Physical Activity Following Spinal Cord Injury: Cardiovascular and Metabolic Outcomes

Executive Summary

Spinal cord injury (SCI) is associated with many changes and disturbances to body function due to the neurological injury. When SCI occurs at or above the first thoracic level (T1) it disrupts the sympathetic spinal pathways exiting the brainstem, which contains the cardiovascular control center that conveys signals to the heart and blood vessels. This loss of “normal neural control over the cardiovascular system” impairs the cardiovascular response to exercise (Gee et al. 2021; Teasell et al. 2000), causes blood pressure fluctuations like orthostatic hypotension (OH) and autonomic dysreflexia (AD) (Claydon & Krassioukov 2006), as well as predisposing people with SCI to acute cardiac events (Collins et al. 2006; Wan & Krassioukov, 2014). Conversely, when injury occurs at or below the T12 level then neural control of the cardiovascular system is essentially normal, and when the injury occurs between T1-T12, the amount of function disruption varies. In addition to changes in cardiovascular function and control, SCI also impacts metabolic function. People with SCI experience accelerated risk for accumulating adipose tissue (e.g., Buchholz & Bugaresti, 2005) and developing metabolic disorders related to lipid (e.g., Emmons et al. 2010) and glucose tolerance (e.g., Battram et al. 2007ª).

Cardiovascular disease is now the leading cause of morbidity and mortality in people with chronic SCI; 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; Garshick et al. 2005; Michael et al. 1999). The Consortium for Spinal Cord Medicine (CSCM) recently released Clinical Practice Guidelines for CMD in SCI (Nash et al. 2019a). These guidelines are the first to establish SCI-specific diagnostic criteria for the cluster of risk factors that coalesce as CMD, as well as population-specific management strategies.

- Obesity is the most prevalent CMD risk factor in the SCI population (Libin et al. 2013; Nash et al. 2019b). A body mass index (BMI) of ≥22 kg/m2 is considered healthy in people with SCI (vs. 30 kg/m2 in non-SCI). The SCI-specific healthy BMI is due to dysregulation in people with SCI and muscle, bone, and collection of adipose tissue (e.g., Ditor et al. 2004; Carpenter et al. 2020; Buchholz & Bugaresti 2005).
- Insulin resistance, or diabetes, uses a cut-off of fasting blood glucose ≥100 mg/dL, the same value as used in persons without SCI. However, it should be noted that laboratory tests for insulin resistance (Aksnes et al. 1996; Duckworth et al. 1980; Jeon et al. 2002; Karlsson et al. 1995b; Palmer et al. 1976) and oral glucose tolerance (Aksnes et al. 1996; Battram et al. 2007b; Bauman et al. 1999; Chilibeck et al. 1999a; Duckworth et al. 1983b; Duckworth et al. 1980; Elder et al. 2004; Gorgey & Gater, 2011a; Jeon et al. 2002; Karlsson et al. 1995b; Lewis et al. 2010; Segal et al. 2007; Wang et al. 2009; Yarar-Fisher et al.

2013a) have routinely found that persons with SCI who have “normal” fasting blood glucose (<100mg/dL) are likely to have impaired glycemic regulation (Aksnes et al. 1996; Bauman et al. 1999; Gorgey & Gater, 2011a; Lewis et al. 2010; Segal et al. 2007; Wang et al. 2009).

- Dyslipidemia has two cut-off criteria: (1) blood triglyceride (TG) concentration ≥ 150 mg/dL, and (2) blood high density lipoprotein cholesterol (HDL-C) concentration of ≤ 40 and ≤ 50 mg/dL for men and women, respectively. The TG concentration cut-off is similar to CMD cut-offs used for people without SCI, but the HDL-C cut-off is population-specific due to the highly reproducible finding of low HDL-C in SCI (Bauman et al. 1992; Gilbert et al. 2014; Krum et al. 1992; La Fountaine et al. 2018; Liang et al. 2007; Lieberman et al. 2014; Washburn & Figoni 1999).
- Generally, a hypertension level for blood pressure is similar to that of the general population (≥ 130 and 85 mmHg for systolic and diastolic blood pressure, respectively). However, in high-level SCI blood pressure can be low for neurogenic reasons that confounds the use of this outcome to reflect cardiovascular disease risk.

Evidence-based guidelines have established the use of physical activity to increase cardiorespiratory fitness and muscular strength in persons with SCI (Martin Ginis et al. 2011). More recently, the CSCM CMD guidelines recommend physical exercise as a primary treatment strategy for the management of CMD in SCI. Though long-term research establishing the absolute connection between physical activity and reduction in CMD does not yet exist, Martin Ginis et al. (2018) state with moderate to high confidence that exercise benefits CMD prevention in persons with SCI. Despite this, people with SCI continually self-report some of the lowest levels of activity among any population in society.

Cardiorespiratory Fitness and Endurance

Cardiorespiratory fitness is a broad term used to measure how well the lungs, heart and muscles work together to use oxygen to perform work. The most common indicator of cardiorespiratory fitness is VO2peak, which represents the maximum capacity to uptake and use oxygen during exercise. In people without SCI, VO2peak is negatively related to the onset of CMD and the risk for all-cause mortality (i.e., higher the VO2peak the less mortality). Although there is no long-term data yet available for the field of SCI, it is likely that the same relationship between VO2peak and risk for CMD exists in people with SCI as in the non-SCI population.

- There is strong, level 1a evidence, from three RCT studies showing that arm cycle ergometry (ACE) training, 3 sessions per week for 8-12 weeks results in increased cardiorespiratory fitness (as assessed by peak rate of whole-body oxygen consumption during exercise)
- Two studies have investigated different forms of combined aerobic exercise and resistance training interventions (Kim et al. 2019; Totosy de Zepetnek et al. 2015). The strongest evidence comes from Kim et al. (2019) who demonstrated Level 1A evidence that such combined exercise, performed for 60min/d, 3d/wk

improved glucose tolerance and HDL cholesterol, whereas similar exercise performed less frequently had no impact on cardiometabolic function (Totosy de Zepetnek et al. 2015).

- There is level 1a evidence (Rosety-Rodriguez et al. 2014; Ordonez et al. 2013) that 12 weeks of armcrank exercise (20-45 min/day, 50-65% heart rate reserve) improves metabolic/immune function in those with mid-to-low thoracic SCI.

- There is level 1a evidence (De Groot et al. 2003) that 8 weeks of 3d/k arm exercise at a low intensity (50-60% heart rate reserve), but not high intensity (70-80% heart rate reserve), improves insulin sensitivity.

FES plus leg or arm cycle ergometry training

- We found fourteen studies that used FES leg cycling exercise (FES-LCE) as a training intervention with cardiorespiratory outcomes, ranging in duration from 6 weeks to 52 weeks. A single RCT study by Gorgey et al. (2017) compared the efficacy of 16 weeks FES-LCE versus arm-cycle ergometry (ACE) training reported that peak oxygen uptake was not significantly changed in either of the intervention groups, nor were resting heart rate or blood pressure. By contrast, of the single-cohort longitudinal studies, most reported concurrent improvements to both VO2peak and POpeak (or endurance time) during or following FES-LEC training.

Body-weight Supported Treadmill Training (BWSTT) and Exoskeleton ambulation training

- Seven BWSTT studies examined people with incomplete SCI who engaged in active walking supported either above ground, or above treadmills with individually-determined body weight support. In general, there were small increases in cardiorespiratory fitness and improvements in submaximal heart rate, indicating a small degree of cardiovascular changes after 4-13 weeks of BWSTT.
- Similarly, observations from the available exercise training studies indicates that exoskeleton-assisted exercise training improves exercise capacity in exoskeleton-specific movements but its improvements do not largely translate to central cardiovascular fitness as determined by conventional arm cycling tests.

Other Exercise or Sport Training

- There is moderate evidence (Level 2) that multi-modal training approaches, 2- 3 times per week for ≥8 weeks improve cardiorespiratory fitness in people with SCI (Pelletier et al. 2015; Yarar-Fisher et al. 2018).
- In studies comparing highly-trained wheelchair athletes with SCI against sedentary individuals with SCI, it is consistently reported that the highly-trained

individuals have improved vascular function but that blood lipids and antioxidant status are not different between cohorts.

- It should be noted that the length of intervention may be important as a higher RCT revealed no significant improvements in cardiorespiratory fitness following only 6 weeks of mutli-modal training (Kim et al. 2019). Further research is needed to indicate the most effective sport training programs and rehabilitation methods in this population.

Wheelchair Propulsion Training

- Eight studies were identified that examined the effect of wheelchair propulsion training on cardiorespiratory fitness and/or endurance. There is level 1b evidence from 1 RCT study showing that low intensity wheelchair propulsion for 2 sessions per week for 16 weeks fails to elicit an increase in ardiorespiratory fitness. Level 2 evidence from two studies (one RCT and one prospective control) shows that increasing exercise intensity, albeit over a shorter 6 to 8 wk training period, also does not result in greater improvements in cardiorespiratory fitness compared to lower intensity wheelchair propulsion.

There is moderate evidence (Level 1b) that behaviour change interventions can improve activity levels and cardiorespiratory fitness in people with chronic (>1 year) SCI (Williams et al. 2021). There is provisional, level 1-4 evidence from two studies that demonstrate a behaviour change coaching intervention designed to promote PA improves cholesterol, HOMA-IR, and blood lipids. Interestingly, in the only study to assess whether following the SCI-specific physical activity guidelines improves cardiometabolic health, it was reported that the exercise group had no improvement in any marker of cardiometabolic disease.

Gaps in the Evidence –

More research is still necessary to clarify important questions in the effects of Physical Activity on Cardiovascular Health in people with SCI. We recommend:

• Larger RCTs with different intervention arms could experimentally demonstrate the optimal types of exercise, as well as the optimal dosage and intensity for better CV fitness, orthostatic tolerance, and specific biomarkers of metabolic health. There is a specific need to determine a clinically-relevant minimum magitude of improvement in cardiorespiratory fitness that results in improved function.

• Longitudinal evidence that establishes the effects of Physical Activity on CV function and levels of chronic disease in people with SCI.

• Including people with SCI of different injury levels and completeness, as well as people of different ages, sex, and race/ethnicity is necessary to determine if there are any differences in effects of PA on CVD health and/or access to PA and CVD health.