Research Article

The influence of level of spinal cord injury on adipose tissue and its relationship to inflammatory adipokines and cardiometabolic profiles

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Objective: Level of injury (LOI) and the role of adipose tissue and its proinflammatory adipokines in cardiometabolic dysfunction following spinal cord injury (SCI) remains poorly understood. We aim to examine the influence of LOI on adipose tissue and its relationship to proinflammatory adipokines and cardiometabolic profiles following SCI.
Design: Cross sectional and correlational study.
Setting: Clinical hospital and academic setting.
Participants: Forty-seven individuals with chronic motor complete SCI (age 43.8±11.5 y, BMI: 27.3±5.3) were classified as having tetraplegia (TSCI; $n=12$) or paraplegia (PSCI; $n=35$).
Intervention: Non applicable.
Outcome Measures: Visceral (VAT) and subcutaneous (SAT) adipose tissue volumes were measured using magnetic resonance imaging. Proinflammatory adipokines (tumor neurosis factor-α, interleukin-6 (IL-6), plasminogen activatable inhibitor-1, thrombin-activatable fibrinolysis inhibitor, and high-sensitivity c-reactive protein) and cardiovascular, carbohydrate, and lipid profiles were assessed according to standard techniques.
Results: VAT volume was greater in TSCI versus PSCI ($p=0.042$); however, after covarying for age this significance was lost ($p>0.05$). IL-6 was significantly elevated in TSCI ($p<0.05$), while other markers of inflammation generally were elevated, but did not reach statistical significance ($p>0.05$). Systolic blood pressure and total cholesterol were significantly lower in TSCI ($p<0.05$), while fasting glucose was significantly lower in PSCI ($p<0.05$). A number of proinflammatory adipokines and cardiometabolic markers significantly correlated with adipose tissue depots by LOI ($p<0.05$).
Conclusion: The results show that LOI does not influence the distribution of adipose tissue, but does influence proinflammatory adipokines and cardiometabolic profiles following SCI. Further research is needed to evaluate impact of lean body mass on these findings.

Keywords: Spinal cord injury, Tetraplegia, Paraplegia, Adipose tissue, Proinflammatory adipokines

Introduction

Spinal cord injury (SCI) can be classified according to level of injury (LOI) as tetraplegia (TSCI), which involves neurologic insult to the cervical spinal cord, or paraplegia (PSCI), involving injury to either the thoracic, lumbar, or sacral spinal cord. It is well documented that following the injury as a result of neurological dysfunction there are drastic alterations in body composition and cardiometabolic profiles.[1,2] Previous research demonstrated that those with SCI are at increased risk for hypertension, carbohydrate and lipid dysfunction, and systemic inflammation.[1–4] Greater

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reductions of lean body mass (LBM) are observed with higher LOI which leads to reductions in energy expenditure and a state of positive energy balance ultimately contributing to a state of obesity. Collectively, these are thought to contribute to the higher prevalence of type-two diabetes mellitus (T2DM) and cardiovascular disease found in the SCI population.[1–4] Two studies reported controversial findings regarding the influence of LOI of obesity: a preliminary report showed that LOI does not influence the distribution of adipose tissue between TSCI and PSCI,[5] while a second study by Inskip *et al.*[6] noted that in rat model one month after the injury central adiposity increased in rats with T3, but not in T10 SCI. Previous findings have suggested that LOI influences metabolic profiles;[5,7–10] however, the role of adipose tissue and its secretory products on these profiles remains poorly understood.

It is increasingly accepted that obesity and obesity-related diseases are inflammatory in nature and characterized by chronic, low-grade inflammation thought to stem from adipose tissue.[11,12] In recent years, adipose tissue has been described as secretory organ releasing a number of signaling molecules called adipokines. Proinflammatory adipokines mediate inflammation and alter physiological function by activating intracellular stress signaling pathways. These pathways interfere with homeostatic mechanisms and are therefore thought to be the link in the pathogenesis of obesity and obesity-related disorders, such as T2DM and cardiovascular disease.[11,13,14]

An important role in the pathogenesis of cardiometabolic dysfunction is played by visceral adipose tissue (VAT), as it directly expresses many proinflammatory adipokines, including tumor necrosis factor-α (TNF-α), interlukin-6 (IL-6), plasminogen activator inhibitor-1 (PAI-1), and thrombin activatable fibrinolysis inhibitor-1 (TAFI-1).[11,15,16] In the able-bodied (AB) population these adipokines are elevated with obesity and contribute to systemic and vascular inflammation due to their access to the hepatic portal vein.[1] In both obese SCI and AB subjects, serum levels of IL-6 were significantly higher than in non-obese healthy participants and in the former group a positive correlation is seen between IL-6 and fasting insulin.[17–20] Plasma levels of PAI-1 were positively correlated with abdominal obesity in chronic SCI, while abdominal sagittal diameter was positively associated with high sensitivity c-reactive protein (hs-CRP),[21] a hepatocyte-derived marker of systemic inflammation that is stimulated by IL-6 and TNF-α and is elevated in chronic SCI.[4,22,23] The results of the aforementioned studies suggest that adiposity and proinflammatory adipokines are greatly contributing, or possibly driving, cardiometabolic dysfunction in the SCI population.

The purpose of the present study was to examine the effect of LOI on adipose tissue and its relationship to proinflammatory adipokines and cardiometabolic profiles in individuals with motor complete SCI. We hypothesized that (1) there would be a significantly greater volume of VAT in TSCI when compared to PSCI, leading to significantly poorer proinflammatory and cardiometabolic profiles in the former group and (2) VAT would correlate with a greater number of proinflammatory adipokines and cardiometabolic profiles by LOI.

Material and methods

Participants

Participants were recruited from a spinal cord dysfunction registry over a period of three years. Forty-seven participants with chronic motor complete SCI (Age 43.8 ± 11.5 y, 38 males/9 females, and BMI: 27.3 ± 5.3) were included in this study. The participants were classified according to their LOI into TSCI ($n=12$, C4-C8) or PSCI ($n=35$, T2-L1; Table 1). All participants completed informed consent that was approved by the local ethical committee at the host institution.

Inclusion criteria were as follows: (1) men and women between the ages of 18 and 65 years old, with maximum age chosen to avoid any confounding effects of age on body composition; (2) C5-L2 motor complete (International Standards for Neurological Classification of Spinal Cord Injury A and B[24]) individuals, as the degree of body composition alterations may vary between complete and incomplete SCI and injuries above C5 have limited hand functions and may be dependent on others to help with meal preparation, which can indirectly influence body composition;[25,26] and (3) a minimum of one year post injury, as by this time adaptations in body composition will be stabilized. Only individuals with motor complete SCI were studied to ensure a homogenous study sample and reduce the possible effects of complete versus incomplete injury on body composition. Exclusion criteria included: (1) those with known orthopedic limitations; (2) smokers or alcohol abusers; (3) type one diabetes mellitus; (4) T2DM requiring insulin; (5) hypothyroidism; (6) preexisting cardiometabolic disease, renal disease, and/or infection; (7) uncontrolled respiratory complications, autonomic dysreflexia, or deep vein thrombosis within the past three months; (8) pressure injuries greater than grade II; and/or (9) individuals with magnetic resonance imaging (MRI) incompatible material (i.e. rods, valves, stents, etc.) implanted for medical purposes.

Table 1 Participant demographics by level of injury.

	Para-SCI (n = 35)	Tetra-SCI (n = 12)
Age (y)	41.46 ± 11.53	50.58 ± 8.81*
Male (M/F)	27/8	11/1
Height (cm)	172.23 ± 9.35	177.48 ± 6.35
Weight (kg)	81.19 ± 15.88	85.72 ± 22.66
Body mass index (kg/m^2)	27.36 ± 4.70	27.24 ± 7.04
Time since injury (y)	13.84 ± 11.55	16.19 ± 11.88
Level of injury	T2-L1	C4-C8

*Significantly different between paraplegia and tetraplegia ($p < 0.05$).

Body composition assessment

Non-contrast abdominal MRIs were obtained with a 1.5-T magnet (General Electric, Waukesha, WI) whole body scanner. T1-weighted imaging was performed using a fast spin-echo sequence with an axial in-phase/out-phase with a repetition time of 500 ms and an echo time of 14 ms, a field of view of 20 cm, and a matrix size of 256×256. After participants were assisted into the supine position on the MRI table, their distal extremities were strapped together to ensure a neutral position and prevent any spastic movement that could contribute to image artifact. Scans were performed with the participants' arms above their head or across their chest if arm range of motion was limited. Transverse slices 4 mm thick were acquired every 4 mm from the xiphoid process to the femoral heads. Images were acquired in a series of two stacks superior and inferior to the intervertebral disc between the fourth and fifth lumbar vertebrae. Using the umbilicus, the L4-L5 intervertebral disc was identified.[12,27–29] The first series of images extended proximally from L4-L5 to the xiphoid process, while the second series of images extended distally from L4-L5 to the femoral heads. During the scan participants were asked to deeply inhale and hold their breath for 10–15 seconds to minimize respiratory motion artifact typically associated with MRI of the abdominopelvic cavity. The use of two stacks of images reduced the breath holding time required for the study participants, especially those with higher SCI. Participants were given earplugs to minimize noise from the MRI magnet. To maintain normal body temperature and deter spasticity, a blanket was provided and participants were instructed to remain motionless.[12]

All images were downloaded to a disk and analyzed using ImageJ (https://imagej.nih.gov/ij) software. Images were automatically segmented into adipose tissue, skeletal muscle, and bone/background based on their intensity, with adipose tissue having the highest intensity and bone/background having the lowest intensity. Cross sectional area (CSA) was automatically calculated by the software by summing the pixels of the tissue and multiplying it by the pixel surface area (field of view divided by matrix size squared), while volume was computed by multiplying the CSA by the image slice thickness and inter-slice space. Visual distinction was used to determine VAT and SAT based on their anatomical locations and the volumes were summed together from consecutive slices for each adipose tissue depot. A ratio of VAT to SAT (VAT:SAT) was calculated.[25] We chose to study volume of adipose tissue as it has been reported to be a better measure of intraabdominal adipose tissue compared to CSA.[30]

Proinflammatory adipokine and cardiometabolic profiles

Following a 12-hour fast, the participants were admitted to the host institution's clinical research center for the collection of plasma proinflammatory adipokines and carbohydrate and lipid profiles. Ten ml of blood was collected for assessment of proinflammatory inflammatory biomarkers and lipids.

A standard intravenous glucose tolerance test (IVGTT) was administered to determine glucose effectiveness (S_G) and insulin sensitivity (S_I) according to previously published procedures.[31] Briefly, an indwelling catheter with an intravenous saline drip (0.9% NaCl) was placed in an antecubital vein, while on a contralateral hand vein another intravenous line was placed. These lines were used to assist with the infusion of glucose and blood sampling throughout the IVGTT. Glucose samples were taken at −6, −4, −2, 0, 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 19, 22, 23, 24, 25, 27, 30, 35, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 minutes after the rapid glucose injection (0.3 g/kg over 30 seconds at time zero). Twenty minutes following the glucose injection, a bolus of insulin (0.02 U/kg) was injected to determine S_I. Blood pressure and heart rate were assessed at 22, 23, and 24 minutes of the IVGTT. Fasting plasma glucose levels were calculated as the mean of −6, −4, −2, and 0 minutes before the administration of the glucose bolus. S_I and S_G were calculated from a least squares fitting of the temporal pattern of glucose and insulin throughout the IVGTT using the minimal model system (MinMod Inc., Pasadena, CA, USA).

Plasma concentrations of TNFα, IL-6, PAI-1 (R&D Systems Inc., Minneapolis, Minnesota, USA), TAFI-1 (Kamiya Biomedical Company, Seattle, Washington, USA), and hs-CRP (ALPCO, Salem, New Hampshire,

USA) were collected and analyzed using a commercially available high-sensitivity enzyme-linked immunosorbent assay. Fasting blood glucose (Wako Chemical USA, Richmond, Virginia, USA), triglycerides (TG; Sigma-Aldrich, St Louis, Missouri, USA), total cholesterol (TC), low-density lipoprotein-cholesterol (LDLC), and high-density lipoprotein-cholesterol (HDLC; Thermo DMA, Austin, Texas, USA) were determined using commercially available colorimetric assays).

Data analysis

Analyses were performed using SPSS 24.0 (IBM, Armonk, New York) and R (R Foundation for Statistical Computing, Vienna, Austria). All values are presented as means ± standard deviation and are not log-transformed. Alpha was set to $p < 0.05$. All data were checked for normality with the Shapiro-Wilk test and box-plots. Values that did not meet parametric standards were log-transformed as this is commonly seen with plasma adipokines and cardiometabolic parameters.[32] Normally distributed variables were evaluated with an independent samples t-test, while non-normally distributed variables were assessed with the Mann–Whitney independent U-test. The mean difference, 95% confidence intervals of the difference, and percent difference were calculated for all adipose tissue, inflammatory, and cardiometabolic variables. Spearman rho correlations were used to evaluate the relationships between adipose tissue depot and inflammatory and cardiometabolic biomarkers between groups. In addition, partial correlations were used to control for systemic inflammation (as measured by hs-CRP) that may result from a secondary complication associated with the chronic SCI.[1] Secondary analysis was performed using analysis of covariance (ANCOVA) to evaluate the effect of age on VAT between the two groups.

Results

There were no significant differences among demographic characteristics ($p > 0.05$), except for age where participants with TSCI were about nine years older than those individuals with PSCI ($p = 0.016$; Table 1). Individuals with TSCI had approximately 38% significantly greater amount of VAT volume versus PSCI ($p = 0.042$; Table 2). All other adipose tissue variables were not significantly different between the groups ($p > 0.05$). In the ANCOVA comparing VAT between TSCI and PSCI, there was a nonsignificant overall group effect ($F = 2.49$, degrees of freedom = 1.00, $p = 0.12$) after using age as a covariate.

Tables 3 and 4 present inflammatory and cardiometabolic profiles between the groups, respectively. IL-6 was significantly greater in TSCI vs. PSCI ($p < 0.05$). All other proinflammatory adipokines were not significantly different between groups ($p > 0.05$); however, individuals with TSCI generally demonstrated higher proinflammatory adipokine profiles compared to PSCI. Systolic blood pressure (SBP) and TC were significantly lower in individuals with TSCI when compared to PSCI ($p < 0.05$), while fasting glucose was significantly lower in PSCI ($p < 0.05$). All other cardiometabolic profiles were not significantly different between the groups ($p > 0.05$).

All correlations between the adipose tissue depots and proinflammatory adipokines and cardiometabolic profiles are presented in Tables 5 and 6, respectively. Significant positive correlations were noted between both depots of adipose tissue and PAI-1 in PSCI (SAT volume: $\rho = 0.425$, $p = 0.014$; VAT volume: $\rho = 0.397$, $p = 0.020$). VAT:SAT significantly correlated with diastolic blood pressure (DBP) in both TSCI and PSCI groups ($\rho = 0.402$, $p = 0.018$ and $\rho = 0.610$, $p = 0.046$, respectively). VAT volume and the VAT to SAT ratio significantly related to insulin sensitivity ($\rho = -0.504$, $p = 0.002$; $\rho = -0.360$, $p = 0.039$, respectively), TG ($\rho = -0.494$, $p = 0.003$; $\rho = -0.445$, $p = 0.008$, respectively), HDLC ($\rho = -0.454$; $p = 0.006$; and $\rho = -0.435$, $p = 0.010$, respectively), and the TC:HDLC ratio ($\rho = 0.507$, $p = 0.002$; $\rho = 0.462$, $p = 0.006$, respectively) in the PSCI group.

When using partial correlations to control for hs-CRP, SAT significantly correlated with PAI-1 in both

Table 2 Adipose tissue by level of injury.

	Para-SCI (n = 35)	Tetra-SCI (n = 12)	Mean Difference	95% CI of the Difference	Percent Difference Between Groups
SAT volume (mL)	4015.81 ± 2173.79	3804.16 ± 1624.21	211.65	−1175.77, 1599.08	5.41%
VAT volume (mL)	2022.48 ± 1247.04	2975.00 ± 1524.50*	−952.52	−1868.76, −36.28	38.12%
VAT/SAT ratio	0.60 ± 0.41	0.80 ± 0.40	−0.20	−0.49, 0.08	28.57%

Note: CI, 95% confidence internal.
*Significantly different between paraplegia and tetraplegia ($p < 0.05$).

Table 3 Inflammatory profiles by level of injury.

	Para-SCI (*n* = 35)	Tetra-SCI (*n* = 12)	Mean Difference	95% CI of the Difference	Percent Difference Between Groups	Able-bodied normal values[55]
Tumor necrosis factor-α (pg/ml)	8.70 ± 0.75	8.92 ± 0.97	−0.22	−0.76, 0.33	2.50%	0.65–1.84
Interleukin-6 (pg/ml)	4.57 ± 3.56	11.3 ±17.62*	16.64	−12.96, −0.5	84.81%	0.26–0.82
Plasminogen activator inhibitor-1 (ng/mL)	68.38 ± 62.08	51.73 ± 32.48	16.64	−21.36, 54.65	141.43%	Not Applicable
Thrombin activatable fibrinolysis inhibitor-1 (ng/ml)	9.86 ± 1.91	9.76 ± 2.99	0.10	−1.39, 1.6	1.02%	Not Applicable
High-sensitivity c-reactive protein (mg/L)	7.08 ± 6.51	8.41 ± 7.99	−1.32	−5.97, 3.33	17.17%	1.65–2.17

Note: CI, 95% confidence internal; Able-bodied normal values adapted from Wyczalkowska-Tomasik *et al.*[55]
* Significantly different between paraplegia and tetraplegia ($p < 0.05$).

Table 4 Cardiometabolic profiles by level of injury.

	Para-SCI (*n* = 35)	Tetra-SCI (*n* = 12)	Mean Difference	95% CI of the Difference	Percent Difference Between Groups
Systolic blood pressure (bmp)	117.43 ± 12.40	105.42 ± 16.50*	12.01	2.9, 21.12	10.78%
Diastolic blood pressure (bmp)	71.00 ± 10.11	64.83 ± 12.28	6.17	−1.03, 13.36	9.08%
Fasting glucose (mg/dL)	93.69 ± 11.04	115.25 ± 51.89*	−21.56	−40.02, −3.11	20.64%
Glucose effectiveness	0.023 ± 0.009	0.017 ± 0.008	0.01	0.00, 0.01	30.00%
Insulin sensitivity	7.92 ± 23.51	1.98 ± 1.14	5.94	−8.47, 20.35	120.00%
Triglycerides (mg/dL)	115.23 ± 55.88	124.17 ± 91.76	−8.94	−53.72, 35.84	7.47%
Total cholesterol (mg/dL)	165.83 ± 31.69	140.58 ± 34.85*	25.24	3.36, 47.14	16.48%
Low density lipoprotein-cholesterol (mg/dL)	101.80 ± 29.14	81.67 ± 35.52	20.13	−0.63, 40.90	21.94%
High density lipoprotein-cholesterol (mg/dL)	36.60 ± 7.93	34.92 ± 9.80	1.68	−3.99, 7.4	4.70%
Total cholesterol/HDL ratio	4.73 ± 1.32	4.21 ± 1.67	0.53	−0.34, 1.39	11.63%

Note: CI, 95% confidence internal.
*Significantly different between paraplegia and tetraplegia ($p < 0.05$).

PSCI ($r = 0.363$, $p = 0.045$) and TSCI ($r = -0.712$, $p = 0.031$), while VAT significantly related to TG ($r = 0.384$, $p = 0.033$), HDLC ($r = -0.393$, $p = 0.029$), and the ratio of TC to HDLC ($r = 0.471$, $p = 0.007$) in PSCI. Additionally, VAT:SAT significantly correlated with TG ($r = 0.541$, $p = 0.002$) in PSCI.

Discussion

In the present study, we aimed to examine the influence of LOI on adipose tissue and its relationship to proinflammatory adipokines and cardiometabolic profiles in motor complete SCI. In the main findings from the current study, we have demonstrated similar patterns of adipose tissue distribution in individuals with TSCI and PSCI. Moreover, IL-6 and fasting glucose was significantly lower in PSCI compared to TSCI, while the former group demonstrated significantly elevated SBP and TC. Despite these observations, TSCI exhibited generally less favorable proinflammatory and cardiometabolic profiles compared to individuals with TSCI.

While not significant after covarying for age, we have shown a 38% greater volume of VAT in individuals with TSCI when compared to PSCI, suggesting higher LOI accumulate greater amounts of intraabdominal adipose tissue. This is in agreement with a preliminary study that showed LOI did not influence VAT or SAT volume or CSA. However, the authors noted the difference in VAT volume between TSCI and PSCI was 200 mL,[5] while the difference in the present study is nearly six times that amount. This was likely due to artifact of a limited sample size in the previous study.[5] The ratio of adipose tissue to LBM may be a better metric than the absolute value of adipose tissue reported in the aforementioned and the present studies.[5,33] This is especially important to consider given the larger reductions of fat free mass in TSCI compared to PSCI.[1,2,34,35] In addition, previous research examining adiposity by LOI has examined either total body or regional adipose tissue without accounting for the depot of the tissue. Spungen *et al.*[35] compared both individuals with TSCI and PSCI to a control group and demonstrated those with TSCI have significantly greater total body fat compared to a control group, while PSCI and the control group were comparable.

Table 5 Spearman rho correlations between adipose tissue and proinflammatory adipokines by level of injury.

	TNF-α	IL-6	PAI-1	TAFI-1	hs-CRP
			Paraplegia SCI (n = 35)		
SAT volume	0.26	0.15	**0.43***	−0.16	0.28
VAT volume	0.25	0.03	**0.40***	−0.12	0.16
VAT/SAT ratio	0.07	−0.07	0.19	−0.13	−0.09
			Tetraplegia SCI (n = 12)		
SAT volume	0.50	0.00	−0.35	−0.12	0.35
VAT volume	0.49	0.30	−0.21	0.15	0.45
VAT/SAT ratio	0.18	0.29	0.24	0.35	0.16

Note: hs-CRP, High-sensitivity c-reactive protein; IL-6, interleukin-6; PAI-1, plasminogen activatable inhibitor-1; SAT, subcutaneous adipose tissue; TAFI-1, thrombin activatable fibrinolysis inhibitor-1; TNF- α, tumor necrosis factor-α; VAT, visceral adipose tissue.
*$p < 0.05$.

Gibson *et al.*,[23] Cirnigliaro *et al.*,[36] and Singh *et al.*[37] showed similar results. Collectively, our data along with the current body of literature demonstrates greater amounts of total adipose tissue in TSCI that may be accounted by the larger quantity of VAT and less LBM when compared to PSCI.

Numerous reports in the AB population suggest proinflammatory adipokines secreted by adipose tissue in the obese population are responsible for metabolic dysfunction that often accompanies obesity.[1,11,38–40] Proinflammatory adipokines IL-6 and TNF-α are both implicated in whole-body insulin resistance via the upregulation of the transcription factor SOCS3.[1,11] Here we show significantly elevated levels of IL-6 in individuals with TSCI. In addition, we also demonstrated that with increasing visceral adiposity there is a positive correlation with IL-6 and TNF-α. Wang *et al.*[4] showed no significant differences between IL-6 and CRP by LOI, while Maruyama *et al.*[21] reported a number of positive correlations among circulating inflammatory adipokines and surrogate measures of obesity in chronic SCI. In both of these studies, a number of these inflammatory markers correlated with markers of insulin resistance, vascular dysfunction, and dyslipidemia.[4,21] In addition, we observed elevated levels of PAI-1 and TAFI-1 in PSCI compared to TSCI and a positive correlation between both adipose tissue depots and PAI-1 and TAFI-1 in the former group, while a negative relationship was observed in TSCI. These adipokines are both primarily involved in inhibiting the breakdown of fibrin clots causing endothelial damage and vascular dysfunction.[1,11] Greater vascular dysfunction may be more prevalent in PSCI, and along with less SNS blunting could contribute to the elevated SBP and DBP we observed in individuals with PSCI compared to TSCI. A greater prevalence of hypertension has also been noted in previous investigations when examining cardiovascular risks between TSCI and PSCI.[41,42] Collectively, this work suggests that TSCI and PSCI may have different proinflammatory profiles and therefore unique cardiometabolic profiles. However, further research is needed to demonstrate the mechanism.

Previous literature has suggested that individuals with TSCI are more susceptible to insulin resistance, impaired glucose tolerance, and dyslipidemia.[7–10] We show TSCI had reduced S_I and S_G and significantly elevated fasting plasma glucose. These results mirror previous studies[5,7,23] and may correspond to significantly less muscle mass and greater visceral adiposity in TSCI versus PSCI, potentially leading to a higher concentration of IL-6 and TNF-α systemically. In addition, IL-6 and TNF-α are both implicated in insulin resistance and dyslipidemia in the AB population and to date, research in this area in the SCI population remains contradictory. Previous reports in TSCI have implicated a greater number of lipid abnormalities than those with PSCI,[10] while others have reported elevated TC, LDLC, and HDLC profiles

Table 6 Spearman rho correlations between adipose tissue and cardiometabolic profiles by level of injury.

	SBP	DBP	FG	S_g	S_I	TG	TC	LDL	HDL	TC/HDL ratio
					Paraplegia SCI (n = 35)					
SAT volume	0.14	−0.24	0.04	−0.19	−0.08	−0.004	0.20	0.03	0.09	0.06
VAT volume	0.18	0.20	0.22	−0.001	**−0.50****	**0.49****	0.17	0.16	**−0.45****	**0.51****
VAT/SAT ratio	0.13	**0.40***	0.10	−0.01	**−0.36***	**0.45****	0.16	0.20	**−0.44***	**0.46****
					Tetraplegia SCI (n = 12)					
SAT volume	−0.42	−0.46	0.19	−0.59	−0.31	0.41	0.25	0.27	−0.25	0.55
VAT volume	−0.20	0.06	0.52	−0.43	−0.20	0.43	0.02	0.06	−0.52	0.54
VAT/SAT ratio	0.28	**0.61***	0.38	−0.01	−0.10	0.39	−0.09	−0.11	−0.52	0.273

Note: Diastolic blood pressure; FG, Fasting glucose; HDL, High density lipoprotein-cholesterol; LDL, low density lipoprotein-cholesterol; S_G, glucose effectiveness; S_I, insulin sensitivity; SBP, systolic blood pressure; TC, total cholesterol; TC/HDL, total cholesterol/HDL ratio; TG, triglycerides.
*$p < 0.05$, **$p < 0.009$.

and a lower TC:HDLC ratio in individuals with PSCI than those with TSCI.[4,8,43–45] We have demonstrated similar results showing elevated TC, LDLC, and HDLC, but a lower TC/HDLC ratio. The relatively elevated HDLC profiles observed in the PSCI group may stem from a larger LBM percentage and better aerobic fitness, which has been implicated in favorable HDLC profiles in PSCI versus TSCI.[44,46,47] With reference to TG, greater levels of inactivity, such as that reported with higher levels of SCI, have been reported to reduce lipoprotein lipase resulting in elevated levels of circulating TG.[43] This observation could account for the elevated levels of TG in the TSCI who have less LBM available for leisure and physical activity versus PSCI. Higher levels of TG have also been previously reported by Schmid *et al.*[43] and Gibson *et al.*[23] Moreover, elevated catecholamine levels have been reported in PSCI due to greater activity of the SNS,[43] which may increase lipolysis and the eventual production of LDLC, thus accounting for the overall increase in TC.

After controlling for hs-CRP, a number of correlations were no longer significant. Given our screening criteria, individuals with any preexisting condition or medical complication that may be inflammatory in nature were excluded from the study. The significant correlations in the present study could be a result of type 2 macrophages in the vascular tree that contribute to a systemic proinflammatory environment, which were lost after controlling for inflammation.[48] Thus, the significant partial correlations may be driven by adipose tissue such that with increasing adiposity there is parallel inflammatory and cardiometabolic dysfunction. To our knowledge, no other literature has conducted such an analysis in the SCI population and future work is needed to reproduce and understand the cause of these findings.

While our findings are novel and extend the current literature in the field of SCI, this study is not without limitations. First, the cross-sectional design of the study makes predictions as to the diagnostic and prognostic value of the evaluated markers and long-term implications difficult. Second, the sample size of TSCI, as well as female participants, was relatively small compared to the PSCI group. This factor may have resulted in a type-two error where we failed to observe a significant difference when there was one due to inadequate power. However, such sample sizes are not uncommon in SCI studies, especially when using advanced imaging technologies.[5,25,33,43] Third, inflammatory and cardiometabolic markers were assessed at a single time point for each participant, thus we were unable to exclude variability of these markers with time. Nonetheless, it has been reported that in approximately 90% of cases, two measurements of CRP taken about 3 months apart were within one quartile of each other.[49] Forth, sex hormones have been implicated in adipose tissue distribution and lipid storage in the AB population, and were not evaluated in the present study.[50] Previous research has demonstrated altered testosterone levels following SCI and its inverse relationship to BMI and insulin sensitivity, thereby potentially contributing to body composition and metabolic profiles.[51,52] Lastly, in our study we assessed circulating levels of proinflammatory adipokines and can therefore not accurately account for other sources of release. Nevertheless, adipose tissue biopsies, especially from VAT, were not feasible for our study and proinflammatory adipokines are not primarily secreted from SAT.[53,54]

Conclusion

This research does not suggest distinctive patterns of adiposity in motor complete TSCI and PSCI given the relatively unique storage sites of adipose tissue and their effect on proinflammatory and cardiometabolic profiles in the AB population. However, proinflammatory adipokines and cardiometabolic profiles showed LOI-based differences such that the latter profiles may stem from greater systemic inflammation present in TSCI compared to PSCI. To further define the influence of level of SCI on obesity and its comorbidities, future studies should assess the effect of LBM on the present findings, as well as match for body fat, age, and gender.

Disclaimer statements

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