Review

Effects of spinal cord injury on body composition and metabolic profile – Part I

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Several body composition and metabolic-associated disorders such as glucose intolerance, insulin resistance, and lipid abnormalities occur prematurely after spinal cord injury (SCI) and at a higher prevalence compared to able-bodied populations. Within a few weeks to months of the injury, there is a significant decrease in total lean mass, particularly lower extremity muscle mass and an accompanying increase in fat mass. The infiltration of fat in intramuscular and visceral sites is associated with abnormal metabolic profiles. The current review will summarize the major changes in body composition and metabolic profiles that can lead to comorbidities such as type 2 diabetes mellitus and cardiovascular diseases after SCI. It is crucial for healthcare specialists to be aware of the magnitude of these changes. Such awareness may lead to earlier recognition and treatment of metabolic abnormalities that may reduce the co-morbidities seen over the lifetime of persons living with SCI.

Keywords: Spinal cord injury, Body composition, Metabolic profile, Muscle mass, Glucose metabolism, Lipid metabolism

Introduction

Spinal cord injury (SCI) causes partial or total interruption of neural signal transmission across and below the level of injury. An estimated 250 000–400 000 individuals have SCI in the USA with approximately 12 000 injuries occurring annually, primarily caused by motor vehicle collisions, sporting accidents, and firearms.[1] The injury is generally categorized by the severity of sensory and motor loss, with injury resulting in absence of sensory and motor function distal to the level of injury categorized as complete, and injury resulting in limited sensation and motor function categorized as incomplete.[2] The loss of somatic and autonomic control results in a limited ability to perform physical activity and a subsequently blunted systemic response to exercise. The clinical consequences of SCI, paired with reduction in physical activity, often result in a deterioration of body composition and metabolic profile.[2–7]

Emerging evidence indicates that there are significant changes in both body composition and metabolic profiles after SCI, which have significant health consequences and lead to several non-communicable diseases. Several studies have sought to determine how increased fat mass (FM) or decreased fat-free mass (FFM) is responsible for disruption in metabolism of lipid, glucose, and insulin. The current evidence is based more on relationships than causality. These studies operate on the hypothesis that physical inactivity and decreases in anabolic hormones after SCI are responsible for deterioration in body composition and associated with metabolic profile disorders. The current review will be divided into two major sections. The first section will include an overview of the major changes in body composition and metabolic profile that occurs after SCI (Part I). The second section includes a summary of the functional electrical stimulation or neuromuscular electrical stimulation

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DOI 10.1179/2045772314Y.0000000245

interventions that showed efficacy in influencing changes after SCI (Part II). We believe that this review will establish a basis for more research in this area. There is growing interest from clinicians, rehabilitation specialists, and the US government (Department of Veterans Affairs and National Institutes of Health) and other countries on waging war against obesity and the associated metabolic health consequences after SCI.

Body composition after SCI

Skeletal muscle, FFM adaptations after SCI

Shortly after injury, individuals with SCI experience rapid and significant skeletal muscle atrophy mainly below the level of injury.[4,5,8–22] Skeletal muscle cross-sectional area (CSA) could be as small as 50% compared to healthy able-bodied (AB) controls.[9] Castro *et al.*, Gorgey and Dudley and others have reported that both individuals with complete and incomplete SCI suffer dramatic muscle atrophy within a few weeks of injury which continues throughout the end of the first year.[9–11] Castro *et al.* studied the effects of complete SCI (C6-T10) on skeletal muscle morphology by analyzing magnetic resonance imaging (MRI) of thigh and leg muscles 6, 11, and 24 weeks post-injury. They found that 6 weeks post-injury, individuals with complete SCI experienced an 18–46% decrease in the size of CSA of sub-lesional skeletal muscles compared to age- and weight-matched AB controls. Additionally, this study reported 12 and 24% decreases in the average CSAs of soleus and gastrocnemius muscles, respectively. The average CSA of quadriceps, hamstrings, and hip adductor muscles decreased by 14–16% within the first 24 weeks of SCI.[9] The average CSA was 45–80% smaller compared to AB controls 24 weeks post-injury. A similar observation was also noted in individuals with incomplete SCI who were found to have 30% smaller CSA of the knee extensors 6 weeks post-SCI compared to AB controls.[10,11] Skeletal muscle continues to atrophy by 43% of the original muscle size 4.5 months post-SCI.[10] The same study noted a three times greater amount of intramuscular fat (IMF) compared to AB controls.[10] Moreover 4.5 months post-SCI, IMF continued to increase by 26% compared to the initial measurement at 6 weeks post-SCI.[10] Increased IMF has been associated with glucose intolerance.[12]

Moreover, SCI has also been shown to greatly affect the relationship between fast and slow twitch muscle fibers; this may arise from paralysis below the level of injury.[13–15] Talmadge *et al.*[14] estimated that by 24 weeks, the vastus lateralis, gastrocnemius, and soleus muscles, approximately 90% of muscle fibers, are fast twitch fibers compared to 6 weeks at baseline. The process typically manifests between 4 and 7 months post-injury and can continue up to 70 months post-injury before plateauing into a steady state of predominantly type IIx, fast-glycolytic twitch muscle fibers.[14,15] This transformation renders the skeletal muscle to be highly fatigable and susceptible to skeletal muscle damage. Bickel *et al.*[16] demonstrated that following acute isometric exercise using electrical stimulation, knee extensors showed significant reduction in torque by 66% post-injury compared to only 33% in AB controls. Moreover, recovery of force between contractions was decreased in persons with SCI compared to AB controls during repetitive isometric actions.[16] Recovery of force is essential to ensure completion of a specific task otherwise fatigue ensues and limits performance. Failure of the muscle force to recover between repetitive contractions may suggest failure of the excitation contraction coupling mechanism or build-up of organic compounds that may interfere with myosin–actin cyclic attachments.

Decline in soft tissue FFM is a key feature in persons with SCI.[5,17–30] In a monozygotic twin study, Spungen *et al.*[17] noticed a significant decline in FFM of twins with SCI compared to their twins without SCI. The study noted a decline in rate of FFM of nearly 4 kg per 5 years, while areas above the level of injury remained unaffected. The same study reported that the monozygotic twins with acquired paraplegia had significantly more total body FM and percentage fat per unit body mass index (BMI) than their AB twins. Those with SCI showed an increase in FM (7%) compared with their AB co-twins.[17] Spungen *et al.*[17] reported that duration or level of injury and advancing age are negatively correlated with percentage of FFM in individuals with SCI. Also completeness and higher level of injury lead to greater decline in FFM compared to those with incomplete SCI. In this study, the percentage of FFM in the arms, legs, trunk, and total mass were 32, 42, 9, and 27% lower in persons with tetraplegia compared to AB controls, respectively.[5] A recent study confirmed the loss of arms' FFM and found that the CSA of wrist extensors in individuals with tetraplegia were 25% smaller compared to AB controls.[19] The findings may suggest that the detrimental upper extremity functions after tetraplegia may be in part due to significant loss in muscle mass.

Bauman *et al.*[23] demonstrated significantly reduced muscle mass and viscera in SCI vs. monozygotic AB twins using whole-body potassium counts (2534 ± 911 vs. 3515 ± 916) with resting energy expenditure (REE) similarly reduced in SCI vs. AB twins (1634 ± 290 vs. 1735 ± 295 kcal/day). Likewise, Monroe *et al.* reported

lower FFM in SCI vs. AB controls (69.2 ± 8.7 vs. 77.2 ± 7.2 kg), with higher FM (30.8 ± 8.7 vs. 22.8 ± 7.2 kg) despite similar BMIs.[24] Considering the health and clinical implications of estimating FFM, Gorgey *et al.*[25] established and validated predictive equations to estimate FFM in persons with SCI. Three equations were developed for whole body, trunk, and leg FFM. These equations can be used by SCI specialists to estimate FFM based on their body weight. Work is in progress to establish similar equations that can capture longitudinal adaptations after SCI.

Energy balance after SCI

After injury, the loss of metabolically active muscle mass results in reduction of basal metabolic rate (BMR) and REE.[24,26] The BMR is commonly measured by indirect calorimeter after overnight fast and complete bed rest for 10–12 hours. The BMR accounts for ~65% of the total daily energy expenditure and may result in significant disturbance of the energy balance.[8,26–28] Previous studies have focused on measuring REE, because it does not require complete bed rest for more than 20 minutes. REE is affected by muscle loss and can result in maladaptive energy balance between energy intake and energy expenditure.[22–27] A significant portion of those with complete SCI has BMR ranged from 900 to 1500 kcal/day. Previous works showed that BMR in persons with complete SCI ranged from 1250 to 1480 kcal/day.[29–32] The lowest end of the range is likely to represent persons with tetraplegia and the other end represents those with paraplegia. It is still unclear whether regional adaptations in body composition may influence parameters of BMR or REE in persons with SCI.[30,32]

Assuming that total energy expenditure (TEE) is 2200 kcal/day in a healthy AB control, this means that REE may represent only 41–54% of TEE in persons with SCI. However, the TEE is diminished in persons with SCI mainly because of the reduction in REE (14–27% lower than AB controls) and physical activity energy expenditure (PAEE, up to 14% lower than AB controls), with no changes in thermic effect of food.[8] This significant reduction in REE is partially explained by reduction in FFM and blunted autonomic actions after SCI. Tanhoffer *et al.*[31] used doubly-labeled water to measure TEE in a community dwelling persons with SCI. Their estimates of REE were in the aforementioned range of 1250–1480 kcal/day. Buchholz *et al.*[8] showed that REE and PAEE represent 61 and 29% of TEE, respectively. This discrepancy in the results between Tanhoffer *et al.*[31] and Buchholz *et al.*[8] could be explained by the fact that estimation of TEE in the former study exceeded 2200 kcal/day. Daily energy expenditure and BMR have also been reported as being directly correlated with level of injury as well as having a possible correlation with blunted sympathetic nervous system activity;[23–28] without appropriate exercise or dietary interventions, this overwhelms the energy balance. The high prevalence of obesity is attributed to the imbalance between energy expenditure and intake within the SCI population.[4,8,26,33] When energy intake equals to energy expenditure, the body maintains energy balance (energy homeostasis). However, when energy intake exceeds energy expenditure, adiposity will occur. There are three strategies that can optimize TEE and reduce weight gain in persons with SCI. First, increase REE by increasing FFM. Second, increase voluntary energy expenditure though exercise. Greater daily leisure time physical activity is associated with improvement in risk factors of cardiovascular conditions after SCI. Third, reduction of calorie intake, through avoidance of drugs that increase appetite (e.g. antidepressants), through manipulations of the ratio of macronutrients (low-carb diet), and possibly through prescription of anorexic drugs.

Hormonal changes and body composition

The effects of reduced levels of testosterone, human growth hormone (GH), and insulin growth factors (IGF) on body composition after SCI have been studied.[34,35] Deterioration in body composition following SCI is attributed to reduced levels of circulating testosterone, human GH, and IGF-1.[34,36,37] Low levels of these hormones can result in a reduced capacity for cellular repair and can lead to a reduced capacity for maintaining lean muscle mass and strength.[34,36–41] Ultimately, low levels of these hormones may indirectly increase the risk for cardiovascular diseases through reduction of FFM and increased body FM.[38–43] Human GH release is blunted and chronically depressed after SCI, as evidenced by reduced levels of IGF-1, a convenient indicator of chronic GH secretion.[34] In the rat and human models, reduction in IGF-1 has been associated with skeletal muscle atrophy and increase in FM accumulation.[37,40] Bauman *et al.*[35] have recently examined the effects of low-dose baclofen therapy (20 mg/day) on plasma IGF-1 deficiency (<250 ng/ml) in persons with SCI. The findings suggested that 8 weeks of baclofen therapy managed to improve plasma IGF-1 but not in a predictable fashion. Diminished levels of circulating testosterone and free testosterone have been postulated to produce alterations in body composition after SCI.[36,42,43] In a recent study, 43% of individuals with SCI had a testosterone level

below 325 ng/dl, with testosterone deficiency linked to the severity of injury.[43] This is accompanied with age-related decline in total serum testosterone up to 0.6% per year.[44]

Spasticity of paralyzed skeletal muscle may defend against skeletal muscle atrophy.[29,35,45,46] Those with a spastic knee extensor (modified Ashworth Score (MAS) > 2) have 22% greater knee extensor CSA and less infiltration of IMF compared to non-spastic individuals with SCI.[35] In a follow-up study, there was a negative association between spasticity and total body and regional FM, and positive associations with between spasticity and percentage FFM, and between FFM and BMR[29] suggesting that spasticity may play a role in several obesity-associated disorders following SCI.[29] This led the same investigators to hypothesize that the inhibitory effects of oral baclofen on spasticity may obliterate the aforementioned effect.[46] Contrary to the hypothesis, oral baclofen administration did not attenuate the protective effects of spasticity on body composition and metabolic profile after SCI and was negatively associated with the homeostatic model assessment index.[46] The positive relationship between spasticity and muscle size as well as lean mass has recently been explained by the effect of spasticity on the circulating plasma IGF-1.[47] Those with MAS greater than 2 have 44% higher plasma IGF-1 than those with lower MAS.[47]

In summary, the above findings suggest that body composition adaptations after SCI occur at cellular, muscular, regional, and whole-body levels. The wide variance and inconsistences in the results may be a factor of using different body composition assessment techniques. These adaptations suggest that loss of lean mass after SCI may be responsible for energy imbalance and increase in adiposity. The evidence suggests that decline in anabolic hormones may be responsible for the overall body composition changes after SCI. Factors similar to spasticity and hormonal disturbances need to be considered when evaluating the extent of lean mass loss after SCI.

FM after SCI

BMI is a well-established criterion for classifying those who are at risk of being overweight or obese. BMI can be calculated by dividing the weight (kg) by the height squared (m^2). Several studies have reported that BMI underestimates the % FM after SCI and recommended the need to lower the BMI criteria to accurately define the magnitude of obesity following SCI.[5,48–53] Laughton *et al.*[49] have suggested lowering the BMI criteria to 22 kg/m^2 to accurately define obesity following SCI. Gorgey and Gater[30] found that 50% of the studied cohort had FM greater than 30% despite their normal BMI because of the lower mass below the level of the injury. Therefore, the use of BMI as an estimate to reflect adiposity in this population is misleading and clear BMI-criteria needs to be well established to define the cut-off points for persons with SCI. This is still problematic for SCI because it depends on age as well as level and completeness of injury. The disagreement between BMI and accurately defining the percentage FM has led several laboratories to accurately evaluate the appropriate methodologies of evaluating body composition in persons with SCI.[35,45] Several techniques are currently being validated against the 4-compartment model assessment of body composition to calculate the error in measuring %FM, which may influence the outcome of each technique in persons with SCI. The details of body composition assessment are beyond the scope of the current review; however, other helpful reviews can be used for this purpose.[4,51]

Evidence supports that two-third of individuals with SCI are either overweight or obese.[4,48,52,53] These reviews raised concerns that the prevalence of obesity after SCI exceeds that of the general population.[4,53] This was established based on the fact that, although obesity is defined as a %FM that exceeds 20%, %FM can easily exceed 30% despite a BMI less than 30 kg/m^2.[3–5,17,18,20] The majority of studies reported an increase in whole body and regional FM after SCI.[5,17,18,20,21,30,54] Spungen *et al.*[5] have demonstrated that 133 men with SCI were 13.1% fatter per unit of BMI compared with age-, height-, and ethnicity-matched AB controls.

Spungen *et al.*[17] reported that twins 16 years post-SCI had 11.7% greater FM in the lower limbs than their twin counterparts without SCI. Spungen *et al.*[5] also reported 8% greater FM in the arms of people with tetraplegia than in people with paraplegia. We have recently established the association between regional adiposity and metabolic profile in persons with SCI. In this study, we provided evidence that 50% of individuals with SCI have BMI less than 30 kg/m^2; however, their %FM easily exceeds 30%.[30] Individuals with tetraplegia have greater leg FM/trunk FM (45%) and leg FM/body FM (26%) and lower trunk FM/body FM (29%) ratios than individuals with paraplegia.[30] %FM increases with age and decreases with physical activity level.[5,32]

Waist circumference (WC) plays a simple role in identifying individuals with SCI who are at risk of developing metabolic syndrome (MS) as well as altered lipid profiles post-injury.[52–63] In the AB population, WC

has been used as an index of central obesity and increasing visceral adipose tissue (VAT) with a WC > 100 cm used as a surrogate for a VAT of >130 cm^2 as measured by MRI.[57,58,61] In a previous SCI study, WC was not related to VAT as measured by MRI.[59] Maki *et al.* have shown that increased WC negatively ($r = -0.42$) associated with HDL-C and positively associated with triglycerides (TG) ($r = 0.57$) after SCI.[56] Increasing VAT has been shown to be strongly correlated to glucose intolerance, insulin resistance, and hyperlipidemia in various populations.[55,60] A recent study showed that after matching WC between individuals with SCI and AB, VAT was greater in persons with SCI compared to matched healthy controls.[55] A VAT CSA greater than 100 cm^2 was found to correspond with elevated cholesterol: high-density lipoproteins ratios and increased fasting plasma glucose levels. This same study also found a direct association between VAT volume and total cholesterol as well as low-density lipoproteins.[60]

The roles of VAT subcutaneous adipose tissue (SAT) influencing the metabolic profile are not clearly understood. Gorgey *et al.* showed that despite visceral adiposity representing only 6% of total body FM in persons with complete SCI,[59] visceral adiposity remains metabolically active and negatively influences the metabolic profile after SCI.[60] The study documented positive relationships between VAT CSA and fasting plasma glucose as well as triglyceride levels.[59] It was previously suggested that a ratio of VAT to SAT greater than 0.4 indicates a high risk of developing metabolic abnormalities. Individuals with SCI have a ratio of VAT to SAT close to 0.7,[59] suggesting that they are at high risk of developing metabolic disorders.[56,64] %FFM varies inversely with VAT and SAT.[59] It is still unclear whether the level of injury influences VAT or SAT distribution between persons with tetraplegia or paraplegia. A preliminary report suggested that despite the metabolic differences between persons with tetraplegia and paraplegia, the level of SCI did not influence the volume or CSA of VAT or SAT.[62] However, an earlier study that used the SCI animal model contradicted these findings and showed that rats with T3 level of injury or above had greater VAT accumulation.[63] The regional role of VAT and SAT in determining the metabolic profile warrants further investigation. Reducing insulin resistance and other metabolic derangements is a valuable goal; studies should examine whether there are rehabilitation strategies that by maintaining FFM through diet and exercise, among other things, can attenuate the infiltration of adipose tissue in non-subcutaneous sites.

Metabolic profile after SCI

A host of processes detrimental to bodily health, including unhealthy blood glucose and lipid levels, have been investigated after SCI.[5–7,23,25] Changes in body composition after SCI have been associated with numerous metabolic sequelae (Table 1), including glucose intolerance, insulin resistance (50–75% of persons with SCI),[7,64,67] hyperlipidemia,[64,68] and cardiovascular diseases.[2–4,69] Unlike AB and other clinical populations, there is not enough evidence explaining what factors trigger such metabolic sequelae after SCI. However, many investigators agree that alterations in body composition are a key element to such deterioration.[2–7] It is also possible that increases in FM are associated with inflammatory biomarkers that trigger MS after SCI.[70]

Persons with SCI are at high risk of developing glucose intolerance or insulin resistance compared to the AB population due to the associated changes in body composition (see above) and lower physical activity levels after paralysis.[64,65,67–73] Duckworth *et al.*[67] previously reported that approximately 50% of patients with chronic SCI had diabetes mellitus (DM) despite having normal fasting glucose levels. Additionally, Bauman and Spungen[64] found that 62% of individuals with tetraplegia and 50% with paraplegia had abnormal oral glucose tolerance test, compared to only 18% in the AB-control group. Aksnes *et al.* noted an association between whole-body insulin-mediated glucose uptake and skeletal muscle mass in tetraplegics, suggesting that loss of muscle mass is the primary reason for insulin sensitivity.[65] Duckworth *et al.*[67] found that insulin-resistant individuals with SCI were more obese than SCI and AB controls and showed insulin levels far exceeding the levels reported in controls. Elder *et al.*[12] reported that accumulation of IMF and skeletal muscle atrophy in the thigh accounted for 70% of glucose intolerance after SCI. Lavela *et al.* documented that DM is age dependent in persons with SCI and increases with aging. Those with SCI who were 45–59 years of age had a higher prevalence of DM than other age-matched veterans.[71] The aforementioned studies suggest that the greater prevalence of glucose intolerance and insulin resistance is an outcome of altered body composition, significant loss of skeletal muscle, and infiltration of IMF.

Defined as multiple risk factors for cardiovascular disease existent in a given person, MS has been reported to effect as many as 55% of individuals with SCI.[73] Metabolic syndrome is defined as a group of metabolic and body composition

Table 1 Associations related to body size, composition, and metabolic markers after SCI

Reference	Participants	Body composition	Metabolic	Other	Conclusions
Wilmet *et al.*[18]	31 SCI within 8 weeks of injury T2–L3 and followed for 1 year	DXA to measure lean mass and fat mass		Spasticity	• Fat mass increased in lower extremity. • Fat-free mass decreased in lower extremity and spasticity attenuates the loss compared to those with flaccid SCI
Maki *et al.*[56]	46 men with spinal cord injury of >6 months duration	Abdominal circumference (AC) was measured in duplicate	Lipid profile		• AC was inversely correlated with HDL-C and positively correlated with LDL-C
Aksnes *et al.*[65]	Nine patients with C5–C7 and 10 patients with age-matched controls	DXA to measure FFM or FM	A euglycemic–hyperinsulinemic clamp procedure to evaluate insulin sensitivity	Muscle biopsy for GLUT-4	• Insulin-mediated glucose transport was 43% lower in tetraplegia compared to controls. • Fiber CSA was 44% smaller in tetraplegia compared to controls. Lean body mass was 19% lower in tetraplegia compared to controls. • Intact peripheral insulin signaling at the skeletal muscle level
Monroe *et al.*[24]	Ten male SCI subjects with levels ranged from C6 to L3 and 59 able-bodied controls	DXA to measure FFM or FM	24-h TEE, RMR, BMR, sleeping metabolic rate was measured over 1 day in the respiratory chamber	• Physical activity • Caloric intake	• Caloric intake and TEE were both 21% lower after SCI compared to controls. • RMR was 20.5% lower after SCI compared to controls. • FFM was significantly associated with both TEE ($r = 082$) and RMR ($r = 0.78$)
Kemp *et al.*[66]	188 Participants with SCI (46% tetraplegia and 54% paraplegia)	Adiposity measured by DXA	Lipid panel	Depression	• Serum total cholesterol, LDL-C, and TG were all higher among persons with paraplegia who were depressed compared to those who were not depressed. • Persons with paraplegia who were depressed had significantly more adiposity than those not depressed
Elder *et al.*[12]	12 complete SCI and 9 able-bodied controls	MRI of thighs to measure muscle CSA and IMF	OGTT		• Skeletal muscle size of thigh was 38% smaller in SCI compared to controls. • IMF was four-fold greater after SCI compared to controls. • Absolute and relative IMF was related to the 90 or 120 min of plasma glucose or plasma insulin ($r^2 = 0.71$–0.40).
Bauman *et al.*[23]	13 pairs of monozygotic twins, 13 of them were with complete and incomplete SCI C5–L1	DXA to measure FFM or FM	BMR or RMR was measured using an indirect calorimeter		• BMR or RMR was significantly lower in twins with SCI compared to their able-bodied co-twins
Edwards *et al.*[55]	Thirty-one men and women ($n = 15$ SCI and 16 AB) participated in a cross-sectional study	Abdominal adipose tissue by computed tomography at L4-L5. Waist circumferences at 3 sites	Serum blood sample for insulin, glucose, lipid panel, and CRP. Plasma adiponectin		• Persons with SCI had a 58% greater VAT, 48% greater mean VAT:SAT ratio than did matched AB controls. • VAT and log insulin ($r = 0.551$, $P < 0.05$) and log HOMA ($r = 0.589$, $P < 0.05$) were significantly correlated.

Gorgey *et al.*[59]	Thirteen individuals with traumatic motor complete SCI	MRI for VAT and SAT. DXA to measure FFM and FM	Fasting plasma glucose, insulin, and lipid concentrations.	• VAT CSA was related to fasting plasma glucose ($r = 0.77$, $P = 0.002$) and to the ratio of cholesterol to HDL-C ($r = 0.71$, $P = 0.006$). • Fasting plasma insulin was negatively related to the VAT CSA and VAT/SAT ratio (both, $r = -0.57$, $P = 0.043$). • VAT volume was related to total cholesterol ($r = 0.57$, $P = 0.043$) and LDL-C ($r = 0.59$, $P = 0.032$)
Gorgey and Gater[62]	32 individuals with motor complete SCI	DXA to measure regional FM in legs and trunk as well as the whole body	RMR, fasting lipid panel and OGTT	• Glucose area under the curve (AUC) was positively related to leg FM ($r = 0.34$, $P = 0.05$). • Strong negative relationships were noted between the ratio of trunk FM to body FM and glucose AUC ($r = -0.38$, $P = 0.03$) and LDL-C ($r = -0.45$, $P = 0.001$). • Whole-body FM was negatively related to HDL-C ($r = -0.49$, $P = 0.007$) after controlling for percentage of trunk FM

abnormalities.[74–76] Persons with SCI have increased levels of TG, low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL). Bauman *et al.*[68] showed that greater than 37% of persons with SCI have HDL-C level less than 35 mg/dl and 18% of this population has LDL-C greater than 160 mg/dl. This dyslipidemia is worsened with aging and leads to accelerated coronary artery disease (CAD) after SCI.[68,69] Nash *et al.*[69] reported that 76% of individuals with paraplegia had HDL-C less than 40 mg/dl and 34% had the Adult Treatment Panel III- defined MS. The increases in non-esterified fatty acids and TG result in elevated VLDL, LDL, and apolipoprotein B, a sub-fraction protein of LDL that has been strongly correlated with CAD. The increased level of TG also reduces the production level of apolipoprotein A, a sub-fraction protein of cardio-protective HDL-C.[4,76,77] The results of increased triglycerides, VLDL, LDL, and decreased HDL-C are associated with higher risk of CAD and peripheral vascular diseases.[4,76–80] The aforementioned phenotype leads to atherogenic profile and increases susceptibility to cardiovascular disease.

Link between body composition and metabolic profile

Evidence suggests that reduction in physical activity and increased fat accumulation can have adverse effects on whole-body carbohydrate and lipid metabolism.[77,79–85] Excessive body fat, especially in the trunk and lower extremities of those with SCI can lead to an increase in the amount of non-esterified fatty acids due to increased lipolysis (Table 1). This takes place even though increased insulin usually suppresses lipolysis under normal levels of adiposity.[76] In a recent study, whole-body FM was negatively associated to HDL-C in 32 individuals with motor complete SCI after controlling for %trunk FM. A similar negative relationship was identified between leg FM and HDL-C.[30] These findings suggest that storage of adipose tissue as ectopic or SAT may impact the metabolic profile differently in persons with SCI.[30]

The increased level of non-esterified fatty acids in the circulating blood increases their influx into muscle and liver cells.[76] This in turn increases the level of triglyceride in the liver which contributes to insulin resistance in the liver.[76] Additionally, increased non-esterified fatty acids in the cells of muscle and liver change cell membrane concentration gradients decreasing passage of glucose into the cells.[76] Non-esterified fatty acid in the muscle causes serine phosphorylation of the insulin

receptors because of an increased number of metabolites within the muscle cells.[78,79] The phosphorylation of the receptors inhibits the activation of GLUT-1 and GLUT-4 (insulin-regulated glucose transporters) receptor translocation to the cell membrane causing decreased facilitation of glucose entrance.[4,78,82]

Likewise, increased fat accumulation in the liver increases insulin resistance and allows increased gluconeogenesis and glucose export out of the liver adding to hyperglycemia which is a precursor of type II DM.[77,79–85] Glucose intolerance is found along with hyperinsulemia, demonstrating that the lack of glucose uptake into the muscle and liver cells is not related to the amount of insulin present in the circulation but rather due to factors inhibiting the ability of muscle and liver cells to receive glucose.[77,80,81] Physical inactivity results in decreased muscle GLUT-4 content which is associated with insulin resistance. Physical inactivity due to bed rest for as little as 7 days results in a significant reduction in insulin sensitivity in inactive muscles.[81,82]

Another important regulator of the relationship between body composition and metabolic profile after SCI is leptin.[86–88] Leptin is a hormone responsible for achieving satiety and maintaining energy homeostasis. Leptin is released by adipose tissue and it is regulated by the adrenergic system.[87,88] Leptin levels are reported to be is ~32% higher in persons with SCI compared to AB controls (7 vs. 4.7 ng/ml).[88] Moreover, it is non-significantly higher in persons with tetraplegia compared to paraplegia. This leads to the development of what is called the leptin paradox. The loss of inhibitory effects of adrenergic control, especially above T6 SCI, may be responsible for such increases in the circulating leptin level after SCI.[86] Despite the higher level of leptin, there is increased adiposity and a diminished stimulatory effect of leptin on resting metabolic rate (RMR).[87]

Manns *et al.*[70] and Gater and Pai[76] agree that increases in FM and other alterations in body composition are in close association with inflammatory biomarkers that trigger MS. The fat cells may be responsible for the release of C-reactive protein (CRP), tumor necrosis alpha and inter-lukin-6. These inflammatory biomarkers have been shown to interfere with insulin signaling and lead to insulin resistance. Liang *et al.*[89] showed that individuals with SCI are more likely to have higher CRP than their age and race-matched AB controls and this is associated with decreased HDL-C. Another study showed that CRP was greater in persons with tetraplegia compared to those with paraplegia. Those with higher CRP had greater WC and percentage body FM.[90]

Conclusion

SCI is associated with a myriad of body composition and metabolic adaptations that are of serious health concerns. Studies have supported the associations between body composition and metabolic profile; however more importantly, interventional trials are needed to see if changing body composition proves to be beneficial. If confirmed, the link between body composition and metabolic health concerns could open a new avenue for prevention and treatment through the restoration of a more healthy body composition. There is a shift in studying whole-body composition to more focused regional composition. In regional adiposity, percentage trunk and leg FM have been shown to be associated with abnormal metabolic profile. Moreover, separation of trunk FM into VAT and SAT indicated that VAT is associated with a spectrum of metabolic abnormalities compared to SAT.

Acknowledgments

The authors apologize that all the outstanding work in this area could not be cited because of the space limitations. We would like to thank Dr. Lance Goetz for his time and effort to proofread and edit our revised manuscript.

Disclaimer statements

Contributors All authors contributed to searching and writing of the review.

Funding ASG is supported by the Department of Veteran Affairs (VA) RR&D.

Conflicts of interest None.

Ethics approval None.

References

1 National Spinal Cord Injury Statistical Center. Spinal cord injury facts and figures at a glance. [accessed on May 1, 2014]. Available from: https://www.nscisc.uab.edu/PublicDocuments/fact_figures_docs/Facts2012FebFinal.pdf.
2 Phillips WT, Kiratli BJ, Sarkarati M, Weraarchakul G. Effects of spinal cord injury on the heart and cardiovascular fitness. Curr Prob Cardiol 1998;23(11):641–716.
3 Kocina P. Body composition of spinal cord injury adults. Sports Med 1997;23(1):48–60.
4 Gater DR, Jr. Obesity after spinal cord injury. Phys Med Rehabil Clin N Am 2007;18(2):333–51.
5 Spungen AM, Adkins RH, Stewart CA, Wang J, Pierson RN, Jr, Waters RL, *et al.* Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Physiol 2003;95(6):2398–407.
6 Bauman WA, Spungen AM. Metabolic changes in persons after spinal cord injury. Phys Med Rehabil Clin N Am 2000;11(1):109–40.
7 Bauman WA, Spungen AM. Carbohydrate and lipid metabolism in chronic spinal cord injury. J Spinal Cord Med 2001;24(4):266–77.

8 Buchholz AC, McGillivray CF, Pencharz PB. Physical activity levels are low in free-living adults with chronic paraplegia. Obes Res 2003;11(4):563–70.
9 Castro MJ, Apple DF, Jr, Hillegass EA, Dudley GA. Influence of complete spinal cord injury on skeletal muscle cross-sectional area within the first 6 months of injury. Eur J Appl Physiol Occup Physiol 1999;80(4):373–8.
10 Gorgey AS, Dudley GA. Skeletal muscle atrophy and increased intramuscular fat after incomplete spinal cord injury. Spinal Cord 2007;45(4):304–9.
11 Shah PK, Stevens JE, Gregory CM, Pathare NC, Jayaraman A, Bickel SC, *et al.* Lower-extremity muscle cross-sectional area after incomplete spinal cord injury. Arch Phys Med Rehabil 2006;87(6):772–8.
12 Elder CP, Apple DF, Bickel CS, Meyer RA, Dudley GA. Intramuscular fat and glucose tolerance after spinal cord injury – a cross-sectional study. Spinal Cord 2004;42(12):711–6.
13 Grimby G, Broberg C, Krotkiewska I, Krotkiewski M. Muscle fiber composition in patients with traumatic cord lesion. Scand J Rehabil Med 1976;8(1):37–42.
14 Talmadge RJ, Castro MJ, Apple DF, Jr, Dudley GA. Phenotypic adaptations in human muscle fibers 6 and 24 wk after spinal cord injury. J Appl Physiol 2002;92(1):147–54.
15 Biering-Sorensen BO, Kristenson IB, Kjaer M, Biering-Sorensen F. Muscle after spinal cord injury. Muscle Nerve 2009;40(4): 499–519.
16 Bickel CS, Slade JM, Dudley GA. Long-term spinal cord injury increases susceptibility to isometric contraction-induced muscle injury. Eur J Appl Physiol 2004;91(2–3):308–13.
17 Spungen AM, Wang J, Pierson RN, Jr, Bauman WA. Soft tissue body composition differences in monozygotic twins discordant for spinal cord injury. J Appl Physiol 2000;88(4):1310–5.
18 Wilmet E, Ismail AA, Heilporn A, Welraeds D, Bergmann P. Longitudinal study of bone mineral content and of soft tissue composition after spinal cord section. Paraplegia 1995;33(11): 674–7.
19 Gorgey AS, Timmons MK, Michener LA, Ericksen JJ, Gater DR. Intra-rater reliability of ultrasound imaging of wrist extensor muscles in humans with tetraplegia. PMR 2014;6(2):127–33.
20 Nuhlicek DN, Spurr GB, Bardoriak JJ, Rooney CB, el Ghatit AZ, Bongard RD. Body composition of patients with spinal cord injury. Eur J Clin Nutr 1988;42(9):765–73.
21 Modlesky CM, Bickel CS, Slade JM, Meyer RA, Cureton KJ, Dudley GA. Assessment of skeletal muscle mass in men with spinal cord injury using dual-energy X-ray absorptiometry and magnetic resonance imaging. J Appl Physiol 2004;96(2):561–5.
22 Castro MJ, Apple DF, Staron RS, Campos GER, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 months of injury. J Appl Physiol 1999;86(1):350–8.
23 Bauman WA, Spungen AM, Wang J, Pierson RN, Jr. The relationship between energy expenditure and lean tissue in monozygotic twins discordant for spinal cord injury. J Rehabil Res Dev 2004; 41(1):1–8.
24 Monroe MB, Tataranni PA, Pratley R, Manore MM, Skinner JS, Ravussin E. Lower daily energy expenditure as measured by respiratory chamber in subjects with spinal cord injury compared with control subjects. Am J Clin Nutr 1998;68(6):1223–7.
25 Gorgey AS, Dolbow DR, Gater DR, Jr. A model of prediction and cross-validation of fat-free mass in men with motor complete spinal cord injury. Arch Phys Med Rehabil 2012;93(7):1240–5.
26 Buchholz AC, Pencharz PB. Energy expenditure in chronic spinal cord injury. Curr Opin Clin Nutr Metab Care 2004;7(6):635–9.
27 Olle MM, Pivarnik JM, Klish WJ, Morrow JR. Body composition of sedentary and physically active spinal cord injured individuals estimated from total body electoral conductivity. Arch Phys Med Rehabil 1993;74(7):706–10.
28 Sedlock DA, Laventure SJ. Body composition and resting energy expenditure and basal metabolic rates of patients with spinal cord injury. Paraplegia 1990;28(7):448–54.
29 Gorgey AS, Chiodo AE, Zemper ED, Hornyak JE, Rodriquez GM, Gater DR. Relationship of spacticity to soft tissue body composition and metabolic profile in persons with chronic motor complete spinal cord injury. J Spinal Cord Med 2010; 33(1):6–15.
30 Gorgey AS, Gater DR. Regional and relative adiposity patterns in relation to carbohydrate and lipid metabolism in men with spinal cord injury. Appl Physiol Nutr Metab 2011;36(1):107–14.
31 Tanhoffer RA, Tanhoffer AI, Raymond J, Hills AP, Davis GM. Comparison of methods to assess energy expenditure and physical activity in people with spinal cord injury. J Spinal Cord Med 2012; 35(1):35–45.
32 Maggioni M, Bertoli S, Margonato V, Merati G, Veicsteinas A, Testolin G. Body composition assessment in spinal cord injury subjects. Acta Diabetol 2003;40(1):183–6.
33 Mollinger LA, Spurr GB, el Ghatit AZ, Barboriak JJ, Rooney CB, Davidoff DD, *et al.* Daily energy expenditure and basal metabolic rates of patients with spinal cord injury. Arch Phys Med Regabil 1985;66(7):420–6.
34 Bauman WA, Spungen AM, Flanagan S, Zhong YG, Alexander LR, Tsitouras PD. Blunted growth hormone response to intravenous arginine in subjects with a spinal cord injury. Horm Metab Res 1994;26(3):152–6.
35 Bauman WA, La Fountaine MF, Cirnigliaro CM, Kirshblum SC, Spungen AM. Low-dose baclofen therapy raised plasma insulin-like growth factor-1 concentrations, but not into the normal range in a predictable and sustained manner in men with chronic spinal cord injury. J Spinal Cord Med 2013;36:476–82.
36 Halstead LS, Groah SL, Libin A, Hamm LF, Priestley L. The effects of an anabolic agent on body composition and pulmonary function in tetraplegia: a pilot study. Spinal Cord 2010;48(1):55–9.
37 Gregory CM, Vandenborne K, Huang HF, Ottenweller JE, Dudley GA. Effects of testosterone replacement therapy on skeletal muscle after spinal cord injury. Spinal Cord 2003;41(1):23–8.
38 Groah SL, Kehn ME. The state of aging and public health for people with spinal cord injury: lost in transition? Top Spinal Cord Inj Rehabil 2010;15(3):1–10.
39 Zmuda JM, Thompson PD, Winters SJ. Exercise increases serum testosterone and sex hormone-binding globulin levels in older men. Metabolism 1996;45(8):935–9.
40 Bauman WA, Kirshblum SC, Morrison NG, Cirnigliaro CM, Zhang RL, Spungen AM. Effect of low-dose baclofen administration on plasma insulin-like growth factor-I in persons with spinal cord injury. J Clin Pharmacol 2006;46(4):476–82.
41 Florini JR, Ewton DZ, Coolican SA. Growth hormone and the insulin-like growth factor system in myogenesis. Endocr Rev 1996;17(5):481–517.
42 Gomez JM. Serum leptin, insulin-like growth factor-i components and sex-hormone binding globulin. Relationship with sex, age and body composition in healthy population. Protein Pept Lett 2007; 14(7):708–11.
43 Durga A, Sepahpanah F, Regozzi M, Hastings J, Crane DA. Prevalence of testosterone deficiency after spinal cord injury. PMR 2011;3(10):929–32.
44 Bauman WA, La Fountaine MF, Spungen AM. Age-related prevalence of low testosterone in men with spinal cord injury. J Spinal Cord Med 2014;37(1):32–9.
45 Gorgey AS, Dudley GA. Spasticity may defend skeletal muscle size and composition after incomplete spinal cord injury. Spinal Cord 2008;46(2):96–102.
46 Gorgey AS, Chiodo AE, Gater DR. Oral baclofen administration in persons with chronic spinal cord injury does not prevent the protective effects of spasticity on body composition and glucose homeostasis. Spinal Cord 2010;48(2):160–5.
47 Gorgey AS, Gater DR. Insulin growth factors may explain relationship between spasticity and skeletal muscle size in men with spinal cord injury. J Rehabil Res Dev 2012;49(3):373–80.
48 Jones LM, Legge M, Goulding A. Healthy body mass index values often underestimate body fat in men with spinal cord injury. Arch Phys Med Rehabil 2003;84(7):1068–71.
49 Laughton GE, Buchholz AC, Martin Ginis KA, Goy RE, SHAPE SCI Research Group. Lowering body mass index cutoffs better identifies obese persons with spinal cord injury. Spinal Cord 2009;47(10):757–62.
50 Clasey JL, Gater DR, Jr. A comparison of hydrostatic weighing and air displacement plethysmography in adults with spinal cord injury. Arch Phys Med Rehabil 2005;86(11):2106–13.
51 Clasey JL, Gater DR, Jr. Body composition assessment in adults with spinal cord injury. Top Spinal Cord Inj Rehabil 2007;12(4):8–19.

52 Buchholz AC, Bugaresti JM. A review of body mass index and waist circumference as markers of obesity and coronary heart disease risk in persons with chronic spinal cord injury. Spinal Cord 2005;43(9):513–8.
53 Gorgey AS, Gater DR, Jr. Prevalence of obesity after spinal cord injury. Top Spinal Cord Inj Rehabil 2007;12(4):1–7.
54 Jones LM, Goulding A, Gerrard DR. DEXA: a practical and accurate tool to demonstrate total and reginal bone loss, lean tissue loss and fat mass gain in paraplegia. Spinal Cord 1998; 36(9):637–40.
55 Edwards LA, Bugaresti JM, Buchholz AC. Visceral adipose tissue and the ratio of visceral to subcutaneous adipose tissue are greater in adults with than in those without spinal cord injury, despite matching waist circumferences. Am J Clin Nutr 2008; 87(3):600–7.
56 Maki KC, Briones ER, Langbein WE, Inman-Felton A, Nemchausky B, Welch M, *et al.* Associations between serum lipids and indicators of adiposity in men with spinal cord injury. Paraplegia 1995;33(2):102–9.
57 You T, Yang R, Lyles MF, Gong D, Nicklas BJ. Abdominal adipose tissue cytokine gene expression: relationship to obesity and metabolic risk factors. Am J Physiol Endocrinol Metab 2005;288(4):E741–7.
58 Carr DB, Utzschneider KM, Hull RL, Kodama K, Retzlaff BM, Brunzell JD, *et al.* Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome. Diabetes 2004; 53(8):2087–94.
59 Gorgey AS, Mather KJ, Poarch H, Gater DR. Influence of motor complete spinal cord injury on visceral and subcutaneous adipose tissue measured by multiaxial magnetic resonance imaging. J Spinal Cord Med 2011;34(1):99–109.
60 Gorgey AS, Mather KJ, Gater DR. Central adiposity associations to carbohydrate and lipid metabolism in individuals with complete motor spinal cord injury. Metabolism 2011;60(6):843–51.
61 Lemieux S, Prud'homme D, Bouchard C, Tremblay A, Despres JP. A single threshold value of waist girth identifies normal-weight and overweight subjects with excess visceral adipose tissue. Am J Clin Nutr 1996;64(5):685–93.
62 Gorgey AS, Gater DR. A preliminary report on the effects of the level of spinal cord injury on the association between central adiposity and metabolic profile. PMR 2011;3(5):440–6.
63 Inskip JA, Plunet W, Ramer LM, Ramsey JB, Yung A, Kozlowski P, *et al.* Cardiometabolic risk factors in experimental spinal cord injury. J Neurotrauma 2010:27(1):275–85.
64 Bauman WA, Spungen AM. Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. Metabolism 1994;43(6):749–56.
65 Aksnes AK, Hjeltnes N, Wahlstrom EO, Katz A, Zierath JR, Wallberg-Henriksson H. Intact glucose transport in morphologically altered denervated skeletal muscle from quadriplegic patients. Am J Physiol 1996;271(3):E593–600.
66 Kemp BJ, Spungen AM, Adkins RH, Krause JS, Bauman WA. The relationships among serum lipid levels, adiposity, and depressive symptomatology in persons aging with spinal cord injury. J Spinal Cord Med 2000;23(4):216–20.
67 Duckworth WC, Solomon SS, Jallepalli P, Heckemeyer C, Finnern J, Powers A. Glucose intolerance due to insulin resistance in patients with spinal cord injuries. Diabetes 1980;29(11):906–10.
68 Bauman WA, Spungen AM, Zhong YG, Rothstein JL, Petry C, Gordon SK. Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury. Paraplegia 1992;30(10): 697–703.
69 Nash MS, Mendez AJ. A guideline-driven assessment of need for cardiovascular disease risk intervention in persons with chronic paraplegia. Arch Phys Med Rehabil 2007;88:751–7.
70 Manns PJ, McCubbin JA, Williams DP. Fitness, inflammation, and the metabolic syndrome in men with paraplegia. Arch Phys Med Rehabil 2005;86(6):1176–81.
71 Lavela SL, Weaver FM, Goldstein B, Chen K, Miskevics S, Rajan S, *et al.* Diabetes mellitus in individuals with spinal cord injury or disorder. J Spinal Cord Med 2006;29(4):387–95.
72 Demirel Ş, Demirel G, Tükek T, Erk O, Yilmaz H. Risk factors for coronary heart disease in patients with spinal cord injury in Turkey. Spinal Cord 2001;39(3):134–8.
73 Nelson MD, Widman LM, Abresch RT, Stanhope K, Havel PJ, Styne DM, *et al.* Metabolic syndrome in adolescents with spinal cord dysfunction. J Spinal Cord Med 2007;30(1):S127–39.
74 Grundy SM, Brewer HB, Jr, Cleeman JI, Smith SC, Jr, Lenfant C. American Heart Association; National Heart, Lung, and Blood Institute. Definition of Metabolic Syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on scientific issues related to definition. Circulation 2004;109(3):433–8.
75 Grundy SM. Obesity, metabolic syndrome, and cardiovascular disease. J Endocrinol Metab 2004;89(6):2592–600.
76 Gater DR, Pai AB. Metabolic disorders. In: Campagnolo DI, Kirshblum S, Nash MS, Heary RF, Gorman PH(eds.) Spinal cord medicine. 2nd ed. Lippincott: Williams & Wilkins; 2011, p. 185–210.
77 Elks ML. Fat oxidation and diabetes of obesity: the Randle hypothesis revisited. Med Hypotheses 1990;33(4):257–60.
78 Gallagher EJ, LeRoith D, Karnieli E. The metabolic syndrome – from insulin resistance to obesity and diabetes. Endocrinol Metab Clin North Am 2008;37(3):559–79.
79 Shulman GI. Cellular mechanisms of insulin resistance. J Clin Invest 2000;106(2):171–6.
80 Sharma D, Shenoy S, Singh J. Effect of electrical stimulation on blood glucose level and lipid profile of sedentary type 2 diabetes patients. Int J Diabetes Dev Ctries 2010;90(4):194–200.
81 Milkines KJ, Richter EA, Dela F, Galbo H. Seven days of bed rest decrease insulin action on glucose uptake in leg and whole body. J Appl Physiol 1991;70(3):1245–54.
82 Stuart CA, Shangraw RE, Prince MJ, Peters EJ, Wolfe RR. Bed rest induced insulin resistance occurs primarily in muscles. Metabolism 1988;37(8):802–6.
83 Kolovou GD, Ananostopoulou KK, Cokkinos DV. Pathophysiology of dyslipidaemia in the metabolic syndrome. Postgraduate Med J 2005;81(956):358–66.
84 Durstine JL, Moore GE, Thompson PD. Hyperlipidemia. In: ACSM's exercise management for persons with chronic diseases and disabilities, 2nd edn. Human Kinetics, Champaign, 2003. vol. 2, p. 142–8.
85 Raal FJ. Pathogenesis and management of the dyslipidemia of the metabolic syndrome. Metab Syndr Relat Disord 2009;7(2):83–8.
86 Bauman WA, Spungen AM, Zhong YG, Mobbs CV. Plasma leptin is directly related to body adiposity in subjects with spinal cord injury. Horm Metab Res 1996;28(12):732–6.
87 Jeon JY, Steadward RD, Wheeler GD, Bell G, McCargar L, Harber V. Intact sympathetic nervous system is required for leptin effects on resting metabolic rate in people with spinal cord injury. J Clin Endocrinol Metab 2003;88(1):402–7.
88 Wang YH, Huang TS, Liang HW, Su TC, Chen SY, Wang TD. Fasting serum levels of adiponectin, ghrelin, and leptin in men with spinal cord injury. Arch Phys Med Rehabil 2005;86(10):1964–8.
89 Liang H, Mojtahedi MC, Chen D, Braunschweig CL. Elevated C-reactive protein associated with decreased high-density lipoprotein cholesterol in men with spinal cord injury. Arch Phys Med Rehabil 2008;89(1):36–41.
90 Gibson AE, Buchholz AC, Martin Ginis KA, SHAPE-SCI Research Group. C-reactive protein in adults with chronic spinal cord injury: increased chronic inflammation in tetraplegia vs paraplegia. Spinal Cord 2008;46(9):616–21.