Exploring the associations between arterial stiffness and spinal cord impairment: A cross-sectional study

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Background/Objective: Elevated aortic arterial stiffness (aortic pulse wave velocity: aPWV) is an independent coronary artery disease predictor among the general population. The purpose of this study was to: (1) report aPWV values in a representative cohort of patients with spinal cord injury (SCI); (2) to compare aPWV values in people with SCI based on neurological level of injury; and (3) to contrast the reported aPWV values with available normal values for the general population.

Methods: Adults with chronic SCI ($n = 87$) were divided into two groups (TETRA group, $n = 37$ and PARA group, $n = 50$). aPWV and potential confounders of aPWV were assessed. Analysis of covariance was used for comparisons between groups and adjusted for the confounders. Subjects' aPWV values were contrasted with reference values for general population determined by "The Reference value for arterial stiffness" collaboration and prevalence of abnormal aPWV defined as greater than or equal to the age-specific 90th percentile was reported.

Results: Prevalence of abnormal aPWV in the cohort was 25.3%. After adjusting for covariates, the mean aPWV values were significantly different between two groups (TETRA: 8.0 (95% confidence interval (CI): 7.5–8.6) m/second, PARA: 9.0 (95% CI: 8.5–9.4) m/second, $P = 0.010$). The prevalence of abnormal aPWV was significantly higher in the PARA group (36%) compared to the TETRA group (11%) ($P = 0.012$).

Conclusions: One-quarter of the total cohort had an abnormal aPWV. Subjects with paraplegia had higher aPWV values and a higher frequency of abnormal aPWV than subjects with tetraplegia. Elevated aPWV in people with SCI, particularly those with paraplegia, may impart significant adverse cardiovascular consequences.

Keywords: Spinal cord injury, Tetraplegia, Paraplegia, Pulse wave velocity, Arterial stiffness, Coronary artery disease

Background

Coronary artery disease (CAD) is a leading cause of mortality in people with spinal cord injury (SCI)¹. CAD tends to develop earlier among individuals with SCI, than their age- and sex-matched peers in the general population.^{1–3} Stiffening of the aortic artery is an emerging risk factor for CAD.⁴ Decreases in arterial elasticity lead to a reduction in the buffering capacity of the vascular system. Consequently, abnormal arterial stiffness results in increased pulse pressure, aortic

impedance, and left ventricular wall tension. This augmentation of the heart's workload is thought to lead to an increase in CAD risk.⁵

Pulse wave velocity (PWV), especially aortic PWV (aPWV, carotid-femoral PWV) is considered the current clinical "gold standard" measurement of arterial stiffness.⁶ PWV is the speed at which the pulse travels along the length of an artery, and it is largely determined by elastic properties of the artery.⁷ aPWV is an important independent risk factor for CAD mortality, non-fatal coronary events, and fatal strokes among patients with traditional cardiovascular risk factors and healthy people.^{4,8–11} Several authors have reported

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that people with SCI have increased arterial stiffness compared to able-bodied controls.^{12–14} However, it is unknown if the frequency and severity of elevated or abnormal arterial stiffness are associated with the individual's neurological impairment. The most common risk factors identified as determinants of aPWV in the able-bodied population are age and mean arterial pressure (MAP).¹⁵ Diabetes status, treatment for dyslipidemia, or hypertension has also been identified as risk factors for increased aPWV in the able-bodied population.¹⁵ In addition, heart rate (HR) is an independent determinant of aPWV.¹⁵ These same risk factors (dyslipidemia, high blood pressure, diabetes) are common among people with SCI,¹⁶ and their prevalence tends to be higher among individuals with tetraplegia compared to individuals with paraplegia except for high blood pressure and high HR.^{17–20} In addition, a majority of the literature on cardiovascular and autonomic function suggests that individuals with tetraplegia have impaired autonomic function,^{21,22} which may contribute to disordered cardiac regulation and abnormalities of the vascular system. This evidence implies that people with tetraplegia may have a greater predilection for elevated arterial stiffness, leading to future development of CAD at a greater frequency when compared to individuals with paraplegia. However, a prior study has demonstrated that elevated HR, which occurs in people with paraplegia,^{20,23} is an independent risk factor of impaired arterial stiffness.²⁴ Rosado-Rivera *et al.*²⁰ reported that individuals with paraplegia experience elevated 24-hour HRs, compared to their peers with tetraplegia and able-bodied controls. These data imply that individuals with paraplegia may be at risk of abnormal arterial stiffness, and the degree of abnormality may be more severe than among individuals with tetraplegia, due to the chronic elevations in HR among paraplegic individuals. In fact, there is evidence suggesting that the relative risk of CAD is 70% greater in those with chronic paraplegia compared to chronic tetraplegia.²⁵ In addition, there is evidence suggesting that people with paraplegia have an increased risk for silent ischemia²⁶ and CAD.²⁷

The purpose of this study was (1) to describe the range of aPWV values among a representative cohort of individuals with SCI in terms of neurological level of injury; (2) to determine if there are differences in arterial stiffness (aPWV) based on neurological level of injury among those with tetraplegia vs. paraplegia, before and after adjustment for potential covariates of aPWV; and (3) to compare their aPWV values with available normal values obtained from able-bodied subjects.¹⁵

Methods

Study design and population

This was a single-center cross-sectional observational study that was conducted at Lyndhurst Centre, Toronto Rehabilitation Institute – University Health Network, Toronto, Canada. We sought to recruit 100 subjects anticipating a 15% dropout rate and a final sample of 85. Consenting English-speaking subjects, ≥ 18 and < 80 years of age, with a stable spinal cord impairment (≥ 2 years post-injury, AIS A–D, C2–T12, with diverse non-traumatic and traumatic etiologies) were included. Subjects underwent medical screening, electrocardiogram, and chart review to ensure eligibility. Individuals with prior or current history of angina, myocardial infarction, atypical chest pain, coronary artery bypass, or prior revascularization, aortic stenosis, uncontrolled arrhythmia or left bundle branch block, hypertrophic cardiomyopathy, severe chronic obstructive pulmonary disease requiring oral steroids or home oxygen, diaphragmatic pacer, and prior stroke were excluded. This study was approved by the University Health Network Research Ethics Board.

Demographic, medical, and anthropometric data

Medical history, current medications, and height were collected through interviews and medical record data abstraction. Information regarding smoking status was collected by interview. Waist circumference was measured at the level of the lowest rib, in centimeters to the nearest decimal, using a non-elastic, flexible measuring tape in a supine position.²⁸ Body weight was measured wearing light clothing and no shoes, in kilograms to the nearest decimal place, using a Stathmos-Lindell Self-indicating Platform Scale (Model 513-417, Stathmos Scale Manufacturing Limited, Milliken, ON, Canada). Body mass index was defined as body mass divided by square of height (kg/m^2).

Arterial stiffness (aPWV)

Subjects were instructed to refrain from exercising 24 hours prior to aPWV testing, and to abstain from caffeine, nicotine, and food for at least 8 hours prior to testing. All PWV data were obtained by two trained technicians in a temperature-controlled room (24°C) between 9:00 A.M. and 1:00 P.M. Following transfer onto a bed, the subject was asked to rest for 20 minutes in the supine position before blood pressure and HR measurements. Brachial systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a mercury sphygmomanometer. Mean blood pressure was calculated as $\text{DBP} + 1/3(\text{SBP} - \text{DBP})$. HR was recorded

using an automated HR monitor (UA-767 Digital blood pressure monitor; Omron, Inc., Tokyo, Japan). Two consecutive blood pressure and HR measures separated by at least 1 minute were averaged. Following blood pressure and HR measurements, waveforms of common carotid artery and common femoral artery were collected simultaneously via two applanation tonometers (SPT-301; Millar Instruments Inc., Houston, TX, USA) or two identical transcutaneous Doppler flowmeters (Smartdop50, Hadeco, Inc., Kanagawa, Japan) to assess aPWV. Doppler flowmeters were used during data collection for the first 12 subjects prior to obtaining the applanation tonometers. In addition, if the pulse waveform could not be detected using applanation tonometry, due to adipose tissue in the region of interest or weak pulse pressure, Doppler flowmeters were used instead ($n = 11$). In total, aPWV data collection for 23 of 87 subjects were obtained using Doppler flowmeter. Transcutaneous blood flow waveforms were recorded using a data acquisition system (Power Lab/16SP; AD Instruments, Inc., Bella Vista, Australia) for subsequent analysis. The blood flow waveform was bandpass filtered (2–30 Hz) and the foot of the blood flow waveform (the start of the sharp systolic upstroke) was identified as the minimum values of the filtered signal.^{29,30} A minimum of 20 simultaneously recorded waveforms were analyzed to determine the pulse transit time between the measurement sites. The distance between the two recording sites was measured across the surface of the body with a non-elastic tape measure. aPWV (m/second) was then calculated using the equation: $(0.8 \times D)/\Delta t$, where D is the distance between measurement sites and Δt is the pulse transit time.³¹ Intra-class correlation of aPWV values obtained with the applanation tonometers vs. the Doppler flowmeters in able-bodied people in our laboratory is $r = 0.968$ ($P < 0.001$). The high test–retest reliability of the aPWV assessments in our laboratory has been confirmed.²⁹ An abnormal aPWV was defined as a standard aPWV above the age-specific 90th percentile of healthy, able-bodied subjects: <30 years: 7.1 m/second, 30–39 years: 8.0 m/second, 40–49 years: 8.6 m/second, 50–59 years: 10.0 m/second, 60–69 years: 13.1 m/second, >70: 14.6 m/second.¹⁵

Diagnosis of metabolic syndrome

Fasting plasma blood glucose, total cholesterol, high-density lipoproteins cholesterol (HDL-C), low-density lipoproteins cholesterol, triglycerides, waist circumference, and resting blood pressure were assessed to screen for metabolic syndrome (MS). The presence of MS or abnormalities in each component of MS were reported and diagnosed according to the criteria from

A Joint Interim Statement of the International Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity (Alberti *et al.*³²). MS component abnormalities were defined by the following criteria: elevated waist circumference >102 cm in men and >88 cm in women; abnormal blood pressure: SBP ≥ 130 mm Hg and/or DBP ≥ 85 mm Hg or the presence of antihypertensive drug therapy; reduced HDL-C: <1.0 mmol/l in men; <1.3 mmol/l in women, or pharmacotherapy for reduced HDL-C; elevated triglycerides: ≥ 1.7 mmol/l or pharmacotherapy for elevated triglycerides; elevated fasting glucose: ≥ 5.6 mmol/l or pharmacotherapy for elevated glucose. We could not specify which lipid disorders were targeted for pharmacotherapy with statin or niacin from the medical screening. Therefore, if subjects had normal HDL-C but were on statin monotherapy for dyslipidemia, we presumed that the treatment was for an abnormal HDL-C and categorized these subjects as having a reduced HDL-C as this is the most common lipid abnormality among individuals with SCI.³³ MS was defined as at least three or more of the above criteria. The total number of MS risk factors was also assessed. Blood chemistry tests were done in 81% (30 of 37) of the TETRA group and 92% (46 of 50) of the PARA group. Therefore, comparison of MS prevalence between the TETRA and PARA groups were completed for 87% (76 of 87) of the total cohort.

Statistical analysis

Statistical analyses were performed using SPSS software (version 20.0; IBM Corporation, Armonk, NY, USA). All continuous variables except for age at injury and duration of injury are expressed as mean $\pm$ SD and categorical variables as n (%). Age at injury and duration of injury are expressed as median, $\pm$ interquartile range because of their skewed distribution. As the influence of sex on aPWV was negligible,¹⁵ we conducted all statistical analysis combining the data for men and women. Differences between the TETRA and PARA groups were examined by Student's t -test for continuous variables except for age at injury and duration of injury and by Fisher's exact test for categorical variables. Differences between the TETRA and PARA groups in age at injury and duration of injury were calculated by Mann–Whitney U test. We compared the mean values of aPWV between TETRA and PARA groups by analysis of covariance (ANCOVA), with adjustment for potential cardiovascular covariates (i.e. age, sex, MAP,

HR, treated hypertension, treated lipidemia, and diabetes)¹⁵ and one SCI-specific covariate, injury severity (AIS A, B or C, D). Prevalence of abnormal aPWV was expressed by percentage and compared between groups using Fisher's exact test. $P < 0.05$ was considered statistically significant. Distribution of aPWV values according to the age categories (20–39, 40–59, and 60–80-year-old) $\times$ neurological level of injury and age $\times$ blood pressure categories (high blood pressure vs. normal blood pressure) are presented. High blood pressure in this analysis was defined by SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg or the presence of antihypertensive drug therapy.

Results

One-hundred and twenty-five individuals were screened. Of the 125 subjects, 100 individuals consented to participation. Of the 100 consented subjects, 10 subjects withdrew their consent and 3 subjects did not meet inclusion criteria. Consequently, 87 subjects met the inclusion criteria and underwent evaluations for aPWV and other cardiovascular parameters. Subjects included 37 with tetraplegia (TETRA: C2–C8, AIS A–D), 50 with paraplegia (PARA: T1–T12, AIS A–D).

Table 1 displays the demographic, anthropometric, and clinical impairment characteristics of the study subjects. Body weight and waist circumference in the TETRA group were significantly higher than that of the PARA group ($P < 0.05$). HR in the TETRA group was significantly lower than that of the PARA group

($P < 0.01$). There were no other significant baseline differences between the TETRA and PARA groups.

The mean aPWV values for the total cohort were 8.6 ± 2.2 m/second. Although it was not statistically significant, there was a trend in the PARA group, who had higher aPWV values compared to the TETRA group (TETRA: 8.1 ± 1.9 m/second, PARA: 8.9 ± 2.5 m/second, $P = 0.07$). After adjusting for important covariates (ANCOVA), the differences in aPWV values among the two groups was statistically significant ($P = 0.010$, Fig. 1). Fig. 2 displays the prevalence of abnormal aPWV. The prevalence of abnormal aPWV values

Figure 1 Mean aPWV in TETRA and PARA groups adjusted for age, sex, MAP, HR, treated hypertension, treated lipidemia, diabetes status, and injury severity (AIS A, B or C, D). Bars indicate 95% CI.

Table 1 Demographics, impairment, medical history, and vital signs of participants, mean $\pm$ SD, median, and interquartile range or number and proportion (%)

N	TETRA (n = 37)	PARA (n = 50)	Total (n = 87)	P
Sex (n, % men)	30 (81.1)	35 (70.0)	65 (74.7)	0.178
Age (years)	50.7 $\pm$ 14.0	46 $\pm$ 13.2	48.1 $\pm$ 13.7	0.117
Duration of injury (years)	13 (5–22)	13 (6–22)	13.0 (6–22)	0.927
Age at injury	33 (20–50)	27 (21–38)	28.0 (21–43)	0.337
AIS (n, % A and B)	21 (56.8)	34 (68.0)	55 (63.2)	0.197
Height (cm)	175 $\pm$ 9.8	174.1 $\pm$ 12.0	174.1 $\pm$ 9.9	0.476
Weight (kg)	84.9 $\pm$ 19.8	77.0 $\pm$ 16.3	80.4 $\pm$ 18.2	0.044*
Body mass index (kg/m ²)	27.7 $\pm$ 5.8	25.3 $\pm$ 4.2	26.4 $\pm$ 5.1	0.058
Waist circumference (cm)	98.6 $\pm$ 13.7	92.5 $\pm$ 13.8	95.1 $\pm$ 14.0	0.045*
Current smokers (n, %)	8 (21.6)	14 (28.0)	22 (25.3)	0.337
Vital signs				
SBP (mm Hg)	116.7 $\pm$ 21.8	121.9 $\pm$ 17.6	119.7 $\pm$ 19.6	0.229
DBP (mm Hg)	75.0 $\pm$ 14.2	78.2 $\pm$ 11.1	76.8 $\pm$ 12.6	0.249
MAP (mm Hg)	88.9 $\pm$ 15.3	92.7 $\pm$ 12.3	91.1 $\pm$ 13.7	0.201
HR (b.p.m.)	59.1 $\pm$ 8.9	64.3 $\pm$ 10.9	62.1 $\pm$ 10.4	0.021*
Medical history				
Treated hypertension (n, %)	3 (81.1)	8 (16.0)	11 (12.6)	0.223
Treated lipidemia (n, %)	3 (81.1)	12 (24.0)	15 (17.2)	0.310
Diabetes (n, %)	3 (81.1)	3 (6.0)	6 (6.9)	0.510

*Significant differences between TETRA and PARA subgroup, $P < 0.05$.

AIS, ASIA Impairment Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure, MAP, mean arterial pressure.

Figure 2 Prevalence of abnormal aPWV in the TETRA ($n = 37$) and PARA ($n = 50$) subgroups and the total cohort ($n = 87$).

Table 2 Distribution of aPWV according to the category of age and neurological level of injury

Age category (n)	Mean $\pm$ SD	Median (Min, Max)
TETRA		
20–39 (8)	6.9 $\pm$ 1.0	7.0 (5.3, 8.3)
40–59 (20)	7.8 $\pm$ 1.5	7.7 (5.5, 10.8)
60–80 (9)	9.8 $\pm$ 2.2	10.2 (5.8, 12.8)
PARA		
20–39 (16)	7.3 $\pm$ 1.6	7.0 (5.1, 10.3)
40–59 (26)	8.8 $\pm$ 1.7	8.4 (5.8, 13.7)
60–80 (8)	12.8 $\pm$ 2.0	11.8 (11.0, 15.5)

was significantly higher in the PARA group (18 of 50) compared to TETRA group (4 of 37) ($P = 0.012$).

aPWV values distinguished by age and by level of lesion are presented in Table 2. There is a systematic rise in aPWV with age and consistently higher aPWV values for the PARA group. aPWV values distinguished by blood pressure groups and age are presented in Fig. 3. There is a systematic rise in aPWV with age and consistently higher aPWV values for the high blood pressure group.

Figure 3 Mean aPWV values according to age and blood pressure categories. (), number of subjects.

Table 3 displays the serum profile and prevalence of MS of the study subjects. Within subjects who completed MS assessments (TETRA: $n = 30$, PARA: $n = 46$, total: $n = 76$), 32.0% (24 of 76) of the total subjects had MS (Table 3). The prevalence of MS was not significantly different between the two groups (TETRA: 33.3%, 10 of 30, PARA: 30.4%, 14 of 46, $P = 0.806$). Fig. 4 displays the prevalence of MS in both abnormal aPWV subjects and normal aPWV subjects. Of those identified with an abnormal aPWV (21 of 76), 48% (10 of 21) met diagnostic criteria for MS.

Discussion

We were able to obtain aPWV values from a broad cross section of adult men and women, with diverse body habitus, health status, and neurological impairment living with chronic SCI in the community. The key findings from this cohort were as follows: (1) obtaining aPWV values from subjects with SCI was feasible; (2) in total (TETRA + PARA), 25% of the subjects had abnormal aPWV values. (3) Subjects with paraplegia had higher aPWV values than subjects with tetraplegia after adjustment for important clinical confounders. (4) The prevalence of abnormal aPWV values indicating an elevated risk of CAD was significantly higher in the PARA group than the TETRA group. (5) Of those identified with an abnormal aPWV, only 48% of subjects met diagnostic criteria for MS. To our knowledge, this is the first report comparing the stiffness of central artery based on neurological level of injury. These findings indicate that there is a high yield from routine assessment of aPWV and that routine surveillance for CAD risk factors, specifically MS and elevated aPWV are feasible, and necessary, given the observed frequency of abnormalities. Roll out of future screening efforts should include the entire SCI population, with priority given to those with paraplegia.

One-quarter of our subjects had an abnormal aPWV, and of those identified with an abnormal aPWV, almost half of them did not have MS. This result implies that the abnormal arterial stiffness may not develop due to only traditional risk factors and current MS criteria may underestimate true CAD risk in individuals with SCI.

Mechanisms that might account for the observed differences in aPWV between subjects with tetraplegia and paraplegia are not clearly delineated. However, one may hypothesize that the observed lower aPWV among individuals with tetraplegia is due to withdrawal of sympathetic tone, resulting in increased distensibility of the artery as demonstrated in sympathectomized rats³⁴ and/or their persisting lower blood pressure.²³

Table 3 Summary of blood profile and MS,³² mean $\pm$ SD, or number and proportion (%)

	TETRA	PARA	Total	P
Serum profile [#]				
Total cholesterol (mmol/l)	4.7 $\pm$ 0.93	4.5 $\pm$ 1.05	4.59 $\pm$ 1.01	0.462
HDL-C (mmol/l)	1.21 $\pm$ 0.34	1.21 $\pm$ 0.26	1.21 $\pm$ 0.29	0.955
LDL-C (mmol/l)	2.85 $\pm$ 0.79	2.73 $\pm$ 0.85	2.78 $\pm$ 0.82	0.524
Triglycerides (mmol/l)	1.44 $\pm$ 0.73	1.42 $\pm$ 1.04	1.37 $\pm$ 0.78	0.905
Fasting glucose (mmol/l)	5.06 $\pm$ 0.55	5.1 $\pm$ 0.84	5.09 $\pm$ 0.73	0.734
Frequency of meeting MS criteria (any) (n, %) [#]				
0 MS criterion	5 (16.7)	9 (41.3)	17 (22.4)	
1 MS criterion	7 (23.3)	17 (28.3)	21 (27.6)	
2 MS criteria	10 (33.3)	14 (41.3)	18 (23.7)	
≥ 3 MS criteria (met MS criterion)	8 (26.7)	18 (47.8)	19 (25.0)	
Frequency of abnormal results by MS criteria (n, %) [#]				
Elevated waist circumference	18 (60.0)	19 (41.3)	37 (48.7)	0.114
Elevated triglycerides	7 (23.3)	13 (28.3)	20 (26.3)	0.639
Reduced HDL-C	12 (40.0)	19 (41.3)	31 (40.8)	0.911
Elevated blood pressure	13 (43.3)	22 (47.8)	35 (46.1)	0.705
Elevated fasting glucose	5 (16.7)	8 (17.4)	13 (17.1)	0.936

[#]Blood chemistry tests were completed for 30 of the 37 subjects in the TETRA group and 46 of the 50 subjects in the PARA group.

Therefore comparison of MS prevalence between TETRA and PARA groups were assessed in 76 of the 87 subjects.

MS, metabolic syndrome; FBG, fasting plasma blood glucose; HDL cholesterol, high-density lipoproteins cholesterol; LDL cholesterol, low-density lipoproteins cholesterol.

We did not see the difference in blood pressure between TETRA and PARA. However, the blood pressure in our study was assessed in the supine position with prior 20 minutes rest in a quiet and temperature-controlled room. Therefore, we do not know our subject's daytime blood pressure in the daily life. West *et al.*²³ found that subjects with tetraplegia exhibited a lower resting SBP in the seated compared with supine position. We assume that most subjects spend their daytime in a seated position. The persisting lower blood pressure experienced during the daytime in individuals with tetraplegia may be a reason for the observed lower aPWV in the TETRA group. Another possible explanation could be that endothelial function, which induces endothelium-dependent dilation in the aortic artery, may be preserved among individuals with tetraplegia, as shown in the femoral artery among people

with SCI.³⁵ On the other hand, it could be hypothesized that the observed higher aPWV among subjects with paraplegia was due to their persistently elevated HR.²⁰ Rosado-Rivera *et al.*²⁰ has previously reported that individuals with paraplegia have elevated 24-hour HRs when compared to individuals with tetraplegia and able-bodied controls. Rosado-Rivera *et al.*²⁰ speculated that the persistently elevated HR in paraplegic individuals may relate to increased sympathetic activity or may reflect vagal dysfunction, or a combination of both sympathetic and vagal pathology. Previous studies with able-bodied subjects have demonstrated associations between chronically elevated HR and increased arterial stiffness and endothelial dysfunction.^{24,36–39} Endothelial and autonomic functions were not assessed in our subjects. Therefore, we cannot comment on their status among our cohort members and how these changes in function affect central arterial stiffness. Further research is required to elucidate the underlying etiology of the observed differences in aPWV among study subjects with paraplegia and tetraplegia.

We compared the aPWV values in our study with available general population reference values.¹⁵ As a result, highly abnormal aPWV was present in 36% of subjects with paraplegia whereas only 10.8% of subjects with tetraplegia had abnormal aPWV. The prevalence of abnormal aPWV in individuals with paraplegia was similar to the prevalence previously shown in people with kidney disease (43%)⁴⁰ and systemic sclerosis (39%).⁴¹ The clinical importance of the threshold abnormal aPWV values used in this study has not been established in the SCI population. However, these aPWV

Figure 4 Prevalence of MS in abnormal aPWV subjects and normal aPWV subjects n (%), assessed in the 76 subjects who completed MS assessment.

results infer a lower CAD-related risk among individuals with tetraplegia vs. paraplegia. Our results are consistent with Groah *et al.*'s²⁵ prior report that the relative risk of CAD in people with paraplegia is higher than those with tetraplegia.

Although the study results clearly demonstrate greater aPWV values among subjects with paraplegia than tetraplegia, this may not mean that individuals with tetraplegia have a lower CAD risk than individuals with paraplegia. Ho and Krassioukov⁴² have reported an observed increase in visceral sympathetic activity with coronary artery constriction during an episode of autonomic dysreflexia, which tends to occur in individuals with SCI above the splanchnic outflow (T6), resulting in myocardial ischemia, even in the absence of CAD. In addition, cardiovascular and metabolic complications such as diabetes,¹⁷ lipid disorders,¹⁸ impaired physical capacity,⁴³ and low levels of physical activity⁴⁴ are frequent and pronounced among people with tetraplegia. Our results and evidence from previous studies suggest that the underlying mechanisms that contribute to the onset and progression of CAD are likely not the same between people with tetraplegia and paraplegia.

This study has limitations that require caution when interpreting and considering the generalizability of the findings reported herein. First and foremost, the clinical importance of an elevated aPWV in chronic SCI is unclear. Large-scale, prospective longitudinal studies are required to determine whether aPWV will predict future CAD mortality and morbidity in people with SCI at rates similar to the general population. Second, although we reported broad range of aPWV values across the cohort, it is unclear at this time if SCI-specific therapeutic and diagnostic thresholds would be lower or higher than the general population. Third, the aPWV values we used as a reference were measured using a different data analysis algorithm. The reference values were based on data using the intersecting tangent algorithm to determine the transit time,¹⁵ whereas we used the point of minimum diastolic pressure detected with bandpass filter to calculate the transit time.^{29,30} However, we believe that the impact of the methodological difference is negligible since the aPWV obtained using two different methods have comparable average variation coefficients (<4%) with high correlation coefficient.⁴⁵ Last, we could not determine if there was a difference in aPWV values between high thoracic SCI (T1–T6) and low thoracic SCI (T7–T12) due to an inadequate sample size. Recently published studies examining the effect of level of lesion on cardiovascular parameters demonstrated that there are lesion-dependent impairments in cardiovascular function.^{23,46} In

addition, we had an inadequate sample size to determine whether or not there are age-dependent differences in the prevalence of increased aPWV.

Conclusions

To our knowledge, this is the first report of the aPWV values and associations between aPWV and neurological level of injury among a large representative cohort of patients with chronic SCI. In total, one-quarter of our subjects had an abnormal aPWV. Among the cohort members, subjects with paraplegia had higher aPWV values than subjects with tetraplegia after adjustment for important clinical confounders. In addition, the prevalence of abnormal aPWV was significantly higher among subjects with paraplegia vs. tetraplegia. Elevated aPWV among those with paraplegia may infer adverse cardiovascular consequences. Given the observed frequency of the abnormal aPWV among this cohort and ease of aPWV acquisition, these data are a strong impetus for future routine aPWV screening of subjects with chronic SCI. In addition, future prospective longitudinal studies are required to determine the clinical implications and associated hazard ratios for adverse CAD-related morbidity and mortality based on the observed elevated aPWV.

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Conflicts of interest None.

Ethics approval The study procedures used in this study were approved by the Research Ethics Board at Toronto Rehabilitation Institute-UHN (TRI REB#09-019).

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