Correlation between Heart Rate Variability and Bladder Sensations During Filling and Voiding Phase of Urodynamic Study in Patients with Myelopathy

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Abstract

Objective: The objective of this study was to correlation between heart rate variability (HRV) and bladder sensations during filling and voiding phase of urodynamic study (UDS) in patients with myelopathy. **Materials and Methods:** Myelopathy patients (traumatic and nontraumatic) within 6 months of illness were included in the study. Demographic data, etiopathological diagnosis, and urinary complaints were noted. UDS was performed and simultaneous HRV calculated at each event of filling and voiding phase by recording and calculating standard deviation of normal-to-normal (NN) interval (SDNN), root mean square of successive differences, total power (TP), average heart rate, high frequency (HF), low-frequency (LF) ratio, and data analyzed. **Results:** The study included 30 patients (23 males) with a mean age of 31.2 years (range 18–60 years, standard deviation 11.6). The mean of LF in normalized units showed an increase from 43.6 ± 14.1 at baseline to 48.9 ± 17.4 at strong desire to void (SDV) and at urgency to 44.1 ± 14.5. HF at baseline 40.4 ± 14.1 reduced to 36.4 ± 12.8 at SDV and rose at urgency to 41.2 ± 13.2. LF/HF at baseline was 1.3 ± 0.8, which increased to 1.6 ± 1.1 at SDV and reduced at urgency to 1.2 ± 0.6. Significant change in mean value was seen in TP ($P = 0.01$) and SDNN ($P = 0.009$) at first desire to void. Significant positive trend was seen in TP ($P = 0.048$) and SDNN ($P = 0.042$) during filling. **Conclusion:** Comparison of HRV measures failed to show significant rise in sympathetic or parasympathetic component in myelopathy patients during UDS and requires more critical evaluation.

Keywords: Heart rate variability, myelopathy, urodynamic study

Introduction

Heart rate variability (HRV) describes the oscillation in interval on an electrocardiogram (ECG) between consecutive RR intervals (also referred as normal-to-normal [NN] intervals) as well as oscillation between consecutive instantaneous heart rates.[1] HRV is currently the only assessment tool that examines the cardiac autonomic modulation in spinal cord injury. The time domain measures are calculated directly from NN intervals on an ECG, and the frequency domain measures are derived using either parametric (e.g. autoregressive model) or nonparametric (e.g. fast Fourier transform) mathematical algorithms.[2,3] The fast Fourier transform is the more commonly used and recommended measure as it is easy to use and apply.[4] It transforms the NN intervals in ECG and provides the amount of variation as a function of frequency. In the calculated power spectrum, each frequency component corresponds to a specific bandwidth and total power (TP) is the total variance.[2,4] HRV in normal population is more, in younger individuals and persons with regular physical activity. Low HRV is an independent predictor of cardiovascular dysfunction and cardiac risk.[4]

Among the time domain measures, the root mean square of the successive differences (RMSSD) of RR interval represents parasympathetic activity, which does not show any change with intact parasympathetic innervation in cervical and thoracic spinal cord injury.[5,6] A reduction in "low frequency" (LF) in cervical injury is seen due to loss of sympathetic control.[6] A higher "high-frequency" and lower LF/HF outcome is seen in complete cervical injury indicating a parasympathetic predominance.[4,6] Recent studies have reported no difference in LF/HF between chronic cervical and thoracic spinal cord injury indicating a maintenance of sympathovagal homeostasis by cardiac autonomic nervous system.[5,6] Cardiovascular deconditioning is cited as another reason for lower HF and higher LF/HF indicating a lower vagal tone on comparing thoracic spinal cord injury with able-bodied participants.[7,8]

Urodynamic study (UDS) has been shown to elucidate the association that exists between the level of spinal cord lesion and the character of recovery of detrusor and sphincter function and is conceptualized as a diagnostic test using no radiation

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and giving maximum information regarding neuroanatomy and pathophysiology.[9,10] Some studies have questioned the reliability of reporting of bladder sensations during the study as they are subjective and dependent on patient reporting.[10-12] A high variability of results have been reported when study was performed by same or different investigators on same patient at different time.[13,14] To prevent subjectivity, International Continence Society (ICS) has recommended objective or semi-objective tests for evaluation of bladder sensations.[12] Despite these shortcomings and some degree of subjectivity, UDS is still considered to be the best method of assessing neurogenic bladder dysfunction in patients with myelopathy and management strategies are based on the findings.

Clinical conditions such as autonomic dysreflexia and micturition syncope have shown a relationship between bladder distension and autonomic function. Recent studies on HRV during UDS in healthy volunteers showed a rise in sympathetic activity during the strong desire to void (SDV).[15] As there is a dearth of information regarding autonomic activity during UDS in patients with myelopathy, our goal was to correlate the HRV parameters with bladder sensations during filling and voiding phase of urodynamics.

Materials and Methods

This prospective cross-sectional interventional study included patients with traumatic or nontraumatic myelopathy with urinary complaints who were admitted for inpatient rehabilitation in the Department of Neurological Rehabilitation in a quaternary university research hospital. The study was conducted between September 2016 and May 2017 and was approved by Institute's Ethics Committee as a nonfunded project. Informed written consent was taken from all the patients before enrolling them for the study. Patients with age between 18 and 60 years were recruited. The duration of injury was 6 months or less as studies report no difference in HRV between cervical and thoracic chronic spinal injury due to maintenance of sympathovagal homoeostasis in the chronic stage of illness/insult.[6] Patients with monophasic spinal cord lesion, stable medical condition with ability to participate in the rehabilitation program for at least 2 h/day were included whereas patients with relapsing-remitting type of illness, Cauda Equina Syndrome and neuromuscular disease were excluded from the study. Participants with medical or surgical urogenital conditions and pregnant women were also excluded from the study.

Urodynamic study

Filling and voiding cystometry was carried out using multichannel pressure recording technology with Life-Tech Urolab Primus (USA) system. All bladder sensations were defined according to ICS guidelines and terminology and comprehensibly explained to the patients before the study.[9] Recordings were made during the filling and voiding phase. Sphincter electromyography was performed to observe sphincter activity and possible synergic/detrusor sphincter dyssynergia-DSD pattern, using surface electrodes. The final urodynamic diagnosis was made, and management determined and instituted consisting of pharmacotherapy, supportive, and behavioral measures.

Heart rate variability recording

Simultaneously, ECG recording was done with Bioharness Zephyr Technology and analyzed for HRV using LabChart 7 AD Instruments. An ectopic free 5-min ECG recording was taken in resting baseline, at the start of filling cystometry, first sensation of filling, first desire to void (FDV), SDV, urgency, and void. Filling and Voiding Cystometry and ECG recordings were performed at the same time of the day, that is, between 9 am to 11 am at the constant room temperature of 25°C in quiet ambience. The data were analyzed for time and frequency domain (linear method) according to standards established by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996).[1]

Time domain measurement of short-term heart rate variability

The time domain parameters are standard deviation of all NN intervals (SDNN), square root of the mean of the sum of squares of differences between adjacent NN intervals (RMSSD) and average heart rate. SDNN is sensitive to all sources of heart rate variation and represents overall HRV, while RMSSD is most sensitive to parasympathetic activity/vagal tone.

Frequency domain measurement of short-term heart rate variability

Using "power spectral density analysis", one can analyze HRV due to sympathetic or parasympathetic influence. The components of frequency domain are TP that is the overall variance, LF power (0.04–0.15) which signifies predominantly sympathetic activity, HF power (0.15–0.4) which indicates parasympathetic activity. LF and HF are often expressed as normalized units. LF/HF ratio indicates sympathovagal balance with an increase ratio signifying a sympathetic overactivity.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences SPSS version 21.0 (IBM, IL, Chicago, USA). Quantitative variables were compared using ANOVA/Kruskal–Wallis test (when the data sets were not normally distributed) between more than two groups. Paired t-test/Wilcoxon ranked sum test (for nonparametric data) was used to compare across filling. Pearson correlation coefficient was used to calculate trend of parameters with respect to filling and its P value is determined using t-test for one mean taking test mean value as 0. $P < 0.05$ was considered statistically significant.

Results

The study included 30 myelopathy patients (7 females and 23 males) with a mean age of 31.2 years (range 18–60 years, standard deviation [SD] 11.6) and a mean duration of insult/injury 2.8 months (range 1–5 months, SD 1.6). Sixteen patients had traumatic spinal cord injury, eight patients had parainfectious cause with acute transverse (long segment) myelitis, three patients had primary spinal tumors, two had tubercular infection with Pott's spine, and one had vascular arteriovenous fistula [Table 1].

Twelve patients had urinary complaints in the form of frequency, urgency, and urge incontinence, nine patients had retention with straining to void and nine patients had mixed urinary complaints.

Ten patients had cervical insult with quadriplegia/paresis and 20 patients had thoracic lesion/injury with paraplegia/paresis. Seventeen patients had a complete injury with the American Spinal Injury Association (ASIA) A, four patients were motor complete with ASIA B, eight patients had incomplete motor lesions (four each in ASIA C and D), and one patient in ASIA E according to ASIA impairment scale [Tables 2 and 3].

The mean of LF in normalized units showed an increase from 43.6 ± 14.1 at baseline to 48.9 ± 17.4 at SDV and to 44.1 ± 14.5 at urgency. HF at baseline 40.4 ± 14.1 reduced to 36.4 ± 12.8 and rose at urgency to 41.2 ± 13.2. LF/HF at baseline was 1.3 ± 0.8, which increased to 1.6 ± 1.1 at SDV and reduced at urgency to 1.2 ± 0.6. Significant change in mean value was observed in TP ($P = 0.01$) and SDNN ($P = 0.009$) at FDV.

On analyzing the data of HRV during UDS, there was no trend seen in average heart rate and RMSSD. A weak positive trend was seen in LF and LF/HF, which was statistically insignificant. A significant positive trend in SDNN ($P = 0.042$) and TP ($P = 0.048$) was observed. A weak negative trend was observed with HF, which was insignificant [Graphs 1 and 2].

Discussion

The results of time and frequency domain measure of short-term HRV in earlier studies suggest that HRV can be used as a useful modality to measure autonomic activity during

Table 1: Type of neurogenic bladder according to urodynamic study and highest level of lesion

Highest level of lesion	Number of cases	Overactive detrusor		Acontractile/underactive detrusor	Normal detrusor
		With DSD	Without DSD		
Cervical	10	2	3	4	1
Thoracic	20	4	4	11	1
Total	30	6	7	15	2

DSD: Detrusor-sphincter dyssynergia

Table 2: Comparison of the mean of heart rate variability parameters with bladder sensation during urodynamic study

Heart rate variability parameter	Normal at resting	Cases at baseline	Cases at start of FC	Cases at FSF	Cases at FDV	Cases at SDV	Cases at urgency
Low frequency	611.5	534.3	445.2	554.5	716.9	654.2	570.3
High frequency	775.8	638.3	569.04	578.5	813.7	745.8	700.8
Low frequency (nu)	43.1	43.6	43.1	44.1	47.5	48.9	44.1
High frequency (nu)	44.8	40.4	42.1	42.03	37.6	36.4	41.2
LF/HF	1.1	1.3	1.3	1.2	1.6	1.6	1.2
Total power	2534.9	2189.04	1898.1	3099.6	3568.6	2325.1	2890.2
Average heart rate	78.2	82.5	80.7	76.3	80.9	83.2	82.7
SDNN	47.5	44.4	41.9	52.5	55.8	48.7	50.8
RMSSD	39.9	37.2	35.2	39.6	44.7	40.8	43.5

FC=Filling cystometry, SDNN=Standard deviation of NN interval, RMSSD=Root mean square of successive RR difference, FSF=First sensation of filling, FDV=First desire to void, SDV=Strong desire to void, nu=Normalized units, HF=High frequency, LF=Low frequency

Table 3: Trend of heart rate variability parameters with respect to filling

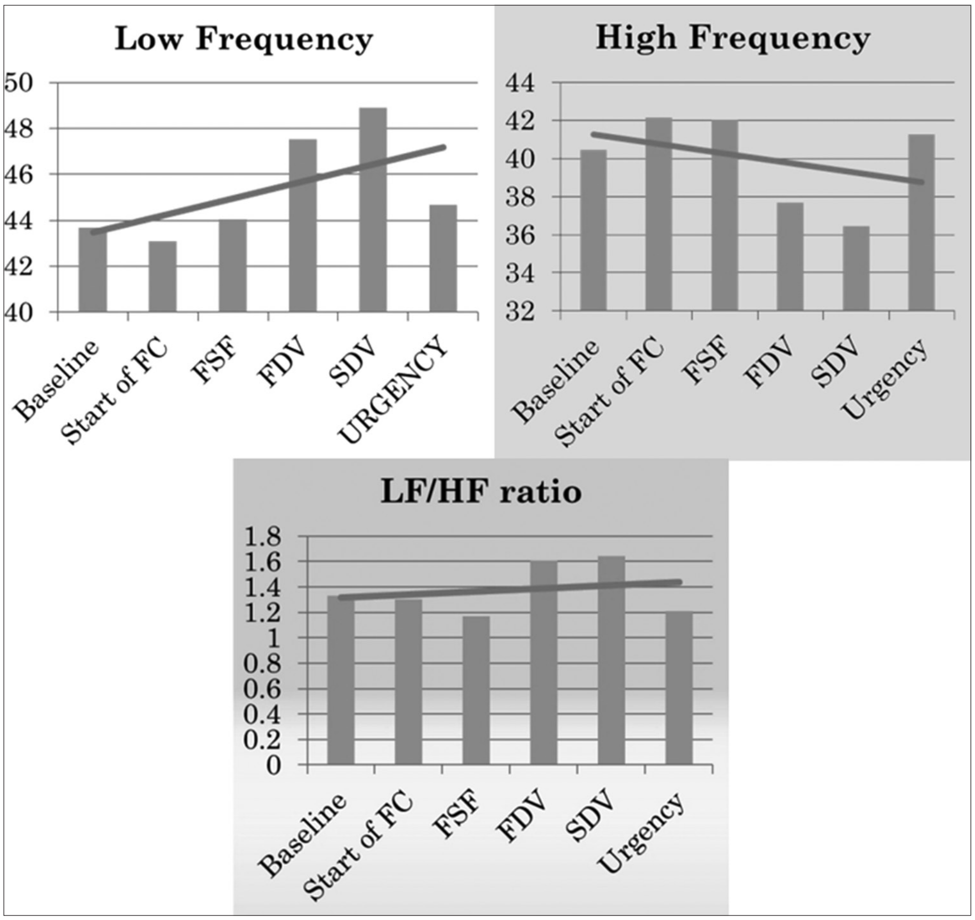
	Sample size	Mean±SD	Median (*r*)	Range	Inter quartile range	*P*
Average heart rate	21	0.06±0.63	0.04	0.94-0.89	0.58-0.59	0.667
HF (nv)	21	−0.18±0.55	−0.22	0.92-0.7	0.65-0.32	0.988
LF/HF	21	0.14±0.54	−0.01	0.68-0.88	0.32-0.74	0.249
LF (nv)	21	0.17±0.54	0.06	0.76-0.96	0.21-0.68	0.165
RMSSD	21	0±0.5	0.01	0.83-0.96	0.29-0.43	1.00
SDNN	21	0.22±0.51	0.27	0.82-0.86	0.047-0.62	0.042
Total power	21	0.18±0.46	0.24	0.8-0.86	0.05-0.6	0.048

RMSSD=Root mean square of successive RR difference, SDNN=Standard deviation of NN interval, nv=Normalized value, HF=High frequency, LF=Low frequency, SD=Standard deviation

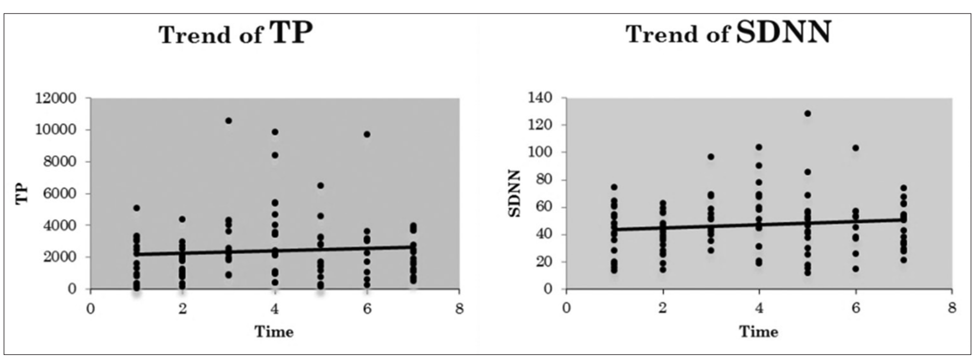
UDS and early recognition of autonomic dysreflexia in the predisposed (which was not observed with any patient in our study during UDS).[2,5,6,8]

Micturition is different from other visceral functions as it is under voluntary control and develops as learned behavior during maturation of nervous system and the neural circuits in bladder control have a phasic pattern of activity when compared to tonic pattern that regulates autonomic activity of cardiovascular system.[16] The normal sensations of bladder are episodic, but duration, intensity, and frequency show an increase in relation to increase in volume.[17,18]

An acute SCI above the sixth thoracic (T6) vertebra disrupts the descending pathways to the sympathetic neurons located in the intermediolateral cell column of the spinal cord T1-L2. The loss of supraspinal control of the sympathetic nervous system results in an increased sympathetic activity below the injury level and a loss of inhibition of the parasympathetic nervous system above the level of damage (intact parasympathetic function).[19] In the present study, we had 14 patients with lesions above D6 level (10 cervical and 4 dorsal myelopathies). Out of these, only five patients had complete/motor complete myelopathy (ASIA A or B) at the time of admission. These patients are more prone



Graph 1: The mean values of heart rate variability parameters at filling phases



Graph 2: Significant positive trend in total power and standard deviation of normal-to-normal

to episodes of autonomic dysreflexia, but none of our patients showed signs during UDS. The explanation for this could be that the patients had started recovering from injury/lesion by the time the UDS was performed.

Distension of the urinary bladder has been shown to cause the vesico-sympathetic reflex which evokes increase in heart rate, blood pressure, and myocardial ischemia in the predisposed patients and a decrease in vagal fiber activity.[20] Accordingly in our study, there was a rise in mean value of LF and LF/HF ratio in comparison to the baseline during various phases of UDS that signifies a raise in sympathetic activity although it was not shown to be statistically significant. HF showed a reduction in mean value during SDV and urgency, which was statistically insignificant (suggests a decline in vagal activity). Time domain measures such as SDNN and RMSSD showed no statistical difference with the baseline during the UDS. Similar results were seen in study by Huang *et al*. comparing 24 spinal cord injury and 12 able-bodied participants, where the spinal cord injured patients showed no significant HRV changes as compared to baseline.[21] Other studies have also shown HRV in able-bodied participants to indicate a rise in sympathetic tone during the SDV due to vesico-sympathetic reflex.[15]

When the trend of HRV parameters was calculated in comparison with the baseline, a significant positive trend was seen in SDNN signifying a rise in sympathetic activity, but no significant trend was seen among other time domain measure, namely RMSSD and average heart rate. The lack of clear autonomic activity can be explained by the loss of supraspinal control of autonomic system in spinal cord injury. In contrast, Mehnert *et al*. in a study with healthy volunteers reported a rise in sympathetic activity during filling phase and the rise in LF/HF ratio as a good indicator for SDV.[15]

On comparing the HRV measures of myelopathy patients with normal age- and gender-matched participants, we observed no significant difference in resting condition. However, during the UDS, there was significant difference with HF measure at SDV as compare to resting condition. This can be interpreted as a rise in parasympathetic activity during void which is well documented.

Conclusion

On comparison of HRV parameters at different events of filling and voiding phases of UDS in myelopathy patients, though alteration in autonomic activity was seen there was no clear indication of predominant sympathetic or parasympathetic activity in the present. The role of HRV in neurogenic bladder to improve the objective evaluation of bladder sensation during UDS requires a more critical evaluation. Further studies are required with larger sample size to interpret the activity of autonomic system and its clinical usefulness during urodynamic procedure in myelopathy patients.

Limitation of the study

The small sample size and short duration of the study might have affected the outcome of the study. The measurement of blood pressure at each phase of the study could have yielded more information.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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