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SPINAL CORD INJURY REHABILITATION EVIDENCE

Cardiovascular Health and Exercise Following Spinal Cord Injury

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Key Points

There is growing evidence that BWSTT can improve indicators of cardiovascular fitness and health in individuals with complete and incomplete tetraplegia and paraplegia.

Interventions that involve FES training a minimum of 3 days per week for 2 months may improve muscular endurance, oxidative metabolism, exercise tolerance, and cardiovascular fitness.

Aerobic and FES exercise training may lead to clinically significant improvements in glucose homeostasis in persons with SCI. Preliminary evidence indicates that a minimum of 30 min of moderate intensity training on 3 days per week is required to achieve and/or maintain the benefits from exercise training.

Aerobic exercise, in a variety of approaches including arm ergometry and FES exercise training may lead to improvements in lipid lipoprotein profile that are clinically relevant for the at risk SCI population.

The optimal training program for changes in lipid lipoprotein profile remains to be determined. However, a minimal aerobic exercise intensity of 70% of heart rate reserve on most days of the week appears to be a good general recommendation for improving lipid lipoprotein profile in persons with SCI.

Table of Contents

Warburton DER, Krassioukov A, Sproule S, Eng JJ (2018). Cardiovascular Health and Exercise Following Spinal Cord Injury. In Eng JJ, Teasell RW, Miller WC, Wolfe DL, Townson AF, Hsieh JTC, Connolly SJ, Noonan VK, Loh E, Sproule S, McIntyre A, Querée M, editors. Spinal Cord Injury Rehabilitation Evidence. Version 6.0. Vancouver: p 1- 68.

Abbreviations

ADL	Activities of Daily Living
BP	Blood Pressure
BWSTT	Body Weight Supported Treadmill Training
CVD	Cardiovascular Disease
EE	Energy Expenditure
FES	Functional Electrical Stimulation
GLUT-4	Glucose Transporters
HDL	High-Density Lipoprotein
HR	Heart Rate
HRR	Heart Rate Reserve
LDL	Low-Density Lipoprotein
OGTT	Oral Glucose Tolerance Test
RPE	Rating of Perceived Exertion
TC	Total Cholesterol
TG	Triglycerides

Cardiovascular Health and Exercise Following Spinal Cord Injury

1.0 Executive Summary

What Cardiovascular problems occur after injury?

There is considerable evidence indicating an earlier onset and/or prevalence of various chronic diseases (including Cardiovascular disease (CVD), type II diabetes, and osteoporosis) in persons with SCI (Yekutiel et al. 1989, Whiteneck et al. 1992, DeVivo et al. 1993, Bauman et al. 1999b, Groah et al. 2001, Garshick et al. 2005, Warburton et al. 2007b). Similar to people without SCI, physical inactivity plays a significant role in the risk for CVD in people with SCI. In fact, the ordinary activities of daily living do not appear to be sufficient to maintain cardiovascular fitness in persons with SCI. Moreover, extremely low levels of physical activity and fitness may lead to a vicious cycle of further decline. Ultimately these changes will have significant implications for the development of CVD (and associated co-morbidities) and the ability to live an independent and healthy lifestyle.

How common are Cardiovascular problems after Spinal Cord Injury?

CVD is a leading cause of mortality in both able-bodied individuals and persons with SCI (Whiteneck et al. 1992). The prevalence rate of symptomatic CVD in SCI is 30–50% in comparison to 5%–10% in the general able-bodied population (Myers et al. 2007). Moreover, the prevalence of asymptomatic CVD has been estimated to be 60%–70% in persons with SCI (Bauman et al. 1993, Bauman et al. 1994). It also appears that persons with SCI have increased CVD-related mortality rates and those with tetraplegia experience mortality at earlier ages in comparison to able-bodied individuals (Whiteneck et al. 1992, DeVivo et al. 1999, Myers et al. 2007). These are alarming statistics, which place a significant burden upon the person with SCI, his/her family, and society as a whole.

What are the risk factors for Cardiovascular problems?

Lesion Level

Cardiac function is strongly influenced by the lesion level; individuals with a T1 lesion will not have any supraspinal sympathetic control, those with a T1-T5 lesion will have partial preservation, while those with an injury below T5 will have full supraspinal sympathetic control of the heart and upper body vasculature (West et al. 2012). Adrenergic dysfunction, poor diet, and physical inactivity are thought to play key roles in the elevated risk for CVD in SCI (Bravo et al. 2004, Warburton et al. 2007b).

Physical Inactivity and Deconditioning

Physical inactivity is a major independent risk factor for CVD and premature mortality in persons with SCI (Warburton et al. 2006, Warburton et al. 2010). Unfortunately, physical inactivity is highly prevalent among persons with SCI and ordinary activities of daily living are not adequate to maintain cardiovascular fitness (Jacobs and Nash 2004, Hoffman 1986). Marked inactivity associated with SCI has been associated with lower high-density lipoprotein (HDL) cholesterol (Schmid et al. 2000, Manns et al. 2005) elevated low-density lipoprotein (LDL) cholesterol (Schmid et al. 2000); triglycerides (Schmid et al. 2000, Manns et al. 2005); total cholesterol levels (Schmid et al. 2000); abnormal glucose homeostasis (Elder et al. 2004, Manns et al. 2005); increased adiposity (Elder et al. 2004, Manns et al. 2005); and excessive reductions in aerobic fitness (Schmid et al. 2000, Manns et al. 2005). Moreover, a reduction in cardiovascular fitness may also lead to a vicious cycle of further decline leading to a reduction in functional capacity and the ability to live an independent lifestyle.

What management options are there for Cardiovascular problems?

Based on preliminary evidence (primarily level 4), it would appear that various exercise modalities (including arm ergometry, resistance training, BWSTT, and FES) may attenuate and/or reverse abnormalities in glucose homeostasis, lipid lipoprotein profiles, and cardiovascular fitness. As such, exercise training appears to be important for reducing the risk for CVD and multiple comorbidities (such as type 2 diabetes, hypertension, and obesity) in individuals with SCI. However, there is little research on SCI in comparison to the general population and other clinical conditions (e.g. chronic heart failure (Warburton et al. 2006, Warburton et al. 2010)). The previously mentioned physical inactivity and deconditioning have important clinical implications for exercise progression, *as the starting workload may need to be low* (e.g., submaximal and performed in bouts with rest in between) and customized to progress slowly due to issues of fatigue, as well as exercise-induced hypotension (Nash et al. 2012).

Non-Pharmacological Options

Aerobic Exercise and Treadmill Training

A common method of aerobic exercise in people with SCI is Body Weight-Supported Treadmill Training (BWSTT) – a harness and treadmill system used to provide a safe environment for stepping and gait without the fear of falling. The amount of unloading (de-weighting) can be adjusted so that the client takes anywhere from all of their weight to no weight at all, and stepping can be assisted by a physical therapist if motor control is limited. There is evidence to suggest that BWSTT can improve indicators of cardiovascular health (e.g., arterial compliance (Ditor et al. 2005b), cardiac autonomic balance (Millar et al. 2009), peak oxygen uptake and heart rate (Jack et al. 2009; Soyupek et al. 2009)) in individuals with complete and incomplete SCI.

There is good evidence from several studies (Hooker and Wells 1989, de Groot et al. 2003, Stewart et al. 2004, El-Sayed and Younesian 2005) to suggest that aerobic exercise training programs (performed at a moderate-to-vigorous intensity 20–30 min/day, three days/week for eight weeks) are effective in improving the lipid lipoprotein profiles of persons with SCI. The optimal training program for changes in lipid lipoprotein profile remains to be determined. However, a minimal aerobic exercise intensity of 70% of HRR on most days of the week appears to be a good general recommendation for improving lipid lipoprotein profile.

Upper Extremity Exercise

If moving the legs is difficult, there is research indicating that upper extremity exercise (e.g., arm cycle ergometry) at a moderate-to-vigorous intensity, three days/week for at least six weeks, improves cardiovascular fitness and exercise tolerance in persons with SCI. The optimal exercise intervention for improving cardiovascular fitness remains to be determined. There is also evidence (de Groot et al. 2003) that high-intensity (70%–80% HRR) exercise can lead to greater improvements in peak power and $VO2_{peak}$ than low-intensity (50%–60% HRR) exercise. There is also evidence to suggest that resistance training at a moderate intensity for at least two days/week also appears to be appropriate for the rehabilitation of persons with SCI (Cooney and Walker 1986, Jacobs et al. 2001, Nash et al. 2001, Mahoney et al. 2005).

Functional Electrical Stimulation (FES)

There is growing evidence from multiple pre-post studies (Berry et al 2012; Griffin et al. 2009; Zbogar et al. 2008; Crameri et al. 2004; Hjeltnes et al. 1997; Mohr et al. 1997; Barstow et al. 1996; Faghri et al. 1992; Hooker et al. 1992) that FES training performed for a minimum of three days per week for two months may be effective for improving musculoskeletal fitness, the oxidative potential of muscle, exercise tolerance, and cardiovascular fitness. Gait training and Neuromuscular electrical stimulation can also increase metabolic and cardiorespiratory response in persons with complete tetraplegia (de Carvalho et al. 2006).

Some evidence indicates that aerobic exercise (often Gait or Treadmill training) paired with FES exercise training programs (performed 30 min/day, three days per week for eight weeks or more) are effective in improving glucose homeostasis in persons with SCI, and that the magnitude of this change is clinically significant (de Groot et al. 2003, Chilibeck et al. 1999, Mohr et al. 2001, Jeon et al. 2002, Jeon et al. 2010).

Limitations of What We Know

The relationship between increasing physical activity and health status of SCI has not been evaluated adequately to date, particularly over the long-term. Well-designed RCTs are required in the future to establish firmly the primary mechanisms by which exercise interventions elicit these beneficial changes. Similarly, further research is required to evaluate the effects of lesion level and injury severity on exercise prescription, such that exercise programs can be developed that address the varied needs of persons with SCI. Moreover, long-term follow-up investigations are required to determine whether training-induced changes in risk factors for CVD translate directly into a reduced incidence of CVD and premature mortality in persons with SCI. Also, there is a need to determine more definitively the relationship of diet and exercise on these risk factors – can diet or exercise alone or diet and exercise together decrease these risk factors?

2.0 Introduction

It is estimated that approximately 85,000 Canadians live with a traumatic or non-traumatic spinal cord injury (SCI) with over 4000 new cases per year in Canada, and of which about half are from traumatic causes (Noonan et al. 2012). In the United States, there are approximately 12,000 cases of SCI per annum (Foundation for Spinal Cord Injury Prevention 2009, Myers et al. 2012). The majority of traumatic SCIs (80%) occur in individuals who are under 30 years of age (ICORD 2003, Rick Hansen Spinal Cord Injury Registry 2004). Persons with SCI currently have an increased life expectancy owing to improvements in medical treatment (Rick Hansen Spinal Cord Injury Registry 2004), and therefore, are susceptible to the same chronic conditions across the lifespan as able-bodied persons. In fact, cardiovascular disease (CVD) is the leading cause of mortality in both able-bodied individuals and persons with SCI (Whiteneck et al. 1992). Unfortunately, there is considerable evidence indicating an earlier onset and/or prevalence of various chronic diseases (including CVD, type II diabetes, and osteoporosis) in persons with SCI (Yekutiel et al. 1989, Whiteneck et al. 1992, DeVivo et al. 1993, Bauman et al. 1999b, Groah et al. 2001, Garshick et al. 2005, Warburton et al. 2007b). The prevalence rate of symptomatic CVD in SCI is 30–50% in comparison to 5%–10% in the general able-bodied population (Myers et al. 2007). Moreover, the prevalence of asymptomatic CVD has been estimated to be 60%–70% in persons with SCI (Bauman et al. 1993, Bauman et al. 1994). It also appears that persons with SCI have increased CVD-related mortality rates and those with tetraplegia experience mortality at earlier ages in comparison to able-bodied individuals (Whiteneck et al. 1992, DeVivo et al. 1999, Myers et al. 2007). These are alarming statistics, which place a significant burden upon the patient, his/her family, and society as a whole.

Cardiac function is strongly influenced by the lesion level; individuals with a T1 lesion will not have any supraspinal sympathetic control, those with a T1-T5 lesion will have partial preservation, while those with an injury below T5 will have full supraspinal sympathetic control of the heart and upper body vasculature (West et al. 2012). Adrenergic dysfunction, poor diet, and physical inactivity are thought to play key roles in the elevated risk for CVD in SCI (Bravo et al. 2004, Warburton et al. 2007b). Additionally, interruption of descendent sympathetic pathways and unopposed vagal tone cause a decrease in compensatory sympathetic activities, elevating the risk for cardiac bradycardia, hypotension, and hypothermia, by lack of sympathetic activity (Grigorean et al. 2009, Krassioukov et al. 2007). Cardiac dysfunctions are often life-threatening in acute SCI; however their risks diminish in chronic SCI (Grigorean et al. 2009). Sympathetic control of the cardiovascular system originates primarily from T1 to T4 spinal segments (Phillips and Krassioukov, 2014). It is important to take into account that individuals with lesions at or above these levels may have an impaired response to exercise.

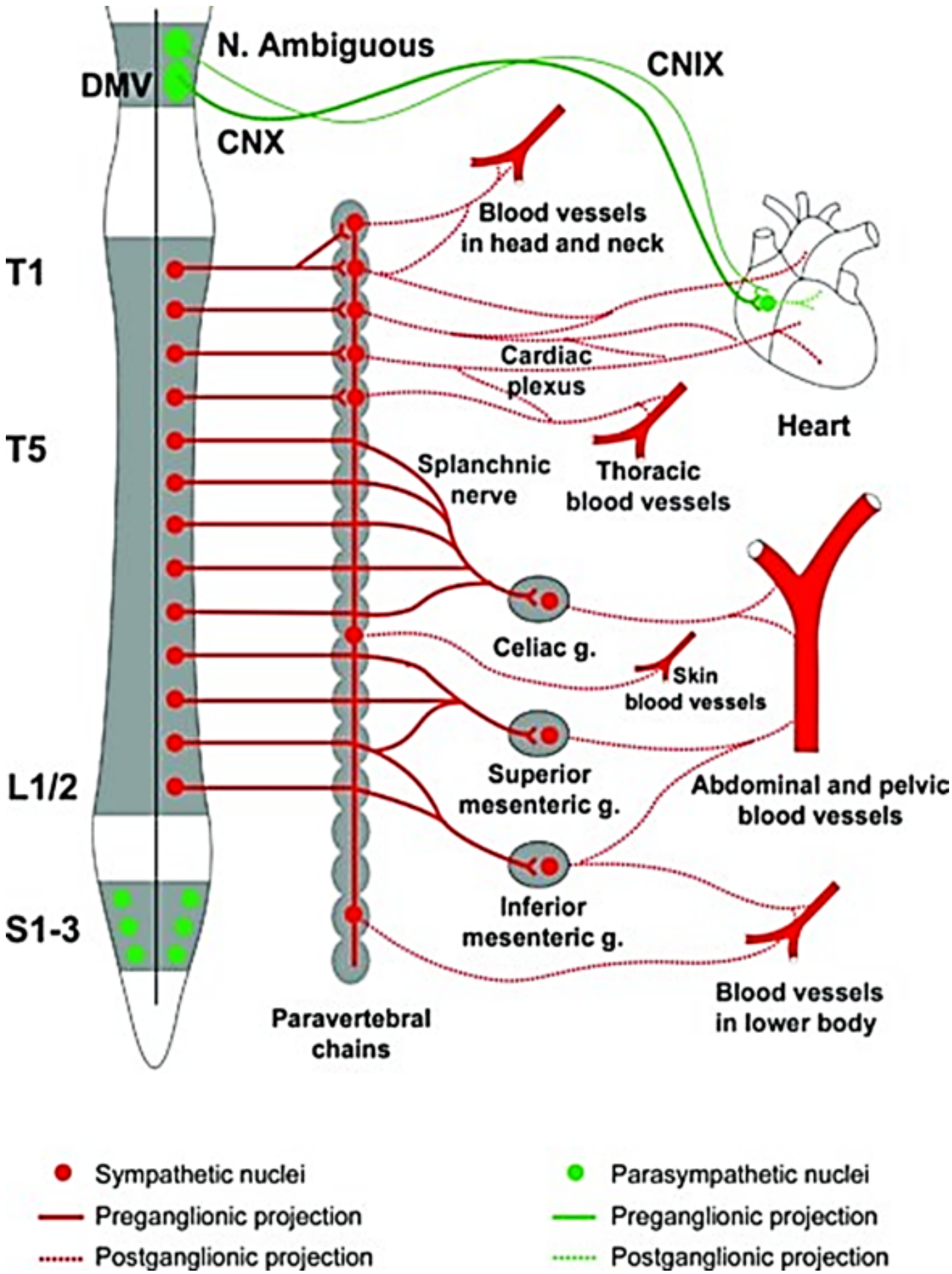


Figure 1 – Schematic diagram illustrating sympathetic and parasympathetic control of the cardiovascular system. Reprinted with permission from Wiley Online Publishing – Phillips AA and Krassioukov AV. Autonomic Consequences of Spinal Cord Injury. In *Comprehensive Physiology,* October 2014; 4(4):1419-53.

Physical inactivity is a major independent risk factor for CVD and premature mortality (Warburton et al. 2006, Warburton et al. 2010). Unfortunately, physical inactivity and marked deconditioning are highly prevalent among persons with SCI (Jacobs and Nash 2004). Also, it appears that the ordinary activities of daily living are not adequate to maintain cardiovascular fitness in persons with SCI (Hoffman 1986). It is likely that low levels of physical activity and fitness (as a result of wheelchair dependency) explain (in part) the increased risk for CVD (Myers et al. 2007). Marked inactivity associated with SCI has been associated with lower high-density lipoprotein (HDL) cholesterol (Schmid et al. 2000, Manns et al. 2005); elevated low-density lipoprotein (LDL) cholesterol (Schmid et al. 2000); triglycerides (Schmid et al. 2000, Manns et al. 2005); total cholesterol levels (Schmid et al. 2000); abnormal glucose homeostasis (Elder et al. 2004, Manns et al. 2005); increased adiposity (Elder et al. 2004, Manns et al. 2005); and excessive reductions in aerobic fitness (Schmid et al. 2000, Manns et al. 2005). It is important to note that SCI presents an additional risk for CVD above that seen in able-bodied individuals owing to the marked decrease in physical activity and injury-related changes in metabolic function (Bravo et al. 2004). Moreover, a reduction in cardiovascular fitness may also lead to a vicious cycle of further decline leading to a reduction in functional capacity and the ability to live an independent lifestyle. Based on the available literature, it is clear that effective exercise interventions are required to slow the progression of multiple risk factors for CVD and other chronic diseases (e.g. obesity, type 2 diabetes) in persons with SCI. In addition, literature from other populations suggest that exercise combined with other healthy lifestyles such as a high fibre, low fat diet may have even further positive impact on cardiovascular health (Golay et al. 2013) and are likely relevant to SCI populations as well (Nash et al. 2012).

The current chapter summarizes and updates the literature regarding the risk for CVD in persons with SCI. This chapter also critically evaluates the level of evidence regarding the effectiveness of varied forms of exercise rehabilitation in increasing cardiovascular fitness and attenuating the risk for CVD in persons with SCI. Table 1 contains a definition of the commonly used terms and/or abbreviations in this chapter.

Table 1: Description of Commonly Used Terms

Term	Definition
Spinal Cord Injury (SCI)	• Refers to persons who have sustained a spinal cord injury.
Cardiovascular Disease (CVD)	• Refers to diseases affecting the circulatory system (i.e., heart and/or blood vessels) including acute myocardial infarction, coronary artery disease, arteriosclerosis, heart valve disease, heart failure, high blood pressure, peripheral vascular dysfunction, congenital heart disease, stroke, and arrhythmias.
Physical Activity	• Refers to all leisure and non-leisure body movements resulting in an increased energy output from the resting condition.
Exercise	• Refers to structured and repetitive physical activity designed to maintain or improve physical fitness.
Aerobic Training	• Refers to an exercise program that incorporates activities that are rhythmic in nature, using large muscle groups at moderate intensities repeated across a week (e.g., 3 to 5 days per week).
Heart Rate Reserve (HRR)	• Refers to the difference between maximal heart rate (HRmax; predicted or determined directly) and resting HR. The %HRR formula takes into account resting and maximal HR to provide an appropriate target HR (or range) for training. • Training Heart Rate = ((HRmax – HRrest) x 40-85%) + HRrest

Term	Definition
	• If an exercise stress test cannot be done, the training heart rate should be set at 20-30 beats above HRrest
MET	• Refers to an estimate of resting metabolic rate while sitting quietly. • 1 MET = 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ or 1 $kcal \cdot kg^{-1} \cdot h^{-1}$
Moderate Intensity Exercise	• Exercise performed at relative intensities of 40-59% HRR, approximately 4-6 METs, or 55-69% of HRmax.
Current General Physical Activity Recommendation	• 150 min of moderate-to-vigorous intensity physical activity per week. • Please note that this is quite distinct from that recommended for SCI and as such should not be used with SCI participants (see below).
Current SCI Physical Activity Recommendation	• Moderate to vigorous intensity aerobic exercise for at least 20 min per session 2 times per week, plus strength training 2 times per week, consisting of 3 sets of 8-10 repetitions of exercise for each major muscle group (SCI Action Canada 2013).
Activities of Daily Living (ADLs)	• Refers to the activities in which one engages during daily life.
Cardiovascular (Aerobic) Fitness	• Refers to the ability to transport and utilize oxygen during prolonged, strenuous exercise or work. It reflects the combined efficiency of the lungs, heart, vascular system and exercising muscles in the transport and utilization of oxygen.
Maximal Aerobic Power (VO_2max)	• The maximum amount of oxygen that can be transported and utilized by the working muscles. Also, commonly referred to as maximal oxygen consumption.
Health-related Physical Fitness	• Involves the components of physical fitness that are related to health status including cardiovascular fitness, musculoskeletal fitness, body composition and metabolism.
Quality of Life	• Refers to an overall satisfaction and happiness with life, and includes the facets of physiological, emotional, functional and spiritual well-being.

3.0 The Risk for Cardiovascular Disease in Persons with SCI

The role of arteriosclerosis (i.e., narrowing and hardening of the arteries) on the development of CVD is clear (Grey et al. 2003). Persons with SCI appear to be particularly susceptible to the development of arteriosclerosis (Bravo et al. 2004). Researchers have revealed that persons with SCI exhibit a series of risk factors for arteriosclerosis and thus CVD (as shown in Table 2).

A healthy endothelium (interior lining of blood vessels) is essential for the protection against arteriosclerosis (Anderson 2003). Increasing evidence has examined the vascular health of persons with SCI (de Groot et al. 2005, Zbogar et al. 2008, Phillips et al. 2011), and the effects of exercise training on vascular health in SCI (see recent systematic review of Phillips et al. 2011). However, the volume and level of evidence is quite limited in comparison to what is known about vascular health in the general population and other chronic conditions (such as heart disease, hypertension, diabetes) (Phillips et al. 2011). The majority (if not all) of the risk factors for CVD in persons with SCI will have a significant negative impact upon vascular health and function. As such, it is likely that vascular dysfunction is a central step in the development of CVD in persons with SCI.

Various authors have demonstrated reduced peripheral vascular function and/or arterial compliance in SCI (Table 1); however, others have highlighted that when appropriate controls are applied certain markers of endothelial function (e.g., endothelium-dependent and -independent vasodilatation of the superficial femoral artery) may not be appreciably different from the general population (de Groot et al. 2004, Thijssen et al. 2008).

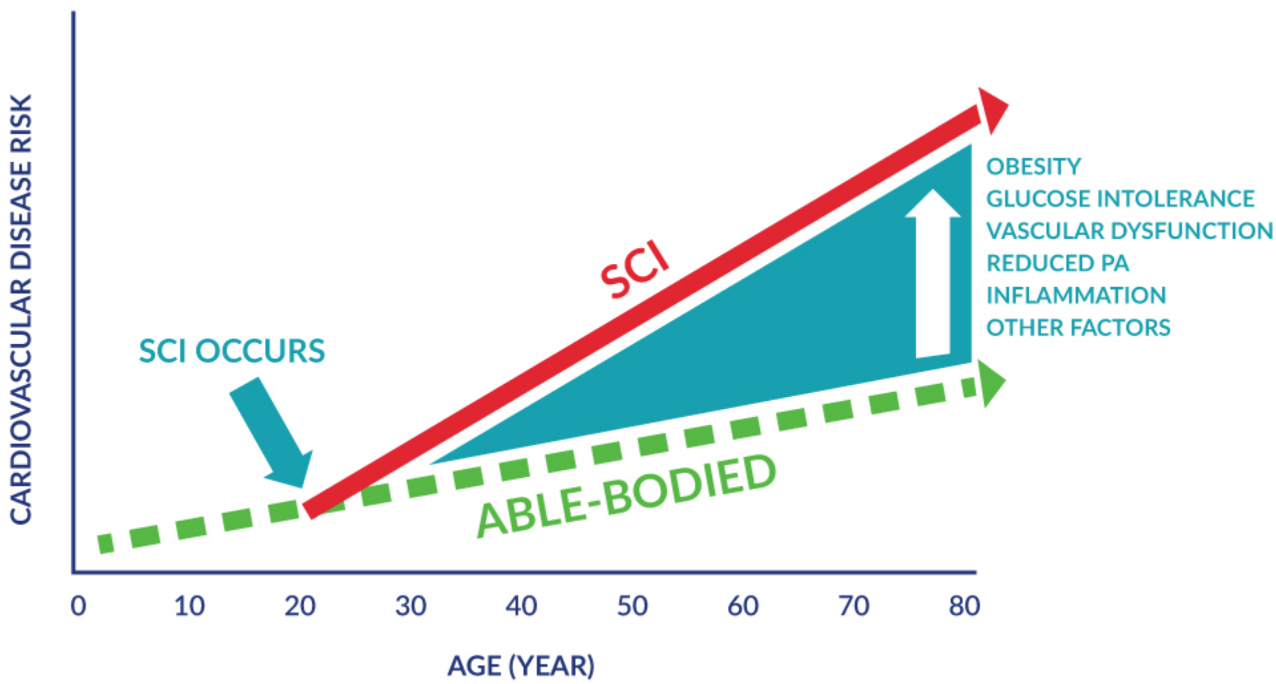


Figure 2: Age related increase and Additional Cardiovascular Disease risk in people with SCI

Adapted from Phillips AA and Krassioukov AV. Contemporary Cardiovascular Concerns after Spinal Cord Injury: Mechanisms, Maladaptations, and Management. Journal of Neurotrauma, 32:1927-1942.

Table 2: Risk factors for Cardiovascular Disease in Persons with SCI

Risk Factor	Literature Support
• Abnormal lipoprotein profiles	(Brenes et al. 1986, Dearwater et al. 1986, Bauman et al. 1992b, Krum et al. 1992, Maki et al. 1995, Dallmeijer et al. 1997, Bauman et al. 1998, Bauman et al. 1999a, Bauman et al. 1999b)
• Abnormal glucose homeostasis	(Myllynen et al. 1987, Bauman and Spungen 2001)
• Increased relative adiposity, elevated body fat and/or reduced lean body mass	(Bauman et al. 1999c, Spungen et al. 2003)
• Reduced peripheral vascular function and/or arterial	(Wecht et al. 2000, Hopman et al. 2002, Wecht et al. 2003, de Groot et al. 2005, Zbogar et al. 2008, Wong et

Risk Factor	Literature Support
compliance	al. 2012, Phillips et al. 2012)
• Increased risk for deep vein thrombosis	(Miranda and Hassouna 2000)
• Abnormal haemostatic and inflammatory markers	(Vaidyanathan et al. 1998, Kahn 1999, Roussi et al. 1999, Kahn et al. 2001, Frost et al. 2005, Lee et al. 2005b)
• Excessive homocysteine (an amino acid)	(Bauman et al. 2001)
• Depressed endogenous anabolic hormone levels (e.g. serum testosterone and growth hormone)	(Claus-Walker and Halstead 1982b, Bauman and Spungen 2000)
• Increased activation of the renin-angiotensin-aldosterone system (a hormone system that regulates blood-pressure and fluid balance).	(Claus-Walker and Halstead 1982a)
• Hypertension	(Lee et al. 2005a)
• Reduced aerobic fitness	(Hoffman 1986)

3.1 Systematic Review

As the body of knowledge is growing in the field of cardiovascular management for spinal cord injury (SCI) it is becoming increasingly important to review the literature and ensure that the information used both in research and in practice is current and evidence based. The aim of this section of the cardiovascular chapter is to provide an overview of the current systematic reviews available in areas related to cardiovascular fitness and health management in SCI population, such as the effect of exercise on cardiovascular risk factors.

Table 3: Systematic Review

Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	Methods Databases	Conclusions
Cragg et al. 2012; Canada Reviewed published articles from 1981 to 2011 N = 30 **Level of evidence:** PEDro scale was used to evaluate studies **Type of study:**	**Method:** Systematically review the management of some potentially modifiable CVD risk factors for the chronic SCI population. Any peer-reviewed human studies or reviews with or without treatments examining CVD risk factors specific to the chronic traumatic SCI population were included. Exclusion criteria include animal studies, non-English. **Database:** MEDLINE/PubMed,	1. One RCT provided level 1 evidence that niacin was efficacious in improving lipid profiles in individuals with chronic tetraplegia. 2. There is no consensus about the optimal frequency of obtaining CRP levels in individuals with SCI. 3. Following SCI, there is consistent evidence of a greater prevalence of abnormal glycemic control relative to able-bodied controls. 1. Several pre-post studies provided level 4 evidence that the use of FES or treadmill

Author Year; Country **Date included in the review** **Total Sample Size** **Level of Evidence** **Type of Study** **Score**	**Methods** **Databases**	**Conclusions**
2 RCT 1 prospective controlled trial 10 Pre-post 17 No intervention AMSTAR: 7	EMBASE, Cochrane Library and hand-searching.	walking favorably influence glycemic control.
Hicks et al. 2011; Canada Reviewed published articles before March 2010 N= 82 (69 chronic, 13 acute SCI) **Level of Evidence:** PEDro scale was used to evaluate studies **Type of study:** Not described AMSTAR: 7	**Methods:** Literature search for published English case studies, experimental and quasi experimental design studies related to fitness benefits of physical activity or exercise training intervention in SCI persons Interventions included exercise and FES. Outcome measures included muscle strength, body composition, physical capacity and functional performance **Databases:** MEDLINE (1950–March 2010, OVID Interface); PsycINFO (1840– March 2010, Scholars Portal Interface); EMBASE (1980–March 2010, OVID Interface); CINAHL (1982–March 2010, OVID Interface); SPORTDiscus (–March 2010).	1. There is strong evidence (level 1 and 2) that exercise, performed 2–3 times per week at moderate-to-vigorous intensity, increases physical capacity (e.g. VO_2 peak) and muscular strength in the chronic SCI population 2. There is insufficient quality evidence to draw meaningful conclusions on its effect on body composition or functional capacity in chronic SCI 3. There were insufficient high-quality studies in the acute SCI population to draw any conclusions 4. Wheelchair ergometry has been shown to significantly increase peak power output (a measure of physical capacity) following 6 weeks of training 4. 16 studies (2 level 1 RCTs) provide strong evidence that combined resistance and aerobic exercise, and functional electrical stimulation (FES)-assisted exercise, produced significant improvements in power output.
Phillips et al. 2011; Canada Reviewed scientific publications from 1950 N=27 **Level of Evidence:** PEDro scale was used to evaluate studies **Type of study:** 1 RCT 8 prospective controlled trials 15 pre-post 2 case-control 1 case report AMSTAR: 6	**Method:** Literature search for articles evaluating the effect of exercise as a therapy to alter arterial function in persons with SCI Interventions included passive leg exercise, FES, single muscle electrical stimulation, upper body continuous aerobic exercise, acute combined arm passive leg exercise and BWSTT. Outcome measures included femoral blood flow velocity, heart rate and vascular measures. **Databases:** MEDLINE, EMBASE, Cochrane Library, ACP Journal Club, DARE, CCTR, CMR, HTA, NHSEED, PsycINFO, SPORTDiscus and CINAHL	Acute combined arm and passive leg exercise: 1. There is currently one paper with level 4 evidence that reported increased leg blood flow in response to combined arm exercise and passive leg movements Stretch-induced contractions: 2. There is currently one paper with level 2 (debatable but reliable results) evidence investigating blood flow changes in response to stretch-induced contractions. With such limited data, it is difficult to interpret the value of this exercise technique Passive leg exercise: 3. There is currently level 1 evidence supporting a passive leg exercise program as a technique to improve vascular function among individuals with paraplegia. Arm exercise: 4. 2 papers (level 3 and level 5) appear to suggest that long-term upper body exercise can improve arterial structure and function in those with SCI.

Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	Methods Databases	Conclusions
Deley et al. 2015 France Systematic Review N= 12 **Level of evidence:** Methodological quality was not assessed **Type of study:** Types of studies included not specified. AMSTAR= 5	**Methods:** A literature search was conducted to identify articles on different FES methods- including cycling, rowing and strengthening. The purpose is to compare the different FES methods, and the intention is to provide practical information for clinicians and people working with FES. Outcome measures include VO2 (L/min), heart rate (beats/min), stroke volume (mL/beat), and cardiac output (L/min). **Databases**: PubMed, Google Scholar	1. Crameri and colleagues suggest that the load applied to paralyzed muscles during an ES strengthening program is an important factor. Indeed, it determines the amount of muscle adaptation that can be achieved, with greater beneficial effects after isometric training in comparison with concentric exercises. 2. Authors reported that the mechanical efficiency of this exercise was low (*8 %) Moreover, this type of training often does not achieve sufficiently high levels of aerobic work and a plateau in training effect is quickly reached.
Warburton et al. 2007; Canada Reviewed published articles from 1980 to March 2006 N=42 **Level of Evidence:** PEDro scale was used to evaluate studies **Type of study:** 35 pre-post 3 prospective controlled trial 4 RCTs AMSTAR: 5	**Methods:** Literature search for English articles regarding the risk of cardiovascular disease (CVD) and the effectiveness of varied exercise rehabilitation programs for CVD in SCI Interventions included treadmill training (BWSTT), upper extremity exercise and FES training. Outcome measures included glucose homeostasis, lipid lipoprotein profiles and blood pressure. **Databases:** PubMed/MEDLINE, CINAHL, EMBASE, PsychINFO	1. Primarily level 4 evidence, which indicates various exercise modalities (including arm ergometry, resistance training, body weight supported treadmill training (BWSTT), and functional electrical stimulation (FES) may attenuate and/or reverse abnormalities in glucose homeostasis, lipid lipo- protein profiles, and cardiovascular fitness 2. There is level 1 and level 4 evidence that both aerobic and FES training (approximately 20–30 min/day, 3 days/week for 8 weeks or more) are effective in improving glucose homeostasis in persons with SCI. 3. There is level 4 evidence from pre-post studies that FES training performed for a minimum of 3 days per week for 2 months may be effective for improving musculoskeletal fitness, the oxidative potential of muscle, exercise tolerance, and cardiovascular fitness. 4. There is level 1 evidence for the role of exercise in the reduction of lipid lipo-protein profiles involved in formation of arteriosclerosis and the reduction of the risk for CVD in persons with SCI. 5. Exercise training appears to be an important therapeutic intervention for reducing the risk for CVD and multiple comorbidities (such as type 2 diabetes, hypertension, obesity) in individuals with SCI.
Deley et al. 2015 Switzerland Narrative Review **Level of evidence:**	**Method:** Narrative review of English publications. The aim of the review is to discuss some evidence-based physiological and methodological consideration for optimal use of FES for training in paraplegia.	1. Most studies reported significant increases in VO2, during FES interventions as compared with resting values. V02 values were also significantly higher during hybrid intervention compared to exercises only involving upper limbs (arm cranking). 2. Most studies reported significant increases

Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	Methods Databases	Conclusions
Methodological quality was not assessed **Type of study:** Types of studies included not specified. AMSTAR:4	Exclusion criteria: English language literature search **Database:** PubMed & Google Scholar	in heart rate during FES sessions with arm cranking, whereas during FES-cycling, heart rate was lower. 3. Functional electrical stimulation (FES), used to facilitate exercise in individuals with spinal cord injury, is associated with major benefits to both the muscular and cardiovascular and pulmonary systems. 4. When used regularly and with appropriate settings, FES exercises have beneficial effects on muscle characteristics, force output, exercise capacity, bone mineral density and cardiovascular parameters. 5. FES rowing might be the most appropriate technique to see training effects on the muscular, cardiovascular, and respiratory levels.
Myers et al. 2012; Dates searched not specified. Number of studies reviewed not specified. **Level of evidence:** Methodological quality was not assessed **Type of study:** Types of studies included not specified. AMSTAR: 4	**Method:** Reviewed the prevalence of CVD and associated cardiometabolic risk markers in SCI and describes the available evidence supporting the benefits of physical activity in persons with SCI. Inclusion/exclusion criteria for articles not specified. **Database:** Databases searched not specified.	1. In 7 low-level studies, lipid profiles in persons with SCI have generally been shown to respond favorably to both diet and exercise intervention. 2. In 2 studies, exercise programs of several weeks duration using arm ergometry or circuit resistance training have been shown to increase HDL in the range 10-20% and to reduce the ratio of total cholesterol to HDL. 3. 3 studies supported the use of circuit training to improve both fitness and lipid profiles in persons with paraplegia. 4. There is a paucity of evidence regarding the effects of physical activity on changes in body mass in persons with SCI. 5. 4 studies support physical activity and fitness level as a determinant of reduced insulin resistance in SCI.
Carlson et al. 2009; USA Reviewed published articles from 1990 to 2008 N= 22 **Level of Evidence:** Methodological quality not assessed **Type of study:** 15 intervention case-series 7 cross- sectional surveys AMSTAR: 4	**Methods:** Literature search for articles written in English evaluating the effect of exercise interventions on carbohydrate and lipid metabolism in adults with chronic SCI. Interventions included active exercise and electrical stimulation ; outcome measures included glucose, insulin, and cholesterol levels **Databases:** MEDLINE (1996–2008), Cochrane Library, bibliographies of identified articles, and expert recommendations	1. Evidence is insufficient to determine whether effects of exercise improves carbohydrate and lipid metabolism disorders among adults with SCI
Hamzaid & Davis 2009;	**Methods:** Literature search for	1. FES-evoked exercise studies demonstrated

Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	Methods Databases	Conclusions
Australia Reviewed published articles from 1830 to 2008 N= 33 **Level of Evidence:** No formal validity assessment was described **Type of study:** 1 RCT, 32 quasi-experimental AMSTAR=4	published articles written in any language and related to functional electrical and neuromuscular stimulation, exercise, health and fitness, and lower limbs of neuromuscular stimulation Interventions include: FES training (cycling, ergometry, rowing, leg muscle contraction, knee extension and treadmill). Outcome measures include: cardiovascular and peripheral blood flow, aerobic fitness, functional exercise capacity, bone mineral density and psychosocial outlook. **Databases:** Ovid MEDLINE (1966- July 31 2008), Ovid MEDLINE Daily Update, PREMEDLINE, Ovide OLDMEDLINE (1950-1965), SPORTDiscus (1830-July 31, 2008), Web of Science (1900- July 31, 2008), Cochrane Library and Database	positive changes within skeletal muscle, enhanced cardiovascular and peripheral blood flow, altered metabolic responses and increased aerobic fitness, and improved functional exercise capacity- strength and endurance 2. Positive bone health improvements with FES-evoked leg training only on some localized areas of bones, particularly in the hips, knee area and shank - FES-induced treadmill walking delivered more positive outcomes than other modalities 3. Bone mineral density changes and alterations of psychosocial outlook were less consistently reported or outcomes were deemed equivocal. 4. FES-evoked leg exercise promotes certain health and fitness benefits for people with SCI

Discussion

Seven systematic reviews examined the effectiveness of cardiovascular and health management in SCI patients. Carlson et al. (2009) focused on the effectiveness of exercise to improve carbohydrate and lipid metabolism disorders in adults with chronic SCI and found that evidence is insufficient to determine whether effects of exercise improves carbohydrate and lipid metabolism disorders in this population. Myers et al. (2012) reviewed the prevalence of CVD and associated cardiometabolic risk markers in SCI focusing on the available evidence supporting the benefits of routine physical activity. They found evidence that lipid profiles in persons with SCI respond favourably to both diet and exercise intervention. They also revealed that the use of arm ergometry or circuit resistance training can increase HDL in the range of 10-20% and reduce the ratio of total cholesterol to HDL. There was also evidence that physical activity and fitness levels were associated with insulin sensitivity in SCI (i.e., higher levels of activity/exercise were associated with lower risk for insulin resistance). Hicks et al. (2011) focused on fitness benefits of physical activity or exercise training intervention in persons with chronic SCI and found strong evidence that exercise could increase physical capacity and muscular strength. Evidence was insufficient however, to draw conclusions in terms of body composition and function. The authors also found that evidence was insufficient to draw any conclusion for the acute SCI population. Phillips et al. (2011) focused on the effect of various modes of exercise on arterial dynamics in patients with SCI and found strong evidence to support passive leg exercise program as a technique to improve vascular function among individuals with paraplegia. The other modes of exercise (acute arm exercise, combined arm and passive leg exercise, stretch induced contraction and arm exercise) presented either insufficient evidence or mixed evidence which makes it difficult to draw any conclusion. Warburton et al. (2007) focused on literature regarding the risk for

CVD and the effectiveness of varied exercise rehabilitation programs in attenuating the risk for CVD in SCI. They found evidence that both aerobic and FES training are effective in improving glucose homeostasis in persons with SCI. They found strong evidence that exercise is effective at reducing lipid lipoprotein profiles involved in the formation of atherosclerosis and the reduction of the risk for CVD in persons with SCI. They also found that FES training may be effective for improving musculoskeletal fitness, the oxidative potential of muscle, exercise tolerance, and cardiovascular fitness in this population. Cragg et al. (2012) focused on the management of modifiable CVD risk factors for the chronic SCI population. They found evidence that niacin was efficacious in improving lipid profiles in individuals with chronic tetraplegia and that the use of FES or treadmill walking favourably influences glycemic control.

4.0 Exercise Rehabilitation and Cardiovascular Fitness

Exercise rehabilitation has been shown to be an effective means of attenuating or reversing chronic disease in persons with SCI. Similar to the general able-bodied population (Warburton et al. 2006), habitual physical activity (beyond activities of daily living) can lead to numerous health benefits that significantly reduce the risk for multiple chronic conditions (in particular CVD) and premature mortality in persons with SCI. However, supporting evidence is relatively low in comparison to the general population and other clinical conditions (e.g. chronic heart failure (Warburton et al. 2006, Warburton et al. 2010)).

The cardiovascular research conducted within the field of SCI has examined predominantly the effects of aerobic exercise and/or functional electrical stimulation (FES) training. In the following sections we will review the literature regarding the effects of varied exercise interventions on the risk for CVD in persons with SCI. Particular attention will be given to the changes in cardiovascular fitness, glucose metabolism, and lipid lipoprotein profiles that occur after training interventions in persons with SCI. The recent systematic review of Phillips et al. (2011) is recommended for a detailed assessment of the effects of different exercise training modalities on vascular health and function. This comprehensive review of the literature reveals that a variety of exercise interventions (including passive exercise, upper body wheeling, FES, and electrically stimulated resistance exercise) can lead to physiologically and clinically relevant improvements in arterial function in persons living with SCI (Phillips et al. 2011). Owing to the relationship between vascular function and CVD, these changes can be associated with a decreased risk for CVD.

It is important to highlight, that our original search included many studies that examined the short term effects of an exercise intervention. However, for inclusion in this chapter the article must have included the examination of the changes in cardiovascular fitness/health that occurred as a result of the training intervention (and not simply the temporal changes in cardiovascular parameters with the exercise modality).

4.1 Treadmill Training

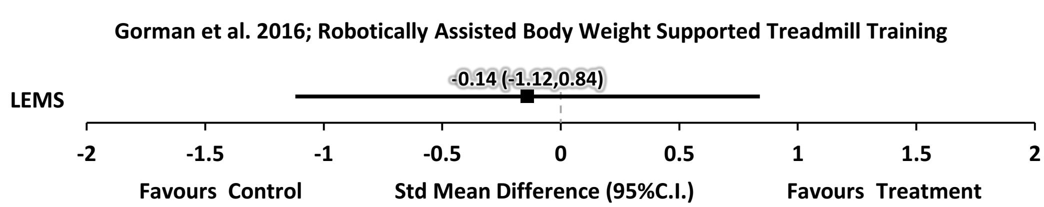
Body-weight–supported treadmill training (BWSTT) is an exercise protocol that has been used to potentially affect a number of domains, including motor recovery, bone density, cardiovascular fitness, respiratory function, as well as quality of life. Traditional BWSTT involves the upright walking on a motor-driven treadmill while a harness (suspended from an overhead pulley system) supports the participant's body weight. Therapists conducting the session determine the magnitude of off-loading of an individual's body weight (Phillips et al. 2004). The treadmill velocity, the amount of body weight supported, and time spent on the treadmill can be individualized (Phillips et al. 2004). Significant resources are often required as the majority of individuals will require one or two assistants to manually help ambulate the lower limbs.

For a more extensive consideration of BWSTT, please visit the section on Lower Limb, Balance and Walking chapter at: https://scireproject.com/evidence/rehabilitation-evidence/lower-limb/gait-retraining-strategies-to-enhance-functional-ambulation/body-weight-treadmill-training/

Table 4: Effects of Body-Weight Supported Treadmill Training on Cardiovascular Fitness and Health

Author Year; Country Score Research Design Total Sample Size	Methods	Outcomes
Alexeeva et al. 2011; USA PEDro = 7 RCT Level 1 N = 35	**Population:** 35 SCI patients (30 male, 5 female, >1 year; AIS 16–70 yrs; injury to at or rostral to the T10; able to rise to standing position with moderate assistance or less, and independently advance at least one leg. **Treatment:** Patients were randomized to 3 groups (body-weight-supported (BWS) walking on a fixed track vs. BWS walking on a treadmill vs. comprehensive physical therapy). The BWS groups used 30% BWS. Patients participated in a 13 week (1 hr/day, 3 d/wk) program. **Outcome measures:** performance values, heart rate, pre- and post-training maximal 10-m walking speed, balance, muscle strength, fitness (VO_2peak), and quality of life.	1. Participants in the BWS walking on a fixed track group achieved the highest average heart rate during training, whereas those in physical therapy had the lowest average heart rate. 2. In all three groups there was a clinically important post-training increase in average normalized VO_2peak (~12% in each group); however, these differences did not achieve statistical significance.
Gorman et al. 2016 USA RCT Level 1 PEDro = 6 N=18	**Population**: 18 individuals chronic motor incomplete spinal cord injury between C4 and L2; >1 y post injury **Treatment**: Participants were randomized to Robotic-Assisted Body-Weight Supported Treadmill Training (RABWSTT) or a home stretching program (HSP) 3 times per week for 3 months. Those in the home stretching group were crossed over to three months of RABWSTT following completion of the initial three month phase. **Outcome Measures:** Peak VO2 was measured during both robotic treadmill walking and arm cycle ergometry: twice at baseline, once at six weeks (mid-training) and twice at three months (post-training). Peak VO2 values were normalized for body mass.	1. The RABWSTT group improved peak VO2 by 12.3% during robotic treadmill walking (20.2 ± 7.4 to 22.7 ± 7.5 ml/kg/min, P = 0.018) Peak VO2 during robotic treadmill walking and arm ergometry showed statistically significant differences.

Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data



Millar et al. 2009; Canada PEDro = 6 RCT with crossover Level 1 N = 7	**Population:** 7 SCI participants (6 male, 1 female, mean age 37.1 ± 7.7 yrs), with C5-T10 level injury, AIS A-C, 5.0 ± 4.4 yrs post-injury **Treatment:** Each participant underwent both body-weight supported treadmill training (BWSTT) and head-up tilt training (HUTT) in random order, for 3 times a week for 4 weeks, separated by a 4 week detraining period. **Outcome Measures:** Heart rate variability; heart rate complexity (what does this capture?); fractal scaling distance score (the correlation of the time between heart beats).	1. No significant difference in heart rate variability after either BWSTT or HUTT training. 2. There was increased sample heart rate complexity after BWSTT, whereas HUTT had no effect. 3. 3. BWSTT, but not HUTT, reduced the fractal scaling distance score in participants.
Fenuta et al. 2014 Canada Prospective Controlled Trial Level 2 N= 14	**Population**: 7 males with incomplete spinal cord injury; mean age= 42.6 ± 4.29y; years post injury= 4.0 ± 0.62y; 7 able bodied males; mean age= 42.7 ± 5.40y; **Treatment**: Steady state locomotion using the same body weight support (BWS) percent was compared in 7 males with incomplete SCI and matched noninjured controls using the Lokomat, Manual Treadmill, and ZeroG. Participants completed walking trials in a randomized order using the Andago GmbH treadmill system or overground ZeroG. EMG electrodes were placed on tibialis anterior, rectus femoris, biceps femoris, and medial gastrocnemius muscles of both legs. **Outcome Measures:** Peak VO2 testing, Heartrate (HR), Lower limb EMG,	1. A strong positive correlation () was found between the flexion: extension strength ratio at the hip in participants with SCI and the amount of BWS required to complete the overground walking session; the higher the flexion: extension ratio, the more support that was required. 2. Lokomat sessions resulted in significantly lower MET values when compared to the Manual Treadmill or ZeroG sessions. 3. For individuals with SCI, average muscle activation tended to be higher for both treadmill conditions compared to the ZeroG session, which could be attributed to increases in TA and BF activity.
de Carvalho et al. 2006; Brazil Prospective Controlled Trial Level 2 N = 21	**Population:** 21 male participants (C4 to C8), all complete with tetraplegia, mean age 32 ± 8 yrs. 11 assigned to the gait group and 10 controls. **Treatment:** BWST training (30%–50%) with neuromuscular electrical stimulation 20 min/day, 2 days/week for 6 months. Control group performed conventional physiotherapy. **Outcome Measures:** blood pressure, oxygen uptake, carbon dioxide production, minute ventilation (volume of gas entering lungs), and heart rate.	1. Gait training (six months) resulted in significant increases in oxygen consumption (36%), minute ventilation (31%), and systolic blood pressure (5%) during the gait phase. In the control group, there were significant increases in resting oxygen consumption and carbon dioxide production (31 and 16%, respectively). 2. Gait training resulted in an increased aerobic capacity due to yielding higher metabolic and cardiovascular stress.
Jeffries et al. 2015 USA Cohort Study Level 2 N=8	**Population:** 8 non-ambulatory individuals with chronic motor complete SCI (7 males, 1 female, T5-T12) and 8 healthy able-bodied (AB) controls. **Treatment:** SCI group- Standing and stepping exercises over a treadmill in a body weight support (BWS) system with manual assistance of lower body kinematics. Weight support was provided by an overhead lift at high (>50% BWS) or low levels (20-35% BWS). AB participants did normal stepping over a treadmill and standing. **Outcome measures:** Oxygen Consumption (VO2) and heart rate during stepping and standing with BWS. VO2 and heart rate responses were assessed in relation to level of BWS.	1. Significant main effect of task on VO2 for SCI and AB groups. There was a significant increase in VO2 with stepping compared with sitting and standing. There was also a significant increase in VO2 when weight support was decreased during stepping. 2. Significant main effect of task on heart rate levels for both SCI and AB groups. There was a significant increase in heart rate with stepping compared with seated and standing. 3. The SCI group also had significant increases in heart rate from seated to standing 4. No difference in heart rate when weight support was decreased during stepping for both groups.

Stevens and Morgan 2015 USA Pre-post Level 4 N=11	**Population:** 11 adults with incomplete SCI (7 males, 4 females, mean age 48). 6 adults with injuries at or above T5 and 5 adults with injury below T5. **Treatment:** 8 weeks of Underwater Treadmill Training (UTT) (3 sessions per week, 3 walking trials per session) incorporating individually determined walking speeds, personalized levels of body weight unloading, and gradual, alternating increases in speed and duration. In weeks 2,4,6, and 8, walking speed was increased by 10%, 20%, 30% and 40% over baseline. **Outcome Measures:** Heart rate	1. None of the interaction tests involving injury level were statistically significant. When averaged over injury level, the interaction between training period and day was significant. 2. Pairwise comparisons revealed that from day 1 to day 6, heart rate fell by 7%, 14% and 17% during training periods 1, 2, 3. All participants exhibited significant decreases in daily submaximal exercise (walking) heart rate for each 2-week period.
Turiel et al. 2011; Italy Pre-post Level 4 N = 14	**Population:** 14 participants (10 males, 4 females; mean age 50.6 ± 17.1 yrs; 2-10 yrs post-injury; 9 paraplegia) with lost sensorimotor function caused by incomplete SCI. **Treatment:** BWSTT assisted with robotic driven gait orthosis for 60 min sessions, 5 d/wk, 6 wk, with 30-50% of body weight supported (reduced as tolerated). **Outcome Measures:** Left ventricular function, coronary blood flow reserve (via dipyrsidamole stress echo), plasma asymmetric dimethylarginine (ADMA) (marker of vascular abnormalities observed in cardiovascular disease and ageing), and plasma inflammatory markers.	1. Significant improvement in the left ventricular diastolic function (i.e., a reduction in isovolumic relaxation time and deceleration time was observed following the training. 2. Significant Increase in coronary reserve flow and reduced plasma ADMA levels was observed in the follow up. 3. Significant reduction in the inflammatory status (C-reactive protein and erythrocyte sedimentation rate).
Jack et al. 2009; UK Pre-post Level 4 N = 2	**Population:** Participant A: female, T9 level injury, age 41 yrs, 2 yrs post-injury; Participant B; male, T6 level injury, age 40, 14.5 yrs post-injury **Treatment:** Body-weight supported treadmill training (BWSTT), three 30-min sessions per week for 16 weeks (participant A) or 20 weeks (participant B) **Outcome Measures:** Measures of cardiopulmonary fitness: oxygen uptake (VO_2); peak heart rate; dynamic O_2 cost	1. Both participants' VO_2 increased after exercise, 8.2 to 10.2 $mL·kg^{-1}·min^{-1}$ for participant A; for participant B, VO_2 increased from 13.8 to 18.2 $mL·kg^{-1}·min^{-1}$ at week 17, after which the VO_2 dropped back to 13.9 $mL·kg^{-1}·min^{-1}$. 2. Peak heart rate increased for both participants after exercise (89 to 119 bmp for participant A, 134 to 157 bpm for participant B). 3. The dynamic O_2 cost decreased for both participants (115 to 29.03 $mL·min^{-1}·W^{-1}$ for participant A, 66.57 to 4.52 $mL·min^{-1}·W^{-1}$ for participant B).
Soyupek et. al. 2009; Turkey Pre-Post Level 4 N = 8	**Population:** 8 incomplete SCI participants, 6 male and 2 female, injury level C6-L1, mean age 40. 8 ±13.9 yrs (range 26-66 yrs) **Treatment:** Body weight supported treadmill training (BWSTT), for 5 times per week for 6 weeks; length of training sessions ranged from 10 to 30 min **Outcome Measures:** Heart rate and blood pressure; Forced expiratory volume in 1 second (FEV1), forced vital capacity (maximum amount of air that can be expelled after maximum inhalation), inspiratory capacity, maximum inspiratory and expiratory pressure	1. The heart rate was significantly lower post-training compared to baseline 2. There were significant improvements of the forced vital capacity and inspiratory capacity in participants post-training compared to baseline 3. There were no significant difference in other parameters between pre- and post-training
de Carvalho and Cliquet 2005; Brazil Pre-post	**Population:** 12 male participants (C4 tp C7) all complete with tetraplegia; Mean age = 33.8 y; Median time post-injury = 77.58 months **Treatment:** Body weight supported treadmill	1. After training, mean systolic blood pressure increased (94 ± 5 mmHg to 100 ± 9 mmHg) at rest and during gait exercise (105 ± 5 to 110 mmHg).

Level 4 N = 12	training (30–50%) with neuromuscular electrical stimulation 20 min/day, 2 days/week for 3 months. **Outcome Measures:** BP and HR.	2. There were no significant changes in post-exercise blood pressure after training.
Ditor et al. 2005a; Canada Pre-post Level 4 N = 8	**Population :** 8 participants (6 males, 2 females), AIS B-C, C4-C5, incomplete, mean age 27.6 yrs, mean 9.6 yrs post-injury. **Treatment:** Progressive, body weight-supported treadmill training, 3 day/week for 6 months. **Outcome Measures:** HR and BP variability, LF/HF ratio (low to high heart beat frequency and is indicative of balanced sympathetic/parasympathetic tone and reduced risk for cardiovascular-related mortality).	1. Significant decrease in resting HR (10.0%) after training. 2. No changes in resting systolic, diastolic, or mean arterial BP after training. 3. Significant reduction in the resting LF/HF ratio after training. 4. There were no significant effects of training on HR and/or blood pressure variability during an orthostatic challenge (60° head up tilt).
Ditor et al. 2005b; Canada Pre-post Level 4 N = 6	**Population:** 6 participants (4 male, 2 female), AIS A and B, C4-T12, mean age 37.7 yrs, mean 6.7 yrs post-injury, motor complete. **Treatment:** Body weight supported treadmill training, 15 min/day (3 bouts of 5 min), 3 days/week for 4 months. **Outcome Measures:** BP, HR, HR variability, BP variability, arterial diameters and mean blood velocities, and arterial blood flow.	1. No changes in femoral or carotid artery cross sectional area, blood flow, or resistance post-training 2. An improvement in femoral artery compliance. 3. No change in resting BP, mean arterial blood pressure, resting HR or heart rate and blood pressure variability after training. 4. 3/6 patients had changes in heart rate and blood pressure variability reflective of increased vagal predominance.

Note: AIS = ASIA Impairment Scale; BP = blood pressure; d = day; hr = hour; HR = heart rate; SCI = spinal cord injury; wk = week; yrs = year. BWSTT = body-weight supported treadmill training.

Discussion

There are two randomized controlled trials (Level 1a) (Millar et al. 2009, Alexeeva et al. 2011), one prospective controlled investigation (Level 2) (de Carvalho et al. 2006), one cohort study (Level 2) (Jeffries et al. 2015) and several pre-post studies (Level 4) have been conducted to examine changes in indicators of cardiovascular fitness/health in SCI after training (de Carvalho and Cliquet 2005a, Ditor et al. 2005a, Ditor et al. 2005b, Jack et al. 2009, Soyupek et al. 2009, Turiel et al. 2011, Stevens and Morgan, 2015).

Four recent investigations examined the effects of BWSTT (Jeffries et al. 2015, Alexeeva et al. 2011, Turiel et al. 2011) and underwater treadmill training (Stevens and Morgan, 2015) on indicators of cardiovascular fitness and/or health. Alexeeva et al. (2011) compared participants randomly assigned to two different BWS ambulation modalities in comparison to traditional physical therapy, and revealed that there were clinically important improvements in normalized VO_2 peak in each group. Turiel et al. (2011) demonstrated that 6 weeks of BWSTT resulted in improvements in resting left ventricular function, coronary blood flow reserve and inflammatory status.

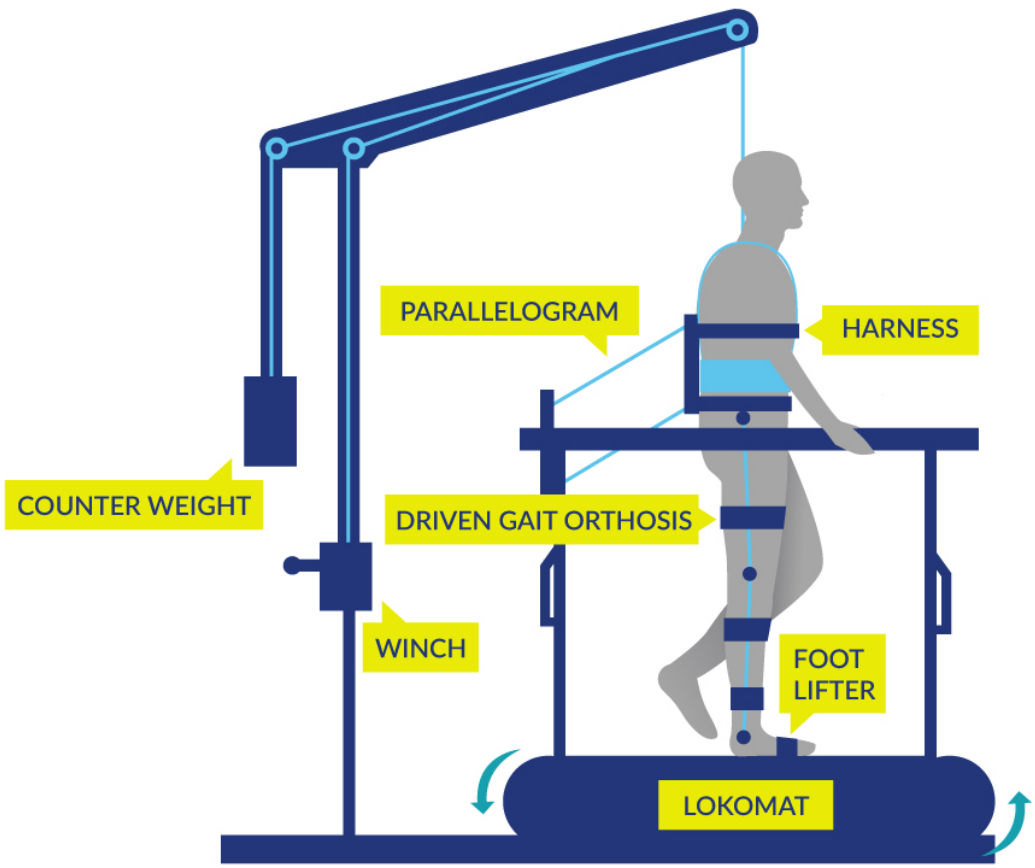


Figure 3 – Lokomat style Body-Weight Supported Treadmill (BWST) – with motor

In 2009, Jack et al. examined two participants (with thoracic injuries) after BWSTT and revealed significant improvements in peak heart rate (HR) and oxygen consumption (VO_2), and a decrease in the dynamic oxygen cost (the rate of oxygen consumption by respiratory muscles as they ventilate the lungs). Soyupek et al. (2009), evaluated eight participants and found significantly lower heart rate post-training and improved forced vital capacity (maximum amount of air that can be expelled after maximal inhalation) and inspiratory capacity.

Stevens and Morgan (2015) examined the effects of 8 weeks of progressive and individualized underwater treadmill training (3 days per week, 3 walking trials per session). They revealed evidence of improved cardiovascular control and function (i.e., reduced submaximal HR) across the training intervention.

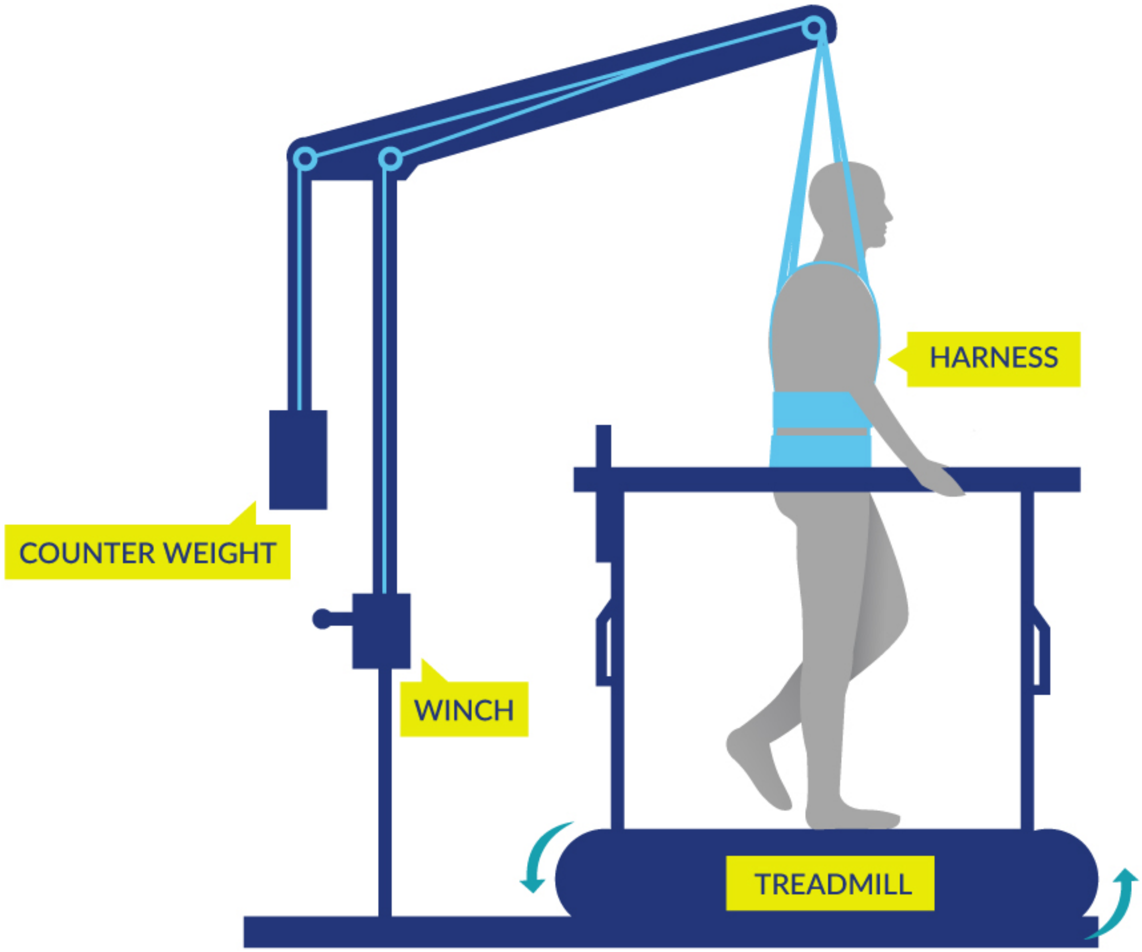


Figure 4 – BWST – manual style (without motor)

Two earlier studies (conducted by the same Canadian research group (Ditor et al. 2005a, Ditor et al. 2005b)) reported that BWSTT did not have substantial group effects on HR and blood pressure in motor-complete participants but did reveal a significant reduction in resting HR in the study that involved individuals with incomplete tetraplegia. There was also evidence that improvements in HR and blood pressure variability may occur after BWSTT in incomplete SCI and a subset of participants with complete SCI. The authors attributed the change in blood pressure variability to reductions in sympathetic tone to the vasculature. These findings have significant physiological relevance since it indicates that both parasympathetic outflow to the heart (as evaluated by heart rate variability) and sympathetic flow to the vasculature (as evaluated by blood pressure variability) can adapt in response to exercise training. This research group also revealed the potential for improvements in vascular health (e.g., arterial compliance) after BWSTT in individuals with motor-complete SCI. There was no indication of the effects of BWSTT on peak oxygen consumption (VO_2peak).

The mechanisms responsible for the improvement in markers of cardiovascular health and regulation in individuals with incomplete SCI remain to be determined. Jack et al. 2009 postulated that an improvement in walking ability likely explained the increase in VO_2peak with training (in individuals with incomplete SCI). They also highlighted how marked atrophy, fast fatiguing lower limbs, and limited neural control may limit the capacity of patients with SCI to make use of their cardiovascular reserve.

Ditor et al. (2005a,b) attributed the training-induced changes in autonomic function to the cardiovascular challenge provided by the upright nature of BSWTT (which potentially could be a sufficient stimulus in individuals with postural hypotension) and the spasticity created during the treadmill training. However, it should also be noted that both weight bearing and the passive movement of the limbs may contribute to the observed changes in these studies.

A Canadian study employing a randomized cross-over design (Millar et al. 2009) revealed that short-term (4 weeks) BWSTT (but not head-up tilt training) led to a significant increase in HR complexity and reduced fractal scaling distance score in persons with SCI. These changes are thought to reflect an improvement in cardiac autonomic balance after short-term BWSTT.

Two investigations (a pre-post study (level 4) and a prospective controlled study (level 2) from the same research group used partial BWSTT (30%–50%) via neuromuscular electrical stimulation assisted by physiotherapists (de Carvalho and Cliquet 2005a, de Carvalho et al. 2006). The first investigation revealed that three months of this form of gait training can result in a significant increase in systolic blood pressure at rest and during gait exercise in males with tetraplegia (de Carvalho and Cliquet 2005b). In the latter study (de Carvalho et al. 2006) the authors revealed that long-term neuromuscular electrical stimulation gait training (six months) resulted in significant increases in VO_2 (36%), minute ventilation (30.5%), and systolic blood pressure (4.8%) during the gait phase. The authors concluded that treadmill gait training combined with neuromuscular electrical stimulation leads to increased metabolic and cardiorespiratory responses in persons with complete tetraplegia.

In a comparison of trials using BWSTT, an interesting discrepancy arises. For instance, in the work of Ditor et al., there was no change in resting blood pressure after BWSTT in individuals with complete or incomplete SCI (Ditor et al. 2005a, Ditor et al. 2005b) whereas the work by de Carvalho and coworkers revealed an increase in resting blood pressure following partial BWSTT (with neuromuscular electrical stimulation) (de Carvalho & Cliquet 2005b, de Carvalho et al. 2006). It is not clear why these discrepancies exist, and, as such, further research is clearly warranted.

It is important to note that while BWSTT may have important cardiovascular benefits, the feasibility of using this treatment over the long term in the home setting is questionable due to the costs of the equipment and assistants to set up the individual and facilitate the leg motions.

Conclusion

There is level 1a evidence (Millar et al. 2009) that BWSTT improves cardiac autonomic balance in persons with tetraplegia and paraplegia (with similar results for varying degrees of lesion level and severity).

There is multiple level 4 evidence (Jack et al. 2009; Soyupek et al. 2009) that BWSTT increases peak oxygen uptake and heart rate, and decreases the dynamic oxygen cost for persons with SCI.

There is Level 2 evidence (Jeffries et al. 2015) that indicates that standing and stepping exercises with BWSTT can increase VO_2 and heart rate levels.

There is Level 4 evidence (Ditor et al. 2005b) that indicates that BWSTT can improve arterial compliance in individuals with motor-complete SCI.

There is Level 4 evidence (Stevens and Morgan, 2015) that 8 weeks of underwater treadmill training decreases walking exercise heart rate.

There is level 2 evidence (de Carvalho et al. 2006) that neuromuscular electrical stimulation gait training can increase metabolic and cardiorespiratory responses in persons with complete tetraplegia.

There is growing evidence that BWSTT (and underwater treadmill training) can improve indicators of cardiovascular fitness and health in individuals with complete and incomplete tetraplegia and paraplegia.

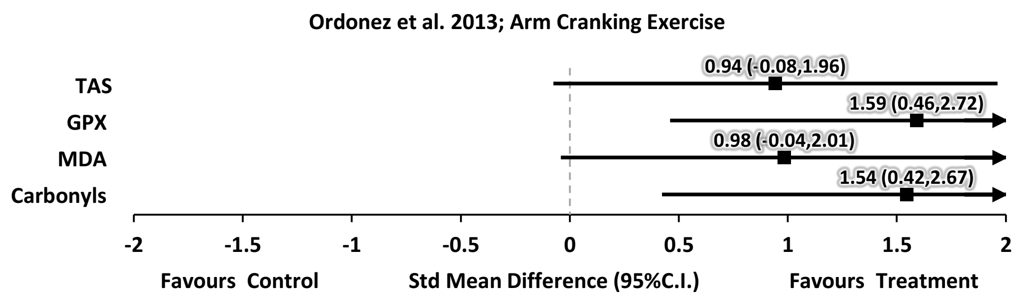
4.2 Upper Extremity Exercise

Given the motor loss of the lower limbs following injury, upper extremity exercise is a logical choice for improving cardiovascular fitness and health. However, improving cardiovascular function can be challenging using the smaller mass of the arms especially when muscle fatigue can often occur before exercise training targets are met. From our search, we found five RCTs, two high quality (de Groot et al. 2003, Ordonez et al. 2013), and three lower quality trials (Davis et al. 1987, Davis et al. 1991, Hicks et al. 2003), two prospective controlled (Hooker and Wells 1989, Hjeltnes and Wallberg-Henriksson 1998), a case report (Tordi et al. 2009), a case-controlled investigation (Jae et al. 2008), one cohort study (Valent et al 2008), and 20 pre-post studies.

Given the large number of studies that have looked at upper extremity exercise, we have tabled only those studies that included a control group consisting of participants with SCI (Table 5).

Table 5: Effects of Upper Extremity Training on Cardiovascular Fitness and Health

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Arm Ergometry		
Ordonez et al. 2013; Italy PEDro=8 RCT Level 1 N=17	**Population:** N=17 male participants with complete SCI at or below the fifth thoracic level (T5); Participants were randomly allocated to the intervention (n=9) or control (n=8) group. *Intervention group:* mean (SD) age: 29.6(3.6) yr; mean (SD) DOI = 54.8(3.4) months. *Control group*: mean (SD) age: 30.2(3.8) yr; mean (SD) DOI = 55.7(3.6) months. **Treatment:** Intervention group performed a 12-week arm-cranking exercise program, 3 sessions/wk, consisting of warming-up (10-15min) followed by a main part in arm-crank (20-30min [increasing 2 min and 30s every 3 wk]) at a moderate work intensity of 50% to 65% of the HR reserve and by a cooling-down period. **Outcome Measures:** Plasmid levels of total antioxidant status, erythrocyte glutathione peroxidase activity malondialdehyde and carbonyl group levels, physical fitness and body composition	1. When compared with baseline results, VO_2peak was significantly increased in the intervention group. 2. Both total antioxidant status and erythrocyte glutathione peroxidase activity were significantly increased at the end of the training program. 3. Plasmatic levels of malondialdehyde and carbonyl groups were significantly reduced following training.

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data 	
de Groot et al. 2003; The Netherlands PEDro = 7 RCT Level 1 N = 6	**Population:** 4 male, 2 female, C5-L1, AIS A (*n* = 1), B (*n* = 1), C (*n* = 4), age 36 yrs. **Treatment:** Interval training (3-min exercise: 2-min rest), 1hr/d, 3d/wk, 8 wks. Randomized to low intensity (50%–60% HRR) or high intensity (70%–80% HRR). **Outcome Measures:** VO_2peak, maximal power output.	1. Greater changes in VO_2peak in the high-intensity (59%) versus low- intensity group (17%).
Davis et al. 1991; Canada PEDro = 4 RCT Level 2 N = 24	**Population:** 8 spina bifida, 16 traumatic, age 17–42 yrs. **Treatment:** Random assignment to (a) control or 1 of 3 arm ergometry programs 2 d/wk, 24 wks: (1) high-intensity long duration (40 min at 70% VO_2peak), (2) high-intensity short duration (20 min at 70% VO_2peak), and (3) low-intensity short duration (20 min at 50% VO_2peak) training. **Outcome Measures:** Cardiac output, HR, VO_2peak, power output, stroke volume.	1. Training increased VO_2peak in the 3 arm ergometry groups (~21%). 2. There were increases in submaximal stroke volume and cardiac output in the high-intensity long and the low- intensity long training groups. 3. The low-intensity short duration training and control groups exhibited small non-significant decreases in stroke volume.
Davis et al. 1987; Canada PEDro = 4 RCT Level 2 N = 14	**Population:** Sedentary SCI (*n* = 9 exercise group, *n* = 5 control group), age 20–39 yrs. **Treatment:** Arm ergometry, 50%–70% VO_2peak, 20–40 min/d, 3d/wk, 16 wks. **Outcome Measures:** BP, HR, power output, VO_2peak, resting left ventricular dimensions, cardiac function.	1. Significant improvement in VO_2peak (31%) and HR (-9.5%) with training. 2. During isometric handgrip exercise, decreased rate-pressure product (HR*BP) (20%) and increased stroke volume (12%–16%).
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data	

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<tr><th>Author, Year;
Country
Score
Research Design
Sample Size</th><th>Methods</th><th>Outcomes</th></tr>
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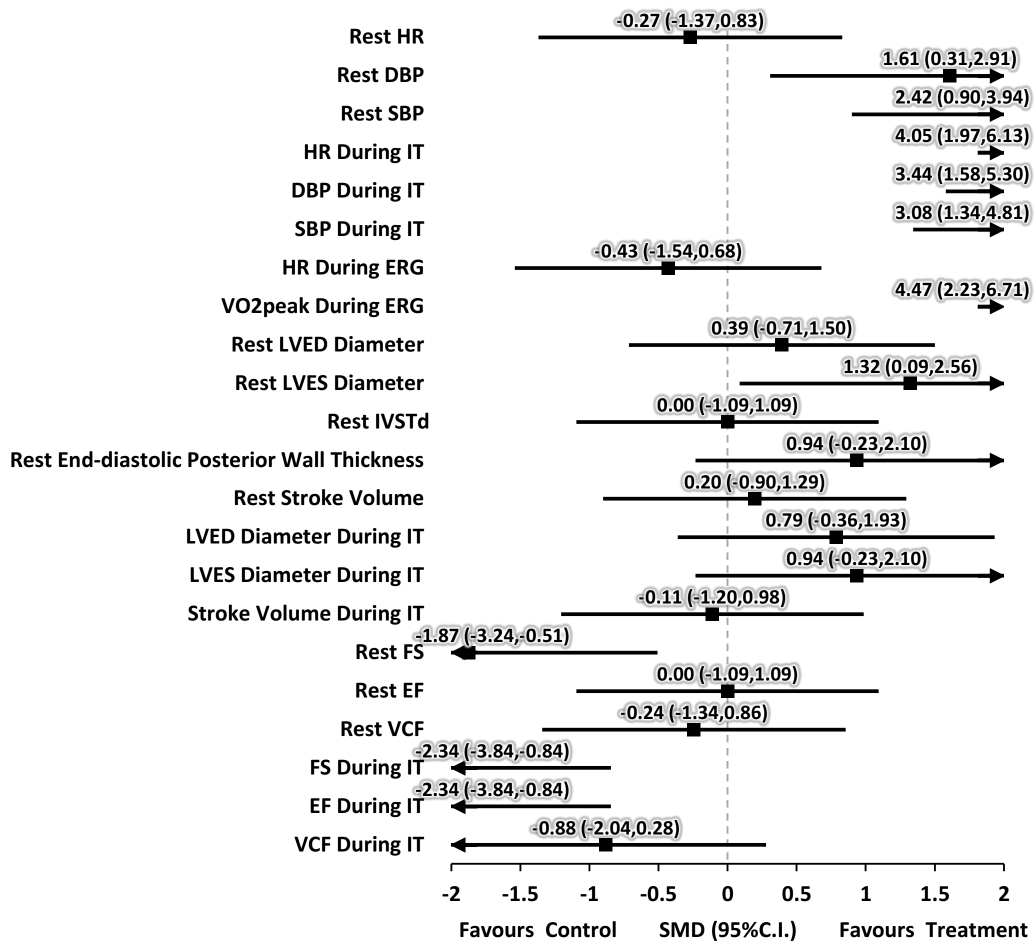
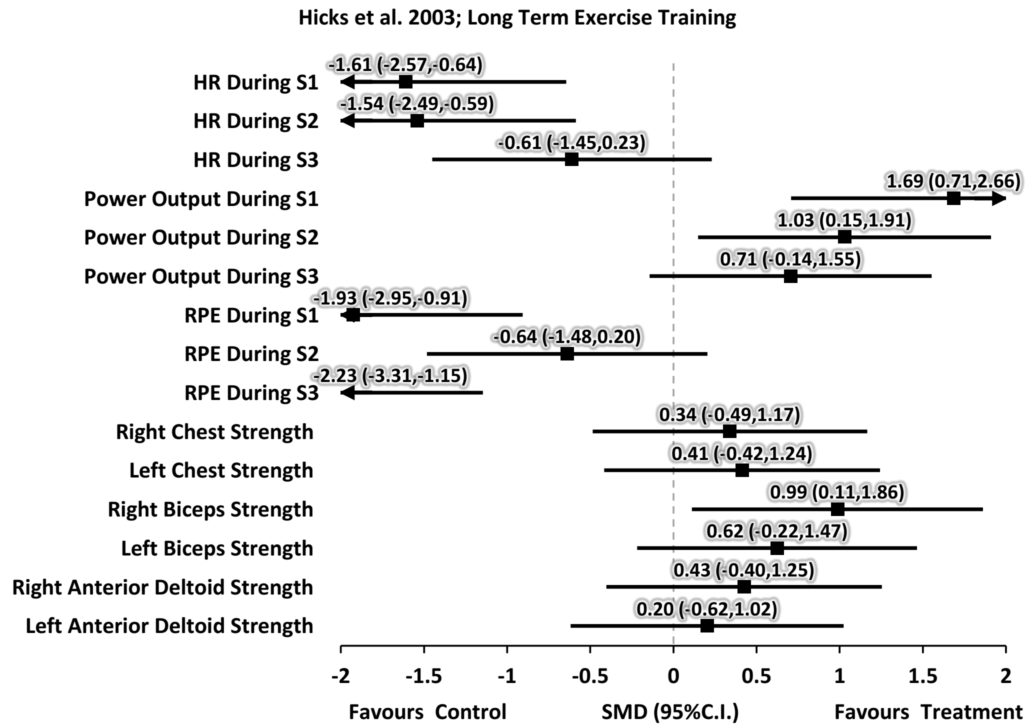
Davis et al. 1987; Arm Cranking



LVES = Left Ventricular End-systolic
LVED = Left Ventricular End-diastolic
IVSTd = End-diastolic Intra-ventricular Septal Thickness

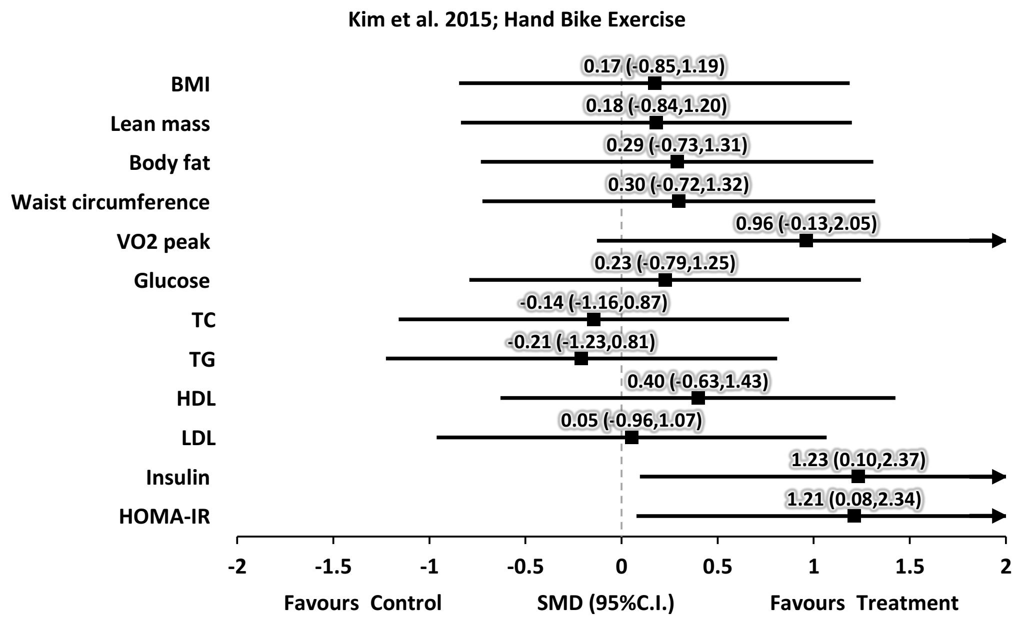
</td></tr>
<tr><td>Hjeltnes and Wallberg-Henriksson, 1998;
Norway
Prospective controlled trial
Level 2
N = 27</td><td>Population: Exercise group: 10 tetraplegia, C6-8, 7 AIS A & 3 AIS B; Control: 10 paraplegia, T7-11, all AIS A.
Treatment: Exercise group: standard rehabilitation + arm ergometry, 30min/d, 3d/wk, 12–16 wks; Control: standard rehabilitation.
Outcome Measures: power output, cardiac function, HR, VO_2, systolic blood pressure, lactate levels, muscular strength, ability to perform activities of daily living.</td><td>1. Persons with tetraplegia increased peak workload (45%) with no change in VO_2peak.
2. Peak workload (45.5%) and VO_2peak (27.7) increased significantly in persons with paraplegia.
3. No change in peak HR, systolic BP, submaximal exercise stroke volume, or cardiac output in either SCI group.</td></tr>
</table>

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Milia et al. 2014 Italy Cohort study Level 2 N=9	**Population:** 9 SCI individuals (2 females, 7 males, mean age of 41) with clinically complete spinal lesions (T4-L1) **Treatment:** One year of exercise training for 3 to 5 hours per week of arm cranking against a workload corresponding to 60% of maximal workload (Wmax). **Outcome measures:** Hemodynamic variables including maximum values of work rate (Wmax), heart rate (HR max), oxygen update (Vo2 max), carbon dioxide production (VCO2 max), respiratory exchange ratio (RER max), pulmonary ventilation (VE max), ventricular filling rate (VFR), end diastolic volume (EDV), mean blood pressure (MBP)	1. After one-year of training, patients reached higher levels in Wmax and VO2 max expressed both in absolute and relative terms. 2. The HR, MBP and EDV responses were significantly increased after one-year training. 3. There were no differences in stroke volume, absolute cardiac output value or VFR absolute values due to training.
Jae et al. 2008; South Korea Case Control Level 3 N = 52 (28 SCI, 24 AB)	**Population**: 28 physically active (trained) competitive wheelchair athletes (below T6). The able-bodied controls (n = 24) were recreationally active age-matched controls. **Outcome Measures**: Measures of arterial structure and function: Common carotid artery intima–media thickness, arterial compliance and b stiffness, and aortic augmentation index (applanation tonometry of radial artery- to capture arterial efficiency)	1. No difference in any of the arterial function indices between groups.
West et al. 2014 Canada Cross-sectional Level 5 N=23	**Population:** 23 elite male paracyclists with SCI (11 with cervical SCI, 12 with thoracic, C3-T8, mean age of 41) at the 2013 Paracycling World Championship **Treatment:** None **Outcome measures**: Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP)	1. No difference in supine SPB and DBP between the thoracic SCI and cervical SCI group. 2. Seated SBP was lower in cervical SCI than the thoracic SCI group. 3. No difference in maximum heart rate for cervical compared to thoracic SCI groups. The average HR was lower in thoracic SCI compared cervical SCI group. 4. Maximum and average HR also tended to be higher in cervical autonomic incomplete compared to autonomic complete. 5. No difference in HR between thoracic autonomic complete vs. incomplete SCI.
Mixed arm and other exercise		
Hicks et al. 2003; Canada PEDro = 5 RCT Level 2 N = 23	**Population:** 18 tetraplegia and 16 paraplegia, AIS A-D, C4-L1, ages 19–65 yrs. **Treatment:** Exercise: 90–120 min/d, 2d/wk, 9 months of arm ergometry (15–30 min, ~70%VO_2max) and circuit resistance exercise; Control group: bimonthly education session. **Outcome Measures:** muscular strength, power output, HR, quality of life ratings.	1. Power output increased by 118% and 45% after training in the tetraplegia and paraplegia groups, respectively. 2. There were progressive increases in strength over the 9 months of training (range 19%–34%).

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data  **ERG = Discontinuous 3-stage Arm Ergometry** **S1 = ERG Stage 1; S2 = ERG Stage 2; S3 = ERG Stage 3**	
	Wheelchair ergometry	
Hooker and Wells 1989; USA Prospective controlled trial Level 2 N = 8	**Population:** Low-intensity group *n* = 6, C5-T7; moderate-intensity group *n* = 5, C5-T9. **Treatment:** Wheelchair ergometry 20 min/d, 3 d/wk, 8 wks: low-intensity (50%–60% max HRR) and moderate-intensity (70%–80% max HRR). **Outcome Measures:** HR, power output, blood lactate, VO_2max, Rating of Perceived Exertion (RPE), lipid profiles.	1. The moderate-intensity group had significantly lower post-training submaximal HR, lactate, and RPE but no changes in oxygen consumption. 2. 70% maximal HRR appears to be the beneficial training threshold.
	Hand-crank Cycling	
Kim et al. 2015 Korea PEDro=5 RCT Level 2 N = 15	**Population:** 15 participants (9 males, 6 females) with SCI (ASIA-A &B, C5-T11). Mean age was 33 and all participants had SCI for more than 6 months. 8 participants allocated to the hand-bike exercise group, 7 participants to the control group. **Treatment:** Participants exercised with the indoor-hand bike for 60min/day, 3 days/week, for 6 weeks under supervision of an exercise trainer. Participants maintained a heart rate of 70% of their maximum. Exercise intensity was gradually increased on a weekly basis using the Borg rating	1. Post-intervention, the exercise group showed significant decrease in BMI, waist circumference, fasting insulin and HOMA-IR levels compared with the control group. 2. The exercise group exhibited significantly lower insulin and HOMA-0R levels, and increase in high density lipoprotein cholesterol after the exercise training period compared with baseline levels. 3. The exercise group also showed

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	of perceived exertion (RPE level 5 to 7). The control group continued with usual activities. **Outcome Measures:** Body mass index (BMI), waist circumference, percent body fat, insulin level, homeostasis model assessment of insulin resistance (HOMA-IR) level, upper body muscle strength (using a dynamometer), V02 peak, lipid metabolite indices (including cholesterol, triglycerides, high & low density lipoprotein cholesterol levels.	significant increases in V02 peak and upper body strength compared with the control group following intervention. 4. No change in glucose, total cholesterol, triglycerides, or low density lipoprotein were observed in the exercise group.

Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data



Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Valent et al. 2008 The Netherlands Cohort Level 2 N = 162	**Population:** Acute SCI participants, level of injury C5 or lower, divided into participants with paraplegia and tetraplegia , and further divided hand–cycling (HC) and non-hand cycling (non-HC) groups according to their rehabilitation protocols; data for 137 participants were available for the clinical rehabilitation period, and 131 for the post-rehabilitation period, 106 were available for both periods, and 162 different participants were tested in total **Treatment:** Hand cycling **Outcome Measures:** Power output; oxygen uptake (VO_2peak); elbow extension strength; measured upon start of active rehabilitation, on discharge, and 1 year after discharge	1. During clinical rehabilitation, a significantly larger increment in peak power output and VO_2peak was found in participants with paraplegia. 2. On average, peak power output increased 6.2W more in HC compared to non-HC participants with paraplegia. 3. Compared with baseline, VO_2peak increased by 29% in HC paraplegics, compared to 8% in the non-HC group. 4. Elbow extension strength increased significantly in the HC compared to the non-HC participants with paraplegia. 5. In contrast to the participants with paraplegia, there was no significant difference between HC and non-HC during rehabilitation for participants with tetraplegia. 6. In the post-rehabilitation period, there was

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
		no significant difference between HC and non-HC groups.
Nooijen et al. 2015 Netherlands Pre-Post Level 4 N=30	**Population:** 30 SCI individuals, 20 paraplegia, 10 tetraplegia, 12 incomplete lesion, 18 complete lesion **Treatment:** Structured hand cycle interval training program during the last 8 weeks of inpatient rehab. Training was more than 2 times per week at intended intensity of Borg score of 4 to 7 on a 10-point scale. **Outcome Measures:** Peak power output and VO_2peak	1.Peak power output and VO2 peak improved significantly after the training period.
Hubli et al. 2014 Canada Cross-sectional Level 5 N=20	**Population:** 20 individuals with motor-complete chronic SCI (C2-T5, 2-29 years post-injury, AIS-A or B). 10 of these individuals were elite hand-cyclists and 10 were sex matched to sedentary individuals with SCI. **Treatment:** None **Outcome measures:** Aortic Pulse Wave Velocity (PWV), discrete brachial blood pressure, heart rate	1. No differences in systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate when resting supine between athletes and non-athletes. 2. Aortic PWV was significantly lower in athletes compared with non-athletes.

Note: AIS = ASIA Impairment Scale; BP = blood pressure; d = day; hr = hour; HR = heart rate; HRR = heart rate reserve; min = minute; RCT = randomized controlled trial; RPE = rating of perceived exertion; SCI = spinal cord injury; wk = week; yrs = year.

Discussion

The reported improvements in aerobic capacity after aerobic arm training in SCI are approximately 20%–30%; however, it is not uncommon for improvements in excess of 50% (DiCarlo 1988). The majority of aerobic training investigations have evaluated the effectiveness of moderate (40%–59% heart rate reserve (HRR) or 55%–69% of maximum HR) to vigorous (60%–84% HRR or 70%–89% of maximum HR) intensity exercise. These studies have used arm ergometry, wheelchair ergometry, and swimming-based interventions. Based on the current level of literature, it appears that moderate intensity exercise performed 20–60 minutes per day for at least three days/week for a minimum of six weeks is effective for improving cardiovascular fitness and exercise tolerance in persons with SCI (Level 1b evidence based on two high-quality RCT's (Ordonez et al. 2013; de Groot et al. 2003) and several lower quality RCTs). Therefore, the generic recommendations provided by many international agencies (i.e., 150 min of moderate-to-vigorous physical activity (Tremblay et al. 2011) can improve the cardiovascular fitness of persons with SCI. However, these recommendations are not optimal as significant changes in aerobic fitness may occur at volumes of exercise well below international recommendations designed for apparently healthy individuals (Ginis et al. 2011). Moreover, there is compelling evidence that the promotion of generic physical activity guidelines may increase the risk of musculoskeletal injury in persons living with SCI. It is also important to note that training intensities may need to be established using a rating of perceived exertion (e.g., RPE) (rather than objective measures of heart rate) in individuals with C1-T6 SCI, which is associated with autonomic denervation of the heart.

RPE 10 POINT SCALE (RATE OF PERCEIVED EXERTION)	
.0	NOTHING AT ALL
.05	VERY, VERY LIGHT
1	VERY LIGHT
2	LIGHT
3	MODERATE
4	SOMEWHAT HARD
5	HARD
6	
7	VERY HARD
8	
9	
10	VERY, VERY HARD

RPE 15 POINT SCALE (RATE OF PERCEIVED EXERTION)	
6	NO EXERTION AT ALL
7	
7.5	EXTREMELY LIGHT (7.5)
8	
9	VERY LIGHT
10	
11	LIGHT
12	
13	SOMEWHAT HARD
14	
15	HARD (HEAVY)
16	
17	VERY HARD
18	
19	EXTREMELY HARD
20	MAXIMAL EXERTION

Figure 5 – Borg Perceived Exertion Scale (15 point) and Modified Perceived Exertion Scale (10 point). Reprinted with permission from CDC and @Gunnar Borg.

An exercise intensity threshold of 70% maximal HR reserve has been advocated for the attainment of training benefits when exercising for the standard 20 min duration (Hooker and Wells 1989, Tordi et al. 2001, Bizzarini et al. 2005). It is also apparent that improvements in exercise capacity and functional status may occur after training without significant changes in VO_2peak, particularly in persons with tetraplegia (Hjeltnes and Wallberg-Henriksson 1998).

Questions remain regarding the primary mechanisms for improvements in aerobic fitness after training. It is unclear whether central (heart and lung) or peripheral (skeletal muscle) adaptations are of key importance. Enhancements have been observed in peripheral muscle function. For instance, investigators have shown intrinsic cellular adaptations in the paralyzed muscle that facilitate oxidative metabolism following BWSTT (Stewart et al. 2004). Only limited investigations, however, have shown an improvement in cardiac function after upper extremity aerobic exercise training (Davis et al. 1987). It could therefore be argued that peripheral adaptations are of primary importance to the improvement in aerobic capacity after this type of aerobic exercise aerobic exercise. However, this statement is somewhat misleading as the majority of studies have not directly evaluated cardiac output during maximal/peak exercise. This is owing to the fact that the assessment of maximal cardiac output during exercise is one of the most difficult procedures in clinical exercise physiology (Warburton et al. 1999a, 1999b). When exercise measures of cardiac function have been taken, improvements in central function have been observed (Davis et al. 1987). Further research examining the primary mechanism(s) of importance for the improved cardiovascular fitness and exercise capacity seen in persons with SCI after aerobic exercise training is warranted. It is also important to highlight that it is often difficult for patients to attain VO_2max during exercise. Moreover, the submaximal prediction of VO_2peak (based on the heart rate response to exercise) is limited owing to the potential impairment in the sympathetic drive to the heart in many persons with SCI. Furthermore, it is often difficult to determine whether the changes in VO_2peak/VO_2max seen after training are related to changes in musculosketelal fitness rather than changes in cardiovascular fitness.

Less is known about the effects of resistance training on cardiovascular fitness. However, the incorporation of resistance training into the treatment of SCI appears to be essential. In fact, muscle weakness and dysfunction are key determinants of pain and functional status in persons with SCI. Previous studies have revealed improvements in maximum aerobic power (Cooney and Walker 1986, Jacobs et al. 2001), exercise tolerance (Jacobs et al. 2001), and musculoskeletal fitness (Jacobs et al. 2001) after resistance training (e.g. circuit training).

As reviewed systematically by Phillips et al. (2011) two papers have evaluated the effects of upper body (arm) exercise on arterial function in SCI (Jae et al. 2008; Tordi et al. 2009). Jae et al. (2008) revealed that there were no significant differences in intima-media thickness, compliance, and beta stiffness index (a measure of arterial elasticity) of the common carotid artery between 28 competitive SCI athletes and 24 age-matched recreationally active able-bodied controls. Tordi and colleagues (2009) revealed (in a case study) that there was an improvement in aortic pulse wave velocity (central aortic stiffness) following six weeks of upper body training (30 min/session, 3 sessions/wk).

Conclusion

There is level 1b (Ordonez et al. 2013) and Level 2 evidence (Davis et al. 1987) that moderate intensity aerobic arm training (performed 20–60 min/day, three days/week for at least 6-8 weeks) is effective in improving the aerobic capacity and exercise tolerance of persons with SCI.

There is level 1b evidence (de Groot et al. 2003) that vigorous intensity (70%–80% HR reserve) exercise leads to greater improvements in aerobic capacity than moderate intensity (50-60% HR reserve) exercise. It should be noted that many individuals with SCI cannot tolerate vigorous intensity initially, to which they must adapt often using a submaximal or interval type approach.

There is level 2 evidence (Milia et al. 2014) that arm cranking against a workload corresponding to 60% of WMax (performed 3-5 hours/day for one year) increases WMax and VO2 max.

There is level 2 evidence (Hjeltnes and Wallberg-Henriksson 1998) that hand cycling exercise increases the power output, oxygen consumption, and muscle strength in individuals with paraplegia, but not tetraplegia during active rehabilitation. Conversely, there is level 4 evidence (Valent et al. 2008) that hand cycling increases power output and oxygen consumption in individuals with tetraplegia. Further research is clearly warranted. There is also level 4 evidence (Nooijien et al. 2015) that hand cycling interval training program increases peak power output and peak VO2 in individuals with paraplegia and tetraplegia.

There is level 3 evidence (Jae et al. 2008) that upper body strength exercise training can improve arterial structure and function in those with SCI.

There is level 5 evidence (Hubli et al. 2014) that aortic pulse wave velocity is significantly lower in athletes (hand cyclists) compared to sedentary individuals with SCI.

The relative importance of changes in cardiac function and the ability to extract oxygen at the periphery in persons with SCI after aerobic training remains to be determined.

Individuals with tetraplegia and paraplegia can improve their cardiovascular fitness and physical work capacity through aerobic arm cycling exercise training which are of moderate intensity, performed 20-60 min day, at least three times per week for a minimum of six to eight weeks. Resistance training at a moderate intensity at least two days per week also appears to be appropriate for the rehabilitation of persons with SCI. It remains to be determined the optimal exercise intervention for improving cardiovascular fitness.

4.3 Functional Electrical Stimulation (FES)

Computer-assisted FES during leg cycling has been shown to be an important and practical means of exercising a relatively large muscle mass in persons with SCI (Hooker et al. 1992). These devices also permit the activation of the skeletal muscle pump during leg cycling. For these reasons, FES training has been advocated widely as an effective treatment strategy for SCI. It is important to note, that the physiological responses to FES training appear to be distinct from arm ergometry training. For instance, arm exercise has been shown to lead to faster VO_2 kinetics (oxygen metabolism/uptake) (at a constant workload), greater changes in HR, and lower post-exercise blood lactates than FES leg cycling (Barstow et al. 2000).

We identified one longitudinal (Berry et al. 2012), one prospective experimental (Fornusek et al. 2014), one post (Hakansson et al. 2012), and 13 pre-post (Ragnarsson et al. 1988, Faghri et al. 1992, Hooker et al. 1992, Barstow et al. 1996, Hjeltnes et al. 1997, Mohr et al. 1997, Gerrits et al. 2001, Hopman et al. 2002, Crameri et al. 2004, Janssen and Pringle 2008, Zbogar et al. 2008, Griffin et al. 2009, Kahn et al. 2010) studies that examined the effectiveness of FES leg cycle ergometry on indices of cardiovascular fitness and/or health in SCI. We also identified 7 pre-post (Pollack et al. 1989, Krauss et al. 1993, Mutton et al. 1997, Gurney et al. 1998, Thijssen et al. 2005, Thijssen et al. 2006, Brurok et al. 2011), 1 RCT (Bakkum et al. 2015) and 1 cross-sectional (Bakuum et al. 2014) investigations that examined hybrid FES (combined leg and arm) on cardiovascular fitness in SCI.

There was one further prospective cohort study (Carty et al. 2012), and 11 pre-post (Jacobs et al. 1997, Nash et al. 1997, Solomonow et al. 1997, Wheeler et al. 2002, de Groot et al. 2005, Sabatier et al. 2006, Stoner et al. 2007, Berry et al. 2008, Jeon et al. 2010, Taylor et al. 2011, Ryan et al. 2013) investigations that examined the effects of other electrically assisted training programs on cardiovascular fitness and/or health.

4.3.1 FES Leg Cycle Ergometry

Table 6: Effects of Functional Electrical Stimulation on Cardiovascular Fitness/Health

Author, Year; Country Score Research Design Sample Size	**Methods**	**Outcomes**
Berry et al. 2012; UK Longitudinal study Level 2 N=11	**Population**: N=11 (9M;2F) participantswith T3-T9 SCI; mean(SD) age: 41.8(7.6) yrs old; at least 2 yrs since injury; all AIS A. **Treatment:** Participants completed a 12-month, home-based progressive FES cycle training programme (up to 5x60min sessions per wk).	1. Oxygen cost and efficiency did not significantly change after training. 2. Total stimulation cost and blood lactate values reduced overall. The high metabolic cost of FES cycling is a result of non-physiological recruitment of predominantly fast muscle fibres. The electrical cost of

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	Outcome Measures: Stimulation cost, oxygen cost, efficiency and markers of anaerobic metabolism were determined before and after 6 and 12 months of training, during constant work-rate tests.	cycling reduced by 37%, probably due to motor unit hypertrophy, and lactate oxidation capacity improved. 3. Respiratory exchange ratios remained relatively high. 1.
Fornusek et al. 2014 Australia Pre-post Level 4 N=8	**Population:** 8 individuals with chronic paraplegia (T4- T11). 7 with complete SCI (AIS- A) and 1 with incomplete SCI (AIS- C) **Treatment:** Participants performed electrical stimulation (ES) on 2 separate sessions one week apart. The first day consists of 5 min of rest followed by 35 min of FES cycling and 15 min intermittent isometric exercise where the pedals were locked in a fixed position using the same ES parameters. The second day, the order and durations of the ES isometric and FES cycling were swapped. **Outcome Measure:** Cardiorespiratory activity (oxygen consumption- VO2, ventilation, tidal volume), heart rate, power output during FES cycling	2. No differences during the first 35 minutes of isometric exercise on each day when comparing the 2 modes of exercise for average rate of oxygen consumption, average heart rate, isometric or minute ventilation. 3. No differences between exercise modes for any peak cardiorespiratory values recorded during the initial 35 minute of exercise or the following 15-minute crossover exercise phase. 4. Both FES cycling and isometric ES induced significant increases from rest values for all cardio respiratory measures.
Kahn et al. 2010; USA Pre-post Level 4 N = 12	**Population:** 14 participants with paraplegia (T1-T10) or tetraplegia (C4-C8); >1 year post injury. 12 participants completed the trial. **Treatment:** FES-leg cycle ergometry training (2 sessions per week for 4 weeks). Each training session consisted of multiple exercise bouts (total 30 min, with 5-min rest period between boots). Stimulation was applied to quadriceps, hamstrings and gluteal muscle groups bilaterally **Outcome Measures:** Thrombin activity, antithrombin III activity, fibrinogen level, coagulation factor levels, cyclic adenosine monophosphate (cAMP) level and platelet aggregation in blood.	1. After the 1st session, significant increase were found for Antithrombin III (103.8 ± 8.9% to 110 ± 6.9%) and camp levels (9.9 ± 2.5% to 15.8 ± 3%) 2. After the eight session, significant increase were found in antithrombine III activity, cAMP levels (17.8 ± 4.2% to 36.5 ± 7.6%) and coagulation factors V and X (respectively 88 ± 27 to 103 ± 23% and 100 ± 40 to 105 ± 7%). In addition, thrombine levels decreased (pre: 12.5 ± 2.0 s to post: 11.1 ± 1.7s) and platelet aggregation was inhibited by 40%.
Griffin et al. 2009; USA Pre-Post Level 4 N = 18	**Population:** 18 SCI participants (age 40 ± 2.4, YPI 11 ± 3.1) with no cardiovascular disease **Treatment:** FES cycling 2-3 times per week for 10 weeks **Outcome Measures:** Cycling power; body composition; ASIA impairment scale (AIS)	1. Cycling power and work done were greater during weeks 8, 9, and 10 compared to week 1 2. Total body mass and lean muscle mass increased significantly after training. 3. Lower extremity total AIS scores and the motor and sensory components of the AIS tests were all significantly higher after training.
Janssen & Pringle 2008; The Netherlands Pre-Post	**Population:** 12 men with SCI (6 tetraplegia and 6 paraplegia), including 4 participants (age 44 ± 14, YPI 13 ± 8) who had previous	1. Significantly higher heart rate (+16%) and power output (+57%) after training, compared to baseline

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Level 4 N = 12	training on ES-LCE **Treatment:** Computer controlled electrical stimulation induced leg cycle ergometry (ES-LCE); total of 18 training sessions with each session lasting 25-30 minutes **Outcome Measures:** Heart rate; power output; oxygen uptake (VO_2); Carbon dioxide production; minute ventilation (volume of gas into lungs)	2. Significantly higher peak values for VO_2 (+29%), carbon dioxide production (+22%), and minute ventilation (+19%)
Zbogar et al. 2008; Canada Pre-Post Level 4 N = 4	**Population:** 4 SCI participants, all female, age 19-51, lesion level C4-T7 **Treatment:** 30-min sessions of FES leg cycle ergometry, 3 times per week for 12 weeks **Outcome Measures:** Large and small artery compliance	1. There was no significant change in large artery compliance. 2. All participants demonstrated increased small artery compliance after training, an average of 63% increase (from 4.2 $\pm$ 1.8 to 6.9 $\pm$ 3.2 $mL \cdot mmHg^{-1} \times 100$)
Crameri et al. 2004; Denmark Pre-post Level 4 N = 6	**Population:** Paraplegia, complete, C6-T7, ages 26–54 yrs, 3–21 yrs post-injury. **Treatment:** FES training 45 min/d, 3 d/wk, 10 wks. One leg: dynamic cycle ergometry involved bilateral quadriceps and hamstring stimulation; contralateral leg: isometric contractions. **Outcome Measures:** muscle biopsies, capillary-to-muscle fibre ratio, muscle proteins, and oxygenation, citrate synthase activity (marker of intact mitochondria).	1. The isometric-trained leg showed larger mean increases in force, increase in type 1 fibres, fibre cross-sectional area, capillary-to-fibre ratio, citrate synthase activity, and relative oxygenation after static training in comparison to baseline and the dynamically trained leg.
Hopman et al. 2002; The Netherlands Pre-post Level 4 N = 9	**Population:** 9 males; Level of injury: thoracic and cervical; Type of injury: AIS A; Time since injury: range 1-22 years. Mean age (including 2 other participants not included in this part of the study) = 40.7±7.2 yrs. **Treatment:** Cycle training was performed by using a computer-controlled leg cycle ergometer with electrodes placed over hamstring, gluteal, and quadriceps muscles. Participants trained for 30 minutes, 3x/week for 6 wks. **Outcome Measures:** Mean arterial pressure, resting blood flow in femoral artery	1. Mean arterial pressure was similar after training compared with values before training. 2. Larger resting blood flow in the femoral artery was found after training. Peak systolic blood flow increased from 1330 ± 550 to 1710 ± 490 $mL \cdot min^{-1}$ and mean blood flow increased from 270 ± 120 to 370 ± 160 $mL \cdot min^{-1}$. 3. Calculated vascular resistance decreased by 30% after 6 weeks of training.
Gerrits et al. 2001; The Netherlands Pre-post Level 4 N = 9	**Population:** 9 males; Age: mean 39.2 yrs, range 26-61; Level of injury: C4-T6, 4 cervical and 5 thoracic; Time since injury: mean 11.1 yrs, range 2-27; Type of injury: 3 AIS B, 5 AIS A, 1 AIS C **Treatment:** All participants trained for 6 weeks, 3 d/wk. A training session consisted of a 30-minute FES-leg cycle ergometry (LCE) exercise. **Outcome Measures:** Longitudinal images and simultaneous velocity spectra of the common carotid and femoral arteries (capturing blood flow); arterial diameters, peak systolic inflow volumes, mean inflow volume, velocity index	1. Increased work output (300%). 2. No change HR and systolic BP. 3. Six weeks of FES-LCE training resulted in an increase in diameter of the femoral artery (pre-training 7.5±1.5 mm vs. post-raining 8.1±1.5 mm) whereas the diameter of the common carotid artery remained unchanged. 4. Velocity index, an indicator for peripheral resistance, decreased from 1.24±0.11 to 1.14±0.12 in the femoral artery; unchanged in common carotid 5. Larger resting inflow volumes of the femoral artery were found after training as peak systolic inflow increased from 1330 ± 550 to

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
		1710 ± 490 mL·min^{-1} and mean inflow volume increased from 270 ± 120 to 370 ± 160 mL·min^{-1}. 6. After training, hyperaemic response is augmented.
Hjeltnes et al. 1997; Norway Pre-post Level 4 N = 5	**Population:** 5 males, complete chronic lesions, 2 C5, 2 C6, 1 C7, 4 AIS A, 1 AIS A/B, age 35 yrs, 10.2 yrs post-injury. **Treatment:** FES leg cycling, 7 x/wk, 8 wks. **Outcome Measures:** DXA (Body composition), VO_2peak.	1. VO_2peak increased (70%) during FES leg cycling but not during arm exercise. 2. Increase in lean body mass (3.0%) and muscle cross-sectional area (21.3%). 3. Decrease in body fat (6.4%).
Mohr et al. 1997; Denmark Pre-post Level 4 N = 10	**Population:** 6 tetraplegia at C6, 4 paraplegia at T4, all complete, ages 27–45 yrs, 3–23 yrs post-injury. **Treatment:** 1-yrs exercise training using an FES cycle ergometer (30 min/d, 3 d/wk). **Outcome Measures:** VO_2max, total work output, blood lactate, muscle properties.	1. 4-fold increase in work output and 12% increase in thigh muscle mass with FES. 2. VO_2max increased 17.5% (6 months) and 19.2% (12 months). 3. Shift toward more fatigue-resistant contractile proteins and a doubling of citric synthase activity.
Barstow et al. 1996; USA Pre-post Level 4 N = 9	**Population:** 9 males, 2 tetraplegia, 7 paraplegia, all AIS A, age 34.4 yrs, 10.1 yrs post-injury. **Treatment:** FES leg-cycle exercise, 30 min (minimum of 24 sessions, 3d/wk). **Outcome Measures:** Work rate, VO_2peak, oxygen pulse.	1. Training significantly increased VO_2peak (10.9%), peak work rate (46.5%), and peak oxygen pulse (12.6%).
Faghri et al. 1992; USA Pre-post Level 4 N = 13	**Population:** 6 paraplegics (5 complete), 7 tetraplegics (all incomplete), C4-C7 and T4-T10, age 30.5 yrs, 8 yrs post-injury. **Treatment:** FES leg cycle, 3 d/wk, 12 wks. **Outcome Measures:** BP, power output, HR, VO_2peak, stroke volume, and cardiac output.	1. Increased resting HR and systolic blood pressure in the tetraplegics, while decreased systolic, diastolic, and mean arterial BP in the paraplegics after training. 2. In both groups, decreased submaximal exercise HR and BP and increased stroke volume after training. 3. After training, submaximal cardiac output increased significantly in the paraplegic group.
Hooker et al. 1992; USA Pre-post Level 4 N = 18	**Population:** 17 males, 1 female, 10 tetraplegia (C5-C7), 8 paraplegia (T4-T11), 7 incomplete, age 30.6 yrs, 6.1 yrs post-injury. **Treatment:** FES leg-cycle training 10–30 min/d, 2–3 d/wk, 12–16 wks. **Outcome Measures:** VO_2peak, power output, cardiac output, stroke volume, total peripheral resistance, and HR.	1. Increase in power output (45%), VO_2peak (23%), cardiac output (13%), HR (11%), and a reduction in total peripheral resistance (-14%) during peak FES leg cycle. 2. No changes in stroke volume (6%), mean arterial BP (-5%), or arteriovenous oxygen difference (+10%). 3. No differences during peak arm cranking exercise for any of the cardiovascular variables.
Janssen and Pringle 2008; The Netherlands Pre-Post Level 4 N = 12	**Population:** All participantst are male, 6 participants with tetraplegia and 6 with paraplegia, including 4 participants (mean (SD) age 44 (14), yrs post-injury 13 (8)) who had previous training on ES-LCE. **Treatment:** Computer controlled ES-LCE;	1. Significantly higher heart rate (+16%) and power output (+57%) after training, compared to baseline 2. Significantly higher peak values for VO_2 (+29%), VCO_2 (+22%), and V_e (+19%) 3. Peak torques were significantly higher for

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	total of 18 training sessions with each session lasting 25-30 minutes. **Outcome Measures:** Heart rate; power output; oxygen uptake (VO_2); Carbon dioxide production (VCO_2); pulmonary ventilation (V_e); peak torque.	most of the relevant muscles
Ragnarsson et al. 1988; USA Pre-post Level 4 N = 19	**Population:** 16 male, 3 females (7 paraplegics T4-T10, 12 tetraplegics C4-C7), ages 19–47 yrs, 2–17 yrs post-injury. **Treatment:** Phase I: quadriceps stimulation with dynamic knee extensions against increasing resistance, 3 d/wk, 4 wks; Phase II: leg-cycle FES, 15-30 min/d, 3 d/wk for 12 wks. **Outcome Measures:** HR, work, BP, and VO_2peak.	1. Most showed an increase in strength and endurance. 2. VO_2peak increased nonsignificantly (14.9%) after training.
Hakansson et al. 2012; USA Post-test Level 4 N=9	**Population:** N = 11 participants (8M;3F) with T4-T12 SCI; mean (SD) age: 28(9) yr old; DOI: 1.25-17 yr; all AIS A **Treatment:** Participants pedaled the ergometer 3x/wk (30 min/session) during the first 3 weeks and once per week during the last 5 weeks. The last 4 weeks (used in analysis) were divided into two 2-week time blocks of StimErg and Stim3, which were randomly assigned. **Outcome Measures:** Work, VO_2, blood lactate	1. Participants performed 11% more work pedaling with Stim3 than with existing stimulation patterns (StimErg). 2. Average VO2 and blood lactate concentrations were not significantly different between Stim3 (442 $mL \cdot min^{-1}$; 5.9 $mmoL \cdot L^{-1}$) and StimErg (417 $mL \cdot min^{-1}$; 5.9 $mmoL \cdot L^{-1}$).

Note: AIS = ASIA Impairment Scale; BP = blood pressure; d = day; FES = functional electrical stimulation; hr = hour; HR = heart rate; min = minute; wk = week; yrs = year.

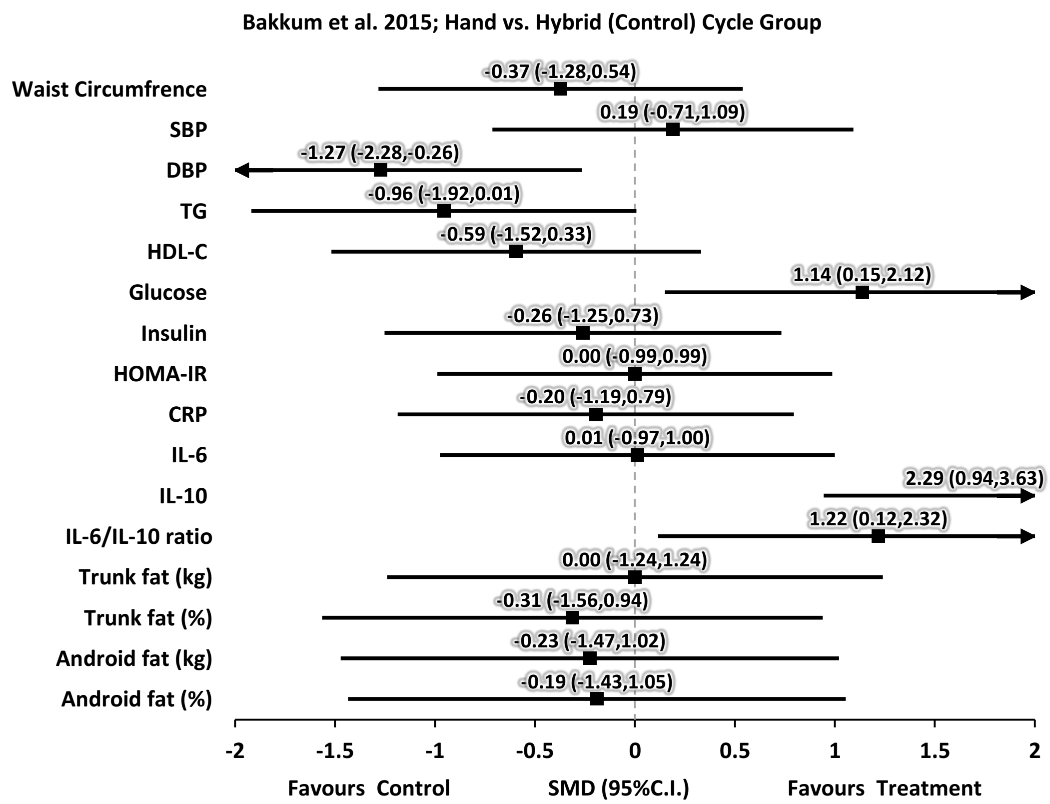
4.3.2 Hybrid FES (Combined Leg and Arm Ergometry)

Table 7: Effects of Hybrid FES Training on Cardiovascular Fitness and Health

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Bakkum et al. 2015 Netherlands PEDro =6 RCT Level 1 N=19	**Population:** 19 participants (18 males, 1 female, C2-L2) with SCI for more than 10 years. **Treatment:** Participants were randomized to the hybrid or hand cycle group. 9 participants on hybrid cycle and 10 participants on hand cycle during 32 individual training sessions within a period of 16 weeks. The duration of each training session increased from 18 to 32 minutes during the program. **Outcome Measures:** Metabolic syndrome (waist circumference, systolic/diastolic blood pressure, high density lipoprotein cholesterol, triglycerides, and insulin resistance),	1. For all metabolic components, inflammatory markers, and visceral adiposity, there were no differences over time between the 2 training groups. 2. Overall reductions were found for waist circumference, diastolic blood pressure, insulin resistance, CRP, IL-6, trunk and android fat percentage.

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	inflammatory status (C-reactive protein, interleukin -6 & -10), and visceral adiposity (trunk and android fat).	

Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data



Brurok et al. 2011; Norway Pre-Post Level 4 N = 6	**Population:** 6 men with SCI in stable neurologic recovery (5 participants – paraplegic AIS A, 1 participant – tetraplegic AIS A) **Treatment:** Aerobic high-intensity hybrid exercise training 3X/week for 8 wks preceded by a 7-wk control period of regular daily activity. Peak tests were performed at three different time points: 1, baseline; 2, control; and 3, post-training. **Outcome measures:** peak stroke volume during hybrid cycling and peak oxygen consumption during hybrid cycling, arm cycle ergometry, and FES leg cycling.	1. Between the control and post training test, there was a significant increase in Hybrid VO2 peak (25.3%) and VO2Peak during arm cycle ergometry (25.9%), and VO2 Peak during FES cycle (25.8%).

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Thijssen et al. 2006; The Netherlands Pre-post Level 4 N = 9	**Population:** 8 males, 1 female, C5-T12, 8 complete AIS A, 1 incomplete AIS C, age 39 yrs, 11 yrs post-injury. **Treatment:** Simultaneous FES cycle ergometry and arm ergometry, 25 min/d, 2 d/wk, 6 wks followed by 6-wks detraining. **Outcome Measures:** Blood flow of thigh, diameter of the femoral artery and flow-mediated dilation.	1. After 2 wks of training, there was a significant increase in baseline and peak blood flow, an increase in femoral artery diameter, and a decrease in femoral artery flow-mediated dilation. 2. Detraining lead to a reversal of baseline and peak thigh blood flow, vascular resistance, and femoral diameter. 3. Detraining did not restore femoral artery flow mediated dilation.
Thijssen et al. 2005; The Netherlands Pre-post Level 4 N = 10	**Population:** 9 males, 1 female, T1-T12, 9 complete, age 39.2 yrs, 1–20 yrs post-injury. **Treatment:** Simultaneous FES cycle ergometry and arm ergometry, 30 min/d, 2–3 d/wk, 4 wks. **Outcome Measures:** VO_2peak, blood flow and vascular resistance, and echo Doppler (diameter and flow-mediated dilation after 13 min of ischemia).	1. Training resulted in increased thigh resting (43.5%) and peak blood flow (17.1%), decreased thigh resting vascular resistance (31.8%), and increased femoral artery diameter. 2. After training, there was an increase in maximal workload (6.8%), VO_2peak (6.1%), and resistance to fatigue.
Gurney et al. 1998; USA Pre-post Level 4 N = 6	**Population:** All male, C4-T10, 4 paraplegia, 2 tetraplegia, ages 23–41 yrs, 5–24 yrs post-injury. **Treatment:** Phase I: FES leg cycle, 3 d/wk, 6 wks; Phase II: FES leg cycle with simultaneous, voluntary arm ergometry, 3 d/wk, 6 wks; Phase III: 8-wks detraining. **Outcome Measures:** VO_2peak, submaximal and maximal HR.	1. Increased VO_2peak (81.7%) and workload with FES leg cycle. 2. After an 8-wk detraining period, peak workload returned to baseline; VO_2peak remained higher.
Mutton et al. 1997; USA Pre-post Level 4 N = 11	**Population:** All male, complete AIS A, C5-6 to T12-L1, age 35.6 yrs, 9.7 yrs post-injury. **Treatment:** 3 phases of exercise training (FES leg-cycle ergometry). Phase I progressive FES leg-cycle exercise to 30 min of exercise; Phase II ~35 sessions of FES-leg cycle ergometry; and Phase III ~41 sessions (30 min each) of combined FES-leg and arm ergometry. **Outcome Measures:** VO_2peak and submaximal physiological parameters (VO_2, HR, blood lactate).	1. In response to FES-leg cycle ergometry training both VO_2peak and peak work rate during graded FES leg exercise (but not graded arm ergometry) testing improved. 2. With hybrid training, VO_2peak (13%) and peak power output (28%) were increased during graded hybrid testing, but not during graded arm or graded FES leg testing alone.
Krauss et al. 1993; USA Pre-post Level 4 N = 8	**Population:** 7 male, 1 female, 7 paraplegia, 1 tetraplegia, age 32 yrs, 13 yrs post-injury. **Treatment:** 2 phase program. Phase I: FES leg cycling 3 d/wk, 6 wks; Phase II: FES leg cycle plus simultaneous arm ergometry for 6 wks. **Outcome Measures:** VO_2peak, HR, workload, peak lactate.	1. After Phase I, arm ergometer VO_2peak (21.9%) and FES leg ergometer VO_2peak (62.7%) increased. 2. After Phase II, the hybrid exercise VO_2peak increased 13.7%. 3. Peak HR only increased with training during FES leg ergometry.
Pollack et al. 1989; USA Pre-post Level 4 N = 11	**Population:** 7 male and 4 female, C4-C6 and T2-T6, complete motor lesions, ages 18–54 yrs, 6–132 months post-injury. **Treatment:** 3 phase program over 13–28 wks. Phase I: quadriceps stimulation (knee extension); Phase II: FES leg cycle with 0–1 kp resistance; Phase III: loaded FES leg cycle, 3 d/wk, 3 wks. **Outcome Measures:** BP, HR, oxygen	1. There were significant increases in endurance time (288%), VO_2peak (95.9%), and HR (16.8%) and decreases in diastolic BP (31.5%) with training.

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	consumption.	
Bakkum et al. 2014 Netherlands Cross-sectional study Level 5 N=9	**Population:** Nine individuals (8 males, 1 female, mean age of 40) with motor complete paraplegia or tetraplegia (6 AIS A, 4 AIS C) **Treatment:** In Session 1, participants performed two 5 minute bouts of Hybrid Cycling at Rate of Perceived Exertions 3 (Light-Moderate) and 6 (Moderate-Vigorous). Hybrid cycling combines handcycling with FES-induced leg cycling. After 48-72 hours of rest, the same participants completed the exact same protocol but with Hand Cycling. **Outcome Measures:** Metabolic rate, cardiorespiratory response (heart rate, oxygen pulse, ventilation)	1. Metabolic rate was higher during hybrid cycling than during hand cycling at equal perceived exertion levels. 2. When compared to Hand Cycling, heart rate and ventilation were higher during hybrid cycling, while oxygen pulse was the same. 3. Heart rate also varied by perceived exercise intensity.

4.3.3 Other Electrically-Assisted Training Programs

Table 8: Effects of Other Electrically Assisted Training Programs on Cardiovascular Fitness and Health

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Other forms of electrically assisted training		
Menendez et al. 2016 Spain PEDro=7 RCT Level 1 N=10	**Population**: 10 individuals- 8 males and 2 females; all wheelchair users; AIS A or B; mean age =46.3 ± 12.9y; years post injury= 12.4 ± 7.8y **Treatment**: All participants received 10 2-h rehabilitation sessions per month, which consisted of standing (tilted) position, passive movements, low-intensity resistance training or electrotherapy and physiotherapy treatment. Ten participants with SCI were assessed in five different sessions. After a familiarization session, four interventions were applied in random order; Whole body vibration (WBV), Electromyostimulation (ES), simultaneous WBV and ES (WBV+ES), and 30 s of WBV followed by 30 s of ES (WBV30/ES30). Each intervention consisted of 10 sets × 1 min ON+1 min OFF. Participants were seated on their own wheelchairs with their feet on the vibration platform (10 Hz, 5 mm peak-to-peak), and ES was applied on the gastrocnemius muscle of both legs (8 Hz, 400 μs). **Outcome Measures:** Popliteal artery blood velocity (BV) and skin temperature (ST) of the calf	1. The simultaneous application (WBV+ES) produced the greatest increase in mean BV (MBV; 36% and 42%, respectively) and peak BV (PBV; 30% and 36%, respectively) during the intervention. 2. This intervention produced the greatest mean increases in MBV (21%) and PBV (19%) during the recovery period. Last, this intervention produced the highest increase in ST during the intervention (2.1 °C).

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Carty et al. 2012; Ireland Prospective cohort Level 2 N=14	**Population:** N = 14 participants with T2-T11 SCI (11M;3F); 11 AIS A, 3 AIS B; mean (SD) age: 45.08 (7.92); mean (SD) yr since injury: 11.22 (11.23). **Treatment:** Four electrodes were placed bilaterally on the quadriceps and hamstrings muscle groups, and subtetanic contractions were elicited using a neuromuscular electrical stimulation device. Training was undertaken for 1 hr, 5d/wk for 8 weeks. Participants increased the stimulation intensity on an incremental wheelchair exercise test of increasing speed and incline as quickly as tolerable to bring them to the desired training intensity as recorded on the Borg scale of rating of perceived exertion (RPE) (between 13 and 15 on RPE). **Outcome Measures:** Incremental treadmill wheelchair propulsion exercise test with simultaneous cardiopulmonary gas exchange analysis to determine VO_{2peak} and HR_{peak}.	1. A significant increase in VO_{2peak} and HR_{peak} between baseline and follow-up was observed. Changes in VO_{2peak} ranged from -1.1% to 57.2%. 2. There was no significant difference in the mean VO_{2peak} change between the 2 groups based on the level of injury (above T6, T6 and below).
Asselin et al. 2015 USA Pre-Post Level 4 N= 8	**Population**: 8 individuals; non-ambulatory persons with paraplegia. **Treatment**: 8 non-ambulatory persons with paraplegia were trained to ambulate with a powered exoskeleton. Once the participant was fitted properly in the device, he or she participated in three training sessions per week. **Outcome Measures:** Measurements of oxygen uptake (VO2) and heart rate (HR) were recorded for 6 min each during each maneuver while sitting, standing, and walking.	1. The average value of VO2 during walking was significantly higher than for sitting and standing. 2. The HR response during walking was significantly greater than that of either sitting or standing. Persons with paraplegia were able to ambulate efficiently using the powered exoskeleton for overground ambulation, providing the potential for functional gain and improved fitness.
Ryan et al. 2013; USA Pre-post Level 4 N=14	**Population:** N = 14 Participants(11M;3F) with motor complete SCI C4-T7 level; AIS A or B; mean (SD) age: 26.7(4.7) yr; mean (SD) time post injury: 7.7 (6.5) yr. **Treatment:** Participants performed resistance exercise training of the knee extensor muscles twice weekly for 16 weeks. Four sets of 10 knee extensions were performed using neuromuscular electrical stimulation. Legs were alternated after 10 repetitions, and training sets were separated by 2 min. **Outcome Measures:** plasma glucose and insulin; thigh muscle and fat mass; quadriceps and hamstrings muscle size and composition; muscle oxidative metabolism.	1. Mean (SD) muscle mass increased in all participants (39(27)%). The mean change (SD) in intramuscular fat was 3(22)%. 2. Phosphocreatine mean recovery time constants (SD) were 102(24) and 77(18)s before and after electrical stimulation-induced resistance training, respectively. 3. No improvement in fasting blood glucose levels, homeostatic model assessment calculated insulin resistance, 2-hour insulin, or 2-hr glucose was observed.
Taylor et al. 2011; USA Pre-post Level 4	**Population:** Six male patients with SCI (T4-T9, ASIA A, within 18 years of injury, and younger than 40 years) **Treatment:** Arms-only rowing and FES rowing. A	1. VO_2peak was greater for FES rowing (20.0 ± 1.9 $mL \cdot kg^{-1} \cdot min^{-1}$, P=.01) than for arms-only rowing (15.7 ± 1.5 $mL \cdot kg^{-1} \cdot min^{-}$

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
N = 6	sub-group (n = 3) completed at least 6 months of a progressive FES row training exercise program with graded exercise tests every 6 months. **Outcome measures:** VO_2peak, peak ventilation, peak respiratory exchange ratio, peak heart rate, and peak oxygen pulse.	^{1}) 2. For 5 participants, the increase in aerobic capacity ranged from 12 to more than 50%. 3. Peak respiratory exchange ratio was higher for arms-only rowing than FES rowing (1.28 ± 0.16 vs. 1.17 ± 0.03, P = 0.14) 4. Peak heart rate was higher for FES rowing than arms-only rowing (179 vs. 170, P = 0.19). 5. Peak oxygen pulse was 35% greater during FES rowing than arms-only rowing (6.90 vs. 9.08, P = 0.0007).
Jeon et al. 2010; Canada Pre-post Level 4 N = 6	**Population:** 6 healthy male participants with paraplegia participated in the study (mean age, 48.6±6y; mean weight, 70.1 ± 3.3 kg; injury levels between T4-5 and T10). **Treatment:** Twelve weeks of FES-rowing exercise training 3 to 4 times a week (600–800 kcal). **Outcome measures:** VO_2peak, plasma leptin, insulin, and glucose levels, insulin sensitivity, body composition.	1. VO_2peak increased from 21.4 ± 1.2 to 23.1 ± 0.8 $mL \cdot kg^{-1} \cdot min^{-1}$ (P = 0.048). 2. Plasma glucose levels were reduced in all 6 patients after the training (pre: 103 ± 7.4 vs. post: 92.5±3.7 $mg \cdot dL^{-1}$); however, this did not reach statistical significance. 3. Plasma leptin levels were significantly decreased after the training (pre: 6.91 ± 1.82 $ng \cdot dL^{-1}$ vs. post: 4.72 ± 1.04 $ng \cdot dL^{-1}$; P = 0.046). 4. Plasma glucose and leptin levels were significantly decreased after exercise training by 10% and 28% (P = 0.028), respectively. 5. Whole-body percent body fat decreased by 5% (pre: 25.5 ±1.8 vs. post: 24.4 ± 1.6%); however, this did not reach statistical significance (P = 0.074) 6. A trend toward fat mass reduction was seen in 4 of the 6 participants; this change did not reach statistical significance (P = 0.08).
Berry et al. 2008 UK Pre-Post Level 4 N = 11	**Population:** 12 SCI participants(10 male, 2 female), with motor and sensory complete T3 to T12 lesion (AIS - A) **Treatment:** Electrically stimulated (ES) cycling training, 236 sessions over 52 weeks **Outcome Measures:** heart rate; O_2 pulse; power output	1. Peak heart rate increased by 13% after 6 months 2. Peak O_2 pulse increased significantly after 6 months 3. Peak power output increased significantly after 3 months and 6 months
Stoner et al. 2007; USA Pre-post Level 4 N = 5	**Population:** 5 males; Age: mean 35.6±4.9 yrs; Level of injury: range C5-T10; Time since injury: mean 13.4±6.5 yrs; Type of injury: AIS A. **Treatment:** Neuromuscular electric stimulation-induced resistance training; the quadriceps femoris muscle group of both legs were trained 2x/week with 4x10 repetitions of unilateral, dynamic knee extensions for 18 weeks. **Outcomes measures:** FMD and resting diameter and arterial range of the posterior tibial artery.	1. FMD improved from 0.08 ± 0.11 (2.7%) to 0.18 ± 0.15 (6.6%) and arterial range improved from 0.36 ± 0.28 mm to 0.94 ± 0.40 mm. Resting diameter did not change.

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Sabatier et al. 2006; USA Pre-post Level 4 N = 5	**Population:** All male, complete AIS A, C5-T10, age 35.6 yrs, 13.4 yrs post-injury. **Treatment:** Home-based electrical stimulation 2 d/wk, 18 wks. **Outcome Measures:** Femoral artery diameter and blood flow, weight lifted, muscle mass, and muscle fatigue.	1. Training resulted in significant increases in weight lifted and muscle mass and a decrease in muscle fatigue. 2. There was no change in femoral artery diameter with training. 3. Resting, reactive hyperaemia, and exercise blood flow did not change significantly with training.
de Groot et al. 2005; The Netherlands Pre-post Level 4 N = 6	**Population:** SCI: 3 male, 3 female, T4-L2, all complete AIS A/B, age 43 yrs, 14.5 yrs post-injury; Controls: 8 able-bodied individuals (4 male, 4 female), age 41 yrs. **Treatment:** Unilateral surface stimulation of the quadricep, tibial anterior, and gastrocnemius muscles, 30 min/d, daily, 4 wks. **Outcome Measures:** Leg circumference, total limb volume, resting mean red blood cell velocity and vessel diameter and blood pressure.	1. An increase in arterial compliance and a decrease in the flow-mediated dilation in the femoral artery of the trained leg, with no changes in these vascular parameters in the femoral artery of the untrained leg, the carotid artery, and the brachial artery. 2. There were no significant training-related changes in resting vessel diameter, blood flow, or shear rate in the femoral, carotid, and brachial arteries.
Wheeler et al. 2002; Canada Pre-post Level 4 N = 6	**Population:** C7-T12, 5 AIS A, 1 AIS C, age 42.5 yrs, 13.8 yrs post-injury. **Treatment:** FES (quadriceps) with arm rowing (70%–75%VO_2peak) 30 min/d, 3 d/wk, 12 wks. **Outcome Measures:** Total rowing distance, VO_2peak, and peak oxygen pulse.	1. Training resulted in significant increases in rowing distance (25%), VO_2peak (11.2%), and peak oxygen pulse (11.4%).
Jacobs et al. 1997; USA Pre-post Level 4 N = 15	**Population:** 12 males and 3 females; Age: mean 28.2 ± 6.8 yrs, range 21.1-45.2 yrs; Time since injury: mean 3.7 ± 3.0 yrs, range 7-8.8 yrs; Type of injury: all AIS A paraplegia; Level of injury: T4-T11 **Treatment:** 32 sessions of functional neuromuscular stimulation ambulation training using a 6-channel system (Parastep ® 1). Participants trained 3 days/week. Typically, three walking trials were completed during each training session. Participants chose ambulation pace and duration. **Outcome measures:** HR, peak VO_2	1. Heart rate was lower throughout sub-peak levels of arm ergometry after the ambulation training. 2. Peak VO_2 increased from 20.0 ± 3.3 $mL \cdot kg^{-1} \cdot min^{-1}$ to 23.0 ±3.6 $mL \cdot kg^{-1} \cdot min^{-1}$ post-training.
Nash et al. 1997; USA Pre–post Level 4 N = 12	**Population**: SCI: T4–T11 **Intervention**: Parastep training (FES with aid of walker), 3 times per week for 12 weeks. Duration based on comfort of the participant. **Outcome measures**: Femoral artery end-diastolic diameter and flow velocity profiles at rest and after 5 min thigh occlusion.	1. Increased resting common femoral cross-sectional area, computed pulse volume, and arterial inflow volume. 2. Peak systolic velocity was not significantly different. 3. After 5-min thigh occlusion, femoral pulse volume, flow velocity integral and arterial inflow volume increased after training.
Solomonow et al. 1997; USA Pre-post Level 4 N = 70	**Population:** All paraplegia, no other details given. **Treatment:** Reciprocating gait orthosis (RGO) 3 hr/wk, 14 wks. **Outcome Measures:** Cardiac output, stroke volume, vital capacity, knee extensor torque, and heart rate at the end of a 30 m walk.	1. There was a non-significant increase in cardiac output (7.1%) and stroke volume (5.0%) after training. 2. There was a significant increase in knee extensor torque (78.2%).

Note: AIS = ASIA Impairment Scale; BP = blood pressure; d = day; FES = functional electrical stimulation; HR = heart rate; min = minute; wk = week; yrs = year; VO_2peak = peak aerobic power.

Discussion

There is a growing body of literature indicating that FES exercise training is an effective way of improving cardiovascular health, peak power output, and exercise tolerance/capacity in persons with SCI (Table 6). These studies generally employ a cycling motion, although rowing and bipedal ambulation have also been evaluated. It appears that moderate-to-vigorous intensity FES training (relative to baseline capacity) may be effective in enhancing cardiovascular fitness in persons with SCI. The majority of the investigations are pre-post designs (level 4) with investigators reporting marked changes in VO_{2max} or VO_{2peak} after FES training. Similar to aerobic training, 20–40% changes in aerobic capacity are often observed after FES training. However, improvements in excess of 70% are not uncommon (Faghri et al. 1992). Harkansson et al. (2012) tested new electrical stimulation timing patterns (Stim3, designed using a forward dynamic simulation to minimize the muscle stress-time integral) to determine whether SCI participants could increase work and metabolic responses when pedaling a commercial FES ergometer, and found that participants performed 11% more work pedalling with Stim3 than with existing stimulation patterns.

Investigations with FES training have also shown an improvement in musculoskeletal fitness. Similar to arm exercise training, limited investigations have shown an improvement in cardiac function after FES training. An investigation has also revealed that the degree of muscular adaptation that can be achieved via FES exercise is dependent upon the load that is applied to the paralyzed muscle (Crameri et al. 2004).

Researchers have also shown that hybrid exercise training (FES leg cycling combined with arm ergometry) may elicit greater changes in peak work rates and VO_{2peak}/VO_{2max} than FES leg- cycling exercise or hand cycling alone (Bakkum et al. 2014, Krauss et al. 1993, Mutton et al. 1997). Moreover, it appears that the physiological adaptations to combined FES leg cycling and arm ergometry training are partially maintained after eight weeks of detraining (Gurney et al. 1998). Other interventions (Table 8) that make use of hybrid FES training have also been shown to improve the exercise capacity and cardiovascular health of persons with SCI. It would appear that the potential adaptations with hybrid exercise may be greater than FES alone; however, further research is required to test this hypothesis.

A series of intrinsic muscle adaptations can also occur after FES training that enhance the ability for oxidative metabolism at the cellular level, which in turn facilitate improved endurance, exercise tolerance and functional capacity. Key intrinsic muscle adaptations that have been observed include an increase in the proportion of type 1 fibres, an enhancement in cross-sectional fibre area, an increase in capillary-to-fibre ratio, a shift towards more fatigue resistant contractile proteins, and an increase in citrate synthase activity (an enzyme important for metabolism). Given the importance of musculoskeletal fitness for health and functional status (Warburton et al. 2001a,b Warburton et al. 2006, Warburton et al. 2010), further research is clearly warranted with persons with SCI. Accordingly, randomized, controlled exercise interventions (both arm and/or FES training) that evaluate concurrent changes in musculoskeletal fitness and health status are particularly needed.

Conclusion

There is level 4 evidence from multiple pre-post studies (Berry et al 2012; Griffin et al. 2009; Zbogar et al. 2008; Crameri et al. 2004; Hjeltnes et al. 1997; Mohr et al. 1997; Barstow et al. 1996; Faghri et al. 1992; Hooker et al. 1992) that FES training performed for a minimum of three days per week for two months may be effective for improving musculoskeletal fitness, the oxidative potential of muscle, exercise tolerance, and cardiovascular fitness.

There is level 2 evidence (Fornusek et al., 2014) that there is no difference in cardiorespiratory responses or peak values between ES leg isometric exercise compared to FES leg cycling.

There is level 4 evidence from multiple pre-post studies (Hopman et al. 2002; Gerrits et al. 2001; Ragnarsson et al. 1988) that FES training may be effective in improving exercise cardiac function in persons with SCI.

There is level 1b evidence (Bakkum et al. 2015) that there there is no difference in metabolic components between the hybrid cycle group and hand cycle group. Both groups experienced beneficial effects on metabolic syndrome components, inflammatory status and visceral adiposity. Conversely, there is level 5 evidence (Bakkum et al. 2014) that metabolic rate, heart rate, and ventilation levels are higher during hybrid cycling than during hand cycling.

There is level 4 evidence (Taylor et al. 2011) that arm-cranking exercise assisted by FES increases peak power output, and may increase oxygen uptake.

There is level 4 evidence (Kahn et al. 2010) that that FES leg cycle ergometry decreases platelet aggregation and blood coagulation in persons with SCI.

There is level 4 evidence (Hakansson et al. 2012) that the use of patterns that minimize the muscle stress-time integral can prolong FES pedaling.

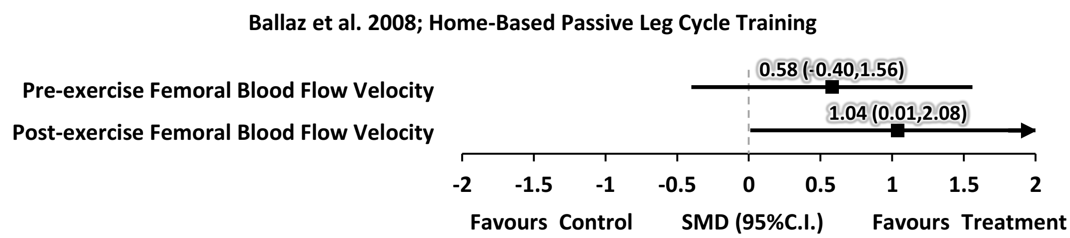
Interventions that involve FES training a minimum of 3 days per week for 2 months may improve muscular endurance, oxidative metabolism, exercise tolerance, and cardiovascular fitness.

4.4 Other Forms of Exercise Interventions

Various forms of exercise interventions have been used in an attempt to improve the health status of persons with SCI (Hopman et al. 1996, Duran et al. 2001, Ter Woerds et al. 2006, Ballaz et al. 2008, Harness et al. 2008). The forms of potential interventions are numerous and varied. As such, it is difficult to systematically review the literature regarding alternative forms of exercise interventions for SCI. Therefore, we have provided a brief summary of studies that have incorporated non-traditional forms of rehabilitation in SCI (Table 9). New technology has potential for physical activity, for example, Gaffurini et al. (2013) used Wii sport video games, and it showed that it had immediate effects on energy expenditure (EE), but training effects were not evaluated.

Table 9: Other Forms of Exercise Interventions

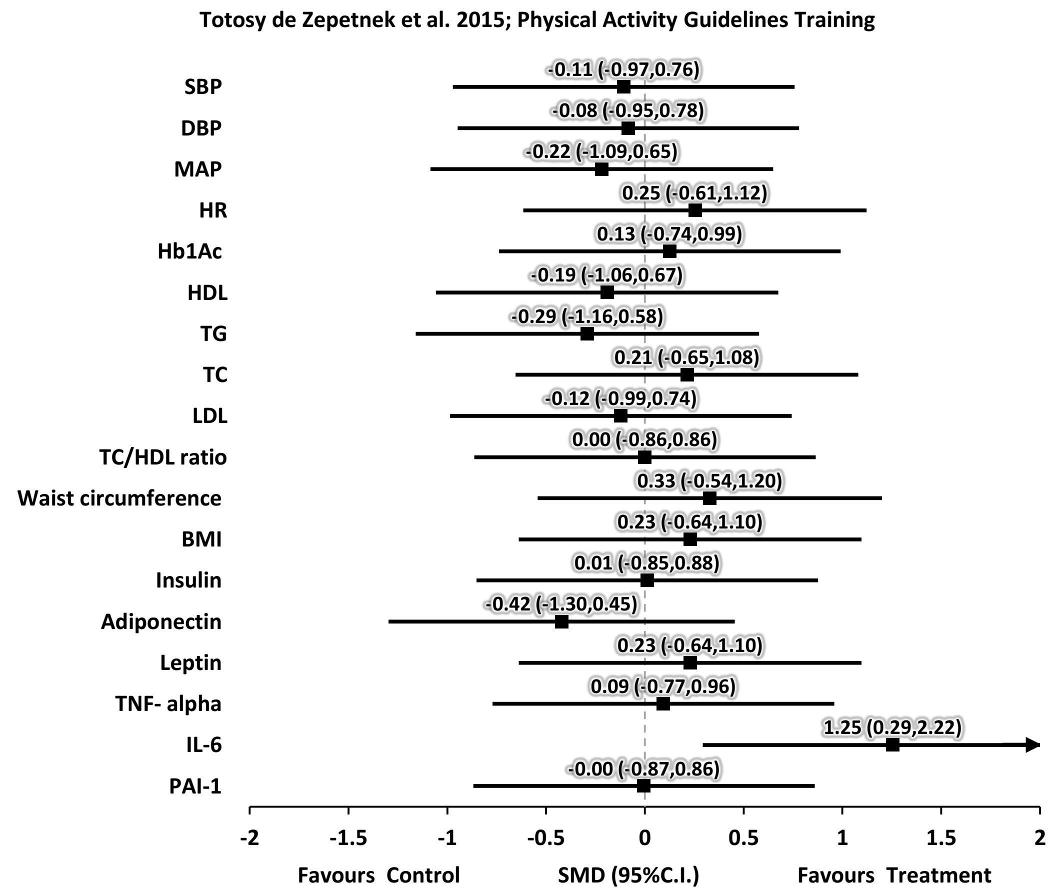
Author Year; Country Score Research Design Sample Size	Methods	Outcomes
	Active Stand Training	
Harkema et al. 2008; USA Pre-Post Level 4 N = 8	**Population:** 8 participants with tetraplegia or paraplegia **Treatment:** Active stand training for 40 and 80 sessions. **Outcome Measures:** Ability to bear weight, blood pressure and heart rate (at rest and in response to an orthostatic challenge).	1. All participants were able to bear more weight after training. 2. There was a significant increase in resting blood pressure in persons with tetraplegia after 80 training sessions (by 24%). 3. Orthostatic tolerance was improved in persons with tetraplegia (i.e., orthostatic hypotension was no longer present after 80 sessions). 4. There were no significant changes in hemodynamic parameters in persons with thoracic SCI.

<table>
<tr><th>Author Year; Country
Score
Research Design
Sample Size</th><th>Methods</th><th>Outcomes</th></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td colspan="3">Passive Cycling Exercise</td></tr>
<tr><td rowspan="2">Ballaz et al. 2008; France
PEDro = 6
RCT
Level 1
N = 17</td><td>Population: 17 participants with chronic paralegia (mean age 48 ± 8, range 35-62), divided into experimental (n = 9) and control (n = 8)
Treatment: passive cycling exercise 6 times weekly for 6 weeks
Outcome Measures: Red blood cell velocity in the common femoral artery; Velocity index (a measure of peripheral vessel resistance) was measured before and after a 10-min session of passive cycling exercise.</td><td>1. Before training, the resting mean blood flow velocity did not differ between groups.
2. In the experimental group, the post-exercise mean blood flow velocity was significantly higher after training.
3. Post exercise velocity index was significantly lower in experimental group after training.</td></tr>
<tr><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data
</td></tr>
<tr><td colspan="3">Prolonged Intense Multi-Modal Exercise (IE)</td></tr>
<tr><td>Harness et al. 2008;
USA
Prospective Controlled Trial
Level 2
N = 29</td><td>Population: 29 SCI participants, divided into intense exercise (n=21, age 37.8 ± 3.6 y, 40 ± 7 months post-injury) and control (age 34.5 ± 2.9 y, 97 ± 23 months post-injury)
Treatment: Intense exercise group: regular participation in an individually designed exercise multi-modal program focused on regaining voluntary motor function below the level of injury for 6 months; participants in the control group dictated their own level of activity
Outcome Measures: AIS scores; Medical Research Council scale (a measure of muscle strength)</td><td>1. The intense exercise group showed significantly greater gains for total AIS motor score compared to the control.
2. 15 participants in the intense exercise group, compared to 0 in the control, had at least one muscle increase in strength from 0 to 1 or more on the Medical Research Council scale.
3. 7 participants in the intense exercise group, compared to 1 in the control, had at least one muscle increase in strength from <3 to ≥3.</td></tr>
<tr><td colspan="3">Quad Rugby</td></tr>
<tr><td>Hopman et al. 1996;
The Netherlands
Pre-post
Level 4
N=21</td><td>Population: Participants divided into 3 groups according to their fitness levels. All participants had a cervical SCI (C4 to C8), tetraplegia.
1. Trained group (T) (n=8): All males; Age: 32.7±12.7; Time since injury: 8.1±10.3; Type of injury: 4 incomplete, 4 complete
2. Untrained group (U) (n=7): 6 males and 1 female; Age: 26.6±6.9; Time since injury:</td><td>1. No significant differences were found in either absolute or relative changes in the physiological responses to arm exercise for submaximal and maximal exercise over 3 or 6 months in U, T, and S groups.</td></tr>
</table>

Author Year; Country Score Research Design Sample Size	Methods	Outcomes
	6.6±5.2; Type of injury: All complete 3. Sedentary group(S) (n=6): 4 males and 2 females; Age: 36.5±10.4; Time since injury: 9.1±3.9; Type of injury: All but one with complete lesion **Treatment:** Untrained and trained group trained once a week and played 2 games/month for 6 months. Training consisted of endurance, sprint, and skill training. The U trained 42.2 min and T 21.3 min above 60% HR_{res} during training. **Outcome Measures:** Physiological responses to maximal and submaximal arm-cranking exercise.	
Passive Exercises		
Ter Woerds et al. 2006; Netherlands Prospective controlled trial Level 2 N=16	**Population:** (1) SCI group: 8 males; Age: 35±8.4; Level of injury: 7 thoracic, 1 thoracic-lumbar, range T2-L1; Type of injury: 6 AIS A, 2 AIS B; Time since injury: 8.3±6.1; Hours of exercise/week: 5.7±3.9. (2) Control group: 8 males; Age: 26±4.5; Hours of exercise/week: 4.7±2.3. **Treatment:** Each participant successively underwent 2 interventions, passive leg movements (10 minutes) and passive cycling (20 minutes). **Outcomes measures:** Leg blood flow, mean red blood cell velocity, diameter of common femoral artery, leg vascular resistance, mean arterial pressure, total peripheral resistance.	1. Blood flow, vascular resistance, and blood pressure in the common femoral artery did not change during or after 2 different passive exercise interventions in the participants with SCI or the control participants.
Wheelchair skills + weight training		
Durán et al. 2001; Colombia Case series Level 4 N=13	**Population:** 12 males and 1 female; Age: 26.3±8.3; Level of injury: All thoracic, T3-T12; Time since injury: 2-120 months; Type of injury: 11 AIS A, 1 AIS B, 1 AIS C. **Treatment:** The program lasted for 16 weeks, with a frequency of 3 sessions (120 minutes) per week. Mobility activities, aerobic resistance, strength, coordination, recreation, and relaxation were combined. The specific aerobic program lasted 11 weeks, including a 4-week adaptation and 1-week enhancement period. Progressively led to 40 minutes of aerobic training at 40% to 60% HR reserve. **Outcome measures:** FIM (functional independence measure), arm crank exercise test, lipid levels	1. Pre-training FIM scores mean 106±7 vs. 113±7 post-training. Highest increase occurred in mobility. 2. Lipid profiles and average resting heart rate did not change. 3. Maximum resistance achieved during arm exercise test increased from 90±24 watts to 110±26 watts. 4. HR at 6 minutes after exercise test decreased from 115±19 bpm to 108±19 bpm.
Whole Body Vibration		

Author Year; Country Score Research Design Sample Size	Methods	Outcomes
Yarar-Fisher et al. 2013 USA Randomized cross-over trial Level 1 N=21	**Population:** 11 males with SCI (C4-T6, ASIA- A or B) and 10 able bodied individuals **Intervention:** 3 whole body vibration (WBV) exercise sessions at 30, 40, 50 Hz. **Outcome measures:** Heart rate, mean arterial blood pressure (MAP), stroke volume (SV), cardiac output (CO), oxygen consumption (VO2), relative changes in oxygenated (HbMbO2), deoxygenated (HHbMb) and total (HbMbtot) heme groups	1. No significant interactions or main effects in either group for HR, MAP, SV, and CO. 2. Both groups demonstrated small but significant increases after WBV in VO_2, [HbMbO2] and [HbMbtot] but the response was greater in the SCI group. 3. Significant decrease in HHbMb was observed in the SCI group.
General Physical Activity		
Totosy de Zepetnek et al. 2015 Canada PEDro=4 RCT Level 2 N=17	**Population:** 23 individuals with SCI from C3-T11. 12 randomly assigned to Physical Activity Guidelines (PAG) training and 11 maintained existing physical activity levels with no guidance or training intensity. **Treatment:** PAG training involving at least 20 minutes of moderate-vigorous aerobic exercise and 3X10 repetitions of upper body strengthening exercise at 2 times per week for 16 weeks. The control group maintained existing physical activity levels with no guidance on training intensity. **Outcome measure:** Blood biomarkers, body composition, arterial structure, arterial stiffness and function (i.e. heart rate, blood pressure, carotid pulse pressure, distensibility)	1. There were decreases in whole body mass, whole body fat, visceral adipose tissue (VAT), and carotid distensibility in the control group. Whereas, the PAG group maintained body composition and carotid stiffness. 2. No other interactions found for other measures of carotid artery structure, indices of regional artery stiffness or vascular function. PAG did not elicit changes in other CVD risk factors. 3. No change in fasting insulin, leptin, adipokines, inflammatory markers, and thrombotic markers in either group
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data	

Author Year; Country Score Research Design Sample Size	Methods	Outcomes



Ravensbergen et al. 2014 Netherlands Longitudinal Level 2 N=110	**Population:** 110 participants, 74% male, 36% cervical lesion, 16% high thoracic lesion, 47% low level lesion, 59% AIS-A, 41% AIS B,C,D. **Treatment:** None. All underwent standard active inpatient rehabilitation **Outcome Measures:** Cardiovascular variables including resting systolic (SAP) and diastolic arterial pressures (DAP), resting and peak heart rates (HR peak), were measured on 5 test occasions: start of inpatient rehab, 3 months later, at discharge and at 1 and 5 years after discharge.	1. No significant change in the prevalence of hypotension during rehabilitation and for 5 years after discharge. 2. No significant change over time in SAP. DAP did not change during the period of rehabilitation but increased in the first 5 years after discharge. 3. SAP and DAP were significantly lower in those with cervical lesions compared with those with high thoracic and low level lesions. 4. No significant change over time in HR peak. HR rest decreased significantly during inpatient rehab and decreased further from time of discharge to 5 years after discharge. Lesion level was negatively associated with HR peak and HR rest and age was negatively associated with HR peak. No significant change in the prevalence of bradycardia over time. Prevalence of an elevated

Author Year; Country Score Research Design Sample Size	Methods	Outcomes
		HR improved during and after rehabilitation.
De Rossi et al. 2014 Brazil Cross-sectional study Level 5 N= 87	**Population:** 58 SCI men (29 sedentary- SCI-S and 29 athletes SCI-A) with at least 1 year of SCI, 50 SCI participants were ASIA A and 8 were ASIA B. 29 able-bodied men (AB) acted as controls. **Treatment:** None **Outcome Measures:** Cumulative training time, body mass index, blood pressure, glucose, lipid fractions, C-reactive protein. Aortic root, Left ventricle and left atrial dimensions, cardiac output, mitral inflow velocity, peak early inflow velocity, peak atrial inflow velocity, peak early/atrial velocity ratio	1. SCI-S presented similar left ventricular (LV) structural and systolic parameters but higher E/Em and lower Em/Am ratios that SCI-A and AB. 2. Tetraplegic athletes had similar features compared with sedentary tetraplegic participants, except for higher E/Em ratio and lower Em values. 3. Paraplegic athletes had similar features compared with sedentary paraplegic individuals, except for higher LV end-diastolic diameter, Em/Am ratio, stroke volume, lower heart rate and relative wall thickness. 4. No correlation detected between training time and cardiac features. In paraplegic athletes, cumulative training time correlated with stroke volume, LV end-diastolic diameter, relative wall thickness, LV mass index and LV end systolic diameter.
Serra et. al 2014 Spain Cross-sectional Level 5 N=78	**Population:** 42 paraplegic participants (T2-T12, AIS A or B) and 36 able bodied (AB) participants. **Treatment:** None. Paraplegic group went about their normal physical activities (22 participants ≥ 3 hrs/week of sport vs. 20 who was active for < 3 hrs/week) **Outcome measures:** Heart Rate variability (HRV)	1. Significant differences between paraplegic and AB participants in some variables in the time domain, frequency domain, and nonlinear analyses. 2. When power was normalized, there were no differences between the two groups. 3. There was reduced variability in paraplegic participants who adopted a sedentary lifestyle. There was only a significant difference in detrended fluctuation in heart rate variability between the sedentary and active paraplegic groups. 4. No differences in autonomic cardiac control between those with different levels of injury (above or below T6).
Schreiber et al. 2014 Cross-sectional Level 5 Brazil N=42	**Population**: 19 SCI men (sedentary- S-SCI) and 23 physically active men (PA-SCI) (ASIA A or B) **Treatment**: None. S-SCI did not perform sports, recreational activity or labor that required physical effort. PA-SCI comprised competing athletes regularly performing wheelchair sports for at least 1 year. **Outcome measures:** Concentration of matrix metalloproteinases (MMPS) and tissue inhibitors of MMPs (TIMPs),	1. PA-SCI participants presented lower pro-MMP-2 and pro-MMP-2/TIMP-2 levels compared to S-SCI participants.. 2. No differences in structural cardiac variables and measurements of systolic function between S-SCI and PA-SCI groups. 3. S-SCI group presented echocardiographic features of reduced LV diastolic function (lower E/A ratio and Em and higher E/Em ratio vales) in comparison with the PA-SCI group.

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcomes**
	echocardiographic parameters (i.e. LV mass, LV diastolic function)	4. The significant difference between the 2 groups for E/A ratio, Em, and E/Em ratio became insignificant after adjustment for pro-MMP-2 levels. (This suggests that pro-MMP-2 might play a role in LV diastolic function improvements induced by regular physical activity in SCI participants.)
Currie et al. 2014 Canada Cross-sectional Level 5 N= 21	**Population:** 8 non-athletic men with SCI and 13 athletic men with SCI. All have tetraplegia (C4 – C8), traumatic motor complete cervical SCI for more than one year. **Treatment:** None. Regular hours of physical activity for both groups **Outcome measures:** Sympathetic function including palmar sympathetic skin responses (SSR) to median nerve stimulation, systolic (SPB) and diastolic blood pressure (DBP) in response to passive sit up. Peak heart rate (HR) during maximal exercise test on electrically braked arm-cycle ergometer.	1. Compared to the athletic group, the non-athletic group exhibited lower peak HR as well as greater reductions in SPB and DPB in response to passive sit-up.
Overground Training For Gait Rehabilitation		
Evans et al. 2015 USA Pre-post Level 4 N= 5	**Population**: 4 males and 1 female; average age 42 ± 9y; chronic spinal cord injury; AIS A. **Treatment**: Expired gases were collected during maximal graded exercise testing and two, 6-minute bouts of exoskeleton-assisted walking overground. **Outcome Measures:** Peak oxygen consumption (V. O2peak), average oxygen consumption (V. O2avg), peak heart rate (HRpeak), walking economy, metabolic equivalent of tasks for SCI (METssci), walk speed, and walk distance.	1. Significant differences were observed between walk-1 and walk-2 for walk speed, total walk distance, V. O2avg, and METssci 2. Exoskeleton-assisted walking resulted in %VO2peak range of 51.5% to 63.2%. The metabolic cost of exoskeleton-assisted walking ranged from 3.5 to 4.3 METssci. -Semen collected by PVS (6 pregnancies) and EEJ.
Stationary Cycling and Uphill Treadmill Walking		
Wouda et al. 2015 Norway PEDro= 6 RCT Level 1 N= 30	**Population**: 22 males and 8 females; mean age 41y; incomplete spinal cord injury; AIS D; 4-14 y post injury **Treatment**: 15 participants with incomplete SCI and 15 control participants performed sub-maximal and maximal exercise tests of both stationary cycling and uphill treadmill walking on separate days. **Outcome Measures:** VO2, VCO2, respiratory exchange ratio (RER), heart rate (HR)	1. RER was significantly higher for the SCI group during the cycle test compared to the uphill treadmill walking test. Control participants exhibited significantly higher peak VO2 during the treadmill test as compared with the cycle test.

Discussion

The evidence supporting non-traditional forms of exercise interventions in SCI is not clear. This is to be expected given the varied training methodologies that can be employed. The lack of concrete information should not however dissuade researchers from considering non-traditional rehabilitation models when for the SCI population. It is clear that novel models of exercise rehabilitation are warranted and desired in the rehabilitation of SCI. For instance, stand locomotor training has been shown to be highly effective in improving blood pressure control and orthostatic tolerance in persons with tetraplegia.

Some modalities of exercise that have been applied with success in able-bodied individuals (such as interactive video games (Warburton et al. 2007a)) or other clinical populations (e.g. interval training (Warburton et al. 2005)) may hold great promise for persons with SCI. As with early research with FES, it is essential that researchers demonstrate innovative thinking that is based upon a strong theoretical foundation. In addition, it is essential to find exercise routines and modalities that an individual can continue with in the long term. Interactive video games or circuit training might offer affordable and accessible approaches that maintain the interest of the person.

Conclusion

There is level 4 evidence (Fisher et al. 2013) that whole body vibration training increases VO2.

There is level 5 evidence (Guilherme et al. 2014, Schreiber et al. 2014) that tetraplegic and paraplegic athletes, with regular physical activity, have improved left ventricular diastolic function. There is level 5 evidence (Currie et al., 2014) that tetraplegic athletes compared to non-athletic group have higher peak HR and lower reductions in systolic and diastolic blood pressure.

There is level 2 evidence (Totosy de Zepetnek et al, 2015) that moderate to vigorous aerobic exercise training maintained body composition and carotid stiffness in individuals with SCI. The training program had no impact on other CVD risk factors.

5.0 Glucose Homeostasis

Glucose intolerance and decreased insulin sensitivity are independent risk factors for CVD (Hurley and Hagberg 1998). Abnormal glucose homeostasis is associated with worsened lipid lipoprotein profiles and an increased risk for the development of hypertension and type 2 diabetes (Hurley and Hagberg 1998, Warburton et al. 2001b, 2001a). It is well-established that habitual physical activity is an effective primary preventative strategy against insulin resistance and type 2 diabetes in the general population (Warburton et al. 2006). Although comparatively less information is available for SCI, it appears that exercise training programs are effective in improving glucose homeostasis (Hjeltnes et al. 1998, Chilibeck et al. 1999, de Groot et al. 2003, Phillips et al. 2004, Mahoney et al. 2005, Jeon et al. 2010). Key terms used when assessing glucose homeostasis are provided in Table 10.

Table 10: Glucose Homeostasis Key Terms

Oral Glucose Tolerance Test (OGTT)	• Involves the ingestion of glucose and the subsequent serial blood analysis of glucose levels to determine the rate of blood glucose removal. Common test used in the diagnosis of diabetes.
Insulin Sensitivity	• Refers to the sensitivity of target cells (muscle, hepatic cells and adipose) to insulin.
Blood Glucose	• Refers to blood levels of glucose (a simple sugar, carbohydrate).

	High fasting blood glucose levels reflects pre-diabetic or diabetic conditions.
Blood Insulin	• Refers to blood levels of insulin (a hormone that regulates carbohydrate metabolism).
Glucose Transporters (GLUT-4)	• Glucose transporters are important membrane proteins that facilitate the transport of glucose through the cellular membrane. GLUT4 is an insulin-regulated glucose transporter located in adipose and muscle tissues.
Glycogen Synthase	• Enzyme involved in the synthesis of glycogen from glucose.
Hexokinase	• An enzyme that acts during carbohydrate metabolism. In the first step of glycolysis, hexokinase phosphorylates (transfers phosphate from ATP) glucose to prepare it for subsequent breakdown for use in energy production.
Citrate Synthase	• Citrate synthase is an important enzyme in the Citric Acid Cycle (Krebs cycle).
Phosphofructokinase	• Phosphofructokinase (PFK) is an important regulatory enzyme of glycolysis.

Table 11: Effects of Exercise Training on Glucose Metabolism in Persons with Spinal Cord Injury

Author, Year; Country Score Research Design Sample Size	**Methods**	**Outcomes**
de Groot et al. 2003; Netherlands PEDro = 7 RCT Level 1 N = 6	**Population:** 4 male, 2 female, C5-L1, AIS A (*n* = 1), B (*n* = 1), and C (*n* = 4), age 36 yrs, 116 d post-injury. **Treatment:** Randomized to low-intensity (50%–60% HRR) or high-intensity (70%–80% HRR) arm ergometry, 20 min/d, 3 d/wk, 8 wks. **Outcome Measures:** VO_2peak, insulin sensitivity, blood glucose.	1. There was a significant difference in insulin sensitivity between groups, with a non-significant decline in the high-intensity group and a significant improvement in the low-intensity group with training. 2. A positive correlation between VO_2peak and insulin sensitivity ($r = 0.68$, $p = 0.02$).
Jeon et al. 2010; Canada Pre-post Level 4 N = 6	**Population:** 6 male participants with paraplegia participated in the study (mean age, 48.6 ± 6.0 y; mean weight, 70.1 ± 3.3 kg; injury levels between T4-5 and T10). **Treatment:** 12 weeks of FES-rowing exercise training 3 to 4 times a week (600–800 kcal). **Outcome measures:** VO_2peak, plasma leptin, insulin, and glucose levels, insulin sensitivity, body composition.	1. VO_2peak increased from 21.4 ± 1.2 to 23.1 ± 0.8 $mL \cdot kg^{-1} \cdot min^{-1}$ (P = 0.048). 2. Plasma leptin levels were significantly decreased after the training (pre: 6.91 ± 1.82 $ng \cdot dL^{-1}$ vs. post: 4.72 ± 1.04 $ng \cdot dL^{-1}$; P = 0.046). 3. Plasma glucose and leptin levels were significantly decreased after exercise training by 10% and 28% (P = 0.028), respectively. 4. Plasma glucose, Leptin levels and Whole body fat decreased but did not reach statistical significance.
Mahoney et al. 2005; USA Pre-post Level 4 N = 5	**Population:** 5 males, complete SCI, C5-T10, AIS grade A, age 35.6 yrs, 13.4 yrs post-injury. **Treatment**: Home-based neuromuscular electric stimulation-induced resistance exercise training, 2 d/wk, 12 wks.	1. All participants had normal fasting glucose levels before and after training. 2. There were no significant changes in blood glucose or insulin with training. However, there was a trend towards reduced plasma glucose levels ($p = 0.074$).

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	Outcome Measures: quadriceps femoris muscle cross-sectional area, plasma glucose, insulin.	
Phillips et al. 2004; Canada Pre-post Level 4 N = 9	**Population:** 8 male, 1 female, incomplete AIS C, C4-T12, 8.1 yrs post-injury. **Treatment:** Body-weight–supported treadmill walking, 3 d/wk, 6 months. **Outcome Measures:** whole-body dual-energy X-ray absorptiometry (to capture body composition and bone density), GLUT4 protein abundance, hexokinase activity, oral glucose tolerance tests, glucose oxidation, CO_2 breath analysis.	1. Reduction in the area under the curve for glucose (-15%) and insulin (-33%). 2. The oxidation of exogenous (ingested) glucose and endogenous (liver) glucose increased (68% and 36.8%, respectively) after training. 3. Training resulted in increased muscle glycogen, GLUT-4 content (glucose transporter) (126%), and hexokinase II enzyme activity (49%).
Jeon et al. 2002; Canada Pre-post Level 4 N = 7	**Population:** 5 male, 2 female, motor complete, C5-T10, ages 30-53 yrs, 3–40 yrs post-injury. **Treatment:** FES leg-cycle training, 30 min/d, 3 d/wk, 8 wks. **Outcome Measures:** oral glucose tolerance test (OGTT), glucose and insulin levels, glucose utilization, insulin sensitivity and levels.	1. There were significantly lower (14.3%) 2-hr OGTT glucose levels after 8 wk of training. 2. Glucose utilization was higher for all 3 participants and insulin sensitivity was higher for 2 of the 3 participants during posttraining 2-hr clamp test.
Mohr et al. 2001; Denmark Pre-post Level 4 N = 10	**Population:** 8 male, 2 female, 6 tetraplegia, 4 paraplegia, C6-T4, age 35 yrs, 12 yrs post-injury. **Treatment:** FES cycling, 30 min/d, 3 d/wk, 12 months; 7 participants completed an additional 6 months (1 d/wk). **Outcome Measures:** insulin-stimulated glucose uptake, oral glucose tolerance test (OGTT), GLUT 4 glucose transporter protein.	1. Insulin-stimulated glucose uptake rates increased after intensive training. 2. With the reduction in training, insulin sensitivity decreased to a similar level as before training. GLUT-4 increased by 105% after intense training and decreased again with the training reduction. The participants had impaired glucose tolerance before and after training, and neither glucose tolerance nor insulin responses to OGTT were significantly altered by training.
Chilibeck et al. 1999; Canada Pre-post Level 4 N = 5	**Population:** 4 male, 1 female, motor complete C5-T8, ages 31–50 yrs, 3–25 yrs post-injury. **Treatment:** FES leg-cycle ergometry training, 30 min/d, 3 d/wk, 8 wks. **Outcome Measures:** glucose transporters (GLUT-4, GLUT-1), oral glucose tolerance test, citrate synthase.	1. Training resulted in increases in GLUT-1 (52%) and GLUT-4 (72%). 2. There was a training-induced increase in citrate synthase activity (56%) and an improvement in the insulin sensitivity index as determined from oral glucose tolerance test.
Hjeltnes et al. 1998; Sweden Pre-post Level 4 N = 5	**Population:** 5 males, C5-C7, all complete AIS A, age 35 yrs, 10 yrs post-injury. **Treatment:** Electrically stimulated leg cycling exercise, 7 d/wk, 8 wks. **Outcome Measures:** peripheral insulin sensitivity, whole body glucose utilization, glucose transport, phosphofructokinase, citrate synthase, hexokinase, glycogen	1. After training, insulin-mediated glucose disposal was increased by 33%. There was a 2.1-fold increase in insulin-stimulated glucose transport. 2. Training led to marked increases in protein expression of GLUT4 (glucose transporter) (378%), glycogen synthase (526%), and hexokinase II (204%) in the vastus lateralis muscle. 3. Hexokinase II activity increased 25%

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
	synthase, blood glucose, plasma insulin.	after training.

Note: AIS = ASIA Impairment Scale; d = day; FES = functional electrical stimulation; HRR = heart rate reserve; min = minute; OGTT = oral glucose tolerance test; RCT = randomized controlled trial; SCI = spinal cord injury; wk = week.

Discussion

The majority of the data is from experimental non-RCT trials. A search of the literature revealed eight investigations (*n* = 54). This included one RCT (de Groot et al. 2003) and seven experimental non-RCT (pre-post) trials (Hjeltnes et al. 1998, Chilibeck et al. 1999, Mohr et al. 2001, Jeon et al. 2002, Phillips et al. 2004, Mahoney et al. 2005, Jeon et al. 2010). The single RCT involved the randomization to two different forms of exercise, and, as such, an exercise condition served as the control (Table 11). The majority (six) of these trials examined the effectiveness of FES training.

Similar to other studies in the field of SCI research, this area of investigation is limited by the lack of quality RCTs. Moreover, the majority of the research relates to the effects of FES training. Limited work has been conducted using aerobic and/or resistance exercise training. As a whole, however, these studies are consistent and reveal several important findings. For instance, the improvements in glucose homeostasis may be the result of increased lean body mass (and associated changes in insulin sensitivity) and increased expression of GLUT-4, glycogen synthase, and hexokinase in exercised muscle.

Consistent with findings in able-bodied individuals (Warburton et al. 2001b, 2001a), the improvement in glucose homeostasis after exercise interventions (e.g., aerobic training or FES) does not appear to be related solely to decreases in body adiposity and/or increases in VO_2max. This is due to the fact that significant improvements in glucose homeostasis can occur with minor changes in body composition (weight and fat to muscle ratios) and/or aerobic fitness.

It is also important to note that there appears to be a minimal volume of exercise required for improvements in glucose homeostasis. For instance, Mohr et al.(Mohr et al. 2001) revealed that beneficial changes in insulin sensitivity and GLUT-4 protein observed during a three days/week FES training program were not maintained when FES training was reduced. (For a more detailed discussion on inter-relationship of diet and SCI, please refer to Nutrition chapter at: https://scireproject.com/evidence/rehabilitation-evidence/nutrition-issues-following-spinal-cord-injury/.)

Conclusion

There is level 1b evidence from 1 RCT (de Groot et al. 2003) and multiple level 4 studies (Chilibeck et al. 1999, Mohr et al. 2001, Jeon et al. 2002, Jeon et al. 2010) that both aerobic and FES training (approximately 20–30 min/day, three days/week for eight weeks or more) are effective in improving glucose homeostasis in persons with SCI.

There is level 4 evidence from multiple pre-post studies that the changes in glucose homeostasis after aerobic or FES training are clinically significant for the prevention and/or treatment of type 2 diabetes.

Aerobic and FES exercise training may lead to clinically significant improvements in glucose homeostasis in persons with SCI. Preliminary evidence indicates that a minimum of 30 min of moderate intensity training on 3 days per week is required to achieve and/or maintain the benefits from exercise training.

6.0 Lipid Lipoprotein Profiles

Abnormal lipid lipoprotein profiles have been associated with an increased risk for CVD (Hurley and Hagberg 1998, Warburton et al. 2001b, 2001a, Warburton et al. 2006). Several studies have revealed worsened lipid lipoprotein profiles in persons with SCI (Brenes et al. 1986, Dearwater et al. 1986, Bauman et al. 1992a, Krum et al. 1992, Maki et al. 1995, Dallmeijer et al. 1997). Routine physical activity has been shown to enhance lipid lipoprotein profiles by reducing triglycerides (TG), increasing HDL, and lowering LDL/HDL in the general population (Warburton et al. 2001b, 2001a, Warburton et al. 2006). Although limited, similar findings have been observed in persons with SCI (Hooker and Wells 1989, Solomonow et al. 1997, Nash et al. 2001, de Groot et al. 2003, Stewart et al. 2004, El-Sayed and Younesian 2005) (Table 12).

Table 12: Effects of Exercise Training on Lipid Lipoprotein Profiles in Persons with Spinal Cord Injury

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
de Groot et al. 2003; Netherlands PEDro = 7 RCT Level 1 N = 6	**Population:** 4 male, 2 female, C5-L1, AIS A (*n* = 1), B (*n* = 1), and C (*n* = 4), age 36 yrs, 116 d post-injury. **Treatment:** Randomized to low-intensity (50%–60% HRR) or high-intensity (70%–80% HRR) arm ergometry; 20 min/d, 3 d/wk, 8 wks. **Outcome Measures:** lipid profiles including total cholesterol (TC), HDL, LDL, triglycerides (TG).	1. The TC/HDL ratio and triglycerides decreased significantly more in the high-intensity group.
Hooker & Wells 1989; USA Prospective controlled trial Level 2 N = 8	**Population:** Low-intensity group: *n* = 6, 3 male, 3 female, C5-T10, age 26–36 yrs, 3 months to 19 yrs post-injury; moderate-intensity group: *n* = 5, 3 male, 2 female, C5-T9, age 23–30 yrs, 2–19 yrs post-injury. **Treatment:** Wheelchair ergometry 20 min/d, 3 d/wk, 8 wks: low-intensity (50%–60% max HRR) and moderate intensity (70%–80% max HRR). **Outcome Measures:** total cholesterol (TC), triglycerides, HDL, LDL.	2. No change in lipid levels in low-intensity group. 3. Significant increases in HDL and decreases in triglycerides, LDL, and the TC/HDL ratio in the moderate intensity group.
El-Sayed et al. 2005; UK Pre-post Level 4 N = 12	**Population:** 5 SCI, lesion below T10, age 32 yrs; 7 AB controls, age 31 yrs. **Treatment:** Arm ergometry, 30 min/d (60%–65%VO_2peak), 3 d/wk, 12 wks. **Outcome Measures:** VO_2peak, peak HR, peak workload, total cholesterol (TC), triglycerides, HDL.	1. Training improved HDL but did not alter TC or triglycerides.
Stewart et al. 2004; Canada Pre-post	**Population:** 8 male, 1 female, incomplete AIS C, C4-T12, 8.1 yrs post-injury. **Treatment:** Body-weight–supported	1. There were significant reductions in TC (-11.2%), LDL (-12.9%), and TC/HDL (-19.8%).

Author, Year; Country Score Research Design Sample Size	Methods	Outcomes
Level 4 N = 9	treadmill training, 3 d/wk, 6 months. **Outcome Measures:** ambulatory capacity (Wernig Walking Scale), cholesterol, HDL, LDL, triglycerides.	
Nash et al. 2001; USA Pre-post Level 4 N=5	**Population:** 5 males, complete lesions T6-L1, age 37.8 yrs, 4.8 yrs post-injury. **Treatment:** Circuit resistance training (50%–60%1 repetition maximum), 3 d/wk, 12 wks. **Outcome Measures:** VO_2peak, time to fatigue, TC, triglycerides, HDL, LDL.	1. There were significant decreases in LDL, LDL/HDL, and TC/HDL after training.
Solomonow et al. 1997; USA Pre-post Level 4 N = 70/33	**Population:** All participants had paraplegia, no other details given. **Treatment:** Reciprocating gait orthosis powered with electrical muscle stimulation, 3 hr/wk, 14 wks. **Outcome Measures:** cholesterol, LDL, HDL	1. There were significant reductions in total cholesterol, LDL, LDL/HDL ratio, and TC/HDL ratio in 8 patients with initially high total cholesterol levels (>200 $mg \cdot dL^{-1}$).

Note: AIS = ASIA Impairment Scale; d = day; HDL = high-density lipoprotein; hr = hour; HRR = heart rate reserve; LDL = low-density lipoprotein; min = minute; RCT = randomized controlled trial; TC = total cholesterol; wk = week; yrs = year.

Discussion

The information regarding the effects of exercise training on lipid lipoprotein profile is derived from one high-quality RCT (level 1b) (de Groot et al. 2003), one nonrandomized, prospective controlled trial (level 2) (Hooker and Wells 1989), and several level 4 studies (Solomonow et al. 1997, Nash et al. 2001, Stewart et al. 2004, El-Sayed and Younesian 2005) (*N* = 110). The majority of the investigations examined a form of aerobic training (either arm ergometry or assisted treadmill walking). Another investigation examined the effects of reciprocating gait orthosis powered with electrical muscle stimulation.

These findings provide level 1b evidence (based on one high-quality RCT and several lower quality studies) for the role of exercise in the reduction of atherogenic lipid lipoprotein profiles and the reduction of the risk for CVD in persons with SCI. It appears that a minimal threshold of training exists for changes in lipoprotein profile. Authors have reported that 70% of maximal HR reserve (for at least 20 min/day, three days/week for eight weeks) is the threshold necessary to achieve significant improvements in lipid lipoprotein profiles. Future research is warranted, however, to quantify the effects of varying forms of exercise (including aerobic exercise, resistance exercise, and FES) on lipid lipoprotein profiles in persons with SCI.

Conclusion

There is level 1b evidence from 1 high quality RCT (de Groot et al. 2003) to suggest that aerobic exercise training programs (performed at a moderate to vigorous intensity 20-30 min/day, 3 days per week for 8 weeks) are effective in improving the lipid lipoprotein profiles of persons with SCI.

Preliminary evidence (level 4; Solomonow et al. 1997) also indicates that the use of a reciprocating gait orthosis with FES training (3 hours/week, for 14 weeks) may improve lipid lipoprotein profiles in SCI.

Aerobic exercise, in a variety of approaches including arm ergometry and FES exercise training may lead to improvements in lipid lipoprotein profile that are clinically relevant for the at risk SCI population. The optimal training program for changes in lipid lipoprotein profile remains to be determined. However, a minimal aerobic exercise intensity of 70% of heart rate reserve on most days of the week appears to be a good general recommendation for improving lipid lipoprotein profile in persons with SCI.

Table 13: Effect of Other Interventions on Cardiovascular Parameters in Persons with Spinal Cord Injury

Kostovski et al. 2015 Norway Randomized controlled crossover trial Level 1 N=12	**Population:** 6 men with long-standing complete tetraplegia (C5-C8), 6 able-bodied men as control group **Treatment:** Capsules with placebo or 2mg melatonin given 4 days before taking a plasma sample. Able-bodied group received no intervention. **Outcome measures:** Hemostatic markers through 24 hour plasma profiles (i.e. Activated factor VII, free TPFI antigen, von Willbrand factor, D-dimer), melatonin concentrations	1. Compared with able-bodied group, the tetraplegic groups with or without melatonin supplementation showed an apparent increase in the circadian variation of fragment 1+2. 2. There was no difference in the circadian pattern for D-dimer.

Table 14: Management of the Risk for Cardiovascular Disease in Persons with Spinal Cord Injury through Aerobic Exercise Training Interventions

Risk factor		Strength of evidence	Literature support, references
Cardiovascular fitness	• Increased exercise tolerance	Level 1b	(Gass et al. 1980, DiCarlo et al. 1983, DiCarlo 1988, Hjeltnes and Wallberg-Henriksson 1998, Jacobs et al. 2002, de Groot et al. 2003, Sutbeyaz et al. 2005)
	• Increased VO_{2max}	Level 1b	(Gass et al. 1980, DiCarlo et al. 1983, Cooney and Walker 1986, DiCarlo 1988, Jacobs et al. 2002, de Groot et al. 2003, El-Sayed et al. 2004, Sutbeyaz et al. 2005)
	• Increased cardiac output	Level 2	(Davis et al. 1987, Davis et al. 1991)
	• Reduced submaximal exercise heart rate	Level 4	(DiCarlo 1988)
	• Increased maximal heart rate	Level 4	(Sutbeyaz et al. 2005)
	• Increased stroke volume	Level 2	(Davis et al. 1987, Davis et al. 1991)
	• Decreased total peripheral resistance	Level 2	(Davis et al. 1987, Davis et al. 1991)
	• Increased power output	Level 1b	(Cooney and Walker 1986, DiCarlo 1988, Hjeltnes and Wallberg-Henriksson 1998, Jacobs et al. 2002, de Groot et al. 2003, Hicks et al. 2003, Sutbeyaz et al. 2005)

Risk factor		Strength of evidence	Literature support, references
	• Intrinsic cellular adaptations that facilitate oxidative metabolism	Level 4	(Stewart et al. 2004)
Lipid lipoprotein profile	• Increased HDL cholesterol	Level 2	(Hooker and Wells 1989, Nash et al. 2001, El-Sayed and Younesian 2005)
	• Reduced LDL cholesterol	Level 1	(Hooker and Wells 1989, Nash et al. 2001, de Groot et al. 2003, Stewart et al. 2004)
	• Reduced triglycerides	Level 1b	(de Groot et al. 2003)
	• Reduced total cholesterol	Level 1b	(Hooker and Wells 1989, de Groot et al. 2003, Stewart et al. 2004)
Glucose homeostasis	• Increased insulin sensitivity, decreased insulin resistance, and/or improved glucose tolerance.	Level 1b	(de Groot et al. 2003)

Note: HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Table 15: Management of the Risk for Cardiovascular Disease in Persons with Spinal Cord Injury through Functional Electrical Stimulation Training Interventions

Risk factor		Strength of evidence	Literature support (references)
Cardiovascular fitness	• Increased exercise tolerance	Level 4	(Pollack et al. 1989, Hooker et al. 1992, Barstow et al. 1996, Mohr et al. 1997, Wheeler et al. 2002, Thijssen et al. 2005)
	• Increased VO_2max/VO_2peak	Level 4	(Pollack et al. 1989, Hooker et al. 1992, Barstow et al. 1996, Hjeltnes et al. 1997, Mohr et al. 1997, Wheeler et al. 2002, Thijssen et al. 2005)
	• Increased cardiac output	Level 4	(Hooker et al. 1992)
	• Reduced submaximal exercise heart rate	Level 4	(Faghri et al. 1992)
	• Increased stroke volume	Level 4	(Faghri et al. 1992)
	• Decreased total peripheral/vascular resistance	Level 4	(Faghri et al. 1992)
	• Increased power output	Level 4	(Faghri et al. 1992, Hooker et al. 1992, Thijssen et al. 2005)
	• Intrinsic cellular adaptations that facilitate oxidative metabolism	Level 4	(Andersen et al. 1996, Mohr et al. 1997, Crameri et al. 2002, Crameri et al. 2004)
Lipid lipoprotein profile	• Reduced LDL cholesterol	Level 4	(Solomonow et al. 1997)
	• Reduced total cholesterol	Level 4	(Solomonow et al. 1997)
Glucose homeostasis	• Increased insulin sensitivity, decreased insulin resistance, and/or improved glucose tolerance.	Level 4	(Jeon et al. 2002)

Note: LDL = low-density lipoprotein.

7.0 References

Alexeeva N, Sames C, Jacobs PL, Hobday L, DiStasio MM, Mitchell SA, Calancie B. Comparison of training methods to improve walking in persons with chronic spinal cord injury: a randomized clinical trial. J Spinal Cord Med 2011; 34: 362-79.

Andersen JL, Mohr T, Biering-Sorensen F, Galbo H, Kjaer M. Myosin heavy chain isoform transformation in single fibres from m. vastus lateralis in spinal cord injured individuals: effects of long-term functional electrical stimulation (FES). Pflugers Arch 1996; 431: 513-8.

Anderson TJ. Nitric oxide, atherosclerosis and the clinical relevance of endothelial dysfunction. Heart Fail Rev 2003; 8: 71-86.

Ballaz L, Fusco N, Cretual A, Langella B, Brissot R. Peripheral vascular changes after home-based passive leg cycle exercise training in people with paraplegia: a pilot study. Arch Phys Med Rehabil 2008; 89: 2162-6.

Bakkum AJT, de Groot S, Onderwater MQ, de Jong J, Janssen TWJ. Metabolic rate and cardiorespiratory response during hybrid cycling versus handcycling at equal subjective exercise intensity levels in people with spinal cord injury. J Spinal Cord Med 2014; 37:758-64

Bakkum AJT, de Groot S, Stolwijk-Swüste ,JM, van Kuppevelt ,DJ, van der Woude ,LHV., Janssen TWJ. Effects of hybrid cycling versus handcycling on wheelchair-specific fitness and physical activity in people with long-term spinal cord injury: a 16-week randomized controlled trial. Spinal Cord. 2015; 53:395-401

Barstow TJ, Scremin AM, Mutton DL, Kunkel CF, Cagle TG, Whipp BJ. Changes in gas exchange kinetics with training in patients with spinal cord injury. Med Sci Sports Exerc 1996; 28: 1221-8.

Barstow TJ, Scremin AM, Mutton DL, Kunkel CF, Cagle TG, Whipp BJ. Peak and kinetic cardiorespiratory responses during arm and leg exercise in patients with spinal cord injury. Spinal Cord 2000; 38: 340-5.

Bauman WA, Adkins RH, Spungen AM, Herbert R, Schechter C, Smith D, Kemp BJ, Gambino R, Maloney R, Waters RL. Is immobilization associated with an abnormal lipoprotein profile? Observations from a diverse cohort. Spinal Cord 1999a; 37: 485-93.

Bauman WA, Adkins RH, Spungen AM, Kemp BJ, Waters RL. The effect of residual neurological deficit on serum lipoproteins in individuals with chronic spinal cord injury. Spinal Cord 1998; 36: 13-7.

Bauman WA, Adkins RH, Spungen AM, Waters RL, Kemp B, Herbert V. Levels of plasma homocysteine in persons with spinal cord injury. J Spinal Cord Med 2001; 24: 81-6.

Bauman WA, Kahn NN, Grimm DR, Spungen AM. Risk factors for atherogenesis and cardiovascular autonomic function in persons with spinal cord injury. Spinal Cord 1999b; 37: 601-16.

Bauman WA, Raza M, Chayes Z, Machac J. Tomographic thallium-201 myocardial perfusion imaging after intravenous dipyrsidamole in asymptomatic subjects with quadriplegia. Arch Phys Med Rehabil 1993; 74: 740-4.

Bauman WA, Raza M, Spungen AM, Machac J. Cardiac stress testing with thallium-201 imaging reveals silent ischemia in individuals with paraplegia. Arch Phys Med Rehabil 1994; 75: 946-50.

Bauman WA, Spungen AM, Adkins RH, Kemp BJ. Metabolic and endocrine changes in persons aging with spinal cord injury. Assist Technol 1999c; 11: 88-96.

Bauman WA, Spungen AM, Raza M, Rothstein J, Zhang RL, Zhong YG, et al. Coronary artery disease: metabolic risk factors and latent disease in individuals with paraplegia. Mt Sinai J Med 1992a; 59: 163-8.

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 1992b; 30: 697-703.

Bauman WA, Spungen AM. Carbohydrate and lipid metabolism in chronic spinal cord injury. J Spinal Cord Med 2001; 24: 266-77.

Bauman WA, Spungen AM. Metabolic changes in persons after spinal cord injury. Phys Med Rehabil Clin N Am 2000; 11: 109-40.

Berry HR, Kakebeeke TH, Donaldson N, Perret C, Hunt KJ. Energetics of paraplegic cycling: adaptation to 12 months of high volume training. Technology and Health Care 2012; 20: 73-84.
Berry HR, Perret C, Saunders BA, Kakebeeke TH, Donaldson Nde N, Allan DB, et al. Cardiorespiratory and power adaptations to stimulated cycle training in paraplegia. Med Sci Sports Exerc 2008; 40: 1573-80.
Bizzarini E, Saccavini M, Lipanje F, Magrin P, Malisan C, Zampa A. Exercise prescription in subjects with spinal cord injuries. Arch Phys Med Rehabil 2005; 86: 1170-5.
Bravo G, Guizar-Sahagun G, Ibarra A, Centurion D, Villalon CM. Cardiovascular alterations after spinal cord injury: an overview. Curr Med Chem Cardiovasc Hematol Agents 2004; 2: 133-48.
Brenes G, Dearwater S, Shapera R, LaPorte RE, Collins E. High density lipoprotein cholesterol concentrations in physically active and sedentary spinal cord injured patients. Arch Phys Med Rehabil 1986; 67: 445-50.
Brurok B, Helgerud J, Karlsen T, Leivseth G, Hoff J. Effect of aerobic high-intensity hybrid training on stroke volume and peak oxygen consumption in men with spinal cord injury. Am J Phys Med Rehabil 2011; 90: 407-14.
Carlson KF, Wilt TJ, Taylor BC, Goldish GD, Niewoehner CB, Shamliyan TA, et al. Effect of exercise on disorders of carbohydrate and lipid metabolism in adults with traumatic spinal cord injury: Systematic review of the evidence. Journal of Spinal Cord Medicine 2009; 32: 361-378.
Carty A, McCormack K, Coughlan GF, Crowe L, Caulfield B. Increased aerobic fitness after neuromuscular electrical stimulation training in adults with spinal cord injury. Arch Phys Med Rehabil 2012; 93: 790-795.
Chilibeck PD, Bell G, Jeon J, Weiss CB, Murdoch G, MacLean I, et al. Functional electrical stimulation exercise increases GLUT-1 and GLUT-4 in paralyzed skeletal muscle. Metabolism 1999; 48: 1409-13.
Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: II (section 2). Partial decentralization of the autonomic nervous system. Arch Phys Med Rehabil 1982a; 63: 576-80.
Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: III. Less quanta of sensory input plus bedrest and illness. Arch Phys Med Rehabil 1982b; 63: 628-31.
Cooney MM, Walker JB. Hydraulic resistance exercise benefits cardiovascular fitness of spinal cord injured. Med Sci Sports Exerc 1986; 18: 522-5.
Cragg JJ, Stone JA, Krassioukov AV. Management of cardiovascular disease risk factors in individuals with chronic spinal cord injury: an evidence-based review. Journal of Neurotrauma 2012; 29: 1999-2012.
Crameri RM, Cooper P, Sinclair PJ, Bryant G, Weston A. Effect of load during electrical stimulation training in spinal cord injury. Muscle Nerve 2004; 29: 104-11.
Crameri RM, Weston A, Climstein M, Davis GM, Sutton JR. Effects of electrical stimulation-induced leg training on skeletal muscle adaptability in spinal cord injury. Scand J Med Sci Sports 2002; 12: 316-22.
Currie KD, West CR, Hubli M, Gee CM, Krassioukov AV. Peak Heart Rates and Sympathetic Function in Tetraplegic Nonathletes and Athletes. Medicine and Science Sports Exercise. 2015;47:1259-64
Dallmeijer AJ, Hopman MT, van der Woude LH. Lipid, lipoprotein, and apolipoprotein profiles in active and sedentary men with tetraplegia. Arch Phys Med Rehabil 1997; 78: 1173-6.
Davis G, Plyley MJ, Shephard RJ. Gains of cardiorespiratory fitness with arm-crank training in spinally disabled men. Can J Sport Sci 1991; 16: 64-72.
Davis GM, Shephard RJ, Leenen FH. Cardiac effects of short term arm crank training in paraplegics: echocardiographic evidence. Eur J Appl Physiol Occup Physiol 1987; 56: 90-6.
de Carvalho DC, Cliquet A, Jr. Energy expenditure during rest and treadmill gait training in quadriplegic subjects. Spinal Cord 2005a; 43: 658-63.
de Carvalho DC, Cliquet A, Jr. Response of the arterial blood pressure of quadriplegic patients to treadmill gait training. Braz J Med Biol Res 2005b; 38: 1367-73.

de Carvalho DC, Martins CL, Cardoso SD, Cliquet A. Improvement of metabolic and cardiorespiratory responses through treadmill gait training with neuromuscular electrical stimulation in quadriplegic subjects. Artif Organs 2006; 30: 56-63.
de Groot P, Crozier J, Rakobowchuk M, Hopman M, MacDonald M. Electrical stimulation alters FMD and arterial compliance in extremely inactive legs. Med Sci Sports Exerc 2005; 37: 1356-64.
de Groot PC, Hjeltnes N, Heijboer AC, Stal W, Birkeland K. Effect of training intensity on physical capacity, lipid profile and insulin sensitivity in early rehabilitation of spinal cord injured individuals. Spinal Cord 2003; 41: 673-9.
de Groot PC, Poelkens F, Kooijman M, Hopman MT. Preserved flow-mediated dilation in the inactive legs of spinal cord-injured individuals. Am J Physiol Heart Circ Physiol 2004; 287: H374-80.
Dearwater SR, LaPorte RE, Robertson RJ, Brenes G, Adams LL, Becker D. Activity in the spinal cord-injured patient: an epidemiologic analysis of metabolic parameters. Med Sci Sports Exerc 1986; 18: 541-4.
Deley G, Denuziller J, Babault N. Functional electrical stimulation: cardiorespiratory adaptations and applications for training in paraplegia. Sports Medicine. 2015; 45:71-82.
De Rossi G, Matos-Souza JR, Babault N. Functional electrical stimulation: cardiorespiratory adaptations and applications for training in paraplegia. Sports Medicine. 2015; 45:71-82.
DeVivo MJ, Black KJ, Stover SL. Causes of death during the first 12 years after spinal cord injury. Arch Phys Med Rehabil 1993; 74: 248-54.
DeVivo MJ, Krause JS, Lammertse DP. Recent trends in mortality and causes of death among persons with spinal cord injury. Arch Phys Med Rehabil 1999; 80: 1411-9.
DiCarlo SE, Supp MD, Taylor HC. Effect of arm ergometry training on physical work capacity of individuals with spinal cord injuries. Phys Ther 1983; 63: 1104-7.
DiCarlo SE. Effect of arm ergometry training on wheelchair propulsion endurance of individuals with quadriplegia. Phys Ther 1988; 68: 40-4.
Ditor DS, Kamath MV, MacDonald MJ, Bugaresti J, McCartney N, Hicks AL. Effects of body weight-supported treadmill training on heart rate variability and blood pressure variability in individuals with spinal cord injury. J Appl Physiol 2005a; 98: 1519-25.
Ditor DS, Macdonald MJ, Kamath MV, Bugaresti J, Adams M, McCartney N, et al. The effects of body-weight supported treadmill training on cardiovascular regulation in individuals with motor-complete SCI. Spinal Cord 2005b; 43: 664-73.
Driussi C, Ius A, Bizzarini E, et al. Structural and functional left ventricular impairment in subjects with chronic spinal cord injury and no overt cardiovascular disease. J Spinal Cord Med. 2014; 37:85-92.
Duran FS, Lugo L, Ramirez L, Eusse E. Effects of an exercise program on the rehabilitation of patients with spinal cord injury. Arch Phys Med Rehabil 2001; 82: 1349-54.
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: 711-6.
El-Sayed MS, Younesian A, Rahman K, Ismail FM, El-Sayed Ali Z. The effects of arm cranking exercise and training on platelet aggregation in male spinal cord individuals. Thromb Res 2004; 113: 129-36.
El-Sayed MS, Younesian A. Lipid profiles are influenced by arm cranking exercise and training in individuals with spinal cord injury. Spinal Cord 2005; 43: 299-305.
Evans N, Hartigan C, Kandilakis C, Pharo E, and Clesson I. Acute cardiorespiratory and metabolic responses during exoskeleton-assisted walking overground among persons with chronic spinal cord injury. Top Spinal Cord Inj Rehabil 2015; 21(2): 122–132.
Faghri PD, Glaser RM, Figoni SF. Functional electrical stimulation leg cycle ergometer exercise: training effects on cardiorespiratory responses of spinal cord injured subjects at rest and during submaximal exercise. Arch Phys Med Rehabil 1992; 73: 1085-93.
Fornusek C, Gwinn TH, Heard R. Cardiorespiratory responses during functional electrical stimulation cycling and electrical stimulation isometric exercise. Spinal Cord. 2014; 52:635-39.
Foundation for Spinal Cord Injury Prevention CC. Spinal cord injury facts: Foundation for Spinal Cord Injury Prevention, Care & Cure 2009. Online available: http://www.fscip.org/facts.htm

Frost F, Roach MJ, Kushner I, Schreiber P. Inflammatory C-reactive protein and cytokine levels in asymptomatic people with chronic spinal cord injury. Arch Phys Med Rehabil 2005; 86: 312-7.
Gaffurini P, Bissolotti L, Calza S, Calabretto C, Orizio C, Gobbo M. Energy metabolism during activity-promoting videogames practice in subjects with spinal cord injury: evidences for health promotion. European Journal of Phys Rehabil Med 2013; 49: 23-9.
Garshick E, Kelley A, Cohen SA, Garrison A, Tun CG, Gagnon D, et al. A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord 2005; 43: 408-16.
Gass GC, Watson J, Camp EM, Court HJ, McPherson LM, Redhead P. The effects of physical training on high level spinal lesion patients. Scand J Rehabil Med 1980;12: 61-5.
Gerrits HL, de Haan A, Sargeant AJ, van Langen H, Hopman MT. Peripheral vascular changes after electrically stimulated cycle training in people with spinal cord injury. Arch Phys Med Rehabil 2001; 82: 832-9.
Ginis KA, Hicks AL, Latimer AE, Warburton DE, Bourne C, Ditor DS, Goodwin DL, Hayes KC, McCartney N, McIlraith A, Pomerleau P, Smith K, Stone JA, Wolfe DL. The development of evidence-informed physical activity guidelines for adults with spinal cord injury. Spinal Cord 2011;49:1088-1096.
Golay A, Brock E, Gabriel R, Konrad T, Lalic N, Laville M, Mingrone G, Petrie J, Phan TM, Pietiläinen KH, Anderwald CH. Taking small steps towards targets - perspectives for clinical practice in diabetes, cardiometabolic disorders and beyond. Int J Clin Pract. 2013;67:322-332.
Gorman PH, Scott W, York H, Theyagaraj M, Price-Miller N, McQuaid J, Eyvazzadeh M, Ivey FM, and Macko RF. Robotically assisted treadmill exercise training for improving peak fitness in chronic motor incomplete spinal cord injury: A randomized controlled trial. J Spinal Cord Med. 2016;39(1):32-44.
Grey E, Bratteli C, Glasser SP, Alinder C, Finkelstein SM, Lindgren BR, et al. Reduced small artery but not large artery elasticity is an independent risk marker for cardiovascular events. Am J Hypertens 2003; 16: 265-9.
Griffin L, Decker MJ, Hwang JY, Wang B, Kitchen K, Ding Z, et al. Functional electrical stimulation cycling improves body composition, metabolic and neural factors in persons with spinal cord injury. J Electromyogr Kinesiol 2009; 19: 614-22.
Grigorean VT, Sandu AM, Popescu M, et al. Cardiac dysfunctions following spinal cord injury. J Med Life. 2009;2(2):133-45.
Groah SL, Weitzenkamp D, Sett P, Soni B, Savic G. The relationship between neurological level of injury and symptomatic cardiovascular disease risk in the aging spinal injured. Spinal Cord 2001; 39: 310-7.
Gurney AB, Robergs RA, Aisenbrey J, Cordova JC, McClanahan L. Detraining from total body exercise ergometry in individuals with spinal cord injury. Spinal Cord 1998; 36: 782-9.
Hakansson NA, Hull ML. Can the efficacy of electrically stimulating pedaling using a commercially available ergometer be improved by minimizing the muscle stress-time integral? Muscle Nerve 2012; 45: 393-402.
Harness ET, Yozbatiran N, Cramer SC. Effects of intense exercise in chronic spinal cord injury. Spinal Cord 2008; 46: 733-7.
Hicks AL, Martin Ginis KA, Pelletier CA, Ditor DS, Foulon B, Wolfe DL. The effects of exercise training on physical capacity, strength, body composition and functional performance among adults with spinal cord injury: A systematic review. Spinal Cord 2011; 49: 1103-1127.
Hicks AL, Martin KA, Ditor DS, Latimer AE, Craven C, Bugaresti J, et al. Long-term exercise training in persons with spinal cord injury: effects on strength, arm ergometry performance and psychological well-being. Spinal Cord 2003; 41: 34-43.
Hjeltnes N, Aksnes AK, Birkeland KI, Johansen J, Lannem A, Wallberg-Henriksson H. Improved body composition after 8 wk of electrically stimulated leg cycling in tetraplegic patients. Am J Physiol 1997; 273: R1072-9.
Hjeltnes N, Galuska D, Bjornholm M, Aksnes AK, Lannem A, Zierath JR, et al. Exercise-induced overexpression of key regulatory proteins involved in glucose uptake and metabolism in tetraplegic persons: molecular mechanism for improved glucose homeostasis. Faseb J 1998; 12: 1701-12.

Hjeltnes N, Wallberg-Henriksson H. Improved work capacity but unchanged peak oxygen uptake during primary rehabilitation in tetraplegic patients. Spinal Cord 1998; 36: 691-8.
Hoffman MD. Cardiorespiratory fitness and training in quadriplegics and paraplegics. Sports Med 1986; 3: 312-30.
Hooker SP, Figoni SF, Rodgers MM, Glaser RM, Mathews T, Suryaprasad AG, et al. Physiologic effects of electrical stimulation leg cycle exercise training in spinal cord injured persons. Arch Phys Med Rehabil 1992; 73: 470-6.
Hooker SP, Wells CL. Effects of low- and moderate-intensity training in spinal cord-injured persons. Med Sci Sports Exerc 1989; 21: 18-22.
Hopman MT, Dallmeijer AJ, Snoek G, van der Woude LH. The effect of training on cardiovascular responses to arm exercise in individuals with tetraplegia. Eur J Appl Physiol Occup Physiol 1996; 74: 172-9.
Hopman MT, Groothuis JT, Flendrie M, Gerrits KH, Houtman S. Increased vascular resistance in paralyzed legs after spinal cord injury is reversible by training. J Appl Physiol 2002; 93: 1966-72.
Hubli M, Currie KD, West CR, Gee CM, Krassioukov AV. Physical exercise improves arterial stiffness after spinal cord injury. J Spinal Cord Med. 2014; 37:782-85.
Hurley BF, Hagberg JM. Optimizing health in older persons: aerobic or strength training? Exercise and Sport Science Reviews 1998; 26: 61-89.
ICORD. SCI Facts and Stats. In: International Collaboration on Repair Discoveries; 2003.
Jack LP, Allan DB, Hunt KJ. Cardiopulmonary exercise testing during body weight supported treadmill exercise in incomplete spinal cord injury: a feasibility study. Technol Health Care 2009; 17: 13-23.
Jacobs PL, Mahoney ET, Nash MS, Green BA. Circuit resistance training in persons with complete paraplegia. J Rehabil Res Dev 2002; 39: 21-8.
Jacobs PL, Nash MS, Klose KJ, Guest RS, Needham-Shropshire BM, Green BA. Evaluation of a training program for persons with SCI paraplegia using the Parastep 1 ambulation system: part 2. Effects on physiological responses to peak arm ergometry. Arch Phys Med Rehabil 1997; 78: 794-8.
Jacobs PL, Nash MS, Rusinowski JW. Circuit training provides cardiorespiratory and strength benefits in persons with paraplegia. Med Sci Sports Exerc 2001; 33: 711-7.
Jacobs PL, Nash MS. Exercise recommendations for individuals with spinal cord injury. Sports Med 2004; 34: 727-51.
Jae SY, Heffernan KS, Lee M, Fernhall B. Arterial structure and function in physically active persons with spinal cord injury. J Rehabil Med 2008; 40: 535-8.
Janssen TW, Pringle DD. Effects of modified electrical stimulation-induced leg cycle ergometer training for individuals with spinal cord injury. J Rehabil Res Dev 2008; 45: 819-30.
Jeffries EC, Hoffman SM, de Leon R, et al. Energy expenditure and heart rate responses to increased loading in individuals with motor complete spinal cord injury performing body weight-supported exercises. Archives of Physical Medicine & Rehabilitation. 2015; 96:1467-73.
Jeon JY, Hettinga D, Steadward RD, Wheeler GD, Bell G, Harber V. Reduced plasma glucose and leptin after 12 weeks of functional electrical stimulation-rowing exercise training in spinal cord injury patients. Arch Phys Med Rehabil 2010; 91: 1957-9.
Jeon JY, Weiss CB, Steadward RD, Ryan E, Burnham RS, Bell G, et al. Improved glucose tolerance and insulin sensitivity after electrical stimulation-assisted cycling in people with spinal cord injury. Spinal Cord 2002; 40: 110-7.
Kahn N, Sinha A, Bauman W. Impaired platelet prostacyclin receptor activity: a monozygotic twin study discordant for spinal cord injury. Clin Physiol 2001; 21: 60-6.
Kahn NN, Feldman SP, Bauman WA. Lower-extremity functional electrical stimulation decreases platelet aggregation and blood coagulation in persons with chronic spinal cord injury: a pilot study. J Spinal Cord Med 2010; 33: 150-8.
Kahn NN. Platelet-stimulated thrombin and PDGF are normalized by insulin and Ca2+ channel blockers. Am J Physiol 1999; 276: E856-62.

Kim DI, Lee H, Lee BS, Kim J, Jeon J. Effects of a 6-Week Indoor Hand-Bike Exercise Program on Health and Fitness Levels in People with Spinal Cord Injury: A Randomized Controlled Trial Study. *Arch Phys Med Rehabil*. 2015;96:2033-40

Kostovski E, Dahm AEA, Mowinckel MC, Stranda A, Skretting G, Osterud B, Sandset PM, Iversen PO. Circadian rhythms of hemostatic factors in tetraplegia: A double-blind, randomized, placebo-controlled cross-over study of melatonin. Spinal Cord. 2015;53:285-90.

Krassioukov AV, Karlsson AK, Wecht JM, et al. Assessment of autonomic dysfunction following spinal cord injury: rationale for additions to International Standards for Neurological Assessment. J Rehabil Res Dev. 2007;44(1):103-12.

Krauss JC, Robergs RA, Depaepe JL, Kopriva LM, Aisenbury JA, Anderson MA, et al. Effects of electrical stimulation and upper body training after spinal cord injury. Med Sci Sports Exerc 1993; 25: 1054-61.

Kressler J, Nash MS, Burns PA, Field-Fote ED. Metabolic responses to 4 different body weight-support locomotor training approaches in persons with incomplete spinal cod injury. Archives of Physical Medicine and Rehabilitation 2013; 94: 1436-42.

Krum H, Howes LG, Brown DJ, Ungar G, Moore P, McNeil JJ, et al. Risk factors for cardiovascular disease in chronic spinal cord injury patients. Paraplegia 1992; 30: 381-8.

Lee MY, Myers J, Abella J, Froelicher VF, Perkash I, Kiratli BJ. Homocysteine and hypertension in persons with spinal cord injury. Spinal Cord 2005a.

Lee MY, Myers J, Hayes A, Madan S, Froelicher VF, Perkash I, et al. C-reactive protein, metabolic syndrome, and insulin resistance in individuals with spinal cord injury. J Spinal Cord Med 2005b; 28: 20-5.

Leicht CA, Griggs KE, Lavin J, Tolfrey K, Goosey-Tolfrey VL. Blood lactate and ventilatory thresholds in wheelchair athletes with tetraplegia and paraplegia. Eur J Appl Physiol. 2014; 114:1635-43.

Lindberg T, Arndt A, Norrbrink C, Wahman K, Bjerkefors A. Effects of seated double-poling ergometer training on aerobic and mechanical power in individuals with spinal cord injury. J Rehabil Med 2012; 44: 893-898.

Mahoney ET, Bickel CS, Elder C, Black C, Slade JM, Apple D, Jr., et al. Changes in skeletal muscle size and glucose tolerance with electrically stimulated resistance training in subjects with chronic spinal cord injury. Arch Phys Med Rehabil 2005; 86: 1502-4.

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: 102-9.

Manns PJ, McCubbin JA, Williams DP. Fitness, inflammation, and the metabolic syndrome in men with paraplegia. Arch Phys Med Rehabil 2005; 86: 1176-81.

Menendez H, Ferrero C, Martin-Hernandez J, Figueroa A, Marin PJ, Herrero AJ. Acute effects of simultaneous electromyostimulation vibration on leg blood flow in spinal cord injury. Spinal Cord 2016; 54: 383-389

Milia R, Roberto S, Marongiu E, et al. Improvement in hemodynamic responses to metaboreflex activation after one year of training in spinal cord injured humans. BioMed Research International. 2014; 2014: 1-9.

Millar PJ, Rakobowchuk M, Adams MM, Hicks AL, McCartney N, MacDonald MJ. Effects of short-term training on heart rate dynamics in individuals with spinal cord injury. Auton Neurosci 2009; 150: 116-21.

Miranda AR, Hassouna HI. Mechanisms of thrombosis in spinal cord injury. Hematol Oncol Clin North Am 2000; 14: 401-16.

Mohr T, Andersen JL, Biering-Sorensen F, Galbo H, Bangsbo J, Wagner A, et al. Long-term adaptation to electrically induced cycle training in severe spinal cord injured individuals. Spinal Cord 1997;35: 1-16.

Mohr T, Dela F, Handberg A, Biering-Sorensen F, Galbo H, Kjaer M. Insulin action and long-term electrically induced training in individuals with spinal cord injuries. Med Sci Sports Exerc 2001; 33: 1247-52.

Mutton DL, Scremin AM, Barstow TJ, Scott MD, Kunkel CF, Cagle TG. Physiologic responses during functional electrical stimulation leg cycling and hybrid exercise in spinal cord injured subjects. Arch Phys Med Rehabil 1997; 78: 712-8.
Myers J, Kiratli J, Jaramillo J. The cardiometabolic benefits of routine physical activity in persons living with spinal cord injury. Current Cardiovascular Risk Reports 2012; 6:323-330.
Myers J, Lee M, Kiratli J. Cardiovascular disease in spinal cord injury: an overview of prevalence, risk, evaluation, and management. Am J Phys Med Rehabil 2007; 86: 142-52.
Myllynen P, Koivisto VA, Nikkila EA. Glucose intolerance and insulin resistance accompany immobilization. Acta Med Scand 1987; 222: 75-81.
Nash MS, Cowan RE, Kressler J. Evidence-based and heuristic approaches for customization of care in cardiometabolic syndrome after spinal cord injury. J Spinal Cord Med. 2012;35:278-292.
Nash MS, Jacobs PL, Mendez AJ, Goldberg RB. Circuit resistance training improves the atherogenic lipid profiles of persons with chronic paraplegia. J Spinal Cord Med 2001;24: 2-9.
Nash MS, Jacobs PL, Montalvo BM, Klose KJ, Guest RS, Needham-Shropshire BM. Evaluation of a training program for persons with SCI paraplegia using the Parastep 1 ambulation system: part 5. Lower extremity blood flow and hyperemic responses to occlusion are augmented by ambulation training. Arch Phys Med Rehabil 1997;78: 808-14.
Nooijen CF, Van Den Brand IL, Ter Horst P, Wynants M, Valent LJ, Stam HJ, Van Den BergEmons,RJ. Feasibility of Handcycle Training during Inpatient Rehabilitation in Persons with Spinal Cord Injury. Arch Phys Med Rehabilitation 2015; 96:1654-57.
Noonan VK, Fingas M, Farry A, Baxter D, Singh A, Fehlings MG, Dvorak MF. Incidence and prevalence of spinal cord injury in Canada: a national perspective. Neuroepidemiology. 2012;38:219-226.
Ordonez FJ, Rosety MA, Camacho A, Rosety I, Diaz AJ, Fornieles G, Bernardi M, Rosety-Rodriguez M. Arm-cranking exercise reduced oxidative damage in adults with chronic spinal cord injury. Archives of Physical Medicine and Rehabilitation 2013; 94:2336-2341.
Phillips AA, Cote AT, Bredin SS, Krassioukov AV, Warburton DE. Aortic stiffness increased in spinal cord injury when matched for physical activity. Med Sci Sports Exerc. 2012;44:2065-2670.
Phillips AA, Cote AT, Warburton DER. A systematic review of exercise as a therapeutic intervention to improve arterial function in persons living with spinal cord injury. Spinal Cord 2011; 49: 702-714.
Phillips SM, Stewart BG, Mahoney DJ, Hicks AL, McCartney N, Tang JE, et al. Body-weight-support treadmill training improves blood glucose regulation in persons with incomplete spinal cord injury. J Appl Physiol 2004; 97: 716-24.
Physical activity guidelines for adults with spinal cord injury. Online accessed on April 20, 2014: http://sciactioncanada.ca/guidelines
Pollack SF, Axen K, Spielholz N, Levin N, Haas F, Ragnarsson KT. Aerobic training effects of electrically induced lower extremity exercises in spinal cord injured people. Arch Phys Med Rehabil 1989; 70: 214-9.
Ragnarsson KT, Pollack S, O'Daniel W, Jr., Edgar R, Petrofsky J, Nash MS. Clinical evaluation of computerized functional electrical stimulation after spinal cord injury: a multicenter pilot study. Arch Phys Med Rehabil 1988; 69: 672-7.
Ravensbergen HJC, de Groot S, Post MWM, Slootman HJ, van dW, Claydon VE. Cardiovascular function after spinal cord injury: Prevalence and progression of dysfunction during inpatient rehabilitation and 5 years following discharge. Neurorehabil Neural Repair. 2014; 28:219-29.
Rick Hansen Spinal Cord Injury Registry. Spinal cord injury facts and statistics. Vancouver, BC: Rick Hansen Spinal Cord Injury Registry; 2004.
Roussi J, Bentolila S, Boudaoud L, Casadevall N, Vallee C, Carlier R, et al. Contribution of D-Dimer determination in the exclusion of deep venous thrombosis in spinal cord injury patients. Spinal Cord 1999; 37: 548-52.
Ryan TE, Brizendine JT, Backus D, McCully KK. Electrically induced resistance training in individuals with motor complete spinal cord injury. Archives of Phys Medicine and Rehabilitation 2013; 94: 2166-73.

Sabatier MJ, Stoner L, Mahoney ET, Black C, Elder C, Dudley GA, et al. Electrically stimulated resistance training in SCI individuals increases muscle fatigue resistance but not femoral artery size or blood flow. Spinal Cord 2006; 44: 227-33.
Schmid A, Halle M, Stutzle C, Konig D, Baumstark MW, Storch MJ, et al. Lipoproteins and free plasma catecholamines in spinal cord injured men with different injury levels. Clin Physiol 2000; 20: 304-10.
Schreiber R, Paim LR, de Rossi G, Matos-Souza JR, Costa e Silva ADA, Souza CM, Borges M, Azevedo ER, Alonso KC, Gorla JI, Cliquet A, Nadruz W. Matrix metalloproteinases and left ventricular function and structure in spinal cord injured subjects. Clinica Chimica Acta. 2014; 437:136-40.
Serra-Ano P, Montesinos LL, Morales J, et al. Heart rate variability in individuals with thoracic spinal cord injury. Spinal Cord. 2015;53:59-63.
Solomonow M, Reisin E, Aguilar E, Baratta RV, Best R, D'Ambrosia R. Reciprocating gait orthosis powered with electrical muscle stimulation (RGO II). Part II: Medical evaluation of 70 paraplegic patients. Orthopedics 1997; 20: 411-8.
Soyupek F, Savas S, Ozturk O, Ilgun E, Bircan A, Akkaya A. Effects of body weight supported treadmill training on cardiac and pulmonary functions in the patients with incomplete spinal cord injury. J Back Musculoskelet Rehabil 2009; 22: 213-8.
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: 2398-407.
Stevens SL, Morgan DW. Heart Rate Response During Underwater Treadmill Training in Adults with Incomplete Spinal Cord Injury. Topics in Spinal Cord Injury Rehabilitation. 2015; 21:40-8
Stewart BG, Tarnopolsky MA, Hicks AL, McCartney N, Mahoney DJ, Staron RS, et al. Treadmill training-induced adaptations in muscle phenotype in persons with incomplete spinal cord injury. Muscle Nerve 2004; 30: 61-8.
Stoner L, Sabatier MJ, Mahoney ET, Dudley GA, McCully KK. Electrical stimulation-evoked resistance exercise therapy improves arterial health after chronic spinal cord injury. Spinal Cord 2007; 45: 49-56.
Sutbeyaz ST, Koseoglu BF, Gokkaya NK. The combined effects of controlled breathing techniques and ventilatory and upper extremity muscle exercise on cardiopulmonary responses in patients with spinal cord injury. Int J Rehabil Res 2005; 28: 273-6.
Taylor JA, Picard G, Widrick JJ. Aerobic capacity with hybrid FES rowing in spinal cord injury: comparison with arms-only exercise and preliminary findings with regular training. PMR 2011; 3: 817-24.
Ter Woerds W, De Groot PC, van Kuppevelt DH, Hopman MT. Passive leg movements and passive cycling do not alter arterial leg blood flow in subjects with spinal cord injury. Phys Ther 2006; 86: 636-45.
Thijssen DH, Ellenkamp R, Smits P, Hopman MT. Rapid vascular adaptations to training and detraining in persons with spinal cord injury. Arch Phys Med Rehabil 2006; 87: 474-81.
Thijssen DH, Heesterbeek P, van Kuppevelt DJ, Duysens J, Hopman MT. Local vascular adaptations after hybrid training in spinal cord-injured subjects. Med Sci Sports Exerc 2005; 37: 1112-8.
Thijssen DH, Kooijman M, de Groot PC, Bleeker MW, Smits P, Green DJ, et al. Endothelium-dependent and -independent vasodilation of the superficial femoral artery in spinal cord-injured subjects. J Appl Physiol 2008; 104: 1387-93.
Tordi N, Dugue B, Klupzinski D, Rasseneur L, Rouillon JD, Lonsdorfer J. Interval training program on a wheelchair ergometer for paraplegic subjects. Spinal Cord 2001; 39: 532-7.
Tordi N, Mourot L, Chapuis A, Parratte B, Regnard J. Effects of a primary rehabilitation programme on arterial vascular adaptations in an individual with paraplegia. Ann Phys Rehabil Med 2009; 52: 66-73.
Totosy de Zepetnek JO, Pelletier CA, Hicks AL, MacDonald MJ. Following the Physical Activity Guidelines for Adults With Spinal Cord Injury for 16 Weeks Does Not Improve Vascular Health: A Randomized Controlled Trial. Archives of Physical Medicine & Rehabilitation. 2015; 96:1566-75

Tremblay MS, Warburton DE, Janssen I, Paterson DH, Latimer AE, Rhodes RE, Kho ME, Hicks A, Leblanc AG, Zehr L, Murumets K, Duggan M. New Canadian physical activity guidelines. Appl Physiol Nutr Metab. 2011;36:36-46; 47-58.

Turiel M, Sitia S, Cicala S, Magagnin V, Bo I, Porta A, et al. Robotic treadmill training improves cardiovascular function in spinal cord injury patients. Int J Cardiol 2011; 149: 323-9.

Vaidyanathan S, Soni BM, Singh G, Mansour P, Watt JW, Sett P, et al. Recurrent urinary infection, raised serum levels of C-reactive protein, and the risk of cardiovascular disease in patients with spinal cord injury: a hypothesis. Spinal Cord 1998; 36: 868-9.

Valent LJ, Dallmeijer AJ, Houdijk H, Slootman HJ, Post MW, van der Woude LH. Influence of hand cycling on physical capacity in the rehabilitation of persons with a spinal cord injury: a longitudinal cohort study. Arch Phys Med Rehabil 2008; 89: 1016-22.

Warburton DE, Bredin SS, Horita LT, Zbogar D, Scott JM, Esch BT, et al. The health benefits of interactive video game exercise. Applied Physiology, Nutrition and Metabolism 2007a; 32: 655-663.

Warburton DE, Charlesworth S, Ivey A, Nettlefold L, Bredin SS. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. Int J Behav Nutr Phys Act 2010; 7: 39.

Warburton DE, Gledhill N, Quinney A. Musculoskeletal fitness and health. Can J Appl Physiol 2001b; 26: 217-37.

Warburton DE, Gledhill N, Quinney A. The effects of changes in musculoskeletal fitness on health. Can J Appl Physiol 2001a; 26: 161-216.

Warburton DE, Haykowsky MJ, Quinney HA, Humen DP, Teo KK. Reliability and validity of measures of cardiac output during incremental to maximal aerobic exercise. Part I: Conventional techniques. Sports Med 1999a; 27: 23-41.

Warburton DE, Haykowsky MJ, Quinney HA, Humen DP, Teo KK. Reliability and validity of measures of cardiac output during incremental to maximal aerobic exercise. Part II: Novel techniques and new advances. Sports Med 1999b; 27: 241-60.

Warburton DE, McKenzie DC, Haykowsky MJ, Taylor A, Shoemaker P, Ignaszewski AP, et al. Effectiveness of high-intensity interval training for the rehabilitation of patients with coronary artery disease. Am J Cardiol 2005; 95: 1080-1084.

Warburton DE, Nicol C, Bredin SS. Health benefits of physical activity: the evidence. Cmaj 2006; 174: 801-9.

Warburton DER, Eng JJ, Krassioukov A, Sproule S, the SCIRE Research Team. Cardiovascular health and exercise rehabilitation in spinal cord injury. Topics in Spinal Cord Injury Rehabilitation 2007b; 13: 98-122.

Wecht JM, de Meersman RE, Weir JP, Bauman WA, Grimm DR. Effects of autonomic disruption and inactivity on venous vascular function. Am J Physiol Heart Circ Physiol 2000; 278: H515-20.

Wecht JM, De Meersman RE, Weir JP, Spungen AM, Bauman WA. Cardiac homeostasis is independent of calf venous compliance in subjects with paraplegia. Am J Physiol Heart Circ Physiol 2003; 284: H2393-9.

West CR, Mills P, Krassioukov AV. Influence of the neurological level of spinal cord injury on cardiovascular outcomes in humans: a meta-analysis. Spinal Cord 2012;50:484-492.

West CR, Gee CM, Voss C, et al. Cardiovascular control, autonomic function, and elite endurance performance in spinal cord injury. *Scand J Med Sci Sports*. 2015; 25:476-85

Wheeler GD, Andrews B, Lederer R, Davoodi R, Natho K, Weiss C, et al. Functional electric stimulation-assisted rowing: Increasing cardiovascular fitness through functional electric stimulation rowing training in persons with spinal cord injury. Arch Phys Med Rehabil 2002; 83: 1093-9.

Whiteneck GG, Charlifue SW, Frankel HL, Fraser MH, Gardner BP, Gerhart KA, et al. Mortality, morbidity, and psychosocial outcomes of persons spinal cord injured more than 20 years ago. Paraplegia 1992; 30: 617-30.

Wong SC, Bredin SS, Krassioukov AV, Taylor A, Warburton DE. Effects of training status on arterial compliance in able-bodied persons and persons with spinal cord injury. Spinal Cord 2013;51:278-81.

Wouda MF, Wejden L, Lundgaard E, and Strøm V. Energetic and cardiovascular responses to treadmill walking and stationary cycling in subjects with incomplete spinal cord injury. Spinal Cord 2016; 54: 51–56.
Yarar-Fisher C, Pascoe DD, Gladden LB, Quindry JC, Hudson J, Sefton J. Acute physiological effects of whole body vibration (WBV) on central hemodynamics, muscle oxygenation and oxygen consumption in individuals with chronic spinal cord injury. Disability & Rehabilitation. 2014; 36:136-45.
Yekutiel M, Brooks ME, Ohry A, Yarom J, Carel R. The prevalence of hypertension, ischaemic heart disease and diabetes in traumatic spinal cord injured patients and amputees. Paraplegia 1989; 27: 58-62.
Zbogar D, Eng JJ, Krassioukov AV, Scott JM, Esch BT, Warburton DE. The effects of functional electrical stimulation leg cycle ergometry training on arterial compliance in individuals with spinal cord injury. Spinal Cord 2008; 46: 722-6.