 511–536.
7. R. D. Berger, S. Akselrod, D. Gordon, R. J. Cohen, *An Efficient Algorithm for Spectral Analysis of Heart Rate Variability*, *IEEE Tr. BME*; Vol. 33 (9), pp. 900 – 904, 1986.
8. P. Castiglioni, *Evaluation of Heart Rhythm Variability by Heart Rate or Heart Period: Differences, Pitfalls and Help from Logarithms*, *Med. Biol. Eng. Comput.* Vol. 33, pp. 323 – 330, 1995.
9. G. A. Myers, et al., *Power Spectral Analysis of HRV in Sudden Cardiac Death: Comparison to other Methods*, *IEEE Trans. Biomed. Eng.*, Vol. 33. No. 12, pp. 1149 – 1156, 1986.
10. K. E. F. Sands, M. L. Appel, L. S. Lilly, F. J. Schoen, G. H. Mudge, and R. J. Cohen, *Power Spectrum Analysis of HRV in Human Cardiac Transplant Recipients*, *Circulation*, Vol. 79, pp. 76 – 82, 1989.
11. J. Philip Saul, *Heart Rate Variability during Congestive Heart Failure: Observations and Implications*, in *Blood Pressure and Heart Rate Variability*, M. Di Rienzo et al, Eds. IOS Press, 1992, pp. 266 – 275.