Participation in moderate-to-vigorous leisure time physical activity is related to decreased visceral adipose tissue in adults with spinal cord injury

Journal:	<i>Applied Physiology, Nutrition, and Metabolism</i>
Manuscript ID	apnm-2017-0304.R1
Manuscript Type:	Article
Date Submitted by the Author:	02-Aug-2017
Complete List of Authors:	Pelletier, Chelsea; University of Northern British Columbia, Omidvar, Maryam; Toronto Rehabilitation Institute - Lyndhurst Centre Miyatani, Masae; Toronto Rehabilitation Institute - Lyndhurst Centre Giangregorio, Lora; University of Waterloo, Craven, B. Catharine; Toronto Rehabilitation Institute - Lyndhurst Centre
Is the invited manuscript for consideration in a Special Issue? :	
Keyword:	spinal cord injury < nervous system, visceral fat < waist circumference, physical activity < exercise, obesity < waist circumference

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Participation in moderate-to-vigorous leisure time physical activity is related to decreased visceral adipose tissue in adults with spinal cord injury

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Abstract

Increased visceral adiposity place individuals with chronic spinal cord injury (SCI) at increased risk of cardiometabolic disease. The purpose of this study was to identify if people with chronic SCI who participate in any moderate-to-vigorous intensity leisure time physical activity (LTPA) have lower visceral adipose tissue (VAT) area compared to those who report none. Participants included 136 adult men ($n = 100$) and women ($n = 36$) with chronic [mean ($\pm$ SD) 15.6 ± 11.3 years post injury] tetraplegia ($n = 66$) or paraplegia ($n = 70$) recruited from a tertiary rehabilitation hospital. VAT area was assessed via whole body dual-energy X-ray absorptiometry (DXA) using a Hologic densitometer and the manufacturer's body composition software. Moderate-to-vigorous LTPA was assessed using the Leisure Time Physical Activity Questionnaire for People with SCI (LTPAQ-SCI) or the Physical Activity Recall Assessment for People with SCI (PARA-SCI). Summary scores were dichotomized into any or no participation in moderate-to-vigorous LTPA to best represent the intensity described in current population-specific physical activity guidelines. Data were analyzed using univariate and multiple regression analyses to identify the determinants of VAT. Overall, the model explained 67% of the variance in VAT area and included time post-injury, age-at-injury, android/gynoid ratio, waist circumference, and moderate-to-vigorous LTPA. Participation in any moderate-to-vigorous LTPA was significantly (95% CI: $(-34.71) - (-2.61)$, $p = 0.02$) associated with VAT after controlling for injury-related and body composition correlates. Moderate-to-vigorous LTPA appears to be related to lower VAT area, suggesting potential for LTPA to reduce cardiometabolic disease risk among individuals with chronic SCI.

Keywords: spinal cord injury, visceral fat, physical activity, obesity

Introduction

Visceral adipose tissue (VAT) is more closely associated with obesity related diseases, including cardiometabolic disease, than other indices of adiposity and is a potent predictor of all-cause mortality in the general population (Katzmarzyk et al., 2012). When compared to subcutaneous adipose tissue (SAT), VAT is highly vascularized, more metabolically active, and negatively impacts an individual's metabolic profile leading to glucose intolerance, insulin resistance, and hyperlipidemia (Fox et al., 2007). It is well established in the able-bodied population that inadequate leisure time physical activity (LTPA) and excessive energy intake are the leading risk factors contributing to central adiposity; both moderate-to-vigorous LTPA (Murbaito et al., 2015) and decreasing sedentary time have been associated with decreased VAT and improved metabolic profile (Philipsen et al., 2015).

Individuals with spinal cord injury (SCI) experience muscle atrophy and increased abdominal and visceral adiposity. These changes in body composition often surpass sarcopenic obesity thresholds, which is one of the most potent predictors of cardiometabolic disease and all-cause mortality in older adults (Atkins et al., 2014; Kim and Choi, 2015; Pelletier et al., 2016).

Estimated rates of obesity in the SCI population range from 20% to 78% and are highly dependent on the assessment method and associated diagnostic criteria (Weaver et al., 2007; Pelletier et al., 2016). Both total VAT and the VAT to SAT ratio are consistently reported as higher among adults with SCI when compared to age and sex matched peers in the general population after controlling for waist circumference (WC) and body mass index (BMI) (Edwards et al. 2008). Individuals with SCI have a 27% increase in VAT for every one-centimeter increase in WC, and a 20% increase in VAT for every one-unit increase in BMI when compared to

matched able-bodied controls (Cirnigliaro et al., 2015). At any given BMI, individuals with SCI have up to a 43% increased VAT volume when compared to the able-bodied population (Cirnigliaro et al., 2015). Previous studies have indicated that neurological level of injury or injury severity (ASIA Impairment Scale) of SCI are not associated with VAT (Gorgey and Gater, 2011; Pelletier et al., 2016). To our knowledge, no prior studies have specifically explored other factors associated with VAT in the SCI population, but variables such as age and sex have been shown to be important influences in the able-bodied population (Kuk et al., 2005).

LTPA is defined as any physical activity that individuals choose to do in their free time and at a mild, moderate, or vigorous intensity. Physical activity guidelines for the SCI population indicate that, for fitness benefits, adults with SCI should engage in 20 minutes of moderate-to-vigorous intensity aerobic physical activity and resistance training 2-days per week (Martin Ginis et al., 2011). While this frequency and intensity of voluntary exercise has been shown to induce fitness benefits after SCI (Pelletier et al., 2015), the effects on specific health outcomes and disease modifying factors including vascular function and body composition are not as well established (Totossy de Zepetnek et al., 2015; Bakkum et al., 2015; Gibbs et al., 2017). Previous cross-sectional investigations have shown a negative association between WC and LTPA in adults with paraplegia (Buchholz et al., 2009) and between trunk fat mass and thrice weekly exercise in adults with tetraplegia (D'Oliveira et al., 2014). Given the metabolic consequences of excessive adipose tissue accumulation (Fox et al., 2007), the identification of effective interventions to decrease VAT is an important therapeutic target for the reduction in cardiometabolic risk in this population. To inform the design of interventions, it is first necessary to elucidate the relationship between the various confounding variables of VAT in a large representative cohort.

The objective of this investigation was to examine if self-reported participation in any moderate-to-vigorous aerobic LTPA is related to VAT in a cohort of community-dwelling individuals with chronic SCI using a cross-sectional study design. The working hypothesis was that participation in any moderate-to-vigorous LTPA would be associated with lower VAT when compared to those who do not engage in moderate-to-vigorous LTPA.

Materials and Methods

Participants

Participants were recruited as part of two cohort studies, the details of which are presented elsewhere (Lala et al., 2013, Miyatani et al., 2014). Eligible participants included adults ≥ 18 years of age, with a chronic SCI (C2 – T12, AIS A-D) at least 2-years prior to enrolment, and the ability to give informed consent. Participants were excluded based on current or prior conditions other than paralysis known to adversely influence bone metabolism, weight $> 123\text{kg}$ (densitometer limit), or women who were pregnant or planning to become pregnant. The relevant institutional research ethics board (University Health Network, Toronto, Ontario, Canada) approved the study protocols and informed consent was obtained from each participant.

Body Composition Assessment

The methodology for the body composition assessments, including anthropometric and DXA scanning protocols are published elsewhere along with descriptive data (Pelletier, et al., 2016). In brief, demographic and anthropometric data were collected through interview and medical chart abstraction, as appropriate. WC (cm) was measured at the level of the lowest rib while in the supine position (Edwards et al., 2008). Whole body dual-energy X-ray absorptiometry (DXA)

scans were completed using a Hologic Discovery W Densitometer and analyzed using commercially available Hologic body composition software (Version 13.4.1:5 Auto Whole Body) to collect VAT area and android/gynoid ratio variables.

LTPA

Mild, moderate, and vigorous LTPA (min/day) was assessed via self-report using either the Leisure Time Physical Activity Questionnaire for People with SCI (LTPAQ-SCI) or the Physical Activity Recall Assessment for People with SCI (PARA-SCI; Latimer et al., 2006, Martin Ginis et al., 2005). As mentioned previously, the sample used in this assessment represents the baseline data from one longitudinal trial and one cross-sectional study that utilized identical DXA protocols and different but related self-reported questionnaires of LTPA. The combination of these two cohorts was necessary to obtain a sample size large enough for our multivariable analysis. Given limitations with the data collected from the PARA-SCI that provides min/day of LTPA based on a 3-day recall and the LTPAQ-SCI that provides min/week of LTPA based on a 7-day recall, we were unable to estimate weekly duration of LTPA across the study cohort. Because current population-specific physical activity guidelines are explicit about intensity of LTPA, the presence of any moderate-to-vigorous LTPA was used as the best available approximation of achieving the guidelines. Thus, LTPA was considered as a dichotomous variable comparing any moderate-to-vigorous intensity LTPA to no moderate-to-vigorous LTPA. In addition, the effect of a one unit change of LTPA on VAT was small; we did not have sufficient power to detect a relationship using LTPA as a continuous variable ($\beta = -0.2$, $p = 0.11$).

LTPA collected using the LTPAQ-SCI were converted to min/day by dividing the total score by seven to be consistent with the data collected using the PARA-SCI. This conversion has been previously validated in a study demonstrating strong and statistically significant correlations between these tools (Martin Ginis et al., 2012). Both the PARA-SCI and the LTPAQ-SCI use the same validated LTPA intensity classification criteria where moderate and vigorous (or heavy) intensity LTPA correspond to 40-59% and >60% VO_2 reserve, respectively (Martin Ginis et al., 2005).

Statistical Analysis

Descriptive statistics, mean and standard deviation for continuous variables, and count and percent for categorical variables, were used to describe the demographic, impairment, and lifestyle risk factors for cardiometabolic disease among the study cohort. Linear regression analysis was used to determine the effect of LTPA on VAT area fulfilling assumptions. Normality was tested using normality plots and Kolmogorov-Smirnov test for continuous variables including age at injury, time post injury, WC, and VAT area.

Based on clinical relevance, possible confounders including age, sex, age at injury, time post injury, WC, android-gynoid ratio, trunk fat mass, level of injury and severity of injury were assessed in a univariate regression analysis. Covariates of VAT area were selected based on a p-value < 0.05 for both Beta and F-change in the univariate regression analysis to be included in the final model using enter method. Android-gynoid ratio was shown to remove the effect of sex better than the sex variable. Although WC is often used as a surrogate for VAT, there are people who appear to have a normal WC but maintain a high amount of VAT due to changes in the

VAT to SAT ratio. Thus, based on the clinical importance and a p-value of <0.01 , WC was included in the final model. The final variables included in the fitted model were age at injury, time post injury, WC, android-gynoid ratio, and moderate-to-vigorous LTPA.

Results of the univariate regression analysis are shown by adjusted R squares to indicate the change of VAT attributed to every determinant and p-value of F-change as an indicator of the significant change due to including the variable (Table 1). Regression coefficients and p-values for each beta in the final multiple regression fitted model were used to determine the effect of each component on the dependent variable (Table 2). A p-value <0.05 was considered statistically significant in the final model. All analyses were performed by SPSS statistical package version 22.

Results

Participants

A total of 136 participants (100 male, 36 female) were included in the analyses that were mean $\pm$ SD 49.1 ± 12.9 years of age and 15.6 ± 11.3 years post-injury and predominantly had motor complete (AIS A-B impairment) paraplegia or low tetraplegia (Table 3).

LTPA Participation

Mean $\pm$ SD total LTPA was 43.5 ± 58.4 min/day and moderate-to-vigorous LTPA was 23.6 ± 33.3 min/day. Moderate-to-vigorous LTPA (min/day) is presented in Figure 1. In total, 54.2% of participants reported any moderate-to-vigorous LTPA while 45.8% reported none.

Visceral Adiposity

Body composition characteristics of participants are presented in Table 3. Mean VAT area was $152.5 \pm 73.4\text{cm}^2$ (range 25 – 373 cm^2).

Determinants of VAT area

As seen in Table 1, univariate regression analysis revealed that participation in any moderate-to-vigorous LTPA was not significantly related to VAT ($R^2 = 0.00$, $p = 0.32$). The variables most strongly associated with VAT were WC ($R^2 = 0.60$, $p = 0.00$) and android/gynoid ratio ($R^2 = 0.45$, $p = 0.00$). Although age at-injury did not reach significance based on beta and F-change ($\beta = 0.63$, 95% CI: -0.04- 1.29), when included in the final multivariate model it was found to have a considerable impact on the effect of LTPA on VAT area based on R square change.

The results of the multiple regression analysis indicate that our model explained 67% of the variance in VAT (Table 2). After removing the influence of age-at-injury, time post-injury, android/gynoid ratio, and WC, moderate-to-vigorous LTPA emerged as a significant factor influencing VAT ($\beta = -18.66$, 95% confidence interval: (-34.71) – (-2.61), $p = 0.02$).

Discussion

Individuals with SCI, particularly those with tetraplegia, are highly susceptible to glucose intolerance, insulin resistance, and dyslipidemia, all of which have been associated with excessive VAT accumulation (Gorgey and Gater, 2011; Fox et al., 2007). Improving health outcomes such as adiposity and metabolic biomarkers can potentially decrease the associated long-term cardiometabolic disease risk and observed morbidity and mortality in this population

(Cragg et al., 2013). Overall, our multivariable model that included injury and body composition correlates was able to explain 67% of the variance in VAT. After controlling for WC, android-gynoid ratio, and time post injury, individuals who self-reported participation in any moderate-to-vigorous LTPA had reduced VAT area; inferring potential health benefits and reductions in cardiometabolic risk.

Previous reports on the impact of LTPA on chronic disease risk factors in adults with SCI have been mixed or inconclusive. Totosy de Zepetnek et al. (2015) reported small decreases in VAT mass and WC, but not traditional cardiovascular blood biomarkers or metabolic syndrome prevalence in a randomized controlled trial based on the moderate-to-vigorous intensity activity defined in the physical activity guidelines for adults with SCI. Bakkum et al., (2015) found no beneficial effects of hybrid functional electrical stimulation leg cycling in comparison to arm cycling alone on visceral adiposity, although improvements in metabolic and body composition outcomes have been noted in other similar training interventions (Gorgey et al., 2012, Griffin et al., 2009). Other novel exercise rehabilitation interventions, such as activity-based therapy have also shown limited effects on trunk fat (Astorino et al. 2014), although few studies have examined VAT specifically. The potential causal relationship between LTPA and VAT should be further investigated in a prospective training study using a supervised, progressive training program meeting current population-specific guidelines for physical activity.

The results of our analyses suggest a relationship with the length of time post-SCI and increasing risk for cardiometabolic disease. As it is widely reported that the risk of other complications increases with injury duration, it is prudent that lifelong rehabilitation modalities be implemented

to prevent the increasing risk of morbidity in this population. Several models of rehabilitation have been proposed for this population that highlight the need for continuous physical activity as individual's transition from rehabilitation to living in the community. Thus, maintaining health and function throughout their lifetime (van der Woude et al., 2013, Rimmer & Henley, 2013). It is also possible that the impact of LTPA on VAT is at least in part mediated by overall functional independence, as individuals with a longer-standing injury tend to report declining functional ability and continued muscle atrophy further contributing to a decreased exercise capacity (Spungen et al., 2003).

The heterogeneity of motor, sensory and autonomic impairments in the SCI population further complicate exercise prescription and physical activity guideline development for this population. Individuals with motor-complete tetraplegia may face challenges achieving an exercise intensity sufficient for cardiometabolic benefit as they may lack the neuromuscular ability to exercise voluntarily at an intensity sufficient to elicit increases in fat utilization and reductions in adipose tissue distribution (Kressler et al., 2014). This is often attributed to the reliance on upper-body exercises among wheelchair users, resulting in decreased caloric expenditure and a lower metabolic yield (Price, 2010). Based on sex and injury characteristics, our sample does represent the heterogeneity of the Canadian SCI population (Noonan et al., 2012), suggesting benefits for all individuals with SCI who engage in moderate-to-vigorous LTPA even though we were unable to detect differences in the relationship between VAT and LTPA based on injury characteristics. Future training interventions should consider the possibility that individuals with motor-complete tetraplegia may not be able to take advantage of this relationship without the use of neuromuscular electrical stimulation. Previous work has demonstrated improvements in VAT,

muscle mass, and metabolic profile following exercise that utilizes electrical stimulated muscle contraction (Gorgey et al., 2012, Griffin et al., 2009), although the costs and availability for the wider SCI population must be considered for public health guidelines.

Relatedly, the impact of voluntary resistance training on VAT, and other health outcomes, in the SCI population remains understudied. While the tendency is to focus on aerobic exercise training in the field of exercise physiology and public health (Steele et al., 2017), resistance training has observed, and possibly equal, benefits to aerobic training on risk of multimorbidity in the able-bodied population (Dankel et al., 2015; Phillips & Winett, 2010). The tools used for this assessment collected overall LTPA, primarily validated for aerobic activity, and we are unable to make any conclusions related to type of LTPA. The importance of both properly measuring resistance training and muscle strength in the SCI population represents an important gap in the literature and may further explain the link between health outcomes and LTPA.

One of the limitations of this study is that LTPA data was collected using self-report rather than an objective measure such as accelerometry. The self-reported nature of physical activity data is often associated with an overestimation of exercise intensity, particularly in sedentary adults and is also dependent on the accurate recall of behaviour (Duncan et al., 2001; Lewis et al., 2007). The data reported in this study represents the baseline data from two cohort studies that utilized different but related SCI-specific LTPA recall questionnaires. While the criterion validity and reliability of these two measures has been established, it does introduce the assumption that a weekly recall is representative of daily activity among the cohort that completed the LTPAQ-SCI. Given the challenges in recruiting individuals with SCI and the high-level resources needed

for DXA-based body composition assessment, we feel this assumption was warranted to provide a sample of sufficient size to conduct multivariable analyses.

To our knowledge, this study was the first to explore the relationship between any moderate-to-vigorous LTPA and VAT in the SCI population. Results of the current cross-sectional assessment indicate that participation in any moderate-to-vigorous LTPA is associated with reductions in VAT after controlling for clinically relevant injury-related and anthropometric correlates. The benefits of LTPA on fitness outcomes in this population are well known; the results of this study suggest there may be cardiometabolic benefits associated with current population-specific physical activity guidelines, however, future work should now focus on improving health outcomes and the mediating factors that influence cardiometabolic morbidity, specifically interventions to reduce VAT accumulation.

Financial Support: This study received funding from the Canadian Institutes for Health Research (CIHR; grant #86521), Craig H Nielsen Foundation (grant #1991150), Ontario Neurotrauma Foundation (grant #2008-SCI-PDF-692; grant #2009-SC-MA-684), and the Spinal Cord Injury Solutions Network (grant #2010-43). Dr. Pelletier received post-doctoral funding from SCI Ontario. Dr. Giangregorio is a CIHR New Investigator, and has received funding from the Ontario Ministry of Research and Innovation and the Canada Foundation for Innovation related to this work. Dr. Craven is a senior scientist funded by the Craig H. Nielsen Foundation (grant #350642).

Conflict of Interest: The authors report no conflicts of interest associated with this manuscript.

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Table 1. Results of univariate regression analysis: The effect of Leisure Time Physical Activity on Visceral Adipose Tissue in participants with chronic SCI^a (n=136)

Variable	β (95% CI)	Adjusted R square	P-value (F change)
Sex	38.22 (10.66-65.78)	0.05	0.01
Age (years)	1.89 (0.98-2.81)	0.10	0.00
Moderate/Vigorous LTPA ^b (Yes/No)	-13.71 (-41.01-13.61)	0.00	0.32
Age at-injury (years)	1.24 (0.50-2.03)	0.06	0.00
Time post-injury (years)	0.19 (-0.92-1.31)	0.00	0.74
Android/Gynoid ratio	209.36 (170.00-248.73)	0.45	0.00
Waist circumference (cm)	4.05 (3.48-4.62)	0.60	0.00

^aSCI=Spinal Cord Injury, ^bLTPA = Leisure Time Physical Activity

Table 2. Results of multiple regression analysis: The effect of Leisure Time Physical Activity on Visceral Adipose Tissue in participants with chronic SCI^a (n=136)

Variable	β	P-value	Adjusted R square	P-value (F change)
Moderate/Vigorous LTPA ^b (Yes/No)	-18.66	0.02	0.00	0.30
Age at-injury (years)	0.63	0.06	0.07	0.00
Time post-injury (years)	1.10	0.01	0.12	0.00
Android/Gynoid ratio	81.10	0.00	0.50	0.00
Waist circumference (cm)	3.08	0.00	0.67	0.00

^aSCI=Spinal Cord Injury, ^bLTPA = Leisure Time Physical Activity

Table 3. Characteristics in participants with chronic SCI^a (n=136)

	All participants	Range	Male	Female
Demographic characteristics				
Sex, n (%)	-	-	100 (73.5)	36 (26.5)
Age (yr), mean (SD ^b)	49.1 (12.9)	22 - 78	48.3 (12.6)	51.2 (13.7)
Smoking, n (%)	32 (23.5)	-	24 (24)	8 (22.2)
Body composition characteristics				
Height (cm), mean (SD)	174.8 (9.5)	148 - 193	178.3 (7.2)	165.1 (8.3)
Mass (kg), mean (SD)	80.7 (19.0)	46 - 137	84.7 (18.1)	69.8 (17.5)
BMI, mean (SD)	26.4 (5.4)	16 - 41	26.6 (5.2)	25.6 (6.1)
Waist circumference (cm), mean (SD)	96.1 (14.1)	65 - 148	98.8 (13.3)	88.5 (13.5)
Android/Gynoid ratio, mean (SD)	0.9 (0.2)	0.4 - 1.5	1.0 (0.2)	0.8 (0.2)
Visceral adipose tissue (cm ²), mean (SD)	152.5 (73.4)	25 - 373	162.6 (69.9)	124.4 (76.5)
Impairment characteristics				
Age at-injury (yr), mean (SD)	33.5 (15.3)	3 - 72	34.3 (15.3)	31.1 (15.3)
Time post-injury (yr), mean (SD)	15.6 (11.3)	2 - 65	14.0 (9.4)	20.1 (14.5)
Impairment distribution, n (%)				
Paraplegia AIS ^c A/B	49 (70.0)	-	35 (35.0)	14 (38.9)
Tetraplegia AIS A/B	37 (56.1)		29 (29.0)	8 (22.0)
Paraplegia AIS C/D	21 (30.0)		16 (16.0)	5 (13.9)
Tetraplegia AIS C/D	29 (43.9)	-	20 (20.0)	9 (25.0)

^aSCI= Spinal Cord Injury, ^bSD = Standard Deviation, ^cASIA impairment scale

Figure Captions

Figure 1. Moderate-vigorous leisure time physical activity (LTPA) distribution (min/day)

Draft

50x40mm (300 x 300 DPI)