ORIGINAL ARTICLE

Cardiovascular Status of Individuals With Incomplete Spinal Cord Injury From 7 NeuroRecovery Network Rehabilitation Centers

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ABSTRACT. Sisto SA, Lorenz DJ, Hutchinson K, Wenzel L, Harkema SJ, Krassioukov A. Cardiovascular status of individuals with incomplete spinal cord injury from 7 NeuroRecovery Network rehabilitation centers. Arch Phys Med Rehabil 2012;93:1578-87.

Objective: To examine cardiovascular (CV) health in a large cohort of individuals with incomplete spinal cord injury (SCI). The CV health parameters of patients were compared based on American Spinal Injury Association Impairment Scale (AIS), neurologic level, sex, central cord syndrome, age, time since injury, Neuromuscular Recovery Scale, and total AIS motor score.

Design: Cross-sectional study.

Setting: Seven outpatient rehabilitation clinics.

Participants: Individuals (N=350) with incomplete AIS classification C and D were included in this analysis.

Interventions: Not applicable.

Main Outcome Measures: Heart rate, systolic and diastolic blood pressure during resting sitting and supine positions and after an orthostatic challenge.

Results: CV parameters were highly variable and significantly differed based on patient position. Neurologic level (cervical, high and low thoracic) and age were most commonly associated with CV parameters where patients classified at the cervical level had the lowest resting CV parameters. After the orthostatic challenge, blood pressure was highest for the low thoracic group, and heart rate for the high thoracic group was higher. Time since SCI was negatively related to blood pressure at rest but not after orthostatic challenge. Men exhibited higher systolic blood pressure than women and lower heart rate. The prevalence of orthostatic hypotension (OH) was 21% and was related to the total motor score and resting seated blood pressures. Cervical injuries had the highest prevalence.

Conclusions: Resting CV parameters of blood pressure and heart rate are affected by position, age, and neurologic level. OH is more prevalent in cervical injuries, those with lower resting blood pressures and who are lower functioning. Results from this study provide reference for CV parameters for individuals with incomplete SCI. Future research is needed on the impact of exercise on CV parameters.

Key Words: Autonomic dysfunction; Blood pressure; Central cord syndrome; Heart rate; Orthostatic hypotension; Rehabilitation; Spinal cord injuries.

SPINAL CORD INJURY (SCI) results not only in devastating paralysis but also in various autonomic dysfunctions, including abnormal cardiovascular (CV) control.[1] The clinical evidence demonstrates that the severity of autonomic dysfunction depends on the level and the completeness of the SCI.[2] The CV dysfunctions are particularly prominent with injuries at or above the sixth thoracic spinal level (fig 1). After a cervical or high thoracic SCI, the parasympathetic control remains intact while the spinal sympathetic system loses supraspinal autonomic control.

To review, the cerebral cortex and hypothalamus provide tonic and inhibitory inputs to the various nuclei within the medulla oblongata, where CV control is coordinated (see fig 1). The parasympathetic control of the heart exits at the level of the brainstem via the vagus nerve. Descending sympathetic pathways provide tonic control to spinal sympathetic preganglionic neurons involved in CV control. Sympathetic preganglionic neurons are found within the lateral horn of the spinal cord in segments T1 through L2 and exit the spinal cord via the ventral roots. They then synapse with postganglionic neurons located in the sympathetic chain (paravertebral ganglia). Finally, the sympathetic postganglionic neurons synapse with the target organs, heart, and blood vessels.

List of Abbreviations

AIS	American Spinal Injury Association Impairment Scale
CI	confidence interval
CV	cardiovascular
DBP	diastolic blood pressure
NRN	NeuroRecovery Network
NRS	Neuromuscular Recovery Scale
OH	orthostatic hypotension
OR	odds ratio
SBP	systolic blood pressure
SCI	spinal cord injury

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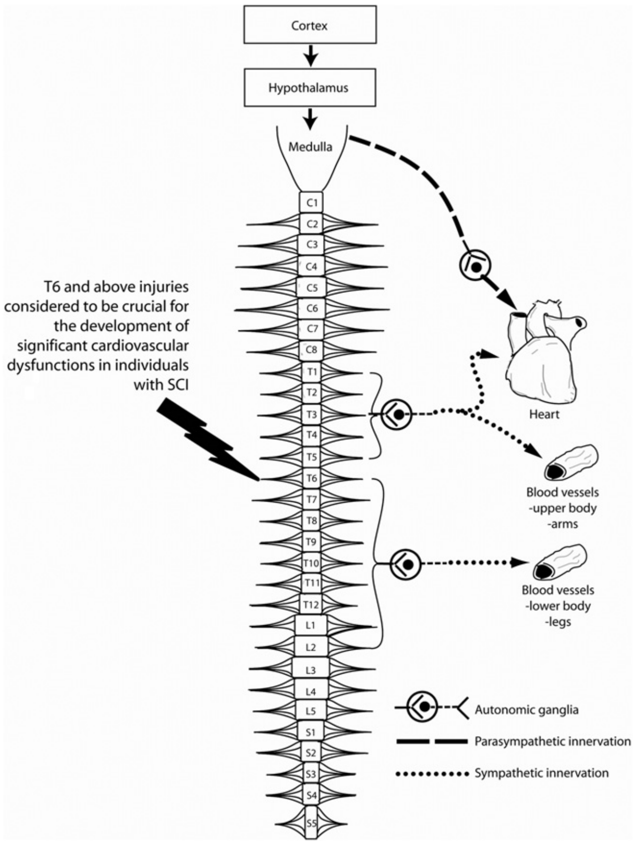

Fig 1. Schematic diagram of autonomic control of CV systems. Afferent feedback for cardiorespiratory functions from the central and peripheral baroreceptors and chemoreceptors is not shown.

As a result of injury to these spinal autonomic pathways, the maintenance of arterial blood pressure and heart rate in individuals with SCI is disrupted, leading to difficulties with participation in rehabilitation in the acute postinjury period and with participation in activities of daily living.[3,4] The appropriate blood pressure and heart rate regulation and reflex response are crucial components of the CV control needed for physical performance and are frequently absent or significantly impaired among individuals with SCI.[5,6] The need for a comprehensive assessment of the CV parameters after SCI has emerged over the years as research performed on individuals with varying levels and severity of SCIs has produced conflicting results with regards to CV outcomes.[5,7,8]

Orthostatic hypotension (OH) is a condition that is commonly seen in both the acute and chronic stages after SCI.[1,7,9] This condition is typically defined as a decrease in systolic blood pressure (SBP) of 20mmHg or more, or a reduction in diastolic blood pressure (DBP) of 10mmHg or more, on changing body position from a supine position to an upright posture, regardless of the presence of symptoms.[2] Furthermore, several studies[4,10,11] in able-bodied populations have documented a strong relationship between OH and CV disease in middle-aged and elderly individuals. OH was found to increase the risk of mortality[4] and coronary heart disease[12] in middle-age and elderly populations. This is particularly important since CV disease is presently the number one cause for morbidity and mortality among individuals with SCI.[3]

The purpose of this analysis was to describe the CV parameters at rest in 2 positions (sitting and supine) and in response to an orthostatic challenge (rapid supine to sit) in a large cohort of patients (N=350) with incomplete SCI. Of note, studies rarely examine CV parameters, including OH, in persons or individuals before SCI and distinguish between high and low thoracic injuries. Some studies examine cervical injuries only[13] or subdivide injuries into cervical, thoracic, and lumbar but do not distinguish between upper and lower thoracic injuries.[8,14] This thoracic distinction is critical to determine the degree to which the components of the sympathetic nervous system are intact. Thus the neurologic level (cervical, high and low thoracic) was an important component in our analysis. Additionally, older age and the sex of individuals with SCI have an impact on CV disease and thus affect CV parameters.[15] Therefore, age and sex were an additional important subanalysis goal. Our sample consisted of patients whose injury durations could be classified as both subacute and chronic, since they were enrolled within months to years after injury. They had an American Spinal Injury Association Impairment Scale (AIS) classification of C and D and were enrolled in the NeuroRecovery Network (NRN) clinical programs. The NRN was initiated, based on basic and clinical scientific evidence,[16] and included individuals with incomplete injuries to determine the outcomes of those most likely to benefit from locomotor training. Our study examined patients enrolled in the NRN clinical programs but who had not yet started locomotor training.

METHODS

Participants

This study included a cross-sectional observational cohort from the Christopher and Dana Reeve Foundation NRN. The NRN is composed of 7 outpatient rehabilitation centers in the United States: Boston Medical Center, Boston, MA; Frazier Rehab Institute, Louisville, KY; Kessler Institute for Rehabilitation, West Orange, NJ; Magee Rehabilitation Hospital, Philadelphia, PA; The Ohio State University Medical Center, Columbus, Ohio; Shepherd Center, Atlanta, GA; and The Institute for Rehabilitation and Research, Houston, TX. We obtained an institutional review board–approved statement of consent before obtaining the clinical information and standardized outcome measures.

Inclusion/Exclusion Criteria

Patients were selected for participation in the NRN locomotor training program and data collection based on medical history and physical examination, including (1) the presence of a nonprogressive spinal cord lesion above T11; (2) no current participation in an inpatient rehabilitation program; (3) no use of chemodenervation or other medications for chemodenervation for spasticity for the 3 months prior; (4) some lower limb movement or visible voluntary contraction; (5) the capacity to generate a lower limb reciprocal alternating flexion/extension stepping pattern in the step training environment; and (6) medical referral by a physician for physical therapy. Patients receiving antispasticity medications were weaned from their use during participation in the NRN program as directed by the NRN physician. All patients received an AIS examination at the time of admission according to the International Standards for Neurological Classification of Spinal Cord Injury.[17] Central cord syndrome was defined as a binary variable indicating whether the lower extremity motor score exceeded the upper extremity motor score by 10 or more.[18] Patients were classified according to the functional classification phase scale called the Neuromuscular Recovery Scale (NRS). The scale includes 7 tasks in the overground environment including sit, sit up,

Table 1: Demographic and Clinical Characteristics for Full Sample and by Neurologic Level

Demographics	Full Sample (N=350)	Cervical (n=271)	High Thoracic (n=46)	Low Thoracic (n=33)
Sex				
Male	267 (76)	211 (78)	33 (72)	23 (70)
Female	83 (24)	60 (22)	13 (28)	10 (30)
AIS				
C	101 (29)	67 (25)	21 (46)	13 (39)
D	249 (71)	204 (75)	25 (54)	20 (61)
Central cord syndrome	35 (10)	35 (13)	0 (0)	0 (0)
Initial NRS phase				
Phase 1	95 (27)	70 (26)	15 (33)	10 (31)
Phase 2	171 (49)	128 (47)	23 (50)	20 (61)
Phase 3/4	84 (24)	73 (27)	8 (17)	3 (9)
Age (y)	42±16	43±16	38±15	39±12
	41 (18, 86)	42 (18, 86)	34 (18, 70)	37 (20, 63)
Time since SCI (y)*	0.9 (0.1, 53.1)	0.9 (0.1, 53.1)	1 (0.1, 10.2)	1.2 (0.1, 15.1)
UE motor score	39±11	35±10	50†	50†
	41 (4, 50)	36 (4, 50)		
LE motor score	31±14	33±14	26±14	27±15
	34 (0, 50)	36 (0, 50)	28 (0, 50)	32 (2, 50)
Total motor score	70±19	68±20	76±14	77±15
	73 (9, 100)	71 (9, 99)	76 (50, 100)	82 (52, 100)

NOTE. Values are n (%) for categorical variables, mean ± SD, or median (minimum, maximum) for continuous variables.
Abbreviations: LE, lower extremity; UE, upper extremity.
*Time since SCI summarized only by median (minimum, maximum) because of heavy right skewness. UE and LE Motor Scores and Total Motor Score are obtained from the American Spinal Injury Association examinations.
†All patients with low thoracic injuries had UE motor scores of 50; 4 patients with high thoracic injuries had UE motor scores of 48, with the rest having scores of 50. High thoracic groups did not differ from the maximal score for the UE motor score and therefore are reported as 50.

reverse sit up, trunk extension, sit to stand, stand, and walking. Four tasks occur in the body weight–supported treadmill environment and include stand retraining, stand adaptability, step retraining, and step adaptability. Further details regarding the NRS scale and NRN structure, administration, and recruitment procedures are reported elsewhere.[19-21]

A total of 350 patients underwent evaluations for resting CV parameters and an orthostatic challenge at NRN enrollment from January 2006 through October 2011 (table 1). Most patients were classified as AIS D (n=249), cervical injuries, with a wide range of ages and times since injury (see table 1).

CV Parameters

SBP, DBP, and heart rate were captured at baseline, before the initiation of a locomotor training program. The resting CV parameters were captured using a specialized testing chair so that the sitting and supine positions could be achieved completely passively (fig 2). Patients were constrained by straps during the test to avoid any volitional muscular contraction that could affect venous return to the heart and heart rate. Additionally, the tests were performed in a quiet area to avoid stimulation that could lead to changes in heart rate. Brachial blood pressure and heart rate were captured using an automated monitoring device (Dinamap[a]). After a 5- to 10-minute quiet period, blood pressure and heart rate were recorded every minute for 3 minutes while the patient was sitting. This was followed by supine positioning where blood pressure and heart rate were again recorded every minute for 3 minutes. These first sitting and supine periods are what we define as the resting CV measurements. Resting hypotension was defined as an SBP of 90mmHg or less, and resting hypertension, an SBP of greater than 140mmHg.[22]

Next, for the orthostatic challenge, individuals were suddenly passively raised from supine to a seated position, so that the trunk was at 85° to 90° vertical at the same time when the knees were allowed to bend to 90°. During this time, blood pressure and heart rate were again monitored immediately and every minute after for up to 10 minutes. After 5 consecutive minutes, if the SBP did not change by ±5mmHg from the previous measurement, the test was considered complete and all measurements were terminated. We define OH according to the American Academy of Neurology consensus statement[2]: a decrease in SBP of 20mmHg or more, or a reduction in DBP of 10mmHg or more, on changing body position from a supine position to an upright posture, regardless of the presence of symptoms.

Data Analysis

Patient characteristics and CV parameters were summarized with means and SDs, medians and extrema for continuous variables, and counts and percentages for categorical variables. Relationships between CV parameters and 8 predictors—neurologic level (cervical, high thoracic, low thoracic), AIS level (C, D), sex, central cord syndrome status (+, –), age, time since SCI, total American Spinal Injury Association motor score, and NRS phase[19,20]—were tested with the fitting of linear mixed-effects models. The use of mixed-effects models was necessitated by the multiple measurements of blood pressure and heart rate in each position (every minute for 3min). Time since SCI was log-transformed before analysis as a result of heavy right skewness. Because of covariation among predictor variables, we adopted the following strategy in fitting our models. Simple (ie, single variable) linear models were fit for each outcome-predictor pairing, and significance tests of each relationship were conducted. The predictors significantly associated with a given outcome at the 0.2 level were included in the multiple linear model for that outcome. In all models, a single intercept term comprised the random effects. Below, we report marginal means with 95% confidence intervals (CIs) for subgroups defined by categorical predictors, and regression coefficients with

Fig 2. An individual with SCI in a specialized testing chair that allows for passive changes in position from sitting to supine and a rapid return to sitting for the orthostatic challenge. Legs are strapped in to avoid spasms during position changes. A chest strap may be used to prevent trunk motion during the maneuver. The person has an automatic blood pressure/heart rate cuff attached to the arm that records data each minute for specified intervals.

95% CIs from the multiple linear models for each outcome. We report *P* values from significance tests of the final, multiple linear models arrived at by the above model-fitting strategy; that is, our final judgment about the significance of an association between outcome and predictor variables was based on the multivariate model. Post hoc pairwise comparisons of CV and quality-of-life measures for neurologic level (the only nondichotomous predictor under consideration) were conducted via the Hochberg procedure.[23] Rates of resting hypotension (SBP<90mmHg), resting hypertension (SBP>140mmHg), and OH (defined above) were estimated, and relationships with the aforementioned predictors were tested through multiple logistic regression models. To define OH per patient, the 3 measurements of blood pressure and heart rate were averaged in the supine position, and the minimum of the 3 measurements after adjustment to the sitting position was selected. All hypothesis tests were conducted at the .05 significance level. All analyses were conducted using the open source R software package.[24]

RESULTS

Patient Characteristics

The 350 patients with incomplete SCI in our sample exhibited characteristics in general correspondence with other samples of NRN data[21]—largely male, widely varying age and time since SCI, with cervical injuries and AIS D classification being most common. The distribution of sex and age were in general correspondence with national averages,[25] while our proportion of patients with cervical injuries (77%) was higher than reported national averages (65%). Ten percent of our sample exhibited central cord syndrome. Motor scores varied considerably and were significantly different among the neurologic levels (Kruskal-Wallis test, $P<.002$).

Associations Between CV Parameters and Patient Characteristics

Neurologic level and age were most commonly associated with CV parameters (table 2, fig 3). SBP, DBP, and heart rate all significantly varied by neurologic level (mixed-effects model, $P<.03$). Both SBP and DBP in all positions were ordered by neurologic level, as patients with cervical injuries exhibited the lowest pressures and patients with low thoracic injuries the highest. Patients with cervical injuries exhibited the lowest average heart rate in all positions, followed by patients with low thoracic injuries and patients with high thoracic injuries. Pairwise post hoc testing demonstrated that only the cervical and low thoracic groups significantly differed with respect to SBP and DBP (Hochberg test, $P<.006$), and these differences were significant in all positions. Patients with high thoracic injuries exhibited higher heart rates than patients with cervical injuries in all positions ($P<.001$), and higher heart rates than patients with low thoracic injuries in the at-rest and postorthostatic challenge sitting positions ($P\leq.02$).

Age was strongly related to all parameters in all positions ($P<.001$, see table 2), with the exception of supine heart rate. Both SBP and DBP increased with age as indicated by the positive regression coefficients ($P<.001$), while sitting heart rate declined ($P<.03$). Time since SCI was negatively related to SBP and DBP in resting positions (sitting at rest, supine) ($P<.02$), but not in the sitting postorthostatic challenge position. Time since SCI and heart rate were not significantly related.

The remaining predictors were less consistently related to the CV parameters. Men exhibited a higher supine SBP (mean, 119mmHg vs 116mmHg) and sitting postchallenge SBP (114mmHg vs 111mmHg) than women, and a significantly lower heart rate sitting at rest (79 vs 83 beats/min) and while supine (69 vs 73 beats/min). Although these differences were statistically significant ($P\leq.04$), they were of small magnitude. Patients with central cord syndrome had a significantly higher heart rate sitting at rest (85 vs 79 beats/min, $P=.004$), while supine (76 vs 70 beats/min, $P=.001$), and sitting postchallenge (82 vs 77 beats/min, $P=.005$), and a lower supine SBP (111mmHg vs 119mmHg, $P=.003$) (fig 4). AIS level, total motor score, and NRS phase were unrelated to any of the CV parameters ($P>.09$, not reported in table 2).

Table 2: Full Sample Summary Statistics for CV Parameters, Adjusted Means by Neurologic Level, and Regression Coefficients for Age and Time Since SCI

Outcome	Position	By Neurologic Level: Cervical	High Thoracic	Low Thoracic	Age	Time Since SCI
SBP (mmHg)	Sitting (at rest)	114 (112–117)	120 (115–126)	130 (124–137)	.36* (.23 to .49)	−.48* (−.79 to −.16)
	Supine	117 (115–119)	119 (114–123)	125 (120–130)	.29* (.18 to .40)	−.31* (−.57 to −.05)
	Sitting (ortho)	113 (111–115)	117 (112–122)	126 (120–132)	.27* (.17 to .38)	NI
DBP (mmHg)	Sitting (at rest)	73 (72–74)	75 (72–78)	82 (78–85)	.16* (.09 to .24)	−.30* (−.48 to −.11)
	Supine	71 (70–72)	71 (68–74)	76 (73–79)	.18* (.12 to .25)	−.21* (−.37 to −.04)
	Sitting (ortho)	72 (71–73)	73 (70–76)	80 (77–84)	.14* (.07 to .21)	−.14 (−.30 to .03)
HR (beats/min)	Sitting (at rest)	78 (76–80)	88 (84–92)	80 (75–85)	−.12* (−.22 to −.02)	−.16 (−.41 to .09)
	Supine	69 (67–70)	76 (72–80)	74 (69–79)	NI[†]	NI[†]
	Sitting (ortho)	76 (74–78)	85 (81–89)	78 (73–82)	−.12* (−.22 to −.02)	−.23 (−.47 to .02)

NOTE. Values are means (95% CI) adjusted for neurologic level, and adjusted regression coefficients (95% CI) for age and log-time since injury.
Abbreviations: HR, heart rate; NI, not included; ortho, orthostatic challenge.
*Significant association ($P<.05$) with CV parameter on multivariate testing.
[†]Not included in multivariate model because of lack of univariate relationship.

Characteristics by Presence of OH

Seventy-five patients (21%) exhibited OH. Most demographic and clinical characteristics did not significantly differ between those who did and did not exhibit OH (table 3). Total motor score was lower for those with OH, and logistic regression showed a significant but weak relationship between total motor score and OH (odds ratio [OR]=.985; 95% CI, .972–.998). Prevalence of OH was ordered by neurologic level of injury, with patients with cervical injuries exhibiting the highest prevalence (23%) and patients with low thoracic injuries the lowest (9%), but differences in OH prevalence among groups were not significant (logistic regression, $P=.19$). Prevalence of OH was ordered by NRS phase, as NRS phase 1 patients exhibited the highest prevalence (28%) and NRS phase 3 patients the lowest (8%). Differences in OH prevalence among NRS phases were significant ($P=.004$), as NRS phase 3 patients were significantly less likely to exhibit OH than NRS phase 2 (OR=.27; 95% CI, .10–.63) and phase 1 (OR=.16; 95% CI, .05–.46) patients.

Supine SBP (120mmHg vs 117mmHg) and DBP (73mmHg vs 71mmHg), the first step of the orthostatic test, did not significantly differ between those who did and did not have OH (Wilcoxon test, $P>.21$) (fig 5). Thus, higher supine SBP was not a contributing factor to the onset of OH; that is, those who had OH did not have OH because they had a higher supine SBP or DBP from which to decline. Importantly, those with OH did exhibit a significantly lower sitting at rest SBP (107mmHg vs 119mmHg, $P<.001$) and DBP (69mmHg vs 75mmHg, $P<.001$). Logistic regression showed that the likelihood of OH significantly decreased with sitting at rest SBP (OR=.96; 95% CI, .94–.99) but not DBP (OR=1.00; 95% CI, .95–1.05).

DISCUSSION

Overview

Results of this cohort study of 350 patients showed that patients with incomplete SCI (AIS C and D) had alterations in

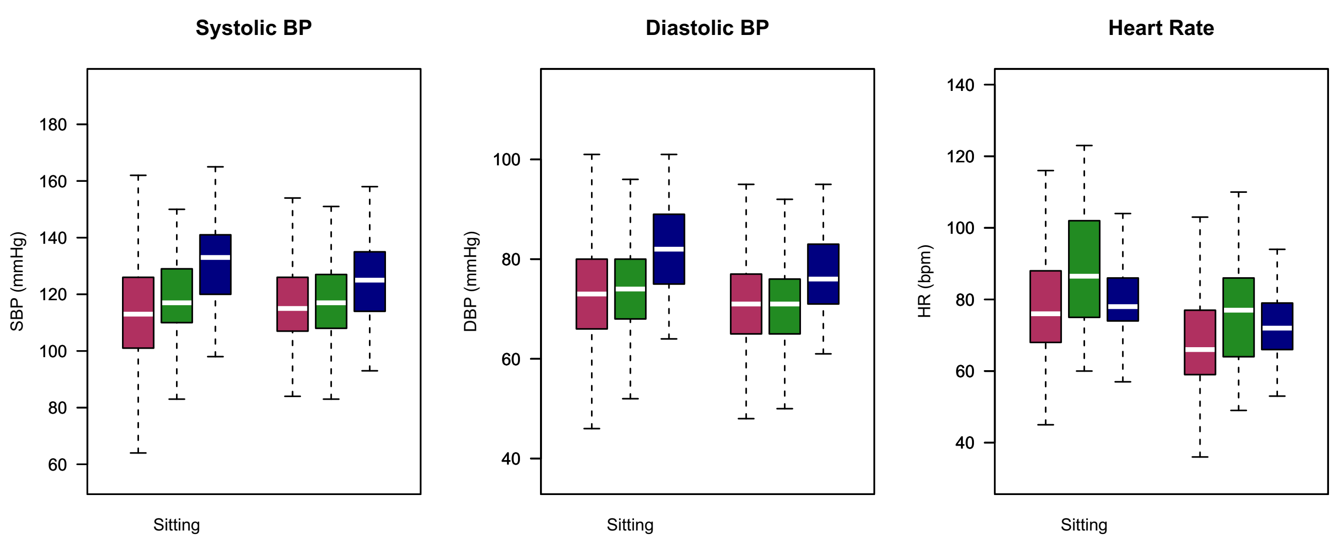

Fig 3. Boxplots of SBP (left panel), DBP (center panel), and heart rate (right panel) in sitting at rest and supine positions for patients with cervical injuries (maroon, n=271), patients with high thoracic injuries (green, n=46), and patients with low thoracic injuries (blue, n=33). All parameters in all positions significantly differed ($P<.03$) over the neurologic levels. Abbreviations: BP, blood pressure; bpm, beats per minute; HR, heart rate.

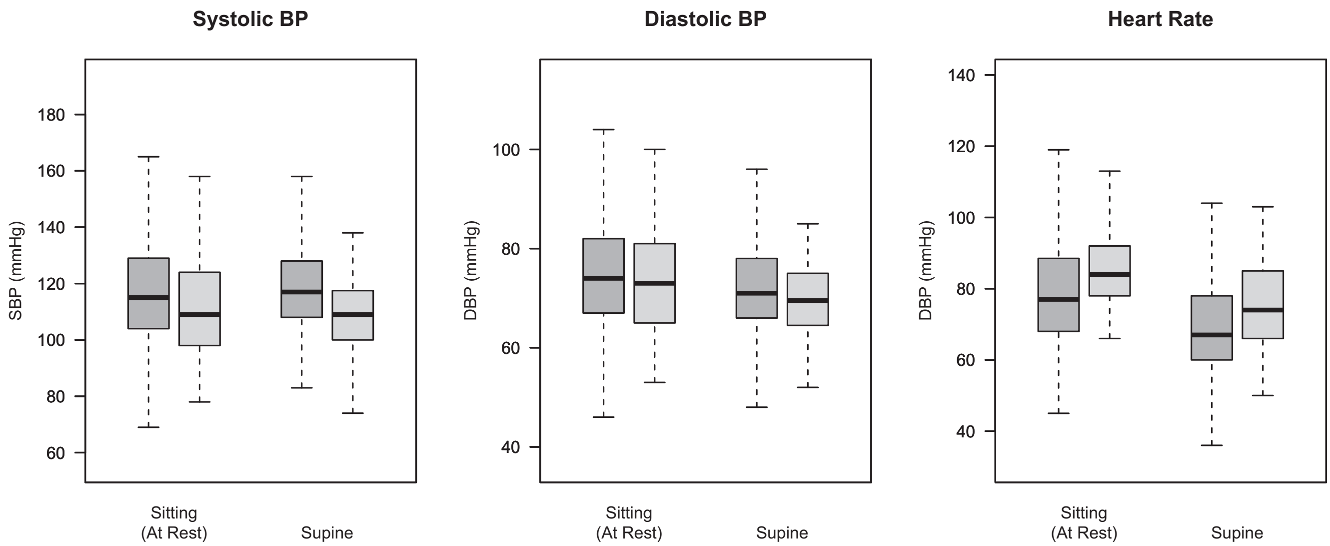

Fig 4. Boxplots of SBP (left panel), DBP (center panel), and heart rate (right panel) in sitting at rest and supine positions for patients with (light gray, n=35) and without (dark gray, n=315) central cord syndrome. Supine SBP and heart rate in all positions significantly differed between groups (*P*<.006). Abbreviation: BP, blood pressure.

CV function that were present even if the time since injury was a few months to several years after injury. Neurologic level and age were associated with the measured CV parameters. Time since injury was negatively related to blood pressure at rest while sitting. Men had higher blood pressures and lower heart rates than women. Positional differences in CV parameters (supine vs sitting) were prevalent. Those with central cord syndrome had lower blood pressures and higher heart rates. AIS level and NRS phase were not related to any of the CV parameters. Twenty-one percent experienced OH during orthostatic stress induced by a sit-up test. This study shows that individuals with incomplete SCI have associations of CV parameters with age and sex similar to noninjured populations, but also have additional effects of the injury related to neurologic level and time of injury.

CV Parameters in Able-Bodied Persons and Those With SCI

Currently, adult blood pressure is considered optimal at 120/80 and is targeted for all ages. Regarding CV risk factors, in persons younger than 50 years, DBP better predicts the risks for heart attack or stroke, whereas after age 50, SBP is a better predictor. By age 60, the SBP is a much better predictor of risk. Taken together, abnormalities in blood pressure, generally higher levels, vary depending on the decade of age and predictors of significant CV events. Depending on the study, when considering DBP among other factors, Krum et al[26] reported a comparable CV disease risk for both persons with SCI and able-bodied persons. On the other hand, Cardus et al[27] used the Framingham risk equation and reported the risk to be similar to that of a deconditioned able-bodied individual. Finally, in 1 study of persons with paraplegia of the same age and time since injury as persons in our study, there was a 14.1% prevalence of hypertension compared with an age- and sex-matched sample from a general Swedish population. They also reported in other studies[28,29] of the same sample of individuals with paraplegia who where wheelchair dependent that the prevalence of hypertension (39.3%) was much higher, and that being older was related to an increased risk of CV disease. Our prevalence rates were much lower (8%) for hypertension. However, in the study by Wahman et al,[15] 33% of individuals had T6 injuries, but no individuals had tetraplegia. Since most individuals in our sample had tetraplegia, this may account for the differences in prevalence rates.

Hypotension, a more common condition in SCI than hypertension, is less common in the noninjured populations. Hypotension for the noninjured is defined as a blood pressure of 90/50 or lower and can result from conditions such as pregnancy, heart failure, blood loss, endocrine disorders, septicemia, and anemia. Hypotension is generally not age related, although inactivity and cardiac conditions in the elderly can result in sudden positional hypotension with symptoms of dizziness and syncope. After SCI, the lesion-related impairment of autonomic function combined with physical deconditioning and the inability to participate in exercise incorporating all muscle groups, creates abnormal CV control compared with able-bodied individuals.[30] Our full sample data demonstrate slightly lower SBP than norms (117mmHg and 120mmHg, respectively); however, when we examine cervical injuries alone (114mmHg for cervical vs 120mmHg for norms), the differences compared with norms are larger. However, when examining our high thoracic injury group (119mmHg vs 120mmHg for norms) and low thoracic injury group (125mmHg vs 120mmHg for norms), the differences compared with norms are not as large as compared with the full sample data. This underscores the importance of examining CV parameters by neurologic level.

Resting Cardiovascular Parameters Related to SCI Studies: Acute Injury Versus Chronic

Our study focused on less acute injuries with an average time since SCI of 3.2 years. One study by Sidorov et al[1] examined the CV parameters in acute SCI at admission and 1 month afterward and found that the supine resting heart rate was significantly lower for patients with cervical injuries (68 beats/min) than for those with upper (91 beats/min) or lower thoracic (98 beats/min) injuries at admission.[1] These values are comparable to those in our study for cervical injuries (69 beats/

Table 3: Demographic and Clinical Characteristics by Presence of OH

Demographics	No OH (n=275)	OH (n=75)
Sex		
Male	209 (76)	58 (77)
Female	66 (24)	17 (24)
Age (y)	42±16	41±17
	41 (18, 86)	40 (18, 76)
Time since SCI (y)	0.9 (0.1, 52)	1.0 (0.1, 53.1)
Central cord syndrome	28 (10)	7 (9)
Initial NRS phase		
Phase 1	68 (24)	27 (36)
Phase 2	133 (48)	38 (51)
Phase 3	77 (28)	7 (9)
Neurologic level		
Cervical	208 (76)	63 (84)
High thoracic	37 (13)	9 (12)
Low thoracic	30 (11)	3 (4)
AIS level		
C	76 (28)	25 (33)
D	199 (72)	50 (67)
UE motor score*	39±10	36±10
	42 (4, 50)	38 (11, 50)
Cervical*	36±10	33±9
	37 (4, 50)	34 (11, 50)
High thoracic	50±1	50±1
	50 (48, 50)	50 (48, 50)
Low thoracic	50	50
LE motor score	32±14	29±15
	35 (0, 50)	30 (0, 50)
Cervical	33±13	30±15
	36 (0, 50)	33 (0, 50)
High thoracic	27±14	19±13
	28 (0, 50)	18 (1, 39)
Low thoracic	27±15	32±17
	32 (2, 48)	29 (16, 50)
Total motor score*	71±19	65±21
	74 (9, 100)	66 (13, 100)
Cervical	69±20	63±21
	72 (9, 99)	66 (13, 96)
High thoracic	77±13	69±13
	78 (50, 100)	68 (51, 89)
Low thoracic	77±15	82±17
	82 (52, 98)	79 (52, 100)

NOTE. Values are n (%) for categorical variables, mean ± SD, or median (minimum, maximum) for continuous variables.
Abbreviations: LE, lower extremity; UE, upper extremity.
*Significantly differed between groups.

min); however, our heart rates for upper (76 beats/min) and lower thoracic (74 beats/min) injuries were much lower. This may be because of the differences in time since injury in our cohort compared with Sidorov's study[1] of acute SCI, in which the patients may also have had greater management of salt/water balance in the hospital setting. With regard to blood pressure, the Siderov study[1] reported resting supine SBP and DBP as 107, 105, and 119mmHg for patients with cervical, upper and lower thoracic injuries, respectively. Our SBP parameters were 117, 119, and 125mmHg for cervical, high and low thoracic injuries, respectively, somewhat higher most likely because of the differences in time since injury (acute vs more chronic).

Claydon et al[5] reported that low SBP is common in the acute period and could persist in individuals with chronic cervical SCI. This study reported resting blood pressure to be significantly lower than an able-bodied control (systolic blood pressure, approximately 95mmHg vs 80mmHg; diastolic blood pressure, approximately 50mmHg vs 40mmHg) and there was no difference in resting heart rate. The most likely reasons for much lower blood pressure values are the differences in time since injury (acute vs chronic) and the single subject example reported.

For chronic injuries, Faghri et al[31] reported SBP and heart rate in sitting and supine for 14 individuals with paraplegia (n=7, T5–10) and tetraplegia (n=7, C4–7) who were injured an average of 6.4 years before testing, and approximately 4 of 15 had incomplete injuries. The average sitting SBP of this group was 108mmHg for all subjects combined, which is lower than our combined SBP in sitting (117mmHg), but their DBP was similar to ours (75mmHg vs 74mmHg). This difference was maintained in the supine position where Faghri[31] also reported SBP to be 124mmHg and DBP to be 82mmHg compared with our data (118mmHg vs 71mmHg). Thus, the main differences in SBP in sitting and supine to our data may be attributable to the degree of completeness of injury, the lack of distinction between upper and lower thoracic injuries, and their small sample size (14 vs 350 in our analysis).

Wecht et al[8] studied 5 individuals with tetraplegia who had chronic injuries (mean duration of injury, 22y); only 1 of the individuals had an incomplete SCI. The authors reported CV parameters in the supine position only. The average heart rates and blood pressures were as follows: heart rate, 67 beats/min; SBP, 97mmHg; and DBP, 65mmHg. In comparison, the CV parameters for our cervical injury group were as follows: heart rate, 69 beats/min; SBP, 71mmHg; and DBP, 121mmHg. While the heart rate values are similar, our blood pressures are considerably higher. These differences between the Wecht[8] study and ours are likely because of the completeness and chronic durations of the injuries.

Our CV parameters were also higher than those we reported previously,[9] which were an average seated SBP of 96mmHg and a DBP of 59mmHg. However, in that study we examined 8 individuals with complete SCI, whereas our present cohort consists only of patients with incomplete SCI. In that previous study,[9] we also reported that DBP was significantly lower for the cervical injury group versus the thoracic injury group (52mmHg and 66mmHg, respectively); however, we did not distinguish between upper and lower thoracic levels. Ditor et al[13] also studied CV parameters in 8 individuals classified as AIS C and D. They reported supine SBP as 117mmHg and DBP as approximately 73mmHg, which was comparable to our 117mmHg SBP and 71mmHg DBP for our cervical injury group. The results from Ditor,[13] although comparable to our study, represented a much smaller sample of individuals who were younger and had on average been injured longer (9.5y vs 3.5y). Despite the similarities in CV parameters in this study compared with ours, age and time since injury are important considerations in analysis and interpretation of these outcomes.

Relationships to Patient Characteristics

Wahman[15] examined individuals with paraplegia (AIS A–C) and reported that age, sex, and SBP were cardiac risk factors found in one third of their sample. The analysis of our cohort indicated that age was also strongly associated with all CV parameters in the seated and supine position and after the orthostatic challenge, and that men exhibited a higher SBP than women in the 3 positions, but a lower seated heart rate. This is in contrast to the study by Wahman et al[28,29] that examined fewer incomplete injuries and whose participants were primarily wheelchair users, compared with our analysis that examined

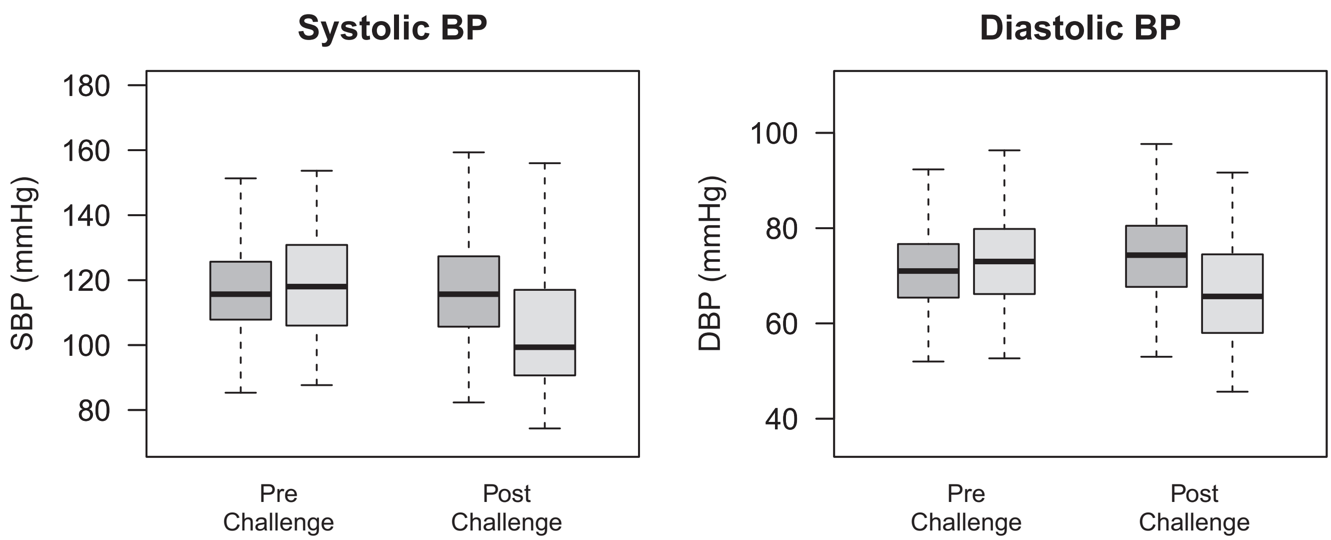

Fig 5. Boxplots of SBP (left panel) and DBP (right panel) in the supine preorthostatic challenge and sitting postorthostatic challenge positions for patients with (n=75, light gray) and without (n=275, dark gray) orthostatic hypotension. Abbreviation: BP, blood pressure.

CV parameters for patients with motor incomplete injuries and who were more likely to be standing and walking.

Our findings emphasize the importance of examining sex, a factor infrequently addressed in current research, and its relationship to CV function. Regarding time since injury, our study additionally demonstrated that it is negatively associated with blood pressure after adjusting for age. In other words, if 2 individuals were exactly the same age but one had a longer duration of injury, that individual would have lower blood pressure values.

OH Related to SCI Studies: Acute Injury Versus Chronic

Sidorov[1] reported that during the first month postinjury, up to 74% of individuals with tetraplegia, compared with 20% for those with paraplegia, had documented episodes of OH for both complete and incomplete SCI. In particular, the incidence of OH was more common in complete injuries for the cervical and high thoracic groups, but no participants had incomplete injuries in the low thoracic group. OH has also been reported to persist during the rehabilitation period after SCI. Other investigators[32] reported that standard mobilization during physiotherapy (eg, sitting or standing) induces blood pressure decreases that are diagnostic of OH in 74% of patients with SCI, and that are accompanied by OH symptoms (such as lightheadedness or dizziness) in 59% of individuals with SCI.[32] This in turn may have a negative impact on the ability of individuals with SCI to participate in rehabilitation. These potential delays in rehabilitation and the development of a variety of complications provide a compelling rationale for the early identification and management of OH in this population.

However, OH not only is evident in the acute period postinjury or during rehabilitation but also has persisted in a significant number of individuals for many years after the initial trauma.[5,7,9] Furthermore, there is evidence that OH in individuals with SCI is associated with a high prevalence of neck pain that significantly delayed their rehabilitation.[1] El Masry[33] has suggested that OH can even lead to neurologic deterioration in individuals who may otherwise have a stable SCI. All these factors could lead to prolonged bed rest, which would increase the likelihood of OH in this population.[34] Other studies[1,32,35] reported the presence of OH among individuals with SCI, although the incidence of OH varied significantly with the time postinjury and the level of SCI. Sidorov[1] and Illman[32] and colleagues documented that up to 74% of individuals with cervical SCI have OH in the acute and early rehabilitation periods, while Claydon and Krassioukov[35] described the presence of OH in individuals with longstanding chronic SCI. However, most individuals in these studies had complete injuries. In our study, we examined only patients with incomplete injuries, and approximately 21% (75 individuals) had OH at enrollment. There was a significantly larger proportion of patients in the cervical injury group with OH (23%) compared with our low thoracic injury group (9%). Our data suggest that even outside the acute management of SCI, the identification and management of OH is important to address in the more chronic periods of rehabilitation or medical care, especially for those with cervical injuries.

Additionally in our study, motor activity, which is represented by the total motor score, was significantly lower for those with OH than those without OH. Therefore, the presence of motor activity and neurologic levels may be important factors to examine with future research. Across NRS phases, there was a significant difference among those with OH, with the highest prevalence in the phase I group where the lowest functional capacity exists. Interestingly, AIS classification or NRS phase classification did not seem to contribute to the presence of OH. Taken together, for an outpatient or an individual with more chronic incomplete SCI, the target group with the greatest potential for demonstrating OH is those with the lower total motor scores and NRS phase 1. These patients should be addressed in future research or given clinical attention.

Effects of Central Cord Syndrome

Our findings identifying that those patients classified (approximately 10%) as having central cord syndrome had a lower supine SBP and a higher heart rate for all 3 positions are novel. One conclusion may be that patients with central cord syndrome may have greater motor resources in the lower limbs that may promote venous return. Furthermore, the lack of trunk and upper limb muscle tone requires the heart rate to increase significantly to maintain blood pressure in the seated position. The presence of central cord syndrome is rarely reported in studies of CV parameters in SCI and should be examined as a unique subgroup in future studies of patients with incomplete SCI.

Study Limitations

There were some factors that we could not control with the patients enrolled and used for this analysis. We were unable to test all patients at the same time of day. Control for daily testing time to account for nocturnal recumbency and meal consumption/fasting are both known to affect CV parameters.[36,37] Lewis et al[36] reported slight variations in day and nighttime blood pressure and heart rate values in the tetraplegia group. Our patients were given a schedule once enrolled in the clinical program that varied between 9 AM and 4 PM, and therefore the differences in time tested across patients could have contributed to the variability of the CV parameters. Additionally, since all patients tested were living at home, it is not expected that many patients were able to arrive in the clinic before 9 AM to 10 AM, thus ruling out the likelihood of nocturnal recumbency. Patients were asked to eat meals before arriving; however, compliance with this request may not have been ideal, thus also potentially contributing to some data variability. No controls were placed on medication intake before the testing period except for predetermined medication exclusions (baclofen or botulinum toxin type A). Midodrine can be prescribed for the treatment of hypotension and OH,[38] but we are unsure whether our results were mitigated by some patients taking this medication.

There was no capture of autonomic symptoms, if present, such as self-report severity, aggravating factors, duration, and time of day.[39] The presence of smoking before testing was not controlled; however, the general effect of smoking is transient[40] and with the time taken for patients to arrive, transfer to the testing chair, and have the CV monitoring system attached, the transient effect of any smoking would have elapsed. The ingestion of caffeine is known to cause vasoconstriction.[41] There was no restriction of caffeine before testing, and the vasoconstrictive effects of caffeine may have persisted during the testing period. Finally, we did not track hydration before testing. The impact of drinking water on CV exercise responses to supine exercise was reported by Humm et al.[42] They found that it had no effect, but drinking water did improve orthostatic tolerance postexercise. While our study did not directly examine orthostatic tolerance or exercise, variations in hydration may have contributed to the variability of our data. With regard to the use of elastic stockings and abdominal binders, most patients at this stage of rehabilitation did not use abdominal binders or elastic stockings, which are more likely used during the acute phase of rehabilitation. We cannot rule out that some patients may have used these supports, which may have affected our data, but Rimaud et al[43] reported that the low pressure generated by elastic stockings may not necessarily influence the venous system to produce improved CV responses. Regarding other potential confounding comorbidities such as diabetes, anemia, or peripheral neuropathy, to our knowledge, our patients did not have these diagnoses.

CONCLUSIONS

This study documented resting CV parameters from the largest cohort of individuals with chronic incomplete SCI reported. These individuals received a standardized assessment of resting CV parameters in 2 positions (sitting and supine) and a standardized orthostatic challenge. Furthermore, this study examined the impact of neurologic levels (cervical, high thoracic, or low thoracic) on CV parameters, whereas many previous studies combine the analysis of injury level or do not distinguish between high and low thoracic levels—a region known to have particular influence on these parameters. It is important to recognize that individuals with incomplete SCI also experience lower blood pressures, especially those with cervical injuries. Additionally, OH can persist months or years after injury. Finally, clinical screening and treatments should be considered, given the prevalence of CV dysfunction, particularly in cervical injuries. Future research is needed on the impact of exercise on CV parameters, and specifically for those individuals with resting hypotension, considering age and sex and neurologic level (cervical, high and low thoracic injuries), as well as for those with motor complete injuries.

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