Physical activity is associated with improved subclinical atherosclerosis in spinal cord injury subjects independent of variation in traditional risk factors ☆

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ARTICLE INFO

Article history:
Received 9 September 2012
Accepted 29 September 2012
Available online 23 October 2012

Keywords:
Paraplegia
Tetraplegia
Intima-media thickness
Exercise

Individuals with spinal cord injury (SCI) exhibit higher atherosclerotic burden in comparison with able-bodied individuals, independent of traditional cardiovascular risk factors [1–4]. Some reports have suggested that physical inactivity plays a role in increasing the cardiovascular risk induced by SCI, since subjects with no voluntary motor function and tetraplegics usually present higher prevalence of cardiovascular diseases than those with incomplete injury and paraplegics, respectively [5,6]. The present study investigated the carotid arteries of physically active (PA-SCI) and sedentary (S-SCI) men with SCI and evaluated the impact of metabolic, inflammatory and hemodynamic parameters in this regard.

Fifty four (30 S-SCI and 24 PA-SCI) men with no motor function below the injury level and >1 year of SCI and 28 sedentary able-bodied men were cross-sectionally evaluated. S-SCI subjects were enrolled from a university hospital outpatient clinic, while able-bodied individuals were recruited from employees and students of the same university. PA-SCI subjects comprised competitive athletes that were regularly performing wheelchair rugby ($n=11$), basketball ($n=11$), handball ($n=1$) and tennis ($n=1$) for >1 year and were enrolled from the School of Physical Education of the university. This latter group had been training in average 11.2 ± 1.3 h/week for 4.3 ± 0.5 years. Exclusion criteria were diabetes mellitus, systemic hypertension, hyperlipidemia [7], current or past smoking, known coronary artery, cardiac or pulmonary disease, cancer, regular medical therapy and clinical evidence of active infection. Fasting serum glucose, lipids and C-reactive protein were measured using standard laboratory techniques. Office blood pressure was measured in the sitting position using validated digital oscillometric device (Omron HEM-705CP, Omron Corp.). Carotid ultrasonography was performed on each subject in the sitting position with a Vivid 3 Pro apparatus as previously described [1,2,8]. Evaluation of cardiac output and peripheral vascular resistance was performed as previously described [2,8]. The study was approved by the Ethics Committee of the State University of Campinas and informed consent was obtained from all participants. The authors certify that they comply with the principles of ethical publishing in the International Journal of Cardiology. All values were expressed as mean ± standard error and median (25–75th percentile) for continuous normal and non-normal variables. Differences in continuous normal and non-normal variables were evaluated by one-way ANOVA followed by Tukey test, and Kruskal–Wallis test followed by Wilcoxon signed rank test, respectively. χ^2 was used to compare categorical variables. General linear model analysis was used to assess differences between groups after adjustment for relevant covariates. A p-value <0.05 was considered significant.

Clinical, hemodynamic and carotid features of enrolled subjects are presented in Table 1. The able-bodied group exhibited higher systolic blood pressure than SCI groups as well as higher diastolic blood pressure and mean blood pressure and lower C-reactive protein levels than the S-SCI group. Conversely, PA-SCI subjects presented lower triglycerides, heart rate and common carotid artery (CCA) resistive index than S-SCI ones. Average CCA intima-media thickness (IMT) and CCA IMT/diameter of PA-SCI subjects were similar to those of able-bodied individuals, but lower than those of S-SCI ones (Fig. 1). Further general linear model analysis revealed that the CCA wall thickness of the S-SCI group remained significantly higher than that of PA-SCI subjects after adjustment for triglycerides, heart rate, and CCA resistive index levels (Fig. 1).

Table 1
Clinical, hemodynamic and carotid features of enrolled subjects.

Variable	Able-bodied ($n=28$)	Sedentary SCI ($n=30$)	Physically active SCI ($n=24$)
Clinical features			
Age, years	30.5 ± 0.9	31.7 ± 1.3	29.1 ± 1.2
Time of injury, years	–	7.7 ± 0.9	9.4 ± 1.1
Tetraplegic, *n* (%)	–	15 (50)	11 (46)
Body mass index, kg/m^2	23.8 ± 0.6	23.6 ± 0.7	22.2 ± 0.7
Glucose, mg/dL	80.8 ± 1.6	82.4 ± 1.6	80.7 ± 0.8
LDL-cholesterol, mg/dL	101.9 ± 8.5	104.1 ± 5.6	97.7 ± 6.0
HDL-cholesterol, mg/dL	45.9 ± 2.4	40.1 ± 1.7	40.1 ± 1.8
Triglycerides, mg/dL	95 (82)	89 (68)	75 (44)**
Log C-reactive protein, mg/dL	−0.95 ± 0.15	−0.39 ± 0.12*	−0.64 ± 0.15
Systemic hemodynamic features			
Systolic BP, mm Hg	119.7 ± 2.5	107.3 ± 2.8*	107.6 ± 3.5*
Diastolic BP, mm Hg	73.2 ± 2.4	66.5 ± 2.3*	68.1 ± 2.6
Mean BP, mm Hg	88.7 ± 2.3	80.1 ± 2.2*	81.3 ± 2.7
Heart rate, b.p.m.	71.1 ± 1.7	77.2 ± 2.2	68.4 ± 2.7**
Cardiac output (L/min)	4.8 ± 0.2	4.8 ± 0.2	4.7 ± 0.3
PVR (dynes × s × cm^{-5})	1515 ± 79	1379 ± 55	1461 ± 77
Carotid features			
CCA diameter, mm	5.32 ± 0.11	5.30 ± 0.10	5.56 ± 0.10
CCA CWT, 10^4 dyn/cm^2	3.17 ± 0.92	2.83 ± 0.10	3.01 ± 0.13
CCA resistive index	0.79 ± 0.02	0.83 ± 0.01	0.78 ± 0.01**
ICA resistive index	0.72 ± 0.02	0.73 ± 0.02	0.73 ± 0.02

Legend. SCI — spinal cord injury; LDL — low density lipoprotein; HDL — high density lipoprotein; BP — blood pressure; PVR — peripheral vascular resistance; CCA — common carotid artery; CWT — circumferential wall tension; ICA — internal carotid artery.
* p at least <0.05 compared to able-bodied subjects.
** p at least <0.05 compared to sedentary SCI subjects.

☆ Funding: This work was supported by grants from FAPESP (2010/16252-0) and CNPq (Proc. 474966/2010-0 and 303539/2010-0), Brazil.

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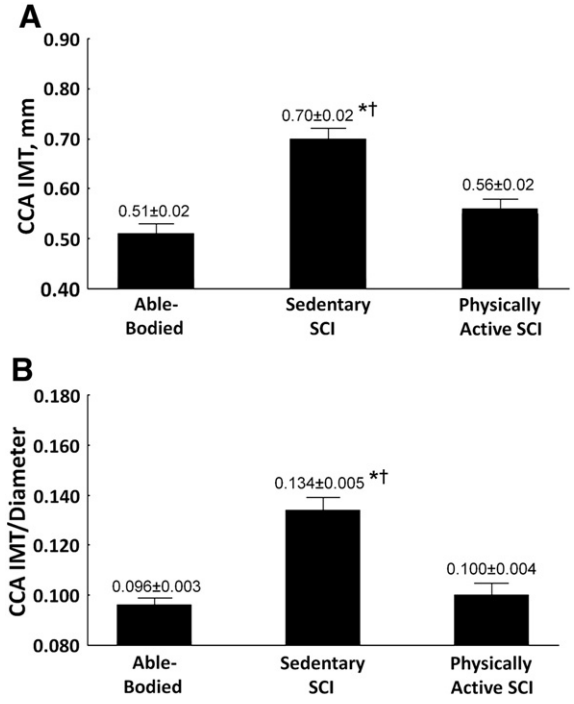

Fig. 1. A. Common carotid artery intima-media thickness (CCA IMT) and; B. CCA IMT/diameter of able-bodied individuals, sedentary SCI subjects and physically active SCI subjects. *$p<0.001$ compared to able-bodied and physically active SCI subjects. †$p<0.01$ compared to physically active SCI subjects adjusted for triglycerides, heart rate and CCA resistive index levels. SCI — spinal cord injury.

This report provided novel knowledge regarding the impact of physical activity on carotid alterations following chronic SCI. First, it demonstrated that the carotid IMT of paraplegic and tetraplegic athletes was markedly lower than that of SCI sedentary individuals and comparable to that of able-bodied subjects. Second, such difference in carotid IMT between the SCI groups was not explained by variation in metabolic (lipid profile, glucose and body mass index), inflammatory (C-reactive protein), systemic hemodynamic (blood pressure, cardiac output, peripheral vascular resistance and heart rate) and local hemodynamic (circumferential wall tension and resistive index) variables. Overall, these findings indicate that physical inactivity *per se* might play a direct role in the development of atherosclerosis in SCI individuals and further suggest that chronic SCI might be a potential human model for the study of the mechanisms by which physical inactivity may stimulate atherogenesis.

One aspect of our protocol that deserves further comments was the strict criteria of subject selection and therefore the homogeneity of our sample. We excluded individuals with obesity, hyperlipidemias, diabetes mellitus, hypertension and smoking, which are commonly seen after chronic SCI [9] and could be potential confounders in the analysis. In addition, we only included SCI subjects without any preserved motor function below the injury level, a feature that is recognizably associated with increased prevalence of cardiovascular disease [5,6]. However, such strict criteria resulted in the inclusion of a relatively small sample size, which might be a potential limitation of our study. In addition, the cross-sectional design limits our ability to infer a causal relationship between regular exercise and reduced atherosclerotic burden in SCI individuals.

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0167-5273/$ – see front matter
http://dx.doi.org/10.1016/j.ijcard.2012.09.222