

Research article

# A retrospective chart review of heart rate and blood pressure abnormalities in veterans with spinal cord injury

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**Objective:** Autonomic impairment may lead to increased prevalence of heart rate (HR) and blood pressure (BP) abnormalities in veterans with spinal cord injury (SCI). In addition, comorbid medical conditions and prescription medication use may influence these abnormalities, including bradycardia, and tachycardia, hypotension, hypertension as well as autonomic dysreflexia (AD), and orthostatic hypotension (OH).

**Design:** A retrospective review of clinical and administrative datasets in veterans with SCI and compared the prevalence rates between clinical values and ICD-9 diagnostic codes in individuals with tetraplegia (T: C1–C8), high paraplegia (HP: T1–T6), and low paraplegia (LP: T7 and below).

**Results:** The prevalence of clinical values indicative of a HR  $\geq$  80 beats per minute was higher in the HP compared to the LP and T groups. A systolic BP (SBP)  $\leq$  110 mmHg was more common in the T compared to the HP and LP groups, whereas the prevalence of a SBP  $\geq$  140 mmHg was increased in the LP compared to the HP and T groups. Diagnosis of hypertension was 39–60% whereas the diagnosis of hypotension was less than 1%. Diagnosis of AD and OH was highest in the T group, but remained below 10%, regardless of categorical lesion level. Antihypertensive medications were commonly prescribed (55%), and patients on these medications were less likely to have high BP. The odds ratio of higher SBP and DBP increased with age and body mass index (BMI).

**Conclusion:** In veterans with SCI, the prevalence of HR and BP abnormalities varied depending on level of lesion, age, BMI, and prescription medication use.

**Keywords:** Spinal cord injuries, Cardiac arrhythmias, Hypotension, Hypertension, Orthostatic hypotension, Autonomic dysreflexia, Tetraplegia, Paraplegia

## Introduction

The Department of Veterans Affairs (VA) currently provides care for approximately 25 000 veterans with spinal cord injuries (SCI),<sup>1</sup> with an estimated lifetime cost for an individual veteran with SCI of between \$1 million and \$5 million, depending on age at onset and severity of injury.<sup>2</sup> The long-term care of veterans with SCI is one of the most costly endeavors to the VA healthcare system. Improvements in post-injury acute and sub-acute care have extended life expectancies in the SCI population<sup>1,2</sup> however, longevity remains below that of

the general population.<sup>2</sup> Moreover, the average age of individuals with SCI is increasing and it is estimated that 80% of veterans with SCI are older than 50 years,<sup>1</sup> predisposing these individuals to increased incidence of age-associated chronic diseases<sup>3</sup> and accelerated cardiovascular aging.<sup>4</sup> As such, health care providers are confronted with the challenge of managing the secondary medical consequences of SCI with chronic conditions which are prevalent in an aging population, including management of cardiovascular disease (CVD). Owing to the lack of specific clinical guidelines for the management of CVD in the SCI population, guidelines used in the general population are followed; however, these treatments may be less

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effective or may worsen cardiovascular homeostasis in persons with SCI due to decentralized autonomic cardiovascular regulation.

The American Spinal Injury Association (ASIA) has developed a classification scale (AIS) to document remaining motor and sensory function following SCI;<sup>5,6</sup> however the degree of autonomic impairment is not considered within these classifications.<sup>7,8</sup> That said, decentralized autonomic cardiovascular control may alter heart rate (HR) and blood pressure (BP) relative to the neurological level of SCI documented using the AIS classification.<sup>9–11</sup> Indeed a recent literature review suggested that individuals with SCI exhibit lesion-dependent changes in cardiovascular function, although direct assessment of autonomic cardiovascular integrity was not reported.<sup>11</sup> In 2005 ASIA, together with the International Spinal Cord Society (ISCoS), began an initiative to develop a standard for the documentation of remaining autonomic function post-SCI, which established definitions for HR and BP abnormalities;<sup>8</sup> however, the proportion of patients with these abnormalities is not known.

There are several methodological issues related to computing prevalence rates of HR and BP abnormalities in the SCI population. First, there is controversy in defining BP and HR abnormality thresholds. The present clinical guideline for diagnosis of hypotension in the general and SCI populations is systolic blood pressure (SBP)  $\leq 90$  mmHg and diastolic blood pressure (DBP)  $\leq 60$  mmHg;<sup>8</sup> however, in 1978 the World Health Organization (WHO) defined hypotension as a SBP  $\leq 110$  mmHg in males and  $\leq 100$  mmHg in females, without regard to DBP.<sup>12</sup> Current guidelines recommended by ASIA and ISCoS for use in the SCI population for bradycardia and tachycardia are HR  $\leq 60$  and  $\geq 100$  beats per minute (bpm),<sup>8</sup> respectively, and although these definitions comply with standards established in the non-SCI population, due to decentralized cardiovascular control, they may not apply to the SCI population. Many individuals with high cord lesions (above T6) maintain a low resting HR without adverse consequences, therefore, a HR below 60 bpm may not reflect a clinical abnormality. In addition, elevated resting HR at thresholds below 100 bpm are associated with accelerated arterial stiffening (AS) with age,<sup>13–15</sup> which has implication for the aging SCI population; therefore, we sought to identify the prevalence of an elevated resting HR  $\geq 80$  bpm in our veterans with SCI. Second, there is debate as to how to compute BP and HR values. In a recent retrospective review of prevalence of low ( $<110/70$  mmHg) and high ( $\geq 140/90$  mmHg) BP in veterans with SCI, BP measurement

was computed as the average of the last three measurements made during a single clinical visit,<sup>16</sup> thus limiting the study's ability to capture variation in HR and BP over the course of several years of clinical observation. In addition, the level of SCI was categorized as either paraplegia or tetraplegia and the prevalence of HR abnormalities (arrhythmias) was not included.<sup>16</sup>

To more accurately assess the prevalence of HR and BP abnormalities in veterans with SCI, a comprehensive medical chart review including multiple clinical visits with a direct comparison of documented clinical values and ICD-9 diagnostic codes for individual patients with SCI was performed. We conducted this retrospective review of the clinical and administrative datasets for veterans with SCI seen at an urban Veterans Affairs Medical Center (VAMC) during FY2004–2008, and compared the prevalence rates of HR and BP abnormalities among individuals with tetraplegia (T: C1–C8), high paraplegia (HP: T1–T6), and low paraplegia (LP: T7 and below). In addition, we report these prevalence rates in conjunction with patient medical history and prescription medication use and examine the association between patient characteristics (age, SCI level, body mass index (BMI), and prescription medication use) and HR and BP.

## Methods

### *Data source and sample*

Data used in this study were derived from VA National Patient Care Database, DSS pharmacy National Data Extract, local VAMC SCI Registry, and the Vital Signs data set extracted from Vista, VA's electronic health record system. The VA National Patient Care Database included data on patient gender, age, race/ethnicity, and diagnosis codes. The SCI registry included information on level of lesion (C1–L5), onset of injury, and type of injury (trauma, non-trauma), but data on completeness of injury and AIS classification were unavailable. The vital signs data included clinical values on HR and BP.

The cohort of eligible veterans with SCI was defined as those with a duration of injury of  $\geq 12$  months who had a routine encounter at the local VAMC during FY 2004–2008 ( $n = 439$ ). Veterans with SCI were identified by diagnosis codes for SCI (ICD-9-CM = 344.0–344.09, 344.1, 950.952.00–952.9), SCI status (tetraplegia, paraplegia) in the Medical SAS Inpatient Datasets, and clinic stop codes (e.g. 210414: SCI urology, 295: SCI observation) in the Medical SAS Outpatient Dataset. From these 439 veterans, we excluded 132 individuals with fewer than 10 BP and HR readings during the study period to ensure that patients were routinely

followed and after further exclusion of 30 veterans with missing level-of-injury data, a total of 277 veterans were included in the analyses. Veterans with SCI with a duration of injury of <12 months were excluded from the study because patients within 1 year of injury might be expected to undergo spontaneous changes in cardiovascular autonomic regulation during the acute and sub-acute period, thus potentially confounding these prevalence data. Routine encounters were identified using the following ICD-9 CM codes: annual physical (99215), urodynamics (51726, 51795–51797, 51722, 76000), and colonoscopy (DRG 45.23, 45.25); vital signs taken during these routine encounters, prior to any clinical procedure, were extracted from the medical record. The study physician (M.G.) examined the records for the day of the visit and identified acute medical illness or infection using ICD-9-CM codes. Most commonly excluded codes for acute medical illness or infection documented at the local VAMC SCI clinic included urinary tract infection (UTI, 599.0), pneumonia (486.0), aspiration (507.0), pressure ulcer (707.04-.07), and deep venous thrombosis (453.8). Any visit indicating these ICD-9-CM codes was excluded from the data set.

#### *Exclusion criteria*

We examined the range of values for SBP, DBP, and HR reported and excluded non-physiological values: SBP < 40 or >300 mmHg; DBP < 20 or >200 mmHg (0.78% of all cases); HR < 30 or >200 bpm (0.23% of all cases). Of the 277 eligible veterans, 212 (77%) were seen every year at the local VAMC during the 5-year study period, 29 (11%) missed 1 year, 16 (5%) missed 2 years, 11 (4%) missed 3 years, and the rest 6 (3%) had data in only one year.

#### *Categorizing clinical values for BP and HR*

The following thresholds were used to categorize BP and HR values from the medical record: SBP: low ( $\leq 90$  mmHg), borderline low (91–110 mmHg), normal (111–139 mmHg), and high ( $\geq 140$  mmHg); DBP: low ( $\leq 60$  mmHg), normal (61–89 mmHg), and high ( $\geq 90$  mmHg); HR: slow ( $\leq 50$  bpm), borderline slow (51–60 bpm), normal (61–80 bpm), borderline fast (81–99 bpm), and fast ( $\geq 100$  bpm). Because multiple HR or BP values were recorded for each patient, we categorized a patient into a particular BP and HR group if  $\geq 50\%$  of all recorded vital signs fell within these predefined thresholds.

#### *Diagnosis of BP and HR abnormalities*

Diagnosis of BP abnormalities was based on the following ICD-9 codes: hypertension: 401.0; 401.1 401.9;

hypotension: 458.1, 458.2; 796.3; autonomic dysreflexia (AD): 337.3; and orthostatic hypotension (OH): 458.0. Diagnosis of HR abnormalities is not readily identifiable in the medical records. Although tachycardia is separately identified by ICD-9 code 785.0, no specific diagnosis code is associated with bradycardia. Instead, cardiac arrhythmias are identified by ICD-9 427.xx, without distinguishing tachycardia or bradycardia. We therefore used only ICD-9 427.xx to identify cardiac arrhythmias. We categorized a patient into a particular BP and HR diagnosis group during a year if any of the above diagnosis codes appeared in the patient's medical records.

#### *Body mass index*

To compute individual's BMI, we examined height and weight values in the records, excluding non-physiological values (i.e. height <60 or >84 inches; weight <80 or >300 lbs); based on these criteria, less than 0.5% of height and weight values were excluded from analysis. For weight, we then examined fluctuations during each year; observations which differed from an annual average weight by >100 lbs or >20% were considered unrealistic and were excluded; less than 1% of values were excluded because of these large variations. For height, we chose the most commonly recorded value for patients who had multiple observations on record. After data cleaning, we re-calculated average annual BMI for each individual and grouped BMI into the following categories: low ( $<19$  kg/m<sup>2</sup>), normal (19–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), and obese ( $\geq 30$  kg/m<sup>2</sup>). Because only 6% of veterans with SCI were in the low BMI group, for statistical analysis we combined the low and normal BMI groups.

#### *Medications*

To examine the influence of medications on the prevalence of BP and HR abnormalities, the study physician (M.G.) examined medications prescribed/dispensed for each visit and categorized them into the following categories: (1) anti-hypertensive medications, (2) anti-hypotensive medications, (3) medications with hypertensive side effects, (4) medications with hypotensive side effects, (5) medications with bradycardic effects, and (6) medications with tachycardic effects. A list of the most common medications prescribed for the patients in our sample within each of the six categories is provided (Table 1).

#### *Chronic conditions*

To examine the influence of chronic conditions on BP and HR abnormalities, the study physician (M.G.) examined all ICD-9 CM diagnosis codes recorded for each

**Table 1 Most commonly prescribed medications in each category**

Anti-hypertensive medications included
1. Beta-blockers
2. Alpha-blockers (selective and non-selective)
3. Angiotensin-converting-enzyme inhibitors
4. Angiotensin-receptor blockers
5. Calcium channel blockers
6. Diuretics
7. Nitrates
Anti-hypotensive medications included
1. Alpha adrenergic agonists
2. Mineralcorticosteroids
Medications with hypertensive side effects included
1. Non-steroidal anti-inflammatory drugs (NSAIDs)
Medications with hypotensive side effects included
1. Anti-cholinergics
2. Opioids
3. Gabapentinoids
4. Benzodiazepines
5. Tricyclic anti-depressants (orthostatic hypotension)
6. Phosphodiesterase inhibitors
7. Selective serotonin re-uptake inhibitors (SSRIs)
Medications with bradycardic effects
1. Beta-blocker
2. Non-dihydropyridine calcium channel blockers
3. Opioids
4. Benzodiazepines
Medications with tachycardic effects
1. Non-selective alpha blocker
2. Dihydropyridine-calcium channel blockers
3. Nitrates
4. Alpha adrenergic agonists
5. Mineralcorticosteroids
6. Non-steroidal anti-inflammatory drugs
7. Anti-cholinergics
8. Gabapentinoids

visit and categorized these in decreasing frequency. We categorized the patient as having a condition if the diagnosis was present in two or more visits during a year.

### Analysis

Group demographics, presence of chronic conditions and medications that affect HR and BP are presented by group. Statistical significance was set at  $\alpha = 0.05$ . We computed the mean, median, minimum, maximum, and proportion of observations which fell into each HR, SBP, and DBP category during each year and by group. We also computed the proportion of patients with each identified chronic condition and medications prescription across all 5 years. Because the trend over time in rates of chronic conditions and prescription medication use were not statistically significant we present 5-year averages for these data.

We used ordered logit models to estimate whether the defined HR, SBP, and DBP abnormality categorical groups differ by level of lesion and other patient characteristics. We chose this model over the less restrictive but more complicated generalized ordered logit models

because tests for parallel lines (i.e. proportional odds) assumptions showed that few variables violated this assumption.<sup>17</sup> We controlled for correlations that occur when individuals have multiple observations. All analyses were performed using Stata 11 (StataCorp, College Station, TX, USA). The main independent variable is level of lesion (HP, LP, reference = Tetra) and we examined the effects of chronic conditions, medication categories, BMI, duration of injury, age, and race on BP and HR prevalence rates among these groups. We included chronic kidney disease (CKD), coronary artery disease (CAD), diabetes mellitus (DM), and hyperlipidemia in our estimation models as they were most commonly diagnosed and were considered to have a potential impact on BP and HR chronically. Estimates from secondary analyses including low prescription rates for anti-hypotensive medications (<1%) and other conditions (e.g. peripheral vascular diseases, smoking) were not statistically significant and were excluded from final models.

To control for the possibility that patients with more medical encounters (i.e. more HR and BP observations) are more likely to be identified as having a HR or BP abnormality, we also controlled for the number of inpatient visits and indicators for year.

## Results

### Patient characteristics

Characteristics of the study groups are presented (Table 2). The average age of the sample was  $63 \pm 14$  years and 84% were older than 50 years. The majority of the veterans with SCI were white males; the average BMI was in the overweight category and nearly one-quarter of these veterans were considered obese. Most of these veterans had a traumatic lesion and slightly more than half of the sample had tetraplegia. Veterans in the T group were significantly younger than those in the HP and LP groups and individuals in the HP group were less likely to have a traumatic lesion compared to the other two groups. Differences in sex, race, BMI, duration of injury, and number of outpatient visits were not statistically different by categorical level of lesion; however, the LP group had significantly fewer inpatient admissions than those in the HP group.

### Commonly prescribed medications

Regardless of injury category, anti-hypertensive medications and medications with hypotensive effects were more commonly prescribed than anti-hypotensive agents and medications with hypertensive effects (Table 3). Prescription rates for anti-hypertensive medications and medications with hypotensive effects were



**Table 2** Demographic characteristics by group

Number of subjects, <i>n</i> (%)	Total		T		HP		LP		
	277 (100%)		151 (55%)		44 (16%)		82 (30%)		
Age (mean years $\pm$ SD)	63 $\pm$ 14		62 $\pm$ 13		66 $\pm$ 16		65 $\pm$ 13		1,2
<50 ( <i>n</i> , %)	44	16%	25	17%	10	23%	9	11%	2,3
50–64 ( <i>n</i> , %)	108	39%	67	44%	9	20%	32	39%	
65–74 ( <i>n</i> , %)	65	23%	33	22%	9	20%	23	28%	
$\geq$ 75 ( <i>n</i> , %)	70	22%	36	17%	16	36%	18	22%	
Males ( <i>n</i> , %)	271	98%	150	99%	42	96%	79	96%	
Race ( <i>n</i> , %)									
White ( <i>n</i> , %)	141	59.7	77	59.7	24	57.1	40	61.5	
Black ( <i>n</i> , %)	95	39.8	52	39.5	18	42.9	25	38.5	
BMI (kg/m <sup>2</sup> )	26.4 $\pm$ 5.4		26.6 $\pm$ 5.4		26.3 $\pm$ 5.9		26.0 $\pm$ 5.1		
Underweight (<19)	13	6%	7	6%	3	8%	3	4%	
Normal (19–24.9)	93	37%	45	35%	14	35%	34	46%	
Overweight (25–29.9)	84	35%	44	35%	16	40%	24	32%	
Obese ( $\geq$ 30)	51	22%	31	24%	7	18%	13	18%	
SCI/D type ( <i>n</i> , %)									
Trauma	206	73%	119	78%	24	52%	63	76%	
Duration of injury (year $\pm$ SD)	18 $\pm$ 15		16 $\pm$ 15		19 $\pm$ 20		20 $\pm$ 15		
Number of outpatient visits $\pm$ SD	149 $\pm$ 108		153.8		145.1		142.3		
Number of inpatient admissions $\pm$ SD	5 $\pm$ 5		5.3		6.1		4.0		3

1, T vs. HP; 2, T vs. LP; 3, HP vs. LP;  $P < 0.05$ .

**Table 3** Overall prescription rate by medication category and level of injury

	Total		T ( <i>n</i> = 691)		HP ( <i>n</i> = 199)		LP ( <i>n</i> = 371)		
	<i>n</i> = 1291								
Antihypertensive medications ( <i>n</i> , %)	683	54.8%	378	54.4%	109	54.5%	196	53.5%	
Antihypotensive medications ( <i>n</i> , %)	3	0.2%	1	0.1%	1	0.5%	1	0.3%	
Medications with hypertensive side effects ( <i>n</i> , %)	215	17.7%	94	13.6%	34	16.3%	87	23.4%	2
Medications with hypotensive side effects ( <i>n</i> , %)	718	57.5%	379	54.8%	116	58.4%	223	60.6%	
Medications with bradycardic side effects ( <i>n</i> , %)	656	52.0%	336	48.6%	114	57.3%	206	55.5%	1,2
Medications with tachycardic side effects ( <i>n</i> , %)	685	54.3%	362	52.4%	103	51.8%	220	59.3%	2

1, T vs. HP; 2, T vs. LP; 3, HP vs. LP;  $P < 0.05$ .

comparable across injury groups; differences between the T and LP groups for medications with hypertensive effects reflects increased prescription of NSAIDs in the LP group. In addition, the data suggest increased prescription rates for medications with bradycardic effects in the HP and LP groups compared to the T group and for medications with tachycardic effects in the LP groups compared to the T group.

### Chronic conditions

The most common chronic conditions diagnosed in veterans with SCI at the local VAMC during FY 2004–2008 are presented (Table 4). Over the 5-year study period, UTI, pressure ulcer, chronic pain, DM, hypercholesterolemia/hyperlipidemia, and kidney/bladder problems were documented for more than a quarter of the patients regardless of injury level. The rate of pressure ulcer and arrhythmias was increased in the HP compared to the LP and T groups. The rate of chronic pain, hypercholesterolemia/hyperlipidemia,

peripheral vascular disease, erectile dysfunction, and CKD was increased in the LP compared to the T group. The rate of CAD was reduced in the T compared to the HP and LP groups; anemia was more common in the HP than the T group.

### Description of HR and BP data

Distribution of mean, median, minimum, and maximum HR and BP averaged across all years is presented by group (Table 5) and over time (Fig. 1A–1C). Average annual number of HR, SBP, and DBP recordings increased from FY 2004 to 2008, but there were no differences across injury category. Mean, median, minimum, and maximum HR were significantly higher in the HP group compared to the T group. Mean, median, minimum, and maximum SBP and DBP were significantly higher in the LP group compared to the T group, and mean and median SBP and DBP also were significantly higher in LP than HP group. During the study period, the distribution of HR values

**Table 4 Overall presence of chronic/recurrent conditions**

	Total (n = 1291)		T (n = 691)		HP (n = 199)		LP (n = 371)		
	n	%	n	%	n	%	n	%	
UTI	567	45.3	319	46.2	95	48.3	153	42.0	
Pressure ulcer	527	41.5	255	36.9	112	55.0	160	42.6	1,3
Pain	501	39.8	239	34.6	78	40.2	184	49.2	2
DM	416	33.0	219	31.7	74	37.8	123	32.7	
Hyper-lipidemia/cholesterolemia	379	30.2	183	26.5	59	30.6	137	36.7	2
Kidney/bladder disorders	323	25.6	178	25.8	51	24.9	94	25.8	
PTSD anxiety	186	14.9	104	15.1	17	9.6	65	17.6	
Depressive disorder	178	14.2	90	13.0	25	13.4	63	16.8	
CAD	174	13.9	69	10.0	36	19.1	69	18.4	1,2
OA	159	12.5	84	12.2	24	11.5	51	13.8	
Anemia	154	12.1	71	10.3	35	17.2	48	12.8	1
GERD	152	12.0	75	10.9	26	12.9	51	13.6	
Bowel dysfunction	134	10.6	69	10.0	34	16.7	31	8.2	3
Benign prostatic hyperplasia	130	10.2	63	9.1	23	11.0	44	11.7	
Urinary incontinence	128	10.2	73	10.6	24	12.4	31	8.2	
Arrhythmia	119	9.5	58	8.4	32	15.8	29	8.0	1,3
Peripheral vascular disease	119	9.3	51	7.4	23	11.0	45	12.0	2
Lung diseases	112	8.8	66	9.6	23	11.0	23	6.1	
Cancer	95	7.4	50	7.2	17	8.5	28	7.4	
Mental disorder	92	7.3	52	7.5	15	7.7	25	6.6	
COPD	75	5.9	43	6.2	13	6.2	19	5.1	
ED	73	5.7	30	4.3	10	4.8	33	8.8	2
CHF	59	4.7	26	3.8	19	9.6	14	3.7	
Substance use	47	3.7	32	4.6	2	1.0	13	3.5	
CKD	48	3.6	17	2.5	9	4.3	22	5.9	2

PTSD, posttraumatic stress disorder; GERD, gastro-esophageal reflux disorder; COPD, chronic obstructive pulmonary disease; ED, erectile dysfunction; CHF, congestive heart failure; CKD, chronic kidney disease.  
 1, T vs. HP; 2, T vs. LP; 3, HP vs. LP significant at  $P < 0.05$  after controlling for time trend

widened, because minimum HR decreased while maximum HR increased (Fig. 1A). Over time the average minimum SBP and DBP decreased significantly but the average maximum SBP and DBP did not change, therefore there was a corresponding decrease in mean and median SBP and DBP (Fig. 1B and 1C).

*Distribution of HR and BP abnormalities: clinical values*

Prevalence rates for extreme HR values (i.e.  $\leq 50$  or  $\geq 100$  bpm) were rare and did not differ by group (Table 6); however, clinical values indicating a HR  $\leq 60$  bpm were significantly lower in the HP compared

**Table 5 Descriptive data for BP and HR clinical values: all years**

	T	HP	LP	
HR				
Average records per year (#)	6.7	7.0	7.4	
Minimum (bpm)	65	68	66	1
Maximum (bpm)	87	92	89	1
Mean (bpm)	75	79	76	1
Median (bpm)	75	78	75	1
SBP				
Average records per year (#)	7.0	7.3	7.9	
Minimum (mmHg)	103	111	115	2
Maximum (mmHg)	138	142	148	2
Mean (mmHg)	120	125	130	2,3
Median (mmHg)	119	124	130	2,3
DBP				
Average records per year (#)	7.0	7.3	7.9	
Minimum (mmHg)	62	62	65	2
Maximum (mmHg)	83	82	86	2
Mean (mmHg)	72	72	75	2,3
Median (mmHg)	72	72	75	2,3

1, T vs. HP; 2, T vs. LP; 3, HP vs. LP;  $P < 0.05$ .

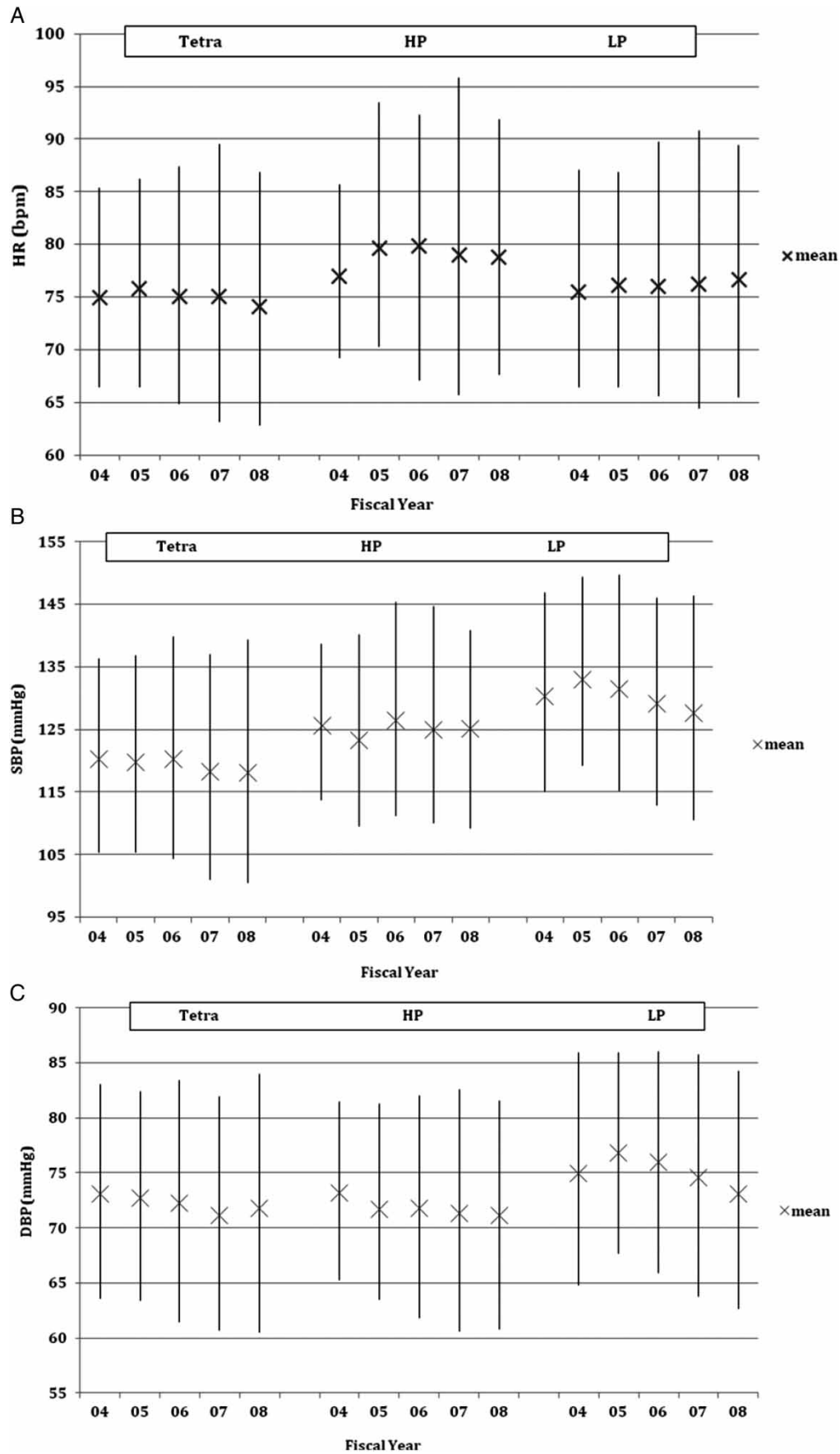


Figure 1 Distribution of mean, minimum, and maximum HR [A], SBP [B] and DBP [C] averaged across all years of observation [FY04-FY08].

**Table 6** Prevalence data for HR and BP abnormalities: all years

	T	HP	LP	
Clinical values				
HR (bpm)				
≤50	1.0%	0.5%	2.4%	
≤60	11.4%	1.6%	11.6%	1,3
≥80	32.1%	43.4%	36.5%	1
≥100	2.1%	4.4%	4.5%	
SBP (mmHg)				
≤90	7.2%	1.6%	0.6%	1,2
≤110	39.1%	23.5%	10.1%	1,2,3
≥140	14.9%	21.9%	24.0%	2
DBP (mmHg)				
≤60	17.5%	12.0%	7.1%	2
≥90	6.0%	2.2%	5.6%	
Diagnoses				
Arrhythmias	8.4%	15.8%	8.0%	1,3
Hypotension	0.3%	0.5%	0.0%	
Hypertension	39.1%	44.2%	59.6%	2,3
AD	6.9%	4.8%	0.0%	
OH	1.3%	0.5%	0.3%	

AD, autonomic dysreflexia; OH, orthostatic hypotension.  
1, T vs. HP; 2, T vs. LP; 3, HP vs. LP;  $P < 0.05$ , controlling for time.

to the T and LP groups. In addition, observation of a clinical value of a HR  $\geq 80$  bpm was significantly increased in the HP compared to the T group. Clinical values indicating a SBP  $\leq 90$  mmHg was significantly higher in the T compared to the HP and LP groups; prevalence of a SBP  $\leq 110$  mmHg was increased in the T compared to the HP and LP groups and was increased in the HP compared to the LP group. Prevalence of a SBP  $\geq 140$  mmHg was significantly increased in the LP compared to the T group. Prevalence of a DBP  $\leq 60$  mmHg was significantly higher in the T compared to the LP group, whereas prevalence rates for clinical value of a DBP  $\geq 90$  mmHg did not differ across study groups.

#### *Distribution of HR and BP: diagnoses*

The distribution of HR and BP diagnoses by ICD-9-CM codes is presented (Table 6). Diagnosis of cardiac arrhythmias was significantly higher in HP group than T and LP groups. On average the rate of hypertension diagnosis was significantly increased in the LP compared to the HP and T groups. Diagnosis of AD was not observed in any patient in the LP group, this diagnosis was relatively low and similar in the T and HP groups. Almost no diagnoses of hypotension or OH were recorded during the study period, regardless of categorical level of lesion.

#### *Multivariate results on patient characteristics associated with HR and BP categories*

We estimated the relationship between patient characteristic and HR, SBP and DBP abnormalities using

ordered logit models (Table 7). Reference groups include the T group; younger than 50 years; low-to-normal BMI; non-traumatic injuries; and white.

#### **Results on HR**

Estimates suggest that higher HR is more likely in the HP group compared to the T group and higher HR is more likely in individuals with the diagnosis of DM. Whereas patients with traumatic lesions, those prescribed anti-hypertensive medications and those with the diagnosis of CAD were significantly less likely to have higher HR.

#### **Results on SBP**

Compared to veterans in the T group, the likelihood of having higher SBP was significantly increased in the HP and LP groups. In addition, the likelihood of higher SBP increases with age in veterans with SCI, doubling (compared to those  $< 50$  years) for 50–64-year olds, quadrupling for those age 65–74 years, and increasing to more than six times for those 75 years or older. Compared to veterans with SCI in the low/normal BMI category, the likelihood of higher SBP more than doubled for those who were obese. Finally, patients prescribed medications with hypotensive side effects were significantly less likely to have high SBP compared to individuals not prescribed these medications.

#### **Results on DBP**

Compared to veterans in the T group, the likelihood of having higher DBP was significantly increased for LP group. Compared to younger veterans with SCI, the likelihood of having higher DBP was more than five



**Table 7** Ordered logit regression results for HR, SBP, and DBP abnormalities

		HR			SBP			DBP		
		OR	SE	P	OR	SE	P	OR	SE	P
Reference	Tetraplegia									
	HP	2.17	0.65	<0.05	1.84	0.54	<0.05	1.68	0.52	<0.1
	LP	1.59	0.45	<0.1	2.77	0.67	<0.01	1.91	0.56	<0.05
Reference	Non-trauma									
	Trauma	0.57	0.15	<0.05	1.08	0.31		1.42	0.46	
Reference	White									
	Black	0.77	0.19		1.38	0.30		1.50	0.40	
	Hispanic	1.01	0.42		1.15	0.39		1.12	0.50	
Reference	<50 years									
	50–64 years	1.29	0.50		2.28	0.69	<0.01	5.20	2.11	<0.01
	65–74 years	1.11	0.50		3.93	1.47	<0.01	3.43	1.30	<0.01
	+75 years	0.60	0.26		5.82	2.31	<0.01	2.52	1.08	<0.05
Reference	Under/normal									
	Overweight	0.78	0.18		1.28	0.28		1.13	0.28	
	Obese	0.73	0.22		2.21	0.61	<0.01	2.09	0.66	<0.05
Medications	Anti-hypertensive	0.73	0.16	<0.05	1.41	0.34		1.54	0.42	
	With hypertensive side effects	1.29	0.30		1.34	0.32		1.79	0.48	<0.05
	With hypotensive side effects	1.26	0.32		0.59	0.13	<0.01	0.93	0.25	
	With bradycardic side effects	0.89	0.23		1.06	0.22		0.77	0.18	
	With tachycardic side effects	0.82	0.19		0.84	0.23		0.80	0.25	
	Chronic Conditions									
	CKD	0.56	0.19	<0.1	0.93	0.58		0.53	0.33	
	CAD	0.52	0.15	<0.05	1.33	0.39		0.91	0.23	
	DM	1.68	0.39	<0.05	1.35	0.33		0.96	0.24	
	Duration of injury	0.99	0.01		0.99	0.01		0.98	0.01	<0.05
	Number of inpatient admits	1.08	0.06		0.98	0.07		1.05	0.07	

Analysis controlled for indicators for FY, all estimates were statistically insignificant.

times higher for those age 50–64 years, more than tripled for those age 65–74 years, and more than doubled for those 75 years or older. Being obese was significantly associated with higher DBP compared to low/normal weight veterans with SCI.

## Discussion

We examined the prevalence of HR and BP abnormalities documented in the medical records among veterans with SCI and the findings suggest: (1) those in the HP group had increased HR across the 5-year observation compared to those in the T group, in addition the prevalence of a HR  $\leq$  60 bpm was reduced and the prevalence of a HR  $\geq$  80 bpm was increased compared to those in the T and LP groups; (2) SBP and DBP were significantly lower and the prevalence of a SBP which meets the WHO definition of hypotension was increased in the T compared to the HP and LP groups and was increased in the HP compared to the LP group; (3) diagnosis of hypotension was less than 1% for all study groups and evidence for prescription of anti-hypotensive medications reflected this low diagnosis rate; yet (4) prevalence of a SBP  $\geq$  140 mmHg was increased in the LP compared to the T group, and diagnosis of hypertension was significantly increased in the LP compared to

the T and HP groups; however, use of prescription anti-hypertensive medications was comparable among the groups; (5) the increased odds ratio of higher SBP and DBP with increasing chronological age and BMI are important clinical findings that warrant further investigation in the SCI population; and (6) regardless of the level of lesion 84% of veterans with SCI are 50 years of age or older, which has significant implication on the clinical management of these individuals to optimize health and longevity.

This is the first retrospective chart review to examine HR across a 5-year time span in veterans with SCI. Although diagnostic codes for HR were not available, clinical data confirm a relatively high prevalence of resting HRs  $\geq$  80 bpm among these veterans. Increased resting HR has been reported in individuals with paraplegia from clinical observations,<sup>18</sup> and we recently conducted a 24-hour study to examine circadian rhythms in individuals with SCI compared to age-matched non-SCI controls.<sup>19</sup> Our data indicate that daytime HR was significantly increased in the HP and LP groups compared to the T and control groups; nighttime HR remained significantly elevated in the LP group.<sup>19</sup> A recent meta-analysis of observational studies on the influence of spinal cord lesion on cardiovascular outcomes failed

to document substantial evidence of elevated HR in those with HP, which may reflect the relatively small representation of studies that reported findings in individuals with a high thoracic lesion (T1–T6).<sup>11</sup> It is reported that persistently elevated HR tends to augment systolic blood flow pulsatility resulting in endothelial dysfunction<sup>20</sup> and increased AS.<sup>14</sup> There is a growing body of literature which reports associations between chronically elevated HR and increased AS, reflecting autonomic imbalance,<sup>21,22</sup> which may have direct relevance to decentralized autonomic cardiovascular regulation in SCI population. Cross-sectional data have identified an association between large vessel stiffening and HR,<sup>14,23</sup> and a longitudinal observation found that increased resting HR was a powerful predictor of the accelerated progression of pulse wave velocity (i.e. surrogate of AS). Thus, individuals with paraplegia with persistently elevated HR may have accelerated vessel degeneration with negative implication on cardiovascular and cerebral vascular function.

There is controversy with regard to the specific threshold below which hypotension should be defined, whether chronic hypotension exists,<sup>24</sup> whether it is a problem or, quite possibly, a benefit to longevity and cardiovascular health.<sup>25–28</sup> However, in 1927, Norris described individuals with low BP as persons who lacked stamina, tired easily, complained of cold extremities, and showed an inability to do prolonged mental or physical work;<sup>29</sup> characteristics very familiar to individuals with high cord lesions. The prevalence of hypotension in our veterans varied significantly depending on which definition was used, and while the diagnosis of hypotension based on a BP  $\leq 90/60$  mmHg was very low (<1%), evidence of clinical BP values below the WHO threshold (i.e. SBP  $\leq 110$  for males and  $\leq 100$  for females) was much higher (10–39%), and persistent hypotension below this threshold has been associated with adverse outcomes in the general population.<sup>30–34</sup> Although several papers suggest that hypotension is the ideal “normal” BP,<sup>26,28</sup> the British Journal of Medicine published a series of papers on the potential association between low BP and mood disorders.<sup>30,33–35</sup> The findings suggest significant associations between hypotension and increased incidence of depression,<sup>30,36–42</sup> anxiety,<sup>38,39</sup> unexplained tiredness,<sup>30,33</sup> and poor perception of well-being.<sup>34</sup> In addition to adverse mood changes, hypotension is also associated with cognitive dysfunction: compared to matched-normotensive controls, individuals with hypotension are reported to have slowed cognitive speed,<sup>43</sup> fewer word recall,<sup>44</sup> decreased accuracy of response,<sup>31</sup> limited attention,<sup>44</sup> and reduced memory and

concentration capacity.<sup>31,32</sup> It should be noted that the threshold used to define hypotension varied among these studies; however, all papers adhered to a threshold above 90/60 mmHg. Therefore, defining and diagnosing hypotension should be a priority in the clinical management of veterans with SCI because nearly one-quarter of the population met the WHO definition of hypotension but less than 1% was prescribed an anti-hypertensive agent or carried a diagnosis of hypotension.

Although the prevalence of a DBP  $\geq 90$  mmHg was relatively low among the study cohort, the observation of a SBP  $\geq 140$  mmHg was more common and nearly one-quarter of the LP group met this criterion. Further, nearly 50% of our sample carried the diagnosis of hypertension and more than 50% were prescribed anti-hypertensive medications. It must be appreciated that a direct association between clinical values indicative of hypertension and a diagnosis was not expected due to appropriate clinical management of the disease. That said diagnosis rates for hypertension were surprisingly high in the T and HP groups, which may reflect the systematic utilization of computerized clinical reminders to apply evidence-based practices in preventive care and chronic disease management adopted by the Veteran Administration.<sup>45–47</sup> However, in special populations such as SCI, the effectiveness of the automatic application of these criteria has not been examined. The discrepancy between the prevalence of the diagnosis of hypertension and the diagnosis of AD in the T (39 vs. 7%, respectively) and HP groups (44 vs. 5%, respectively) was also surprising. The incidence of AD has been reported to be between 48 and 90% during rehabilitation in individuals with tetraplegia and HP (above T6),<sup>48–50</sup> and the prevalence increases with time post-injury.<sup>49</sup> The reduced prevalence of the diagnosis of AD in the T and HP groups may reflect the infrequent occurrence of the signs and symptoms during routine physical. It is also possible that when extreme, less “acceptable” values were observed in the clinical setting, measurements were re-taken and more “acceptable” values recorded. Furthermore, the expected BP elevation during provocative screenings (i.e. urodynamics and colonoscopy) is often treated immediately but not documented in the medical record as a diagnosis.

Current literature in the general population suggests that BP increases with age<sup>51–53</sup> and a study in a Japanese community reported that there was a 0.32 mmHg/year increase in SBP from ages 24–79 years.<sup>54</sup> In normal aging, increasing SBP is associated with increased hazards ratio of coronary heart disease,<sup>55</sup> and increased incidence of white matter

hyperintensities on neuro-imaging of the brain.<sup>52</sup> In an aging population high BP is one of the most important risk factors for stroke,<sup>56,57</sup> and a recent paper reported that incidence of stroke was 5-fold increased in patients with SCI compared to age-, sex- and propensity score-matched controls, and the incidence of ischemic stroke was higher than that of hemorrhagic stroke.<sup>58</sup> Mortality risk from stroke was significantly increased in individuals with a 10 mmHg increase in SBP in higher BMI categories.<sup>56</sup> The finding of significantly increasing odds ratio of high SBP and DBP with increasing age in veterans with SCI may have implication for increased incidence of CHD, and two recent studies reported significantly increased CVD risk in individuals with paraplegia compared to age-matched controls.<sup>59,60</sup> The significant age- and BMI-associated increases in BP documented here in veterans with SCI should be studied in more depth through longitudinal observation.

### Study limitations

These data represent the medical record over a 5-year period among veterans with SCI at one urban VAMC and may not represent veterans or non-veterans in other geographic locations. Very few female veterans were represented in the medical record (<2%); therefore extrapolation of these results to a female SCI population is precluded. Limitations inherent in retrospective studies, which include but are not limited to: incomplete or inaccurate documentation, variation in interpretation of data and missing data verification, should be considered when interpreting our results. However, previous studies have shown that coding in the VA medical data sets are generally reliable.<sup>61</sup> Inaccuracies in data entry or diagnostic coding in the medical records cannot be accounted for in this retrospective review and we acknowledge that if a HR or BP recording seems out-of-the-ordinary, the clinic nurse may not record the value, which would contribute to an underestimation of these abnormalities in the medical record. Neurological classification of injury was limited to the level of lesion; reliable information on the completeness of injury or AIS classification was not available in the medical record during the study period, although a recent report suggests that completeness of motor and sensory innervation does not correlate with the autonomic completeness of lesion.<sup>62</sup> Because clinical data may fluctuate over time, instead of a cross-sectional snapshot of patients we have used a longitudinal study design and included data from multiple years on a set of relatively stable VA-users of veterans with SCI. In our multivariable analysis effects of secular changes over time, e.g. transition from manual data entry to

electronic data recording, were controlled for; therefore, unless these secular changes have differential effects on the outcomes, they should not bias our multivariate results. It should be noted that the relationships shown in this study are associations, not causations. Finally, distinction between AD and hypertension from the medical record was not clear and the data reported therefore must be interpreted with caution, particularly in those with lesions above T6.

### Conclusion

In veterans with SCI, the prevalence of HR abnormalities varied depending on level of lesion, prescription medication usage and coincident medical conditions; prevalence of BP abnormalities varied depending on the level of lesion, age, and prescription medication usage. While our results suggest association between these factors and not causation, prescription medication use and co-incident medical conditions should be considered when documenting these vital signs in the medical record in persons with SCI.

Although there is no consensus on the thresholds which should be used to define HR and BP abnormalities, we recommend clinical documentation of HR and BP in association with the concurrent medication use and medical conditions, due to the significant associations documented herein, along with demographic and lesion-specific information, for long-term tracking of these vital signs in the SCI population. Until there is an evidence-based consensus on the definitions of HR and BP thresholds, distinguishing specific abnormalities among individuals with SCI will remain elusive. However, it must be appreciated that before safe and effective approaches to the management of the secondary medical complications becomes a routine part of clinical practice, we need a better understanding of the prevalence of these abnormalities in the SCI population.

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