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REVIEW ARTICLE

Heart rate variability: a review

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Abstract Heart rate variability (HRV) is a reliable reflection of the many physiological factors modulating the normal rhythm of the heart. In fact, they provide a powerful means of observing the interplay between the sympathetic and parasympathetic nervous systems. It shows that the structure generating the signal is not only simply linear, but also involves nonlinear contributions. Heart rate (HR) is a nonstationary signal; its variation may contain indicators of current disease, or warnings about impending cardiac diseases. The indicators may be present at all times or may occur at random—during certain intervals of the day. It is strenuous and time consuming to study and pinpoint abnormalities in voluminous data collected over several hours. Hence, HR variation analysis (instantaneous HR against time axis) has become a popular noninvasive tool for assessing the activities of the autonomic nervous system. Computer based analytical tools for in-depth study of data over daylong intervals can be very useful in diagnostics. Therefore, the HRV signal parameters, extracted and analyzed using computers, are highly useful in diagnostics. In this paper, we have discussed the various applications of HRV and different linear, frequency domain, wavelet domain, nonlinear techniques used for the analysis of the HRV.

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1 Introduction

Heart rate variability (HRV), the variation over time of the period between consecutive heartbeats, is predominantly dependent on the extrinsic regulation of the heart rate (HR). HRV is thought to reflect the heart's ability to adapt to changing circumstances by detecting and quickly responding to unpredictable stimuli. HRV analysis is the ability to assess overall cardiac health and the state of the autonomic nervous system (ANS) responsible for regulating cardiac activity.

HRV is a useful signal for understanding the status of the ANS. HRV refers to the variations in the beat intervals or correspondingly in the instantaneous HR. The normal variability in HR is due to autonomic neural regulation of the heart and the circulatory system [111]. The balancing action of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) branches of the ANS controls the HR. Increased SNS or diminished PNS activity results in cardio-acceleration. Conversely, a low SNS activity or a high PNS activity causes cardio-deceleration. The degree of variability in the HR provides information about the functioning of the nervous control on the HR and the heart's ability to respond.

Past 20 years have witnessed the recognition of the significant relationship between ANS and cardiovascular mortality including sudden death due to cardiac arrest [69, 115, 120]. Numerous numbers of papers appeared in connection with HRV related cardiological issues [8, 13, 57, 58, 64, 87, 97, 112] reiterates the significance of HRV in assessing the cardiac heath. The interest in the analysis of HRV (i.e., the fluctuations of the heart beating in time,) is not new. Furthermore, much progress was achieved in this field with the advent of low cost computers with massive computational power, which fueled many recent advances.

Tulen and Man in t'veld [125] have found that, HR, diastolic blood pressure (BP), mid-frequency band power of HR and systolic BP, and plasma adrenaline concentrations showed significant increase when changed from supine to sitting to standing posture. Viktor et al. [132] have studied the variation of HR spectrogram and breathing rates in lateral and supine body positions. Recently, new dynamic methods of HRV quantification have been used to uncover nonlinear fluctuations in HR, that are not otherwise apparent. Several methods have been proposed: Lyapunov exponents [105], 1/*f* slope [64], approximate entropy (ApEn) [93] and detrended fluctuation analysis (DFA) [91].

Heart rate variability, i.e., the amount of HR fluctuations around the mean HR, can be used as a mirror of the cardiorespiratory control system. It is a valuable tool to investigate the sympathetic and parasympathetic function of the ANS. The most important application of HRV analysis is the surveillance of postinfarction and diabetic patients. HRV gives information about the sympathetic-parasympathetic autonomic balance and thus about the risk for sudden cardiac death (SCD) in these patients. HRV measurements are easy to perform, noninvasive, and have good reproducibility, if used under standardized conditions [46, 63].

Kovatchev et al. [65] have introduced the sample asymmetry analysis (SAA) and illustrate its utility for assessment of HR characteristics occurring, early in the course of neonatal sepsis and systemic inflammatory response syndrome (SIRS). Compared with healthy infants, infants who experienced sepsis had similar sample asymmetry in health, and elevated values before sepsis and SIRS ($p = 0.002$). Cysarz et al. [29] have demonstrated that the binary symbolization of RR interval dynamics, which at first glance seems to be an enormous waste of information, gives an important key to a better understanding of normal heart period regularity. Furthermore, differential binary symbolization still enables the identification of nonlinear dynamical properties.

Recently, Verlinde et al. [129] have compared the HRV of aerobic athletes with the controls and showed that the aerobic athletes have an increased power in all frequency bands. These results are in accordance with values obtained by spectral analysis using the Fourier transform, suggesting that wavelet analysis could be an appropriate tool to evaluate oscillating components in HRV. But, in addition to classic methods, it also gives a time resolution. Time-dependent spectral analysis of HRV using the wavelet transform was found to be valuable for explaining the patterns of cardiac rate control during reperfusion. In addition, examination of the entire record revealed epochs of markedly diminished HRV in two patients, which attribute to vagal saturation [123]. A method for analyzing HRV signals using the wavelet transform was applied to obtain a time-scale representation for very low-frequency (VLF), low-frequency (LF) and high-frequency (HF) bands using the orthogonal multiresolution pyramidal algorithm [44]. Results suggest that wavelet analysis provides useful information for the assessment of dynamic changes and patterns of HRV during myocardial ischaemia. Time-frequency parameters calculated using wavelet transform and extracted from the nocturnal heart period analysis appeared as powerful tools for obstructive sleep apnoea syndrome diagnosis [104]. Time-frequency domain analysis of the nocturnal HRV using wavelet decomposition could represent an efficient marker of obstructive sleep apnoea syndrome [104]. Its added ease of use and interpretation is of interest in considering the high prevalence of sleep-related breathing disorders in a general middle-aged, at-risk population. Recently, Schumacher et al. [114] have explained the use of linear and nonlinear analysis in the analysis of the HR signals. The affect of ANS, BP, myocardial infarction (MI), nervous system, age, gender, drugs, diabetes, renal failure, smoking, alcohol, sleep on the HRV are discussed in detail.

Power spectral analysis of beat-to-beat HRV has provided a useful means of understanding the interplay between autonomic and cardiovascular functionality. Mager et al. [73] have developed an algorithm that utilizes continuous wavelet transform (CWT) parameters as inputs to Kohonen's self-organizing map (SOM), for providing a method of clustering subjects with similar wavelet transform signatures . Bracic et al. [18] have analyzed human blood flow in the time-frequency domain, and used the wavelet transform (Morlet) which gives good time resolution for high frequency components and good frequency resolution for LF components . Recently, HR (using Morlet wavelet as mother wavelet) for different cardiac arrhythmias was proposed (Oliver et al. 2004). Shimojima et al. [118] have used Morlet mother wavelet to evaluate the performance of frequency power spectrum during QRS in intraventricular conduction abnormalities (IVCA). They have observed that there is reduction of the low frequency power in IVCA and the increased power and number of peaks in high frequency range in IVCA with MI.

1.1 The autonomic nervous system

The ANS have sympathetic and parasympathetic components. Sympathetic stimulation, occurring in response to stress, exercise and heart disease, causes an increase in HR by increasing the firing rate of pacemaker cells in the heart's sino-atrial node. Parasympathetic activity, primarily resulting from the function of internal organs, trauma, allergic reactions and the inhalation of irritants, decreases the firing rate of pacemaker cells and the HR, providing a regulatory balance in physiological autonomic function. The separate rhythmic contributions from sympathetic and parasympathetic autonomic activity modulate the heart rate (RR) intervals of the QRS complex in the electrocardiogram (ECG), at distinct frequencies. Sympathetic activity is associated with the low frequency range (0.04–0.15 Hz) while parasympathetic activity is associated with the higher frequency range (0.15–0.4 Hz) of modulation frequencies of the HR. This difference in frequency ranges allows HRV analysis to separate sympathetic and parasympathetic contributions evident. This should enable preventive intervention at an early stage when it is most beneficial.

1.2 HRV and blood pressure

Several structural and functional alterations of the cardiovascular system that are frequently found in hypertensive individuals may increase their cardiovascular risk beyond that induced by the BP elevation alone. Electrocardiographic evidence of left ventricular hypertrophy (LVH) and strain are associated with increased morbidity and mortality. HRV is significantly reduced in patients with LVH secondary to hypertension or aortic valve disease. Cardiac vagal nerve activity is influenced by the arterial baroreflex. The amplitude of respiratory sinus arrhythmia (HRV) has been found to correlate with baroreflex sensitivity which is reduced in hypertension and diabetes. This reduction in baroreflex sensitivity is correlated with cardiac LVH.

A method to describe relationships between short-term BP fluctuations and heart-rate variability in resting subjects was analyzed in the frequency domain [9, 14–16]. Relationships between pressure and interval variability indicate that the 10-s variability, which indicate in systolic pressure, leads the interval variation by two to three beats and manifest in cross-spectra. However no such lag is found between the respiration-linked variations in systolic pressure. And later they [14–16] have proposed a simple model to interpret the results of spectral analysis of BP and HR data. The baroreflex equation of the model describe the data only in the region of respiratory frequencies. The shape of the phase spectrum of systolic pressures against intervals was modeled by difference equations. But no physiological interpretation of these equations was given. They have proved that, the spectral properties of the input signal can not be recovered fully from the interval spectrum, nor from the spectrum of counts, the more so as physiological series of events were not be generated by an ideal integrated pulse frequency modulation (IPFM) model [14–16]. Recently, the European Society of Hypertension working group on baroreflex and cardiovascular variability, in which 11 centres participated, has produced a comprehensive database which is available for testing and comparison of methods [66]. Recently, Westerhof et al. [137] have proposed a cross-correlation baro-flex sensitivity (xBRS) technique for the computation of time-domain baroreflex sensitivity on spontaneous BP and HRV using EUROBAVAR data set. They proved that, the xBRS method may be considered for experimental and clinical use, because the values yielded were correlated strongly with and was close to the EUROBAVAR averages.

1.3 HRV and myocardial infarction

A predominance of sympathetic activity and reduction in parasympathetic cardiac control has been found in patients with acute MI [108]. Sympathetic activity decreases the fibrillation threshold and predisposes to ventricular fibrillation (VF). Vagal activity increases the threshold and appears to protect against malignant ventricular tachyarrhythmias [117, 138]. The degree of respiratory sinus arrhythmia shows a linear relation with parasympathetic cardiac control [61, 75] and thus can be used as a prognostic tool in patients, who have had a MI. It was shown that, the HRV decreases with the recent MI [21, 22]. Despite the beneficial effects on clinical variables, exercise training did not markedly alter HRV indexes in subjects after MI [32]. A significant decrease in SDRR and HF power in the control group suggested an ongoing process of sympathovagal imbalance in favor of sympathetic dominance in untrained patients after MI with new-onset left ventricular dysfunction.

1.4 HRV and nervous system

Disorders of the central and peripheral nervous system have effects on HRV. The vagally and sympathetically mediated fluctuations in HR may be independently affected by some disorders. All normal cyclic changes in HR are reduced in the presence of severe brain damage [71] and depression [21, 22]. HRV was less accurate than the Glasgow Coma Scale in predicting outcome. But it was easily accessible and may provide information about the patient's neurologic status [67]. In serial determinations, the rate of return of normal HRV may reflect the subsequent state of neuronal function.

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. There is conflicting reports about the HRV and the major depression. It is proved that, in physically healthy depressed adults the HRV does not vary from healthy subjects [113].

1.5 HRV and cardiac arrhythmia

A complex system like cardiovascular system cannot be linear in nature and by considering it as a nonlinear system, can lead to better understanding of the system dynamics. Recent studies have also stressed the importance of nonlinear techniques to study HRV in issues related to both health and disease. The progress made in the field using measures of chaos has attracted the scientific community to apply these tools in studying physiological systems, and HRV is no exception. There have been several methods of estimating invariants from nonlinear dynamical systems being reported in the literature. Recently, Fell et al. [39] and Radhakrishna et al. [99] have tried the nonlinear analysis of ECG and HRV signals, respectively. Also, Paul et al. (2002) showed that coordinated mechanical activity in the heart during VF may be made visible in the surface ECG using wavelet transform. Owis et al. [86] have used nonlinear dynamical modeling in ECG arrhythmia detection and classification. Acharya et al. [1–4] have classified the HRV signals using nonlinear techniques, and artificial intelligence into different groups. Dingfie et al. [46] have classified cardiac arrhythmia into six classes using autoregressive (AR) modeling.

1.6 HRV in diabetes

Diabetes can cause severe autonomic dysfunction and can be responsible for several disabling symptoms, including SCD. Although traditional measures of autonomic function are able to document the presence of neuropathy, in general they are only abnormal when there is severe symptomatology. Thus by the time changes in function were evident, the natural course of autonomic neuropathy was well established. HRV and SCD Ventricular tachyarrhythmias represent a leading cause of SCD in the community.

The pathophysiology of SCD was probably an interaction between an abnormal anatomical substrate such as coronary artery disease with associated myocardial scarring, LVH or cardiomyopathy, and transient functional disturbances which trigger the terminal dysrhythmia. This may include factors such as ischaemia, premature beats, electrolyte disturbance and fluctuations in autonomic balance.

The decreased beat-to-beat variability during deep breathing in diabetic neuropathy was first reported by Wheeler and Watkins [139] and confirmed by many others [92]. In studies comparing cardiac autonomic function tests and HRV indices (based on both short (5-min) and 24-h ECG recordings), show that, in diabetic patients without abnormal function tests, HRV was lowered [92]. It was concluded that cardiac (parasympathetic) autonomic activity was diminished in diabetic patients before clinical symptoms of neuropathy become evident [92, 119, 134].

1.7 HRV and renal failure

In patients with renal failure, autonomic function tests have been done [37, 146], followed by HRV indices [41] and spectral analysis of HR [10]. Although autonomic function tests revealed predominant impairment of the PNS [146], spectral analysis exhibited a strong reduction in the HR power spectrum at all frequency ranges, both sympathetically and parasympathetically [10]. The relationship between HRV parameters and electrolyte ion concentrations in both pre- and post-dialysis [124]. The 5-min HRV of 20 chronic renal failure (CRF) patients were analyzed. Results revealed that calcium is negatively correlated to the mean of RR intervals and normalized HF power after hemodialysis. A model of baroreflex control of BP was proposed in terms of a delay differential equation and was used to predict the adaptation of short-term cardiovascular control in CRF patients [68]. They showed that in CRF patients, the mean power in the LF band was higher and lower in the

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