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Exercise to mitigate cardiometabolic disorders after spinal cord injury

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Abstract

The cardiometabolic disorder (CMD) is a syndrome caused by coalescing of cardiovascular, endocrine, pro-thrombotic, and inflammatory health risks. Together, these risks confer a hazard as health-threatening as coronary artery disease or type2 diabetes, whether an individual has a diagnosis of coronary disease or diabetes, or not. CMD is most often defined by three or more of five clinically assessed risk components, notably obesity, insulin resistance, hypertension, hypertriglyceridemia, and depressed high-density lipoprotein cholesterol.

Evidence currently suggests that worldwide CMD is expanding at a pandemic rate, and it is known that people living with spinal cord injuries (SCI) qualify for the diagnosis at more than 50% of the prevalence of a non-disabled cohort. A recent evidence-based guideline warned of the current state of CMD following SCI and recommended early lifestyle intervention incorporating exercise and prudent nutrition as a first-line disease counter-measure. This monograph will define the CMD following SCI, explore its underlying pathophysiology, and provide evidence that recommends exercise for CMD health hazards after SCI.

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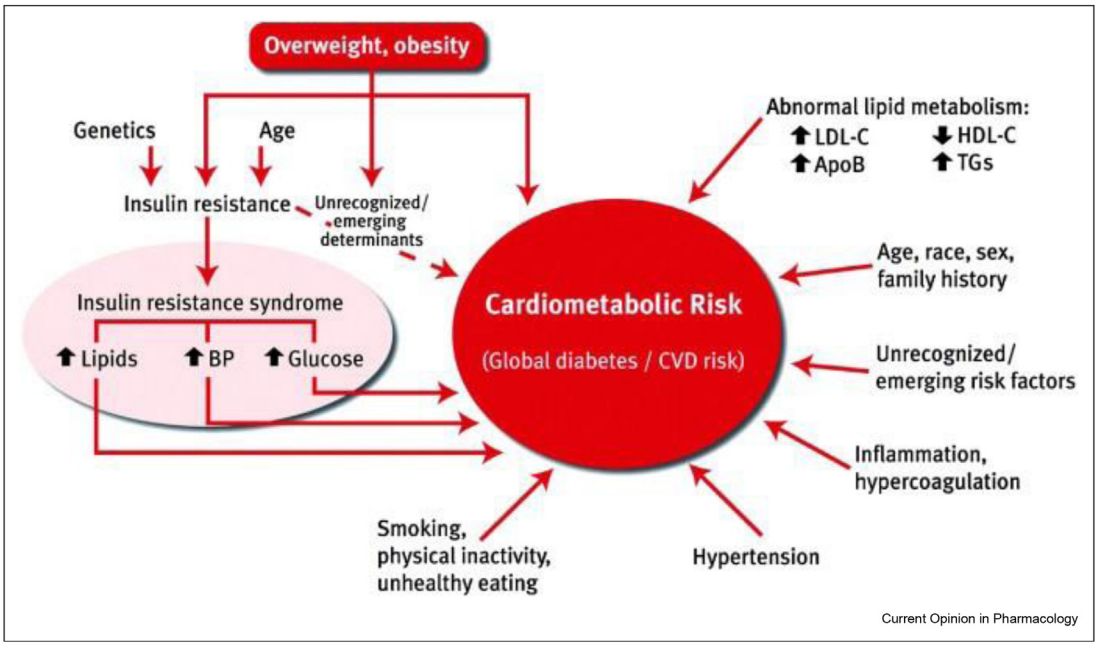
Cardiometabolic disease after spinal cord injury

An accelerated trajectory of all-cause cardiovascular disease (CVD) is notable among chronic health risks observed after SCI [1] and is reported to accelerate all-cause cardiovascular morbidity and mortality [2]. The source for this excessive risk has been attributed, in part, to CVD risk factors that resemble those established in the non-disabled population [3]. However, the atherogenic dyslipidemia observed after SCI deviates from the routine clinical pattern of elevated total cholesterol (TC) and elevated low-density lipoprotein cholesterol and instead reports low levels of the cardioprotective high-density lipoprotein cholesterol (HDL-C) and an exaggerated postprandial hypertriglyceridemia [4,5]. Post-SCI dyslipidemia is also associated with marked physical deconditioning [1,6,7] and systemic inflammation [8–10], which have known linkage with rapidly developing neurogenic obesity [11], insulin resistance [9], and type 2 diabetes mellitus [12]. When compared with non-disabled cohorts, excessive risks for these health hazards have all been reported after SCI [1]. They have also been linked with diminished resting and exercise energy expenditure [13] and a daily nutrient intake of the SCI population that is excessive in total calories relative to the daily need [14].

The hazards of cardiometabolic disease (CMD) and standards for disease identification and management after SCI have recently been defined in an evidence-based guideline [15]. The cardiometabolic condition is an interrelated disorder of cardiovascular, renal, metabolic, pro-thrombotic, and inflammatory health hazards (Figure 1), which is recognized as a distinct disease entity by most of the world's medical authorities [1,7]. While still lacking a fully unified diagnosis, the American Heart Association and the National Institutes of Health (NIH) National Heart Lung Blood Institute (NHLBI) define CMD as the co-occurrence of any three medical hazards described in Table 1. This definition is similar but not identical to the diagnoses of the World Health Organization, the American Diabetes Association, the World Heart Federation, and others [16].

While physical deconditioning is not included among the five archetypical diagnostic criteria of obesity, insulin resistance, dyslipidemia, and hypertension, it is still highlighted universally as a cause for CMD after SCI [17]. Exercise conditioning is thus a favored treatment approach [18–20]. Reconditioning exercise is especially

Figure 1



Interrelated cardiometabolic risks. From: Leiter et al. Cardiometabolic Risk in Canada: A Detailed Analysis and Position Paper by the Cardiometabolic Risk Working Group. Position Statement. 27(2), E1-E33, 2011.

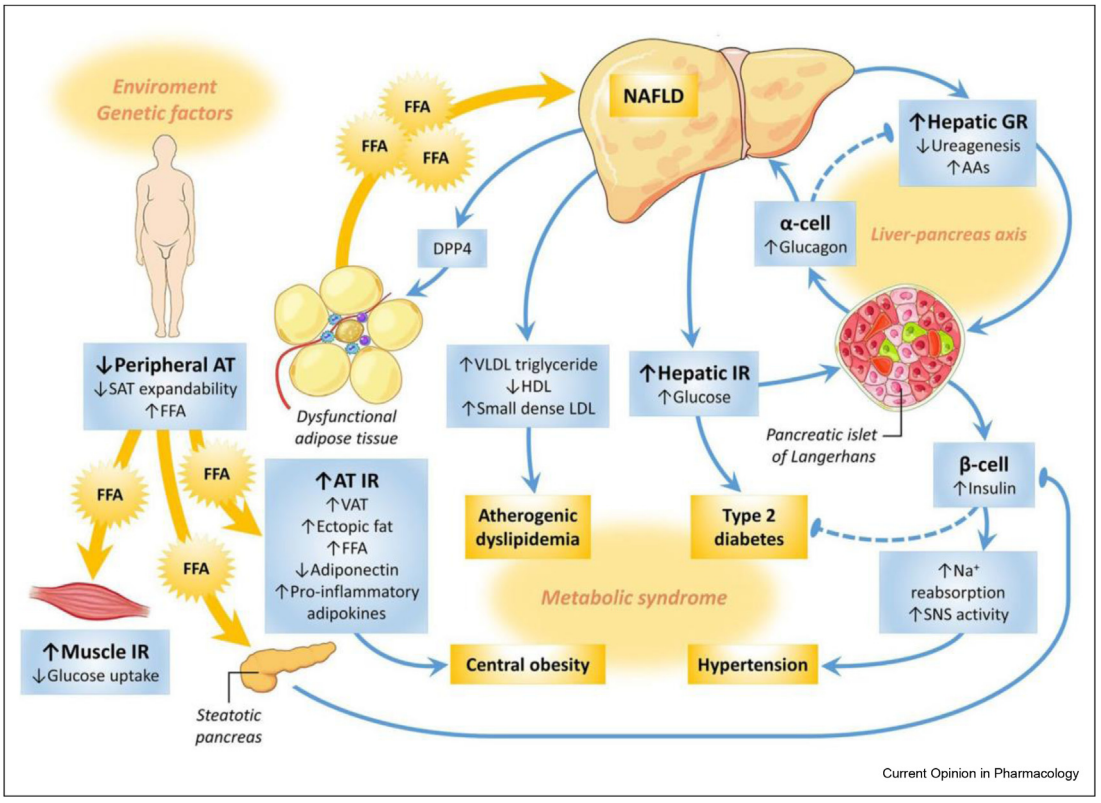
important for those with SCI, where fitness levels are well below those of the non-disabled population [21], and at the lowest end of the human fitness continuum [22]. Low levels of resting metabolism after SCI are sometimes a lifestyle choice that comes about from exercise abstention [23] but can also result from diminished resting metabolism of paralyzed muscles, altered sublesional fuel homeostasis, and diminished sympathetic nervous system activity accompanying cord injuries below the first thoracic vertebrae. Deconditioning can also ensue limited exercise options and opportunities, transportation barriers, financial obstacles, need for specially adapted equipment, and architectural barriers to the use of exercise engagement [23]. Notwithstanding the cause(s), physical deconditioning contributes to the decline in health and function experienced throughout the lifespan and is associated with other secondary complications, including prevalent pain [7,15].

Cardiometabolic pathophysiology after spinal cord injuries

Adipose tissue has recently been identified as the primary mediator of cardiometabolic pathophysiology in humans (Figure 2), and is especially abundant in persons with SCI [11,25]. More than just sarcopenic obesity [26], neurogenic obesity in SCI is the result of motor paralysis, sympathetic blunting, neurogenic anabolic dysfunction, neurogenic osteoporosis, and blunted satiety resulting in a profound reduction in total energy expenditure that can rarely be matched through decreased energy intake without intentional and fairly extreme dietary restriction [11,27]. In the simplest terms, adipose tissue accumulates as total daily energy intake exceeds total daily energy expenditure, which comprises basal/resting metabolic rate, the thermic effect of food, and the thermic effect of activity [28–30]. A recent systematic review of resting metabolic rate after SCI demonstrated significant disparities between estimated and measured metabolic rate, furthering the notion that indirect calorimetry should be used to determine metabolic needs for those with SCI, particularly as it relates to dietary intervention [14,28,31,32]. The resulting positive energy balance translates to relative body fat (% BF) of 22–44% in persons with SCI, while body mass index (BMI) varied between 17 and 27 kg/m^2 [25,33], well below the World Health Organization's definition of obesity at 30 kg/m^2 [34]. Whether using the American Society of Exercise Physiologists' (ASEP) definition of obesity as > 22% BF for men and >35% BF for women [35,36] or the SCI-corrected body mass index (BMISCI) suggested by SCI clinicians [1,37,38], the prevalence of obesity in persons with SCI falls between 67 and 97%, well above that of the non-SCI population [11,25,39].

Adipose tissue and its associated macrophages produce many pro-inflammatory cytokines, including tumor necrosis factor-α (TNFα), interleukin-6 (IL-6), interleukin-1 b (IL-1b), monocyte chemoattractant protein 1 (MCP-1), and nuclear factor kappa-light-chain-

Figure 2



Pathophysiology of obesity and metabolic syndrome. Environmental factors influence gene expression inducing the gain of adipose tissue (AT). When subcutaneous adipose tissue capacity is reached, free-fatty acids (FFA) mobilize and are deposited in visceral and ectopic fat (e.g., liver, skeletal muscle, and heart). FFA deposition in muscle inhibits insulin-mediated glucose uptake (i.e., insulin resistance, IR), reducing lipolysis and increasing non-esterified FFA flux to the liver, resulting in hepatic IR (enhancing gluconeogenesis) and hepatic lipogenesis and atherogenic dyslipidemia. Hepatic glucagon resistance to amino acid (AA) production reduces ureagenesis, resulting in hyper-aminoacidemia and glucagon resistance (GR); increased glucagon production from pancreatic α-cells accelerates hepatic gluconeogenesis. FFA deposit in the pancreas where β-cell dysfunction is caused by lipotoxicity; hyperglycemia, and insulin resistance (IR) results. Hyperinsulinemia stimulates sodium reabsorption and increased sympathetic nervous system activity, contributing to hypertension (HTN). AT becomes more IR and releases pro-inflammatory adipokines, decreasing the anti-inflammatory adiponectin. Triglycerides and toxic metabolites in the liver induce lipotoxicity, mitochondrial dysfunction,and endoplasmic reticulum stress, resulting in hepatic damage, apoptosis, and fibrosis (nonalcoholic liver disease, NAFLD). The damaged hepatocytes release dipeptidyl peptidase 4 (DPP4), which stimulates AT macrophage inflammation, promoting further IR. Adapted from Godoy- Matos et al., Diabetology & Metabolic Syndrome, 2020,12,60. https://doi.org/10.1186/s13098-020-00570-y, licensed under a Creative Commons Attribution 4.0 International License: https://creativecommons.org/licenses/by/4.0/.

Table 1

CMD diagnosis for persons with and without SCI [11].

Three of more of:	Waist circumference[a]	• Men >40 inches (102 cm) • Women >35 inches (88 cm)
	Plasma TG	• ≥ 150 mg/dL (1.7 mmol/L)
	HDL-C cholesterol	• Men <40 mg/dL (1.03 mmol/L) • Women <50 mg/dL (1.29 mmol/L)
	Elevated blood pressure	• ≥ 130/85 mmHg or use of medication for hypertension
	Fasting glucose	• ≥ 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia

[a] NOTE: Use of waist circumference is not validated in persons with SCI. Substitute definitions of obesity using a: > 22% body fat when using 3- or 4-compartment modeling or b) BMI ≥22 kg/m^2.

enhancer of activated B cells (NFκB), as well as several hormones including angiotensinogen, angiotensin II and the adipokines leptin, adiponectin, and resistin that modulate systemic inflammation, insulin resistance, hypertension, appetite, energy metabolism, and lipid metabolism, respectively [11,40]. TNF-α and IL-6 suppress insulin receptor substrates 1 and 2 (IRS-1, IRS,2) and glucose transporter-4 (GLUT4) and upregulate suppressor of cytokine signaling-3 (SOCS3), causing insulin resistance [11,41,42]. TNF-α, IL-6, and IL-1b also activate NFκB, which further blocks phosphorylation of IRS-1 and IRS-2, limiting the phosphoinositide 3-kinase (PI3K) cascade required to activate GLUT4 migration to the cell membranes [11,43]. TNF-α, IL-1B, and NFκB also induce pancreatic β-cell apoptosis in the later stages of type 2 diabetes mellitus, reducing the endogenous production of insulin [44]. Obesity-induced hypertension in SCI is mediated by the renin-angiotensin-aldosterone system, sympathetic nervous system activation, natriuretic peptide catabolism, leptin resistance, and renal compression caused by visceral adipose tissue [11,45–49]. Under conditions of insulin resistance, visceral adipose tissue contributes to lipolysis, hypertriglyceridemia and the accelerated production of non-esterified free-fatty acids (NEFA), increasing hepatic production of apolipoprotein-B (apo-B), low-density lipoprotein (LDL-c) and very-low-density lipoprotein (VLDL-C); conversely apolipoprotein-A (apo-A) production is slowed, reducing high-density lipoprotein (HDL-c). Additionally, cholesteryl ester transfer protein (CETP) activity is increased, promoting the exchange of triglycerides (TG) with cholesterol esters between lipoproteins, rendering much of the remaining HDL-c dysfunctional [11,50]. In short, unprecedented % BF in persons with SCI largely contributes to obesity-related metabolic dysfunction, with multiple studies demonstrating metabolic syndrome prevalence is greater than 50% [25,39,51], well above that noted in the non-SCI population.

Recent recommendations for exercise reconditioning in adults with SCI

Exercise is a fundamental element for maintaining physical capacity and cardiovascular and metabolic health in persons of all ages and health states. The unified American College of Sports Medicine (ACSM) and WHO guidelines [52] prescribe exercise and provide physical activity guidelines for supporting health and wellness in the non-disabled population, which are also recommended for individuals with SCI "to the best of their abilities". The latter inclusive language encourages everyone with an SCI - even those with extensive impairments - to make best efforts to avoid sedentary behaviors. These guidelines are in substantial agreement with both the ACSM Guidelines for Exercise Testing and Prescription [53] and the Physical Activity Guidelines for Adults with SCI that were established for SCI Action Canada [54]. They are also similar to the Physical Fitness for Special Populations (PFSP) "Physical Fitness for Individuals with Spinal Cord Injury" recommendations of the American Physical Therapy Association [cited in Ref. [15]].

The earliest exercise programs for persons with SCI primarily focused on enhancing cardiorespiratory fitness and aerobic power using arm, wheelchair, or electrical stimulation hybrid training [55–58]. Not surprisingly, more recent activities have used more intense exercise protocols incorporating high-intensity interval training (HIIT) [18,59] and circuit resistance training (CRT) [60–63], which broaden the benefits of conditioning and better match the lifestyle needs of persons with SCI.

Most recent studies undertaking exercise conditioning of persons with SCI report improved fitness as evidence by enhanced physical capacity, muscular strength, and functional performance [59,64]. Others report increased anaerobic power [60], an element of fitness deemed necessary to sustain function when wheeling uphill on ramps, crossing rocky or high-friction terrain, or performing in selected sports and recreation activities [65]. Fewer studies find reduced body fat mass [66], unless also incorporating dietary modifications of lowered caloric intake and less saturated fat [67]. As recent evidence reports that the three CMD component risks of obesity, insulin resistance, and low HDL-C are most commonly found in persons with early SCI [9,68], incorporation of moderate-intense exercise intensities best target the component risks comprising medical hazards of those with SCI.

Exercise as a countermeasure to cardiometabolic risks after SCI

Evidence supports the adoption of exercise is a practical approach for mitigating CMD and its risks for persons with SCI, and should be recommended by health care professionals following SCI as a non-pharmacological intervention [37]. Recent guidelines for physical exercise after SCI have addressed the benefit of activity countermeasures for cardiometabolic risk [15,54]. Participation should include at least 30 min of moderate-to vigorous-intensity aerobic exercise 3 times per week [54] or at least 150 minutes of moderate-intensity exercise per week as can be tolerated [15]. Exercise sessions can be fulfilled by 30–60 min performed 3–5 days per week or by exercising for at least 3, 10-min sessions per day [15]. This volume of physical exercise addressed by current guidelines is associated with 532–1064 kcal per week of energy expenditure.

A critical factor in the mitigation of CMD with exercise is targeting an increase in energy expenditure to promote

a negative energy balance and decrease adipose tissue. To promote adipose tissue loss and prevent weight regain, The American College of Sports Medicine recommends 250–300 min per week of moderate-intensity activity with an energy expenditure equivalent to approximately 2000 kcal per week [69]. However, the ability to increase exercise energy expenditure is innately reduced after SCI. With the current SCI exercise guidelines of 150 min per week, persons with SCI are often unable to achieve recommended moderate-intensity exercise of 10.5 mL O_2/kg/min. This exercise intensity is equivalent to an energy expenditure of 532 kcal per week and would take about seven weeks to lose one pound of adipose tissue (equal to 3500 kcal). Therefore, consideration should be made to double SCI exercise guidelines and adopt recommendations to achieve 300 min of exercise per week to expend over 1000 kcal. This is supported by a recent study that reported improvements in body composition and decreased CMD risk factors after functional electrical stimulation (FES) leg cycling for 300 min per week [70].

Following an exercise session, energy expenditure remains elevated and does not immediately return to a pre-activity level, a concept referred to as excess post-exercise oxygen consumption [20]. In individuals with SCI, excess post-exercise oxygen consumption is elevated for up to 30 min, as reported by two studies using FES cycling and arm crank exercise [71,72]. Further, compared to a reliance on glucose oxidation during an exercise session, with post-exercise recovery, there is a shift in substrate partitioning to an increased dependence on fat oxidation. Exercise modalities involving interval or resistance training that incorporates intermittent high-intensity contraction rely on muscle glycogen depletion during exercise to increase post-exercise fat oxidation. Following FES exercise [73] and circuit resistance training [61], post-exercise shifts to fat oxidation may be a consequence of the vastly glycolytic nature of these exercise modes [20]. The influence of physical exercise on fat as a fuel is significant, as energy stored as fat has been reported to predict cardiovascular disease risk factors after SCI independent of activity and fitness levels [74].

Accordingly, the low rates of exercise energy expenditure after SCI necessitate a compound intervention approach with a strong emphasis on high-volume exercise plus caloric restriction following a healthy dietary pattern to promote a negative energy balance that mitigates the CMD component risk factors.

Conclusions

CMS risk factors are disturbingly prevalent in individuals with SCI and pose health hazards that challenge health and function throughout the lifespan. An overweight or obese body habitus, insulin resistance, and low levels of cardioprotective HDL-C are the most common of these hazards and occur more often than reported in the non-disabled population. Heightened surveillance for risk, and adoption of healthy living recommendations specifically directed toward significant risks for weight control and glycemic management, should be incorporated as a priority for disease prevention. While physical fitness is not included among the five guideline risks of CMD, moderate-intense exercise should be considered an essential component of this plan. Best practice would also incorporate calorie-adjusted nutrition to achieve optimal body mass and insulin sensitivity and preserve activity, health, and independence throughout the lifespan.

Author statement

Mark Nash: Conceptualization, Methodology, Investigation, Writing – review & editing, Project administration; Gary Farkas: Conceptualization, Methodology, Investigation, Writing – review & editing; Eduard Tiozzo: Conceptualization, Methodology, Investigation, Writing – review & editing; David Gater: Conceptualization, Methodology, Investigation, Writing – review & editing.

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Conflict of interest statement

Nothing declared.

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The investigators computed the prevalence of cardiometabolic disease using the American Heart Association/National Heart, Lung, and Blood Institute guideline (CMS diagnosis as sum of risks ≥3 method) for overweight/obesity, insulin resistance, hypertension, and dyslipidemia. After adjustment for multiple comparisons, injury level and AIS grade were unrelated to CMS or risk factors. However 32.1% of subjects with SCI had CMS when using the sum of risks or HOMA2/QUICKI model, respectively. This is nearly double the prevalence of the non-disabled population. Overweight/obesity and (pre)hypertension were highly prevalent (83% and 62.1%, respectively), with risk for overweight/obesity being significantly associated with CMS diagnosis (sum of risks, $\chi 2 = 10.105$; adjusted P = .008). Insulin resistance was significantly associated with CMS when using the HOMA2/QUICKI model ($\chi 2 = 21.23$, adjusted P < .001). Of the 279 subjects, 76.4% were at moderate to high risk from elevated CRP, which was significantly associated with CMS determination (both methods; sum of risks, $\chi 2 = 10.198$; adjusted P = .048 and HOMA2/QUICKI, $\chi 2 = 10.532$; adjusted P = .04).The study concluded that CMS risk factors were prevalent in individuals with SCI/D. Overweight/obesity, hypertension, and elevated CRP were common. The findings called for surveillance for risk, and adoption of healthy living recommendations specifically directed toward weight reduction, hypertension management, and inflammation control.

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The investigators examined current exercise guidelines for SCI, which focus predominantly on relative short durations of moderate-intensity aerobic upper-body exercise, yet contemporary evidence suggests this is not sufficient to induce meaningful improvements in risk factors for the prevention of cardiometabolic disease in this population. They suggest these guidelines require re-examination and propose that high-intensity interval training (HIIT) may be a viable alternative exercise strategy to promote vigorous-intensity exercise and prevent cardiometabolic disease in persons with SCI. They present strong evidence to suggest that HIIT is superior to moderate-intensity aerobic exercise for improving cardiorespiratory fitness, insulin sensitivity, and vascular function. The potential application and safety of HIIT in this population is also discussed. Increasing exercise intensity could offer a simple, readily available, time-efficient solution to improve cardiometabolic health in persons with SCI.

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Physical inactivity after SCI leads to profound deconditioning. The Investigators established reference values of cardiorespiratory fitness applicable to the general, untrained spinal cord injury (SCI) population by colaescing data from 12 published studies. Participants were 153 men and 26 women (age, 18–55y) with chronic SCI (N = 179) were included. Participants completed a progressive resistance exercise test to determine peak oxygen consumption (Vo2peak). Percentile ranking (poor<20%; fair; 20%–40%; average, 40%–60%; good, 60%–80%; excellent, 80%–100%) was used to establish reference values. For the primary outcome measure (Vo2peak), persons with paraplegia had significantly higher values than did persons with tetraplegia (P < .001). Regression analysis revealed that motor level of injury was associated with 22.3% of the variability in Vo2peak (P < .001), and an additional 8.7% was associated with body mass index (P < .001). No other measure accounted for additional significant variability. Key determinants of fitness were motor level of injury and body habitus, yet most variability in aerobic capacity was not associated with standard measures of SCI status or demographic characteristics.

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The Investigators formed the first evidence-based Panel from the Consortium for Spinal Cord Medicine of the Paralyzed Veterans of America to address CMD after SCI. They reported emergence of all-cause cardiovascular diseases (CVD) and CVD-related risks as significant health hazards for persons with SCI and established a foundational standard for identification and management of cardiometabolic risks. The evidence rating confirmed that persons with SCI are frequently sedentary, overweight, dyslipidemic and at elevated risk for insulin resistance, thus placing them in jeopardy of developing CMD. The panel made detailed recommendations for exercise, nutrition, and pharmacotherapy that would best mitigate this risk.

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Recent literature would suggest the prevalence of metabolic syndrome in persons with spinal cord injury (SCI) is higher than that of the general population, although no large cohorts have yet been reported. The current retrospective investigation represents a cross- sectional cohort of 473 veterans with SCI from a single center in the mid-Atlantic region of the United States for whom modified International Diabetes Federation (IDF) criterion variables for the metabolic syndrome were available in the computerized personal record system (CPRS). These variables included a surrogate marker of obesity appropriate to SCI (Body Mass Index (BMI) $\geq$ 22 kg/m2), as well as indicators of diabetes, dyslipidemia and hypertension. Results showed over 57% of the veterans had metabolic syndrome by modified IDF criteria, including 76.7% with BMI $\geq$22 kg/m2, 55.1% with or under treatment for hypertension, 49.7% with or previously diagnosed with diabetes mellitus, and 69.7% with or under treatment for high density lipoprotein (HDL) cholesterol under 40 mg/dl. The Investigators concluded that metabolic syndrome and its constituent components are more prevalent in veterans with SCI than in the general population, suggesting a greater need for identification and treatment interventions in this specialty population.

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People with chronic paraplegia frequently experience dyslipidemias characterized by depressed levels of high-densitylipoprotein cholesterol (HDL-C) and elevated levels of low- density lipoprotein cholesterol (LDL-C). These anormal lipid profiles andpoor fitness levels increase their risk for cardiovascular disease. The investigators tested whether circuit resistance exercise training improves both upper-extremity fitness and the atherogenic lipid profile in persons with chronic paraplegia. A homogeneous cohort of 5 men with neurologically complete spinal cord injuries at T6 to L1 underwent 3 months of exercise training using uninterrupted resistance and endurance exercises of the upper extremities. Training was performed 3 times a week on alternating days. Results of graded arm exercise testing showed a 30.3% improvement in peak oxygen consumption a 33.5% increase in time to fatigue ($P < .01$) and a 30.4% increase in peak power output ($P < .05$). A 25.9% lowering of LDL-C ($P < .05$) and 9.8% elevation of HDL-C ($P < .05$) were observed after training. These changes reduced the average LDL-C- to- HDL-C ratio by 1 unit ($P < .05$) and the TC-to- HDL-C ratio from 5.0 ± 1.1(mean ± SO) to 3.9 ± .7 ($P < .05$). This change reflected a cardiovascular risk reduction of almost 25%; the TC/ HDL-C declined from the high-risk score of 5.0 to near the desired score of 3.5. These findings support the beneficial effects of circuit exercise resistance training on fitness and atherogenic lipid profiles in persons with chronic paraplegia.

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Exercise conditioning of people with SCI often focuses on young persons in excellent health. Here the Investigators examined effects of circuit resistance exercise (CRT) training on muscle strength,

endurance, anaerobic power, and shoulder pain in middle-aged men with paraplegia who began training with pain. Seven men aged 39–58 years with motor- complete paraplegia from T5 to T12 and confirmed shoulder pain were studied. Subjects underwent a 4-month CRT program using alternating resistance maneuvers and high-speed, low-resistance arm exercise. One-repetition maximal force was measured before training and monthly thereafter. Pretraining and post-training peak oxygen uptake (Vo2peak) was measured by graded arm testing. Anaerobic power was measured before and after training using a 30-s Wingate Anaerobic Test. Shoulder pain was self-evaluated by an index validated for people with spinal cord injury (Wheelchair Users Shoulder Pain Index [WUSPI]). Strength increases ranging from 38.6% to 59.7% were observed for all maneuvers (P range, .005–.008). Vo2peak increased after training by 10.4% (P = .01), and peak and average anaerobic power increased by 6% (P = .001) and 8.6% (P = .005), respectively. WUSPI scores were significantly lowered, with almost half of subjects reporting complete resolution of shoulder pain. The Investigators found that CRT improved muscle strength, endurance, and anaerobic power in middle-aged men with paraplegia while significantly reducing their extant shoulder pain.

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This prospective case series analyzed effects of a comprehensive lifestyle intervention program in three patients with chronic paraplegia having major risks for the cardiometabolic syndrome (CMS).Treatment was an intense 6-month program of circuit resistance exercise, nutrition using a Mediterranean diet and behavioral support, followed by a 6-month extension (maintenance) phase involving minimal support. The primary goal was a 7% reduction of body mass. Other outcomes analyzed insulin resistance using the HOMA-IR model, and plasma levels of fasting triglycerides and high-density lipoprotein cholesterol. All participants achieved the goal for 7% reduction of body mass and maintained the loss after the MP. Improvements were observed in 2/3 subjects for HOMA- IR and high-density lipoprotein cholesterol. All participants improved their risk for plasma triglycerides. A lifestyle intervention program involving circuit resistance training, a calorie- restrictive Mediterranean-style diet and behavioral support, results in clinically significant loss of body mass and effectively reduced component risks for CMS and diabetes. These results were for the most part maintained after a 6-month MP involving minimal supervision.

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Most studies of CMD risk following SCI describe individuals in the chronic phase of their recovery. Here the Investigators described the prevalence of cardiometabolic disease (CMD) at spinal cord injury (SCI) rehabilitation discharge; (2) compared this with controls without SCI; and (3) identified factors associated with increased CMD. 95 patients aged 18–70 years, with SCI (neurologic levels of injury C2-L2, American Spinal Injury Association Impairment Scale grades A-D), and enrolled within 2 months of initial rehabilitation discharge were studies. A control group (n = 1609): age/sex/body mass index–matched entries in the National Health and Nutrition Examination Education Survey (2016–2019) (N = 1704). Percentage of participants with SCI with CMD diagnosis, prevalence of CMD determinants within 2 months of rehabilitation discharge, and other significant early risk associations were analyzed using age, sex, body mass index, insulin resistance (IR) by fasting glucose and Homeostasis Model Assessment (v.2), fasting triglycerides, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol, total cholesterol, and resting blood pressure (systolic and diastolic). Participants with SCI had significantly higher diastolic blood pressure and triglycerides than those without SCI, with lower fasting glucose and HDL-C. 74.0% of participants with SCI vs 38.5% of those without SCI were obese when applying population-specific criteria (P < .05). Low HDL-C was measured in 54.2% of participants with SCI vs 15.4% of those without (P < .05). IR was not significantly different between groups, but was still in the high risk strata. 31.6% of participants with SCI had ≥3 CMD determinants, which was 40.7% higher than those without SCI (P < .05). Interplay of lipids and lipoproteins (i.e., total cholesterol:HDL-C ratio and triglyceride:HDL-C ratio) were associated with elevated risk in participants with SCI for myocardial infarction and stroke. The only significant variable associated with CMD was age (P < .05). Individuals with SCI have an increased CMD risk compared with the general population; obesity, IR, and low HDL-C are the most common CMD risk determinants; age is significantly associated with early CMD.

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