Involvement of Autonomic Nervous System in Isometric Handgrip in Healthy Young Subject

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Abstracts: Background: HRV can be considered a relatively simple, noninvasive and sensitive method for studying autonomic modulation, purpose of the present study was to determine whether readily measured blood pressure (BP) indices and responses to autonomic reflex tests could be used as surrogates of short-term heart rate variability. Different Methods were used to evaluate sympathetic and Parasympathetic activity. Results: The autonomic function tests and heart rate variables were recorded and data was tabulated for Statistical evaluation. A two tailed P value less than or equal to 0.05 (5%) were considered statistically significant. Heart Rate Variability in Male Mean R-R interval and SDNN of time domain analysis were highly significant on comparing supine to standing (P<0.001),Similarly LF, HF power, Total Power and LFnu of frequency domain analysis were highly significant on comparing supine to standing (P<0.001) and in Females also it is same. Conclusion : Considering the results our data indicate a decrease in HRV that seems to be expressions of a reduction in autonomic modulation in postural change from supine to standing erect both in male and female subjects. The findings suggestive of a shift in cardiac autonomic regulation towards sympathetic activation in response to real life stressors which also includes the decrease in parasympathetic modulation and no significant correlation between readily measured blood pressure indices to heart rate variables in both male and female groups, we suggest that mean heart rate, SBP, DBP and RPP cannot be used as surrogates of HRV. However, observations need to be made in healthy subjects belonging to various age groups and in patients with conditions known to be associated with autonomic deregulation. [Chand K et al NJIRM 2011; 2(4) : 95-105]

Key Words: Autonomic nervous system, Heart rate variability,triangular index

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Introduction: The term heart rate variability (HRV) conventionally describes the beat-to-beat fluctuations in the heart rate or the variations in consecutive RR intervals. The HRV is mainly caused by efferent modulations of the S.A node. In 1965 by Hon and Lee [1] appreciated first clinical application of the HRV. Later, Wolf et al. [2] found assoc0iations between a higher risk of post infarction mortality and reduced HRV. Akselrod et al. [3] described the relation between quantitative evaluations of the beat-to-beat cardiovascular control by the power spectral analysis of the heart rate fluctuations.

The frequency domain analysis obtained by mathematical processing of the RR intervals is well accepted to assess the neural mechanisms controlling the heart rate. Thereby two main spectral components which are considered as markers of the sympathetic and parasympathetic control of the heart have been discriminated: a high frequency component (HF) which ranges from 0.4-0.15 Hz and a low frequency one (LF) ranging from 0.15-0.04 Hz. Furthermore, the HRV measure is apparently easy to derivate because of the availability of new, digital, high-frequency, long- and short term multi channel electrocardiogram (ECG) recordings.

Heart rate variability (HRV) is related to lifestyle in adults. Endurance trained athletes have been noted to show profound bradycardia (lower resting heart rate) compared with sedentary control which implicated enhanced vagal and/or diminished sympathetic activity [5, 6, 7]. Thus, physical activity was thought to affect positively the indexes of the HRV in healthy humans as well as in patients.

Regular physical exercise in adults has beneficial effect on autonomic control of the heart, with decreased resting heart rate often accompanied

with increase in HRV [8, 9]. Disturbed sleeping patterns or lack of sleep effect HRV. Shift workers and patients with sleep apnoea have deranged HRV [10, 11]. Smoking impairs the sympatho-vagal balance and decreases the HRV in healthy adults [12, 13] and in heavy smokers vagal modulation of the heart is blunted [14]. In adolescent HRV decreases with augmented BMI [15] as it does with blood glucose levels [16] and risk factor influence on autonomic heart rate control is present before manifest cardiovascular disease [17]. The relationship between HRV and lifestyle is not well studied in children and adolescents and it is not known at what age the relationship is established. There is a modification of HRV with age, which represents the evolution of the autonomic nervous system [18]. LF, HF and total power increase from 0–6 years, followed by a decrease to adulthood [19]. Early life individual differences in HRV can be explained by hereditary factors [20], diabetic neuropathy [21] or an underdeveloped ANS in prematurely born children [22].Decreased HRV is associated with risk for cardiac events in adults [23] and is a predictor of imminent hypertension [24,25]. A decreased HRV is related to an increased risk of death and HRV could have a predictive value for life expectancy and health [23]. HRV changes due to lifestyle factors precedes or parallels the development of cardiovascular disorders, i.e. it should present also in healthy adolescents, where long-term effects of poor lifestyle has not yet generated manifest cardiovascular disease.

The purpose of the present study was to determine whether readily measured blood pressure (BP) indices and responses to autonomic reflex tests could be used as surrogates of short-term heart rate variability (HRV), which is an established marker of autonomic regulation of SA node. Therefore, we examined the correlation between short-term HRV and heart rate (HR), BP indices viz. systolic pressure, diastolic pressure, pulse pressure (PP), and rate-pressure product (RPP), during supine and standing erect

Material and Methods: The study was approved by Ethical Committee. Present study was conducted in the Department of Physiology, Kamineni institute of medical sciences, Sreepuram, Narketpally, Nalgonda (Dt), Andhra Pradesh. 75 Male and 75 Female, healthy young individuals from various socioeconomic groups residing in Narketpally & students of Kamineni institute of medical sciences were randomly selected belonging to the age group of 18-22yrs. Informed consent was obtained from each subject.

Inclusion Criteria included All male and female subjects should belong to the specified age range. Female subjects selected for study were on 10th - 12th day of their menstrual cycle. They should maintain good health recommended for that age, as evaluated by general physical examination without any known respiratory, cardiovascular illness, or any disorder which can interfere the autonomic responses. Normal 12 lead ECG, blood pressure for the particular age group.

Exclusion Criteria was subject having History of metabolic or cardiovascular diseases. History of Hypertension (sitting blood pressure > 140/90 mmHg). History of alcohol / smoking. History of intercurrent illness (e.g. Pyrexia, Diarrhea). History of drug intake. History of unstable body weight (change of >1% within the month before the study). Ages below 18 years and above 21 years.

Instruments used were ECG V: 52 [HRV analysis software], Digital Electronic Blood Pressure Monitor, Hand Grip Dynamometer, Stop Watch and Weighing Machine

The protocol was explained and informed consent was obtained from each of the participant. The subject was asked to relax in supine position for 30 minutes in the laboratory and then the autonomic function tests were performed on the subjects.

The body weight of the subjects was measured using a pedestal type of weighing scale with a maximum capacity of 150 kg. The body weight was considered to the nearest of 0.1 kg. Height without footwear was measured using a vertical scale (Avery, India) with an accuracy 0.5 cms and was rounded to the nearest 0.01 m. BMI is calculated: BMI = weight (kg) / height squared (m^2) RPP was calculated as SP × HR × 10–2 and expressed in units of mm Hg × beats per min × 10–2.
Each subject in supine position was subjected for standard Lead II recording of ECG for five minutes in

eyes closed relaxed state which is simultaneously analyzed by the software. Similarly the test was done when the subject is standing erect eyes closed relaxed state for five minutes.

Heart rate variability analysis: A chest lead ECG was recorded throughout supine, standing, deep breathing and Valsalva maneuver using the ECG V: 52 system (Niviqure Meditech pvt. Ltd). Beat to-beat variations in instantaneous HR were derived offline using a rate-detector algorithm. For computing HRV indices during supine rest and tilt, recommendations of the Task Force on HRV were followed [4]. A 5-min ECG was acquired at a sampling rate of 1000 Hz during supine rest and during standing erect; with the subjects breathing normally at 12–18 per min. RR intervals were plotted using the ECG V: 52 software. An RR series was extracted using a rate-detector algorithm after exclusion of artefacts and ectopic. A stationary 256 second RR series was chosen for analysis. In the time domain, the standard deviation of normal-to-normal RR intervals (SDNN) was taken as an index of overall HRV. The RR series was resampled at 4 Hz, the mean and trend removed, a Hann window applied and the 1024 data point series transformed by fast Fourier transformation. Low frequency (LF) and high frequency (HF) spectral powers were determined by integrating the power spectrum between 0.04 and 0.15 Hz and 0.15 and 0.4 Hz respectively. Total power was calculated by integrating the spectrum between 0.004 and 0.4 Hz and includes very low frequency, LF and HF components. Spectral powers are expressed in absolute units of milliseconds squared. LF and HF powers are also expressed in normalized units as described.

Following Autonomic Function Tests were done using standard method [26]

Tests to evaluate sympathetic system activity

1. Resting Heart Rate
2. Systolic Blood Pressure (SBP)
3. Diastolic Blood Pressure (DBP)
4. Blood Pressure response to sustained handgrip

Test to evaluate parasympathetic system activity

1. Valsalva Ratio
2. Heart Rate Response to deep breathing.

Statistical evaluation was performed using the SPSS (version 11.0). All the parameters measured were expressed in terms of mean ± SD. Pearson correlation coefficient was used for correlation matrix , Non-parametric Wilcoxon signed rank test was applied to analyze the changes in the heart rate variability parameters because of non-normal distribution of the data. A two tailed P value less than or equal to 0.05 (5%) were considered statistically significant.

Result: The anthropometric parameters, autonomic function tests and heart rate variability variables were recorded in all the subjects. The data so obtained was tabulated with respect to various autonomic function tests and heart rate variability which were statistically treated and analyzed separately for males and females.Baseline Characteristics of different genders Age and anthropometric measurements are expressed as mean ± SD along with the range of the variable in Table 1.

Table 1 Baseline Characteristics of different genders

Characteristics	Males (n = 75)	Females (n = 75)
Age (years)	19.69 ± 0.93 [18-22]	19.6 ± 1.16 [18-22]
Height (meters)	1.65 ± 0.042 [1.58-1.74]	1.60 ± 0.05 [1.52-1.75]
Weight (Kilograms)	62.10 ± 4.96 [50-76]	55.88 ± 6.43 [44-72]
BMI (Kg/m2)	22.58 ± 1.74 [19.04-26.29]	21.77 ± 2.65 [16.89-30.35]

Resting cardiovascular parameters Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Pulse Pressure (PP), Heart Rate (HR) and Rate pressure Product (RPP) are presented for male in Table 2 and female in Table 6.

Autonomic function test parameters Parasympathetic component represented by hear rate changes during Valsalva manoeuvre and during deep breathing test. Sympathetic component by change in diastolic blood pressure to sustained isometric hand grip test along with change in pulse pressure are tabulated in Table 3 and 7 for male and female respectively.

Heart Rate Variability Parameters in Male Table 4 shows a comparison of heart rate variability parameters to different positions i.e. supine and

standing, both the time domain and frequency domain analysis were used as parameters of heart rate variability, statistical test applied was Wilcoxon-matched pairs test as the data was skewed Mean R-R interval and SDNN of time domain analysis were highly significant on comparing supine to standing (P<0.001)

Similarly LF, HF power, Total Power and LFnu of frequency domain analysis were highly significant on comparing supine to standing (P<0.001)

Heart Rate Variability Parameters in Female Table 8 shows a comparison of heart rate variability parameters to different positions i.e. supine and standing, both the time domain and frequency domain analysis were used as parameters of heart rate variability, statistical test applied was Wilcoxon-matched pairs test as the data was skewed Mean R-R interval and SDNN of time domain analysis were highly significant on comparing supine to standing (P<0.001) Similarly LF, HF power, Total Power and LFnu of frequency domain analysis were highly significant on comparing supine to standing (P<0.001) Correlation matrix, showing correlations between resting heart rate, blood pressure indices and short term heart rate variability indices in Male and Female The correlation between short term heart rate variability indices SDNN, LF, HF and total power along with LFnu, Valsalva ratio, heart rate difference to deep breathing to resting blood pressure and heart rate during supine rest Mean heart rate, Systolic blood pressure, diastolic blood pressure, pulse pressure and rate pressure product are BP and HR indices on application of Pearson correlation coefficient test for normally distributed data and spearman's rank correlation test for correlation of RR interval spectral powers to various indices.

Table 2: Resting cardiovascular parameters in Male

Parameter	Mean ± SD	Range
Systolic Pressure	118.17 ± 6.56	106 – 136
Diastolic Pressure	76.98 ± 3.64	70 – 84
Pulse Pressure	41.18 ± 5.89	27 – 56
Heart Rate	73.53 ± 3.88	64 – 82
Rate Pressure Product SP X HR X 10-2	86.96 ± 7.44	68 – 107

Table 3: Autonomic function test parameters in Male

Parameter	Mean ± SD	Range
Valsalva Ratio	1.67 ± 0.36	1.14 – 2.66
I – E HR Difference	25 ± 3	17 – 35
Increase in diastolic pressure During IHG (mm Hg)	35 ± 2.73	30 – 41
Change in Pulse Pressure During IHG (mm Hg)	9.96 ± 0.85	8 – 12

Table 4: HRV Parameters in Male

Parameter	Supine	Standing	P value*
Mean R – R (ms)	888.52 ± 102.8	770.19 ± 89.10	<0.0001
SDNN (ms)	45.57 ± 5.63	43.8 ± 5.41	<0.0001
LF power (ms2)	114.13 ± 24.53	240.62 ± 51.72	<0.0001
HF power (ms2)	173.61 ± 13.42	81.06 ± 6.26	<0.0001
Total power (ms2)	966.62 ± 75.25	718.74 ± 55.96	<0.0001
LF nu	39.31 ± 5.11	74.21 ± 4.13	<0.0001

*Significant, Wilcoxon-matched pairs test applied

Table 5: Correlation matrix, showing correlations between resting heart rate, blood pressure indices and short term heart rate variability indices in Male

	Mean HR	SBP	DBP	PP	RPP	DBP (IHG)
SDNN	0.3	-0.1	0.02	-0.1	0.1	0.133
LF power	0.2	0.08	0.05	-0.1	0.2	0.12
HF power	0.2	-0.04	-0.03	-0.02	0.07	0.99
Total power	0.2	-0.03	-0.03	-0.02	0.07	0.99
LF nu	0.1	0.09	-0.05	0.2	0.2	-0.2
Valsalva ratio	0.2	0.08	-0.06	0.1	0.2	0.12
I-E HR difference	0.06	-0.2	-0.009	-0.2	-0.09	0.5

Data (n=75) are expressed as Pearson or Spearman correlation coefficient, whichever is appropriate

Table 6: Resting cardiovascular parameters in Female

Parameter	Mean ± SD	Range
Systolic Pressure	108.49 ± 4.36	100 – 118
Diastolic Pressure	71.41 ± 3.70	62 – 79
Pulse Pressure	37.08 ± 4.68	24 – 45
Heart Rate	74.81 ± 3.42	68 – 82
Rate Pressure Product SP X HR X 10-2	81.11 ± 3.85	72.8 – 88

Table 7: Autonomic function test parameters in Female

Parameter	Mean ± SD	Range
Valsalva Ratio	1.74 ± 0.38	0.74 – 2.77
I – E HR Difference	27 ± 3	19 – 36
Increase in diastolic pressure During IHG (mm Hg)	29.6 ± 4.96	18 – 43
Change in Pulse Pressure During IHG (mm Hg)	7.76 ± 3.62	1 – 17

Table 8: HRV Parameters in Female

Parameter	Supine	Standing	P value*
Mean R – R (ms)	858.40 ± 85.92	756.12 ± 75.68	<0.0001
SDNN (ms)	43.69 ± 4.34	41.41 ± 4.11	<0.0001
LF power (ms2)	108.99 ± 24.05	229.63 ± 50.67	<0.0001
HF power (ms2)	161.24 ± 13.39	67.65 ± 5.62	<0.0001
Total power (ms2)	1067.2 ± 88.64	714.22 ± 59.32	<0.0001
LF nu	39.95 ± 5.69	76.77 ± 4.55	<0.0001

*Significant, Wilcoxon-matched pairs test applied

Results as displayed in Table 5 and 9 suggested there was no correlation between resting heart rate, blood pressure indices to short term heart rate variability indices in both the groups of male and female.

Table 9: Correlation matrix, showing correlations between resting heart rate, blood pressure indices and short term heart rate variability indices in female

	Mean HR	**SBP**	**DBP**	**PP**	**RPP**	**DBP (IHG)**
SDNN	-0.09	-0.05	-0.08	0.02	-0.1	0.007
LF power	0.3	0.03	0.1	-0.09	0.3	0.06
HF power	-0.04	-0.03	-0.2	0.2	-0.06	0.18
Total power	-0.04	-0.03	-0.2	0.16	-0.06	0.18
LF nu	0.3	0.05	0.3	-0.2	0.3	-0.03
Valsalva ratio	0.3	0.03	0.2	-0.09	0.3	0.06
I-E HR difference	0.08	-0.03	0.2	-0.2	0.05	-0.08

Data (n=75) are expressed as Pearson or Spearman correlation coefficient, whichever is appropriate.

Discussion: The focus of this study is on non-invasive, quantitative tests of autonomic function that are currently used in autonomic laboratories.

1. There is the concept that the evaluation is not only an extension of the clinical examination but also that the repertoire of tests is best interpreted together. It is somewhat simplistic to ascribe a single function to a single test. The particular clinical question may require the selection of a specific battery tailored to answer the question at hand.
2. The majority of tests of autonomic function evaluate end-organ responsiveness so that end-organ failure itself can affect test results.

There are several special clinical reasons for utilizing tests of autonomic function. There is increasing evidence that the function of unmyelinated and small myelinated peripheral nerve fibers may improve as neuropathy improves these fiber populations are at least as amenable to improvement as somatic fibres. There is good clinical evidence that sympathetic fibers have a great propensity to regenerate. Autonomic cardiovascular indices correlate with function, such as cardiovascular exercise performance. As the cardiovascular autonomic neuropathy worsens, the cardiovascular performance and systemic peripheral resistance responses become more abnormal, so that autonomic neuropathy may contribute to exercise intolerance. Another reason

for autonomic evaluation is that patients with autonomic failure show an increase in mortality. Blood pressure instability (requiring pharmacologic treatment) predicts increased intra-operative mortality. [27, 28]

The analysis of the heart rate variability (HRV) has been applied to several examinations in different research areas as well as in clinical studies. The spectra of the power spectral analysis in particular phenomenon are non invasive insight in the vegetative control of the heart due to the classification of the sympathetic and parasympathetic activity with respective frequency bands. Therefore the sympathetic activity is classed with low (LF 0.15-0.04 Hz) and the vagal activity with high frequency (HF 0.4-0.15 Hz) fluctuations. The HF consists of pure vagal whereas the LF of a composition of sympathetic and vagal activity which may not be numerically quantized. Only the ratio between the sympathetic and parasympathetic activity may be expressed by the normalized LF and HF units as well as the LF/HF ratio which is often designated as a marker of the sympathovagal balance. Similarly in time domain analysis Mean R-R interval and SDNN indicates overall heart rate variability without pointing the single component in precise. Yet, the physiological significance of each HRV parameters and its correlations remains unknown so that provocation tests, e.g. the orthostatic test, are applied specifically to unbalance the autonomic nervous control of the heart which results in modulated HRV results. The present study was carried with specific aims in both male and female To test whether readily measured blood pressure indices and responses to classic autonomic reflex tests could be used as surrogates of short term heart rate variability. To study correlation between short term heart rate variability indices and autonomic responses and isometric hand grip in a group of subjects.

The present study evaluated 75 male and 75 female subjects in the age group of 19.69 ± 0.93 yrs and 19.6 ± 1.16yrs respectively with BMI of 22.58 ± 1.74 in males and 21.77 ± 2.65 in females Resting cardiovascular parameters Heart rate, Systolic and diastolic blood pressure were recorded and rate pressure product was calculated using heart rate and systolic blood pressure as tabulated.

Autonomic function test parameters Valsalva ratio a complex global index of sympathetic and parasympathetic effects and heart rate response to deep breathing was calculated for parasympathetic component. The pressor response to sustained isometric handgrip i.e. change in pulse pressure and changes in diastolic pressure is taken as index of sympathetic modulation

Relationship of HRV parameters to position: A heart rate variability index to change in position, SDNN which encompasses all components responsible for RR variability, is a simple domain measure of overall HRV. High frequency spectral power reflects parasympathetic modulation of RR interval at controlled respiratory frequency. LF power in absolute units of power quantifies baroreflex-mediated modulation of RR intervals in the 0.04-0.15 Hz range. Changes in sympathetic as well as vagal nerve traffic to the heart are thought to contribute to LF power. Total power is also an index of overall HRV. At least in physiologic states characterized by sympathetic excitation, low frequency spectral power expressed in normalized units of power (LFnu) has been shown to be a useful non-invasive index of sympathovagal balance.

Our results both in male and female group showed a decrease in Mean RR, increase in LFnu and decrease in HF power during standing erect are well known concomitants of sympathetic excitation, which is associated with an increase in mean heart rate, reduces the magnitude of respiratory sinus arrhythmia In the experimental manoeuvre from supine to standing induces a shift of the sympathovagal balance toward a sympathetic activation, as expected our study confirmed that Mean RR is associated with the progressive sympathetic activation and parasympathetic withdrawal accompanying this manoeuvre, we also noted that LFnu can track the gradual increase in the cardiac sympathetic modulation and HFnu exhibits a reciprocal trend as a result of the relationship between LFnu and HFnu as shown in Total spectral power

Our results were similar to results obtained by Malliani, A et al [29] In the supine position healthy subjects always present LF and HF components, the latter often are being greater in adolescence and

smaller in adulthood. In the active upright position (or during passive tilt), in addition to an increase in heart rate and to small adjustments in blood pressure, a marked change occurs, as a rule, in the spectral profile the LF component is increased, whereas the HF component is reduced. Variance usually decreases in the upright position, causing a reduction in the absolute value of both spectral components. Hence, in the upright position, LF tends to be decreased, in its absolute values, by the reduction of variance but also tends to be increased, in nu, by the greater concentration of power in this part of the spectrum Numerous data, collected in various experimental conditions involving human and animal studies, have been summarized previously [30] to support the assumptions that

1) The respiratory rhythm of heart period variability (HF) is a marker of vagal modulation (an issue widely accepted);
2) The rhythm corresponding to vasomotor waves and present in heart period and arterial pressure variability (LF) is a marker of sympathetic modulation of, respectively, heart period and vasomotion
3) The reciprocal relation existing in the R-R variability spectrum between LFnu and HFnu is a marker of the state of the sympathovagal balance modulating sinus node pacemaker activity (also deducible from LF/HF, which, like any ratio, can emphasize the opposite changes).

This hypothesis does not imply that LF and HF components should be confined to sympathetic and vagal activities, respectively: actually, the opposite is true, because they are simultaneously present in the discharge of both autonomic outflows. However, a rhythm, being a flexible and dynamic property of neural networks, should not necessarily be restricted to one specific neural pathway to carry a functional significance [30] (as in the case of different electroencephalogram patterns).Qi Fu1 et al [31] Eleven healthy young men and eleven age-matched pre-menopausal women were studied and concluded that the menstrual cycle affects sympathetic neural responses but not sympathetic baroreflex sensitivity during orthostasis, though upright vasomotor sympathetic activity is not clearly different between men and women. Not only sympathetic but also cardiovagal baroreflex sensitivity is similar between sexes and menstrual phases during a hypotensive stimulus. However, cardiovagal baroreflex mediated bradycardia during a hypertensive stimulus is different between sexes but not affected by the menstrual cycle. Thus, other factors rather than sympathetic baroreflex control mechanisms contribute to sex differences in orthostatic tolerance in young humans

Correlation matrix, to study correlations between resting mean heart rate, blood pressure indices and short term heart rate variability indices in Male and Female: In our study on comparing the normally distributed data of cardiovascular variables mean resting heart rate, systolic blood pressure, diastolic blood pressure, pulse pressure and rate pressure product to that of non normally distributed data of heart rate variability indices SDNN, LF, HF, TP, LFnu, did not show any correlation between these two variable components both in male and female group of subjects de Boer et al. [32] developed a beat-to-beat model of the human circulation using a set of differential equations and the following principles of operation:
(1) The baroreflex regulates heart rate and peripheral vascular resistance;
(2) Windkessel properties characterize the systemic arterial tree;
(3) Contractile properties of the ventricular myocardium follow Starling's law; and
(4) Respiration exerts mechanical effects on BP.

The model attributes LF power to a resonance in the circulatory control system, produced by a slow time constant for reflexive sympathetically mediated responses to beat-to-beat blood pressure changes. The resonance can be up- or down-regulated by the state of baroreflex activity. The model of deBoer et al. predicts that changes in BP would lead HR changes at 0.1 Hz through a delayed sympathetic response. Changes in HR would depend on summed effects of sympathetic and vagal effects, with the sympathetic response delaying the overall response. At the respiratory frequency (0.2 – 0.3Hz), BP and HR changes would occur with little delay, because of fast parasympathetic control.

In essence, the response of the sympathetic nervous system behaves as a low band pass filter, with a peak response at 0.1 Hz and little response at frequencies above 0.2 Hz. Systolic blood pressure would lead to changes in heart rate, via the baroreflex. In general the results of this study fit with the de Boer model Raine Virtanen et al. [33]

Age, gender, heart rate, and blood pressure affect HRV in an important way the studies were not primarily focused on these variables, but attempted rather to control the effects of age and gender and of heart rate and blood pressure by running multivariate regression analyses of the data. Although reported only in one group, advanced age was related to decrease HRV in all studies. Gender differences were also identified particularly in the normalized components of HRV. In a group of older subjects, higher diastolic blood pressure was an independent determinant of reduced HF component of HRV in multivariate regression analysis that tested several factors related to insulin resistance. Although in young subjects revealed an association between PP and BRS, PP was not independently associated with any measure of HRV. This suggests that PP does not have any significant effect on tonic autonomic cardiovascular control and that it affects baroreflex-mediated heart rate fluctuations.

In a study of cardiac sensitivity of males and females relates, at least in part, to the pattern of blood pressure increase and is independent of basal heart period (mean RR) values. Although males and females behave similarly when their blood pressure is elevated slowly to a steady-state level, they differ significantly when abrupt rises in blood pressure occur. The difference may infer a relatively weaker vagal response to rapid activation of baroreceptors evoked by the bolus method. These authors have reported that a similar pressor response to stressors among males and females involve different gender-related hemodynamic mechanisms. Greater myocardial reactivity (increased HR and cardiac output) contributes more to the pressor response in females than in males, whereas an enhanced vascular reactivity plays a greater role in the pressor response to stressors in males.

In contrast to our study report Madan Mohan et al [34] reported that positive correlation between PP and LF power during supine rest and the possible basis for this was mentioned as greater PP, loading of high-pressure baroreceptor afferents is greater and consequently, the reflex modulation of RR interval is also higher. A significant positive correlation between RPP and the change in LF nu (i.e. LF nu during tilt – LF nu during supine rest) is possibly because of sympathetic excitation during head-up tilt. In other parameters of SDNN, Mean HR, SBP, DBP on comparing to heart rate variability parameters did not show any significant correlation In an another attempt of comparing the Valsalva Ratio and effect of deep breathing with reference to heart rate were also correlated to resting heart rate and blood pressure indices which exhibited no statistically significant correlation on comparing both the normally distributed data and on correlation of isometric hand grip exercise change in diastolic blood pressure to heart rate variability indices showed no significant statistical correlation Saul and coworkers [35] made a convincing case that there is no need to postulate changes of vagal-cardiac nerve traffic to explain the RR-interval variability; such variability can be explained simply on the basis of the kinetics of sinoatrial node responses to acetylcholine. During slow breathing, responses to acetylcholine are expressed more fully than during rapid breathing, when responses to one mainly expiratory bolus of acetylcholine merge with responses to the next, and fluctuations of RR intervals are minimized. They may apply to the numerator as well as the denominator of the sympathovagal equation; during periods of slow breathing (which healthy people have), LF and respiratory-frequency centre frequencies may be the same. Thus, moderate changes of arterial pressure, which alter vagal-cardiac nerve activity, do not change HF RR-interval fluctuations, and changes of breathing frequency and depth, which profoundly alter HF RR-interval fluctuations, may not change vagal-cardiac nerve activity at all.

The HR response to a brief isometric handgrip task is largely due to cardiovagal withdrawal. The observations that isometric hand grip test did not have significant correlation in either group in this task supports this conclusion. From this perspective, the sex independent HR responses suggest that

they either display greater vagal withdrawal, or have a greater end-organ response to a given level of vagal withdrawal to this type of physiological stress.

The finding of greater physiological responses in both groups during handgrip exercise is consistent with earlier observations during orthostatic stress. Nonetheless, the current findings may contrast with the earlier conclusions that cardiovagal control of HR is more pronounced in women. However, the differences may relate to task specific responses and/or to the fact that we measured the HR response rather than spectral power at particular frequencies. Such measures were not possible during this study due to the short duration of handgrip task One of the criticisms of comparing HRV values collected under different conditions is that the variability of the heart rate may be dependent on the heart rate itself. A unique aspect of this study was the expression of HRV as the coefficient of variation of R-R intervals. Whereas this method of characterizing variability relative to the mean behaviour of the system is rather simple and straightforward, to our knowledge HRV has not been expressed in this fashion.

The data from this investigation suggest that coefficient of variation provides some unique information about cardiac chronotropic control. That is to say that the exercise induced changes during isometric hand grip exercise of R-R intervals were different from the changes in mean R-R intervals and SDNN. From these findings one could hypothesize that a changes in the isometric hand grip exercise reflects parasympathetic withdrawal without an increase in sympathetic activation. However, the meaningfulness of this parameter is not that clear. Rather, we report these findings in the context to determine the physiological correlates and the predictive validity of the correlation to R-R intervals. Grossman and Kollai [36] mentioned RR-interval fluctuations to ripples on a sea of varying depths. In their study suggested of no arguments in the sympathovagal literature that support the view that it is the fluctuations of nerve traffic (the ripples on the surface of the sea) rather than the absolute levels (the depth of the sea) that are important. Such justification is necessary. What evidence indicates that during moderate changes of arterial pressure, the physiologically relevant variable is the nearly constant fluctuations of vagus nerve traffic rather than the varying absolute levels of vagus nerve traffic that are proportional to arterial pressure

Limitations of our study Despite the large number of experimental and clinical studies published the measurement of HRV is still a research technique and not a routine clinical tool. There are several potential reasons that can explain this situation. First, the pathophysiological mechanism of HRV establishing the direct link between mortality and reduced HRV is still not fully elucidated. Second, the clinical application of HRV assessment is limited by a lack of standardized methodology due to variability of the parameters according to gender, age, drug interferences and concomitant diseases. Third, despite the relative evidence of the robust character of parameters such as SDNN and the HRV index, there is still no consensus about the most accurate HRV parameter for clinical use. Fourth, the sensitivity, specificity and positive predictive accuracy of HRV are limited. Particularly, its positive predictive accuracy is modest, ranging from 14 to 40%. It has, however, a higher negative predictive value ranging from 77 to 98%. Finally, conflicting results have been found regarding HRV measured after MI, suggesting that this technique may be insufficient by itself to adequately risk stratify these high risk patients.

Conclusion: HRV can be considered a relatively simple, non-invasive and sensitive method for studying autonomic modulation of sinus node. Our data indicate a decrease in HRV that seems to be expressions of a reduction in autonomic modulation in postural change from supine to standing erect both in male and female subjects. The findings are suggestive of a shift in cardiac autonomic regulation towards sympathetic activation in response to real life stressors which also includes the decrease in parasympathetic modulation in sinus node.

As our results suggested no significant correlation between readily measured blood pressure indices to heart rate variables in both male and female groups, we suggest that mean heart rate, SBP, DBP and RPP cannot be used as surrogates of HRV. However, observations need to be made in healthy

subjects belonging to various age groups and in patients with conditions known to be associated with autonomic deregulation.

References:

1. EH, Lee, ST, Electronic evaluations of fetal heart rate patterns preceding fetal death: further observations, Am J Obstet Gynecol, 1965:87:814-826.
2. Wolf, MM, Varigos, GA, Hunt, D, Sloman, JG, Sinus arrhythmia in acute myocardial infarction, Med J Aust, 1978: 2:52-52.
3. Akselrod, S, Gordon, D, Ubel, FA, Shannon, DC, Barger, AC, Cohen, RJ, Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat to beat cardiovascular control, Science, 1981: 213:220-222.
4. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, Heart rate variability: standards of measurements, physiological interpretation and clinical use, Circulation,1996:93:1043-1065.
5. Catai, A. M, et al, Effects of aerobic exercise training on heart rate variability during wakefulness and sleep and cardiorespiratory responses of young and middle-aged healthy men, Braz J Med Biol Res, 2002:35(6):741-752.
6. Kouidi, E, Haritonidis, K, Koutlianos, N, Deligiannis. A, Effects of athletic training on heart rate variability triangular index, Clin Physiol & Func Im, 2002:22:279-284.
7. Melanson, E.L, Resting heart rate variability in men varying in habitual physical activity, Med Sci Sports Exerc, 2000:32(11):1894-1901.
8. Hottenrott K, Hoos O, Esperer HD Heart rate variability and physical exercise. Current status. Herz. 2006:31:544–552.
9. Tuomainen P, Peuhkurinen K, Kettunen R, Rauramaa R. Regular physical exercise, heart rate variability and turbulence in a 6-year randomized controlled trial in middle-aged men: the DNASCO study. Life Sci 2005:77:2723–2734.
10. Furlan R, Barbic F, Piazza S, Tinelli M, Seghizzi P, Malliani A. Modifications of cardiac autonomic profile associated with a shift schedule of work. Circulation 2000:102:1912–1916.
11. Gula LJ, Krahn AD, Skanes A, Ferguson KA, George C, Yee R, Klein GJ Heart rate variability in obstructive sleep apnea: a prospective study and frequency domain analysis. Ann Noninvasive Electrocardiol 2003:8:144–149.
12. Alyan O, Kacmaz F, Ozdemir O, Maden O, Topaloglu S, Ozbakir C, Metin F, Karadede A, Ilkay E. Effects of cigarette smoking on heart rate variability and plasma N-terminal pro-B-type natriuretic peptide in healthy subjects: is there the relationship between both markers? Ann Noninvasive Electrocardiol 2008:13:137–144.
13. Karakaya O, Barutcu I, Kaya D, Esen AM, Saglam M, Melek M, Onrat E, Turkmen M, Esen OB, Kaymaz C. Acute effect of cigarette smoking on heart rate variability. Angiology 2007:58:620–624.
14. Barutcu I, Esen AM, Kaya D, Turkmen M, Karakaya O, Melek M, Esen OB, Basaran. Cigarette smoking and heart rate variability: dynamic influence of parasympathetic and sympathetic maneuvers. Ann Noninvasive Electrocardiol 2005:10:324–329.
15. Rabbia F, Silke B, Conterno A, Grosso T, De Vito B, Rabbone I, Chiandussi L, Veglio F. Assessment of cardiac autonomic modulation during adolescent obesity. Obes Res 2003:11:541–548.
16. Singh JP, Larson MG, O'Donnell CJ, Wilson PF, Tsuji H, Lloyd-Jones DM, Levy D Association of hyperglycemia with reduced heart rate variability (The Framingham Heart Study). Am J Cardiol 2000:86:309–312.
17. Jensen-Urstad M, Jensen-Urstad K, Ericson M, Johansson J. Heart rate variability is related to leucocyte count in men and to blood lipoproteins in women in a healthy population of 35-yearold subjects. J Intern Med 1998:243:33–40.
18. Silvetti MS, Drago F, Ragonese P. Heart rate variability in healthy children and adolescents is partially related to age and gender. Int J Cardiol2001:81:169–174.
19. Finley JP, Nugent ST. Heart rate variability in infants, children and young adults. J Auton Nerv Syst 1995:51:103–108.
20. Singh JP, Larson MG, O'Donnell CJ, Tsuji H, Corey D, Levy D. Genome scan linkage results for heart rate variability (The Framingham Heart Study). Am J Cardiol 2002:90:1290–1293.
21. Colhoun HM, Francis DP, Rubens MB, Underwood SR, Fuller JH. The association of

heart-rate variability with cardiovascular risk factors andcoronary artery calcification: a study in type 1 diabetic patients and the general population. Diabetes Care 2001:24:1108–1114.
22. Longin E, Gerstner T, Schaible T, Lenz T, Konig S. Maturation of the autonomic nervous system: differences in heart rate variability in premature vs. term infants. J Perinat Med 2006:34:303–308.
23. Tsuji H, Larson MG, Venditti FJ Jr, Manders ES, Evans JC, Feldman CL, Levy D Impact of reduced heart rate variability on risk for cardiac events. The Framingham Heart Study. Circulation 1996:94:2850–2855.
24. Schroeder EB, Liao D, Chambless LE, Prineas RJ, Evans GW, Heiss G. Hypertension, blood pressure, and heart rate variability: The Atherosclerosis Risk in Communities (ARIC) study. Hypertension 2003:42:1106–1111.
25. Singh JP, Larson MG, Tsuji H, Evans JC, O'Donnell CJ, Levy D. Reduced heart rate variability and new-onset hypertension: insights into pathogenesis of hypertension: the Framingham Heart Study. Hypertension 1998:32:293–297.
26. Ewing D. J. Autonomic function testing (clinical) – Michael Poon's Shrine of neurology. 1985, 1988 in www.Autonomic function testing.
27. Burgos LG, Ebert TJ, Asiddao C, et al. Increased intraoperative cardiovascular morbidity in diabetics with autonomic neuropathy. Anesthesiology 1989: 70:591-597.
28. Knuttgen D, Weidemann D, Doehn M. Diabetic autonomic neuropathy:abnormal cardiovascular reactions under general anesthesia. Klin Wochenschr 1990:68:1168-1172.
29. Malliani, A, The pattern of sympathovagal balance explored in the frequency domain, News Physiol Sci, 1999:14:111-117.
30. Malliani, A., M. Pagani, F. Lombardi, and S. Cerutti. Cardiovascular neural regulation explored in the frequency domain. Circulation 1991: 84: 482–492.
31. Qi Fu1, Kazunobu Okazaki, Shigeki Shibata, Robin P. Shook, Tiffany B. VanGunday, M. Melyn Galbreath, Miriam F. Reelick and Benjamin D. Levine. Menstrual cycle effects on sympathetic neural responses to upright tilt. J Physiol. 2009: 587: (9):2019–2031
32. DeBoer RW, Karemaker JM, Strackee J. Hemodynamic fluctuations and baroreflex sensitivity in humans: a beat-to-beat model. Am J Physiol 1987: 253:H680–9.
33. Raine Virtanen. Association between autonomic regulation and cardiovascular risk factors in middle-aged subjects. Publications of the National Public Health Institute, A4/2007, 90 .
34. Madan Mohan, Prakash.E.S, Bhavanani.A.B. Co-Relation between heart rate variability, Blood pressure, Heart rate and pressure reactivity to isometric hand grip in healthy young male subjects.IJPP.2005: 49(2); 132-138
35. Saul JP, Berger RD, Albrecht P, Stein SP, Chen MH, Cohen RJ. Transfer function analysis of the circulation: unique insights into cardiovascular regulation. Am J Physiol. 1991:261:H1231–H1245.
36. Grossman P, Kollai M. Respiratory sinus arrhythmia, cardiac vagal tone, and respiration: within- and between-individual relations. Psychophysiol. 1993:30:486–495.