Autonomic Cardiovascular Control in Paralympic Athletes with Spinal Cord Injury

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ABSTRACT

WEST, C. R., S. C. WONG, and A. V. KRASSIOUKOV. Autonomic Cardiovascular Control in Paralympic Athletes with Spinal Cord Injury. *Med. Sci. Sports Exerc.*, Vol. 46, No. 1, pp. 60–68, 2014. **Introduction**: Disruption of autonomic control after spinal cord injury (SCI) results in life-threatening cardiovascular dysfunctions and impaired endurance performance; hence, an improved ability to recognize those at risk of autonomic disturbances is of critical clinical and sporting importance. **Purpose**: The objective of this study is to assess the effect of neurological level, along with motor, sensory, and autonomic completeness of injury, on cardiovascular control in Paralympic athletes with SCI. **Methods**: Fifty-two highly trained male Paralympic athletes (age, 34.8 ± 7.1 yr) from 14 countries with chronic SCI (C2–L2) completed three experimental trials. During trial 1, motor and sensory functions were assessed according to the American Spinal Injury Association Impairment Scale. During trial 2, autonomic function was assessed via sympathetic skin responses (SSR). During trial 3, cardiovascular control was assessed via the beat-by-beat blood pressure response to orthostatic challenge. **Results**: Athletes with cervical SCI exhibited the lowest seated blood pressure and the most severe orthostatic hypotension ($P < 0.025$). There were no differences in cardiovascular function between athletes with different American Spinal Injury Association Impairment Scale grades ($P > 0.96$). Conversely, those with the lowest SSR scores exhibited the lowest seated blood pressure and the most severe orthostatic hypotension ($P < 0.002$). Linear regression demonstrated that the combined model of neurological level and autonomic completeness of SCI explained the most variance in all blood pressure indices. **Conclusion**: We demonstrate for the first time that neurological level and SSR score provide the optimal combination of assessments to identify those at risk of abnormal cardiovascular control. We advocate the use of autonomic testing in the clinical and sporting classification of SCI athletes. **Key Words:** TETRAPLEGIA, PARAPLEGIA, EXERCISE, BLOOD PRESSURE, SYMPATHETIC SKIN RESPONSE

BASIC SCIENCES

Cardiovascular complications after spinal cord injury (SCI) have been well documented in humans and animal models (11,18). One of the most critical determinants of cardiovascular dysfunction after SCI is the degree of descending vasomotor control that remains intact after injury (14). Studies in rodents and humans have demonstrated that descending vasomotor pathways are primarily in the dorsal aspect of the lateral funiculus (8,24,26,27). Because the majority of SCI results from compression and contusion (12) rather than complete transection, it is plausible that the dorsolateral aspects of the cord may remain intact and provide some descending vasomotor control even in the face of neurologically (motor and sensory) complete SCI. In this respect, we have recently reported inconsistencies between motor/sensory completeness of injury and autonomic completeness of injury in patients with SCI (4). The concept of autonomic completeness of injury has only recently emerged in the literature; hence, the majority of studies that have reported physiological responses of patients or athletes with SCI have typically not accounted for autonomic completeness of injury in their study cohort (22,36). Instead, investigators tend to group individuals by clinical or sporting classification. The current clinical and sporting assessments of SCI are predominantly based on motor and sensory functions and therefore examine only the integrity of the corticospinal tract (motor function), the spinothalamic tract (pinprick sensation), and the dorsal columns (light touch) (13). Hence, the integrity of vasomotor pathways is currently not assessed during either clinical or sporting classification.

The identification of individuals with intact vasomotor pathways is of critical sporting importance. We recently reported that Paralympic wheelchair rugby athletes who had partially or fully intact descending vasomotor control were able to perform markedly better during tests of aerobic capacity and endurance performance (38). Furthermore, disruption of descending vasomotor control appears to be a prerequisite for impaired blood pressure control (orthostatic hypotension (OH) and autonomic dysreflexia) (19). Accordingly, we believe that tests of autonomic function may help

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identify whether a particular athlete can gain a physiological benefit from intentionally inducing autonomic dysreflexia during competition, a practice known as boosting (16). Boosting is currently banned by the International Paralympic Committee because of both the unfair performance advantage (29) and more importantly the risks it poses to athletes' health (see the succeeding part of this article). Unfortunately, identifying those athletes who boost is difficult because a "boosted" blood pressure can still be within normal limits because of severe resting hypotension in this population (37). In a recent investigation into the incidence of boosting in Paralympic sport, it was reported that approximately 20% of surveyed athletes self-reported boosting during competition (1). An improved ability to identify those athletes who could boost is clearly required.

In addition to the direct sporting significance of being able to identify those at risk of autonomic cardiovascular dysfunction, there are also clinical benefits. For example, individuals with SCI are tasked with the daily problem of managing unstable blood pressure, which is characterized by periods of marked hypotension (5) and instances of severe hypertension during autonomic dysreflexia (19). Hypotension and autonomic dysreflexia usually coexist and can result in sequelae of life-threatening consequences (7,10). Also, during the last decade, cardiovascular diseases have emerged as the number one cause of morbidity and mortality among individuals with SCI (9,23). It is proposed that altered cardiovascular control and frequent alterations in blood pressure during autonomic dysreflexia may contribute to this heightened risk of cardiovascular disease (36). Thus, recognition of those individuals who are at risk of cardiovascular dysfunction could vastly improve their overall health and well-being.

The importance of reliable documentation of autonomic function in the SCI population has started to be recognized clinically, where standards to document remaining autonomic function are now in place (17). Although this is a step in the right direction, there is still no validated physiological assessment to determine autonomic completeness of SCI in the clinical setting. In the sporting setting, there is neither any documentation of autonomic function nor a test for autonomic completeness of injury. This lack of testing is likely due to the dearth of knowledge regarding the incidence of abnormal cardioautonomic control in Paralympic athletes, the lack of an easy-to-use bedside assessment of autonomic function, and a poor understanding of the factors that cause disordered cardioautonomic control. To address this shortcoming, the primary aim of the present study was to conduct a cross-sectional analysis of blood pressure control in Paralympic athletes with SCI. A secondary aim was to investigate whether autonomic testing may provide a useful adjunct to the classification of Paralympic athletes. We hypothesized that Paralympic athletes with SCI would exhibit a neurological level-dependent and autonomic completeness of injury-dependent impairment in cardiovascular function. We also hypothesized that the combined knowledge of neurological level and autonomic completeness of injury would provide the strongest estimate of impaired blood pressure regulation in this population.

METHODS

Participants

All procedures were approved by the institutional ethics committee and the International Paralympics Committee. All participants provided written informed consent. A total of 52 male Paralympic wheelchair athletes with SCI (C4–L1, American Spinal Injury Association Impairment Scale (AIS) A–D; age, 34.8 ± 7.1 yr, 15.8 ± 7.9 yr postinjury) volunteered to take part in the study. All participants represented their country at the London 2012 Paralympic Games, competing in wheelchair rugby (n = 26), wheelchair basketball (n = 10), track and field (n = 8), wheelchair tennis (n = 5), and swimming (n = 3). None of the participants smoked or had a history of cardiopulmonary disease. Some participants were taking medication for spasticity (Baclofen, n = 8) and overactive bladder (Ditropan, n = 13). Participants had been training for their relevant sport for at least 3 yr and took part in regular exercise training of at least 10 $h \cdot wk^{-1}$ (range, 10–32 $h \cdot wk^{-1}$). Training varied between sports but primarily consisted of sports-specific training along with general conditioning sessions.

Experimental Design

All measurements were made during one visit to the cardiovascular health clinic at the London 2012 Paralympic Games. Participants were assessed on noncompetition days. On arrival at the laboratory, participants were asked to void their bladder and fill out a questionnaire relating to their injury. Participants were also asked to self-report incidence of autonomic dysreflexia; specifically, they were asked, "Do you have any episodes of autonomic dysreflexia, a condition where your blood pressure rises very fast, usually resulting in symptoms such as severe headache, sweating, excessive spasms, hot/cold flushes, and nasal congestion?" To determine the effect of neurological level, motor/sensory completeness of injury, and autonomic completeness of injury on cardiovascular function, participants completed three experimental trials. Trial 1 consisted of motor/sensory examination for the determination of AIS grade. Trial 2 consisted of an electrophysiological assessment of the integrity of autonomic pathways via recordings of sympathetic skin responses (SSR). Trial 3 consisted of a cardiovascular assessment via beat-by-beat arterial blood pressure measurements at rest and during orthostatic stress (15). Participants were required to avoid caffeine for 4 h and food for 2 h before assessment.

Methods of Measurement

Motor and sensory assessment. Neurological classification was conducted according to the International Standards for Neurological Classification of Spinal Cord

Injury (ISNCSCI) to determine AIS grade and neurological level of injury (the last spinal cord segment with full preserved sensory and motor function) (13). The ISNCSCI classification examines motor function (integrity of corticospinal tracts) along with pinprick (integrity of spinothalamic tract) and light touch sensation (integrity of dorsal columns). Individuals are then classified into one of five categories: motor and sensory complete (AIS A), motor complete and sensory incomplete (AIS B), motor and sensory incomplete (AIS C–D), and normal motor and sensory functions (AIS E). Neurological classification of SCI was conducted by one of the authors who has >20 yr of experience in the neurological classification of individuals with SCI.

SSR. Participants rested supine, with room temperature maintained at 23°C. After a 10-min rest, SSR was obtained by electrical stimulation of the median nerve at the wrist. To ensure that SSR reflected the integrity of the sympathetic nervous system rather than the integrity of the peripheral nerve, we also collected SSR in response to deep inspiratory maneuvers (33). The SSR measures changes in skin conductance after activation of sweat glands in response to various stimuli, such as peripheral nerve stimulation or acoustic stimulation (3). In this respect, the SSR tests the integrity of the sympathetic cholinergic pathways and acts as a proxy for the integrity of descending autonomic pathways (34). Self-adhesive recording electrodes were applied bilaterally to the palmar and dorsal cervices of the hands and feet. SSR was recorded simultaneously from both hands and feet for 8 s and sampled at a band pass of 3 Hz to 3 kHz. To minimize the well-known habituation and adaptation of these responses, stimuli were applied in random order and with variable time delays (minimum delay, 90 s) (2). An SSR was deemed present when there was a clear positive deflection from baseline. Any potential that coincided with muscle spasm, limb movement, or cough was excluded from the analysis. Five recordings with stimulations (0.2-ms duration, 10- to 20-mA intensity) at each site were obtained. Similarly, five recordings were obtained at each site in response to deep inspiration, where participants were asked to breathe in quickly and deeply. Responses to median nerve stimulation and deep inspiration were quantified by the number of SSR elicited at each site (20), and the average across all four sites was reported. Data were continuously collected using an analog-to-digital converter (PowerLab/16SP model ML795; ADInstruments, Colorado Springs, CO) interfaced with a computer and stored for subsequent offline analysis (PowerLab version 7.2, ADInstruments). Because of technical difficulties with our SSR machine, we only collected SSR data on 40 athletes.

Baseline cardiovascular assessment. Participants were asked to transfer to the supine position for the measurement of baseline blood pressure and HR. Once supine, participants were fitted with a one-lead ECG and a finger plethysmograph (Finometer; Finapres Medical Systems BV, Arnhem, The Netherlands) for the beat-by-beat assessment of HR and arterial blood pressure, respectively. An automated blood pressure cuff (DINAMAP PRO 300V2; GE Medical Systems Information Technologies, Tampa, FL) was also fitted over the brachial artery and inflated every minute to calibrate the finger plethysmograph. Supine HR, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded during 10 min of rest using an analog-to-digital converter (PowerLab/16SP Model ML795, ADInstruments) interfaced with a computer. Data were stored for subsequent offline analysis (PowerLab version 7.2, ADInstruments).

Orthostatic challenge (sit-up test). After 10 min of baseline recordings, HR, SBP, and DBP were assessed during a 10-min sit-up test (4). Briefly, participants were moved to an upright seated position with the legs hanging off the side of the bed at 90°. This "sit-up" position mimics that experienced while seated in a wheelchair, except the lower legs and feet are unsupported. Participants were instructed to not assist in the "sit-up" procedure. The change (delta) in SBP between supine and seated SBP was used to determine the severity of OH. The cutoff for determining the presence or absence of OH was a ≥20 mm Hg reduction in SBP on assumption of the upright position (6). The test was terminated prematurely if the participant exhibited signs of presyncope. HR and blood pressure data were averaged over 30-s intervals, and the largest reduction in blood pressure was used to define the presence or absence of OH.

Data Analyses

Multiple analyses were conducted to determine the effect of neurological level, motor/sensory completeness of injury (AIS grade), and autonomic completeness of injury (average SSR score) on blood pressure control. When participants were grouped by neurological level, the following designations were used: C3–C5, C6–C8, T1–T5, and T6–L2. When participants were grouped by AIS grade, the following designations were used: AIS A, AIS B, and AIS C–D. Further subanalyses were carried out by neurological level and motor/sensory completeness of injury for cervical individuals only (C3–C8, AIS A; C3–C8, AIS B; and C3–C8, AIS C–D). Finally, when participants were grouped by average four-site SSR score, the following designations were used: no preservation (score, 0–1), some preservation (score, 2–3), and full preservation (score, 4–5).

Statistics

A one-way ANOVA with Bonferroni-corrected pairwise comparisons was used to assess between-group differences in all continuous cardiovascular variables. Pearson χ^2 was used to assess between-group differences in self-reported autonomic dysreflexia and the relation between incidence of autonomic completeness and motor/sensory completeness of injury. The association between SSR score and delta SBP was assessed using the Spearman rank coefficient. Univariable and multiple linear regression were used to determine predictors of blood pressure. For linear regression, average SSR score and neurological level of injury remained as a three- and four-level categorical predictor, respectively. The SSR

TABLE 1. Effect of lesion level, American Spinal Injuries Association class, and SSR on cardiovascular parameters.

	n	SBP (mm Hg)			DBP (mm Hg)			HR (bpm)			Time to Onset of OH (min)
		Supine	Seated	Delta	Supine	Seated	Delta	Supine	Seated	Delta	
Level of injury											
C2–C5	13	115 ± 12	94 ± 17**,***	−21 ± 12**,***	66 ± 6	52 ± 9**,***	−14 ± 6**,***	63 ± 10	81 ± 11	18 ± 6	4.1 ± 1.4
C6–C8	19	116 ± 8	96 ± 15**,***	−20 ± 14**,***	64 ± 4	55 ± 9	−10 ± 8***	60 ± 10***	79 ± 13	20 ± 11***	5.2 ± 3.0
T1–T5	7	120 ± 6	117 ± 5	−4 ± 5	64 ± 4	63 ± 4	−2 ± 3	64 ± 3	74 ± 8	10 ± 6	N/A
T6–L2	13	124 ± 12	126 ± 12	1 ± 6	72 ± 10	71 ± 12	−1 ± 6	71 ± 8	83 ± 9	12 ± 5	N/A
AIS class											
AIS A	30	117 ± 10	106 ± 21	−10 ± 14	66 ± 7	59 ± 12	−7 ± 9	67 ± 8	82 ± 9*	15 ± 7**	4.0 ± 2.0
AIS B	15	116 ± 8	105 ± 12	−12 ± 13	67 ± 6	59 ± 9	−8 ± 6	59 ± 10	74 ± 9**	15 ± 6**	4.8 ± 1.9
AIS C–D	7	126 ± 16	105 ± 27	−21 ± 19	70 ± 14	61 ± 19	−9 ± 9	64 ± 13	88 ± 16	24 ± 15	6.3 ± 4.0
AIS class by lesion level											
Cervical AIS A	15	113 ± 10	92 ± 19	−21 ± 13	64 ± 5	51 ± 9	−14 ± 8	65 ± 9	83 ± 8	18 ± 7	4.0 ± 2.0
Cervical AIS B	11	115 ± 9	99 ± 9	−16 ± 12	66 ± 6	57 ± 9	−9 ± 6	56 ± 9	72 ± 10	17 ± 5	4.8 ± 1.9
Cervical AIS C–D	6	124 ± 5	98 ± 19	−26 ± 20	64 ± 4	53 ± 10	−11 ± 9	60 ± 13	86 ± 19	26 ± 17	6.3 ± 4.0
SSR score											
0–1	18	114 ± 9**	96 ± 14*,**	−18 ± 11*,**	66 ± 6	54 ± 9*,**	−12 ± 7*,**	64 ± 10	79 ± 12	15 ± 5	4.0 ± 1.9
2–3	14	120 ± 8	116 ± 11	−4 ± 8	68 ± 6	64 ± 7	−4 ± 6	64 ± 11	76 ± 11	13 ± 6	N/A
4–5	8	127 ± 14	127 ± 13	0 ± 6	72 ± 13	71 ± 15	0 ± 6	72 ± 6	83 ± 6	11 ± 6	N/A

Note that time to OH is reported only for athletes who developed OH according to clinical guidelines (6).
*Significantly different vs group 2 ($P < 0.05$).
**Significantly different vs group 3 ($P < 0.05$).
***Significantly different vs group 4 ($P < 0.05$).
N/A,not applicable because no individual developed clinically defined OH.

scores of the 4–5 group and the T6–L2 group were used as the reference groups within the multiple regression model. Statistical significance was accepted at $P < 0.05$. All analyses were conducted using Stata 12 (StataCorp, College Station, TX).

RESULTS

Effect of neurological level on cardiovascular and autonomic parameters. In the supine position, there were no differences in HR, SBP, or DBP between any groups (all $P > 0.057$, Table 1). In the seated position, SBP was lower in the cervical versus the thoracic groups (all $P < 0.005$). Seated DBP was lower in C2–C5 versus T1–T5 and T6–L2 ($P < 0.001$). Delta SBP in response to sit-up was greater in the cervical versus the thoracic groups ($P < 0.010$, Fig. 1); hence, there was a greater incidence of clinically defined OH in those with cervical ($n = 15$) versus thoracic SCI ($n = 0$, $P < 0.0001$). Incidence of self-reported autonomic dysreflexia differed significantly by neurological level ($P < 0.001$), being more common in cervical versus thoracic groups.

FIGURE 1—*Top panel*: SBP in response to sit-up test stratified by neurological level. *Vertical dotted line* denotes transition to upright posture. *Horizontal bar* denotes statistically different in cervical vs thoracic groups at those time points ($P < 0.05$). *Bottom panel*: Group mean ± 95% CI for the maximum change in SBP (ΔSBP) in response to sit-up test. Note that individuals with a cervical injury exhibited a greater degree of OH that reached statistical significance after 3 min of sit-ups.

TABLE 2. Group mean ± SD for the number of present SSR to median nerve stimulation and deep inspiration stratified by level of injury and motor/sensory completeness of injury.

		Median Nerve Stimulation				Deep Inspiration			
	n	Left Palmar	Right Palmar	Left Plantar	Right Plantar	Left Palmar	Right Palmar	Left Plantar	Right Plantar
Lesion level									
C2–C5	10	0.7 ± 1.6*,** (0–5)	0.9 ± 1.9*,** (0–5)	0 ± 0 (0–0)	0 ± 0 (0–0)	0.9 ± 1.9*,** (0–5)	0.9 ± 1.9*,** (0–5)	0 ± 0 (0–0)	0 ± 0 (0–0)
C6–C8	11	1.2 ± 1.9*,** (0–5)	1.3 ± 2.0*,** (0–5)	0.6 ± 1.5 (0–5)	0.3 ± 0.9 (0–5)	1.2 ± 2.0*,** (0–5)	1.0 ± 2.0*,** (0–5)	0.6 ± 1.6 (0–5)	0.5 ± 1.5 (0–5)
T1–T5	7	4.4 ± 1.1 (2–5)	4.3 ± 1.5 (1–5)	1.1 ± 2.0 (0–4)	1.1 ± 2.0 (0–4)	4.3 ± 1.6 (2–5)	3.7 ± 2.2 (1–5)	1.6 ± 2.3 (0–4)	1.4 ± 2.4 (0–4)
T6–L2	12	4.9 ± 0.3 (4–5)	4.9 ± 0.3 (4–5)	2.0 ± 2.3 (0–5)	1.8 ± 2.3 (0–5)	4.9 ± 0.3 (4–5)	4.9 ± 0.3 (4–5)	2.4 ± 2.4 (0–5)	2.0 ± 2.4 (0–5)
AIS class									
AIS A	24	3.2 ± 2.2 (0–5)	3.3 ± 2.2 (0–5)	0.9 ± 1.7 (0–5)	0.7 ± 1.6 (0–5)	3.0 ± 2.4 (0–5)	3.0 ± 2.4 (0–5)	1.0 ± 1.9 (0–5)	0.9 ± 1.8 (0–5)
AIS B	12	1.7 ± 2.4 (0–5)	1.6 ± 2.3 (0–5)	0.7 ± 1.6 (0–5)	0.7 ± 1.7 (0–5)	1.7 ± 2.4 (0–5)	1.7 ± 2.4 (0–5)	0.9 ± 1.7 (0–5)	0.8 ± 1.7 (0–5)
AIS C–D	4	3.3 ± 2.1 (0–5)	3.8 ± 2.5 (0–5)	2.0 ± 2.5 (0–5)	1.8 ± 2.1 (0–4)	3.0 ± 2.4 (0–5)	2.9 ± 2.4 (0–5)	2.5 ± 2.8 (0–5)	2.5 ± 2.9 (0–5)

Note that the maximum score is 5 for each site. Values in parentheses represent the range.
*Significantly different vs T1–T5 ($P < 0.05$).
**Significantly different vs T6–L2 ($P < 0.05$).

Delta HR was greater in C6–C8 versus T6–L2 ($P = 0.041$). Univariable regression analyses revealed that neurological level significantly predicted seated SBP ($r^2 = 0.50$), seated DBP ($r^2 = 0.41$), delta SBP ($r^2 = 0.43$), and delta DBP ($r^2 = 0.43$).

There was also a neurological level-dependent impairment in SSR score whereby those in the C2–C5 or the C6–C8 group exhibited a lower average SSR score than those in either the T1–T5 or the T6–L2 group (all $P < 0.013$, Table 2). Within each neurological level group, however, there was a wide range of responses with some individuals exhibiting no SSR and others exhibiting complete preservation of SSR. There were no differences in the number of responses elicited by median nerve stimulation or deep inspiration. Only 10 individuals exhibited complete preservation of plantar SSR, and the majority ($n = 8$) of those were present only in individuals with an injury between T6 and L2. Two individuals with cervical SCI also exhibited an intact plantar SSR, both of whom were classified as AIS D. There was a positive correlation between delta SBP in response to sit-up and remaining SSR score (rho = 0.52, $P = 0.0001$).

Effect of motor/sensory completeness of injury on cardiovascular and autonomic parameters. In the supine position, there were no differences in SBP or DBP between AIS A, AIS B, and AIS C–D groups (all $P > 0.110$, Table 1). Similarly, there were no differences in either seated or delta SBP and DBP between different AIS groups (all $P > 0.26$), nor was there a between-group difference in incidence of clinically defined OH ($P = 0.405$). Incidence of self-reported autonomic dysreflexia was not different between AIS groups ($P = 0.839$). When we further analyzed completeness of injury by neurological level, there were still no differences in SBP, DBP, or HR in any position between cervical AIS A, cervical AIS B, and cervical AIS C–D groups (all $P > 0.87$). There were no differences in SSR score between participants in different AIS groups (all $P > 0.41$, Table 2). Motor/sensory completeness of injury was not related to autonomic completeness of injury (Table 3).

Effect of autonomic completeness of injury on cardiovascular parameters. In the supine position, participants with a 0–1 SSR score exhibited a lower SBP than those with an SSR score of 4–5 ($P = 0.023$, Table 1).

TABLE 3. Relation between incidence of autonomic completeness and motor/sensory completeness of injury.

	Autonomic Complete	Autonomic Incomplete
Total sample ($n = 40$)		
Motor/sensory complete	9	15
Motor/sensory incomplete	9	7
Cervical only ($n = 21$)		
Motor/sensory complete	8	1
Motor/sensory incomplete	9	3
Thoracic only ($n = 19$)		
Motor/sensory complete	1	4
Motor/sensory incomplete	0	14

Motor and sensory completeness of injury was assessed using the ISNCSCI. Autonomic completeness of injury was inferred from the presence (SSR score of 2–5, incomplete) or absence (SSR score of 0–1, complete) of an SSR to median nerve stimulation. There were no differences between groups in the total sample ($\chi^2 = 1.36$, $P = 0.24$) or when the sample was stratified by cervical ($\chi^2 = 0.64$, $P = 0.42$) or thoracic injury ($\chi^2 = 0.28$, $P = 0.59$).

On assumption of the seated position, those with an SSR score of 0–1 exhibited a lower SBP compared with those with an SSR score of 2–3 or 4–5 (both $P < 0.001$, Fig. 2); hence, delta SBP was greatest in those with 0–1 score versus both the other groups ($P = 0.001$), and those with an SSR score of 0–1 exhibited the highest incidence of clinically defined OH ($n = 8$) versus both the other groups ($n = 0$, $P = 0.001$). DBP was not different by SSR score in the supine position (all $P > 0.084$) but followed the same pattern in the seated position (all $P < 0.009$). HR was not different in any position. Incidence of self-reported autonomic dysreflexia differed significantly by SSR scores ($P = 0.002$), being most common in those with an SSR score of 0–1 and nonexistent in those with an SSR score of 4–5. Univariable regression analyses revealed that SSR group significantly predicted supine SBP ($r^2 = 0.19$), seated SBP ($r^2 = 0.51$), seated DBP ($r^2 = 0.33$), delta SBP ($r^2 = 0.44$), and delta DBP ($r^2 = 0.42$). To identify whether SSR provides a useful adjunct to neurological level alone, we conducted multiple linear regression (Table 4). For all blood pressure variables, the combined model of neurological level and SSR score explained more variance than either neurological level or SSR alone. We also found that SSR group significantly predicted seated SBP and delta DBP independent of neurological level.

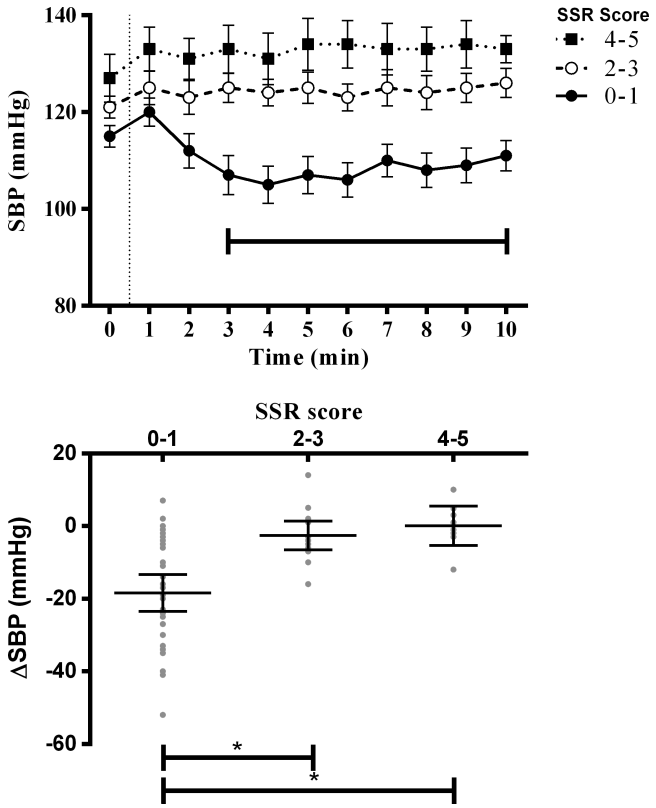

FIGURE 2—*Top panel*: SBP in response to sit-up test stratified by SSR (averaged over five stimulations at four sites). *Vertical dotted line* denotes transition to upright posture. *Horizontal bar* denotes statistically different in those with no remaining autonomic function (score 0–1) vs those with partial (score 2–3) or full (score 4–5) remaining autonomic function at those time points ($P < 0.05$). *Bottom panel*: Group mean ± 95% CI for the maximum change in SBP (ΔSBP) in response to sit-ups. Note that individuals with an autonomically complete injury exhibited a greater degree of OH that reached statistical significance after 3 min of the sit-up test.

TABLE 4. Summary of multiple linear regression.

	B	SE	CI (L, U)	*P* value
Seated SBP (0.64)				
Level of injury				
T6–L2	Ref			
T1–T5	−7.4	5.6	−18.8, 4.0	0.196
C6–C8	−15.5	6.8	−29.3, −1.6	0.029
C2–C5	−24.1	6.9	−37.9, −10.1	0.001
SSR score				
4–5	Ref			
2–3	−7.9	5.2	−18.5, 2.7	0.130
0–1	−16.1	6.9	−30.1, −2.0	0.026
Delta SBP (0.59)				
Level of injury				
T6–L2	Ref			
T1–T5	−3.3	4.1	−11.7, 5.0	0.425
C6–C8	−9.4	4.9	−19.5, 0.6	0.067
C2–C5	−16.5	5.0	−26.7, −6.2	0.002
SSR score				
4–5	Ref			
2–3	−2.0	3.8	−9.8, 5.8	0.606
0–1	−8.1	5.1	−18.5, 2.1	0.115
Seated DBP (0.48)				
Level of injury				
T6–L2	Ref			
T1–T5	−7.5	4.4	−16.6, 1.5	0.100
C6–C8	−10.6	5.4	−21.5, 0.4	0.058
C2–C5	−16.7	5.4	−27.8, −5.7	0.004
SSR score				
4–5	Ref			
2–3	−5.7	4.1	−14.1, 2.7	0.177
0–1	−7.4	5.4	−18.6, 3.6	0.180
Delta DBP (0.58)				
Level of injury				
T6–L2	Ref			
T1–T5	−3.3	4.1	−11.7, 5.0	0.425
C6–C8	−9.4	4.9	−19.6, 0.7	0.067
C2–C5	−16.5	5.0	−26.7, −6.2	0.002
SSR score				
4–5	Ref			
2–3	−1.9	3.8	−9.8, 5.8	0.606
0–1	−8.1	4.0	−18.8, −0.1	0.047

Delta, change in blood pressure between supine and seated position. Note that italicized values in parentheses reflect adjusted r^2 values for the combined model.
B, coefficient; CI, confidence interval; L, lower CI; U, upper CI; ref, referent.

DISCUSSION

The novel finding of the current study is that the addition of autonomic testing to neurological level alone improves the ability to predict those at risk of impaired blood pressure control. Furthermore, in the largest cross-sectional analyses of cardiovascular and autonomic function of Paralympics athletes to date, we show that autonomic completeness of injury is closely related to abnormal cardiovascular control, independent of neurological level and motor/sensory completeness of injury.

Blood pressure control. We report a neurological level-dependent impairment in blood pressure control, whereby athletes with cervical injuries exhibit a lower seated SBP, a greater delta SBP, and a higher incidence of clinically defined OH than those with thoracic injury. Interestingly, we found no difference in SBP during supine rest between groups of different injury levels. This finding is different from our recent meta-analysis (37) and our previous study

in untrained individuals with SCI (4), both of which demonstrated that individuals with cervical SCI have a lower resting supine SBP than those with thoracic injuries. It is possible that the regular exercise training undertaken by the Paralympic athletes in the current study resulted in improved resting blood pressure compared with that typically reported in the untrained patient population. Alternatively, the athletes in the current study may have succeeded in reaching the peak of Paralympic performance because they have enhanced cardiovascular function compared with the wider SCI population. Within the first 5 min of sit-up, athletes with cervical SCI exhibit a high incidence of clinically defined OH, which is consistent with that in the untrained population (4), suggesting chronic exercise training does not improve orthostatic intolerance. It is of note that athletes with a high thoracic injury did not exhibit OH. This is in agreement with our previous findings in the untrained population (4) but contradicts the general consensus in the literature that preserved central sympathetic control of the critical splanchnic bed (T6–T12) is required to maintain blood pressure in the upright posture (31,32). Although the majority of individuals with high thoracic SCI in the current study exhibited some preservation of descending autonomic control, it was limited to a palmar response. That no individual with high thoracic SCI exhibited a plantar SSR response suggests that the critical splanchnic bed was also likely devoid of supraspinal sympathetic input. This implies that other compensatory mechanisms allow these individuals to maintain blood pressure during orthostatic stress.

HR control. Athletes with cervical and high thoracic SCI exhibited resting supine bradycardia compared with individuals with low thoracic/lumbar SCI. This finding was anticipated in cervical individuals, but not in high thoracic individuals who are usually reported to exhibit a resting HR that is similar to uninjured individuals (37). Indeed, it has been previously reported in animal models of SCI that there is increased sympathetic activity in the portions of the thoracic spinal cord immediately rostral to the injury (21). Thus, one may expect an accelerated resting HR in individuals with a T1–T5 injury. Because exercise is known to reduce resting HR in able-bodied individuals (28), it is possible that the combination of partial interruption of descending sympathetic control and a history of chronic exercise training explains this finding. In response to sit-up, there was a greater tachycardia in those with cervical SCI compared with those with thoracic SCI, a finding that is presumably due to a greater loading of the arterial baroreflex. In the untrained SCI population, however, we reported that individuals with cervical and thoracic SCI exhibit a similar degree of tachycardia during orthostatic stress (4). This difference suggests that untrained individuals may exhibit dysfunction of the baroreflex, and exercise training may help to normalize such impairments. In agreement with this postulate, it has been consistently reported that baroreflex function is impaired after SCI (25); however, the effect of exercise on baroreflex function in the SCI population remains to be determined.

Effect of completeness of injury on autonomic cardiovascular control. Using histopathological techniques to examine axonal degeneration in the spinal cord, we have previously demonstrated that the degree of axonal loss in the area traversed by the descending vasomotor fibers is a critical determinant of the clinical severity of cardiovascular dysfunction (8). Although we make no histopathological measures in the present study, we used SSR score as a proxy for the integrity of the descending autonomic pathways. Similar to our findings for neurological level, those with an SSR score of 0–1 (autonomic complete) exhibited the lowest seated SBP, the greatest delta SBP, the highest incidence of clinically defined OH, and they self-reported the highest incidence of autonomic dysreflexia. Multiple linear regression revealed that the effects of SSR on seated SBP and delta DBP were independent of neurological level. This implies that in addition to neurological level, cardiovascular function/dysfunction after SCI is also dependent on the degree of autonomic sparing. It is of note that we found a similar seated SBP and no evidence of OH in those with partial (SSR score of 2–3) and full autonomic sparing (SSR score of 4–5), which suggests only a small amount of sparing is required to retain normal blood pressure control. This is consistent with findings in animal models, where rodents with high thoracic SCI that exhibit partial sparing of autonomic fibers do not get autonomic dysreflexia (35).

To examine the intricate relation between neurological level, autonomic completeness of injury, motor/sensory function, and cardiovascular function, we conducted multiple linear regression. Although neurological level was the strongest univariable predictor of abnormal blood pressure regulation, the additional knowledge of autonomic completeness of injury improved the ability to predict those at risk of abnormal blood pressure control. Conversely, there was no relation between any blood pressure variable and motor/sensory completeness of injury. This is reflected in our finding that motor/sensory completeness/incompleteness agrees with autonomic completeness/incompleteness only approximately 50% of the time (Table 3). This is intuitive, considering that the location of the tracts assessed during the ISNCSCI classification does not include assessment of the tracts that contain descending vasomotor and sympathetic cholinergic fibers.

Clinical and sporting significance. For individuals with cervical SCI, there was a large discord between motor/sensory completeness of injury and autonomic completeness of injury. For example, 10 out of 12 athletes with cervical SCI were classified as motor/sensory incomplete but were autonomically complete. Although this was improved in thoracic SCI, more than one in four athletes were still misclassified as having a complete/incomplete SCI on the basis of only the motor/sensory assessment. An autonomic complete injury implies an athlete may be at risk of disordered blood pressure control and impaired endurance performance and may partake in the dangerous practice of boosting. Thus, identifying

autonomic completeness of injury is critical for athlete health and for exercise performance. Previously, it has been shown that approximately 20% of Paralympic athletes with SCI self-reported boosting before competition (1). Our current finding that more than 60% of Paralympic athletes with SCI have an autonomically complete injury suggests that the true incidence of boosting may be higher than previously thought. We postulate that if autonomic completeness of injury was to be included into the sporting/clinical classification, then individuals at risk of disordered blood pressure control could be targeted with specific education about how to manage their blood pressure and the dangers of boosting. Also, incorporating such testing into sports classification could help to "level the playing field" and ensure athletes with a similar degree of autonomic dysfunction are classified into the same sporting class. To this end, we believe the addition of autonomic testing would provide a useful adjunct to the classification of wheelchair athletes, especially in those sports that incorporate a strong endurance component.

Limitations. Because this study was conducted during the London 2012 Paralympic Games, we were unable to specify that athletes did not take part in any physical activity for at least 24 h before measurements or were unable to restrict medication intake. Although we ensured all athletes were assessed on a noncompetition day, there is a small chance that prior exercise may have exerted a carry-over effect; however, we believe any effect would be minimal because, even in the hypertensive literature, it has been reported that any effects of prior exercise on resting blood pressure are usually abated within 12–16 h (30). A further potential limitation is that some of our athletes were taking Baclofen or Ditropan to manage spasticity and neurogenic bladder, respectively. Baclofen has been shown to lower blood pressure, and Ditropan may increase blood pressure; thus, it is possible that medication may have exerted an effect on blood pressure. To investigate this potential "medication effect," we conducted a subanalysis and compared those taking Baclofen versus no medication and Ditropan versus no medication by neurological level. We found no differences between any medication groups, suggesting any effect of medication was marginal and superseded by other predictors. Despite athletes remaining on Baclofen during the cardiovascular assessments, there were some instances of spasms during the sit-up test. These spasms, however, were rare and did not require the test to be interrupted, nor did they produce any noticeable alterations in hemodynamics as assessed with the Finometer.

CONCLUSIONS

In line with our hypothesis, we report for the first time that Paralympic athletes with SCI exhibit a neurological level-dependent and autonomic completeness-dependent impairment in blood pressure regulation, whereby those with the highest injuries and greatest disruption to autonomic control exhibit the most severe impairments in cardiovascular control. Knowledge of the degree of autonomic dysfunction may significantly improve the ability to predict those individuals most at risk of impaired blood pressure regulation and those who are most likely to gain a sporting benefit from boosting. We advocate the addition of autonomic testing to the sporting movement to help "level the playing field" for Paralympic athletes and to potentially prevent a life-threatening cardiovascular event related to SCI.

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