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Autonomic Nervous System Assessment- Wide Role of Heart Rate Variability Analysis- A Review

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ABSTRACT *Besides the various routinely performed tests for the evaluation of autonomic nervous system, the Heart Rate Variability (HRV) emerges as a newer and advance test. HRV is analyzed by time domain and frequency domain methods where mean and standard deviation of RR interval and power spectral density of RR series is taken into consideration respectively. Poincare plot is also reflects short and long term variability. This all methods helpful for evaluating the sympathetic and parasympathetic status and its interaction could be quantifiable. HRV act as a tool for understanding various physiological & clinical diseases which affects the normal rhythm of heart rate. It is cost effective, easy to test and it suggested HRV measurement is used for diagnostic and research purposes for the benefit of mankind.*

INTRODUCTION

The autonomic nervous system is essential to maintaining physiologic homeostasis in health and responding to illness. Its integrative functions coordinate input from peripheral and visceral afferent nerves to maintain a dynamic balance among organ systems. Its adaptive functions react moment by moment to the various forms of stress experiences by the body. The autonomic nervous system thus regulates and coordinates such physiological functions as blood pressure and heart rate, respiration, body temperature, sweating, lacrimation, nasal secretion, pupillary size, gastrointestinal motility, urinary bladder contraction, sexual physiology, and blood flow to the skin and many organs.(1)

The individual with the disturbance of the ANS shows complex clinical abnormalities. The diagnosis of autonomic neuropathy is often difficult to established, since clinical symptoms generally appear late in the course of the disease and may be non specific. In case of progressive autonomic failure there is degeneration of both preganglionic and postganglionic neuron of autonomic nervous system which leads to inability to maintain the blood pressure in the erect posture (orthostatic or postural hypotension), constipation, incontinence of urine, impotence, paralysis of accommodation, papillary areflexia, and disturbances of sweating and lose of lacrimation.

The autonomic functions test assessment is an important part of evaluation of peripheral and central nervous system. Its diagnosis is indirect, often being based on the measurement of physiological variables (reflexes) which are controlled by ANS. These test are reliable, reproducible, simple, quick to carry out and all non invasive. One important point in these tests is that here Stimulus is given and response is recorded and it is objectively quantifiable (2).

Some of the routinely used tests to detect the autonomic functions are classified into parasympathetic and sympathetic function tests.(2)

Parasympathetic Functions Test-
- Standing to lying ratio(S/L ratio)
- Immediate heart rate response to standing(30:15 R-R ratio)
- Valsalva ratio
- Tachycardia ratio
- Heart rate variation with respiration: Sinus arrhythmia

Sympathetic Functions Test-
- QT/QS2 ratio
- Sympathetic(galvanic) skin response
- Hand grip test
- Cold pressor test

Besides above given summary of tests, one of the significant non invasive tests is Heart rate variability analysis. There has been a growing interest over the last 30 years in studying the oscillations of the heart rate (HR) calculated from the electrocardiogram (ECG).These oscillations are termed as heart rate variability (HRV).

HISTORY OF HEART RATE VARIABILITY

The variation in signals like heart rate and blood pressure was remaining always interesting for physician. It was Stephan hales (1773) who documented earliest finding of these cardiovascular variations in blood pressure, when no ECG or other modern instruments were available for analyzing heart rate variability (HRV) signals. In 1778, Albrecht Von Haller observed that the healthy heart beat was not absolutely regular and their fluctuations were in a rhythm with respiration. Carl Ludwig in 1847 also recorded the pulse rate oscillations along with the inspiratory and expiratory state of respiration in dog. This change is known as respiratory sinus arrhythmia. HRV research was somewhat neglected until later century. In 1965, Hon and Lee reported reduction in beat to beat variability in fetus which is further correlated with fetal variability. It was Ewing and colleagues in 1970 that investigating the short term R-R interval difference to detect autonomic neuropathy in diabetic patients. In 1981, Akselrod et al & Marple (1981) incorporated the analysis of the HRV in clinical field. Kleiger et al. 1987, Farrell et al. 1991, Bigger et al. 1992,all confirmed the relationship of decline in HRV with increased risk for arrthymic events and mortality in patient of myocardial infarction. Akselrod et al (1985) observed the baroreflex related and thermoregulation related HRV other than respiratory sinus arrthymia.(3)

PHYSIOLOGICAL BACKGROUND OF THE HRV

Actually heart rate is depolarization of sinus node. Hear rate depict the balance of influences from the sympathetic and parasympathetic (vagus) nerves. In heart, vogues nerve (parasympathetic) innervates SA node, AV pathway and atrial muscle while sympathetic nerve innervate the entire heart including SA node, AV conducting pathways and atrioventricular muscle (3). Sinus node is innervated by both autonomic divisions so interection between sympathetic centre and vagal centre determines the final outcome of heart rate. Increased

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parasympathetic (vagal) activity has a decreasing effect on the heart rate mediated by release of acetylcholine which has short latency period thus parasympathetic activation to be regulated on a beat to beat basis. The vagal mediators exert their influence more quickly on the heart and principally high frequency power of the HRV spectrum(4).Sympathetic activity has reverse role due to release of norepinephrine which has a slower time course. Sympathetic mediators exert their influences over longer period of time and are reflected in the low frequency power (LFP) Thus the dynamics between parasympathetic and sympathetic activity causes a continuous oscillation of the heart rate which is called HRV. Thus at any point in time the ratio between LFP: HFP is a proxy of sympatho-vagal balance (4).

HRV act as a tool for examining the sympathetic and parasympathetic functions of the Autonomic nervous system (ANS).It also considered as a reflection of various physiological factors which affects the normal rhythm of heart rate. HRV can be used as a quantitative marker of autonomic nervous system. There are so many physiological and clinical disease which affects HRV. (5)

Clinical application of HRV analysis-

- Myocardial infarction and angina pectoris Diabetic neuropathy
- Congestive heart failure
- Malignant arrhythmias and sudden cardiac death Essential hypertension
- Cardiovascular surgery
- Assessment of risk in neurologic disorders- Severe head injury and brain death Acute brainstem stroke
- Evaluation outcomes in sepsis and shock Fetal and neonatal monitoring.

MEASUREMENT OF HEART RATE VARIABILITY

According to the standards set forth by the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology in 1996, there are two methods of analysis of HRV data: time-domain and frequency-domain analysis.

Time-domain methods

The time-domain parameters are the simplest ones calculated directly from the raw RR interval time series. The simplest time domain measures are the mean and standard deviation of the RR intervals. (Table-1) The prefix NN stands for normal-to-normal intervals (i.e. intervals between consecutive QRS complexes resulting from sinus node depolarization). In practice, RR and NN intervals usually appear to be same. (6)

Table 1: Commonly used time domain measures

AVNN*	Average of all NN intervals
SDNN*	Standard deviation of all NN intervals
SDANN	Standard deviation of the averages of NN intervals in all 5-minute segments of
	a 24-hour recording
SDNNIDX	Mean of the standard deviations of NN intervals in all 5-minute segments of a
	24-hour recording
rMSSD*	Square root of the mean of the squares of differences between adjacent NN
	intervals
pNN50*	Percentage of differences between adjacent NN intervals that are greater than
	50 ms

*** Short term HRV statistics**

Furthermore, there are some geometric measures like the HRV triangular index and TINN that are determined from the histogram of RR intervals.

RR triangular index The integral of the sample density distribution of RR intervals divided by the maximum of the density distribution

Baseline width of the minimum square di erence triangular interpolation of the maximum of the sample density distribution of RR intervals

Frequency domain methods

In the frequency-domain analysis power spectral density (PSD) of the RR series is calculated. Methods for calculating the PSD estimate may be divided into nonparametric [e.g. fast Fourier transform (FFT) based] and parametric [e.g. based on autoregressive (AR) models] methods.

The PSD is analyzed by calculating powers and peak frequencies for different frequency bands. (Table 2).For the FFT based spectrum powers are calculated by integrating the spectrum over the frequency bands. The parametric spectrum, on the other hand, can be divided into components and the band powers are obtained as powers of these components. This property of parametric spectrum estimation has made it popular in HRV analysis (7).

Table 2: Commonly used frequency-domain measures

TOTPWR*	Total spectral power of all NN intervals up to 0.04 Hz
ULF	Total spectral power of all NN intervals up to 0.003 Hz
VLF*	Total spectral power of all NN intervals between 0.003 and 0.04 Hz
LF*	Total spectral power of all NN intervals between 0.04 and 0.15 Hz
HF*	Total spectral power of all NN intervals between 0.15 and 0.4 Hz
LF/HF*	Ratio of low to high frequency power

*** Short-term HRV statistics (VLF = spectral power between 0 and 0.04 Hz.)**

Nonlinear methods

It is realistic to presume that HRV also contains nonlinear properties because of the complex regulation mechanisms controlling it. The interpretation and understanding of many nonlinear methods is, however, still insufficient. One simple and easy to comprehend nonlinear method is the so called Poincar´e plot. It is a graphical presentation of the correlation between consecutive RR intervals. The geometry of the Poincar´e plot is essential. A common way to describe the geometry is to fit an ellipse to the graph. The ellipse is fitted onto the so called line-of-identity at 45◦ to the normal axis. The standard deviation of the point's perpendicular to the line-of-identity denoted by SD1 describes short-term variability which is mainly caused by respiratory sinus arrhythmia (RSA). The standard deviation along the line-of-identity denoted by SD2 describes long-term variability (6).

Table: 3 Non linear measures (Poincare plot)

SD1	The standard deviation of Poincare plot perpendicular to the line of identity
SD2	The standard deviation of Poincare plot along the line of identity

INTERPRETATION

NN50 and RMSSD quantitate short-term HRV and they reflect alterations that are almost wholly mediated by vagal tone. These parameters are considered as vagal indexes.

Measurement of risk RR interval changes, such as SDRR index, pNN50% and RMSSD aim to evaluate parasympathetic activity, which, of course, is directly responsible for rapid HR fluctuation.(8)

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The HF power spectrum is evaluated in the range from 0.15 to 0.4 Hz. This band reflects parasympathetic (vagal) tone and fluctuations caused by spontaneous respiration known as respiratory sinus arrhythmia.

The LF power spectrum is evaluated in the range from 0.04 to 0.15 Hz. This band can reflect both sympathetic and parasympathetic tone.

The VLF power spectrum is evaluated in the range from 0.0033 to 0.04 Hz. The physiological meaning of this band is most disputable. With longer recordings it is considered representing sympathetic tone as well as slower humoral and thermoregulatory effects. There are some findings that in shorter recordings VLF has fair representation of various negative emotions, worries, rumination etc.

The TP is a net effect of all possible physiological mechanisms contributing in HR variability that can be detected in 5-min recordings, however sympathetic tone is considered as a primary contributor.

The LF/HF Ratio is used to indicate balance between sympathetic and parasympathetic tone. A decrease in this score might indicate either increase in parasympathetic or decrease in sympathetic tone. It must be considered together with absolute values of both LF and HF to determine what factor contributes in autonomic disbalance.(9)

CONCLUSION

Heart rate variability is a strong and independent physiological marker of autonomic tone. Its analysis diagnoses the sympathetic tone, parasympathetic tone and its interaction can be calculated. The HRV in clinical field is used very little despite the fact that HRV have established prognostic relations. The field of HRV is fascinating and opens the window of various researches. HRV can be recorded at bedside in both adults and children. It is cost effective, easy to test and it suggested HRV measurement is used for diagnostic and research purposes for the benefit of mankind.

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