

# Time and Frequency Domain Analysis of Heart Rate Variability (HRV) In Response to Cold Stress in Subjects with Family History of Hypertension

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## ABSTRACT

**Objective:** Autonomic nervous system plays a crucial role in the development of hypertension and autonomic dysfunction underlies the initiation and maintenance of hypertension. Elevated blood pressure has been known to be a huge risk factor for cardiovascular disease later in life and leads to increased morbidity and mortality. In this study, we aimed to study the effect of cold stress on heart rate variability and prevalence of cardiovascular risks in subjects with hypertensive parents

**Methods:** A total of 30 subjects and 30 healthy controls were recruited in the study. Their anthropometrical and cardiovascular parameters were recorded. For recording HRV, the resting cardiac cycles (R-R intervals) signals at spontaneous respiration were recorded for 5 min in supine position after 15 min of supine rest. The HRV was recorded in both groups using Polar S810i heart rate monitor before, during and after the cold pressor test (CPT).

**Results:** Analysis was done for baseline and post-CPT period within the study group, in both time and frequency domain components of HRV. Two time domain parameters; SDNN and RMSSD were found to differ significantly pre and post-CPT, with both of the parameters being more in the post-CPT period, as it can be seen from the table 4.

**Conclusion:** RMSSD was decreased (p value= 0.042) and SDNN was increased (p value= 0.048: borderline) post-CPT in subjects with family history of hypertension, suggesting that some amount autonomic dysfunction is manifested at early age.

**Key words:** HRV, CPT, Blood pressure

## INTRODUCTION

Autonomic nervous system plays a crucial role in the development of hypertension and autonomic dysfunction underlies the initiation and maintenance of hypertension. <sup>[1]</sup> Elevated blood pressure has been known to be a huge risk factor for cardiovascular disease later in life and leads to increased morbidity and mortality. <sup>[2]</sup> Cardiac autonomic function can be measured by beat-to-beat changes in the heart rate. The standard deviation of normal R-R intervals (SDNN) reflects cardiac vagal activities in the time domain. A power spectral density analysis provides the frequency component of heart rate

variability (HRV). The low-frequency component (LF) (0.04 to 0.15 Hz) is predominantly under sympathetic control with vagal modulation. Parasympathetic activity is the major contributor to the high-frequency (HF) (0.15 to 0.40 Hz) component. The LF/HF ratio displays the index of sympathovagal balance. <sup>[3]</sup>

A study done in healthy normotensive males with normal BMI where subjects were divided into two groups; those with normotensive parents (control group) and those with the hypertensive parents (study group) and cardiovascular response to whole body isotonic exercise was measured. <sup>[4]</sup> It was

found that basal LFnu (normalized unit) and LF/HF ratio were significantly higher while the basal HFnu was significantly lower in the study group compared to control group. This study concluded that a difference in basal systolic blood pressure, a higher LFnu and a lower HFnu found in offspring of hypertensive parents may be an early marker of cardiovascular change in subjects with a genetic predisposition to hypertension.

In another similar study done on healthy young males dividing them into two groups; normotensive subjects with normotensive parents (control group) and another normotensive subjects with hypertensive parents (study group) where blood pressure, heart rate (HR), indices of short term HRV during supine rest and quiet standing, HR variation during timed controlled deep breathing was compared between the two groups, it was found that LF power was significantly increased in the study group.<sup>[5]</sup> HF power was decreased in the study group. LF nu increased and HF nu decreased during standing in study group. SDNN was significantly decreased in the study group during standing and there was decrease in the total variability in the study group. During the controlled deep breathing HF in power was significantly reduced in the study group compared control group.

Evaluating family history at the levels of parents, grandparents, siblings and children a study found that prevalence of hypertension was higher among subjects with family history of hypertension compared to those who didn't.<sup>[6]</sup>

Recently, a study done on college students with confirmed diagnosis of prehypertension to assess the effects of heart rate variability biofeedback on cardiovascular responses and autonomic sympathovagal modulation following stressor tasks, there was a significant decrease in heart rate and respiration rate and a significant increase in blood volume pulse amplitude after the HRV-BF intervention.<sup>[7]</sup> For the HRV analysis, HRV-BF significantly reduced the ratio of

low-frequency power to high-frequency power (the LF/HF ratio) and increased the normalized high-frequency power (HFnu) during the stress tests, and an added benefit over slow abdominal breathing by improving HRV was also observed.

A study has shown that hypertensive, with high-normal BP and normotensives groups were comparable in terms of mean HR and low-frequency (LF) power expressed in normalized units at rest and during quiet standing, the standard deviation of normal-to-normal RR intervals (SDNN) during supine rest, LF and high-frequency spectral powers during supine rest and HRVdb were lowest in hypertensive, indicating diminished baroreflex modulation of RR intervals in hypertensive's.<sup>[8]</sup> In contrast, LF power was highest in subjects with high-normal BP during supine rest and this is possibly because of higher BP variability.

Another study had shown that hypertensive and normotensive subjects participating CPT and IHGT (Ischemic Hand Grip Test) as sympatho-excitatory stressors, evoked greater increases in mean arterial blood pressure in hypertensive participants compared with normotensive participants.<sup>[9]</sup> Resting HF power, which is a parameter of HRV associated with parasympathetic cardiac modulation, was lower in hypertensive participants and was negatively correlated with systolic blood pressure and mean arterial pressure across all participants. There were no differences in HRV or forearm blood flow responses to the CPT or IHGT between groups. This study supports the notion that autonomic dysfunction is likely to contribute to the pathogenesis of hypertension. During the last few decades, researchers have recognized the significance of the relationship between autonomic system and cardiovascular mortality.<sup>[10]</sup> So the rationale of our study is to assess the difference in the effect of physiological stress (CPT) on autonomic nervous system activity by measuring heart rate variability on the subjects with and without family history of

hypertension. Through this study we will be able to explore the hereditary risk that an individual carries to develop any autonomic dysfunction and its effect on cardiovascular status.

No studies have been done on assessment of autonomic function (such as post stress HRV) for estimating the future risk of hypertension in young adults who had family history of hypertension. Therefore, our aim is to assess the changes in HRV in relation to physiological stress (CPT) in hypertension young adults who have family history of hypertension.

**METHODS**

A total of 30 subjects and 30 healthy controls were recruited in the study. Their anthropometrical and cardiovascular parameters were recorded. All subjects were normotensive (resting systolic BP - 120 mmHg and diastolic BP - 80 mmHg), nondiabetic, and not taking over-the-counter or prescription medications or supplements with primary or secondary cardiovascular effects (e.g., statins, anti-hypertensives, anticoagulants, antidepressants, etc.). Subject self-identify as to whether their father or mother have been diagnosed with high BP (diastolic blood pressure greater than 90 mm Hg or systolic blood pressure greater than 140 mm Hg on at least three times); a positive response for either (or both) parents were subsequently used to determine family history status. Negative family history indicate that neither parent has high BP and comprise the control group while subjects with a positive family history indicate that either parent has high BP and comprise the test group. For recording HRV, the resting cardiac cycles (R-R

intervals) signals at spontaneous respiration were recorded for 5 min in supine position after 15 min of supine rest. The HRV was recorded in both groups using Polar S810i heart rate monitor before, during and after the cold pressor test (CPT).

**STATICAL ANALYSIS:** For analysis of HRV and parameters recorded the R-R intervals recorded in the watch were transmitted to the computer using an infra-red device. The computer installed with Polar Precision Performance software detected the recording sent from the wrist unit. HRV software was installed in the computer and the HRV recording was analysed.

**RESULTS**

**Anthropometric variables:** The mean and the standard deviation of anthropometric variables, namely age weight, height and body mass index of the study group (with family history of hypertension) and the control group are tabulated below. There is no statistically significant difference between the two groups shown in table 1.

Table 1. Analysis of anthropometric variables

	Study group	Control group	Statistical Significance
Age (yrs)	21.57±1.01	21.6±1.92	NS
Weight (kg)	69.57± 6.39	66.9±10.53	NS
Height (cm)	173.14 ± 6.68	172.73± 4.96	NS
BMI (kg/m <sup>2</sup> )	23.26 ± 2.42	22.39± 3.06	NS

**Inter-group analysis in pre-CPT baseline phase:**

Analysis of baseline values of time and frequency domain components were compared between the study and the control group. No statistically significant difference was observed between the groups shown in table 2.

Table 2. Analysis of baseline values

	Study group	Control group	Statistical Significance
	Median ( Q1-Q3)	Median (IQR: Q1-Q3)	
SDNN (ms)	74.66 (49.53 - 81.1)	72.21 (63.55 - 81.6)	NS
RMSSD(ms)	61.45 (32.08 - 72.79)	52.78 (44.84 - 70.52)	NS
NN50	117.00 (45.50 - 169.5)	86 (62 - 131)	NS
pNN50 (%)	33.47 (11.55 - 47.11)	27.54 (20.14 - 42.67)	NS
LF (ms <sup>2</sup> )	1043.65 (539.17 - 2019.12)	1770.2 (947.59 - 2132.15)	NS
HF (ms <sup>2</sup> )	1189.54 (371.10 - 2610.25)	727.47 (421.12 - 1578.45)	NS
LFnu	56.31 (39.75 - 67.53)	59.11 (44.95 - 78.1)	NS
HFnu	43.57 (32.38 - 59.97)	40.32 (21.66 - 54.97)	NS
LF/HF	1.30 (0.66 - 2.1)	1.47(0.84 - 3.67)	NS
TP (ms <sup>2</sup> )	3671.50 (1740.50 - 6715)	4400 (2658.5 - 7111.5)	NS

**Inter-group analysis in post-CPT phase:**

Similarly, analysis of post-CPT values of time and frequency domain components were done comparing the study and the control group. There was no statistically different finding in both groups shown in table 3.

**Intra-group analysis for Study group:**

Analysis was done for baseline and post-CPT period within the study group, in both time and frequency domain components of HRV. Two time domain parameters; SDNN and RMSSD were found to differ significantly pre and post-CPT, with both of the parameters being more in the post-CPT period, shown in table 4.

**Table 3. Analysis of post-CPT values**

	Study group	Control group	
	Median (IQR: Q1-Q3)	Median (IQR: Q1-Q3)	Statistical Significance
SDNN (ms)	77.94 (57.67 - 99.24)	81.52 (61.54 - 92.01)	NS
RMSSD(ms)	57.11(48.79- 81.76)	53.84(37.78 -75.16)	NS
NN50	115.50(84.25- 150.5)	87(40.5 -132)	NS
pNN50 (%)	31.50(27.08- 48.07)	30.42(11.4 -40.46)	NS
LF (ms <sup>2</sup> )	1216.80(873.26- 1890.22)	1458.7(1006.64 -2342.95)	NS
HF (ms <sup>2</sup> )	840.01(639.19- 1657)	770.22(440 -1586.45)	NS
LFnu	55.61(45.89- 61.9)	72.7(47.79 -77.08)	NS
HFnu	44.29(38.01- 53.8)	27.26(22.83 -52.2)	NS
LF/HF	1.25(0.85- 1.63)	2.67(0.92 -3.39)	NS
TP (ms <sup>2</sup> )	3808.00(2302.75- 7245.5)	5435(32.69 -7914)	NS

**Table 4. Intra group analysis for Study group**

	Baseline	Post-CPT	
	Median (IQR: Q1-Q3)	Median (IQR: Q1-Q3)	Statistical Significance
SDNN (ms)	74.66(49.53- 81.1)	77.94(57.67- 99.24)	<b>P= 0.048</b>
RMSSD(ms)	61.45(32.08- 72.79)	57.11(48.79- 81.76)	<b>P= 0.042</b>
NN50	117.00(45.50-169.5)	115.50(84.25- 150.5)	NS
pNN50 (%)	33.47(11.55- 47.11)	31.50(27.08- 48.07)	NS
LF (ms <sup>2</sup> )	1043.65(539.17- 2019.12)	1216.80(873.26- 1890.22)	NS
HF (ms <sup>2</sup> )	1189.54(371.10- 2610.25)	840.01(639.19- 1657)	NS
LFnu	56.31(39.75- 67.53)	55.61(45.89- 61.9)	NS
HFnu	43.57(32.38- 59.97)	44.29(38.01- 53.8)	NS
LF/HF	1.30(0.66- 2.1)	1.25(0.85- 1.63)	NS
TP (ms <sup>2</sup> )	3671.50(1740.50- 6715)	3808.00(2302.75- 7245.5)	NS

**Intra-group analysis for Control group:**

Similarly, analysis was also done for baseline and post-CPT period within the control group, in both time and frequency

domain components of HRV. However, the parameters were not found to differ significantly pre and post-CPT shown in table 5.

**Table 5. Intra group analysis for Control group**

	Baseline	Post-CPT	
	Median (IQR: Q1-Q3)	Median (IQR: Q1-Q3)	Statistical Significance
SDNN (ms)	72.21(63.55 -81.6)	81.52(61.54 -92.01)	NS
RMSSD(ms)	52.78(44.84 -70.52)	53.84(37.78 -75.16)	NS
NN50	86(62 -131)	87(40.5 -132)	NS
pNN50 (%)	27.54(20.14 -42.67)	30.42(11.4 -40.46)	NS
LF (ms <sup>2</sup> )	1770.2(947.59 -2132.15)	1458.7(1006.64 -2342.95)	NS
HF (ms <sup>2</sup> )	727.47(421.12 -1578.45)	770.22(440 -1586.45)	NS
LFnu	59.11(44.95 -78.1)	72.7(47.79 -77.08)	NS
HFnu	40.32(21.66 -54.97)	27.26(22.83 -52.2)	NS
LF/HF	1.47(0.84 -3.67)	2.67(0.92 -3.39)	NS
TP (ms <sup>2</sup> )	4400(2658.5 -7111.5)	5435(32.69 -7914)	NS

**DISCUSSION**

In our study, time and frequency domain of heart rate variability in response to cold stress were analysed and compared among the subjects with and without

hypertensive parents. We found that none of the parameters under both time and frequency domain were significantly related to family history of hypertension. Unlike our findings, the study done by Camm et al.,

2004; Muralikrishnan et al., 2011 found that basal LFnu (normalized unit) and LF/HF ratio were significantly higher while the basal HFnu was significantly lower in the study group compared to control group, LF power was significantly increased in the study group. HF power was decreased in the study group. Chen et al., 2016 found reduction in the ratio of low-frequency power to high-frequency power (the LF/HF ratio) and increment in the normalized high-frequency power (HFnu) during the stress tests. In the present study in intra-group comparison of HRV parameters, only SDNN (p value = 0.048) and RMSSD (p value = 0.041) were found to be having significant correlation pre and post-CPT in the study group while there was no significant relation in other time and frequency domain parameters. However, this is only mild correlation. The decreased RMSSD post-CPT in the study group indicates that there is decreased parasympathetic tone in subjects with family history of hypertension. This is consistent with existing views that decreased parasympathetic tone is one of the factors leading to hypertension in adults. Therefore, it can be seen that autonomic changes start to manifest at an early age, possibly resulting in increased risk of having hypertension later in life. However, the significance seen is borderline, thus further studies are required to validate the findings. Moreover, no parameter was found to be having significant relation in pre and post-CPT conditions in the control group.

## CONCLUSION

Elevated blood pressure has been known to be a huge risk factor for cardiovascular disease with studies suggesting that the autonomic nervous system plays a crucial role in the development of hypertension. Cardiac autonomic function can be measured by beat-to-beat changes in the heart rate, which consists of time and frequency domain components. It was seen from our study that RMSSD was decreased (p value= 0.042)

and SDNN was increased (p value= 0.048: borderline) post-CPT in subjects with family history of hypertension, suggesting that some amount autonomic dysfunction is manifested at early age.

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