Published in final edited form as:
Arch Phys Med Rehabil. 2015 June ; 96(6): 1071–1079. doi:10.1016/j.apmr.2015.01.018.

Prevalence of Abnormal Systemic Hemodynamics in Veterans with and without Spinal Cord Injury

Jill M. Wecht, EdD[1,3,4], **Joseph P. Weir, PhD**[5], **Marinella Galea, MD**[2,4], **Stephanie Martinez, BS**[1], and **William A. Bauman, MD**[1,2,3,4]

[1]The Center of Excellence, James J. Peters VAMC, Bronx, NY

[2]Medical Service, James J. Peters VAMC, Bronx, NY

[3]Department of Medicine, The Icahn School of Medicine, Mount Sinai, New York, NY

[4]Department of Rehabilitation Medicine, The Icahn School of Medicine, Mount Sinai, New York, NY

[5]Department of Health, Sport and Exercise Sciences, The University of Kansas, Lawrence, Kansas

Advances in the clinical management of patients with acute and chronic spinal cord injury (SCI) have contributed to extended life expectancies; however longevity in those with SCI remains below that of the general population.(1) Reduced longevity in the SCI population has been attributed to increased incidence of age-associated chronic illnesses,(2) premature cardiovascular aging,(3) and increased prevalence of heart disease, stroke (4) and diabetes mellitus, (5) compared to the general population. In fact, cardiovascular disease (CVD) is now a leading cause of morbidity and mortality in the SCI population, which may be amplified due to increased risk factors such as inactivity, chronic inflammation, and impairment in autonomic cardiovascular control.(6)

The American Spinal Injury Association (ASIA) impairment scale (AIS) is used to document remaining motor and sensory function following SCI; (7, 8) however, the degree of autonomic nervous system impairment is not considered within this classification schema. (9, 10) That said, impaired autonomic control of the cardiovascular system after SCI results in measurable changes in heart rate (HR) and blood pressure (BP) that loosely reflect the level and completeness of SCI documented using the AIS classification, (11, 12) but may also reflect orthostatic positioning.(6, 12, 13) The impact of these changes in HR and BP on cardiovascular health and longevity is not fully appreciated in the SCI population; however, prior to identifying the consequences of these cardiovascular abnormalities, prevalence rates of HR and BP values which fall outside the expected normal range should be documented.

Correspondence: Dr. Jill M. Wecht, Center of Excellence: Medical Consequences of Spinal Cord Injury, James J. Peters VA Medical Center; Rm. 7A-13, 130 West Kingsbridge Rd., Bronx, NY 10468, (718) 584-9000 Ext. 3122, Fax: (718) 741-4675, JM.Wecht@va.gov.

Disclosure:
We certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on us or on any organization with which we are associated AND, if applicable, we certify that all financial and material support for this research (eg, NIH or NHS grants) and work are clearly identified in the title page of the manuscript.

The International Standards to Document Autonomic Function (post-SCI) initially established guidelines for the assessment of HR and BP abnormalities in 2009, (10) which was updated in 2012, but the thresholds remained consistent. (14) Specifically, bradycardia is defined as a HR ≤ 60 beats/minute (bpm) and tachycardia as a HR ≥ 100 bpm. (14) Hypotension is defined as a systolic BP (SBP) ≤ 90 mmHg and a diastolic BP (DBP) ≤ 60 mmHg; hypertension is SBP ≥ 140 and/or DBP ≥ 90 mmHg. (14) While these definitions comply with standards established in the non-SCI population, due to decentralized cardiovascular control, they may not be appropriate for use in the SCI population. In addition, relatively recent evidence has emerged which associates adverse outcomes in the general population using other HR (15, 16) and BP (17-21) thresholds. Beyond the clinical consequences of alterations in HR and BP, persons with SCI may experience loss of independence and life quality related to the inability to adequately maintain cardiovascular homeostasis; however, until we gain a better understanding of the prevalence of these abnormalities, the development and testing of effective treatment strategies will not be a priority.

Therefore, the goal of this investigation was to assess HR and BP in veterans with (SCI) and without SCI (non SCI). Similar to a recent report, (6) we hypothesized that level of SCI (i.e., the higher the lesion level the greater the prevalence of abnormal HR and BP recordings) and orthostatic positioning (i.e., increased prevalence of abnormal HR and BP recordings in the seated versus the supine position) would influence the prevalence of HR and BP abnormalities. In addition, we hypothesized that the prevalence of comorbid cardiovascular medical conditions, current smoking status, age and use of prescription anti-hypertensive (anti-HTN) medications would influence the prevalence of HR and BP abnormalities in veterans with and without SCI.

METHODS

Subjects

All investigative procedures were performed at an urban Veterans Affairs Medical Center (VAMC) in a convenience sample of veterans with and without SCI. The subjects were not matched but were recruited based on willingness to volunteer and having met the inclusion criteria. Veterans with and without SCI were approached and asked to participate in the study during their annual physical examination or in a waiting room area prior to being seen for a routine clinical follow-up appointment. None of the subjects was receiving clinical care for an acute illness or infection, which was ascertained via medical history questionnaire and verified in the medical record. Prior to initiating data collection procedures, subjects were asked questions related to their personal characteristics, which included a complete medical history, prescription medication use, and information pertaining to any chronic medical conditions, which wasverified via electronic medical chart review and corrected if needed. Subjects were then transferred to a clinic bed for instrumentation and a period of quiet rest in the supine position prior to data collection. All study procedures were approved by the local IRB.

Data Collection Procedures

Resting HR and BP assessments were measured for 5 minutes in the supine position in all subjects, for 5 minutes while seated in the veterans with SCI and for 5 minutes while standing in the veterans without SCI; data were recorded at minutes 0, 1, 2, 3, 4 & 5 for a maximum of six recordings in each position. Recording of HR and BP assessments were made using an automated sphygmomanometer BP cuff (Dynamap Pro 300, [GE Healthcare, Buckinghamshire, UK]), which was placed around the upper right arm. Data collection began in the supine position for all subjects and once complete subjects were either transferred to their wheelchair (SCI) or were asked to stand (non-SCI).

Operative Definitions

We examined the incidence of a resting HR ≥ 80 bpm among veterans with and without SCI because of the possible association between persistent cardiac acceleration (CA) and vascular degeneration and cardiac mortality.(16, 22, 23) An average resting HR above 80 bpm in either the supine or upright positions was used to classify individuals with potential CA. Systolic hypotension (HYPO) was defined according to the World Health Organization (W.H.O.) as a systolic BP (SBP) ≤ 110 mmHg for males and ≤ 100 mmHg for females.(24) The W.H.O. definition of hypotension is without regard to diastolic BP (DBP); however, a recent article reported increased mortality in veterans with a DBP ≤ 70 mmHg, and as such, the incidence of a DBP ≤ 70 mmHg was determined in our veterans with and without SCI. (21) The American Autonomic Society (AAS) and the American Academy of Neurology (AAN) have defined orthostatic hypotension (OH) as a fall in SBP of ≥ 20 mmHg and/or a fall in diastolic BP (DBP) ≥ 10 mmHg.(25-28) Individuals were classified as having OH if the change in either SBP or DBP met the AAS and AAN definition within the first 3 minutes of assuming an upright position. In addition, participants were categorized as being hypertensive (HTN) if their average SBP in either the supine or upright positions was ≥ 140 and/or their average diastolic BP (DBP) was ≥ 90 mmHg. The observed HR and BP recordings were averaged across the available number of values (maximum 6) and participants were classified according to their average HR and BP in each of the two orthostatic positions.

Data Analysis

Data were analyzed using SPSS version 21. For purposes of data analysis, veterans with SCI were categorized by the neurological level of lesion with specific reference to sympathetic cardiovascular innervation (SCI status); tetraplegia (tetra: C3-C8), high thoracic (T1-T5) or low thoracic (T7-L2) lesions. Differences among the groups for subject characteristics and baseline hemodynamics were tested using one-way analysis of variance models. Statistical significance for the ANOVA models was set at the $p<0.05$ level, and were adjusted for multiple comparisons with Tukey HSD. To statistically assess the effect of group categorization, the data were analyzed using binary logistic regression with presence or absence of the specific condition (separate analyses for CA, HYPO, OH & HTN) coded as the dependent variable. Pairwise group differences for these prevalence rates were compared using univariate chi-square analyses. From the resulting logit calculations, prevalence rates (in percentages) were calculated. In addition, following significant omnibus effects in the

logistic regression analyses, 95% confidence intervals (CI) were constructed about the respective prevalence rates for each group,(29) and pairwise differences between groups for prevalence rates were assessed using confidence intervals, as previously described.(30) Finally, we entered covariates into the significant logistic regression models to determine if the contribution of these variables added to the prediction model. The covariates included: chronological age, smoking status (Y, N), number of cardiovascular diagnoses, HTN diagnosis (Y, N), and use (Y, N) and number of prescribed anti-HTN medications. For the SCI group alone we also entered injury specific demographics as covariates into the binary models, including: duration of injury (years) and motor complete (AIS A & B) versus incomplete (AIS C & D) lesions.

RESULTS

Two-hundred forty two subjects signed consent to participant, of which 62 veterans with SCI and 160 veterans without SCI completed all study procedures; 15 subjects did not complete testing and 5 were non-veterans. The study population consisted of predominantly male veterans (97%) and ranged in age from 21-88 years. Characteristics of the study groups are presented (Table 1); the high thoracic group was significantly younger than the tetra group and body mass (kg) was significantly reduced in the high thoracic compared to the other 3 groups. The duration of injury in our veterans with SCI ranged from 1 to 54 years and 60% of the SCI study group sustained a complete motor injury (AIS A & B). Duration of injury and AIS classification were entered into the logistic regression models for the SCI groups; however, neither variable contributed to the prediction of the cardiovascular abnormalities beyond that explained by SCI status alone.

Resting supine and upright hemodynamics are presented (Figures 1-3). These data show that, regardless of orthostatic position, resting HR was significantly reduced in the tetra group compared to the other 3 groups (Figure 1). Although supine SBP did not differ among the study groups (Figure 2A), upright SBP was reduced in the tetra group compared to the non-SCI and low thoracic groups (Figure 2B). In the non-SCI veterans, supine DBP was significantly increased compared to the 3 SCI groups (Figure 3A) and upright DBP was increased compared to the tetra and low thoracic groups (Figure 3B). Of note, average HR was ≥ 80 bpm while upright in the non-SCI veterans and regardless of orthostatic position in veterans with high thoracic lesions. Further, average DBP was ≤ 70 mmHg while supine in the high thoracic group and regardless of orthostatic position in the tetra group.

Prevalence rates for medical history which is related to the most prevalent cardiovascular conditions is presented (Table 2). Current smoking status did not differ among the study groups. However, overall omnibus effects were significant for cardiovascular diagnoses, HTN diagnosis alone and the use of anti-HTN medications. The diagnosis of CVD, which included HTN, diabetes mellitus, high cholesterol, lipids, triglycerides, heart or vascular disease, was lower in high thoracic compared to the other 3 groups; however, this group effect was eliminated with addition of chronological age. The diagnosis of HTN alone was reduced in veterans with high thoracic and cervical lesions compared to the non-SCI and low thoracic veteran groups, use of prescription anti-HTN medications was increased in the

low thoracic group compared to the other 3 groups, and was increased in the non-SCI compared to the tetra group.

The probability and omnibus χ^2 effects for HR and BP abnormalities relative to group affiliation is presented (Table 3). Prevalence rates for HTN and OH did not differ among the study groups. However, the omnibus tests from the binary logistic regression analyses for group differences were statistically significant for CA, systolic and diastolic HYPO. The prevalence of CA was reduced in the tetra group compared to the other 3 groups. The prevalence of systolic HYPO was increased in the tetra group compared to the other three groups, and the prevalence of diastolic HYPO was reduced in non-SCI veterans compared to the 3 groups of veterans with SCI.

To examine the influence of the aforementioned covariates, additional logistic regression models were constructed with the individual covariates included in the models (Table 4). For all analyses, the covariates were not significant with the exception of age and number of anti-HTN medications in the CA model; however, even with these covariates included in the model, “group” was still a significant predictor of CA ($p < 0.01$).

DISCUSSION

In this investigation we sought to determine prevalence rates for HR and BP abnormalities in veterans with SCI compared to a veteran cohort without SCI. The data suggest that SCI status, but not AIS classification or duration of injury, contributes to the prevalence of CA, systolic and diastolic HYPO. In addition, SCI status contributed to the reduced prevalence of the diagnosis of HTN and the use of anti-HTN medications in those with higher cord lesions. Although our data suggest that the prevalence of OH, systolic and diastolic HTN did not differ significantly among the groups, regardless of SCI status, the diagnosis of HTN was increased in the non-SCI and low thoracic veteran groups compared to veterans with high cord lesions (above T6).

We have noted increased resting HR in individuals with paraplegia compared to individuals with tetraplegia and non-SCI controls in laboratory observations (31, 32) as well as over the course of a typical 24-hour day. (33) The present data suggest that more than 50% of veterans with high and low thoracic lesions and those without SCI have a resting HR above 80 bpm. The reported consequences of persistently elevated HR include increased cardiovascular morbidity, (34) atherosclerosis and cardiovascular mortality, (22, 35) hypertension, (36) and accelerated progression of arterial stiffness, (16) and, as such, persistently elevated HR constitutes an emerging cardiovascular risk factor. (15) The relevance of applying these findings derived from studies performed in the general population to persons with SCI has not yet been established. However, CVD is a leading cause of mortality in the SCI population, (37) increased diagnosis of HTN has been reported in veterans with paraplegia compared to veterans with tetraplegia, (38) and increased arterial stiffness is reported among individuals with SCI compared to matched non-SCI controls. (39-41) Furthermore, similar to prior reports (38, 42) the present data suggest that nearly three-quarters of the low thoracic population carry the diagnosis of HTN, whereas the

significantly reduced prevalence of HTN found in our high thoracic group was fully accounted for by age.

Increased prevalence of systolic HYPO in the tetra and high thoracic groups was not surprising and can be attributed to decentralized sympathetic outflow to the vasculature. (12, 13, 43) An unexpected finding was that the prevalence of systolic HYPO was doubled in veterans with low thoracic lesions compared to veterans without SCI and was comparable to the high thoracic group. Level of lesion in the low thoracic group ranged from T7-L1 and systolic HYPO was predominantly in those with lesions at or above T10, in whom sympathetic control of the splanchnic vascular bed would likely be partially decentralized. Although we found relatively increased use of prescription anti-HTN medications in veterans with low thoracic lesions, this incidence rate did not contribute to the prevalence of systolic HYPO in this group. There is a growing body of literature which suggests that persistently low systolic BP is associated with cognitive dysfunction (18, 44-46) and mood disorders. (17, 20, 47) We demonstrated that hypotensive individuals with SCI perform more poorly on tasks of memory and attention processing compared to matched (for incidence of traumatic brain injury) normotensive individuals with SCI. (48) In addition, we reported that individuals with SCI, as well as their clinical care providers, were able to ascribe adverse health-related quality of life effects, which stem from persistent hypotension. (49) However, because most individuals with persistently low systolic BP remain asymptomatic, treatment is very rare, and in fact, the present data indicate that although nearly one-third of the SCI population studied had systolic HYPO only 3 patients (1 high thoracic and 2 tetra) were prescribed an anti-HYPO medication.

In addition to systolic HYPO, more than 50% of the SCI population had diastolic HYPO, defined as a DBP ≤ 70 mmHg, regardless of level, AIS classification, or duration of injury; whereas the prevalence of diastolic HYPO was 30% in the non-SCI veterans. A recent study conducted in a large veteran population (n=14,270) documented, via retrospective chart review, increased all-cause mortality after adjusting for comorbidities in veterans with a DBP ≤ 70 mmHg.(21) These investigators reported a higher incidence of diastolic HYPO in their population (49%) compared to our findings in the non-SCI veterans; however their veterans with diastolic HYPO were nearly a decade older (68±9 years) than our non-SCI veterans with diastolic HYPO (59±14 years).(21) Moreover, the prevalence of a diastolic HYPO was increased in all three SCI groups studied (56%) compared to both groups of non-SCI veterans, and the mean age of the diastolic HYPO group among veterans with SCI was 58±14 years. The mortality risk associated with diastolic HYPO in individuals with SCI is not known, but age, cardiovascular diagnoses and prescription anti-HTN medications did not account for group differences in this prevalence rate.

Interestingly, the prevalence of OH did not differ significantly among our study groups, and ranged between 22% (high thoracic) and 36% (tetra). Age did not contribute to the prevalence of OH in our study population; however, the prevalence rate of OH appears to be higher than previously reported in otherwise healthy middle-aged males (12%), (50) regardless of SCI status. This has significant clinical implication because OH is associated with increased morbidity and mortality in otherwise healthy asymptomatic individuals (i.e., those that do not complain of dizziness, lightheadedness, nausea, blurred vision, etc.).

(51-58) It should be noted that we reported BP from manual sphymomanometry at the brachial artery; however, a recent report suggests markedly higher prevalence rates for OH using beat-to-beat BP recordings in men 65+ years old.(59)

We hypothesized that, due to impaired sympathetic vasomotor tone, veterans with high cord lesion (above T6) would have a relatively low incidence of the diagnosis of HTN compared to veterans with low cord lesions (T7 and below) and those without SCI. The data support our hypothesis in that the diagnosis of CVD in general, and HTN in particular, was reduced, and as a result use of prescription anti-HTN medications was lower, in veterans with spinal cord lesions above T6. A recent paper documented, through medical chart review, the prevalence of HTN diagnosis in veterans without SCI as 68.4% compared to a prevalence of 56.6% in veterans with SCI. (38) We found a similar prevalence of the diagnosis of HTN in our non-SCI veterans, but due to our differentiation of level of injury relative to the origin of sympathetic vasomotor control, our findings in veterans with SCI differ from those reported by Barry et al. (38) Specifically, the incidence of the diagnosis of HTN was higher in our veterans with SCI below T7 (72.7%), but the incidence was significantly lower in those with lesions above T6 (≈22%). It is therefore important to consider level of injury relative to peripheral sympathetic vasomotor control when reporting the incidence of HTN in persons with SCI.

Of interest, two-thirds of the veterans with tetraplegia studied carried the diagnosis of diabetes mellitus, which may have clinical relevance. Twenty years ago our group reported abnormalities in carbohydrate and lipid metabolism in 67% of veterans with tetraplegia (age: 47±2 years) residing in the New York City metropolitan area.(60) In a second publication we reported that 23% of subjects with complete tetraplegia (age: 38±1 years) were diabetic. (61) It should be appreciated that the incidence of DM increases with advancing age, (60) and today, 90% of our veterans with tetraplegia are older than 50; 57% are older than 60.

Study Limitations

A limitation of this study is that there was no assessment of autonomic dysreflexia (AD) in veterans with SCI. The definition of AD includes an increase in BP ≥ 20/10 mmHg, which may be associated with symptoms including pounding headache, profuse sweating and piloerection above lesion.(62) We were unable to assess the prevalence of AD, which stems from an unrestrained outpouring of norepinephrine from the post-synaptic sympathetic ganglia due to noxious or non-noxious stimuli below the level of lesion, because our data were collected in a resting state. However, elevation in resting BP, which we attributed to HTN, may reflect AD, particularly in individuals with high cord lesions. Large variability in BP is a concern in the SCI population, and because our data were calculated from average BP recordings during a single clinical visit, we may have underestimated the prevalence rates of BP and HR abnormalities and we recognize that these data may not adequately reflect overall cardiovascular hemodynamics in our veterans. It should be noted that the groups were recruited from a convenience sample of veterans with and without SCI, and were not matched for demographic data or medical history; therefore group comparisons should be interpreted with caution and extrapolation to the general VA may be inappropriate. In addition, comparisons for the prevalence of cardiovascular diagnoses,

medications and cardiovascular abnormalities in the group with high thoracic lesions should be interpreted with caution because of the small sample size and the lower chronological age compared to the other groups. Also, because a greater percentage of veterans without SCI and those with low thoracic lesions were prescribed anti-HTN medications than veterans with high thoracic and cervical lesions, the use of these agents may have served to bias the analyses. Finally, it should be noted that there were too few women in our study population to discern any unique characteristics of gender on prevalence rates for the hemodynamic abnormalities documented.

In conclusion, our data support the notion that SCI status conveys appreciable cardiovascular risk for increased prevalence of CA, systolic and diastolic HYPO. In addition, prevalence of OH appears to be increased in our veterans with and without SCI at an earlier age than previously reported. Because cardiac acceleration and persistent and episodic hypotension are associated with adverse cognitive and mood consequences, as well as increased morbidity and mortality in the general population, the increased prevalence of these conditions in the SCI population should be considered a priority for clinical investigations and in the management of the health and wellbeing of these individuals. These findings provide a foundation for the development of a national registry describing cardiovascular parameters in the veteran population.

Acknowledgments

Grant Support:

This research was supported by the Veterans Affairs Rehabilitation Research and Development Service (Grants # B9212C & B6999R).

Abbreviations

AAN	American Academy of Neurology
AAS	American Autonomic Society
AD	Autonomic Dysreflexia
AIS	ASIA Impairment Scale
ASIA	American Spinal Cord Injury Association
BP	Blood Pressure
CA	Cardiac Acceleration
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
HR	Heart Rate
HTN	Hypertension
HYPO	Hypotension
IRB	Institutional Review Board

OH	Orthostatic Hypotension
SBP	Systolic Blood Pressure
SCI	Spinal Cord Injury
Tetra	Cervical lesions (C3-C8)
VAMC	Veterans Affairs Medical Center
WHO	World Health Organization

REFERENCES

1. Spinal Cord Injury Facts and Figures at a Glance. 2012. https://wwwnsciscuabedu
2. Garshick E, Kelley A, Cohen SA, Garrison A, Tun CG, Gagnon D, et al. A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord. 2005; 43(7):408–16. [PubMed: 15711609]
3. Groah SL, Charlifue S, Tate D, Jensen MP, Molton IR, Forchheimer M, et al. Spinal cord injury and aging: challenges and recommendations for future research. Am J Phys Med Rehabil. 91(1):80–93. [PubMed: 21681060]
4. Cragg JJ, Noonan VK, Krassioukov A, Borisoff J. Cardiovascular disease and spinal cord injury: results from a national population health survey. Neurology. 2013; 81(8):723–8. [PubMed: 23884034]
5. Cragg JJ, Noonan VK, Dvorak M, Krassioukov A, Mancini GB, Borisoff JF. Spinal cord injury and type 2 diabetes: results from a population health survey. Neurology. 2013; 81(21):1864–8. [PubMed: 24153440]
6. West CR, Mills P, Krassioukov AV. Influence of the neurological level of spinal cord injury on cardiovascular outcomes in humans: a meta-analysis. Spinal Cord. 2012; 50(7):484–92. [PubMed: 22391687]
7. Marino RJ, Barros T, Biering-Sorensen F, Burns SP, Donovan WH, Graves DE, et al. International standards for neurological classification of spinal cord injury. J Spinal Cord Med. 2003; 26(Suppl 1):S50–6. [PubMed: 16296564]
8. Maynard FM Jr. Bracken MB, Creasey G, Ditunno JF Jr. Donovan WH, Ducker TB, et al. American Spinal Injury Association. International Standards for Neurological and Functional Classification of Spinal Cord Injury. Spinal Cord. 1997; 35(5):266–74. [PubMed: 9160449]
9. Krassioukov AV, Karlsson AK, Wecht JM, Wuermser LA, Mathias CJ, Marino RJ. Assessment of autonomic dysfunction following spinal cord injury: rationale for additions to International Standards for Neurological Assessment. Journal of rehabilitation research and development. 2007; 44(1):103–12. [PubMed: 17551864]
10. Alexander MS, Biering-Sorensen F, Bodner D, Brackett NL, Cardenas D, Charlifue S, et al. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord. 2009; 47(1):36–43. [PubMed: 18957962]
11. Groah SL, Weitzenkamp D, Sett P, Soni B, Savic G. The relationship between neurological level of injury and symptomatic cardiovascular disease risk in the aging spinal injured. Spinal Cord. 2001; 39(6):310–7. [PubMed: 11438852]
12. Claydon VE, Krassioukov AV. Orthostatic hypotension and autonomic pathways after spinal cord injury. Journal of neurotrauma. 2006; 23(12):1713–25. [PubMed: 17184183]
13. Claydon VE, Steeves JD, Krassioukov A. Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord. 2006; 44(6):341–51. [PubMed: 16304564]
14. Krassioukov A, Biering-Sorensen F, Donovan W, Kennelly M, Kirshblum S, Krogh K, et al. International standards to document remaining autonomic function after spinal cord injury. J Spinal Cord Med. 2012; 35(4):201–10. [PubMed: 22925746]
15. Palatini P. Elevated heart rate: a “new” cardiovascular risk factor? Prog Cardiovasc Dis. 2009; 52(1):1–5. [PubMed: 19615486]

16. Palatini P, Parati G. Persistently elevated heart rate accelerates the progression of arterial stiffness. J Hypertens. 2010; 28(4):653–6. [PubMed: 20625244]
17. Barrett-Connor E, Palinkas LA. Low blood pressure and depression in older men: a population based study. Bmj. 1994; 308(6926):446–9. [PubMed: 8124175]
18. Duschek S, Matthias E, Schandry R. Essential hypotension is accompanied by deficits in attention and working memory. Behav Med. 2005; 30(4):149–58. [PubMed: 15981893]
19. Elias MF, Robbins MA, Schultz NR Jr. Pierce TW. Is blood pressure an important variable in research on aging and neuropsychological test performance? J Gerontol. 1990; 45(4):P128–35. [PubMed: 2195104]
20. Pilgrim JA, Stansfeld S, Marmot M. Low blood pressure, low mood? Bmj. 1992; 304(6819):75–8. [PubMed: 1737142]
21. Tringali S, Oberer CW, Huang J. Low Diastolic Blood Pressure as a Risk for All-Cause Mortality in VA Patients. Int J Hypertens. 2013; 2013:178780. [PubMed: 23606946]
22. Palatini P. Heart rate as a risk factor for atherosclerosis and cardiovascular mortality: the effect of antihypertensive drugs. Drugs. 1999; 57(5):713–24. [PubMed: 10353296]
23. Tomiyama H, Hashimoto H, Tanaka H, Matsumoto C, Odaira M, Yamada J, et al. Synergistic relationship between changes in the pulse wave velocity and changes in the heart rate in middle-aged Japanese adults: a prospective study. J Hypertens. 2010; 28(4):687–94. [PubMed: 20051904]
24. Arterial hypertension. Report of a WHO expert committee. World Health Organ Tech Rep Ser. 1978; (628):7–56. [PubMed: 103326]
25. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. J Neurol Sci. 1996; 144(1-2):218–9. [PubMed: 8994128]
26. The Consensus Committee of the American Autonomic Society; American Academy of Neurology. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. Neurology. 1996; 46(5):1470. [PubMed: 8628505]
27. Kaufmann H. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. Clin Auton Res. 1996; 6(2):125–6. [PubMed: 8726100]
28. The definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. Journal of the autonomic nervous system. 1996; 58(1-2):123–4. [PubMed: 8740670]
29. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Statistics in medicine. 1998; 17(8):857–72. [PubMed: 9595616]
30. Altman D, Machin D, Bryant TN, Gardner MJ. Statistics with Confidence 2nd Edition. British medical journal. 2000
31. Wecht JM, Rosado-Rivera D, Jegede A, Cirnigliaro CM, Jensen MA, Kirshblum S, et al. Systemic and cerebral hemodynamics during cognitive testing. Clin Auton Res. 2012; 22(1):25–33. [PubMed: 21792728]
32. Wecht JM, Zhu C, Weir JP, Yen C, Renzi C, Galea M. A prospective report on the prevalence of heart rate and blood pressure abnormalities in veterans with spinal cord injuries. J Spinal Cord Med. 2013; 36(5):454–62. [PubMed: 23941793]
33. Rosado-Rivera D, Radulovic M, Handrakis JP, Cirnigliaro CM, Jensen AM, Kirshblum S, et al. Comparison of 24-hour cardiovascular and autonomic function in paraplegia, tetraplegia, and control groups: implications for cardiovascular risk. J Spinal Cord Med. 2011; 34(4):395–403. [PubMed: 21903013]
34. Palatini P. Elevated heart rate as a predictor of increased cardiovascular morbidity. J Hypertens Suppl. 1999; 17(3):S3–10. [PubMed: 10489092]
35. Palatini P, Casiglia E, Julius S, Pessina AC. High heart rate: a risk factor for cardiovascular death in elderly men. Archives of internal medicine. 1999; 159(6):585–92. [PubMed: 10090115]
36. Palatini P, Julius S. Relevance of heart rate as a risk factor in hypertension. Curr Hypertens Rep. 1999; 1(3):219–24. [PubMed: 10981069]
37. Sabre L, Rekand T, Asser T, Korv J. Mortality and causes of death after traumatic spinal cord injury in Estonia. J Spinal Cord Med. 2013; 36(6):687–94. [PubMed: 24090049]

38. Barry W, St Andre JR, Evans CT, Sabharwal S, Miskevics S, Weaver FM, et al. Hypertension and antihypertensive treatment in veterans with spinal cord injury and disorders. Spinal Cord. 2013; 51(2):109–15. [PubMed: 23147130]
39. Miyatani M, Masani K, Oh PI, Miyachi M, Popovic MR, Craven BC. Pulse wave velocity for assessment of arterial stiffness among people with spinal cord injury: a pilot study. J Spinal Cord Med. 2009; 32(1):72–8. [PubMed: 19264052]
40. Wecht JM, Weir JP, DeMeersman RE, Spungen AM, Bauman WA. Arterial stiffness in persons with paraplegia. J Spinal Cord Med. 2004; 27(3):255–9. [PubMed: 15478529]
41. Phillips AA, Cote AT, Bredin SS, Krassioukov AV, Warburton DE. Aortic stiffness increased in spinal cord injury when matched for physical activity. Med Sci Sports Exerc. 2012; 44(11):2065–70. [PubMed: 22688833]
42. Lee MY, Myers J, Abella J, Froelicher VF, Perkash I, Kiratli BJ. Homocysteine and hypertension in persons with spinal cord injury. Spinal Cord. 2006; 44(8):474–9. [PubMed: 16331308]
43. Teasell RW, Arnold JM, Krassioukov A, Delaney GA. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil. 2000; 81(4):506–16. [PubMed: 10768544]
44. Duschek S, Schandry R. Cognitive performance and cerebral blood flow in essential hypotension. Psychophysiology. 2004; 41(6):905–13. [PubMed: 15563343]
45. Duschek S, Schandry R. Reduced brain perfusion and cognitive performance due to constitutional hypotension. Clin Auton Res. 2007; 17(2):69–76. [PubMed: 17106628]
46. Duschek S, Weisz N, Schandry R. Reduced cognitive performance and prolonged reaction time accompany moderate hypotension. Clin Auton Res. 2003; 13(6):427–32. [PubMed: 14673692]
47. Rosengren A, Tibblin G, Wilhelmsen L. Low systolic blood pressure and self perceived wellbeing in middle aged men. Bmj. 1993; 306(6872):243–6. [PubMed: 8443523]
48. Jegede AB, Rosado-Rivera D, Bauman WA, Cardozo CP, Sano M, Moyer JM, et al. Cognitive performance in hypotensive persons with spinal cord injury. Clin Auton Res. 2010; 20(1):3–9. [PubMed: 19842013]
49. Carlozzi NE, Fyffe D, Morin KG, Byrne R, Tulsky DS, Victorson D, et al. Impact of blood pressure dysregulation on health-related quality of life in persons with spinal cord injury: development of a conceptual model. Arch Phys Med Rehabil. 2013; 94(9):1721–30. [PubMed: 23499779]
50. Shin C, Abbott RD, Lee H, Kim J, Kimm K. Prevalence and correlates of orthostatic hypotension in middle-aged men and women in Korea: the Korean Health and Genome Study. J Hum Hypertens. 2004; 18(10):717–23. [PubMed: 15116144]
51. Benvenuto LJ, Krakoff LR. Morbidity and mortality of orthostatic hypotension: implications for management of cardiovascular disease. Am J Hypertens. 2011; 24(2):135–44. [PubMed: 20814408]
52. Fedorowski A, Stavenow L, Hedblad B, Berglund G, Nilsson PM, Melander O. Orthostatic hypotension predicts all-cause mortality and coronary events in middle-aged individuals (The Malmo Preventive Project). Eur Heart J. 2010; 31(1):85–91. [PubMed: 19696189]
53. Masaki KH, Schatz IJ, Burchfiel CM, Sharp DS, Chiu D, Foley D, et al. Orthostatic hypotension predicts mortality in elderly men: the Honolulu Heart Program. Circulation. 1998; 98(21):2290–5. [PubMed: 9826316]
54. Maule S, Milazzo V, Maule MM, Di Stefano C, Milan A, Veglio F. Mortality and prognosis in patients with neurogenic orthostatic hypotension. Funct Neurol. 27(2):101–6. [PubMed: 23158582]
55. Rockwood MR, Howlett SE, Rockwood K. Orthostatic hypotension (OH) and mortality in relation to age, blood pressure and frailty. Arch Gerontol Geriatr. 2012; 54(3):e255–60. [PubMed: 22240412]
56. Rose KM, Eigenbrodt ML, Biga RL, Couper DJ, Light KC, Sharrett AR, et al. Orthostatic hypotension predicts mortality in middle-aged adults: the Atherosclerosis Risk In Communities (ARIC) Study. Circulation. 2006; 114(7):630–6. [PubMed: 16894039]
57. Schatz IJ, Lessons from the Honolulu Heart Program. Orthostatic hypotension predicts mortality. Clin Auton Res. 2002; 12(4):223–4. [PubMed: 12357271]

58. Xin W, Lin Z, Mi S. Orthostatic hypotension and mortality risk: a meta-analysis of cohort studies. Heart.

59. Cooke J, Carew S, Quinn C, O'Connor M, Curtin J, O'Connor C, et al. The prevalence and pathological correlates of orthostatic hypotension and its subtypes when measured using beat-to-beat technology in a sample of older adults living in the community. Age and ageing. 2013; 42(6): 709–14. [PubMed: 23934598]

60. Bauman WA, Spungen AM. Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. Metabolism: clinical and experimental. 1994; 43(6):749–56. [PubMed: 8201966]

61. Bauman WA, Adkins RH, Spungen AM, Waters RL. The effect of residual neurological deficit on oral glucose tolerance in persons with chronic spinal cord injury. Spinal Cord. 1999; 37(11):765–71. [PubMed: 10578247]

62. Krassioukov A, Warburton DE, Teasell R, Eng JJ. A systematic review of the management of autonomic dysreflexia after spinal cord injury. Arch Phys Med Rehabil. 2009; 90(4):682–95. [PubMed: 19345787]

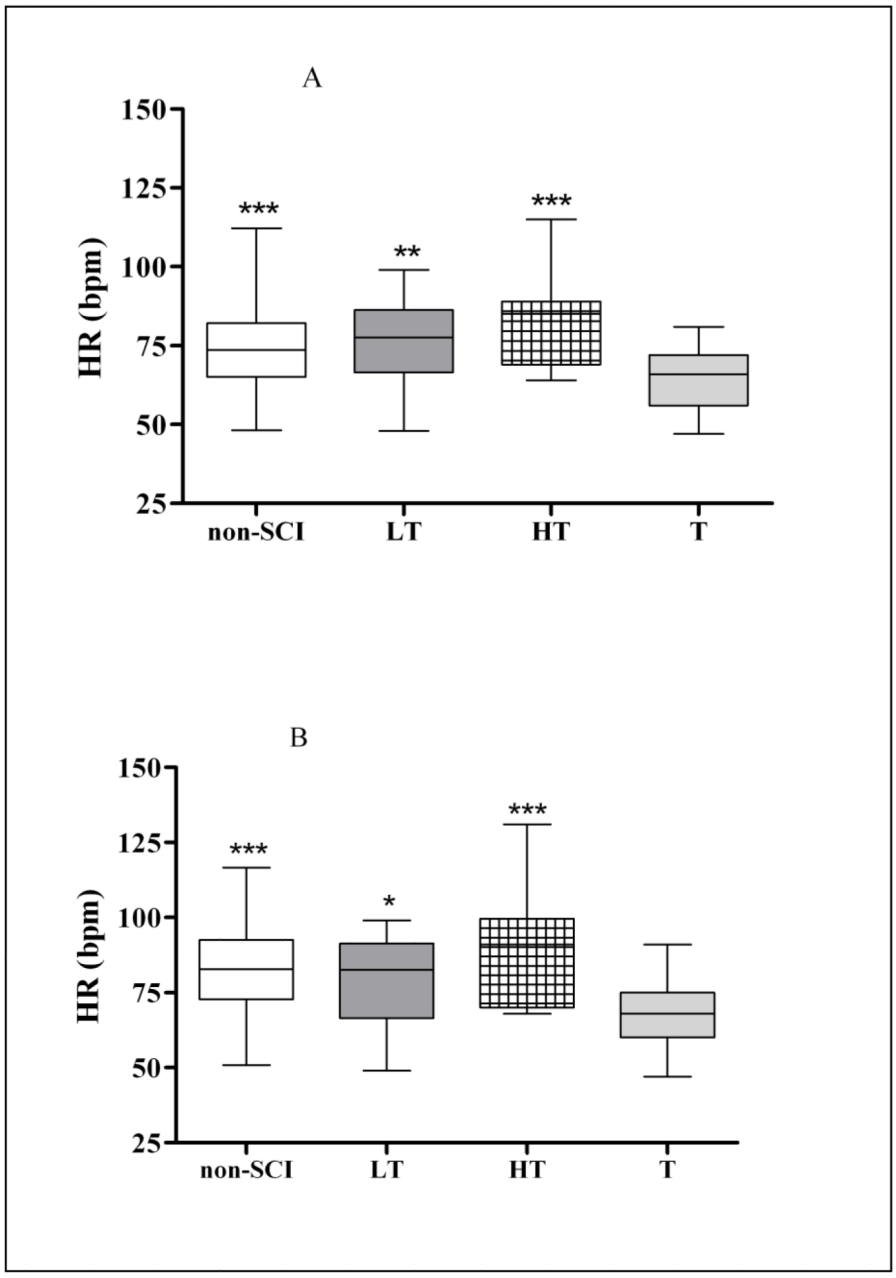

Figure 1.

Box plot demonstrating the mean, max and min resting Heart Rate (HR: bpm) in the supine [A] and upright [B] positions among non-SCI veterans (open bar) and veterans with low thoracic (LT: dark gray bars), high thoracic (HT: hatched bars) and cervical lesions (T: light gray bars). * $p<0.05$; ** $p<0.01$; *** $p<0.001$ versus the Tetra group.

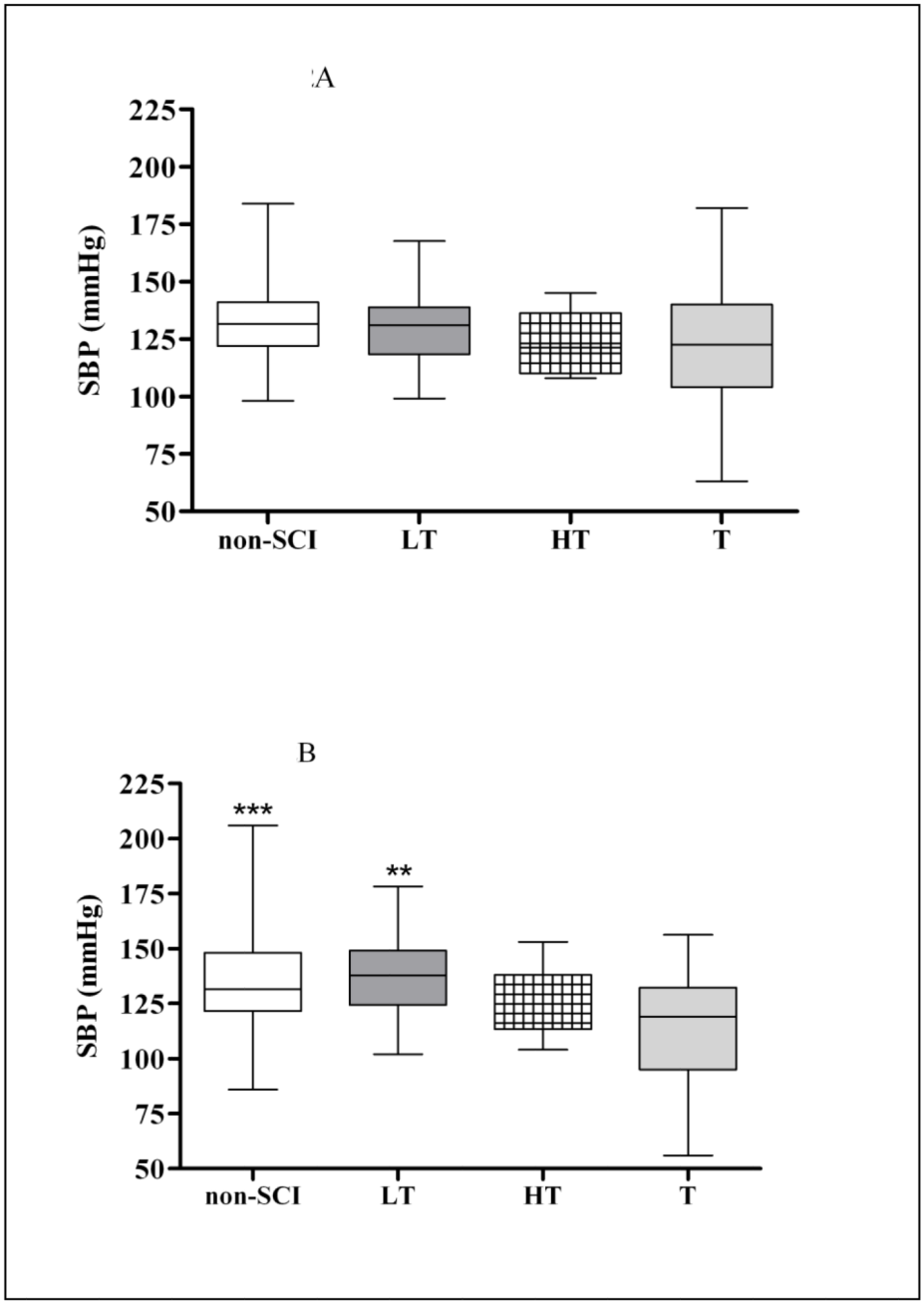

Figure 2.

Box plot demonstrating the mean, max and min resting Systolic Blood Pressure (SBP: mmHg) in the supine [A] and upright [B] positions among non-SCI veterans (open bar) and veterans with low thoracic (LT: dark gray bars), high thoracic (HT: hatched bars) and cervical lesions (T: light gray bars). ** $p<0.01$; *** $p<0.001$ versus the Tetra group.

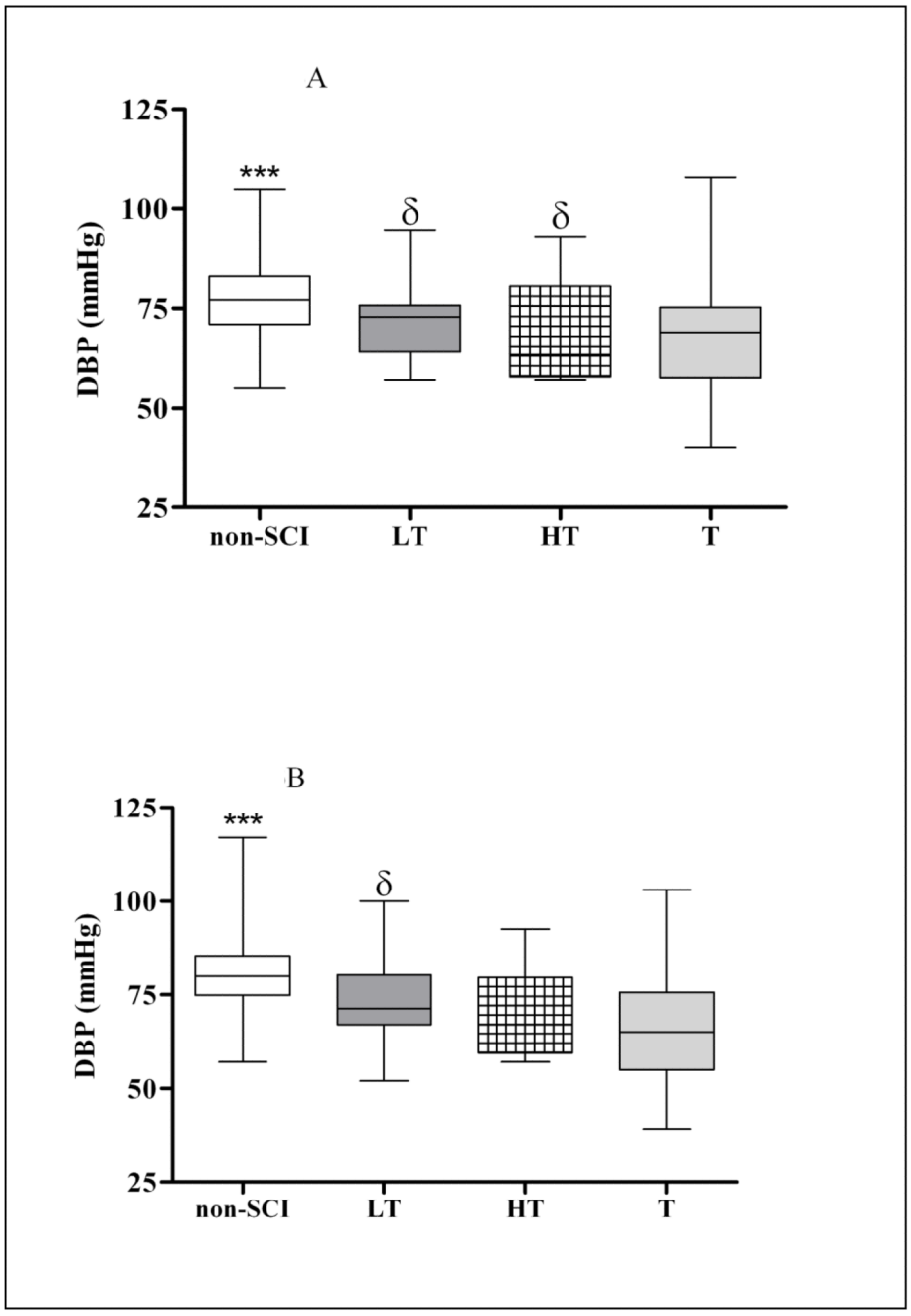

Figure 3.

Box plot demonstrating the mean, max and min resting Diastolic Blood Pressure (DBP: mmHg) in the supine [A] and upright [B] positions among non-SCI veterans (open bar) and veterans with low thoracic (LT: dark gray bars), high thoracic (HT: hatched bars) and cervical lesions (T: light gray bars). *** $p<0.001$ versus the Tetra group; δ $p<0.05$ versus the non-SCI group.

	non-SCI n=160	Low Thoracic n=22	High Thoracic n=9	Tetra n=31
Age (y)	57±11	57±10	48±20	60±11*
Age range (y)	21-88	32-73	22-83	37-79
HT (m)	1.78±0.08	1.78±0.06	1.78±0.07	1.76±0.33
WT (kg)	88±18	88±30	64±27***	86±26
BMI (kg/m^2)	28.5±5.7	29.0±7.1	23.0±4.0	27.4±6.2
Female Gender (n)	3	1	1	1
Duration (y)	NA	21±13	18±18	20±14
Level of SCI	NA	T7-L2	T1-T5	C3-C8
AIS A	NA	12 (55%)	6 (67%)	11 (36%)
AIS B	NA	2 (9%)	1 (11%)	5 (16%)
AIS C	NA	5 (23%)	1 (11%)	9 (29%)
AIS D	NA	3 (14%)	1 (11%)	6 (19%)

y=years; HT=height; m=meters; WT=weight; kg=kilograms; BMI=body mass index

* p<0.05

** p<0.01 versus HP group:

*** p<0.000 versus all other groups:

Table 2

Cardiovascular Medical History

	non-SCI	Low Thoracic	High Thoracic	Tetra	χ^2	*p value*
Current Smokers	30.0%	31.8%	11.1%	25.8%	*1.991*	*0.574*
Cardiovascular Diseases Diagnoses	70.6%	72.7%	22.2%	64.5%	*8.877*	*0.031*
HTN Diagnosis	66.9%	72.7%	22.2%	22.6%	*28.109*	*0.000*
Diabetes Mellitus	26.3%	31.2%	11.1%	67.7%	*2.090*	*0.554*
High Cholesterol, Lipids, Triglycerides	31.9%	45.4%	22.2%	38.7%	*2.451*	*0.484*
Heart & Vascular Disease	12.5%	9.1%	0.0%	12.9%	*2.535*	*0.459*
anti-HTN Medications	65.6%	81.8%	44.5%	41.9%	*11.117*	*0.011*
α^1:-blockers	14.4%	9.1%	11.1%	6.5%	*1.994*	*0.574*
β-blockers	20.0%	31.8%	33.3%	16.1%	*2.700*	*0.440*
Calcium Channel-blockers	25.0%	31.8%	0.0%	3.2%	*15.498*	*0.001*
ACE and ARBs	39.4%	59.1%	11.1%	22.6%	*10.799*	*0.013*
Nitrates	3.8%	4.6%	0.0%	6.5%	*1.188*	*0.756*
Diuretics	37.5%	22.7%	0.0%	9.7%	*18.560*	*0.000*
anti-HYPO Medications	0.0%	0.0%	11.1%	6.5%	*10.673*	*0.014*
α-agonists	0.0%	0.0%	11.1%	3.2%	*1.994*	*0.574*
Mineralocorticoids	0.0%	0.0%	0.0%	3.2%	*3.965*	*0.265*

Table 3
Cardiovascular Abnormalities: Probability

	non-SCI	Low Thoracic	High Thoracic	Tetra	χ^2	*p value*
Cardiac Acceleration (≥ 80 bpm)	56.2%	54.5%	66.7%	16.1%	*19.219*	*0.000*
Systolic Hypotension (≤ 110 mmHg)	13.7%	22.7%	22.2%	38.7%	*9.794*	*0.020*
Diastolic Hypotension (≤ 70 mmHg)	30.0%	54.5%	66.8%	67.8%	*21.061*	*0.000*
OH (≥−20/10 mmHg fall)	24.4%	22.7%	22.2%	35.5%	*1.761*	*0.623*
Systolic Hypertension (≥ 140 mmHg)	41.9%	45.5%	22.2%	32.3%	*2.579*	*0.461*
Diastolic Hypertension (≥ 90 mmHg)	18.1%	4.5%	22.2%	9.7%	*4.646*	*0.200*

Table 4

A: Significant Multiple Regression Results

	CA			systolic HYPO			diastolic HYPO		
	B	***SE***	***p value***	***B***	***SE***	***p value***	***B***	***SE***	***p value***
Constant	1.775	0.791	0.025	−2.674	0.973	0.006	−1.42	0.774	0.067
Group dummy code X1	−2.392	0.690	0.001	0.761	0.523	0.146	1.345	0.486	0.006
Group dummy code X2	0.250	0.790	0.752	0.370	0.894	0.679	1.681	0.770	0.029
Group dummy code X3	−0.101	0.474	0.830	0.661	0.573	0.249	1.115	0.474	0.019
age (years)	−0.030	0.014	0.039	0.021	0.017	0.213	0.011	0.014	0.417
smoking (y/n)	−0.102	0.325	0.754	0.070	0.403	0.861	0.337	0.326	0.302
CVD diag (y/n)	1.238	0.751	0.099	0.485	0.627	0.440	0.379	0.614	0.537
HTN diag (y/n)	−0.477	0.860	0.579	−1.440	0.792	0.069	−0.988	0.745	0.185
anti-HTN meds (y/n)	0.679	0.625	0.278	0.418	0.680	0.539	−0.330	0.610	0.588
anti-HTN meds (#)	−0.539	0.193	0.005	−0.086	0.253	0.735	0.284	0.177	0.110

B: Non-significant Mutiple Regression Results

	OH			systolic HTN			diastolic HTN		
	B	***SE***	***p value***	***B***	***SE***	***p value***	***B***	***SE***	***p value***
Constant	−1.536	0.857	0.073	−0.787	0.79	0.319	−0.89	0.997	0.372
Group dummy code X1	0.497	0.529	0.347	0.016	0.520	0.975	−0.731	0.843	0.386
Group dummy code X2	0.045	0.895	0.960	−0.256	0.898	0.776	0.374	0.936	0.689
Group dummy code X3	−0.221	0.558	0.693	0.153	0.488	0.755	−1.660	1.052	0.115
age(years)	−0.006	0.015	0.673	−0.013	0.014	0.373	−0.031	0.018	0.081
smoking (y/n)	0.593	0.343	0.084	−0.106	0.329	0.748	0.005	0.429	0.990
CVD diag (y/n)	0.580	0.661	0.380	1.031	0.640	0.107	1.127	0.916	0.219
HTN diag (y/n)	−1.213	0.803	0.131	0.542	0.741	0.464	−0.785	1.045	0.453
anti-HTN meds (y/n)	0.879	0.648	0.175	−0.584	0.631	0.355	0.953	0.837	0.255
anti-HTN meds (#)	0.245	0.183	0.179	−0.787	0.790	0.319	−0.890	0.997	0.372

Constant=non-SCI; X1=Tetra [1,0,0]; X2=High Thoracic [0,1,0]; X3=Low Thoracic [0,0,1]

CVD diag (y/n)=yes/no cardiovascular disease diagnoses; HTN diag (y/n)= yes/no diagnosis of hypertension

anti-HTN meds (y/n)= yes/no prescribed anti-hypertensive agents; anti-HTN meds (#)=number of prescribed anti-hypertensive agents