

Original Article

Assessment of Autonomic Dysfunction in Chronic Complete Spinal Cord Injury by Heart Rate Variability

Navin BP¹, Joshi Mrinal², Dube Amitava³

Abstract

Objectives: Non-invasive assessment of cardiac autonomic dysfunction in spinal cord injury (SCI) by means of heart rate variability analysis (HRV). Also, to assess the effect of postural change on neural outflow.

Setting: Rehabilitation research center, Sawai Man Singh Hospital, Jaipur.

Participants: 110 patients with SCI were screened, of whom, 12 patients aged between 20 and 30 years with chronic complete SCI and neurological level of T6 or above were included. An equal number of age and sex matched healthy individuals were the controls.

Interventions: Five minute ECG recording, first in supine position and then in sitting position was done.

Outcome measures: Frequency domain measures of heart rate variability.

Results: No significant differences were observed between both the groups in supine rest. On sitting, the absolute power of the low frequency (LF) and high frequency (HF) components were significantly less in the SCI patients than that in the controls. A significantly increased LF-to-HF ratio along with a higher mean heart rate (HR) was observed in the controls on postural change.

Conclusion: On change of posture, the controls showed a physiologically patterned response, which was not observed in the SCI patients. The loss of this homeostatic mechanism in the SCI subjects was observed, which may reflect a dysfunctional autonomic nervous system interplay in patients with complete SCI.

Key words: Autonomic nervous system, autonomic dysreflexia, heart rate variability, spinal cord injury, sympathetic nervous system.

Introduction:

Autonomic dysfunction causes life threatening disturbances in both the acute and chronic phases of spinal cord injury (SCI)¹. Autonomic dysreflexia (AD) is a constellation of signs or symptoms in SCI above T5-T6 level in response to noxious or non-noxious stimuli below the level of injury². It is caused by disconnection of spinal sympathetic centres from supraspinal control^{3,4}.

Most tests of autonomic function as of this date have been developed for able bodied individuals and are not necessarily applicable to patients with SCI⁵. Autonomic tests have not been very well described in SCI patients⁶. Both in the acute and chronic stages of SCI, cardiovascular disorders are among the most common causes of death⁷⁻⁹.

Heart rate variability (HRV) analysis, is an evaluation of the rhythmical beat to beat oscillations which provide a basis to appreciate the complex interplay between the neural outflow in sympathetic and parasympathetic systems^{10,11}. The measures of heart rate variability may be used as reproducible indices of autonomic cardiovascular regulation in SCI¹².

Heart rate power spectra can be analysed in short term electrocardiogram (ECG) recordings¹³. The spectral analysis of heart rate variability is similar to the spectral analysis of visible light except that, the frequencies of interest in HRV are in a range of <1Hz¹⁰. Three main spectral components are observed in short term ECG recordings of 2 to 5 minutes: HF (high frequency),

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LF (low frequency) and VLF (very low frequency) components¹³. The genesis and the constituent parameters of HRV have been an issue of contention and intrigue. Using pharmacological blockade, it has been observed that the vagal influences appear to be present in both the low frequency (LF) and high frequency (HF) components of HRV during supine and upright postures, while sympathetic activity contributes to the low frequency component of HRV only during upright posture¹⁴. The genesis of very low frequency (VLF) component is much less defined¹⁵.

The objective of the study was to noninvasively assess cardiac autonomic dysfunction in patients with SCI by short term HRV analysis and to observe the effect of change in posture on the neural outflow.

Materials and Methods:

The present study was a hospital based comparative evaluation done in the Departments of Physical Medicine and Rehabilitation and Physiology at Sawai Man Singh Medical College, India, wherein patients in the indoor ward of the Department of Physical Medicine and Rehabilitation were recruited for the proposed research protocol. Ethical clearance was obtained from the institution's ethical clearance committee. Informed and written consent were taken prior to start of the study.

Patients with chronic (≥ 6 months post-injury) complete SCI, in the age range of 20 to 30 years with a neurological level of T6 or above were included in the study. As aging has an effect on parameters of HRV, a range of 10 years was chosen for age in the inclusion criteria. An equal number of age and sex matched healthy individuals acted as controls.

Patients with a traumatic brain injury, acute SCI (<6 months post-injury), non-traumatic SCI, incomplete SCI or those with systemic illness such as diabetes mellitus, renal failure, heart failure or cardiac arrhythmia were excluded. Patients with severe spasticity or pressure ulcers interfering with proper positioning were excluded. Patients were instructed to stop anticholinergics 12 hours prior to the study. Patients and controls were instructed to abstain from caffeinated drinks, tea, alcohol or smoking for at least 12 hours prior to the study. They did not perform physical exercise for at least 24 hours prior to the study and were asked not to take any solid food by mouth two hours prior to the study.

Neurological examination was done on the day of the study and ASIA impairment scale¹⁵ was used to evaluate the severity of neurological impairment. The

participants were instructed to empty the bladder (if not on continuous bladder drainage by a suprapubic or transurethral catheter) then to relax, lie down quietly for about 20 minutes prior to the HRV testing, for stabilisation of the cardiovascular parameters. They were instructed to be awake throughout the period of study. Five minutes short term ECG based recordings with a sampling rate of 500Hz was done using HRV Soft_version1.1 (AIIMS and MICT, New Delhi) with an ambient room temperature maintained between 24°C and 25°C. The study was initially done in supine position followed by postural change to sitting position with both knees in flexion. The R-wave (QRS complex) fiducial point identification and manual editing was done. This was followed by offline analysis of the data in frequency domain. The data was expressed as mean \pm s.d.

Statistics: The statistical analyses were performed using "R" version 2.10.1¹⁶ and RKWard¹⁷. Raw data was used for the analysis. Data was tested for normality using Kolmogorov and Smirnov distributions. Comparison between and within groups was performed using Wilcoxon rank-sum test with continuity correction. Unpaired t-test was used to compare the demographic variables between the patients and controls. The level of significance was set at $p < 0.05$.

Results:

One hundred and ten patients with SCI were screened for fulfilling the inclusion and exclusion criteria. The present study comprised 12 male patients with a chronic complete SCI, whom eight patients were complete tetraplegics with a cervical SCI and four patients had complete paraplegia with thoracic SCI (Table 1).

There were no significant differences between age of the patients (mean 25.66 years, SD 2.6) and the controls (mean 25.08 years, SD 1.72). Although, we had assessed two female patients, we had to exclude them from the analysis for reasons that statistical comparisons could not be made due to the small sample size in this particular sex group. One male patient was excluded from the analysis due to the presence of ectopics in the ECG recording. Mean time since trauma to testing was 24.8 \pm 21.7 months.

A. Comparison between SCI patients and controls

Supine position: No significant differences could be observed between both the groups in frequency domain of HRV and mean heart rate (HR) in supine rest.

Sitting position: The absolute power of the low frequency (LF) and high frequency (HF) components were significantly less in the SCI patients (Figs 1 and 2) than

that in the controls ($p=0.038$ and 0.044 , respectively). The mean heart rate (HR) was significantly higher in the SCI group than that observed in the control group ($p=0.0001$).

B. Effect of postural change in SCI patients

No significant differences could be appreciated in the frequency domain on change of posture from supine to sitting position in the SCI patients. The mean heart rate (HR) was significantly high in the sitting position (Fig 3) than in the supine position ($p=0.004$).

C. Effect of postural change in controls

A significantly increased LF-to-HF ratio was observed on sitting position (Fig 4) as compared to that in supine position ($p=0.034$).

A significant increase in power in the low frequency (LF) range expressed in normalised units (Fig 5) and a significant decrease in the power in the high frequency (HF) range expressed in normalised units (Fig 6) was observed ($p=0.042$). The mean heart rate (HR) was

significantly high in the sitting position as compared to that in supine position ($p=0.0038$).

Discussion:

In 10 healthy subjects, using ganglion blockade it has been observed that the R-R variability under supine resting conditions with spontaneous breathing, at all measured frequencies is predominantly controlled by autonomic neural activity¹⁸.

The present study observed no significant difference in resting heart rate in supine position between patients with complete SCI and that of controls. This finding is in agreement with the study by Gao *et al*¹⁹ who observed a similar trend in their study on nine SCI individuals (lesion C4-T5). They demonstrated significantly low total body noradrenaline spillover with similar baroreceptor reflex sensitivity and haemodynamic profile compared to that observed in able-bodied controls at rest. Otsuka *et al*²⁰ noted that trained complete tetraplegic men had a lower heart rate at rest when compared with untrained

Table 1: Characteristics of the SCI Patients

Sl. No	Age (years)	Vertebral level	Neurological level	Autonomic dysreflexia (+ present; - absent)	Time since injury (months)
1	29	#C5	C5	+	60
2	24	#C5	C4	+	77
3	29	D/L C4-C5	C4	+	11
4	26	#C4-C6	C4	+	11
5	25	#D/LC4-C5	C5	+	22
6	21	#C7	C6	-	34
7	22	D/L C6-C7	C7	+	13
8	25	D/L C4-C5	C7	+	10
9	29	#T3, T10	T5	+	20
10	27	#T6	T5	-	16
11	25	#T2-T4	T5	+	12
12	26	#D/L T6-T7	T6	+	12

Table 2: Values Expressed as Mean \pm SD for Different Parameters of Heart Rate Variability in SCI Patients and the Controls during Rest and while Sitting

Parameters	Supine patient	Supine control	Sitting patient	Sitting control
LFnu (normalised units)	46.47 \pm 21.29	50.61 \pm 9.51	62.87 \pm 22.28	58.98 \pm 16.83
HFnu (normalised units)	53.52 \pm 21.29	49.39 \pm 9.51	37.12 \pm 22.28	41.01 \pm 16.83
LF:HF	1.21 \pm 0.99	1.09 \pm 0.39	4.08 \pm 6.19	1.9 \pm 1.4
VLF power (msec ² /Hz)	2097.8 \pm 4697	852.9 \pm 295	2990.4 \pm 5277	1189.24 \pm 1150.5
LF power (msec ² /Hz)	689.02 \pm 926.13	677.53 \pm 294.7	478.91 \pm 353	791.27 \pm 404.1
HF power (msec ² /Hz)	896.4 \pm 1135	762.99 \pm 654.94	312.73 \pm 31.74	569.86 \pm 347.56
Mean heart rate (HR in beats/minute)	75.16 \pm 11.43	67.33 \pm 9.17	91.16 \pm 7.29	72.33 \pm 8.6

tetraplegic men and controls. Moreover, no significant differences could be appreciated in the frequency domain parameters of HRV in supine position between the two groups in the present research work, which is in agreement with the previous studies of Otsuka *et al*²⁰ and Koh *et al*²¹. Otsuka *et al*²⁰ found no differences in the R-R interval power spectra among trained complete tetraplegic men, untrained complete tetraplegic men and that of the controls. However, in contrast to the findings of the present study, Guzzetti *et al*²² observed significantly

high power spectral density of HF component with absent or reduced LF component (expressed in normalised units) at rest in patients with complete quadriplegia than in the controls. In the present study, a LF component could be appreciated in patients with complete quadriplegia at rest. Claydon and Krassioukov⁵ on the other hand observed a long R-R interval profile, increased HF power with a reduced LF:HF ratio in patients with cervical SCI implicating parasympathetic predominance in such patients.

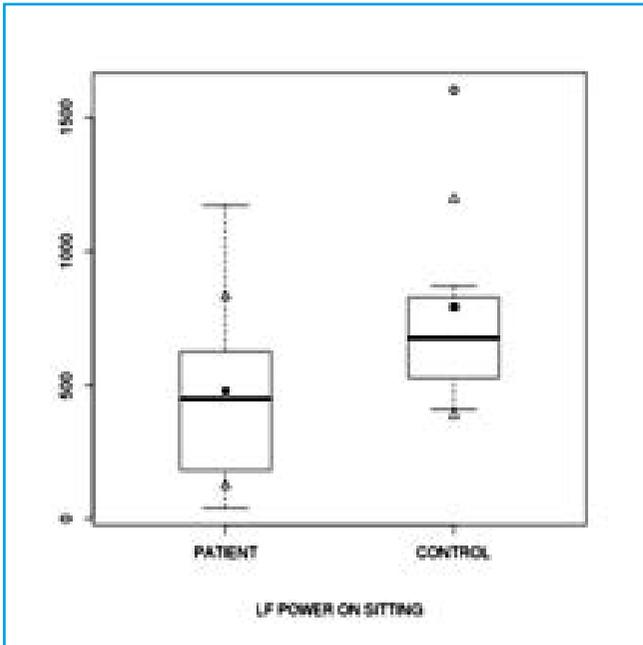


Fig 1

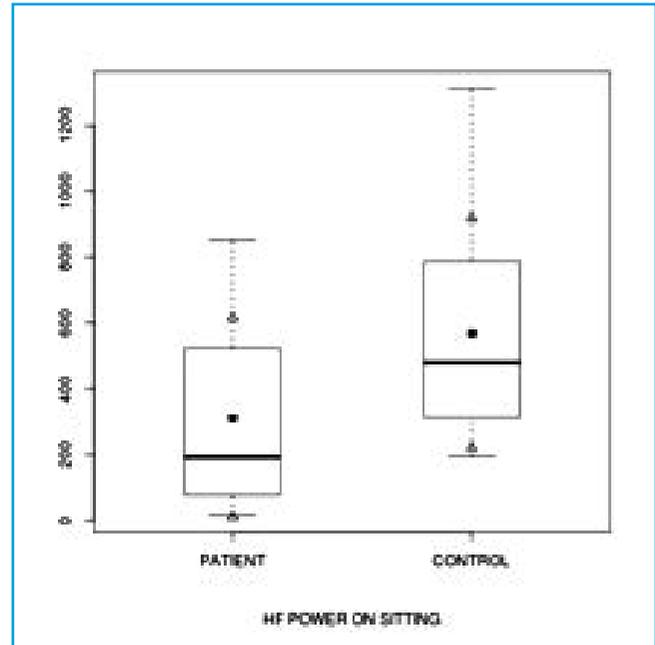


Fig 2

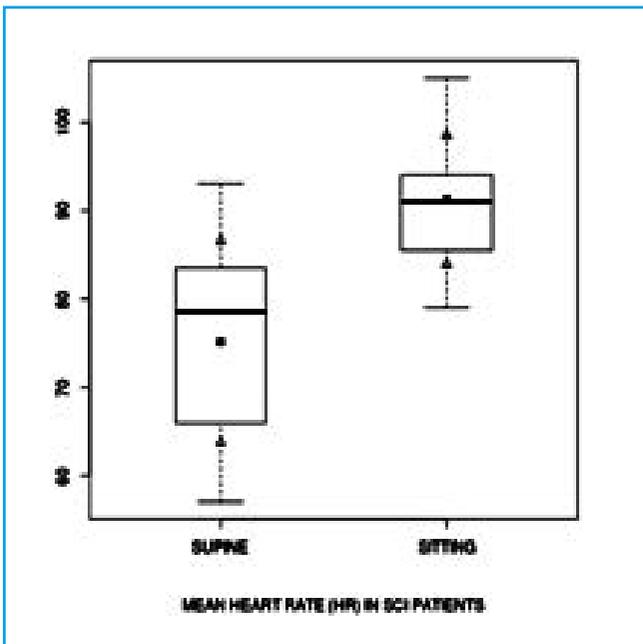


Fig 3

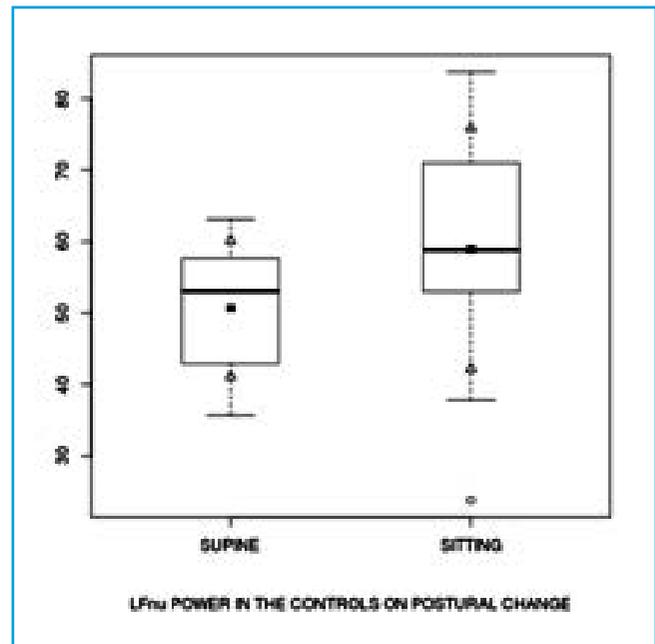


Fig 4

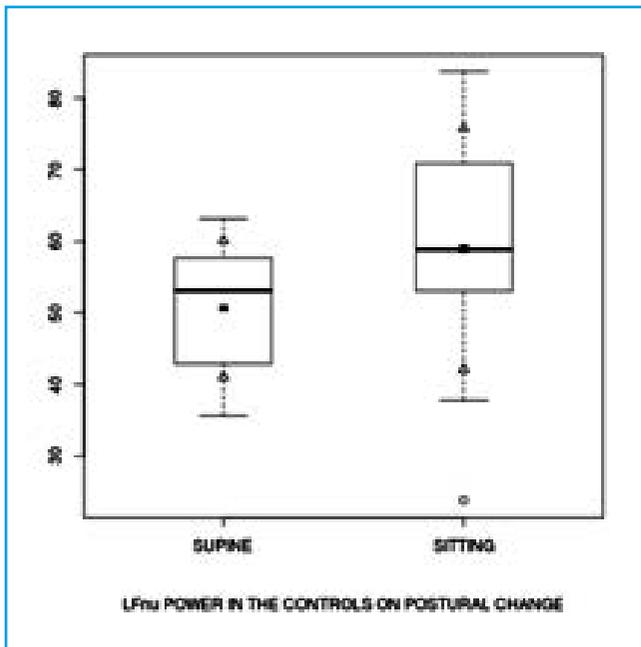


Fig 5

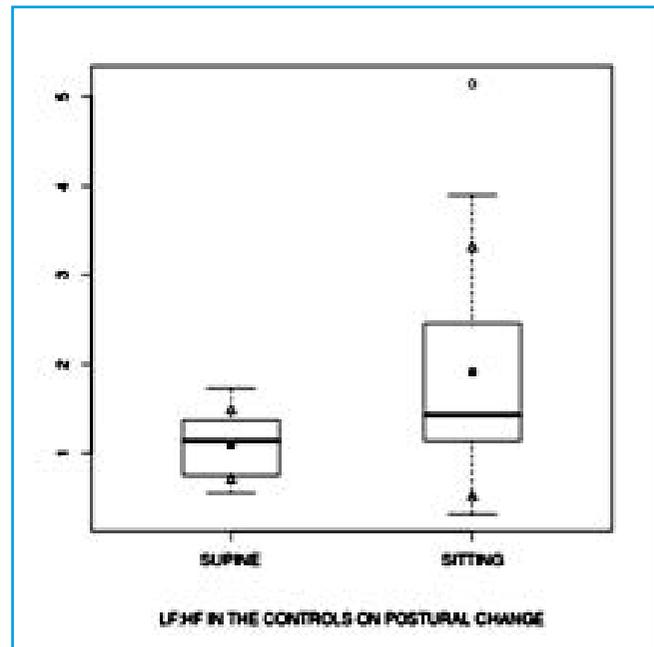


Fig 6

It is known that some of the autonomic disturbances are transient, whereas, others continue to persist for life²³. A new balance is reached few months after SCI²³. In the present study, all the SCI patients were in the chronic phase post-injury. A new balance in the stable chronic phase of SCI, probably offers an explanation to the comparable autonomic neural modulations as observed by the insignificant differences in the frequency domain measures of HRV at rest.

A significantly reduced absolute power of LF and HF components of the frequency domain of HRV along with a significantly high mean heart rate (HR) could be appreciated in complete SCI patients on sitting as compared to that observed in the control population. It has been suggested that an increase in heart rate (HR), in association with a decrease in the power of LF and HF in the upright position, reflects vagal withdrawal with little increase in sympathetic drive to the heart⁵. Wecht *et al*²⁴ have reported significantly low LF:HF ratio, low LF power and a reduced heart rate in tetraplegics as compared to that of controls. A blunted heart rate response to vagal withdrawal (as elicited through head-up tilt maneuver in the experimental design) in tetraplegics (5 of the 7 tetraplegics so studied had an incomplete lesion) was observed by Wecht *et al*²⁴ in their study and the plausible rationale attributed to the observed phenomenon put forward by them is a reduced sympathetic cardiac modulation, limited ability of vagal withdrawal to influence heart rate (HR) and/or altered SA

node responsiveness to vagal withdrawal. However, in contrast to the above observations, an increase in heart rate with reduced absolute power of LF and HF components of HRV was observed in sitting position in patients with complete SCI in the present study, a finding that could be attributed to an intrinsic vagal withdrawal mechanism along with decreased sympathetic outflow.

Claydon and Krassioukov⁵ observed that the R-R interval decreased significantly in SCI patients and controls in upright position. An higher heart rate in both trained and untrained persons with tetraplegia on change of position from supine to 60 degree was observed by Otsuka *et al*²⁰. The observation in the present study, is similar to the above studies.

In the upright position, an increase in normalised LF power and LF:HF ratio along with a decrease in the normalised HF power has been observed in the controls but not in SCI patients⁵. Similar results have been noted in the present study, a finding that reflects increased sympathetic with subsequent reduced parasympathetic modulation of the heart due to baroreflex mechanism.

Conclusions:

On change of posture, the controls showed a physiologically patterned response, which was not observed in the SCI patients. The loss of this homeostatic mechanism in the SCI patients was observed. SCI patients with a complete lesion may exhibit a dysfunctional autonomic nervous system interplay, wherein, the sympathovagal interplay

seems to be working on a different neuronal work-space which seems to be characteristic of SCI patients, as compared to the control population in the present study. The small sample size is an important limitation of the present study. Further research to demonstrate the effects of rehabilitation interventions on the cardiovascular autonomic control in SCI patients is needed.

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