

Review Article:
HEART RATE VARIABILITY
A Remarkable Tool to Assess Sympathovagal Balance

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ABSTRACT

An electrocardiography (ECG) recording is not only an information source of heart electrical and mechanical functions, but also a source of information about cardiac autonomic functions. The latter, can be analyzed by various methods, including by performing a heart rate interval analysis, termed as heart rate variability (HRV), from a short or long term ECG recording. This paper highlights the methods how to do analyses, the physiological relevance in understanding HRV, and various factors may interfere HRV in normal subjects. Prolonged activation of sympathetic activities is correlated with bad prognosis, whereas chronic parasympathetic dominance has been considered cardioprotective. Indicating the dominance of either sympathetic or parasympathetic tones, HRV may act as a remarkable prognostic determining tool, especially in association with cardiovascular issues.

Keywords: heart rate variability, autonomic function, sympathovagal balance

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INTRODUCTION

The Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) defines heart rate variability (HRV) as the magnitude of heart rate fluctuations around the mean heart rate. The focus of this measurement is the oscillation in the interval between consecutive heart beats, also called normal-to-normal (NN) intervals or R to R (RR) intervals, as well as between consecutive instantaneous heart rates. Typically, it usually uses the R wave as the marker and reference point of analysis (McMillan 2002). Numerous factors continuously modulate heart rate through autonomic nerve and neurohumoral pathways. The activation of sympathetic and parasympathetic nerves results in net effects of increases and decreases in heart rate respectively. Thus, a study of heart rate fluctuations provides information about cardiac vagal tone, sympathovagal balance (Winsley 2002) and interactions between the cardiovascular and neurological systems (Bergfeldt & Haga 2003). Despite the existence of normal variation of dominant autonomic components, a chronic sympathetic activation is pathologic and has been associated with poor cardiovascular prognosis (McMillan 2002). On the other hand, parasympathetic dominance seems to confer cardioprotection (McMillan 2002).

METHODOLOGY

There are two main methods used to measure HRV namely time domain and frequency domain analysis (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Time domain analysis is a conventional statistical analysis of beat-to-beat heart rate quantification. It is usually presented in form of a cardiogram and histograms of RR intervals or delta RR intervals (Figure 1 and 2). The cardiogram, a geographical display of RR interval series, represents the interval (time) between consecutive R waves, measured in milliseconds (Kamen 1996). The simplest time domain variable is standard deviation of NN interval (SDNN, where NN represents the RR interval of only normal, non-ectopic, non-artifact beats), and is a statistic representing all of the cyclic components responsible for variability in the period of recording. Other measures commonly calculated include the mean of NN interval, standard deviation of average NN interval (SDANN), the square of root mean squared differences of successive NN intervals (RMSSD), the number of intervals where the difference of successive beats is larger than 50 ms (NN50) and the proportion of NN50 in total number of NN intervals (pNN50) (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). RMSSD and

pNN50 reflects the power of high frequency (HF) in frequency domain analysis (Ueda et al. 2002).

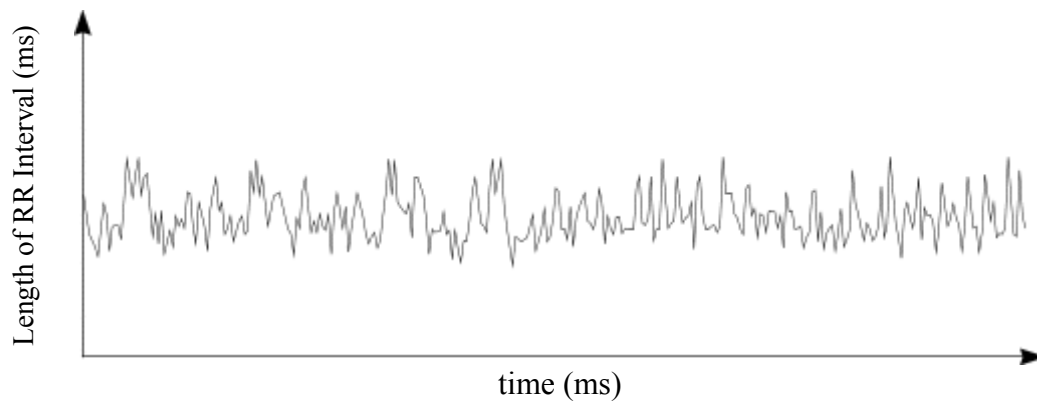


Figure 1. Cardiogram, indicates the occurrence of RR intervals from time to time (in ms)

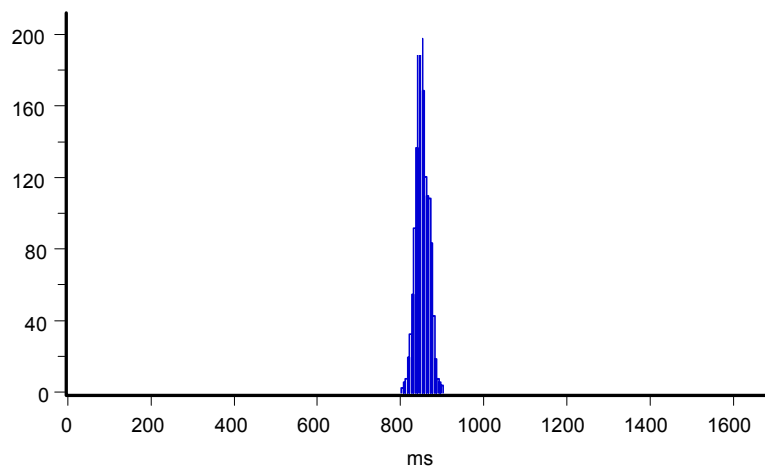


Figure 2. Histogram, summarizes the number of RR intervals occurred in certain duration.

The frequency domain analysis, usually presented in form of spectrum of frequencies (Figure 3), is believed to be more accurate in differentiating the two autonomic components of HRV signals. Most methods used to convert the time domain signal into the frequency domain involve the use of mathematical transformations, which decompose the signals into the sum of sine waves of different amplitude and frequency. Then, spectral analysis technique is used to analyze the transformed signals (Kamen 1996). The frequencies commonly used in HRV studies are very low frequency (VLF; 0.003-0.004 Hz), low frequency (LF; 0.04-0.15 Hz), and high frequency (HF; 0.15-0.4 Hz). Other frequency domain measures include total power (TP), which reflects variance of all NN intervals, and ratio of low frequency to high frequency (LF/HF). Frequency domain components are usually presented in absolute value of power (millisecond squared) or in normalized units (nu, only for LF and HF). The power spectrum

reflects the amplitude of heart rate fluctuation at certain frequencies. Normalization (nu) represents the relative value of each power component in proportion to TP minus VLF, minimizing the effects of the changes in total power to the LF and HF components during the sympathetic or parasympathetic activation (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

Other relatively new methods used in HRV analysis are nonlinear methods, which are determined by complex interactions of variables such as hemodynamic, electrophysiological and humoral changes, as well as by regulations of autonomic and central nervous system (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). One of techniques used in these methods is poincaré plot, which is a scatter plot of

current RR interval (vertical axis, interval to next R wave) against the preceeding RR interval (horizontal axis, interval to previous R wave) (Kamen 1996). Although this semi-quantitative technique has not been applied to a large population, it is still potentially powerful (Kamen & Tonkin 1995). Ueda et al. (2002)

found strong correlations between the length of scatter plots and TP and VLF, the width of scatter plots correlates with HF; and the sum width and length of scatter plots correlates with TP (Figure 2.9) (Ueda et al. 2002).

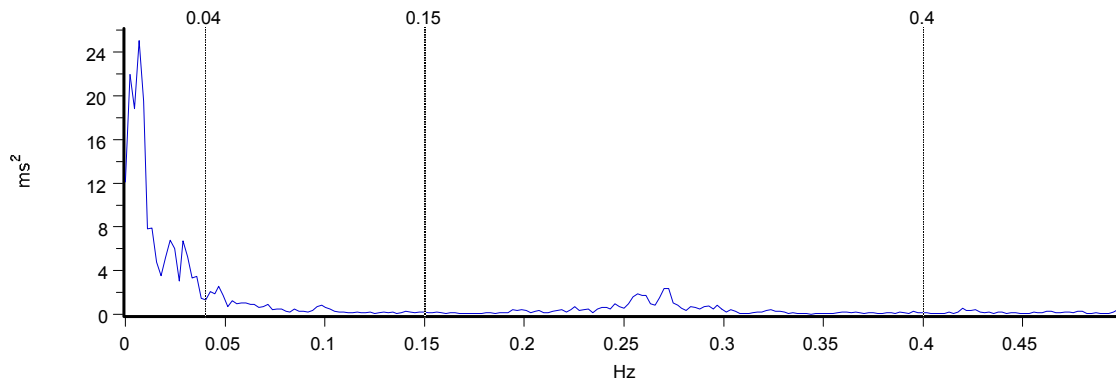


Figure 3. Spectrum of frequencies of HRV

MEANINGS OF FREQUENCY DOMAIN MEASURES

Akselrod et al. (1981) proposed that typically there are three peaks (low, mid and high frequency peaks) in spectral (frequency domain) analysis (Figure 4). The first peak centered at about 0.02-0.09 Hz, related to thermoregulatory fluctuation in vasomotor tone. The second one, related to baroreflex-mediated regulation, located at frequency of 0.09-0.15 Hz. The third peak was around respiratory frequency and highly influenced by respiratory rate. Akselrod et al. named the peaks as low, mid, and high frequency peaks (Akselrod et al., 1981). Recently, these peaks have been re-classified as very low, low and high frequency (van Ravenswaaij-Arts et al. 1993).

There are two types of recordings namely short-term (two-to-five minute) and long-term (24 hours) recordings. Short-term recording data are preferably investigated by using frequency domain methods, whereas long time recordings are best analyzed by using time domain methods. Although some time-domain measures such as SDNN and RMSSD can also analyze short term data, a longer recording of at least 20 minutes is required in order to provide enough representative data, especially for geometric methods (part of time domain methods) (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996).

HRV IN NORMAL INDIVIDUALS

The changes of RR interval in normal individuals occur frequently and irregularly. In a study of 25 normal subjects, Ewing, Nielson and Travis (1984) reported that changes of successive RR intervals greater than 50 ms occurred 150-250 times per hour during waking and 350-450 times per hour during sleeping, indicating an increase in vagal activity during sleep (Ewing et al. 1984). The number of these events decreases gradually with age (Ewing et al. 1991).

Pharmacological studies on autonomic control in modulating heart rate revealed the origin of various heart rate frequencies. Blockade of cardiac parasympathetic activities by either vagotomy (Horner et al. 1996) or by using anticholinergic agents (e.g., atropine) resulted in abolished peaks of HF power and a substantial reduction in LF peaks (Jokkel et al. 1995; Pomeranz B et al. 1985). When a beta blocker (e.g., propranolol) was added to the vagal blockade, the peaks of LF power vanished with no changes in HF power (Horner et al. 1996; Pomeranz et al. 1985). On the other hand, administration of propranolol alone increased both LF and HF peaks, which was likely as the result of unopposed vagal activation. Addition atropine to propranolol produced similar result as atropine alone. Hence, HF represents vagal tone and provides an index of cardiac vagal activity; and LF represents combined vagal and sympathetic activities (Houle & Billman 1999; Jokkel et al. 1995; Pomeranz et al. 1985). As vagal excitations strongly correlate with respiration

rhythms, respiratory sinus arrhythmia (RSA) may also provide information about cardiac vagal activities (Eckberg 1983; Hayano et al. 1994; Katona & Jih 1975). Sympathetic tone outflow is indicated by LF/HF ratio (Nakagawa et al. 2001), which is also a measure of sympathovagal balance. Experts proposed that VLF originates from the influences of thermoregulation and

renin-angiotensin system (Akselrod et al. 1981; van Ravenswaaij-Arts et al. 1993; Winsley 2002). Akselrod et al. (1985) found that ACE blockade increased the power of VLF, although parasympathetic activities still strongly influenced VLF, indicated by marked decreases in VLF after vagal blockade (Taylor et al. 1998).

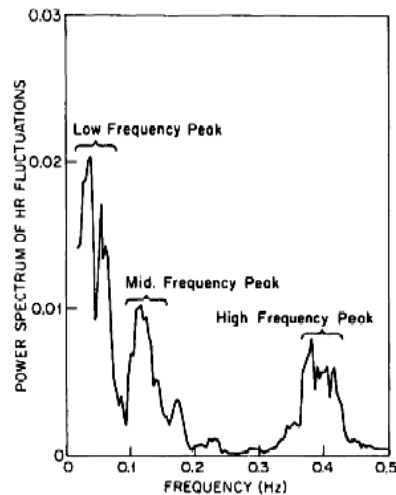


Figure 4. Three main peaks in the spectrum of HR fluctuations (Akselrod et al. 1981).

Postural effects on heart interval variations have been studied extensively. During rest on supine position, parasympathetic activity was dominant, showed by high HF and low ratio of LF/HF. During standing or passive head-up tilt, the sympathetic tone increased and vagal activity was inhibited, indicated by increases of LF power (Figure 5) (Nakagawa et al. 2001; Pagani et al., 1986; Pomeranz et al. 1985; Scavini et al. 1998). Compared to men, women have a greater power of HF during supine, but a smaller increase in LF during tilt (Barnett et al. 1999). Pomeranz et al. (1985) studied postural effects on HRV by applying a muscarinic anticholinergic agent (i.e., atropine) and a beta-adrenergic blocker (i.e., propranolol) to subjects (Table 1). These results support the concept that HF represents vagal activity, whereas LF is contributed by both vagal and sympathetic activities (Pomeranz et al. 1985).

Many studies investigated the relationship between respiration and alteration of heart rate. Controlled respiration resulted in a marked increase in the high-frequency component, and a reduction of LF component and of LF/HF ratio at rest. During tilt, the increase in LF/HF ratio was significantly smaller than for supine lying (Pagani et al. 1986; Scavini et al., 1998). Hayano et al. (1994) found similar reductions of LF during controlled breathing. However, they found no

significant changes in high frequency when paced breathing was performed at spontaneous frequency during supine lying and tilt. Further, they reported that HF increased with increasing respiratory rate (Hayano et al., 1994).

Long-term exercise training is associated with increases in both vagal activity and heart rate variability (Winsley 2002). Compared to sedentary people, athletes have lower resting heart rates and lower heart rate responses to submaximal exercise intensities. Aerobic exercise training for three months increased cardiovagal baroreflex sensitivity significantly in previously sedentary persons (Monahan et al. 2000). Thus, the long-term exercise effect is cardioprotective and has been recognized as a nonpharmacological intervention for arrhythmias in clinical settings (Billman 2002).

In clinical setting, HRV has been widely used in assessing autonomic nerve functions in various fields such as in cardiology, neurology, endocrinology, anesthesiology, pediatrics, obstetrics as well as in psychiatry (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996).

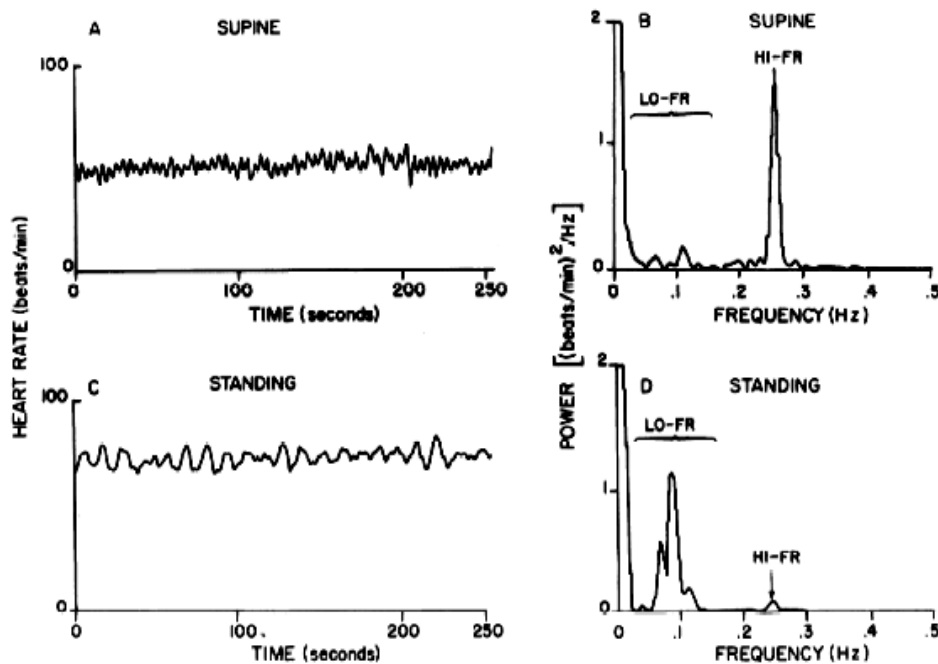


Figure 5. HRV in postural changes (supine and standing). A and C, cardiogram. B and D, power spectrum (Pomeranz B et al., 1985).

Table 1. Effects of autonomic blockade on LF and HF in supine and standing positions (Pomeranz B et al., 1985).

Posture	Day 1		Day 2	
	Atropine	Atropine + Propranolol	Propranolol	Propranolol + Atropine
<i>Low frequency (0.04–0.12 Hz)</i>				
Supine	-84† ±4.6	-83* ±5.6	+47 ±23.3	-90† ±2.5
Standing	-72* ±4.4	-89* ±1.7	-73* ±5.3	-90* ±2.6
<i>High frequency (0.224–0.28 Hz)</i>				
Supine	-92* ±4.2	-80* ±1.7	+18 ±25.0	-92* ±2.9
Standing	-95† ±1.8	-93† ±1.1	+11 ±48.9	-96* ±1.1

Values are means ± SE. * $P < 0.05$. † $P < 0.01$.

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