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Abstract
Passive leg cycling and functional electrical stimulation are interventions used to improve the cardiovascular function in persons with spinal cord injury. Although the volume of evidence in support of these techniques is relatively limited, current findings have demonstrated their capacity to improve arterial function in the patients living with spinal cord injury. We proposed that a novel strategy is to alternate the application of passive leg cycling and functional electrical stimulation, which may elicit a synergistic cardiorespiratory response to exercise, leading to marked enhancements in cardiovascular function. This approach has the potential to improve the quality and efficacy of clinical exercise rehabilitation for persons with spinal cord injury, improve their cardiovascular health, and reduce their risks associated with cardiovascular disease. Health & Fitness Journal of Canada 2016;9(3):59-65.

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Introduction
A spinal cord injury (SCI) may temporarily or permanently change the spinal cord’s sensory, motor, and/or autonomic function (Chin et al., 2016). In addition to physical inactivity (as a result of lower-body paralysis), chronic autonomic disturbances (e.g., autonomic dysreflexia and orthostatic hypertension) can increase the risk of cardiovascular disease (CVD) in SCI (Phillips and Krassioukov, 2015). Since CVD is the leading cause of rehospitalisation and mortality in the SCI population (Phillips and Krassioukov, 2015), considerable research has focused on improvements in cardiovascular health.

The health benefits of physical activity are well documented. Physical activity is a primary and secondary preventative strategy against more than 25 chronic diseases including CVD (Warburton et al., 2006). As a result of wheelchair dependency, low levels of physical activity can lead to imbalances in glucose homeostasis, abnormal lipoprotein profiles and increased adiposity, all of which are risk factors associated with CVD (Warburton et al., 2006). Hence, physical activity is an important contributor to cardiovascular health in the SCI population.

Currently, two physical activity strategies used in SCI clinical exercise rehabilitation programs are passive leg cycling (PLC) and functional electrical stimulation (FES). In PLC, the legs are moved by a cycle ergometer at a constant rate (Menéndez et al., 2015), or moved by the concurrent (hybrid) exercise of the arms facilitated by arm ergometry (Stefanizzi and Overend, 1998). In contrast, FES-assisted leg cycling induces passive muscle contraction to generate motions of leg cycling (Ballaz et al., 2007).
Although the volume of evidence in support of these techniques is relatively limited, both techniques have been shown to improve indicators of cardiovascular function in persons living with SCI.

The primary purpose of this narrative review and commentary is to evaluate contemporary research regarding the use of PLC and FES, and to provide an evidence-based recommendation that may potentially improve the cardiovascular response generated in these passive leg exercises. We propose that by alternating the application of PLC and FES, a synergistic cardiovascular response may be elicited, leading to marked enhancements in cardiovascular function in the SCI population.

**Key Findings**

Recent advancements in pre-clinical SCI research produced novel evidence demonstrating that PLC can contribute significantly to improvements in cardiovascular function (West et al., 2014; West et al., 2015). In both studies conducted by West and his colleagues, rats were randomly assigned into three experimental groups over a period of 4 months: uninjured, complete SCI at the third thoracic vertebrae (T3-SCI), and T3-SCI with passive hind-limb cycling. The first major finding was that passive hind-limb cycling reduced cardiac dysfunction associated with the first week of T3-SCI (West et al., 2014). In contrast, non-cycling T3-SCI rats were observed to have left ventricular fibrosis, elevations in TGFβ1-Smad3 mRNA (a biomarker of myocardial fibrosis), and reductions in indicators of cardiovascular function, including end-diastolic volume, stroke volume, and cardiac output. It was postulated that fibrosis remodelled the heart in a manner that diminished its capacity for normal venous return. Furthermore, in cycling rats week 4 post-SCI, myocardial fibrosis was prevented, all aforementioned cardiac dysfunctions were reversed, and indicators of cardiovascular function were 20-30% higher relative to non-cycling T3-SCI rats (West et al., 2014). These findings suggest that passive leg cycling is sufficient to improve aerobic capacity, and as elaborated by Lujan and DiCarlo (2014), that increasing venous return may be a prerequisite to prevent or reverse cardiac dysfunction in the SCI population.

In the subsequent study, West et al. (2015) measured the change in autonomic dysreflexia in rats. Autonomic dysreflexia is a symptom post-SCI characterized by acute, uncontrolled hypertension, which is also observed in humans with SCI. Following 4 weeks of passive hind-limb cycling, histological assessments revealed that passive hind-limb cycling significantly reduced the severity of autonomic dysreflexia in T3-SCI rats (West et al., 2015). The finding that passive hind-limb cycling was sufficient to improve cardiovascular function in rats provided evidence at the molecular level that supported previous research findings regarding the use of PLC in clinical exercise rehabilitation programs for persons living with thoracic SCI (Ballaz et al., 2007; Ballaz et al., 2008).

A case series by Ballaz et al. (2007) examined the influence of PLC on acute changes in the blood flow velocity in the common femoral artery of 15 adults with chronic thoracic SCI. A Doppler ultrasound was used to measure the maximum and minimum velocities of red blood cells in the common femoral artery of participants pre- and post-10 minutes of PLC performed in a sitting position. Calculations revealed that PLC
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significantly increased the mean blood flow velocity in the common femoral artery by 30%, and significantly reduced vascular resistance in the common femoral artery by 6% in adults with thoracic SCI. These findings demonstrated that PLC contributed to improving cardiovascular function in the thoracic SCI population (Ballaz et al., 2007).

In a follow-up investigation, Ballaz et al. (2008) conducted a pilot study to examine whether or not home-based PLC could induce similar peripheral vascular changes in 17 adults with thoracic SCI. In this randomized controlled intervention, participants were required to perform 36 PLC sessions at home over 6 weeks. The results revealed that performing longitudinal PLC training significantly increased the acute mean blood flow velocity in the common femoral artery by 47% in comparison to the control group (Ballaz et al., 2008).

The findings by Ballaz and colleagues provided evidence that PLC was sufficient to improve aspects of cardiovascular function in persons living with thoracic SCI. The theory was that alternative motions in PLC increased peripheral blood flow in the lower limbs by passively activating muscle pumps, which resulted in increased venous return and subsequent elevations in end-diastolic volume, cardiac output, and stroke volume. These observations can be explained, in part, by evidence at the molecular level (West et al., 2014; West et al., 2015). The notion that passively activating muscle pumps can lead to marked improvements in cardiovascular function is also consistent with findings in research regarding the use of hybrid exercises in SCI rehabilitation; the concurrent exercise of the arms and legs have been shown to elicit even greater cardiorespiratory responses in comparison to traditional ergometer-assisted PLC, because it is suggested that concurrent exercises utilize larger muscle mass (Hasnan et al., 2013; Phillips et al., 2011).

Collectively, evidence in pre-clinical and clinical research provides support for the use of PLC to improve cardiovascular function in humans with thoracic SCI. However, the volume of evidence and consistency in findings in this field of research are relatively low.

Evidence shown by Woerds et al. (2006) revealed that PLC did not significantly increase common femoral artery blood flow in 8 chronic thoracic SCI and 8 able-bodied adults. Common femoral artery blood flow was measured (using Doppler ultrasound) before, during, and after 2 separate interventions: 10 min of passive movements (flexion on and extension of the lower limbs induced by a machine), and 20 min of PLC in a sitting position. The results revealed no significant changes in common femoral artery blood flow, vascular resistance, and systolic blood pressure between groups, irrespective of the intervention. These findings showed that in a thoracic SCI population, passive pumping of leg muscles was insufficient in evoking significant increases in common femoral artery blood flow.

This finding by Woerds and colleagues is consistent with the conclusion drawn by Hasnan et al. (2013), that a single intervention type (in this case, FES) may be insufficient in promoting aerobic fitness in the SCI population. Regardless, there is evidence to show that the health benefits accrued from FES treatment may not be elicited to the same extent in a PLC.
intervention, which highlights the value of FES.

The use of FES was explored in one study by Krause et al. (2008), which investigated the individual effect of FES and PLC regarding changes in muscle tone spasticity among five patients with thoracic SCI. In this randomized crossover study, each participant engaged in two separate interventions of passive cycling performed in a sitting position: PLC on a cycle ergometer, and FES-assisted cycling. The level of muscle spasticity was measured pre- and post-intervention. Results revealed that in comparison to baseline values, performing FES-assisted cycling significantly reduced muscle spasticity of the lower limbs by 68%, while performing PLC using a cycle ergometer significantly reduced muscle spasticity of the lower limbs by only 12% (Krause et al., 2008). Of particular clinical importance is that in the thoracic population, spasticity of the lower limbs is a symptom that often interferes with an individual’s capacity to perform passive leg exercises (Krause et al., 2008). Because a reduction in their capacity to perform passive leg exercises can limit the cardiovascular gains associated with this form of exercise, therapeutic strategies that reduce muscle spasticity of the lower limbs can indirectly improve the cardiovascular health in patients with thoracic SCI. Thus, the findings in this study highlight the clinical importance of FES treatment.

The use of FES was also investigated by Johnston et al. (2009) in a randomized controlled study that assessed aerobic improvements in 30 children with chronic SCI at various levels. Participants either performed PLC on a cycle ergometer, FES-assisted leg cycling, or no cycling (but received FES therapy as a control) for 6 months. By comparing cardiorespiratory measures, vascular measures, and blood lipid profiles at baseline and post-intervention, it was observed that FES-assisted leg cycling only resulted in significantly higher gains in peak oxygen uptake, and non-cycling FES therapy led to significant reductions in cholesterol levels. The lack of significant relationships between therapeutic strategies (FES or PLC) and cardiovascular outcomes suggested that passive leg exercises alone may be insufficient in generating significant cardiovascular responses in the thoracic SCI population, a statement that is consistent with the conclusion drawn by Hasnan et al. (2013).

Based on the current lines of evidence, our analysis is that passive leg exercises may be able to induce a greater cardiovascular response when the application of these exercises is coupled in an alternative manner.

The pairing of therapeutic strategies was explored in a study conducted by Menéndez et al. (2015). These authors investigated the effects of simultaneous FES and vibration on leg blood flow in 10 patients with thoracic SCI. In this randomized crossover study, each patient participated in four interventions in a seated position: whole body vibration, FES, simultaneous whole body vibration and FES, and 30 sec of whole body vibration followed by 30 sec of FES. Blood flow velocity was measured (via Doppler ultrasonography) in the popliteal artery pre- and post-intervention. Three key findings emerged from this study: 1) participants who engaged in the sole application of FES were observed to have the smallest increase in mean and peak blood flow velocity relative to all interventions; 2) when participants engaged in 30 sec of whole body vibration
followed by 30 sec of FES, the mean and peak blood flow velocities were significantly greater than when FES was applied alone; and 3) participants who engaged in the simultaneous application of whole body vibration and FES were observed to have the greatest significant increase in mean and peak blood flow velocity relative to all interventions. It could be interpreted that when FES was paired with vibration, the benefits from each therapeutic strategy generated a synergistic effect that elicited significantly greater improvements in cardiovascular response to stimuli.

The findings by Menéndez et al. (2015) provide novel insight on how passive leg exercises can be applied to improve cardiovascular function in the thoracic SCI population, such as the pairing of two therapeutic strategies. We propose a novel clinical exercise rehabilitation strategy for the thoracic SCI population involving the alternation of PLC and FES application. Involving a variety of exercise interventions is suggested to improve arterial function in persons with SCI (Phillips et al., 2011). We believe that alternating the application of PLC and FES can elicit a synergistic response in cardiovascular function similar to the marked enhancements in cardiovascular responses observed in participants who received the paired FES-vibration treatment (Menéndez et al., 2015). Although alternating two treatments may not be time- and cost-effective, the cardiovascular benefits may potentially be greater.

Our postulation is that the cardiovascular benefits associated with the applications of FES and PLC can be accrued synergistically. Alternating the two interventions can maximize the cardiovascular stimulus and related benefits, and minimize the risks associated with the prolonged application of a single intervention. For instance, reductions in muscle spasticity could allow patients to complete their passive leg exercises without interruption, and may subsequently lead to enhanced cardiovascular benefits. Furthermore, alternating interventions can minimize risks associated with overuse injuries, such as fatigue, neurological damage and bone fracture observed in prolonged FES treatments (Ballaz et al., 2007). Thus, alternating the application of FES and PLC may potentially improve the overall physical activity experience and cardiovascular function in ways that a single intervention cannot achieve. The role of alternating PLC and FES in improving cardiovascular function in persons living with thoracic SCI requires further research. The justification for further research stems from a relatively limited volume of evidence in this field.

Conclusion
Our narrative and commentary address one knowledge gap in research methodology in the area of SCI clinical exercise rehabilitation, which is the approach of alternating the application of PLC and FES to improve the cardiovascular function in the thoracic SCI population. Because the health benefits of PLC and FES may be accrued in a synergistic manner, such an approach may lead to marked enhancements in blood flow in the lower limbs of persons living with thoracic SCI, and by extension, improvements in cardiovascular function and health. This outcome is desirable because persons living with chronic thoracic SCI experience a 50% reduction in blood flow velocity (Ballaz et al., 2007). Blood stasis as a result of poor lower limb
circulation reduces venous return, which can lead to subsequent decreases in several measures of cardiovascular function, including cardiac output, stroke volume, and end-diastolic volume. (Ballaz et al., 2007). A decline in cardiovascular health can lead to CVD, which is the leading cause of rehospitalisation and mortality in the SCI population. The approach of alternating the application of PLC and FES offers novel insight into future research regarding SCI rehabilitation. Potential findings in this discipline can build and extend upon existing (yet limited) evidence-based recommendations for the use of PLC and FES in SCI clinical exercise rehabilitation programs.

Authors’ Qualifications
The authors’ qualifications are as follows: Henry Lai, BSc, BKIN; Darren Warburton, MSc, PhD, HFFC-CEP.

References


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