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ORIGINAL ARTICLE

Observational Study

Altered heart rate variability and pulse-wave velocity after spinal cord injury

Hsi-Kai Tsou, Kuan-Chung Shih, Yueh-Chiang Lin, Yi-Ming Li, Hsiao-Yu Chen

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Abstract

BACKGROUND

Heart rate variability (HRV) and pulse-wave velocity (PWV), indicators of cardiac function, are altered in patients with spinal cord injury (SCI), suggesting that autonomic cardiac function and arterial stiffness may underlie the high risk of cardiovascular complications in these patients. No study has simultaneously investigated HRV and PWV in the same patients.

AIM

To evaluate cardiovascular complications in SCI patients by comparing HRV and PWV between patients with and without SCI.

METHODS

In this cross-sectional pilot study, patients with (n = 60) and without SCI (n = 60) were recruited from December 7, 2019 to January 21, 2020. Each participant received a five-minute assessment of HRV and the cardiovascular system using the Medicore HRV Analyzer SA-3000P. Differences in HRV and PWV parameters between participants with and without SCI were statistically examined.

RESULTS

We observed a significant difference between participants with and without SCI with respect to the standard deviation of all normal-to-normal intervals, square root of the mean sum of squared successive risk ratio interval differences, physical stress index, total power, very-low frequency, low frequency, high frequency, and arterial elasticity.

CONCLUSION

Patients with SCI have weaker sympathetic and parasympathetic activity as well as lower arterial elasticity compared to those without, suggesting that SCI may increase cardiac function loading.

Key Words: Acceleration plethysmography; Cardiac function; Heart rate variability; Pulse wave velocity; Spinal cord injury

Core Tip: Noninvasive, simultaneous assessment of heart rate variability and pulse-wave velocity showed that patients with spinal cord injury have weaker sympathetic and parasympathetic activity and lower arterial elasticity compared to those without. These findings indicate that increased cardiac function loading may underlie the high risk of cardiovascular complications in patients with spinal cord injury. Continuous dynamic monitoring of heart rate variability and pulse-wave velocity could be integrated into care programs for spinal cord injury patients to inform the development of measures to reduce stress and increase vitality.

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INTRODUCTION

Spinal cord injury (SCI) that causes total or partial disability is a catastrophic event that often leads to multiple complications[1,2]. Patients with high-level SCI commonly have sympathetic nervous system hypofunction, resulting in cardiovascular complications including hypotension, cardiac dysrhythmias, orthostatic hypotension, and autonomic dysreflexia[3,4]. As a result, coronary artery disease is the leading cause of death among people with SCI[5]. Over a decade of research on the effects of SCI on the cardiovascular system[6-8] has revealed a clear correlation between cardiovascular disorders and SCI. However, the physiological mechanisms underlying cardiovascular disorders associated with SCI vary between patients, and their elucidation requires further investigation[9]. Numerous recent studies of cardiac function in SCI patients have investigated heart rate variability (HRV), the change in time between heartbeats. The complex oscillations of the heart allow the cardiovascular system to rapidly adjust to sudden physical and psychological challenges to homeostasis[10]. HRV is an indicator of cardiac autonomic activity, as cardiac function is directly related to sympathetic and parasympathetic nervous system activity[11]. Measurable HRV parameters are divided into frequency and time domains. Frequency domain analysis separates HRV into its component rhythms that operate within different frequency ranges: ultra-low frequency (ULF), very-low frequency (VLF), low frequency (LF), and high frequency (HF)[12,13]. The ratio of LF to HF power (LF/HF ratio) estimates the ratio sympathetic to parasympathetic nervous system activity, and the total power (TP) is the sum of the energy in the VLF, LF, and HF bands in short-term recordings[12]. Time domain parameters include the mean normal-to-normal (NN) intervals during the entire recording and the standard deviation between NN intervals (SDNN), which reflects the ebb and flow of all the factors that contribute to heart rate variability[12].

The root mean square of successive differences between normal heartbeats (RMMSD) reflects the beat-to-beat variance in heart rate and is used to estimate the vagally-mediated changes reflected in HRV [12]. These HRV parameters have been investigated in SCI patients to better understand the factors underlying the association between SCI and cardiovascular complications.

Compared to able-bodied control subjects, patients with cervical SCI were found to have reduced supine and upright power in the LF range, while those with thoracic SCI had reduced supine HF power [8]. Compared to subjects without SCI, thoracic SCI patients had altered HRV parameters, including the SDNN, TP, VLF power, and LF power[14]. In another study evaluating changes in HRV and skin perfusion in response to postural changes, no changes were found in individuals with SCI, while healthy individuals exhibited significant changes in the sympathovagal balance[15]; these observations suggest SCI-induced impairment of microvascular function. In addition, the higher level of neurological impairment in patients with SCI suggests reduced sympathetic activity due to disordered cardio-vascular control[16]. Nevertheless, an investigation of obstructive sleep apnea and nocturnal blood pressure (BP), both of which commonly occur in SCI, found no relationship between HRV and obstructive sleep apnea severity or BP as signs of autonomic dysfunction in SCI patients[17]. Cardiac parasympathetic activity is associated with LV filling at rest and during elevated cardiac vagal tone in healthy individuals but not in SCI patients, whose autonomic function does not influence LV; this observation indicates a lack of connection between parasympathetic and cardiovascular function in SCI patients[13].

Pulse-wave velocity (PWV), the velocity of the blood pressure wave as it travels between 2 sites within the arterial system, is a measure of arterial stiffness[18]. This parameter can be assessed noninvasively using acceleration plethysmography. PWV was first used to evaluate cardiac function in SCI patients 2009[5] and since has been widely used to evaluate arterial parameters in SCI patients[19-21]. In particular, significant elevations in PWV appear to indicate greater cardiovascular risk in patients with cervical and thoracic SCI[21]. However, to the best of our knowledge, HRV and PWV have not been evaluated simultaneously in individuals with SCI. Therefore, this cross-sectional study aimed to measure both HRV and PWV at the same time in people with and without SCI to comprehensively assess the influence of SCI on cardiac function and arterial stiffness.

MATERIALS AND METHODS

Study design and participants

This cross-sectional study recruited patients diagnosed with SCI (SCI group) and those without history of neurological injury (non-SCI group) between December 7, 2019 and January 21, 2020. Participants in the non-SCI group were patients admitted to the study hospital for causes other than neurological injury. Inclusion criteria for all participants, regardless of group, were age 20–80 years and without bipolar disorder or psychosis. Only patients with SCI who were able to maintain basic life functions independently or with the assistance of a caregiver 6 mo after SCI were included. Patients with SCI with severe spasticity or brain trauma or who were undergoing mechanical ventilation or oxygen therapy were excluded.

Ethical considerations

The study protocol was approved by the Institutional Review Board of Taichung Jen-Ai Hospital (JAHIRB-108-73). All participants provided signed informed consent prior to participating in the study.

Procedures

All participants were first asked to complete a questionnaire to provide their demographic and clinical characteristics, as described previously[22]. Subsequently, the HRV and PWV of each participant were measured simultaneously using the Medicore HRV Analyzer SA-3000P (Medicore, Seoul, Korea) according to the manufacturer's instructions [23] in a room that was maintained with bright indoor lighting, no external noise, and a comfortable ambient temperature (20 °C–25 °C). Participants were instructed to avoid consuming coffee, tea, alcohol, and other potentially irritating foods for 2 h before the measurement and not to wear any metal objects during the measurement. A fingertip sensor was attached to the participant's left index finger, held at the same height as the heart. Participants were instructed to sit upright in a chair or wheelchair with backrest, to avoid closing their eyes or falling asleep, and to maintain normal breathing throughout the 5-minute measurement period.

Heart rate variability parameters

The SA-3000P analyzer measures time and frequency domain HRV parameters[23]. Time domain parameters assessed include the mean HRT over a given time period, SDNN, RMSSD (which reflects parasympathetic regulation of the heart), and the physical stress index (PSI). Frequency domain parameters included TP (< 0.4 Hz) (which reflects sympathetic nervous system activity), VLF (0.0033 – 0.04 Hz), LF (0.04 – 0.15 Hz), and HF (0.15–0.4 Hz). Frequency domain parameters assessed include the

LF norm [calculated as LF/ (TP−VLF) × 100], HF norm [calculated as HF/(TP−VLF) × 100], and LF/HF ratio, as previously described[23].

Pulse-wave velocity parameters

The SA-3000P analyzer performs acceleration plethysmography to measure PWV, which reflects arterial elasticity[23]. The pulse waves generated by cardiac constriction travel to different parts of the body at different rates. Infrared sensors detect these differences in the rate of arterial pulse wave travel (Figure 1). Increases in PWV reflect greater arterial wall thickness and stiffness[23]. Parameters calculated from PWV include the differential pulse wave index (DPI) [calculated as (b−c−d)/a], eccentric constriction power (EC) (b/a), arterial elasticity (AE) (c/a), and remaining blood volume (RBV) (d/a) (Figure 1)[23]. In addition, vascular age was estimated based on the wave pattern detected, with each of 7 wave patterns corresponding to an arterial age level (1–7)[20]. Only the number of patients with each type of wave pattern was determined in this study; no actual 'vascular age' can be calculated using the SA-3000P data.

Statistical analysis

The SA-3000P analyzer converted the original data files to CSV format, which then were imported into SPSS 24.0 (IBM Corp., Armonk, NY, United States) for all statistical analyses. Descriptive statistics of the study population were performed. Continuous variables are expressed as the mean ± SD, and categorical variables are presented as *n* (%). For normally distributed data, the *t*-test was conducted to examine differences between groups. Non–normally-distributed data were analyzed using Fisher's exact test and the Mann–Whitney *U* test. $P < 0.05$ was established as statistically significant.

RESULTS

Demographic and clinical characteristics

A total of 120 participants [60 patients with SCI (SCI group) and 60 without (non-SCI group)] were included in this cross-sectional pilot study. The demographic and clinical characteristics of the two groups are presented in Table 1. The mean ages of the SCI and non-SCI groups were comparable (P = 0.09). The SCI group had 45 males and 15 females, and the non-SCI group had 15 males and 45 females. Regardless of SCI status, the majority of all participants (82.5%) had a high school, university, or graduate school diploma, worked as freelancers (30.83%), were married or cohabiting (50.83%), and practiced a combination of Taoism and Buddhism (40.00%). At least one comorbidity was present in 29 patients (48.3%) in the SCI group, including hypertension (20%), diabetes (8.3%), and pneumonia (6.7%) (Table 1). In contrast, 17 patients (28.3%) in the non-SCI group had at least one comorbidity, including hypertension (13.3%), asthma (5.0%), and hyperlipidemia (5.0%). In the SCI group, 36 patients (60.0%) were taking at least one medication, including a hypoglycemic, antihypertensive, and anticoagulant agents and others. In contrast, 11 patients (18.3%) in the non-SCI group were taking at least one medication, including hypoglycemic and antihypertensive agents and others (Table 1). The clinical characteristics of the SCI group are summarized in Table 2, in which patients with SCI were further divided into two subgroups: paraplegia (n = 30) and tetraplegia (n = 30). For all included patients with SCI, the mean SCI duration was 16.73 years, and the main cause of SCI was automobile accident (51.67%) (Table 2). Most patients had cervical spine injuries (47.30%), followed by thoracic spine injuries (31.08%), lumbar (20.27%), and sacral injuries (1.35%). The majority of patients with paraplegia had thoracic spine injuries (46.34%), while most patients with tetraplegia had cervical spine injuries (81.82%). Four patients had incomplete paraplegia, 26 patients had complete paraplegia, 22 patients had incomplete tetraplegia, and 8 patients had complete tetraplegia (Table 2).

Comparison of HRV parameters between patients with and without SCI

All HRV parameters were treated as continuous variables (Table 3). Subsequently, the mean HRV parameters were compared between patients with and without SCI. The mean SDNN, RMSSD, PSI, TP, VLF, LF, and HF differed significantly between SCI and non-SCI groups (all $P < 0.05$). In contrast, no significant between-group differences were observed in the mean HRT, LF/HF ratio, LF norm, or HF norm (Table 3). The HRT, SDNN, RMSSD, PSI, TP, and LF/HF ratio also were treated as categorical variables and compared between the 2 groups (Table 3). The SDNN, RMSSD, PSI, and TP differed significantly between the SCI and non-SCI groups (all $P < 0.05$). No significant between-group differences were observed in the HRT or LF/HF ratio (Table 3). Most participants in both groups had normal mean HRT (SCI, 75%; non-SCI, 81.67%) (Table 3). SDNN was low in most SCI patients (75%) and normal in most non-SCI participants (66.67%). RMSSD was very low in the majority of SCI patients (68.33%)and normal in most non-SCI patients (65%). PSI was very high in most SCI patients (70%) and normal in most non-SCI patients (65%). Very low TP was observed in 86.67% SCI patients and 53.33% of non-SCI patients. A normal LF/HF ratio was observed in 50% of SCI patients and 55% of non-SCI patients (Table 3).

Table 1 Demographic and clinical characteristics of patients with or without spinal cord injury

	SCI (n = 60)	Non-SCI (n = 60)	P value
Age, yr	49.92 ± 11.61	45.93 ± 13.99	0.09
Sex			
Male	45 (75.0%)	15 (25.0%)	< 0.001[a]
Female	15 (25.0%)	45 (75.0%)	
Education level			
Elementary school	2 (3.3%)	1 (1.7%)	< 0.001[a]
Junior high school	6 (10.0%)	0 (0.0%)	
Senior high/vocational school	32 (53.3%)	6 (10.0%)	
Five-year junior college	6 (10.0%)	6 (10.0%)	
University	14 (23.3%)	21 (35.0%)	
Graduate school	0 (0.0%)	26 (43.3%)	
Occupation			
Freelancer	37 (61.7%)	0 (0.0%)	< 0.001[a]
Teacher	1 (1.7%)	17 (28.3%)	
Public servant	1 (1.7%)	15 (25.0%)	
Service industry	4 (6.7%)	10 (16.7%)	
Others	17 (28.3%)	18 (30.0%)	
Marital status			
Unmarried	27 (45.0%)	20 (33.3%)	0.01[a]
Married/cohabiting	24 (40.0%)	37 (61.7%)	
Divorced	8 (13.3%)	1 (1.7%)	
Widowed	1 (1.7%)	2 (3.3%)	
Religion			
None	13 (21.7%)	22 (36.7%)	0.14
Taoism/Buddhism	24 (40.0%)	24 (40.0%)	
Christianity/Catholicism	14 (23.3%)	6 (10.0%)	
Folk belief	9 (15.0%)	8 (13.3%)	
Comorbidity			
No	31 (51.7%)	43 (71.7%)	0.04[a]
Yes	29 (48.3%)	17 (28.3%)	
Heart attack	3 (5.0%)	1 (1.7%)	0.62
Diabetes	11 (8.3%)	2 (3.3%)	0.02[a]
Kidney disease	2 (3.3%)	2 (3.3%)	1.00
Pneumonia	4 (6.7%)	0 (0.0%)	0.12
Hypertension	12 (20.0%)	8 (13.3%)	0.46
Asthma	1 (1.7%)	3 (5.0%)	0.62
Hyperlipidemia	0 (0.0%)	3 (5.0%)	0.24
Malignant tumor	0 (0.0%)	1 (1.7%)	1.00
Medication			
No	24 (40.0%)	49 (81.7%)	< 0.001[a]
Yes	36 (60.0%)	11 (18.3%)	

Hypoglycemic agent	11 (18.3%)	2 (3.3%)	0.02[a]
Antihypertensive agent	12 (20.0%)	6 (10.0%)	0.20
Anticoagulant	2 (3.3%)	0 (0.0%)	0.50
Others	21 (35.0%)	5 (8.3%)	0.001[a]

SCI: Spinal cord injury.
[a]Statistically significant ($P < 0.05$).

Table 2 Clinical characteristics of the spinal cord injury group

Variables	SCI patients (*n* = 60)	Subgroup	
		Paraplegia (*n* = 30)	Tetraplegia (*n* = 30)
Age, yr	49.92 ± 11.61	51.53 ± 12.39	48.30 ± 10.73
Duration of injury, years	16.73 ± 11.05	17.67 ± 12.96	15.80 ± 8.88
Cause of injury			
Car accident	31 (51.67%)	12 (40.00%)	19 (63.33%)
Fall from high place	11 (18.33%)	5 (16.67%)	6 (20.00%)
Sports injury	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hit by a heavy object	1 (1.67%)	1 (3.33%)	0 (0.00%)
Lesions	6 (10.00%)	4 (13.33%)	2 (6.67%)
Other	11 (18.33%)	8 (26.67%)	3 (10.00%)
Injured region			
Cervical	35 (47.30%)	8 (19.51%)	27 (81.82%)
Thoracic	23 (31.08%)	19 (46.34%)	4 (12.12%)
Lumbar	15 (20.27%)	13 (13.71%)	2 (6.06%)
Sacral	1 (1.35%)	1 (2.44%)	0 (0.00%)
Level of injury			
Complete tetraplegia	8 (13.33%)	-	8 (26.67%)
Incomplete tetraplegia	22 (36.67%)	-	22 (73.33%)
Complete paraplegia	26 (43.33%)	26 (86.67%)	-
Incomplete paraplegia	4 (6.67%)	4 (13.33%)	-

SCI: Spinal cord injury.

Pulse-wave velocity parameters

The PWV parameters, including DPI, EC, AE and RBV, were treated as continuous variables and expressed as the mean ± SD (Table 4). The mean AE differed significantly between the SCI and non-SCI groups ($p < 0.05$). No significant between-group differences were observed in the mean DPI, EC, or RBV (Table 4). Vascular age was assessed based on a 7-level scale[23]. In Table 4, vascular age, HRT, SDNN, RMSSD, PSI, TP, and LF/HF ratio were also treated as categorical variables and compared between patients with and without SCI (Table 4). Vascular age and AE differed significantly different between patients with and without SCI ($P < 0.05$). No significant between-group differences were observed in the DPI, EC, or RBV (Table 4). The majority of patients in the SCI group (55.00%) and non-SCI group (33.3%) had a Level 2 vascular age (Table 4). The DPI was normal or good in nearly all patients in the SCI and non-SCI groups (86.6% and 96.7%, respectively). The AE was normal in most patients in the SCI and non-SCI groups (55% and 51.67%, respectively).

Table 3 Comparison of heart rate variability parameters between patients with and without spinal cord injury

	SCI (n = 60)	Non-SCI (n = 60)	P value
Continuous variables			
HRT	79.93 ± 13.19	77.03 ± 9.90	0.18[b]
SDNN	27.11 ± 18.45	34.30 ± 11.18	< 0.001[a,c]
RMSSD	21.54 ± 17.65	25.19 ± 9.51	< 0.001[a,c]
PSI	125.42 ± 126.02	58.68 ± 63.64	< 0.001[a,c]
TP	813.78 ± 2211.10	989.19 ± 671.65	< 0.001[a,c]
LF/HF ratio	1.80 ± 2.52	1.98 ± 2.68	0.20[c]
VLF	519.54 ± 1903.98	443.89 ± 372.20	0.001[a,c]
LF	179.09 ± 319.20	299.85 ± 292.49	< 0.001[a,c]
HF	115.16 ± 133.82	245.45 ± 276.53	< 0.001[a,c]
LF norm	51.33 ± 20.21	55.78 ± 18.33	0.21[a]
HF norm	48.67 ± 20.21	44.22 ± 18.33	0.21[a]
Categorical variables			
HRT			
Low (≤ 60)	1 (1.7%)	2 (3.3%)	0.51[d]
Normal (60–90)	45 (75.0%)	49 (81.7%)	
High (> 90)	14 (23.3%)	9 (15.0%)	
SDNN			
Low (≤ 30)	45 (75.0%)	20 (33.3%)	< 0.001[a,d]
Normal (> 30)	15 (25.0%)	40 (66.7%)	
RMSSD			
Low (≤ 20)	41 (68.3%)	21 (35.0%)	< 0.001[a,d]
Normal (> 20)	19 (31.7%)	39 (65.0%)	
PSI			
Normal (≤ 50)	18 (30.0%)	39 (65.0%)	< 0.001[a,d]
High (> 50)	42 (70.0%)	21 (35.0%)	
TP			
Low (≤ 1000)	52 (86.7%)	32 (53.3%)	< 0.001[a,d]
Normal (> 1000)	8 (13.3%)	28 (46.7%)	
LF/HF ratio			
Low (≤ 0.5)	15 (25.0%)	9 (15.0%)	0.42[d]
Normal (0.5-2.0)	30 (50.0%)	33 (55.0%)	
High (> 2.0)	15 (25.0%)	18 (30.0%)	

HRT: Heart rate over a given period of time; SDNN: Standard deviation of all normal-to-normal intervals; RMSSD: Square root of the mean of the sum of the squares of differences between adjacent normal-to-normal intervals; PSI: Physical stress index; TP: Total power; LF/HF: The ratio or low frequency to high frequency; VLF: Very low frequency; LF: Low frequency; HF: High frequency.

[a]Statistically significant (P < 0.05).

[b]T-test.

[c]Mann–Whitney U test.

[d]Fisher's exact test.

DISCUSSION

In this pilot study assessing HRV parameters and vessel conditions of patients with and without SCI, we

Table 4 Comparison of pulse-wave velocity parameters between patients with and without spinal cord injury

	SCI (n = 60)	Non-SCI (n = 60)	P value
Continuous variables			
DPI	-63.57 ± 44.51	-75.12 ± 46.32	0.17
EC	-88.59 ± 16.95	-88.67 ± 18.05	0.98
AE	-21.17 ± 15.27	-7.18 ± 17.29	< 0.001[a]
RBV	-27.65 ± 17.88	-30.08 ± 17.67	0.38
Categorical variables			
Vascular age			
Level 1	6 (10.0%)	18 (30.0%)	0.01[a]
Level 2	33 (55.0%)	20 (33.3%)	
Level 3	4 (6.7%)	11 (18.3%)	
Level 4	15 (25.0%)	10 (16.7%)	
Level 5	1 (1.7%)	1 (1.7%)	
Level 6	1 (1.7%)	0 (0.0%)	
DPI			
Poor	8 (13.3%)	2 (3.3%)	0.12
Normal	26 (43.3%)	25 (41.7%)	
Good	26 (43.3%)	33 (55.0%)	
EC			
Poor	12 (20.0%)	6 (10.0%)	0.24
Normal	28 (46.7%)	28 (46.7%)	
Good	20 (33.3%)	26 (43.3%)	
AE			
Poor	24 (40.0%)	12 (20.0%)	0.001[a]
Normal	33 (55.0%)	31 (51.7%)	
Good	3 (5.0%)	17 (28.3%)	
RBV			
Poor	8 (13.3%)	6 (10.0%)	0.56
Normal	21 (35.0%)	27 (45.0%)	
Good	31 (51.7%)	27 (45.0%)	

DPI: Differential pulse wave index; EC: Eccentric constriction power; AE: Arterial elasticity; RBV: Remaining blood volume;
[a]Statistically significant (P < 0.05).

observed significantly lower SDNN, RMSSD, TP, LF, and HF and significantly higher PSI and VLF in those with SCI. These results suggest that patients with SCI have weaker cardiac load function, higher pressure, lower vitality, and weaker sympathetic and parasympathetic activity compared to those without SCI. Accordingly, the SCI patients were more prone to mental and physical fatigue and abdominal discomfort. Overall, simultaneous decreases in the HRV frequency domains TP, LF, and HF were more likely in people under great long-term cardiovascular pressure, demonstrating a relationship between autonomic function and fatigue status. The relationship between autonomic function and fatigue was demonstrated previously in populations of different ages[24]. In the present pilot study, vascular age assessment showed that arterial elasticity was generally poorer among those with SCI compared to those without, suggesting inferior vasculature in SCI patients. Correspondingly, SCI patients exhibited relatively weaker cardiac function and vascular conditions, higher remaining blood volume and vessel resistance, and poorer circulation and metabolism than did those without SCI. A previous study also showed that chronic SCI correlates with changes in vascular structure that result in lower elasticity of the blood vessel walls, in turn increasing cardiovascular risk[25]. Lee *et al*[26]

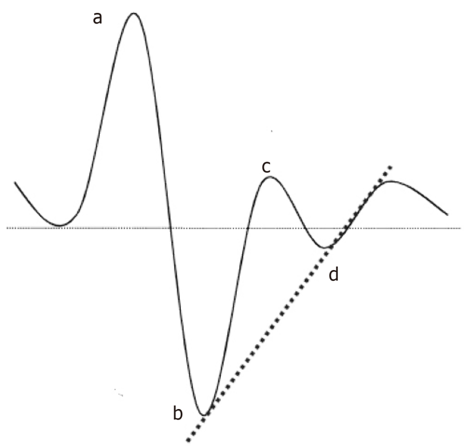

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Figure 1 Pulse wave velocity waveform. a: Basic point to evaluate autologous platelet-rich gel wave form; b: Cardiac constriction power (cardiac output)-the deeper (-) value is better shape; c: Arterial elasticity-higher (+) value is better; d: Remaining blood volume-higher value, smaller (-) value is better.

reported that elevated PWV in SCI patients indicates that central arterial stiffness is a powerful index of cardiovascular health associated with accelerated cardiovascular decline. The authors concluded that the higher risk of arterial stiffness resulted from autonomic dysfunction, vascular remodeling, and low physical activity levels over time. In addition to pharmacological treatments, lifestyle and dietary interventions are suggested to ameliorate these developments in people with SCI.

An Australian study by Craig *et al*[27] used HRV assessment to explore the relationship between daytime sleepiness and autonomic dysfunction in people with and without SCI. The authors observed weak cardiac function and reduced daytime sympathetic nervous system activity in those with SCI, causing them to tire readily and become sleepy during the day. However, the authors observed no significant difference in parasympathetic activity between people with and without SCI[27]. The present study supports these previous findings of low cardiac function and sympathetic activity in those with SCI. Specifically, we found in our Taiwanese cohort that SCI patients were also characterized by low parasympathetic activity, suggesting that they were not only prone to insomnia, neurosis, and metabolic syndrome, but also vulnerable to complications such as diabetes.

Our results also are consistent with those of many previous studies assessing HRV and PWV parameters. However, while the present study used simultaneous measurement of HRV and PWV using an HRV analyzer[23,24], previous studies applied various techniques to simultaneously measure HRV[13,15-17] and PWV parameters[5,19-21] separately. The SA-3000P HRV analyzer is a non-invasive and quick evaluation tool that can detect cardiovascular complications after SCI, facilitating appropriate early intervention. In the present and previous studies, HRV alterations (particularly lower SDNN) were predictive of progressive coronary artery disease in people with SCI and were found more frequently in those with a sedentary lifestyle and without regular physical exercise[14]. Physical exercise after SCI is shown to increase sympathetic activity and may help minimize the risk of cardiac arrhythmias and prevent sudden cardiac death in those with cervical SCI[28]. Fatigue is also associated with altered HRV parameters and greater risk of cardiovascular sequelae after SCI; appropriate levels of exercise as well as sufficient sleep and dietary measures are recommended as anti-fatigue and anti–cardiovascular-risk strategies[16]. Regarding PVW, the present study found significant differences in the AE between patients with and without SCI but not in the vascular age, DPI, EC, or RBV. The results of other studies, however, are inconsistent regarding the cause-and-effect relationship between hypertension and arterial stiffening in SCI patients[20]. Although repeated episodes of hypertension over time are recognized as stimuli for vascular remodeling, some authors found no relationship between autonomic dysreflexia and aortic augmentation indices[21].

Karri *et al*[29] developed a novel modality for diagnosing neuropathic pain after SCI, finding that people with SCI and chronic neuropathic pain demonstrated significantly lower SDNN, RMSSD, HF, and LF than did able-bodied adults. This finding is also consistent with the findings of the present study. El-Kotob *et al*[30] used HRV as a surrogate measure of cardiac autonomic function in chronic traumatic SCI patients in Canada, showing a positive relationship between HF and LF. The present study also identified this relationship in Taiwanese people with SCI. While we found that most previous studies focused on HRV analysis, we also noted that they rarely discussed vascular age. The present pilot study found that comprehensive evaluation of HRV and vascular age indicators addresses the full spectrum of poor AE, SDNN, and RMSSD in those with SCI. Studies have shown that physical activity, painting, respiratory training, music therapy, and nature therapy have the potential to reduce stress and improve HRV-related disorders and blood vessel structure[28,31-34]. Changes in the autonomic system, for example, are readily observed in response to physical exercise in individuals with SCI. Adjustments occur in the cardiac autonomic system as a result of exercise-induced remodeling of damaged axons, which increases sympathetic activity and may help to minimize risk of arrhythmia or sudden cardiac death in those with cervical SCI[28]. Kyriakides *et al*[31] examined the effects of regular physical workouts (four-hour sessions once a week for three months) on reducing the HRV of people with SCI, reporting that all HRV metrics improved in SCI patients who engaged in this exercise program. Other interventions have applied various relaxation techniques to reduce HRV. Chang *et al*[32] used painting as an intervention to help participants relax the mind, relieve stress, and stabilize the HRV. According to Ditterline *et al*[33], respiratory training performed 5 d a week for 4 wk effectively improved both sympathetic and parasympathetic nervous system function and further resulted in improved HRV in individuals with chronic SCI. Audio stimulation with music was used as a therapeutic approach to reduce fatigue, increase comfort and relaxation, and induce sympathetic and parasympathetic activity in cancer survivors, confirming the effectiveness of music in improving HRV parameters in this patient population[34]. Nature therapy was also evaluated in adult male SCI patients; visual stimulation with bonsai trees induced mental and physical relaxation, reduced stress, promoted parasympathetic activity, and ultimately improved HRV in these patients[35]. Self-management strategies are also suggested to assist people with SCI in improving self-care skills that may ultimately help to prevent complications after SCI[22]. Together, the results of these studies suggest the importance of developing a care program that can reduce stress, increase vitality, and improve cardiovascular function in SCI patients. Implementing such a program may help people with SCI to improve cardiac function and load, reduce stress, and increase vitality, autonomic function, and vascular health. Based on the results of the present study and those in the related literature, our follow-up study will seek to develop an evidence-based care program that can reduce stress, increase vitality, and support cardiovascular health in patients with SCI.

The present pilot study has several limitations. All data analyzed were from Taiwanese subjects; similar studies of patients in other countries are needed to confirm the applicability of these findings to other populations. Because the study was closed, we were not able to conduct sex-matched sampling. Therefore, the unmatched sex ratio is a limitation of this pilot study. We did not perform subgroup analysis based on the level of injury (*e.g.*, tetraplegia *vs.* paraplegia) to address differences between types of SCI. The large standard deviation in the time elapsed after SCI may affect study results to some degree. Continuous monitoring of dynamic HRV and PWV would be of greater clinical significance than the assessments employed in this pilot study, and continuous monitoring will be included in our future research. Large-scale, cohort-matched multi-center studies in different countries are needed to expand and confirm the findings of the present study.

CONCLUSION

Analysis of HRV and PWV parameters showed that cardiac function loading is elevated in SCI patients, resulting in stress and a decline in vitality. SCI patients have weaker sympathetic and parasympathetic activity than do those without SCI, increasing their risk of mental and physical fatigue and abdominal discomfort. Cardiovascular assessment demonstrates that SCI patients also have lower arterial elasticity. HRV and PWV data can be obtained non-invasively, such that continuous dynamic monitoring of HRV and PWV could be integrated into care programs for SCI patients, along with measures aiming to reduce stress and increase vitality.

ARTICLE HIGHLIGHTS

Research background

While a clear correlation has been established between spinal cord injury and cardiovascular disorders, the underlying mechanism is not fully understood. Heart rate variability (HRV) and pulse-wave velocity (PWV), indicators of cardiac function, are altered in patients with spinal cord injury, implicating autonomic cardiac function and arterial stiffness in this mechanism.

Research motivation

While studies have independently assessed HRV or PWV in patients with spinal cord injury, simultaneous assessment to gain a broader view of their cardiovascular condition has not been reported.

Research objectives

The study objective is to elucidate the mechanism underlying cardiovascular complications in spinal cord injury (SCI) patients

Research methods

Short-term HRV and PWV parameters were compared between patients with and without spinal cord injury. All assessments were made using the Medicore HRV Analyzer SA-3000P, which measures HRV time and frequency domain parameters and uses acceleration plethysmography to measure PWV.

Research results

Factors that differed significantly between participants with and without spinal cord injury included the standard deviation of all normal-to-normal intervals, square root of the mean sum of squared successive RR interval differences, physical stress index, total power, very-low frequency, low frequency, high frequency, and arterial elasticity.

Research conclusions

Patients with spinal cord injury have weaker sympathetic and parasympathetic activity as well as lower arterial elasticity compared to those without, suggesting that SCI may increase cardiac function loading.

Research perspectives

Further investigation is needed using multi-center, cohort-matched studies with continuous assessment of HRV and PWV. This non-invasive assessment could be integrated into care programs for SCI patients as an indicator of the need for measures to reduce stress and increase vitality.

FOOTNOTES

Author contributions: Tsou HK and Chen HY contributed to study conception and design; Tsou HK, Chen HY, Shih KC, Lin YC and Li YM contributed to data collection; Tsou HK, Chen HY and Shih KC did data analysis and interpretation; Tsou HK, Chen HY and Shih KC contributed to drafting of the article; Tsou HK and Chen HY did the critical revision of the article.

Institutional review board statement: The study protocol was approved by the Institutional Review Board of Taichung Jen-Ai Hospital (JAHIRB-108-73). All participants provided signed informed consent prior to participating in the study.

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Data sharing statement: All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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