Pulse Wave Velocity (PWV) for Assessment of Arterial Stiffness Among People with Spinal Cord Injury: A Pilot Study

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Abstract

BACKGROUND: The most significant complication and leading cause of death for people with spinal cord injury (SCI) is coronary artery disease (CAD). It has been confirmed that Aortic pulse wave velocity (PWV) is an emerging CAD predictor among able-bodied individuals. No prior study has described PWV values among people with SCI.

PURPOSE: To compare: Aortic (the common carotid to femoral artery) PWV, Arm (the brachial to radial artery) PWV, and Leg (the femoral to posterior tibial artery) PWV in people with SCI (SCI group) to that of age, gender, height and weight matched able-bodied controls (non-SCI group).

METHODS: Subjects included 12 men with SCI and nine age, gender, height and weight matched non-SCI controls. Subjects with a history of CAD or current metabolic syndrome were excluded. Aortic, Arm and Leg PWV was measured using the echo Doppler method.

RESULTS: Aortic PWV (Mean ± SD) in the SCI group (1274 ± 369cm/sec) was significantly higher (P<0.05) than in the non- SCI group (948 ± 110cm/sec). There were no significant between group differences in the mean Arm PWV (SCI: 1152±193cm/sec,
non-SCI: 1237±193cm/sec) nor the mean Leg PWV (SCI: 1096±173cm/sec, non-SCI: 994±178cm/sec) values.

**CONCLUSIONS:** Aortic PWV was higher among the SCI group compared to the non-SCI group. The higher mean Aortic PWV values among the SCI group compared to the non-SCI group indicated a higher risk of CAD among SCI subjects in the absence of metabolic syndrome.

**Key Words:** Arterial stiffness; Pulse wave velocity; Spinal cord injuries; Doppler ultrasound, Coronary artery disease, Diagnosis
Introduction

Coronary artery disease (CAD) is the most significant complication and leading cause of mortality after spinal cord injury (SCI)\(^1\). Individuals with chronic SCI have higher cardiovascular mortality rates and cardiovascular mortality occurs at earlier ages when compared to the able-bodied population\(^2\text{-}^4\). Stiffening of the central or cardiothoracic arteries is a significant independent risk factor for CAD in able-bodied people\(^5\text{-}^7\). Decreases in the elastic properties of arteries reduce their buffering capacity, leading to increased pulse pressure, aortic impedance, and left ventricular wall tension. All of which augment the workload of the heart, thereby increasing CAD risk. Several indices have been used to quantify the stiffness of the peripheral and cardiothoracic arteries. These include: 1) measuring Pulse Wave Velocity (PWV); 2) relating changes in arterial diameter to distending pressure; and 3) assessing arterial pressure wave forms. Of the above indirect methods for measuring arterial stiffness, PWV is the most widely accepted technique\(^8\). PWV has been a useful noninvasive measure to assess arterial stiffness and severity of CAD among able bodied people in a number of previous studies\(^9\text{-}^{11}\).
PWV is the velocity of the blood pressure wave as it travels a known distance between two anatomic sites within the arterial system, and is determined by the elasticity and other properties of the artery\textsuperscript{12}. PWV values positively correlate with arterial distensibility and stiffness. Three locations or the measurement of PWV have been proposed: 1) trunk (Aortic PWV); 2) arm (Arm PWV); and 3) leg (Leg PWV). Aortic PWV is the established index for measuring arterial stiffness.

Aortic PWV values have been directly linked with cardiovascular mortality, fatal and nonfatal coronary events and fatal strokes in patients with low and high levels of traditional CAD risk factors\textsuperscript{9-11,13-15}. For example, Aortic PWV values $\geq$1300 cm/sec are a strong predictor of cardiac mortality among hypertensive patients\textsuperscript{13}. Among people with hypertension, a 500 cm/sec increment in Aortic PWV is an independent predictor of both cardiovascular mortality (odds ratio=1.34) and all-cause mortality (odds ratio=1.51)\textsuperscript{14}. Although Leg PWV and Arm PWV have not been studied to the same extent, it has been suggested that these peripheral PWV measures are insensitive to physical activity levels and/or aging compared to Aortic PWV in able-bodied people\textsuperscript{16,17}. 

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Several CAD risk factors have been identified as determinants of PWV in the able-bodied population these include: obesity\textsuperscript{18-20}, diabetes\textsuperscript{21, 22}, hypercholesterolaemia\textsuperscript{23} and hypertension\textsuperscript{9, 24}, poor cardiorespiratory fitness\textsuperscript{25, 26}, and low physical activity\textsuperscript{27}. These same CAD risk factors are common among people with SCI\textsuperscript{28-32}. In addition, people with SCI above the splachnic outflow (T6) have autonomic dysfunction, which may contribute to disordered cardiac regulation and abnormalities of the vascular system. Thus, it was hypothesized that people with chronic SCI will have an increased risk of adverse vascular health and increased arterial stiffness as measured by PWV.

The purpose of this study was to compare Aortic PWV in people with chronic SCI (SCI group) to that of age, gender, height and weight matched able-bodied controls (non-SCI group), and to compare Arm PWV and Leg PWV in these same groups to determine if differences exist in the values obtained.

\textbf{Methods}

\textit{Subjects:} The SCI group was comprised of fifteen subjects with SCI (C3-T10, AIS A, B and C). The non-SCI group was comprised of 11 age, height and weight matched sedentary
able bodied controls). SCI subjects were recruited via a poster campaign from Toronto Rehab’s Lyndhurst Centre. Non-SCI subjects were recruited from the staff and friends of the authors affiliated with the Lyndhurst Centre. Subjects did not participate in any regular exercise or endurance-type wheelchair exercise beyond their normal activities of daily living for 6 months prior to enrolment. All subjects were nonsmokers for at least 1 year prior to the study. No subjects reported a prior history of CAD, pulmonary disease, diabetes mellitus or metabolic syndrome. The subject’s current medications were recorded. No subjects were taking medications known to interfere with the cardiovascular system.

A 12 lead EKG, was done to screen for arrhythmia, or prior myocardial infarction. The subjects’ fasting serum blood sugar, glycosylated hemoglobin (HbA1C), Total Cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL), Triglycerides (TG), C-Reactive Protein (CRP) and Apolipoprotein (A and B) levels, resting blood pressure (BP) and waist circumference were measured to screen for metabolic syndrome. Heart rate and BP were recorded from the right antecubital fossa using a stethoscope and hand-held dynamometer. Metabolic syndrome was defined as per the
American Heart Association Guidelines as ≥ 3 or more of the following criteria: abdominal obesity (waist circumference ≥102 cm for men); dyslipidemia (TC/HDL >4 or LDL >2.5); glucose intolerance (fasting blood sugar >7 mmol/L); elevated CRP (>3mg/dl); or hypertension (BP >140/90 mmHg).

Fifteen SCI subjects and 11 non-SCI subjects were screened for enrolment in the study. Five subjects’ data were excluded from the analysis; three subjects due to having metabolic syndrome; one subject for an arrhythmia (atrial fibrillation) which interfered with PWV measurement; and one subject for an incomplete assessment. In total, 12 SCI subjects and 9 Non-SCI subjects were included in the study. The study protocol was approved by the Toronto Rehab Research Ethics Board.

*Pulse wave velocity (PWV):* PWV was measured from the foot, blood flow waves were recorded at two points along the path of the arterial pulse wave. PWV was calculated from the measured wave latency and the distance traveled between the two arterial recording sites (Figure 1)\textsuperscript{10, 15, 17, 33, 34}. Two identical transcutaneous Doppler flowmeters (Smartdop50, Hadeco, Inc., Kanagawa, Japan) were used to obtain the PWV values at three
locations: (1) between the carotid and the femoral arteries (Aortic PWV); (2) between the femoral and posterior tibial arteries (Leg PWV); and, (3) between the brachial and radial arteries (Arm PWV) (Figure1B). Distance traveled by the pulse was measured over the surface of the body with a tape measure as the distance (D) between recording sites (cm). A minimum of 20 sequentially recorded wave forms were analyzed and averaged. All PWV data were obtained by two trained technicians between 10AM and 1PM to avoid circadian changes in PWV values. Measurement of PWV was conducted after abstinence from caffeine and an overnight fast of at least 8 hours. Flow measurements were obtained sequentially in the arm, aorta and then the leg over a 40 minute time period. Arterial pulse waves were digitized for off-line analysis with signal-processing software (Chart 5.5.5, AD Instruments, Australia). PWV was determined over the three arterial segments as PWV= D/ \Delta t (cm/sec), where \Delta t was determined from time delay between the proximal and the distal foot of the wave form (Figure1A). The foot of the wave was identified as the commencement of the sharp systolic upstroke. All analyses were performed by a trained technician blinded to the subject’s group assignment (SCI or non-SCI).
The test-retest variability of PWV measures in our laboratory was established by sequential measurement of 9 able-bodied males (21 ~ 39 yrs) on two separate days. The intraclass correlation coefficients for test-retest reliability were 0.730 ~ 0.972 for each PWV value. The mean PWV combined for the three sites was 1095 ±238 versus 1057 ±210 cm/sec for trial 1 versus trial 2 (not significant).

Statistical Analysis: The statistical analyses were performed using StatView (Version 5.0) software. Demographic, anthropometric and PWV data are expressed as mean±SDs. The SCI and non-SCI subjects were compared by the nonparametric Mann-Whitney U-test because of the small group size. A two sided P value of <0.05 was considered significant.

Results

There were no significant differences between groups in the baseline demographic or anthropometric parameters including: age, height, weight, heart rate and BP (Table1). The mean duration of injury of the SCI subjects was 20 ±13 years (Mean±SD). Mean Aortic PWV in the SCI group (1274±369cm/sec) were significantly higher (P<0.05) than that of the non-SCI group (948±110cm/sec) (Figure 2a). There were no statistically significant
differences between the SCI group and the non-SCI group (Figure 2b, c) in either Arm PWV (SCI: 1152 ± 193 cm/sec, non-SCI: 1237 ± 193 cm/sec) (P=0.434) nor Leg PWV (SCI: 1096 ± 173 cm/sec non-SCI: 994 ± 178 cm/sec) values (P=0.145).

Discussion

Aortic PWV values in the SCI group were higher than those of able-bodied controls (non-SCI group), while there were no significant differences between the SCI and non-SCI groups in Arm PWV and Leg PWV values. Recently reported Aortic PWV values in healthy able-bodied individuals 24 to 62 years of age ranged from 600 to 1000 cm/s. Among hypertensive subjects, Aortic PWV values ranged from 1100 to 1500 cm/s. Arm and Leg PWV values in healthy able-bodied individuals ranged from 840 to 1200 cm/s and from 920 to 1050 cm/s, respectively. The values for PWV documented herein are comparable with those previously reported for able-bodied individuals within the same age range.

Additionally, we found that Aortic PWV values among healthy SCI subjects were higher than the age-matched non-SCI subjects. Aortic PWV values in the SCI group were
equally high compared to the values (>1300 cm/sec) associated with an increased risk of developing CAD in Blacher’s report\textsuperscript{13}. These results suggest that the SCI group has a high risk of CAD. Screening protocols to diagnose and prevent CAD related mortality are urgently needed.

In contrast to the Aortic PWV result, there were no significant differences between the SCI group and non-SCI group in either Arm PWV or Leg PWV. These results concur with a prior study reporting that Aortic PWV is sensitive to daily activity and aging while Leg and Arm PWV values are not\textsuperscript{16, 17}. This sensitivity of the PWV of central versus peripheral arteries may be related to their distinct roles in hemodynamic regulation. Compared with the central arteries whose cushioning function damps fluctuations in flow, the peripheral arteries do not exhibit the same extent of pulsatile changes in diameter\textsuperscript{35} and, as such, may not undergo the adaptations leading to a loss of elasticity. However, previous studies, which investigated femoral arterial stiffness by augmentation index (AI)\textsuperscript{36} and arterial compliance\textsuperscript{37, 38} among people with SCI, demonstrated that stiffness of femoral artery in people with SCI was higher than that of able-bodied people. The reasons for this
discrepancy is not clear, however, the use of the PWV methodology as opposed to the AI and arterial compliance to assess arterial stiffness may in part explain the discrepancy between our finding of normal leg PWV values and prior publications reporting elevated femoral AI and decreased arterial compliance values among patients with SCI. The PWV method measures pulse wave latency over the femoral and posterior tibial arteries as opposed the femoral artery alone when assessing the AI or arterial compliance.

Although there are no prior studies determining PWV in people with SCI, three previous studies investigated arterial stiffness using other measures of arterial stiffness: the AI\textsuperscript{36} and arterial compliance\textsuperscript{37, 38} and compared them to those of able-bodied controls. de Groot et al. and Schmidt-Trucksass et al. (2000) reported that arterial compliance of the superficial femoral and carotid artery were significantly lower in subjects with SCI compared to non-SCI subjects\textsuperscript{37, 38}. Wecht et al. (2004) reported that arterial stiffness evaluated by AI was high in a group of people with paraplegia compared with an able-bodied group\textsuperscript{36}. Moreover, premature and advanced coronary atherosclerosis was found in persons with SCI compared with able-bodied people using electron beam
tomography\textsuperscript{39}. Our observation of increased aortic arterial stiffness supports prior reports of premature CAD in the SCI population.

Mechanisms which may potentially account for higher Aortic PWV among SCI subjects include: 1) structural changes in the vessel as a result of long-term sympathectomy and increased collagen content in the vascular wall\textsuperscript{40}; or, 2) functional changes in the endothelium due to decreased regional blood flow. Decreased regional blood flow as a result of inactivity impedes endothelium function and subsequently inhibits nitric oxide production, which is a mediator of endothelium dilatation\textsuperscript{38}. Although the relative importance of structural and functional changes in vascular tone is unknown, these may relate to both disordered cardiac regulation and inactive lifestyles after SCI. The mechanism(s) which account for the current results are unknown.

The current study has limitations that require caution when interpreting and generalizing the findings reported herein. Firstly, the reliability of PWV values for people with SCI has not been reported. Secondly, this pilot study had a small sample size. Thirdly, adjustments for confounding variables including: the subject’s injury level, duration of
injury and physical activity levels, which impact CAD risk, were not done. Future studies may want to use validated measures such as the PARA-SCI\textsuperscript{31} to quantify activity and explore the relationship between PWV and activity. Lastly, it is uncertain if the high PWV values reported reflect the presence of CAD among the subjects’ in this study. Further investigations with larger representative samples of SCI subjects are needed to determine the relationship between the increased arterial stiffness and the development/onset of atherosclerotic and asymptomatic CAD among people with SCI.

To our knowledge, this is the first study describing Aortic PWV in people with SCI. High Aortic PWV values were found in subjects with SCI compared to age, gender, height, and weight matched able-bodied subjects indicating a higher risk of CAD among SCI subjects. Arm PWV and Leg PWV were found to be insensitive to the differences between the two groups. PWV is potentially a good screening test to assess CAD risk among people with chronic SCI. However, this pilot study merely measured PWV among people with SCI. Further study is needed to confirm the reproducibility of PWV measures among people with SCI. Further study of the PWV method's reliability, validity and responsiveness while
considering the potential confounding effects of: age, duration of injury, impairment and physical activity on PWV among subject's with SCI are needed.

Acknowledgements

The author (Masae Miyatani) is a fellow funded by Canadian Paraplegic Association Ontario. The authors acknowledge the support of Toronto Rehab who receives funding under the provincial rehabilitation research program from the Ministry of Health and Long Term Care in Ontario.
References


**Figure legends**
**Figure 1.** A: Determination of time delay of waveform B: Scheme of Pulse wave velocity (PWV) measurement. $\Delta t$: Time delay of waveform; CA: Carotid artery; FA: Femoral artery; BA: Brachial artery; RA: Radial artery; PTA: Posterior tibial artery; D Aortic: Distance of between CA and FA; D Arm: Distance of between BA and RA; D Leg: Distance of between FA and PTA.

**Figure 2.** Pulse wave velocity (PWV) in subjects with spinal cord injury (SCI) and able bodied controls (non-SCI).
Table 1 Subject characteristics

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<th>non-SCI group</th>
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<tr>
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<tr>
<td>Age (yr)</td>
<td>45.9 ± 7.8</td>
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<td>Heart rate (beats/min)</td>
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<td>65.4 ± 8.0</td>
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Data are means±SD
Figure 1

A

FA Blood Flow

PTA Blood Flow

Time Delay of waveform

Time (sec)

6 6.5 7 7.5 8

B

• Calculation of PVW
  (1) Aortic PWV (cm/sec) =
      D Aortic / TD between CA and FA
  (2) Arm PWV (cm/sec) =
      D Arm / TD between BA and RA
  (3) Leg PWV (cm/sec) =
      D Leg / TD between FA and PTA
Figure 2

A

Aortic PWV (cm/sec)

SCI | non-SCI

P<0.05

B

Arm PWV (cm/sec)

SCI | non-SCI

C

Leg PWV (cm/sec)

SCI | non-SCI