CARDIOVASCULAR FITNESS IN INDIVIDUALS WITH CERVICAL SPINAL CORD INJURY

by

Amira Tawashy

B.Sc. (Biopsychology), University of British Columbia, 2005

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE STUDIES

(Rehabilitation Sciences)

THE UNIVERSITY OF BRITISH COLUMBIA

(Vancouver)

April 2009

© Amira Tawashy

ABSTRACT

Background: The prevalence of cardiovascular disease in individuals with cervical spinal cord injury (SCI) is high, yet research surrounding the improvement of cardiovascular fitness in this population is lacking.

Purpose: 1) To systematically review the published literature to assess the effects of exercise modality, time since injury, injury severity, and training on VO_2peak values in individuals with cervical SCI; 2) to develop an aerobic exercise program to enhance aerobic capacity in a patient undergoing primary rehabilitation from a motor-complete C5/6 SCI.

Methods:

Part 1. A systematic review of the literature was undertaken to identify published studies measuring VO_2peak in individuals with cervical SCI. Scatterplots were generated to illustrate the effects of exercise modality, time since injury, and injury severity on VO_2peak. Effect sizes were calculated for the response to training on VO_2peak.

Part 2. Using the American College of Sports Medicine (ACSM) guidelines, an aerobic exercise program was developed for individuals with cervical SCI. Activity stations were designed to challenge aerobic capacity while minimizing muscular fatigue. The program was trialed on one subject with a C5 AIS A SCI undergoing sub-acute rehabilitation from injury.

Results: The literature review identified 40 studies reporting VO_2peak in individuals with cervical SCI. Scatterplots illustrated that VO_2peak was influenced by injury severity, but not exercise modality. Effect sizes for VO_2peak ranged from 0 to 21 (using pre-training standard deviations) in response to training. The case study of an individual with a C5 AIS A SCI showed that participation in the aerobic training program facilitated increased exercise tolerance, both in terms of exercise duration and exercise intensity. Measures of cardiovascular health, taken before and after training, showed increases in peak oxygen uptake and orthostatic tolerance over the 2 month course of the program.

Conclusions: The systematic review provided further evidence that VO_2peak is related to injury severity. The training studies reviewed suggest that it is possible for individuals with tetraplegia to gain cardiovascular benefits from aerobic training. The subject in our case study exhibited several signs of improved exercise tolerance over the 2 month program, indicating potential cardiovascular improvement from the exercise training.

TABLE OF CONTENTS

Abstract ii
Table of Contents iv
List of Tables vi
List of Figures vii
List of Abbreviations viii
Acknowledgments ix
Statement of Co-Authorship x

CHAPTER 1: Introduction 1
1.1 Introduction 1
1.2 Selected cardiovascular concepts 2
Stroke Volume 3
Autonomic cardiovascular control 3
Blood pressure control 6
1.3 Selected cardiovascular complications 7
Orthostatic Hypotension 7
Metabolic Syndrome 8
1.4 Measuring cardiovascular fitness 9
1.5 Cardiovascular de-conditioning and cardiovascular fitness 10
Aerobic exercise for individuals with cervical SCI 11
Aerobic training during sub-acute rehabilitation 12
1.6 Purpose 15
1.7 Research questions and hypothesis 16
1.8 References 18

CHAPTER 2: Cardiovascular capacity after cervical SCI: A systematic review 23
2.1 Overview 24
2.2 Introduction. 26
2.3 Methods. 29
2.4 Results. 32
Study characteristics 34
Testing modality and protocol 34
Cardiovascular capacity shortly after injury 45
The effect of training on VO_2peak 45
2.5 Discussion 51
Testing modality and protocol 52
VO_2peak and lesion characteristics 52
The effect of training on VO_2peak 53
Limitations 57
2.6 References 58

CHAPTER 3: Aerobic exercise during early rehabilitation from cervical SCI: A case report 64
3.1 Overview 65
3.2 Introduction 66

3.3 Methods. 68
Patient history and examination.....68
Intervention.....69
Outcome measures.....71
3.4 Results.....74
Training intervention.....74
Cardiovascular assessments.....77
Orthostatic hypotension: Sit up Test.....78
Timed functional wheeling 79
Subjective perception of the program.....80
3.5 Discussion 80
Limitations 83
3.6 References 85

CHAPTER 4: Conclusions and General Discussion.....88
4.1 Overview 88
4.2 Evaluation of the literature.....88
4.3 Evaluation of the in-patient exercise program 89
4.4 Clinical implications 90
4.5 Future work.....92
4.6 Summary 93
4.7 References 94

APPENDICES
Appendix A: Consent form 95
Appendix B: AIS 100
Appendix C: Electrode placement for ECG leads.....102
Appendix D: VO_2peak protocol 103
Appendix E: BORG RPE Scale.....104
Appendix F: Psychometric properties of outcome measures.....105
Appendix G: Ethics approval.....106

LIST OF TABLES

Table 2.1: Quality criteria for assessment of cohort studies 31
Table 2.2: Cross sectional studies measuring VO_2peak in individuals with tetraplegia: Protocol descriptions 36
Table 2.3: Longitudinal studies which measured VO^2peak in individuals with tetraplegia.....40
Table 2.4: Cardiovascular training studies.....48
Table 3.1: Exercise progression guidelines 71
Table 3.2: Participant Satisfaction Scale 74
Table 3.3: Cardiovascular results.....78

LIST OF FIGURES

Figure 1.1: Autonomic nervous system.....4
Figure 2.1: Flowchart for systematic search/selection of papers 33
Figure 2.2: VO_2peak elicited during ACE vs. Injury Level.....41
Figure 2.3: VO_2peak elicited during WCE vs. Injury Level.....43
Figure 2.4: VO_2peak elicited during FES vs. Injury Level 43
Figure 2.5: VO_2peak vs. Length of Injury.....45
Figure 3.1: Exercise program progression.....76
Figure 3.2: Sit-up Test.....79

LIST OF ABBREVIATIONS

ACSM – American College of Sports Medicine
AIS – American Spinal Injury Association Impairment Scale
BP – Blood pressure
CINAHL – Cumulative Index to Nursing and Allied Health Literature
HR – Heart rate
mL/kg/min – Millilitres of oxygen per kilogram body mass per minute
PO – Power output
RER – Respiration exchange ratio
RPE – Rate of perceived exertion
SCI – Spinal cord injury
SD – Standard deviation
VO_2peak – Peak oxygen consumption
W – Watts

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my supervisor, Dr. Janice Eng, who has given me invaluable guidance and support over the years. I cannot thank you enough for giving me the chance to explore and enjoy this experience. To my thesis committee: thank you to Dr. Bill Miller for his advice throughout the project; to Dr. Andrei Krassioukov for his dedication to many hours of testing; and to Dr. Bill Sheel for acting as external examiner for my thesis defense.

To all the members of the Rehabilitation Research Lab over the past few years, your knowledge, laughter, and commitment to success made this a great time for me. Chihya, your dedication and cheerful disposition were invaluable. And Jocelyn, you have been like a sister to me - I truly don't know where I would have been without you.

And lastly, I would like to thank my family from the bottom of my heart. Your never ending support and love challenged me to pursue this degree whole-heartedly and embrace life with open arms.

Statement of Co-Authorship

This thesis contains one research study which was conducted by the candidate, Amira Tawashy, under the supervision of Dr. Janice Eng and with guidance from Dr. Bill Miller and Dr. Andrei Krassioukov, and one systematic review conducted under the supervision of Dr. Janice Eng. The collection, analysis, and documentation of the research study and systematic review were primarily the work of the candidate.

Chapter 1: Introduction

1.1 Introduction

Spinal cord injury (SCI) is a devastating condition often affecting young and healthy individuals. The estimated number of Canadians currently living with SCI is 36 000, with approximately 1,050 new injuries occurring each year (Canadian Paraplegic Association, 2004). This debilitating condition not only creates enormous physical and emotional costs to individuals but is also a significant financial burden to society at large. Health care costs for people living with SCI range from $1.25 million - $25 million over a lifetime (Canadian Paraplegic Association, 2004). Although the medical management of SCI has improved dramatically over the last 30 years, there are still many unknowns with regard to inducing successful regeneration, especially in the chronic SCI state (Houle and Tessler, 2003). Not surprisingly, the common misconception still equates the term “walking” with “cure” (Anderson, 2004). Today, as it stands, one appropriate approach to SCI research is to learn from the people living with SCI about what is truly important to improving their quality of life, and to develop treatments and programs leading to partial function and recovery as per <u>their</u> priorities (Anderson, 2004). The mismatch of desired outcomes with outcomes usually targeted by researchers is a concern to the SCI population. Thus, the value of current research will depend on its relevance to those problems that strongly impact quality of life (Anderson, 2004).

Though significant progress has been made with regards to reducing mortality rate during the first 2 years post-SCI, there has been no substantial change in either

annual mortality rates after the second year post-SCI or life expectancy as measured from the second anniversary of injury or later (Strauss et al., 2006). People with SCI are susceptible to the same chronic conditions as their able-bodied counterparts. In particular, the leading cause of death in both populations is cardiovascular disease (CVD) (Garshick et al., 2005); though this occurs earlier (Garshick et al., 2005) and is more prevalent (Garshick et al., 2005; Myers et al., 2007) in individuals with SCI, with rates of symptomatic CVD reaching 30-50% in the SCI population (compared to 5-10% in the general, age-matched able-bodied population) (Myers et al., 2007). The risk of developing CVD increases with injury severity: tetraplegic injuries are associated with a 16% higher risk of all CVDs (Myers et al., 2007). Cardiovascular disease is especially disconcerting for individuals with cervical SCI as it can further exacerbate functional limitations resulting from the initial injury, thereby (i) posing a major threat to independent living; (ii) exponentially increasing financial care requirements; and (iii) negatively affecting quality of life (Noreau et al., 1993).

1.2 Selected cardiovascular concepts

The heightened risk of CVD in this population is attributable, in part, to the major physiological changes unique to a cervical SCI. Muscle paralysis imposes a more sedentary lifestyle (due to limited exercise options) and diminishes the activity of the skeletal muscle pump in the lower limbs (thereby decreasing the heart's stroke volume), while neurological dysfunction blunts the heart's "normal" chronotropic response to physical activity by decreasing stroke volume and sympathetic activity. These adverse physiological changes increase in magnitude with increasing severity of injury (Krassioukov et al., 2007) and individuals with cervical SCI at increased risk for cardiovascular disease.

1.2.1 Stroke Volume

Stroke volume is considerably lower in individuals with SCI compared to their age-matched counterparts (Nash et al., 1996). Lower stroke volume is associated with venous pooling in the lower extremities. This venous pooling causes low systemic blood pressures and reduced cardiac pre-load. As size, architecture, and function of the human heart are affected by peripheral circulatory blood volume and systemic pressures; these altered circulatory dynamics change the structure of the heart and subsequently alter its pumping efficiency (Cooper and Tomanek, 1982). Consequently, the functional capacity of the SCI heart is dependant upon injury level. In persons with tetraplegia, the chronic reduction of cardiac pre-load and decreased myocardial volume inevitably causes the left ventricle to atrophy (Nash et al., 1991). In contrast, individuals with paraplegia achieve near normal cardiac outputs by increasing their resting heart rate in order to compensate for lower stroke volumes (Hopman et al., 1998).

1.2.2 Autonomic cardiovascular control

In able bodied individuals, heart rate and blood pressure are controlled by both the parasympathetic and sympathetic components of the autonomic nervous system (Mathias, 1995). The parasympathetic system generally serves to decrease heart rate at rest whereas the sympathetic system counteracts the parasympathetic nervous system in response to a deviation from homeostasis (i.e. emergency or exercise). Consequently, when activated, the sympathetic system increases heart rate, myocardial contractile force, and peripheral vascular resistance. Parasympathetic control of the cardiovascular system is through the vagus nerve

(Cranial Nerve X), which exits the brain stem and synapses with postganglionic neurons within the myocardium. The parasympathetic nervous system does not innervate the peripheral vasculature. In contrast, sympathetic control of the cardiovascular system is through nerve tracts descending the spinal cord, which exit with motor nerves in the thoracolumbar segments (Claydon et al., 2006).

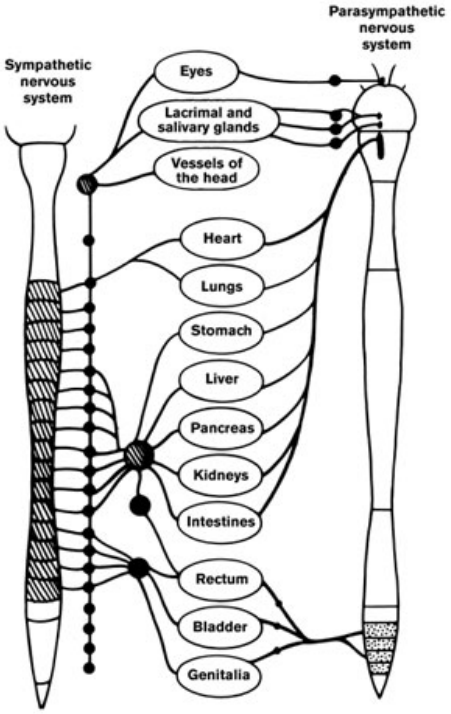


Figure 1.1 Autonomic Nervous System Modified from The Dana Guide to Brain Health (Bloom et al., 2009)**.**

SCI alters normal sympathetic innervation. Descending spinal sympathetic cardiovascular pathways exit the spinal cord at T1-T4. Consequently, cardiovascular control can be severely disrupted in individuals with cervical and high thoracic SCIs due to an imbalance between the sympathetic and parasympathetic nervous systems. Specifically, disruption of the sympathetic cardiovascular pathways results in sympathetic hypo-activity and unopposed parasympathetic control (Claydon et al., 2006).

The disrupted sympathetic nervous system also interferes with normal cardiovascular function through diminished innervation of the adrenal medulla. The adrenal medulla is innervated by cholinergic preganglionic sympathetic neurons - most of which originate between T5 and T9 (Bravo et al., 2004). Normally, the adrenal medulla releases epinephrine and norepinephrine into the blood in response to stress or exercise. Cardiovascular effects of these catecholamines are increased heart rate and blood pressure, and blood vessel constriction. SCI alters the catecholamine response to physical exercise. Whereas the able-bodied person will show an exponential increase in free plamsa epinpephrine and norepinephrine during maximal tests, the tetraplegic individual will exhibit only small increases of these same catecholamines - indicating no considerable stimulation of the sympathetic nervous system (Bravo et al., 2004). The loss of sympathetic outflow to the heart and adrenals seen in individuals with lesion levels above T5 result in bradycardia (Krassioukov et al., 2007). These individuals show a blunted chronotropic response to exercise and are unable to attain their age-predicted maximal heart rate, with peak heart rates of individuals with cervical injuries rarely exceeding 120 beats per minute (Freyschuss and Knutsson, 1969). Any minor cardiac acceleration (increase in heart rate) during exercise is attributed to the withdrawal of vagal tone (i.e. de-activation of the parasympathetic nervous system) and not increased sympathetic drive. Consequently, maximal cardiac output is significantly reduced and overall ability to transport oxygen to peripheral tissues is diminished in these individuals.

1.2.3 Blood pressure control

Blood pressure is continuously regulated by the autonomic nervous system, balancing the opposing effects of the sympathetic and parasympathetic nervous systems. Baroreceptor activity also contributes to the maintenance of blood pressure homeostasis. Baroreceptors are stretch receptors (located in the aortic arch, carotid sinus, and coronary arteries) that modulate sympathetic and parasympathetic outflow, in response to changes in arterial pressure, in order to maintain blood pressure homeostasis (Claydon et al., 2006). Common causes of hypotension are as follows: (1) Hypovolemia, often induced by hemorrhage or insufficient fluid intake; (2) Decreased cardiac output, including the use of beta-blockers (despite normal blood volume); (3) Excessive vasodilation, usually due to autonomic dysfunction (decreased sympathetic output and/or increased parasympathetic activity); and (4) decreased baroreflex activity.

The effect of SCI on normal cardiovascular function and blood pressure is evident even during the initial hours after injury. The well known “spinal shock” is a transient state of hypoexciteability of the isolated spinal cord and is associated with flaccid paralysis of muscles and impairment of spinal autonomic function (Ditunno et al., 2004). Dilation of blood vessels (coincident with spinal shock), combined with impaired autonomic function, often results in severe hypotension and persistent bradycardia (Bravo et al., 2004) and is termed “neurogenic shock” (Atkinson and Atkinson, 1996). Over time, as spinal shock subsides (a few days to weeks), cardiovascular control in individuals with cervical SCI remains disrupted due to the imbalance between sympathetic and parasympathetic nervous systems and dysfunctional baroreceptor reflex control (Mathias and Frankel, 1999).

1.3 Selected cardiovascular complications

1.3.1 Orthostatic Hypotension

Orthostatic hypotension (OH) is a common form of low blood pressure, precipitated by a change in position towards vertical (i.e. lying to sitting, sitting to standing). It is defined as a decrease in systolic blood pressure of $\geq$ 20 mm Hg or a decrease in diastolic blood pressure of $\geq$ 10 mm Hg when the subject moves from a supine to upright posture, regardless of whether symptoms occur (Shatz et al., 1996). Symptoms may include dizziness, nausea, or light-headedness with physical signs of pallor, diaphoresis, or loss or consciousness. Generally, OH is caused by cerebral hypoperfusion. Any factor decreasing either cardiac output or total peripheral vascular resistance diminishes cerebral perfusion (Kenny, 2003). Thus, common causes of OH are similar to those of general hypotension: hypovolemia, cardiac insufficiency, venous pooling, excessive use of diuretics or vasodilators, dehydration, anemia, or prolonged bed-rest. Although OH has been observed in all age groups, it occurs most frequently in the elderly population. Aging blunts baro-reflex activity (manifested as reduction in heart rate response to hypotensive stimuli); increases susceptibility to hypovolemia (due to excessive salt wasting by the kidneys); and diminishes cardiac output and systemic arterial pressure (Kenny, 2003).

In individuals with acute cervical and high thoracic SCI, clinical measurements of cardiovascular parameters often reveal severe blood pressure drops during orthostatic challenge tests, reflecting the presence of OH (Krassioukov and Claydon, 2006; Sidorov et al., 2007). This is likely attributable to excessive pooling of blood in the viscera and extremities due to the absence (or low level) of sympathetic nervous

activity and loss of reflex vasoconstrictor effect of arterial baroreceptors (Mathias, 1995). Individuals with lesions above T6 lack sympathetic outflow to the renal vascular beds and therefore cannot sufficiently vasoconstrict the blood vessels of the abdomen. This causes severe drops in blood pressure, especially with changes in body position from supine to sitting. Additionally, baroreflex function during orthostatic stress has been found to be abnormal in individuals with both high (Munakata et al., 2001) and low (Wecht et al., 2003) SCI lesions, suggesting that baroreceptor impairment may also contribute to orthostatic intolerance in individuals with SCI. The likelihood of experiencing OH is greater in patients with higher spinal cord lesions, and therefore is more common in those individuals with tetraplegic injuries than those with paraplegic injuries (Claydon and Krassioukov, 2006).

OH can significantly complicate and delay rehabilitation from the initial injury: Illman and colleagues found that 58.9% of patients with acute SCI experienced symptomatic OH with mobilization (Illman et al., 2000). Symptomatic OH can lead to immobility and prolonged bed-rest which are factors which have been cited to contribute to a variety of complications such as pressure sores, contractures, and pneumonia, and can further increase the likelihood of OH (Sidorov et al., 2007). Although OH was previously thought to occur solely in the acute period following SCI, it has been shown that it can persist for years, and often becomes worse with time (Claydon and Krassioukov, 2006).

1.3.2 Metabolic Syndrome

Metabolic syndrome is a pre-diabetic state characterized by a group of metabolic risk factors. The American Heart Association considers this syndrome to be a major risk

factor for heart disease (American Heart Association, 2007), with its presence roughly doubling the risk of CVD mortality (Myers et al., 2007). Risk factors closely associated with metabolic syndrome are as follows: obesity (as measured by increased waist circumference); atherogenic dyslipidemia (high triglycerides, low high-density lipoprotein [HDL] cholesterol, high low-density lipoprotein [LDL] cholesterol, and increased apolipoprotein B), high blood pressure, insulin resistance, and proinflammatory conditions (high C-reactive protein [CRP]) (Lee et al., 2005).

The prevalence of the metabolic syndrome and its individual components has been shown to be present in 23% of individuals with SCI, approximately double that of age-matched able-bodied individuals (Lee et al., 2005). After SCI, there is a tendancy toward elevated LDL cholesterol and total cholesterol as well as lower HDL cholesterol levels (Bauman and Spungen, 2000). CRP is elevated in both acute and chronic SCI (Myers et al., 2007) and has been found to be significantly associated with the presence of other well-known CVD risk factors, including multiple lipid abnormalities, metabolic syndrome, and insulin resistance in this population (Lee et al., 2005). The mean high-sensitivity CRP level in these subjects placed them in the high-risk group on the basis of normatives established for ambulatory individuals. Not surprisingly, individuals with tetraplegia tend to have a greater number of lipid abnormalities than their paraplegic counterparts (Myers et al., 2007). The reduced physical function associated with cervical SCI leads to sedentary lifestyles and lower energy expenditures, both of which contribute to a variety of related metabolic abnormalities associated with inactivity including insulin resistance, lower HDL levels, and greater susceptibility to vascular inflammation (Lee et al., 2005).

1.4 Measuring cardiovascular fitness

Cardiovascular fitness reflects the maximal amount of oxygen consumed during each minute of near maximal exercise. Maximum oxygen uptake (VO_2max) is generally accepted as the gold standard for assessing cardiovascular fitness. Values for maximal oxygen consumption (VO_2max) can range from 10mL/kg/min in able-bodied individuals with cardiovascular and respiratory diseases, to more than 80mL/kg/min in elite runners and cross-country skiers (Plowman and Smith, 2007). In individuals with SCI, the VO_2max test is most often assessed by either arm cycle ergometry (ACE) or wheelchair ergometry (WCE). However, the inherent weakness of the upper limbs can cause arm fatigue to limit the VO_2max test : In able bodied subjects, VO_2max as measured by arm work is approximately two thirds that achieved with cycling or running (Glaser et al., 1979). Thus, the term VO_2peak (the highest VO_2 value elicted from the maximal exercise test) is a more appropriate term to use when describing testing of individuals with SCI to attain VO_2 data. It has been long known that VO_2peak is associated with injury severity in this population (Burkett et al., 1990). Reported VO_2peak values in individuals with SCI range from approximately 6 mL/kg/min in individuals with tetraplegia (Dallmeijer and van der Woude, L.H., 2001; Lewis et al., 2007) to as high as 37 mL/kg/min in individuals with paraplegia (Cooper et al., 1992). Recently, VO_2peak has been assessed using a variety of other modalities (e.g. functional electrical stimulation leg cycle ergometry (FES-LCE), body-weight supported treadmill, handcycle), in addition to the standard ACE and WCE methods; however, a set of comparative values for different exercise modalities has yet to be compiled. Chapter 2 of this thesis uses a systematic review to quantify the effects of exercise modality and testing protocol on VO_2peak in individuals with cervical SCI.

1.5 Cardiovascular de-conditioning and cardiovascular fitness

Cardiovascular de-conditioning, secondary to prolonged periods of inactivity, is a modifiable risk factor predisposing individuals with SCI to CVD (American College of Sports Medicine and Johnson, 2000), OH (Sidorov et al., 2007) and metabolic syndrome (Lee et al., 2005). Literature addressing the need for people with SCI to adopt habitual exercise as part of a healthy lifestyle is abundant (Jacobs and Nash, 2004) and clients have indicated that they consider exercise to be an important aspect of their functional recovery (Anderson, 2004; O'Neill S.B., Maguire S., 2004). Physical activity is needed if persons with SCI are to reach and maintain the level of physical fitness that is desirable for their function in daily life. By improving their physical fitness, individuals with SCI may be able to decrease the incidence and severity of OH, thereby mitigating delays in initial rehabilitation (Sidorov et al., 2007), decrease their risk for chronic CVD (Dearwater et al., 1986), decrease their risk factors for metabolic syndrome (Lee et al., 2005), and ultimately decrease physical strain during their activities of daily living (Janssen et al., 1996).

1.5.1 Aerobic exercise for individuals with cervical injury

Our current knowledge surrounding the effects of aerobic training in the SCI population is garnered primarily from studies of individuals with paraplegia (Jacobs et al., 2000; Tordi et al., 2001), the results of which demonstrate significant cardiovascular improvement due to aerobic training in individuals with SCI. Although the documented duration and frequency of successful aerobic exercise training programs vary, it is generally agreed that the intensity threshold required to induce training benefits for individuals with chronic SCI is 70% of maximal heart rate for a

minimal duration of 20 minutes over a period of at least 4 weeks (Hooker and Wells, 1989). However, given that arm exercises incorporate a relatively small muscle mass, the primary factors limiting performance during aerobic exercise are likely peripheral in nature; thus, local fatigue of the highly stressed arm musculature may occur despite sufficient systemic oxygen availability (De Groot et al., 2003). Consequently, many studies exploring aerobic exercise for the SCI population utilize interval training as it allows a longer cumulative exercise duration (De Groot et al., 2003; Hicks et al., 2003; Tordi et al., 2001). For example, Tordi et al. (2001) ran a wheelchair ergometer program consisting of six successive mini-workouts of 5 minutes each (Tordi et al., 2001). During each mini-workout, a 4-min period of moderate exercise (base) was followed by a 1-min period of intense exercise (peak). Initially, the base level was set at 50% of maximal tolerated power (MTP) and the peak at 80% MTP. The peak and base loads were alternately re-adjusted by 10% as HR declined in response to the exercise. Four weeks of this training program resulted in an 18.5% increase in VO_2peak in five subjects with paraplegia.

Due to the sympathetic insufficiency associated with cervical SCI, the training results seen in the above studies cannot be generalized to individuals with tetraplegia. Unfortunately, because of the cardiovascular autonomic dysfunction associated with injuries above T5, individuals with cervical SCI are often excluded from cardiovascular training studies. Thus, knowledge concerning the cardiovascular effects of training program for individuals with cervical injuries is severely lacking.

1.5.2 Aerobic training during sub-acute rehabilitation

Individuals sustaining a motor-complete cervical SCI can experience up to four weeks in bed during acute care (Illman et al., 2000). The negative cardiovascular consequences of such prolonged bed-rest have been well documented in the able-bodied population (Saltin et al., 1968) and are particularly detrimental for individuals with cervical SCI. Aerobic exercise during sub-acute rehabilitation may halt the cardiovascular deterioration resulting from prolonged immobility. Further, cardiovascular training is needed if persons with SCI are to reach and maintain the level of cardiovascular fitness that is desirable for function in daily life. Therefore, the effort to achieve optimal levels of fitness, through sustained aerobic activity, should ideally start during primary rehabilitation itself (De Groot et al., 2003).

Though the rationale for aerobic exercise to start during rehabilitation is compelling, it is a topic that is currently understudied by the SCI research community. To date, only a small number of training studies during sub-acute rehabilitation from SCI have been published. Most of the recent ones involve novel exercise therapies (e.g. Functional Electrical Stimulation (Chilibeck et al., 1999), Body Weight Supported Treadmill Training (Dobkin et al., 2006) rather than conventional methods (e.g. wheeling, arm ergometry), so the knowledge surrounding aerobic exercise during SCI rehabilitation is scarce. Consequently there are no evidence-based guidelines for promoting and prescribing exercise for this population nor is it not considered a key component of their rehabilitation.

To our knowledge, only two studies have explored use of aerobic exercise as an adjunct to primary rehabilitation (Bizzarini et al., 2005; De Groot et al., 2003). De

Groot et al. (2003) investigated the effect of training intensity on the physical capacity of six individuals undergoing primary rehabilitation from an SCI and Bizzarini et al. (2005) evaluated the effect of training on the metabolic parameters of 21 individuals undergoing primary rehabilitation from an SCI. De Groot et al.'s program was three days/week for 8 weeks while Bizzarini et al.'s was five days/week for 6 weeks. Both programs aimed to maintain target heart rates between 70% and 80% of maximum. In deGroot et al.'s study, participants were randomly assigned to one of two groups: low intensity (LI) exercise training (40-50% HRR; n=3) or high intensity (HI) exercise training (70-80% HRR; n=3). Both training groups demonstrated significant increases in VO_2peak after the exercise program (150%, HI; 117%, LI). However, this increase was significantly greater in the HI group than it was in the LI group (6.67 ml/kg/min $\pm$ 3.8, HI; 3.00 ml/kg/min $\pm$ 0.0, LI). Furthermore, blood lipid profiles revealed that TG and TC/HDL dropped more in the HI group than they did in the LI group. The HI group's baseline TG values (range 1.5 - 2.6 mmol/L) decreased 41% after exercise training (post-test range: 0.8-1.8 mmol/L), in comparison to only a 5% drop in the LI group (0.9-3.8 vs.1.0-3.8 mmol/L). TC/HDL baseline ratios decreased 23% to post-test (median 5.3 (pre-test) vs. 4.0 (post-test)) in the HI group compared to a 0% decrease in the LI group (median 4.0). Although results showed a trend toward more favorable lipid profile after high intensity exercise training, changes in the individual components TC, HDL, and LDL were not significant between groups. Participants in Bizzarini et al.'s study completed 90 minute, daily training session, which consisted of discontinuous exercise on arm and wheelchair ergometers and strength training on pulley machines. They were monitored every 2 weeks and training was modulated with the aim of maintaining a target heart rate between 70% and 80% of maximum.

Participants increased their workload throughout the study without any metabolic signs of overtraining.

These two studies provide support that recently injured SCI individuals can (a) benefit from early exercise and (b) sustain a relatively high physical strain during early rehabilitation. However, the study by De Groot et al. (2003) (n=6) included only one individual with cervical SCI who was injured more 6 months prior to participating in the program and Bizzarini et al.'s study (2005) did not include any individuals with complete cervical SCI, nor did they use any cardiovascular assessments. No study has assessed the feasibility (nor the effects) of an exercise program designed specifically for individuals with cervical SCI participating in sub-acute rehabilitation. Because they are severely limited by autonomic nervous system impairments and paralysis, individuals with tetraplegia are not always able to participate in programs designed for individuals with full upper body strength and intact autonomic control of the cardiovascular system. Chapter 3 of this thesis outlines the process used to develop an aerobic exercise program to enhance aerobic capacity in a patient undergoing primary rehabilitation from a motor-complete C5/6 SCI.

1.6 Purpose

The purpose of this thesis was twofold:

1) To undertake a systematic review to:

a) Quantify the effects of exercise modality, time since injury, injury severity, and training on VO_2peak in individuals with cervical SCI ; and

b) Analyze the protocols used to assess VO_2peak in individuals with cervical SCI.

2) To outline the process used to develop an exercise program to enhance aerobic capacity in a patient undergoing primary rehabilitation from a motor-complete C5/6 SCI.

1.7 Research questions and hypothesis

Cardiovascular capacity after cervical spinal cord injury: A systematic review.

1.7.1 Research question 1: Does exercise modality, time since injury, injury severity, and training effect VO_2peak in individuals with cervical SCI?

Hypothesis: VO_2peak values will be similar across exercise modalities using the same musculature (i.e. upper limb vs. lower limb).

Hypothesis: Time since injury, injury severity, and training will alter VO_2peak values.

Aerobic exercise during early rehabilitation from cervical spinal cord injury: A case report

1.7.2 Research question 2: Is it feasible to design an aerobic training program for individuals with cervical SCI?

Hypothesis: An exercise program for individuals with cervical SCI which minimizes muscle fatigue, thereby facilitating aerobic capacity, can be developed.

1.7.3 Research question 3: Can an individual with motor-complete cervical SCI sustain an aerobic training program and improve cardiovascular function during sub-acute rehabilitation?

Hypothesis 1: An individual with cervical SCI will be able to sustain an aerobic training program during sub-acute rehabilitation with minimal adverse effects.

Hypothesis 1: Aspects of cardiovascular function (VO_2peak, OH, lipid profile) will improve after participation in an aerobic training program.

1.8 References

1. American College of Sports Medicine, and Johnson, E. P. (2000). ACSM's Guidelines for Exercise Testing and Prescription. Lippincott Williams & Wilkins:

2. American Heart Association. (2007).

3. Anderson, K. D. (2004). Targeting recovery: priorities of the spinal cord-injured population. J Neurotrauma. **21,** 1371-1383.

4. Atkinson, P. P., & Atkinson, J. L. D. (1996). Spinal shock. **71,** 384-389.

5. Bauman, W. A., and Spungen, A. M. (2000). Metabolic changes in persons after spinal cord injury. Phys Med Rehabil Clin N Am. **11,** 109-140.

6. Bizzarini, E., Saccavini, M., Lipanje, F., Magrin, P., Malisan, C., and Zampa, A. (2005). Exercise prescription in subjects with spinal cord injuries. Arch Phys Med Rehabil. **86,** 1170-1175.

7. Bloom, F. E., Beal, M. F., & Kupfer, D. J. (2009). The Dana guide to brain health - Autonomic Disorders.

8. Bravo, G., Guizar-Sahagun, G., Ibarra, A., Centurion, D., and Villalon, C. M. (2004). Cardiovascular alterations after spinal cord injury: an overview. Curr Med Chem Cardiovasc Hematol Agents. **2,** 133-148.

9. Burkett, L. N., Chisum, J., Stone, W., and Fernhall, B. (1990). Exercise capacity of untrained spinal cord injured individuals and the relationship of peak oxygen uptake to level of injury. Paraplegia. **28,** 512-521.

10. Canadian Paraplegic Association. (2004). Canadian Paraplegic Association. Statistical data [on-line].

11. Chilibeck, P. D., Jeon, J., Weiss, C., Bell, G., and Burnham, R. (1999). Histochemical changes in muscle of individuals with spinal cord injury following functional electrical stimulated exercise training. Spinal Cord. **37,** 264-268.

12. Claydon, V. E., Steeves, J. D., and Krassioukov, A. V. (2006). Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord. **44,** 341-351.

13. Claydon, V. E., and Krassioukov, A. V. (2006). Orthostatic hypotension and autonomic pathways after spinal cord injury. J Neurotrauma. **23,** 1713-1725.

14. Cooper, G., and Tomanek, R. J. (1982). Load regulation of the structure, composition, and function of mammalian myocardium. Circ Res. **50,** 788-798.

15. Cooper, R. A., Horvath, S. M., Bedi, J. F., Drechsler-Parks, D. M., and Williams, R. E. (1992). Maximal exercise reponse of paraplegic wheelchair road racers. Paraplegia. **30,** 573-581.

16. Dallmeijer, A. J., and van der Woude, L.H. (2001). Health related functional status in men with spinal cord injury: relationship with lesion level and endurance capacity. Spinal Cord. **39,** 577-583.

17. De Groot, P. C. E., Hjeltnes, N., Heijboer, A. C., Stal, W., and Birkeland, K. (2003). Effect of training intensity on physical capacity, lipid profile and insulin sensitivity in early rehabilitation of spinal cord injured individuals. Spinal Cord. **41,** 673-679.

18. Dearwater, S. R., LaPorte, R. E., Robertson, R. J., Brenes, G., Adams, L. L., and Becker, D. (1986). Activity in the spinal cord-injured patient: an epidemiologic analysis of metabolic parameters. Medicine & Science in Sports & Exercise. **18,** 541.

19. Ditunno, J. F., Little, J. W., Tessler, A., and Burns, A. S. (2004). Spinal shock revisited: a four-phase model. Spinal Cord. **42,** 383-395.

20. Dobkin, B., Apple, D., Barbeau, H., Basso, M., Behrman, A., Deforge, D., Ditunno, J., Dudley, G., Elashoff, R., and Fugate, L. (2006). Weight-supported treadmill vs over-ground training for walking after acute incomplete SCI. Neurology. **66,** 484-493.

21. Freyschuss, U., and Knutsson, E. (1969). Cardiovascular control in man with transverse cervical cord lesions. Life Sci. **8,** 421-424.

22. Garshick, E., Kelley, A., Cohen, S. A., Garrison, A., Tun, C. G., Gagnon, D., and Brown, R. (2005). A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord. **43,** 408-416.

23. Glaser, R. M., Sawka, M. N., Laubach, L. L., and Suryaprasad, A. G. (1979). Metabolic and cardiopulmonary responses to wheelchair and bicycle ergometry. J Appl Physiol. **46,** 1066-1070.

24. Hicks, A. L., Martin, K. A., Ditor, D. S., Latimer, A. E., Craven, C., Bugaresti, J., and McCartney, N. (2003). Long-term exercise training in persons with spinal cord injury: effects on strength, arm ergometry performance and psychological well-being. Spinal Cord. **41,** 34-43.

25. Hooker, S. P., and Wells, C. L. (1989). Effects of low-and moderate-intensity training in spinal cord-injured persons. Medicine & Science in Sports & Exercise. **21,** 18.

26. Hopman, M. T. E., Dueck, C., Monroe, M., Philips, W. T., and Skinner, J. S. (1998). Limits to maximal performance in individuals with spinal cord injury. Int J Sports Med. **19,** 98-103.

27. Houle, J. D., and Tessler, A. (2003). Repair of chronic spinal cord injury. Exp Neurol. **182,** 247-260.

28. Illman, A., Stiller, K., and Williams, M. (2000). The prevalence of orthostatic hypotension during physiotherapy treatment in patients with an acute spinal cord injury. Spinal Cord. **38,** 741-747.

29. Jacobs, P. L., and Nash, M. S. (2004). Exercise Recommendations for Individuals with Spinal Cord Injury. Sports Medicine. **34,** 727.

30. Jacobs, P. L., Nash, M. S., and Rusinowski, J. R. (2000). Circuit training provides cardiorespiratory and strength benefits in persons with paraplegia. Med Sci Sports Exerc. **33,** 711-717.

31. Janssen, T. W., van Oers, C. A., Rozendaal, E. P., Willemsen, E. M., Hollander, A. P., and van der Woude, L. H. (1996). Changes in physical strain and physical capacity in men with spinal cord injuries. Med Sci Sports Exerc. **28,** 551-559.

32. Kenny, R. A. (2003). Syncope in the elderly: diagnosis, evaluation, and treatment. J Cardiovasc Electrophysiol. **14,** S74-7.

33. Krassioukov, A., and Claydon, V. E. (2006). The clinical problems in cardiovascular control following spinal cord injury: an overview. PBR. **152,** 227-233.

34. Krassioukov, A. V., Karlsson, A. K., Wecht, J. M., Wuermser, L. A., Mathias, C. J., and Marino, R. J. (2007). Assessment of autonomic dysfunction following spinal cord injury: Rationale for additions to International Standards for Neurological Assessment. J Rehabil Res Dev. **44,** 103-112.

35. Lee, M. Y., Myers, J., Hayes, A., Madan, S., Froelicher, V. F., Perkash, I., and Kiratli, B. J. (2005). C-reactive protein, metabolic syndrome, and insulin resistance in individuals with spinal cord injury. J Spinal Cord Med. **28,** 20-25.

36. Lewis, J. E., Nash, M. S., Hamm, L. F., Martins, S. C., and Groah, S. L. (2007). The Relationship Between Perceived Exertion and Physiologic Indicators of Stress

37. Mathias, C. J., and Frankel, H. L. (1999). Autonomic disturbances in spinal cord lesions. Autonomic Failure: A Textbook of Clinical Disorders of the Autonomic Nervous System. 494–513.

38. Mathias, C. J. (1995). Orthostatic hypotension: causes, mechanisms, and influencing factors. Neurology. **45,** S6-11.

39. Munakata, M., Kameyama, J., Nunokawa, T., Ito, N., and Yoshinaga, K. (2001). Altered Mayer wave and baroreflex profiles in high spinal cord injury&ast.

40. Myers, J., Lee, M., and Kiratli, J. (2007). Cardiovascular Disease in Spinal Cord Injury: An Overview of Prevalence, Risk, Evaluation, and Management. American Journal of Physical Medicine & Rehabilitation. **86,** 142.

41. Nash, M. S., Montalvo, B. M., and Applegate, B. (1996). Lower extremity blood flow and responses to occlusion ischemia differ in exercise-trained and sedentary tetraplegic persons. Arch Phys Med Rehabil. **77,** 1260-1265.

42. Nash, M. S., Bilsker, S., Marcillo, A. E., Isaac, S. M., Botelho, L. A., Klose, K. J., Green, B. A., Rountree, M. T., and Shea, J. D. (1991). Reversal of adaptive left ventricular atrophy following electrically-stimulated exercise training in human tetraplegics. Paraplegia. **29,** 590-599.

43. Noreau, L., Shephard, R. J., Simard, C., Pare, G., and Pomerleau, P. (1993). Relationship of impairment and functional ability to habitual activity and fitness following spinal cord injury. Int J Rehabil Res. **16,** 265-275.

44. O'Neill S.B., Maguire S. (2004). Patient perception of the impact of sporting activity on rehabilitation in a spinal cord injuries unit. Spinal Cord. **42,** 627-630.

45. Plowman, S., and Smith, D. (2007). Exercise physiology for health, fitness, and performance. Lippincott Williams & Wilkins:

46. Saltin, B., Blomqvist, G., Mitchell, J. H., Johnson, R. L.,Jr, Wildenthal, K., and Chapman, C. B. (1968). Response to exercise after bed rest and after training. Circulation. **38,** VII1-78.

47. Shatz, I. J., Bannister, R., Freeman, R. L., Goetz, C. G., Jankovic, J., Kaufmann, H. C., Koller, W. C., Low, P. A., Mathias, C. J., and Polinsky, R. J. (1996). American Autonomic Society Consensus Statement. The definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. Neurology. **46,** 1470-1471.

48. Sidorov, E. V., Townson, A. F., Dvorak, M. F., Kwon, B. K., Steeves, J., and Krassioukov, A. V. (2007). Orthostatic hypotension in the first month following acute spinal cord injury. Spinal Cord. **46,** 65.

49. Strauss, D. J., DeVivo, M. J., Paculdo, D. R., and Shavelle, R. M. (2006). Trends in life expectancy after spinal cord injury. Arch Phys Med Rehabil. **87,** 1079-1085.

50. Tordi, N., Dugue, B., Klupzinski, D., Rasseneur, L., Rouillon, J. D., and Lonsdorfer, J. (2001). Interval training program on a wheelchair ergometer for paraplegic subjects. Spinal Cord. **39,** 532-537.

51. Wecht, J. M., De Meersman, R. E., Weir, J. P., Spungen, A. M., and Bauman, W. A. (2003). Cardiac autonomic responses to progressive head-up tilt in individuals with paraplegia. Clinical Autonomic Research. **13,** 433-438.

Chapter 2: Cardiovascular capacity after cervical spinal cord injury: A systematic review[1]

[1] A version of this chapter will be submitted for publication. Tawashy, AE., Eng, JJ. Cardiovascular capacity after spinal cord injury: A systematic review.

2.1 OVERVIEW

Background: The prevalence of cardiovascular disease in individuals with cervical spinal cord injury (SCI) is high, yet research surrounding the measurement and improvement of cardiovascular fitness in this population is lacking.

Purpose: To systematically review the published literature to assess the effects of exercise modality, time since injury, injury severity, and training on VO_2 peak. values in individuals with cervical SCI.

Methods: The key words 'spinal cord injury', 'paraplegia', 'tetraplegia', and 'quadriplegia' were entered in combination with 'exercise' and 'oxygen consumption'. Studies were described with respect to population, testing modality and protocol, and training regime. Scatterplots were generated to assess the relationship between lesion level and VO_2peak for testing modalities. Effect sizes were calculated for the response to training on VO_2peak.

Results: The literature review identified 40 studies reporting VO_2peak in individuals with cervical SCI. Scatterplots illustrated that VO_2peak was influenced by injury severity, but not exercise modality. Effect sizes for VO_2peak ranged from 0 to 21 in response to training.

Conclusions: The exercise literature concerning individuals with cervical SCI is limited in quantity. This review revealed a wide range of VO_2peak values. In general,

VO_2peak increased with decreasing severity of injury. Higher intensity training seemed to elicit higher effect sizes for VO_2peak.

2.2 Introduction

Physical capacity can be described as the capacity of the cardiovascular system, muscle groups, and the respiratory system to provide a level of physical activity (Stewart et al., 2000). It is reduced in individuals with spinal cord injury (SCI), particularly those with cervical injuries, due to the direct loss of motor control and sympathetic activity below the level of lesion. Low physical capacity coupled with wheelchair dependancy severely reduces the ability to maintain an active lifestyle, and is a major contributor to cardiovascular disease. Similar to the able-bodied population (Garshick et al., 2005), the leading cause of death in individuals with SCI is cardiovascular disease (CVD) (Garshick et al., 2005); though this occurs earlier (Garshick et al., 2005) and is more prevalent (Garshick et al., 2005; Myers et al., 2007) in the latter. The risk of developing CVD increases with injury severity: tetraplegic injuries are associated with a 16% higher risk of all CVDs (Myers et al., 2007). The heightened risk of CVD in this population is attributable, in part, to the major physiological changes unique to a cervical SCI. Muscle paralysis imposes a more sedentary lifestyle (due to limited exercise options) and diminishes the activity of the skeletal muscle pump in the lower limbs (thereby decreasing the heart's stroke volume), while neurological dysfunction blunts the heart's "normal" chronotropic response to physical activity by decreasing stroke volume and sympathetic activity. Low cardiovascular fitness can lead to a vicious cycle of further decline as it results in reduced functional capacity and thus threatens the ability to live independently.

Maximum oxygen uptake (VO_2max) is generally accepted as the gold standard measurement for assessing cardiovascular fitness (Stewart et al., 2000). VO_2max is the highest amount of oxygen an individual can take in, transport, and utilize to

produce ATP aerobically while breathing air during heavy exercise (Plowman and Smith, 2007). Physiological criteria for reaching VO_2max are as follows : 1) a lactate value greater than 8mmol/L; 2) a heart rate $\pm$ 12 beats/minute of predicted maximal heart rate; 3) a respiratory exchange ratio of ≥1.0; and 4) a plateau in VO_2 with subsequent increases in exercise intensity (Plowman and Smith, 2007). A rating of perceived exertion of equal or greater than 17 is often used as a psychophysiological criterion (Howley et al., 1995). In individuals with SCI, the VO_2max test is most often assessed by a graded exercise test using either arm cycle ergometry (ACE) or wheelchair ergometry (WCE). However, the inherent weakness of the upper limbs can cause arm fatigue which may limit the VO_2max test. In able bodied subjects, VO_2max as measured by arm work is approximately two-thirds that achieved with cycling or running (Glaser et al., 1979). Thus, the term VO_2peak (the highest rate of aerobic metabolism elicited from the maximal exercise test (Stewart et al., 2000)) is a more appropriate term to use when describing testing of individuals with SCI to attain VO_2 data (Burkett et al., 1990). However, it has been noted that there is often a lack of information given as to whether a true VO_2 peak has been attained (i.e. eliciting a maximal effort) when working with this population (Burkett et al., 1990). Recently, VO_2 peak has been assessed using a variety of other modalities (e.g. functional electrical stimulation leg cycle ergometry (FES-LCE); body-weight supported treadmill; handcycle), in addition to the standard ACE and WCE methods. However, a set of comparative values for the different exercise modalities has yet to be determined.

There are several inherent problems that occur when an attempt is made to compare research findings between exercise studies from individuals with SCI. Firstly,

although it has been established that VO_2peak is associated with injury severity in this population (Burkett et al., 1990), many investigators choose to group all subjects together (e.g. paraplegic with tetraplegic) because of small subject numbers. Some authors include individual data as well as mean data, however this is not universal practice. Secondly, within the current literature, reported fitness levels vary greatly. This is likely due to a wide range of participant characteristics (duration and severity of injury) and testing methodologies, both of which hamper generalizations and comparisons.

Unfortunately, in order to create homogeneous subject pools, some researchers limit participation in their studies to individuals with injuries below the sixth thoracic nerve as these subjects maintain complete autonomic sympathetic control of the cardiovascular system. So, although research regarding physical capacity in SCI is not lacking per se, knowledge surrounding cardiovascular fitness in individuals with cervical injuries is sparse in comparison to those with paraplegia. For individuals with tetraplegia, failure of sympathetically driven cardiac acceleration results in severely decreased cardiac output and reduces oxygen transport to the muscle, thus systemically limiting ability to reach VO_2peak. The significant reduction in the amount of innervated musculature further limits the ability to reach VO_2peak. Consequently, this population is an understudied one in the exercise literature. Thus, the purpose of this review is to narrow the focus of physical capacity to those individuals with cervical injuries. Accordingly, the main objective of this study is to undertake a systematic review of the literature to:

1) Quantify the effects of exercise modality, time since injury, injury severity, and training on VO_2peak in individuals with cervical SCI.

2) Analyze the protocols used to assess VO_2peak in individuals with cervical SCI.

2.3 Methods

Data search

The electronic databases of PubMed (MEDLINE), CINAHL, and Ovid (Embase) were systematically searched with the following (combinations of) keywords : 'spinal cord injury', 'paraplegia', 'tetraplegia', and 'quadriplegia', combined with 'exercise', and/or 'oxygen consumption'. The search was limited to the English language and included publications up to September 2008. After this first selection of studies, all hits were investigated in detail. The reference lists of all included articles were scanned for further literature. To be included in this review, studies were required to meet the following inclusion criteria:

1) The research population was comprised entirely of individuals with spinal cord injury.

2) Inclusion of $\geq$ 5 individuals with a tetraplegia

3) No more than 20% of subjects had a injury below the 8th cervical nerve

4) The component of peak oxygen uptake (VO_2peak) was measured in the study.

Each study population was described via age, injury severity, length of injury (LOI), and activity level. Studies were subdivided into 'complete injuries' (all participants had motor-complete SCIs); 'incomplete injuries' (all participants had motor-incomplete SCIs); or 'mixed injuries; (the study included participants with both complete and incomplete injuries). In the event that completeness of injury was not explicitly stated, the study was put in the 'mixed injuries' category. This was the case for the

majority of studies using the Stoke Mandeville Functional Sports Classification. The modality and protocol used to determine VO_2peak were described. Data was extracted from either text or graphs. We presented VO_2peak in mL/kg/min. Where VO_2 was presented in L/min (and body mass was not reported), we used the average mass of the entire cohort (72.0 kg) to compute an estimate of the VO_2peak for that study. Training protocols were described with respect to exercise intensity, training frequency, and program duration. We assessed the methodological quality of each training study by using a 9-item assessment scale designed for cohort studies (Centre for Reviews and Dissemination, 2001; Zwicker and Harris, 2009). Items required a yes/no response (yes = 1; no = 0) and measured factors such as sufficient description of groups, comparability of groups, blinded outcome measurement etc (Table 2.1). The maximum possible score is 10. Scores of $\geq$7 were considered to indicated strong studies; 4 to 6 moderate, and <4 weak.

Table 2.1. Quality criteria for assessment of cohort studies

	Circle one:	Comment
Is there sufficient description of the groups and the distribution of prognostic factors?	Y N	
Are the groups assembled at a similar point in their disease progression?	Y N	
Is the "exposure" reliably ascertained?	Y N	
Were the groups comparable on all important confounding factors?	Y N	
Was there adequate adjustment for the effects of these confounding variables?	Y N	
Was outcome assessment blind to exposure status?	Y N	
Was follow-up long enough for the outcomes to occur?	Y N	
What proportion of the cohort was followed-up?	< 50% (0) 50-75% (1) > 75% (2)	
Were drop-out rates and reasons for drop-out similar across intervention and unexposed groups?	Y N	
Quality Assessment Score (one point for each Y response plus corresponding score for % of cohort remaining)	**/10**	

Scatterplots were generated to explore the effect of lesion level on VO_2 peak for each exercise modality (ACE, WCE, and FES). A weighting system was developed, assigning scores to injury levels, in order to effectively graph the data. A C5 injury was assigned 5 points, a C6 injury assigned 6 points and so forth, such that all participants were assigned a point value. The values for each study were summed and divided by that study's number of participants. Thus, a study with 7 participants (2 with C5 injuries, 3 with C7 injuries, 2 with C8 injuries) had an injury score of 6.7

We were also interested in exploring VO_2peak early after injury. Early after cervical SCI, cardiovascular function is not stable, due to reconciliation of neurogenic shock and permanent autonomic disturbances. We extrapolated and consolidated the VO_2peak values from a series of longitudinal studies in order to generate a scatterplot documenting the relationship between VO_2peak and length of injury (LOI) over the first 24 months post-injury.

2.4 Results

After searching the different databases, 1829 articles were identified. Following screening of titles and abstracts for consistency with inclusion criteria, 86 papers were selected as potentially relevant. After reading the articles, 43 studies were excluded because a) the population was not SCI specific: the study included individuals with impairments other than SCI (n=2); b) the population was mixed: more than 20% of the subject pool had injuries below T1 (n=7); c) the study did not include individuals with tetraplegia (n=14); d) the study population was less than 5 individuals (n=8); e) the study did not include VO_2peak values; and f) the data was presented in an article already included in the review (n=3) (Figure 2.1).

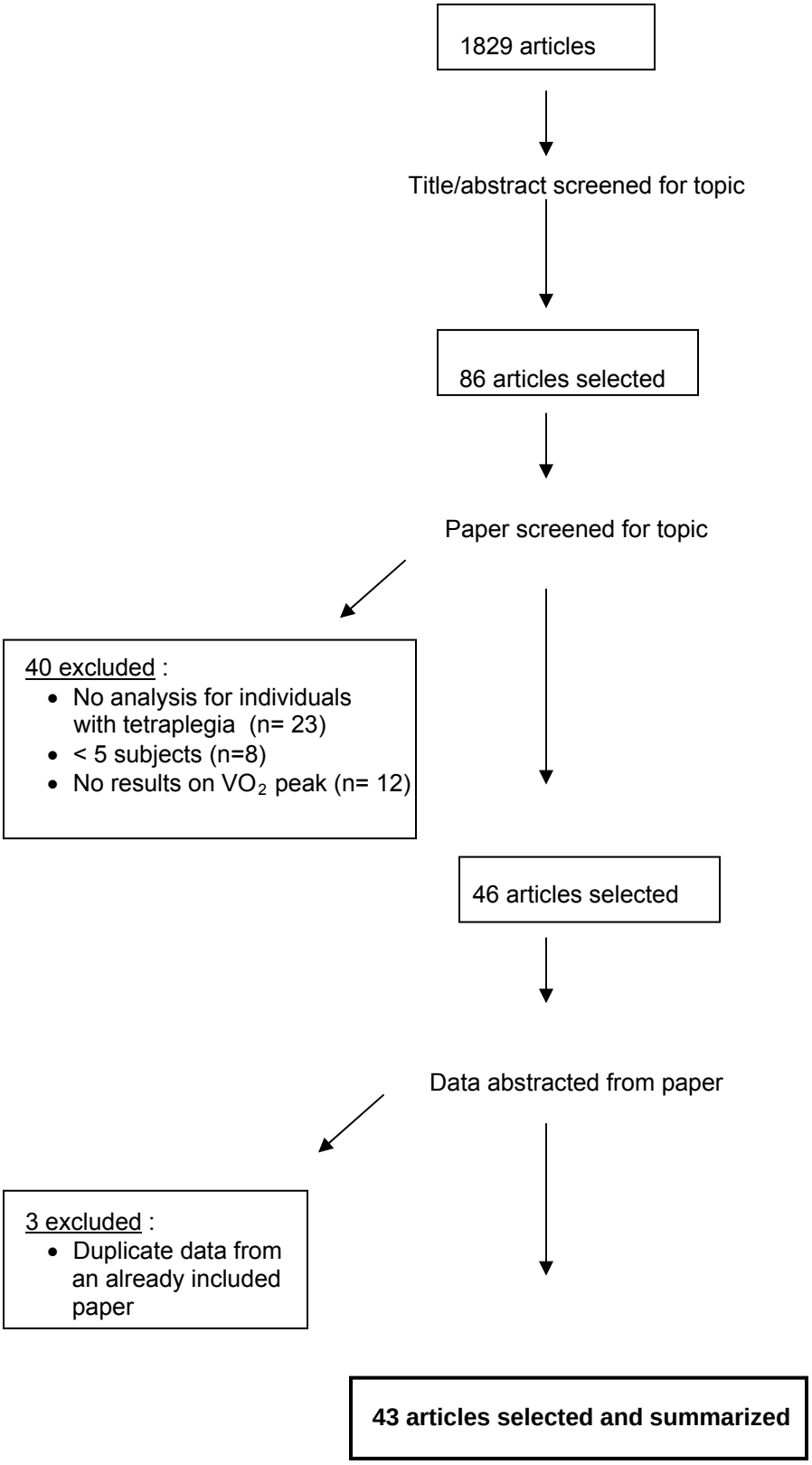


Figure 2.1 Flowchart for the systematic search and selection of papers.

Study characteristics

Data from the 36 cross-sectional studies were extracted (Table 2.2). Study populations differed considerably in size and composition. The number of subjects per study ranged between 5 and 47 with a mean value of 13 subjects per study. The mean age was 31.1 years (SD = 4.5). The studies included in this section of the review included participants with injury durations of longer than one year. The six longitudinal studies are summarized in Table 2.3. Participants in these studies had relatively recent SCIs (LOI $\leq$ 2 years). Seven studies reporting the cardiovascular effects of training programs are presented in Table 2.4.

Testing modality and protocol

Fourteen studies used arm cycle ergometry (ACE); 14 studies used wheelchair ergometry (WCE); 3 studies used FES-cycling; and 2 studies used hand-cycling (Table 2.2). There was considerable variability with respect to the protocol (e.g. the starting power output (PO) or velocity, and the subsequent increments in intensity) used for the VO_2peak tests. Three studies did not give sufficient detail to replicate the protocol used to ascertain VO_2peak. Seven studies stated that they required all subjects to void their bladder prior to testing in order to control for dysreflexic increases in blood pressure.

The 14 ACE studies generally increased PO (approximately 5 Watts/min) in order to increase intensity. Most (n= 13) increased intensity at equal increments (e.g. 2 W/min), though Hopman (1996) estimated each participant's peak PO based on their level of injury, completeness of lesion, training level, sex, and strength of the upper limbs (formula not given) and then increased intensity by 20% of this peak PO every 30 seconds. The majority of WCE studies increased speed each minute

(approximately 1-5km/hr) in order to increase intensity. Thus, similar to most ACE studies, the WCE studies increased intensity at equal increments (e.g. increased speed by 3km/hr each minute). Some WCE studies increased both speed and resistance (either via a pulley system on the treadmill or an eletronically braked roller) in order to increase intensity (e.g. each minute saw a 0.56 m/sec speed increase and a 10% resistance increase). Gass (1980) used a unique method, alternating between speed and gradient increases as a means of increasing intensity

Table 2.2 Cross-sectional studies measuring VO_2peak in individuals with tetraplegia: Protocol descriptions

Arm Cycle Ergometry								
Author/Year	**N**	**Age**	**Injury Level**	**Length of Injury (years)**	**Activity Level**	**Continuous/ Discontinuous**	**Protocol**	**VO_2peak mL/kg/min (SD)**
(Lewis et al., 2007)	10	/	C5-C8	/	Untrained	Discontinuous	3 min stages; increase 100kpm/stage	6.73 (3.27)
(Goosey-Tolfrey et al., 2006)	8	29	C5-C7	/	Athletes	Continuous	2 min stages; increase 5W/stage	13.4 (2.37)
(Hopman et al., 2004)	6	25.8	C4-C8	/	Moderately trained	Continuous	Increase 3-5W/min	12.2 (1.8)
(Jacobs et al., 2002)	16	35.3	C5-C7	8	/	Discontinuous	2 min stages (2 min ex + 1 min rest); increase 10W/stage	10.91 (3.68)
(Lassau-Wray and Ward, 2000)	5	32.4	C4-C5	/	/	Continuous	Increase 5W/min	11.5 (2.46)
	5	29.6	C6-C8	/	/	Continuous	Increase 5W/min	18.8 (3.3)
(Uijl et al., 1999)	6	31.5	C5-C6	10.7	/	Continuous	Increase 3-6W/min	10.6 (2.3)
(Hopman et al., 1998)	5	28	C5-C8	7	Moderately trained	Discontinuous	Increase 2-10W/min	12.7 (2.1)
(Hjeltnes et al., 1997)	5	35	C5-C7	10.2	Sedentary	Discontinuous	5 min stages (3 min ex + 2 min rest); increase 20W/stage	11
(Hopman et al., 1996)	6	36.5	C4-C8	9.1	Sedentary	Continuous	Increase 20% of estimated max PO/30 sec	7.4 (2.7)
	7	26.6	C4-C8	6.6	Sedentary	Continuous	Increase 20% of estimated max PO/30 sec	8.1 (3.1)
	8	32.7	C4-C*	8.1	Trained	Continuous	Increase 20% of estimated max PO/30 sec	14.0 (5.7)
(McLean and Skinner, 1995)	14	33.8	C5-T1	11.7	Not trained	Discontinuous	5 min stages (3.6 min ex + 1.4 min rest); increase 2-15W/stage	10.6
(Lasko-McCarthey and Davis, 1991b)	14	28.9	C6	7	/	Continuous	Increase 4W/min	11 (2.7)
	10	28.9	C7-C8	10.8	/	Continuous	Increase 4W/min	16.8 (4.5)
(Figoni et al., 1988)	11	27.3	C5-C7	10	Untrained	Discontinuous	4 min stages (3 min ex + 1 min rest); increase 5W/stage	10.15 (3.58)
(DiCarlo, 1988a)	8	23.6	C5-C7	8.5	Not trained	Continuous	2 min stages: Increased pedal rate by 10rpm/stage (started at .5kg resistance/50rpm)	12.1 (0.54)
Mean	**7.7**	**31**	**/**	**9.4**	**/**	**/**	**/**	**11.0**

Wheelchair Ergometry								
Author/Year	**N**	**Age**	**Injury Level**	**Length of Injury (years)**	**Activity Level**	**Continuous/ Discontinuous**	**Protocol**	**VO_2peak mL/kg/min (SD)**
(Janssen et al., 2002)	59	32.8	C4-C8	6.8	Sedentary-active	Continuous	0.56 (meter/sec)/min; Increase resistance 10%/min (individualized)	12.6 (6.6)
(Schmid et al., 2001)	6	36.7	C7	10.5	Sedentary	Continuous	10km/hr; Increase 10W/3 min	27.5 (10.86)
(Dallmeijer and van der Woude, L.H., 2001)	10	26.3	C5-C6	4.1	/	Continuous	Increase resistance 10%/min (individualized)	9.25
	9	45.9	C6-C8	8.4	/	Continuous	Increase resistance 10%/min (individualized)	6.78
	7	35.7	C4-C8	2.9	/	Continuous	Increase resistance 10%/min (individualized)	15
(Schmid et al., 1998)	25	33.8	C7 & up	10.9	/	Discontinuous	Increase 5W/3 min	10.27 (2.39)
(Dallmeijer et al., 1997)	8	30.6	C4-C8	7.4	Athletes	Continuous	0.56 meter/sec; Increase resistance 10%/min	15.6 (0.49)
	5	26	C4-C8	6.3	Untrained	Continuous	0.56 meter/sec; Increase resistance 10%/min	8.2 (0.27)
	7	39.6	C4-C8	5.6	Sedentary	Continuous	0.56 meter/sec; Increase resistance 10%/min	9.68 (0.26)
(Janssen et al., 1996)	8	34.3	C4-C8	17.8	/	Continuous	5 min stages (3 min ex + 2 min active rest); Increase power output each stage	13.6 (3.4)
(Dallmeijer et al., 1996)	12	28.7	C6 & up	5.3	/	Continuous	0.83 (meter/sec); Increase resistance 10%/min	7.7
	7	39.1	Below C6	10.1	/	Continuous	0.83 (meter/sec); Increase resistance 10%/min	11.4
	6	33.5	Cervical	3.1	/		0.83 (meter/sec); Increase resistance 10%/min	15
(Bhambhani et al., 1995)	8	33.6	Cervical	/	Untrained	Continuous	5km/hr for 5 min + 2 (km/hr)/2 min	14.9 (4)
	8	31.8	Cervical	/	Trained	Continuous	5km/hr for 5 min; Increase 2(km/hr)/2 min	19.8 (4.3)
(Bhambhani et al., 1994)	7	30.6	C5-C8	/	/	Continuous	5km/hr for 5 min; Increase 2(km/hr)/2 min	15.5 (2.6)

Author/Year	N	Age	Injury Level	Length of Injury (years)	Activity Level	Continuous/ Discontinuous	Protocol	VO_2peak mL/kg/min (SD)
(Dallmeijer et al., 1994)	6	37.3	Cervical	/	/	/	Protocol cited elsewhere	12. 9
(Janssen et al., 1993)	9	32.9	Cervical	14.6	/	Discontinuous	5 min stage (3 min ex + 2 min rest); Velocity: 0.83 m/sec; Increase 0.05(W/kg)/stage	13.63 (3.05)
(Noreau et al., 1993)	25	/	C6 & up	/	/	/	/	10.5 (3.7)
	22	/	C7-C8	/	/	/	/	14.5 (4.5)
(Lasko-McCarthey and Davis, 1991a)	12	29.1	C4-C6	7.3	Untrained	Continuous	Increase 4W/min	9.4 (3.2)
	10	28.9	C7-C8	10.8	Untrained	Continuous	Increase 4W/min	15.1 (4)
(Eriksson et al., 1988)	12	29	Cervical	9	Untrained	Continuous	Speed increased 1-3(km/hr)/min	12.17 (0.16)
	8	32	Cervical	14	Trained	Continuous	Speed increased 1-3(km/hr)/min	15.35 (0.34)
	6	31	Cervical	10	/	Continuous	Speed increased 1-3(km/hr)/min	16.21 (2.75)
(Coutts et al., 1985)	8	/	Cervical	/	/	Continuous	40 pushes/min; Increase 10 (push/min)/min	9.5 (2.97)
(Coutts et al., 1983)	8	27	Cervical	/	/	Continuous	10-15(N/cm)/min	15.3 (3.7)
(Gass et al., 1980)	7	34.4	C5-T1		Sedentary	Continuous	(2 min@ 2km/hr; Increase gradient 2% for 2mins; Increase speed 0.5km/hr for 2 mins) until exhaustion	9.5 (4.6)
Mean (SD)	**11**	**33.6**	**/**	**9.7**	**/**	**/**	**/**	**13.2**
FES-leg cycle Ergometry								
Author/Year	**N**	**Age**	**Injury Level**	**Length of Injury (years)**	**Activity Level**	**Continuous/ Discontinuous**	**Protocol**	**VO_2peak mL/kg/min (SD)**
(Dela et al., 2003)	6	33	C6-C7	11.3	/	Discontinuous	15 min of exercise at low intensity + 15 min of exercise at high intensity	20.5 (3.9)
(Hopman et al., 1998)	5	28	C5-C8	7	Moderately trained	Discontinuous	/	13.4 (1.4)
(Hjeltnes et al., 1997)	5	35	C5-C7	10.2	Sedentary	Discontinuous	11 min stages (2 min warm-up + 6 min exercise + 5 min rest) until exhaustion	7.5
Mean (SD)	**5.3**	**32.8**	**/**	**9.7**	**/**	**/**	**/**	**13.5**

Hand-cycle on a wheelchair treadmill								
Author/Year	**N**	**Age**	**Injury Level**	**Length of Injury (years)**	**Activity Level**	**Continuous/ Discontinuous**	**Protocol**	**VO_2peak mL/kg/min (SD)**
(Valent et al., 2007)	10	41	C7-C8*	8.5	Untrained	Discontinuous	Speed on treadmill was set to 4-7km; 2.5 min stages (2 min exercise + 30 sec rest); PO increased 2-5.25W/stage	15.6 (4.59)
	10	40	C5-C6*	10.3	Untrained	Discontinuous		13.3 (4.47)
(Janssen et al., 2001)	10	35	C5-C8	9.7	Trained	Discontinuous	Speed on treadmill set to 5-7km; PO increased 5W/min	14.2 (3.8)
Mean (SD)	**10**	**38.7**	**/**	**9.5**	**/**	**/**	**/**	**14.4**

***** All participants had motor-complete injuries.

Table 2.3 Longitudinal studies which measured VO_2peak in individuals with tetraplegia

Author/Year	N (baseline)	Age	Injury Level	Stage of Rehabilitation (baseline)	VO_2peak
(de Groot et al., 2008)	21	38.5	Cervical	Start of inpatient rehab	12.3 (3.4)
(Valent et al., 2008)	9	/	Cervical	Start of inpatient rehab	10.8 (3.4)
(Haisma et al., 2007)	17	/	Cervical	End of inpatient rehab	15 (4.6)
(Haisma et al., 2006)	22	39	Cervical	Start of inpatient rehab	12.1 (3.6)
(Hjeltnes and Wallberg-Henriksson, 1998)	10	25	C6-C8	Start of inpatient rehab	11.64 (3.3)
(Hjeltnes, 1986)	14	28	C5-C8	Start of inpatient rehab	10.9
Mean (SD)	15.5	32.6	/	/	12.1

(Gass et al., 1980). Lasko-McCarthey (1991a and 1991b) used three different protocols (intensity increases of 2,4, 6, and 8 W/min) in order to ascertain the optimal work rate increment for eliciting VO_2peak in individuals with tetraplegic SCI. Using both ACE and WCE modalities, they found that VO_2peak was protocol-dependant, as both faster (6 and 8W increases/min) and slower (2W increases/min) protocols significantly underestimated VO_2peak (found using the 4 W increases/minute protocol).

The mean VO_2peak during ACE (14 studies, 144 participants)) was 11.6 mL/kg/min (range : 6.7 – 18.8); the mean VO_2peak during WCE (17 studies, 325 participants)) was 13.1 mL/kg/min (range : 6.78 – 27.5); and the mean VO_2peak during FES (3 studies, 16 participants)) was 13.5 mL/kg/min (range : 7.5 – 20.5) (Table 1). Thus, the three modalities spanned similar ranges. In general, as lesion severity decreased, VO_2peak increased (Figure 2.2).

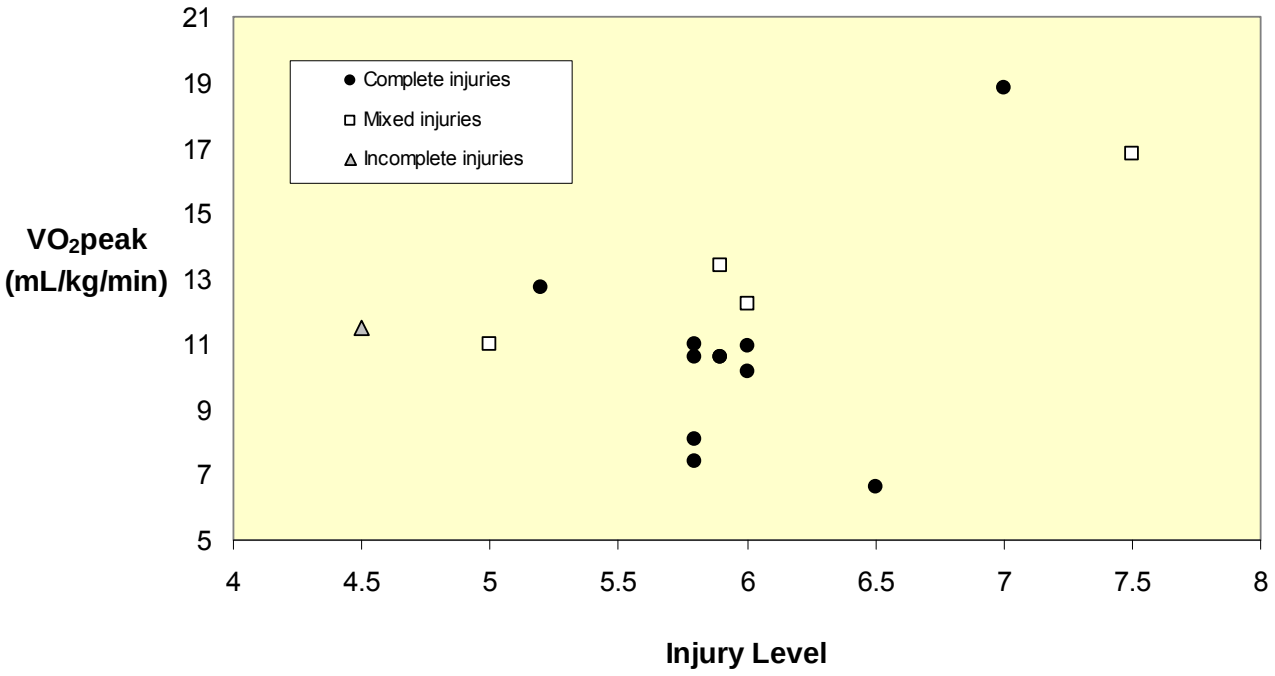


Figure 2.2 VO_2peak elicted during ACE vs. Injury level from 14 studies (n=144 participants)

Higher level injuries elicited lower VO_2peak results. Similarly, those studies including participants with incomplete injuries tended to show higher mean VO_2peak values than those using only participants with complete injuries. One ACE study (VO_2peak: 18.8 mL/kg/min) is notably higher than the others (Figure 2.2). The five participants in this study (Lassau-Wray and Ward, 2000) had motor- complete C6-C7 injuries, but no information was given about their fitness levels. This study utilized a continuous protocol, with 5W increases per minute. On the other hand, one ACE study (VO_2peak: 6.63; injury level: 6.5) is exceptionally low. The ten participants in this study (Lewis et al., 2007) had motor-complete injuries (C5-C8), but no information was given about their fitness levels or time since injury. This study used 3 minute stages with an increase of 100kpm/stage (16.3 Watts) to ascertain VO_2peak. One WCE study's particularly high mean VO_2peak values (VO_2peak: 27.5; SD: 10.26 mL/kg/min) were elicited from professional athletes (n=6), but the completeness of their injury was not specified (Schmid et al., 2001) (Figure 2.3). One of the subjects in this study had a T5 injury and thus, taking into consideration the relatively large standard deviation, may have skewed the results upward.

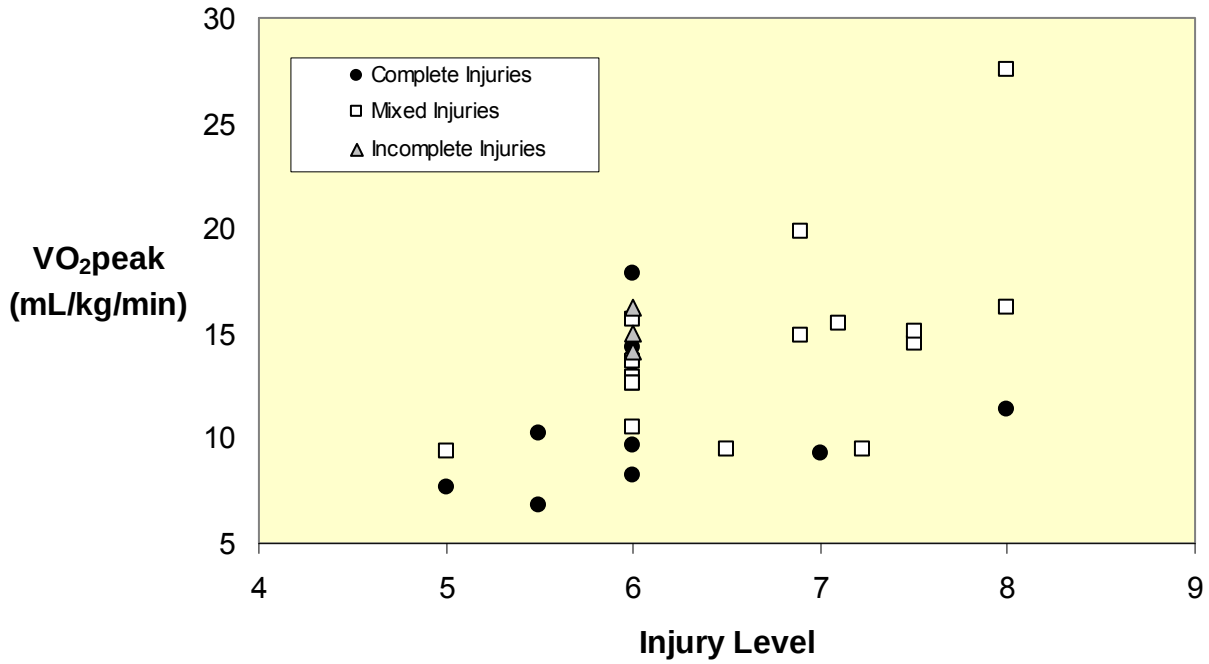


Figure 2.3 VO_2peak elicited during WCE vs. Injury level from 17 studies (n=325 participants)

VO_2peak values elicited by FES are similar to those found during voluntary upper extremity exercise (Figure 2.4)

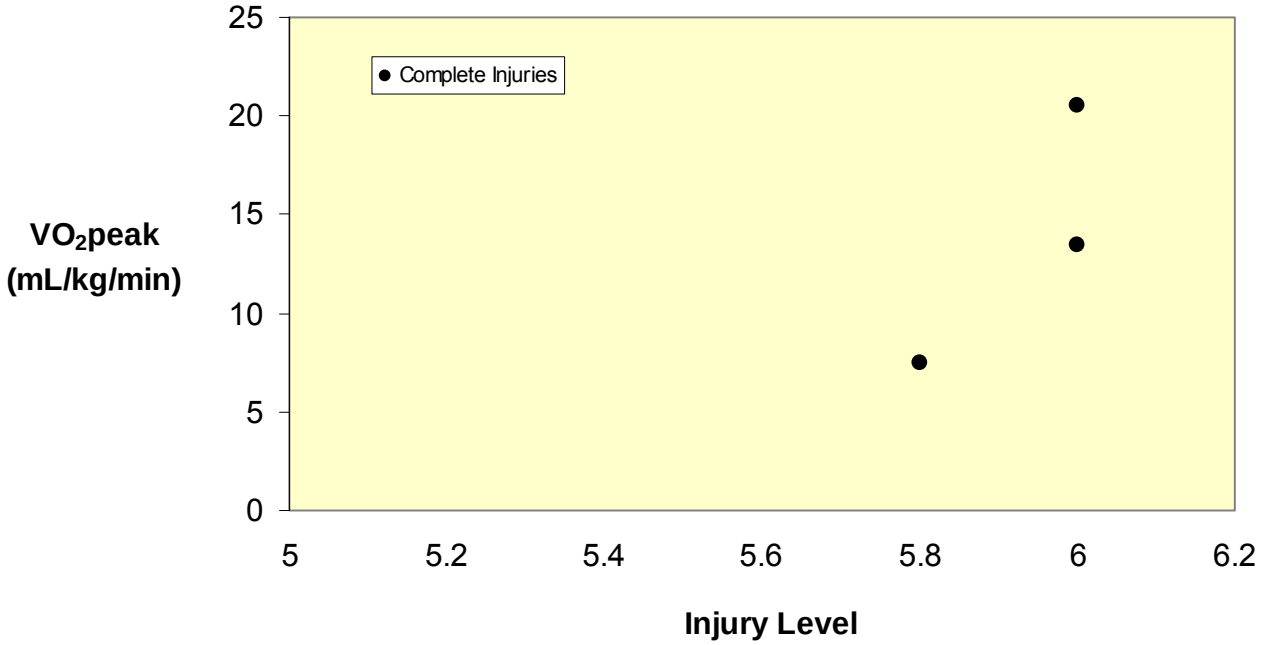


Figure 2.4 VO_2peak elicited during FES vs. Injury level from 3 studies (n=16 participants)

Individual studies support the finding that similar VO_2peak values can be elicited from ACE and WCE in individuals with cervical SCI. Using the same subject pool, Lasko-McCarthey et al. reported VO_2 peak in two different studies (one explored the protocol-dependence of VO_2 peak during ACE (Lasko-McCarthey and Davis, 1991b) and the other explored the protocol-dependence of VO_2 peak during WCE (Lasko-McCarthey and Davis, 1991a). Using a protocol of 4Watt increases/min on both ACE and WCE, the VO_2 peak results from ten tetraplegic subjects (injuries C7-C8) were similar using WCE (15.1 mL/kg/min) compared to ACE (16.8 mL/kg/min). Hopman et al. (1998) also found that different testing modalities resulted in similar VO_2 peak values: their study of five subjects with motor-complete tetraplegia (C5-C6) showed that a maximal ACE test yielded a mean VO_2 peak of 12.7 (2.1) mL/kg/min, while a maximal ACE test with the addition of FES-LCE elicited a mean VO_2 peak of 13.4 (1.4) mL/kg/min. On the other hand, Hjeltnes et al. (1997) carried out a single study in which their subjects (five individuals with motor complete C5-C7 SCI) undertook VO_2peak tests via two different modalities: 1) ACE and 2) FES-leg cycle ergometry (FES-LCE). Results from the ACE test (11 mL/kg/min) were higher than those from the FES-LCE test (7.5 mL/kg/min).

One study elicited VO_2peak in individuals with complete tetraplegia via a passive walking-like exercise (Higuchi et al., 2006). VO_2peak was considered to have been reached once subjects reached voluntary fatigue during an incremental test of passive walking on an Easy Stand Glider 6000 (Altimate Medical Int., Morton, MN, USA). This apparatus is used in the standing position; when the subjects swing their arms back and forth, their legs simultaneously move passively in a walking like motion. The mean VO_2peak elicited from seven subjects on this device was 17.6 mL/kg/min.

Cardiovascular capacity shortly after injury

Four of the six studies represented in the VO_2peak/time since injury graph are from a series of articles written from the same Dutch research group; thus, some subjects may be represented more than once (Figure 2.5). VO_2peak appears to increase through in-patient rehabilitation (approximate LOI < 1 year) and then level off there-after. In fact, in one study (n=17), VO_2peak values decreased slightly after discharge from in patient rehabilitation (discharge: 15.0 mL/kg/min; 1 year post discharge: 14.3 mL/kg/min) (Haisma et al., 2007).

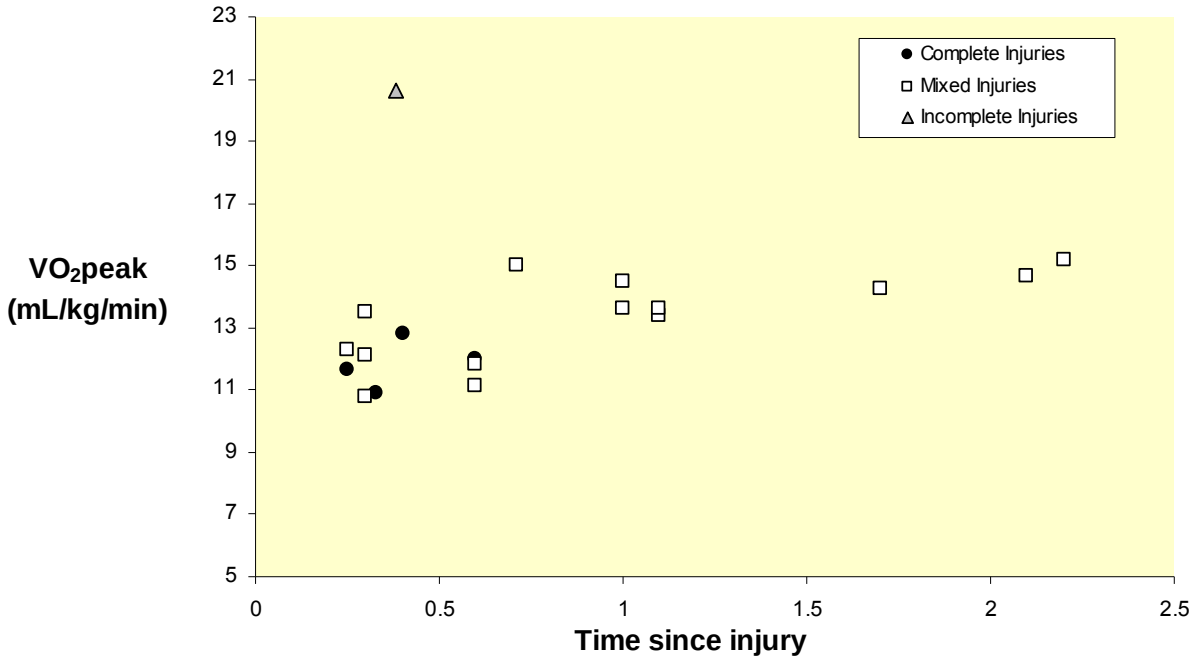


Figure 2.5 VO_2peak vs. Length of injury from 6 studies (n=93 participants)

The effect of training on VO_2peak

Seven studies explored the cardiovascular effects of a training program (total participants = 57) (Table 2.4). Training programs varied in frequency (mean 3 session/wk; range 1 – 7 sessions/wk), duration (range 8 weeks – 6 months), and intensity (minimal supervision – individualized training progressions). These programs yielded varying results, with some studies showing large training effects (net VO_2peak change: 11.4 mL/kg/min (DiCarlo, 1988b)) and others showing a

minimal training effect (net VO_2peak change: 0.41 mL/kg/min (Dallmeijer et al., 1997)). Effect sizes were larger when calculated using the pre-intervention SDs than when using the post-intervention SDs. The smallest effect size (0.11) was seen after six months of weekly rugby training sessions (one to two hours in duration) (Dallmeijer et al., 1997). These training sessions included wheelchair endurance training, arm strength training, and a training to improve ball skills and wheelchair handling. On the other hand, the largest effect size (21) was seen after 2 months of thrice weekly ACE training (DiCarlo, 1988b). Participants in this program trained at 50-60% of their heart rate reserve and slowly increased duration from 15 minutes during the first week to 30 minutes by the end of the training program. VO_2peak results from Hjeltnes' study (1997) were training specific: FES-LCE training resulted in higher VO_2peak values on an FES-LCE exercise test, but not on an ACE exercise test (Hjeltnes et al., 1997).

Four of the training studies assessed the effect of a training intervention without the use of a control group (DiCarlo, 1988b; Gass et al., 1980; Hjeltnes et al., 1997; McLean and Skinner, 1995). The studies by Dallmeijer et al. (1997) and Hopman et al. (1996) used three groups: 1) a trained group (who had been actively participating in the rugby program for at least two years); 2) an untrained group (who started the rugby program at the time of the study); and 3) a sedentary control group (who remained inactive for the duration of the study). The effect of training on VO_2peak as measured by ACE (Hopman et al., 1996) and WCE (Dallmeijer et al., 1997) is presented for Group 2, the untrained group (Table 2.3). However, minimal changes in VO_2peak were reported for all groups. The study by Carvalho et al. (2005) included a control group (n=10) who participated in two standard therapy sessions per week.

VO_2, assessed by a knee extension exercise, increased slightly over the 6 month period (3.45 mL/kg/min at baseline; 4.62 mL/kg/min at post-test).

Table 2.4 Cardiovascular training studies

Study	*Sample size*	*Injury Severity*	*Length of Injury (years)*	*Age*	*Training protocol*	*Test modality*	*Pre-training VO_2peak (mL/kg/min)*	*Post-training VO_2peak (mL/kg/min)*	*Net change (m/kg/min)*	*Effect size (based on pre SD)*	*Effect size (post SD)*	*QOS*
(Gass et al., 1995)	7	C5-T4* (motor complete)	11.7 (4.8)	34.4 (10.9)	WCE training (5 sessions/wk; 7 weeks)	WCE	9.5 (4.6)	12.7 (5.9)	3.2	0.69	0.54	6
(DiCarlo, 1988a)	8	C5 – C6 (lesion severity not specified)	8.5 (6.4)	23.6 (4.2)	ACE training (3/wk; increased duration: 15min-30min; 8 weeks)	ACE	12.1 (0.54)	23.5 (3.1)	11.4	21	3.68	5
(McLean and Skinner, 1995)	7 (sit)	C5-T1 (motor complete)	9.3 (12.5)	34.3 (12.1)	30 ACE training sessions (3/wk for 30 mins) in either sit or supine positions	ACE	9.9	10.8	.96	N/A	N/A	9
	7 (supine)	C5-T1 (motor complete)	14.1 (6.4)	33.3 (7.0)			11.3	12.1	.83	N/A	N/A	
(Dallmeijer et al., 1997)	5	C4-C8 (motor complete)	6.3 (4)	26 (7.1)	Quad rugby (1 session/ wk) for 6 months	WCE	8.1 (3.7)	8.5 (4.9)	.41	0.11	0.02	8
(Hopman et al., 1996)	5	C4-C8 (motor complete)	6.3 (4)	26 (7.1)	Quad rugby (1 session/ wk) for 6 months	ACE	8.1 (3.1)	Final VO_2 not reported (only change score given)	0	0	0	8

Study	*Sample size*	*Injury Severity*	*Length of Injury (years)*	*Age*	*Training protocol*	*Test modality*	*Pre-training VO_2peak (mL/kg/min)*	*Post-training VO_2peak (mL/kg/min)*	*Net change (m/kg/min)*	*Effect size (based on pre SD)*	*Effect size (post SD)*	*QOS*
(Hjeltnes et al., 1997)	5	C5-C7 (motor complete)	10.2 (3.4)	35 (3)	FES-LCE (7 sessions/wk) for 10 weeks	ACE	11 (1.6)	11 (1.6)	0	0	0	8
	5	C5-C7 (motor complete)	10.2 (3.4)	35 (3)	FES-LCE (7 sessions/wk) for 10 weeks	FES-LCE	7.5 (1.8)	12.5 (1.4)	5	2.8	2.0	
(de Carvalho and Cliquet, 2005)	21	C4-C7 (motor complete)	6.8 (4.9)	32.9 (8.5)	FES of quadriceps (5 months) + BWSTT (2/week; 20 mins; 6 months)	BWSTT + FES	7.0 (1.8)*	9.6 (2.5)*	2.6	1.4	0.56	9

* A VO_2 peak test was not actually performed; this value is the highest value taken during a walking test.
QOS = Quality of study score

Twenty-three of the 36 cross-sectional studies did not report the criteria used to determine if VO_2peak had been reached (i.e. maximal exercise). For those studies that did state the criteria, it ranged from objective measurements (e.g. plateau of VO_2 despite increases in intensity; a respiration exchange ratio (RER) >1.0 (Dallmeijer et al., 1996)) to subjective ratings of perceived exertion (RPE) of 17 or greater on the BORG RPE scale (Jacobs et al., 2002). Jacobs et al. (2002) noted that all their subjects with tetraplegia (n=16) attained at least a 17 (out of 20) on the BORG RPE scale with peak heart rates in accord with the ACSM guidelines for maximal effort (American College of Sports Medicine and Johnson, 2000), stating this indicated the subjects had reached appropriate end-points for test termination. Conversely, Dallmeijer et al. (1996) stated that five of their subjects with tetraplegia (n=25) did not reach one of the objective criteria for maximal exercise performance. Similarly, Hopman et al. (2004) stated that none of their participants with tetraplegia (n=6) met any of the criteria for maximal exercise (whereas all the individuals with paraplegia and all the able-bodied controls did).

None of the reviewed studies stated there were any adverse effects to the exercise testing or that any subjects had to prematurely stop the testing for any reason other than volitional fatigue. However, Schmid (1998) commented that the individuals with complete tetraplegia in their study showed an inadequate blood pressure regulation during exercise and that this was less apparent in incomplete tetrapegia.

2.5 Discussion

The literature surrounding exercise in people with cervical SCI is limited in quantity. Subject pools are small and/or heterogeneous (caused by variation in lesion level, completeness of lesion, and time since injury) thus limiting the generalizeablity of the results. Although we aimed to minimize this heterogeneity by focusing on cervical injuries and grouping studies based on lesion severity (complete vs. incomplete) and time since injury (chronic vs. early injury), we had to exclude a large number of articles due to mixed populations (e.g. no individual analysis for cervical injuries). In terms of exercise response, it is well known that individuals with cervical injuries are limited both by their available musculature as well as by their sympathetic autonomic impairment. It is also assumed that individuals with incomplete injuries have some sparing in terms of innervated muscle mass and/or autonomic function. Thus, it is difficult to compare results from studies with heterogeneous subject populations (e.g. groups containing individuals with both tetraplegic and paraplegic injuries and/or groups with both complete and incomplete injuries).

In addition to heterogeneous populations, the different maximal exercise test protocols to measure physical capacity (e.g. continuous or discontinuous, intensity increments, and the duration of exercise stages) likely influence test results, thereby limiting the extent to which the studies can be compared and interpreted. It has been shown that fast protocols (those with large work rate increments) and slow protocols (those with small work rate increments) cause underestimations of true VO_2 peak values (found using intermediate-speed protocols) (Lasko-McCarthey and Davis, 1991b). This is likely because fast protocols cause individuals to terminate early due to insufficient muscle strength needed to accommodate the large work rate

increments during the final stages of the test ; whereas slow protocols (longer test durations) : 1) cause significant increases in core body temperature (thus resulting in re-distribution of blood/oxygen to cutaneous circulation rather than the exercising musculature) and 2) require extremely high motivation on the part of the subject (Lasko-McCarthey and Davis, 1991b).

Testing modality and protocol

The large variation in testing protocols used in the studies included in this review makes comparison across studies difficult. For example, the ACE study yielding the lowest value in Figure 2.2 (VO_2peak: 6.63; injury level: 6.5 (Lewis et al., 2007)) used 3 minute stages, increasing intensity by 100kpm/stage (16.3 Watts) to ascertain VO_2peak. These results are well below those of other studies which used the recommended 5W/min intensity increases (Lasko-McCarthey and Davis, 1991b) (e.g.18.8 mL/kg/min (Lassau-Wray and Ward, 2000); 12.2 mL/kg/min (Hopman et al., 2004)). The assumption follows that the individuals in Lewis et al.'s study could not maximally stress the cardiovascular system and were likely limited by peripheral factors (i.e. local muscular fatigue) rather than central cardiovascular factors, thus resulting in an underestimation of VO_2peak. In fact, Jacobs et al. (2002) previously stated that persons with cervical-level SCI typically attribute local muscular fatigue and soreness in the arms and shoulders, rather than cardiorespiratory fatigue, as the reason they are unable to continue a maximal arm ergometry test.

VO_2peak and lesion characteristics

Our systematic review provides further evidence that VO_2peak is related to lesion severity: VO_2peak decreases with increasing lesion level and individuals with

incomplete lesions elicit higher VO_2peak values than individuals with complete lesions. Dallmeijer et al. (1996) showed that 66% of the variance in VO_2peak can be explained by severity of the lesion. Higher level injuries cause greater reduction in functional muscle mass and strength available for use in exercise tests in comparison to lower level injuries. Incomplete injuries allow for more autonomic and musculature sparing than complete lesions. The resulting increases in sympathetic autonomic function would allow for greater chronotropic response to exercise, and would therefore facilitate higher VO_2peaks in this group in comparison to those with complete injuries. Similarly, more available musculature would decrease venous pooling, thus increasing cardiac pre-load and increasing cardiac output to the exercising upper limb muscles.

The results from this systematic review suggest that VO_2peak may be influenced by time since injury. In the first year post-injury, dissipation of neurogenic shock and natural recovery likely play a large part in the observed increase in VO_2peak values. In the second year post-injury, cardiovascular capacity may decrease as individuals are discharged from the in-patient rehabilitation centre and experience the multi-faceted challenges of community re-integration, which can limit physical activity, thus facilitating a sedentary lifestyle.

The effect of training on VO_2peak

The results from this review suggest that an exercise program can positively effect VO_2peak. However, these results need to be interpreted with caution as the available evidence is weak due to small sample sizes and lack of control groups. Without a comparable control group, any change in the dependant variable is attributed to the

intervention (Eng et al., 2008), despite the presence of extraneous effects un-related to the training. The use of a control group can capture any non-training influences (such as familiarization to the outcome measure or increasing length of injury) and allow them to be removed during the calculation of effect size (Carlson and Schmidt, 1999). Accordingly, mean effect sizes for single group pre-test post-test designs are larger than effect sizes for studies using control group designs (Lipsey and Wilson, 1993). Weak evidence is not a shortcoming unique to exercise research in this population. Single group pre-test post-test designs are frequently used to evaluate training programs as situational constraints often make use of control groups impractical in field settings (Carlson and Schmidt, 1999). In fact, the majority of SCI rehabilitation literature is limited by methodological insufficiencies, due to small, heterogeneous samples, few randomized controlled trials, and a lack of consensus on appropriate outcome measures (Eng et al., 2008).

Given the paucity of rigorous research in this area, the available evidence tentatively suggests that it is possible to achieve an aerobic training effect in individuals with tetraplegia. It appears that a threshold of exercise is required for quantifiable aerobic effects. For example, the study by Dallmeijer et al. (1997) of the effect of once weekly Quad rugby training was insufficient to produce an increase in VO_2peak, while the study by DiCarlo (1988) of thrice weekly ACE training produced a large net change in VO_2peak. However, it is unclear as to whether any improvements in VO_2peak are related to central cardiovascular (i.e. heart's ability to deliver blood to the tissues) or peripheral (metabolic capacity of the exercising muscle) adaptations. The minimal muscle mass involved during volitional arm exercise in individuals with cervical SCI may not increase the body's metabolic rate sufficiently to cause central training

adaptations. Consequently, it has been suggested that most of the changes observed post-training are likely due to peripheral adaptations (i.e. increases in capillary density and metabolic capacity of the exercising muscles) (Figoni, 1993). The results from Hjeltnes (1998) suggest that VO_2peak is training specific (Hjeltnes and Wallberg-Henriksson, 1998). They showed that 8 weeks of FES-LCE training did not change VO_2peak value as determined via an ACE test; but did on the subsequent FES-LCE test (Hjeltnes and Wallberg-Henriksson, 1998). This is similar to results found in the able-bodied population: VO_2max was found to be higher for runners and non-athletes during exercise on the treadmill and higher for cyclists during exercise on the cycle-ergometer (Moreira-da-Costa M. et al., 1984). These authors suggested that the quantitative effects of training on cardiovascular and respiratory functions may only be appropriately evaluated by using an ergometer which requires an activity similar to that usually performed by the subjects.

The variation in effect sizes for the response to training on VO_2peak reflected a wide variety of training programs. Dallmeijer et al. (1997) noted that the training frequency and/or intensity in their study were probably not of sufficient magnitude to elicit training effects in their subjects, citing the once per week frequency as the most likely explanation for this finding (Dallmeijer et al., 1997). On the other hand, DiCarlo (1988) found significant increases in VO_2peak values after two months of intense aerobic training (DiCarlo, 1988b). Because the majority of the evidence presented in this systematic review used the single group pre-test post-test design, we calculated effect sizes using both the pre-training standard deviation (SD) and the post-test SD for the trained group. Glass et al. (1981) argue for the use of the SD from the dependant variable measure in the untrained population (i.e. the SD calculated at

baseline in training studies). They state that post-training SDs may be altered by individual differences which cause participants to learn at different rates, thus resulting in more variable scores. Indeed, Carlson and Schmidt (1999) found that SDs were, on average, larger for post-training assessments than for baseline assessments. Though this mean increase did not meet statistical significance, effect size calculations, based on post-training SDs, would be smaller than those calculated with baseline SDs, as seen in Table 2.3.

Functionally, a 2 point increase in VO_2peak (measured in mL/kg/min on an ACE) has been shown to correlate with significant improvements on a wheelchair skills test (Kilkens et al., 2005). DiCarlo (1988b) also found that his subjects could wheel 1km farther during a 12 minute endurance test after the two month training program (2.1 km vs. 1.2 km). So, although the large change in VO_2peak seen in his study was measured via the same as the training (ACE), the cardiovascular benefits from the training were apparent across exercise modalities. It remains to be seen whether an increase in VO_2peak measured by FES, such as the one noted by Hjeltnes (1998), would have a similar functional benefit. However, as McLean and Skinner (1995) noted, increases in VO_2peak would likely be of little benefit if they do not generalize to functional tasks in the sitting position in which the majority of individuals with cervical SCI perform most of their activities of daily living.

Dallmeijer et al. (1996) noted that despite abiding by the recommendations of Lasko-McCarthey(1991b), some of their participants with tetraplegia were not able to reach the objective criteria for maximal exercise performance. The inability to reach the objective criteria used to determine VO_2peak is likely not limited to this study alone,

leading to the assumption that this may be an underreported phenomenon during exercise testing of individuals with cervical SCI. This leads to further questioning regarding the validity of using the traditional VO_2peak criteria (originally designed for the able-bodied population) to ascertain cardiovascular capacity in individuals with cervical SCI.

Limitations

This review includes articles from as early as 1980. Thus, some heterogeneity exists due to the use of the older Stoke Mandeville Functional Sports Classification (SMFSC) rather than the newer, American Spinal Injury Association Impairment Scale (AIS) classification system (American Spinal Injury Association., 1992). The SMFSC classifies injuries based on neurological level, with no regard for completeness of the lesion, whereas the AIS system accounts for incomplete lesions (both sensory and motor). Thus, it was not possible to group earlier studies based on injury completeness as this information was often not provided. Secondly, using the mean body weight from the data available to calculate VO_2peak in mL/kg/min may have affected our results. Lastly, we did not include any non-peer reviewed literature and thus may have excluded some potentially relevant information.

2.6 References

1. American College of Sports Medicine, and Johnson, E. P. (2000). ACSM's Guidelines for Exercise Testing and Prescription. Lippincott Williams & Wilkins:

2. American Spinal Injury Association. (1992). Standards for neurological and functional classification of spinal cord injury. American Spinal Injury Association: Chicago,

3. Bhambhani, Y. N., Burnham, R. S., Wheeler, G. D., Eriksson, P., Holland, L. J., and Steadward, R. D. (1995). Ventilatory threshold during wheelchair exercise in untrained and endurance-trained subjects with quadriplegia. Adapted Physical Activity Quarterly. **12,** 333-343.

4. Bhambhani, Y. N., Holland, L. J., Eriksson, P., and Steadward, R. D. (1994). Physiological responses during wheelchair racing in quadriplegics and paraplegics. Paraplegia. **32,** 253-260.

5. Burkett, L. N., Chisum, J., Stone, W., and Fernhall, B. (1990). Exercise capacity of untrained spinal cord injured individuals and the relationship of peak oxygen uptake to level of injury. Paraplegia. **28,** 512-521.

6. Carlson, K. D., and Schmidt, F. L. (1999). Impact of experimental design on effect size: Findings from the research literature on training. J Appl Psychol. **84,** 851-862.

7. Centre for Reviews and Dissemination. (2001). Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews. CRD Report 4. 2nd edn. York Publishing Services: York, United Kingdom,

8. Coutts, K. D., Rhodes, E. C., and McKenzie, D. C. (1985). Submaximal exercise responses of tetraplegics and paraplegics. J Appl Physiol. **59,** 237-241.

9. Coutts, K. D., Rhodes, E. C., and McKenzie, D. C. (1983). Maximal exercise responses of tetraplegics and paraplegics. Journal of Applied Physiology Respiratory Environmental and Exercise Physiology. **55,** 479-482.

10. Dallmeijer, A. J., and van der Woude, L.H. (2001). Health related functional status in men with spinal cord injury: relationship with lesion level and endurance capacity. Spinal Cord. **39,** 577-583.

11. Dallmeijer, A. J., Hopman, M. T., Angenot, E. L., and van der Woude, L. H. (1997). Effect of training on physical capacity and physical strain in persons with tetraplegia. Scand J Rehabil Med. **29,** 181-186.

12. Dallmeijer, A. J., Hopman, M. T., van As, H. H., and van der Woude, L. H. (1996). Physical capacity and physical strain in persons with tetraplegia; the role of sport activity. Spinal Cord. **34,** 729-735.

13. Dallmeijer, A. J., Hopman, M., Angenot, E., and LHV. (1997). Effect of training on physical capacity and physical strain in persons with tetraplegia. Scand J Rehabil Med. **29,** 181-186.

14. Dallmeijer, A. J., Kappe, Y. J., Veeger, D. H., Janssen, T. W., and van der Woude, L. H. (1994). Anaerobic power output and propulsion technique in spinal cord injured subjects during wheelchair ergometry. J Rehabil Res Dev. **31,** 120-128.

15. de Carvalho, D. C., and Cliquet, A.,Jr. (2005). Energy expenditure during rest and treadmill gait training in quadriplegic subjects. Spinal Cord. **43,** 658-663.

16. de Groot, S., Dallmeijer, A. J., Post, M., Angenot, E., and LHV. (2008). The longitudinal relationship between lipid profile and physical capacity in persons with a recent spinal cord injury. Spinal Cord. **46,** 344-351.

17. Dela, F., Mohr, T., Jensen, C. M. R., Haahr, H. L., Secher, N. H., Biering-Sorensen, F., and Kjaer, M. (2003). Cardiovascular control during exercise: Insights from spinal cord-injured humans. Circulation. **107,** 2127-2133.

18. DiCarlo, S. E. (1988a). Effect of arm ergometry training on wheelchair propulsion endurance of individuals with quadriplegia. Phys Ther. **68,** 40-44.

19. DiCarlo, S. E. (1988b). Effect of arm ergometry training on wheelchair propulsion endurance of individuals with quadriplegia. Phys Ther. **68,** 40-44.

20. Eng, J. J., Teasell, R. W., Miller, W. C., Wolfe, D., and Townson, A. (2008). Spinal Cord Injury Rehabilitation Evidence (SCIRE).

21. Eriksson, P., Lofstrom, L., and Ekblom, B. (1988). Aerobic power during maximal exercise in untrained and well-trained persons with quadriplegia and paraplegia. Scand J Rehabil Med. **20,** 141-147.

22. Figoni, S. F. (1993). Exercise responses and quadriplegia. Med Sci Sports Exerc. **25,** 433-441.

23. Figoni, S. F., Boileau, R. A., Massey, B. H., and Larsen, J. R. (1988). Physiological responses of quadriplegic and able-bodied men during exercise at the same V[dot]O_2. Adapted Physical Activity Quarterly. **5,** 130-139.

24. Garshick, E., Kelley, A., Cohen, S. A., Garrison, A., Tun, C. G., Gagnon, D., and Brown, R. (2005). A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord. **43,** 408-416.

25. Gass, E. M., Harvey, L. A., and Gass, G. C. (1995). Maximal physiological responses during arm cranking and treadmill wheelchair propulsion in T4-T6 paraplegic men. Paraplegia. **33,** 267-270.

26. Gass, G. C., Watson, J., Camp, E. M., Court, H. J., McPherson, L. M., and Redhead, P. (1980). The effects of physical training on high level spinal lesion patients. Scand J Rehabil Med. **12,** 61-65.

27. Glaser, R. M., Sawka, M. N., Laubach, L. L., and Suryaprasad, A. G. (1979). Metabolic and cardiopulmonary responses to wheelchair and bicycle ergometry. J Appl Physiol. **46,** 1066-1070.

28. Glass, G. V., McGaw, B., and Smith, M. L. (1981). Meta-analysis in social research. Sage Publications:

29. Goosey-Tolfrey, V., Castle, P., Webborn, N., and Abel, T. (2006). Aerobic capacity and peak power output of elite quadriplegic games players. BJSM online. **40,** 684-687.

30. Haisma, J. A., Bussmann, J. B., Stam, H. J., Sluis, T. A., Bergen, M. P., Dallmeijer, A. J., de Groot, S., and LH. (2006). Changes in physical capacity during and after inpatient rehabilitation in subjects with a spinal cord injury. Arch Phys Med Rehabil. **87,** 741-748.

31. Haisma, J. A., van der Woude, L. H., Stam, H. J., Bergen, M. P., Sluis, T. A., de Groot, S., Dallmeijer, A. J., and Bussmann, J. B. (2007). Prognostic models for physical capacity at discharge and 1 year postdischarge from rehabilitation in persons with spinal cord injury. Arch Phys Med Rehabil. **88,** 1694-1703.

32. Higuchi, Y., Kitamura, S., Kawashima, N., Nakazawa, K., Iwaya, T., and Yamasaki, M. (2006). Cardiorespiratory responses during passive walking-like exercise in quadriplegics. Spinal Cord. **44,** 480-486.

33. Hjeltnes, N., Aksnes, A. K., Birkeland, K. I., Johansen, J., Lannem, A., and Wallberg-Henriksson, H. (1997). Improved body composition after 8 wk of electrically stimulated leg cycling in tetraplegic patients. American Journal of Physiology- Regulatory, Integrative and Comparative Physiology. **273,** 1072-1079.

34. Hjeltnes, N. (1986). Cardiorespiratory capacity in tetra- and paraplegia shortly after injury. Scand J Rehabil Med. **18,** 65-70.

35. Hjeltnes, N., and Wallberg-Henriksson, H. (1998). Improved work capacity but unchanged peak oxygen uptake during primary rehabilitation in tetraplegic patients. Spinal Cord. **36,** 691-698.

36. Hopman, M. T., Houtman, S., Groothuis, J. T., and Folgering, H. T. (2004). The effect of varied fractional inspired oxygen on arm exercise performance in spinal cord injury and able-bodied persons. Arch Phys Med Rehabil. **85,** 319-323.

37. Hopman, M. T., Dallmeijer, A. J., Snoek, G., and van der Woude, L. H. (1996). The effect of training on cardiovascular responses to arm exercise in individuals with tetraplegia. Eur J Appl Physiol. **74,** 172-179.

38. Hopman, M. T. E., Dueck, C., Monroe, M., Philips, W. T., and Skinner, J. S. (1998). Limits to maximal performance in individuals with spinal cord injury. Int J Sports Med. **19,** 98-103.

39. Howley, E. T., Bassett Jr, D. R., and Welch, H. G. (1995). Criteria for maximal oxygen uptake: review and commentary. Medicine & Science in Sports & Exercise. **27,** 1292.

40. Jacobs, P. L., Mahoney, E. T., Cohn, K. A., Sheradsky, L. F., and Green, B. A. (2002). Oral creatine supplementation enhances upper extremity work capacity in persons with cervical-level spinal cord injury. Arch Phys Med Rehabil. **83,** 19-23.

41. Janssen, T. W. J., Dallmeijer, A. J., Veeger, D. H., and van der Woude, L.H.V. (2002). Normative values and determinants of physical capacity in individuals with spinal cord injury. JRRD. **39,** 29-39.

42. Janssen, T. W., Dallmeijer, A. J., and van der Woude, L. H. (2001). Physical capacity and race performance of handcycle users. J Rehabil Res Dev. **38,** 33-40.

43. Janssen, T. W., van Oers, C. A., Hollander, A. P., Veeger, H. E., and van der Woude, L. H. (1993). Isometric strength, sprint power, and aerobic power in individuals with a spinal cord injury. Med Sci Sports Exerc. **25,** 863-870.

44. Janssen, T. W., van Oers, C. A., Rozendaal, E. P., Willemsen, E. M., Hollander, A. P., and van der Woude, L. H. (1996). Changes in physical strain and physical capacity in men with spinal cord injuries. Med Sci Sports Exerc. **28,** 551-559.

45. Kilkens, O. J., Dallmeijer, A. J., Nene, A. V., Post, M. W., and LH. (2005). The longitudinal relation between physical capacity and wheelchair skill performance during inpatient rehabilitation of people with spinal cord injury. Arch Phys Med Rehabil. **86,** 1575-1581.

46. Lasko-McCarthey, P., and Davis, J. A. (1991a). Effect of work rate increment on peak oxygen uptake during wheelchair ergometry in men with quadriplegia. Eur J Appl Physiol Occup Physiol. **63,** 349-353.

47. Lasko-McCarthey, P., and Davis, J. A. (1991b). Protocol dependency of VO2max during arm cycle ergometry in males with quadriplegia. Med Sci Sports Exerc. **23,** 1097-1101.

48. Lassau-Wray, E. R., and Ward, G. R. (2000). Varying physiological response to arm-crank exercise in specific spinal injuries. J Physiol Anthropol Appl Human Sci. **19,** 5-12.

49. Lewis, J. E., Nash, M. S., Hamm, L. F., Martins, S. C., and Groah, S. L. (2007). The Relationship Between Perceived Exertion and Physiologic Indicators of Stress During Graded Arm Exercise in Persons With Spinal Cord Injuries. Arch Phys Med Rehabil. **88,** 1205-1211.

50. Lipsey, M. W., and Wilson, D. B. (1993). The efficacy of psychological, educational, and behavioral treatment. Am Psychol. **48,** 1181–1209.

51. McLean, K. P., and Skinner, J. S. (1995). Effect of body training position on outcomes of an aerobic training study on individuals with quadriplegia. Arch Phys Med Rehabil. **76,** 139-150.

52. Moreira-da-Costa M., Russo A.K., Piçarro I.C., Silva A.C., Leite-de-Barros-Neto T., Tarasantchi J., and Barbosa A.S. (1984). Maximal oxygen uptake during exercise using trained or untrained muscles. Braz J Med Biol Res. **17,** 197-202.

53. Myers, J., Lee, M., and Kiratli, J. (2007). Cardiovascular Disease in Spinal Cord Injury: An Overview of Prevalence, Risk, Evaluation, and Management. American Journal of Physical Medicine & Rehabilitation. **86,** 142.

54. Noreau, L., Shephard, R. J., Simard, C., Pare, G., and Pomerleau, P. (1993). Relationship of impairment and functional ability to habitual activity and fitness following spinal cord injury. Int J Rehabil Res. **16,** 265-275.

55. Plowman, S., and Smith, D. (2007). Exercise physiology for health, fitness, and performance. Lippincott Williams & Wilkins:

56. Schmid, A., Huonker, M., Barturen, J. M., Stahl, F., Schmidt-Trucksass, A., Konig, D., Grathwohl, D., Lehmann, M., and Keul, J. (1998). Catecholamines, heart rate, and oxygen uptake during exercise in persons with spinal cord injury. J Appl Physiol. **85,** 635-641.

57. Schmid, A., Schmidt-Trucksass, A., Huonker, M., Konig, D., Eisenbarth, I., Sauerwein, H., Brunner, C., Storch, M. J., Lehmann, M., and Keul, J. (2001). Catecholamines response of high performance wheelchair athletes at rest and during exercise with autonomic dysreflexia. Int J Sports Med. **22,** 2-7.

58. Stewart, M. W., Melton-Rogers, S. L., Morrison, S., and Figoni, S. F. (2000). The measurement properties of fitness measures and health status for persons with spinal cord injuries. Arch Phys Med Rehabil. **81,** 394-400.

59. Uijl, S. G., Houtman, S., Folgering, H. T., and Hopman, M. T. (1999). Training of the respiratory muscles in individuals with tetraplegia. Spinal Cord. **37,** 575-579.

60. Valent, L. J., Dallmeijer, A. J., Houdijk, H., Slootman, H. J., Post, M. W., and van der Woude, L. H. (2008). 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. **89,** 1016-1022.

61. Valent, L. J., Dallmeijer, A. J., Houdijk, H., Slootman, J., Janssen, T. W., Hollander, A. P., and van der Woude, L. H. (2007). The individual relationship between heart rate and oxygen uptake in people with a tetraplegia during exercise. Spinal Cord. **45,** 104-111.

62. Zwicker, J. G., and Harris, S. R. (2009). Quality of life of formerly preterm and very low birth weight infants from preschool age to adulthood: A systematic review. Pediatrics. **121,** e366-e376.

Chapter 3. Aerobic exercise during early rehabilitation from cervical spinal cord injury: A case report[2]

[2] A version of this chapter has been submitted for publication. Tawashy, AE., Eng, JJ., Krassioukov AV., Miller WC., Sproule S. Aerobic exercise during early rehabilitation from cervical spinal cord injury: A case report

3.1 Overview

Background: Individuals with spinal cord injury (SCI), particularly those with tetraplegic injuries, are at risk for cardiovascular-related illnesses. There is a compelling need to address poor cardiovascular health as early as possible after cervical SCI.

Purpose: To illustrate the process of aerobic exercise prescription during inpatient rehabilitation from cervical SCI.

Methods: The patient was a 22 year old man who had sustained a complete C5 SCI, due to a diving accident, 12 weeks prior to participating in an aerobic exercise program. We developed an aerobic exercise program that aimed to facilitate aerobic capacity while minimizing muscular fatigue.

Results: The participant attended 18 sessions over a 2 month period. Exercise tolerance increased both in terms of exercise duration and exercise intensity. Measures of cardiovascular health, taken before and after training, showed substantial increases in peak oxygen uptake (20%) and orthostatic tolerance over the course of the program.

Conclusions: This patient experienced typical complications associated with acute SCI (e.g. orthostatic hypotension, urinary tract infections). He exhibited several signs of improved exercise tolerance over the 2 month program, indicating potential cardiovascular improvement from the exercise training.

3.2 Introduction

Cervical spinal cord injury (SCI) significantly disrupts connections in the spinal cord, causing severe muscle paralysis, loss of sensation, and autonomic dysfunction. Physical inactivity, a direct result of the injury, significantly increases the risk of cardiovascular disease (CVD). Accordingly, CVD is the leading cause of death in individuals with SCI (Garshick et al., 2005), with tetraplegic injuries associated with a 16% higher risk of developing the disease than paraplegic injuries (Myers et al., 2007). CVD and low cardiovascular fitness lead to a vicious cycle of further decline as they can result in reduced functional capacity and thus threaten the ability to live independently.

For individuals with tetraplegia, failure of sympathetically driven cardiac acceleration results in severely decreased cardiac output and reduces oxygen transport to the muscle. This autonomic dysfunction, in combination with physical inactivity, predisposes individuals to metabolic syndrome. Metablic syndrome, a pre-diabetic state characterized by a group of metabolic risk factors (obesity, high blood pressure, insulin resistance, and atherogenic dyslipidemia (Lee et al., 2005)) is considered to be a major risk factor for heart disease (American Heart Association, 2007), with its presence roughly doubling the risk of CVD mortality (Myers et al., 2007). Metabolic syndrome has been shown to be present in 23% of individuals with SCI, with the highest incidence of the disease apparent in persons with tetraplegia (Myers et al., 2007). Another cardiovascular dysfunction observed in acute (Sidorov et al., 2007) and chronic (Claydon and Krassioukov, 2006) SCI is orthostatic hypotension (OH). OH can significantly complicate and delay rehabilitation from cervical SCI as 58.9% of patients experience symptomatic OH with mobilization (Illman et al., 2000)). It has

even been suggested that OH can lead to neurological deterioration in individuals who may otherwise have a stable SCI (El Masry, 1993). As prolonged bed rest and cardiac insufficiency are two primary causes of OH in the able-bodied population (Claydon et al., 2006; Mathias, 1995), it is assumed that severe cardiovascular de-conditioning in the initial months post-SCI increase the risk of OH, thereby threatening efficient rehabilitation.

It is critical to address cardiovascular function as early as possible after newly sustained SCIs. Individuals with acute, motor-complete cervical SCI can experience up to four weeks in bed during acute care (Illman et al., 2000). The negative cardiovascular consequences of such prolonged bed rest have been well documented in the able-bodied population (Saltin et al., 1968) and are particularly detrimental for individuals with cervical SCI. Thus, cardiovascular training during sub-acute rehabilitation may halt the cardiovascular deterioration resulting from prolonged immobility and improve OH symptoms. Cardiovascular training is needed if persons with SCI are to reach and maintain the level of cardiovascular fitness that is desirable for function in daily life. Therefore, the effort to achieve optimal levels of fitness, through sustained aerobic activity, should start during primary rehabilitation itself.

Despite compelling rationale to optimize physical fitness levels in this population, research investigating conventional aerobic exercise (e.g. wheeling, arm ergometry) during sub-acute rehabilitation is scarce. There are currently no guidelines for prescribing aerobic exercise for individuals with cervical SCI, nor is it an integral part of sub-acute rehabilitation. To our knowledge, only two studies have explored use of aerobic exercise as an adjunct to primary rehabilitation (Bizzarini et al., 2005; De

Groot et al., 2003). These studies aimed to maintain an exercise frequency of three to five days per week at an intensity of 70%-80% heart rate reserve (HRR). However, the study by deGroot et al (2003) (n=6) included only one individual with cervical SCI who was injured more 6 months prior to participating in the program and the study by Bizzarini et al (2005) did not include any individuals with complete cervical SCI, nor did they use any cardiovascular assessments.

No study has assessed the feasibility (nor the effects) of an exercise program designed specifically for individuals with cervical injuries. Because they are severely limited by autonomic nervous system impairments and paralysis, individuals with tetraplegia are not always able to participate in programs designed for individuals with full upper body strength and intact autonomic control of the cardiovascular system. The purpose of this case report is to outline the process used to develop an exercise program to enhance aerobic capacity in a patient undergoing primary rehabilitation from a motor-complete C5/6 SCI. Secondary outcomes included measures of OH, lipids, functional wheeling, and program satisfaction.

3.3 Methods

Patient history and examination

The subject was a 21 year old male (62 kg; 188 cm) admitted for in-patient rehabilitation following a traumatic SCI due to a swimming injury. He spent 50 days in acute care before transferring to the in-patient rehabilitation centre. Due to medical management of his injury (cervical collar) and the development of a deep vein thrombosis, baseline assessments for the study were completed 6 weeks following admission to the rehabilitation centre and the exercise regime commenced 3 months

after the subject sustained his injury. The participant provided informed consent prior to participating in the study. This project was approved by the local hospital and university research ethics board.

American Spinal Injury Association (ASIA) Impairment Scale (AIS) examination(Marino et al., 2003) showed a C5 sensory/C6 motor AIS-A SCI, with an overall motor score of 20/100. He had full passive shoulder range of motion. At the initiation of the exercise program, the participant was able to do some activities of daily living (ADLs) with assistance. He could tolerate a full day in his manual wheelchair and expressed no complaints of pain, shortness of breath, or cough. He was managing occasional OH with abdominal binders and Thrombo-Embolic Deterrent stockings. He was participating in daily physical therapy (1 hour) and occupational therapy (1 hour) which included range of motion, functional mobility, ADL, and wheelchair skills training.

Intervention: Development of the exercise program

The American College of Sports Medicine (ACSM) recommends a minimum exercise frequency of three times per week and minimum duration of 20-30 minutes(American College of Sports Medicine and Johnson, 2000). The ACSM suggests that an exercise intensity of 70%-80% of HRR is necessary to produce training effects in de-conditioned that individuals (American College of Sports Medicine and Johnson, 2000). Designing an effective aerobic exercise program for individuals with tetraplegia is challenging due to physiological and musculoskeletal considerations. Cervical SCI disrupts sympathetic outflow to the heart, resulting in an inability to attain age-predicted maximal heart rates (peak heart rates rarely exceed 120 beats per

minute). Thus, exercise intensity cannot be monitored solely via heart rate (HR) and must include subjective ratings of perceived exertion. Secondly, because arm exercises incorporate a relatively small muscle mass, the primary factors limiting performance may be peripheral in nature; thus local fatigue of the highly stressed arm musculature may occur despite sufficient systemic oxygen availability(De Groot et al., 2003). Accordingly, we utilized interval training to facilitate longer cumulative exercise durations and incorporated a number of activities to minimize muscle fatigue and boredom.

We developed a circuit that included four activities (arm ergometry, boxing, sliding motion, and wheeling), two of which were repeated for a total of six timed stations, to be performed three times/week. The circuit was designed to be 30 minutes in duration, with each station lasting 5 minutes. Intensity was monitored via HR monitor and perceived exertion. Both exercise duration and intensity progressed over the course of the program in accordance with the ACSM guidelines for exercise progression for individuals with chronic conditions (American College of Sports Medicine and Johnson, 2000): (1) Duration: Stations initially consisted of three minutes of exercise followed by two minutes rest (18 cumulative minutes of exercise) and increased to 4.5 minutes exercise followed by 30 seconds rest (27 cumulative minutes of exercise); (2) Intensity: Target work rates (HR as determined from initial VO_2 peak tests and corresponding level on the 20 item Borg Ratings of Perceived Exertion (RPE) scale(Borg, 1970)) were initially set to 50% HRR and increased to 70%-80%HRR. Progression guidelines are presented in Table 3.1.

Table 3.1 Exercise progression guidelines.

Exercise Progression (Using Intermittent Exercise)					
Level	RPE (20 point Borg Scale)	Total minutes at RPE	Exercise minutes	Rest minutes	Reps
1	12-14	18	3	2	6
2	12-14	21	3.5	1.5	6
3	12-14	24	4	1	6
4	14-16	24	4	1	6
5	14-16	27	4.5	.5	6
6	14-18 (1 min at RPE 14 + 1 min at RPE 18) X 2	24	4	1	6

The participant was considered able to progress to the next level of exercise if all of the following criteria are met:

- Able to complete the time-goal (exercise minutes) of current level without pain or over-bearing fatigue (fatigue which interferes with ADLs or regular therapy as reported by the participant)

- Able to complete the RPE-goal of current level without pain or over-bearing fatigue (fatigue which interferes with ADLs or regular therapy as reported by the participant)

Outcome Measures

All assessments were taken at three time points: 1) Baseline (prior to exercise program); 2) Mid-point (40 days after the first training session); and 3) Final (80 days after the first training session).

Primary Outcome Measure

Cardiopulmonary status: VO_2peak. A maximal graded exercise test was performed prior to the initiation of training to assess cardiopulmonary status. The protocol for assessing VO_2 peak for individuals with SCI is well established (Lasko-McCarthey and Davis, 1991b) and has been documented previously (Hol et al., 2007). Briefly,

the test consisted of one minute of arm cycling against no resistance at a comfortable cadence (generally between 50-70 rpm) followed by subsequent work load increases of 5 Watts/min (Lasko-McCarthey and Davis, 1991a) until volitional exhaustion. Peak VO_2 and HR were collected during the test and the participant rated his perceived exertion using Borg's RPE scale immediately following the test.

Secondary Outcome Measures

Functional capacity: 6-MAT. As a measure of functional capacity, the participant completed a single-stage, six minute sub-maximal arm ergometer task, shown to be valid and reliable within the SCI population (Hol et al., 2007). He cycled on an arm cycle ergometer (Monark Rehab Trainer 881E, Vansbro, Sweden), against 5 Watts of resistance at a comfortable cadence (between 50-70 rpm) for six minutes. During the arm cycling, the subject wore a HR monitor (Polar A3; Polar electro Inc; Woodbury, NY, USA) and the same non-rebreathing face mask used for the VO_2peak test. HR was recorded every five seconds. An average HR over a 30 second period, taken during the last minute of this test, was used to determine functional capacity. Immediately following the test, the participant rated his perceived exertion using Borg's RPE scale.

Lipid Profile. Serum levels of TC, HDL, low density lipoprotein (LDL), and triglycerides (TG) were analyzed from fasting blood samples.

Orthostatic Tolerance: Sit-up Test. The presence of OH was assessed by the Sit-up Test (Claydon and Krassioukov, 2006). In the supine position, the participant was fitted with a 12-lead ECG. Systolic (SAP), diastolic (DAP), and mean (MAP) blood

pressures were measured with a calibrated DINAMAP monitor (Critikon Inc, Tampa, Florida, USA). A cuff was placed on the participant's right bicep and an oximeter placed on his left index finger. Baseline HR and BP recordings were made during a 10 minute supine rest period. The participant was then passively moved into an upright seated position by raising the head of the plinth by 90 degrees and dropping the base of the plinth by 90 degrees from the knees. This "sit-up" position is essentially the same as when seated in a wheelchair. The participant was informed as to the importance of the maneuver being passive, and was instructed not to assist in the "sit-up" procedure. The upright position was maintained for 10 minutes, during which time HR and BP measurements were continued. Specifically, values from the 3rd minute after assuming the upright posture are reported. OH was defined as a decrease in SBP of $\geq$ 20mmHg or DBP of $\geq$ 10mmHg when upright, whether or not symptoms occurred (Shatz et al., 1996). Visual signs of OH (e.g. yawning, pallor) and subjective symptoms (e.g. light-headedness, dizziness) were also recorded.

Timed functional wheeling. The subject completed two items from the Functional Tasks for Persons Who Self-Propel a Manual Wheelchair (May et al., 2003). As reliability of this measure is reported for each task individually (i.e. single-item results can be used (May et al., 2003), we used the timed forward wheeling (distance 23m) and ramp ascent (10m ramp; 1:12 grade) tasks for this study.

Subjective perception of the program

One week after exercise completion, the participant completed a 7 item questionnaire regarding his satisfaction with the program (Table 3.2). We designed the questionnaire based on a literature review of satisfaction criteria and input from two

SCI rehabilitation researchers. The items within each category were rated on an ordinal scale from 0 to 5. A rating of 5 indicated the subject was extremely satisfied with the program, and a rating of 0 indicated he was not satisfied. We calculated a total score from this questionnaire, with a higher score indicating higher satisfaction.

Table 3.2 Participant Satisfaction Scale

I am interested in how you feel about the exercise program you participated in over the past 2 months. Please tell me how you would rate the following (response categories were (1) not at all satisfied; (2) somewhat satisfied; (3) satisfied; (4) very satisfied; (5) extremely satisfied).

1. How satisfied were you with the frequency of the program (3 times/week)?
2. How satisfied were you with the duration of the program (30 minutes)?
3. How satisfied were you with the content of the program (6 stations)?
4. How satisfied were you with the intensity of the program (12-16 on the BORG scale)?

For each of the following statements, please tell me how manageable/ beneficial/enjoyable you found the exercise program (for example, response categories for #1 were (1) not at all manageable; (2) somewhat manageable; (3) manageable; (4) very manageable; (5) extremely manageable).

1. How manageable is the program given an in-patient rehabilitation schedule?
2. How beneficial did you find the program?
3. How enjoyable did you find the program?

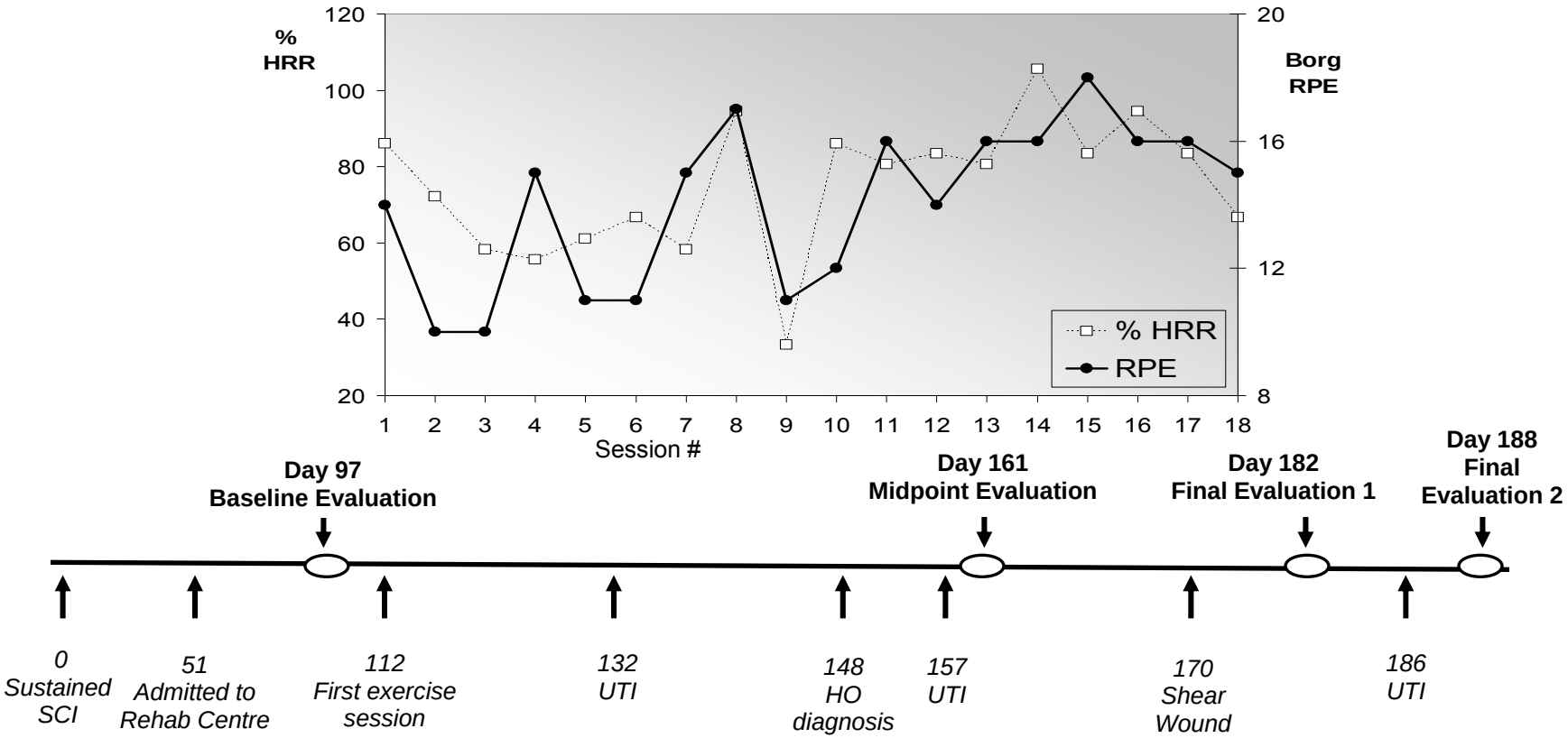
Results

Training intervention

This patient had expressed interest in participating in the exercise program upon admission to the rehabilitation centre. Although he eagerly attended 18 of 35 scheduled exercise sessions over a 2.5 month period (average attendance 2 sessions/ week), his participation in the program (and required assessment sessions) was disrupted by several common medical setbacks (Figure 3.1). Seventeen

sessions were missed due to: statutory holidays and/or recreation day trips out of the centre (n=5), specialist appointments out of the centre (n=4), or illness/ fatigue (n=8). During the course of the exercise program, the participant contracted three urinary tract infections (confirmed by urine culture), developed heterotropic ossification over his right hip (confirmed on x-ray and bone scan), and developed a shear wound on his left ischial tuberosity. Though every effort was made to reschedule sessions when possible (i.e. to compensate for recreation programs/holidays or specialist appointments), this was not always feasible as he was very active in his rehabilitation program (he participated in most recreation opportunities) and enjoyed spending time with family and friends.

Figure 3.1 Exercise program progression



SCI: spinal cord injury; UTI: urinary tract infection (as confirmed by urine culture); HO: Heterotrophic Ossification diagnosis confirmed by x-ray.

*Two "final tests" were conducted because the subject felt too ill to continue with testing on day 182 (subsequent testing confirmed a urinary tract infection). Thus, the assessments were re-administered once the subject felt well enough to perform the tests and results from final test 2 were analyzed.

The progression of the exercise program, with regards to average HR and RPE, is presented in Figure 3.1. Exercise duration increased by 6 minutes (18 to 24 minutes) and exercise intensity increased both in terms of average RPE (Borg rating: 10: “light effort” to 18: “very hard effort”) and %HRR (56% to 106%) throughout the program. Average RPE over the first half of the program was a Borg rating of 12 (“moderately hard”) and average %HRR was 65%. Over the second half of the program, the average Borg rating increased to 15 (“hard”) and average %HRR achieved was 85%.

Cardiovascular assessments (Table 3.3)

Cardiopulmonary Status: VO_2peak. Peak HR increased from 109 beats/min (baseline) to 117 beats/min (end-point evaluation). Peak VO_2 increased from 11.78mL/kg/min (baseline) to 13.72mL/kg/min (end-point). Power output, measured during the peak cardiovascular stress test, increased from 20Watts (baseline) to 30Watts (end-point) over the two month period.

Functional capacity: 6-MAT. VO_2 and HR were lower at the end-point evaluation than they were at baseline, indicating less effort was required to cycle at similar power outputs.

Lipid Profile. Lipid changes were minimal. HDL values increased from 1.08 (baseline) to 1.30 (end-point), while the TC/HDL ratio decreased 0.03 (baseline: 1.98 vs. end-point: 1.95) over the course of the exercise program.

Table 3.3 Cardiovascular results

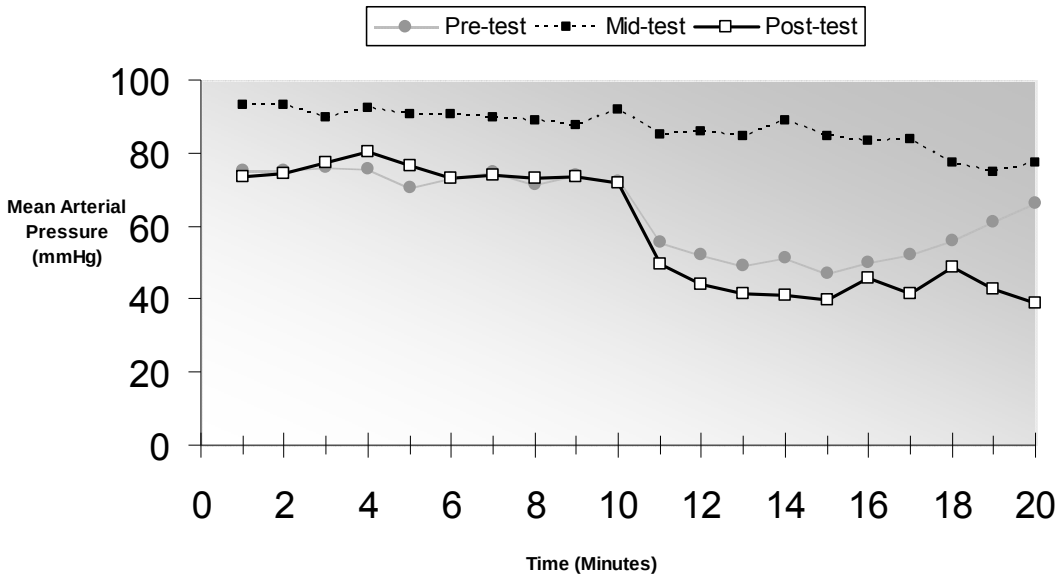
	Baseline	Mid-point	Post-test
Stress test (peak values)			
VO_2 (mL/kg/min)	11.78	14.16	13.72
VO_2 (L/min)	0.73	1.02	0.85
Heart rate (Beats/min)	109	115	117
VE/VO_2	50.88	48.50	56.48
Power Output (Watts)	20	20	30
Borg RPE	19	19	19
6-MAT (average values)			
VO_2 (mL/kg/min)	8.47	8.68	7.59
Heart rate (Beats/min)	110	114	99
Borg RPE	11	16	11
Lipid Profile (mmol/L)			
Triglycerides (TG)	0.41	0.50	0.41
HDL Cholesterol	1.08	1.11	1.30
LDL Cholesterol	0.87	0.75	1.05
TG/LDL ratio	1.98	1.88	1.95

Orthostatic Hypotension: Sit-up Test.

The participant's response to orthostatic challenge increased from baseline to mid-point evaluation (Figure 3.2). At baseline evaluation, three minutes after passive movement from lying to sitting, the subject's SBP decreased from 107.3mmHg to 75 mmHg and DBP decreased from 58.2mmHg to 37mmHg, confirming the presence of OH. These drops in BP were accompanied by feelings of dizziness and light-headedness. At the mid-point evaluation, BP did not incur a large drop at the 3 minute mark (as was observed in the baseline testing) and the participant had no complaints of adverse symptoms. Due to an acute UTI however, these improvements were not apparent during the end-point evaluation session. Dehydration and fatigue (common consequences of a UTI) likely impaired orthostatic tolerance (Mathias, 1995). However, the participant's HR at the 3rd minute after sit-up during the end-point

evaluation (101 beats/min) was 14 beats higher than the baseline evaluation (87 beats/min), indicating improvement in chronotropic compensation during the orthostatic challenge.

Figure 3.2 Sit-up Test



	Supine (average of 10 minutes)			3-minute			Average of last 3 minutes		
	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR
Pre program	107.3	58.2	72.8	75	37	87	86.7	49.3	90.7
Mid-point	124	75.6	59.6	112	72	67	98	66.7	87.7
Post program	111.1	57.8	76.9	62	32	101	67.7	32	98.3

* SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate

Timed functional wheeling.

The participant showed improvements on the two wheeling tests, with substantially faster times to cover (1) the flat distance: 19 seconds (baseline) to 12 seconds (end-point); and (2) the ramp: 23 seconds (with 4 rest breaks) at baseline, to 12 seconds (without stopping) at end-point.

Subjective perception of the program.

The participant rated the program 31 out of a possible 35 points, with a score of 3 on items 3 and 5 (satisfaction with content and manageability of the program) and scores of 5 (extremely satisfied) on all other items. He stated that each station had its own unique challenges and functional outcomes. For example, he noticed and appreciated increases in hand-eye coordination, balance, and body awareness from practicing the boxing station. He also believed that using the arm ergometer was instrumental in alleviating some mild shoulder pain, stating that this was likely due to the balanced strengthening of the push-pull motion. He also commented on the psychological benefits of exercise, reporting that the "biggest thing" about the program was that the exercise increased his mood, stating that "it [the exercise] is good for the body and even more importantly, good for the mind".

3.5 Discussion

The aerobic exercise program we developed appeared to be a feasible addition to this participants' inpatient rehabilitation schedule. Increased exercise tolerance, evident during both training and testing sessions, suggested gains in aerobic capacity, and orthostatic testing indicated improved orthostatic tolerance. The participant also commented on the psychological benefits of aerobic exercise.

The activities and intensity used in our program were modified to continually challenge the subject's increasing capacity for exercise (as measured by changes in HR and RPE). Careful adjustment of exercise prescription is of utmost importance for the SCI population as training intensities must not compromise the muscles required

for wheeling and transferring, yet must be intense enough to induce training effects (Martin Ginis and Hicks, 2007). The participant was able to sustain a relatively high physical effort during in-patient rehabilitation without compromising standard therapy or suffering over-bearing fatigue. Although the three day/week protocol seemed relatively manageable at the outset of the program, participating in three sessions per week was often difficult. Medical complications and numerous specialist appointments out of the centre impeded regular adherence to the program. These disturbances are commonly encountered during SCI rehabilitation (Chen et al., 1999) and need to be recognized and accounted for during realistic implementation of any program. Thus, while three sessions per week is often thought to be optimal for exercise training, it has been noted that twice weekly programs may be more suitable for individuals with SCI as they offer similar benefits to those of more frequent training, yet provide an easier prescription with which to comply (Martin Ginis and Hicks, 2007).

The participant exhibited several signs of improved exercise tolerance (e.g. sustained increases in exercise duration and intensity) throughout the program, indicating potential cardiac or peripheral skeletal muscle adaptations to the exercise training. Aerobic changes during exercise (sustained elevation of HRR and RPE) seemed to occur over the second half of the program. This was likely due to the fact that the participant was i) accustomed to the exercises and thus could challenge himself with respect to intensity; and ii) able to sustain longer exercise durations. He showed a 2 $mL \cdot kg^{-1} \cdot min^{-1}$ change in VO_2peak (with a corresponding 10W increase in power output) from baseline evaluation to end-point evaluation. Functionally, this has previously been shown to positively relate to wheelchair wheeling performance: a 2

$mL \cdot kg^{-1} \cdot min^{-1}$ change in VO_2peak was sufficient to increase ability and time to complete a Wheelchair Circuit in 74 individuals with SCI (Kilkens et al., 2005). Similarly, our participant showed improvements on the two wheeling tests, indicating a concomitant increase in functional wheeling power.

We found that orthostatic tolerance improved after 6 weeks of aerobic exercise in the participant. HR responses to orthostatic stress are normally due to baroreflex-mediated parasympathetic (vagal) withdrawal and sympathetic activation (Mathias, 1995). However, because of his cardiovascular sympathetic insufficiency, it is likely that any increase in HR during orthostatic challenge was predominantly due to baroreflex-mediated reductions in vagal tone. While there is some evidence to support exercise's role in increasing barereceptor activity in the able-bodied population (Convertino and Adams, 1991), similar research in the SCI population is scarce, though Engelke has suggested it may play a similar role for individuals with SCI (Engelke et al., 1992).

Previous studies have reported unfavourable lipid profiles in persons with SCI and have suggested that low levels of HDL are mainly due to low physical activity, secondary to wheelchair dependency (Dearwater et al., 1986). Though De Groot (2003) demonstrated that a physical activity program enhanced the lipid profiles of individuals undergoing primary rehabilitation from SCI (De Groot et al., 2003), Solomonow (1997) found that those with normal cholesterol levels did not exhibit a change in HDL or LDL after a 14 week exercise program (Solomonow et al., 1997). As our participants' lipid profile was within the normal guidelines (Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert

Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 2001), minimal changes were observed.

The medical complications mentioned in this case report are common occurrences during in-patient rehabilitation from cervical SCI (Chen et al., 1999). Clinicians and scientists undergoing research with an in-patient SCI population need to be aware of the typical interruptions in rehabilitation. Though exercise participation in this study was complicated by various medical setbacks, the participant was able to manage the training sessions, suggesting this program is a feasible addition to standard therapy. Thus, it would appear from the results of this case study, that a patient with a motor-complete C5 SCI is able to sustain a relatively high physical effort during initial rehabilitation without compromising standard therapy or suffering over-bearing fatigue. With early aerobic training, we may be able to mitigate cardiovascular deterioration and metabolic alterations, thereby decreasing cardiovascular risk factors and achieving optimal physical fitness for function in daily life.

Limitations

The present study has limitations that must be taken into consideration. Firstly, our participant was a recently injured individual undergoing sub-acute rehabilitation, thus physiologic change may have been influenced by the usual rehabilitation program and natural processes of adaptation and/or recovery. Adding elements of a controlled experiment is necessary to address internal validity concerns regarding the effects of history or maturation. Secondly, the difficulty in accurately measuring exercise intensity in individuals with tetraplegia cannot be over-looked. Though the Borg scale

$_2$ at high exercise intensities in individuals with tetraplegia (Lewis et al., 2007). However, HRR generally mirrored RPE throughout the program, indicating the Borg scale provided a reflection of this participant's exertion.

3.6 References

1. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2001). JAMA. **285,** 2486-2497.

2. American College of Sports Medicine, and Johnson, E. P. (2000). ACSM's Guidelines for Exercise Testing and Prescription. Lippincott Williams & Wilkins:

3. American Heart Association. (2007).

4. Bizzarini, E., Saccavini, M., Lipanje, F., Magrin, P., Malisan, C., and Zampa, A. (2005). Exercise prescription in subjects with spinal cord injuries. Arch Phys Med Rehabil. **86,** 1170-1175.

5. Borg, G. (1970). Perceived exertion as an indicator of somatic stress. Scand J Rehabil Med. **2,** 92-98.

6. Chen, D., Apple, D. F., Hudson, L. M., and Bode, R. (1999). Medical complications during acute rehabilitation following spinal cord injury—current experience of the model systems. Arch Phys Med Rehabil. **80,** 1397-1401.

7. Claydon, V. E., Steeves, J. D., and Krassioukov, A. V. (2006). Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord. **44,** 341-351.

8. Claydon, V. E., and Krassioukov, A. V. (2006). Orthostatic hypotension and autonomic pathways after spinal cord injury. J Neurotrauma. **23,** 1713-1725.

9. Convertino, V. A., and Adams, W. C. (1991). Enhanced vagal baroreflex response during 24 h after acute exercise. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. **260,** 570-575.

10. De Groot, P. C. E., Hjeltnes, N., Heijboer, A. C., Stal, W., and Birkeland, K. (2003). Effect of training intensity on physical capacity, lipid profile and insulin sensitivity in early rehabilitation of spinal cord injured individuals. Spinal Cord. **41,** 673-679.

11. Dearwater, S. R., LaPorte, R. E., Robertson, R. J., Brenes, G., Adams, L. L., and Becker, D. (1986). Activity in the spinal cord-injured patient: an epidemiologic analysis of metabolic parameters. Medicine & Science in Sports & Exercise. **18,** 541.

12. El Masry, W. S. (1993). Physiological instability of the spinal cord following injury. Paraplegia. **31,** 273-275.

13. Engelke, K. A., Shea, J. D., Doerr, D. F., and Convertino, V. A. (1992). Enhanced carotid-cardiac baroreflex response and elimination of orthostatic hypotension 24 hours after acute exercise in paraplegics. Paraplegia. **30,** 872-879.

14. Garshick, E., Kelley, A., Cohen, S. A., Garrison, A., Tun, C. G., Gagnon, D., and Brown, R. (2005). A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord. **43,** 408-416.

15. Hol, A. T., Eng, J. J., Miller, W. C., Sproule, S., and Krassioukov, A. V. (2007). Reliability and validity of the six-minute arm test for the evaluation of cardiovascular fitness in people with spinal cord injury. Arch Phys Med Rehabil. **88,** 489-495.

16. Illman, A., Stiller, K., and Williams, M. (2000). The prevalence of orthostatic hypotension during physiotherapy treatment in patients with an acute spinal cord injury. Spinal Cord. **38,** 741-747.

17. Kilkens, O. J., Dallmeijer, A. J., Nene, A. V., Post, M. W., and LH. (2005). The longitudinal relation between physical capacity and wheelchair skill performance during inpatient rehabilitation of people with spinal cord injury. Arch Phys Med Rehabil. **86,** 1575-1581.

18. Lasko-McCarthey, P., and Davis, J. A. (1991a). Effect of work rate increment on peak oxygen uptake during wheelchair ergometry in men with quadriplegia. Eur J Appl Physiol Occup Physiol. **63,** 349-353.

19. Lasko-McCarthey, P., and Davis, J. A. (1991b). Protocol dependency of VO2max during arm cycle ergometry in males with quadriplegia. Med Sci Sports Exerc. **23,** 1097-1101.

20. Lee, M. Y., Myers, J., Hayes, A., Madan, S., Froelicher, V. F., Perkash, I., and Kiratli, B. J. (2005). C-reactive protein, metabolic syndrome, and insulin resistance in individuals with spinal cord injury. J Spinal Cord Med. **28,** 20-25.

21. Lewis, J. E., Nash, M. S., Hamm, L. F., Martins, S. C., and Groah, S. L. (2007). The Relationship Between Perceived Exertion and Physiologic Indicators of Stress During Graded Arm Exercise in Persons With Spinal Cord Injuries. Arch Phys Med Rehabil. **88,** 1205-1211.

22. Marino, R. J., Barros, T., Biering-Sorensen, F., Burns, S. P., Donovan, W. H., and Graves, D. E. (2003). International standards for neurological classification of spinal cord injury. J Spinal Cord Med. **26,** S49-S56.

23. Martin Ginis, K. A., and Hicks, A. L. (2007). Considerations for the development of a physical activity guide for Canadians with physical disabilities. Appl Physiol Nutr Metab. **32,** S135-S147.

24. Mathias, C. J. (1995). Orthostatic hypotension: causes, mechanisms, and influencing factors. Neurology. **45,** S6-11.

25. May, L. A., Butt, C., Minor, L., Kolbinson, K., and Tulloch, K. (2003). Measurement reliability of functional tasks for persons who self-propel a manual wheelchair. Arch Phys Med Rehabil. **84,** 578-583.

26. Myers, J., Lee, M., and Kiratli, J. (2007). Cardiovascular Disease in Spinal Cord Injury: An Overview of Prevalence, Risk, Evaluation, and Management. American Journal of Physical Medicine & Rehabilitation. **86,** 142.

27. Saltin, B., Blomqvist, G., Mitchell, J. H., Johnson, R. L.,Jr, Wildenthal, K., and Chapman, C. B. (1968). Response to exercise after bed rest and after training. Circulation. **38,** VII1-78.

28. Shatz, I. J., Bannister, R., Freeman, R. L., Goetz, C. G., Jankovic, J., Kaufmann, H. C., Koller, W. C., Low, P. A., Mathias, C. J., and Polinsky, R. J. (1996). American Autonomic Society Consensus Statement. The definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. Neurology. **46,** 1470-1471.

29. Sidorov, E. V., Townson, A. F., Dvorak, M. F., Kwon, B. K., Steeves, J., and Krassioukov, A. V. (2007). Orthostatic hypotension in the first month following acute spinal cord injury. Spinal Cord. **46,** 65.

30. Solomonow, M., Reisin, E., Aguilar, E., Baratta, R. V., Best, R., and D'Ambrosia, R. (1997). Reciprocating gait orthosis powered with electrical muscle stimulation (RGO II). Part II: Medical evaluation of 70 paraplegic patients. Orthopedics. **20,** 411-418.

Chapter 4: General Discussion

4.1 Overview

Due to the high prevalence of cardiovascular disease in individuals with SCI, particularly those with cervical SCI, there is a need to increase the body of knowledge surrounding aerobic exercise for this unique population. Specifically, with early aerobic training, we may be able to mitigate cardiovascular deterioration and metabolic alterations, thereby decreasing cardiovascular risk factors. Our results suggest that individuals with motor-complete cervical SCI are able to sustain a relatively high physical effort during initial rehabilitation without compromising standard therapy or suffering over-bearing fatigue. The work of this thesis provides the grounds for more rigorous trials of cardiovascular training during in-patient rehabilitation from cervical SCI.

4.2 Evaluation of the literature

The results from the systematic review (chapter 2) show that VO_2peak values recorded from individuals with cervical SCI varied widely. This is likely due to subject heterogeneity in variables such as fitness level, time since injury, and injury severity, as well as a wide variety of testing protocols and testing modalities. Our systematic review identified a number of testing modalities, most of which appeared to elicit VO_2peak values spanning similar ranges. Though recommendations have been given as to which protocols seem to most accurately estimate VO_2peak in individuals with tetraplegia (Lasko-McCarthey and Davis, 1991a; Lasko-McCarthey and Davis, 1991b), the protocols documented in the literature vary considerably.

Although it is apparent from the systematic review that VO_2peak increases with decreasing injury severity, heterogeneous subject groups make it difficult to compare VO_2peak values across studies and severely limit the generalizeability of results. Given the wide variety of muscular innervation and autonomic sparing in this population, it would be optimal to conduct sub-group analysis controlling for the varying physical abilities and cardiovascular responses to exercise. Although the systematic review suggests that individuals with tetraplegia show cardiovascular benefits from exercise training, the effect sizes of training on VO_2peak vary considerably and there is a notable lack of rigorous controlled trials. Consequently, the intensity, frequency, and duration required for optimal aerobic training effects in this population have yet to be determined.

4.3 Evaluation of the in-patient exercise program

The aerobic exercise program we developed appeared to be a feasible addition to this participants' inpatient rehabilitation schedule. The subject was able to sustain a relatively high physical effort without compromising standard therapy or suffering over-bearing fatigue. However, participating in three sessions per week was often difficult. He was not immune to the typical complications commonly encountered during SCI rehabilitation (urinary tract infections, pressure ulcers, heterotopic ossification (Chen et al., 1999). Such disturbances are rarely noted in the SCI exercise literature, yet they need to be recognized and accounted for during realistic implementation of any program.

The participant exhibited several signs of improved exercise tolerance throughout the program, indicating potential cardiac or peripheral skeletal muscle adaptations to the

exercise training. The aerobic changes, as measured by his VO_2peak tests, were within the ranges noted in our systematic review. While a 2 point change in VO_2 peak has previously been shown to be sufficient to increase ability and time to complete a functional Wheelchair Circuit (Kilkens et al., 2005), it would be an overstatement to assume that the changes noted in our subject were solely from the aerobic program as he was also participating in wheelchair skills training classes and was becoming exceedingly more efficient maneuvering his wheelchair. The changes seen on the Sit-up test, though promising, must be interpreted with caution as dissipation of neurogenic shock and natural recovery likely played a large part in the improved orthostatic tolerance. However, this case report documented the feasibility of participating in aerobic exercise during sub-acute rehabilitation from cervical SCI. Our participant was able to maintain an elevated heart rate and RPE during exercise, demonstrating his ability to sustain high intensity exercise. He showed improved exercise tolerance over the course of the program, suggesting potential central or peripheral adaptations to the training. And, he commented on the psychological benefits of participating in aerobic exercise during rehabilitation from SCI.

4.4. Clinical implications

The long term aim of this project was to develop an aerobic exercise program that could be implemented as a group therapy class for individuals with cervical SCI. Accordingly, there are a few points that require consideration.

Firstly, one of the unique aspects of this program was that it was continually modified to challenge our participant. Particularly in this population, careful adjustment of

exercise prescription is of utmost importance as training intensities must not compromise the muscles required for wheeling and transferring, yet must be intense enough to induce training effects (Martin Ginis and Hicks, 2007). Clearly, it is relatively easy to modify a program to meet the changing needs of one individual. However, this poses some legitimate concerns when monitoring numerous clients. In a group setting, it is imperative that each participant be educated on the importance of maintaining his/her prescribed intensity level. As this program is comprised of various, time-controlled activity stations, each participant would be able to train at their own level, while maintaining the continuity of the class.

We increased both exercise time and exercise intensity to continually challenge our participant. Intensity was monitored each session via both HR and RPE. Exercise intensity was prescribed at the beginning of each class by setting a goal RPE (e.g. 16). The participant subsequently reported his RPE at time-points throughout the class and was verbally encouraged to maintain or adjust his effort accordingly. HR was used as an extrinsic motivator; each time the participant reported his RPE, he was made aware of his HR. He became motivated by this objective measure and was constantly working to increase his HR response. We acknowledge that using a HR monitor may not be feasible in a group therapy setting. For our one participant, RPE generally mirrored HR throughout the exercise sessions, suggesting that the Borg RPE scale provided a reflection of this participant's exertion. However, it is not known whether HR and RPE would have a similar relationship in a larger sample.

Thirdly, we accommodated for our participant's busy schedule as best as possible and every effort was made to "make up" for missed sessions. Despite our efforts, his

average attendance was about twice per week. Clearly, a group class does not accommodate for individual schedule changes, so attending three sessions per week would likely be difficult. On the other hand, a set group class may encourage rehabilitation therapists to organize therapy sessions accordingly, thus decreasing scheduling conflicts and increasing participation in the class.

Lastly, the emotional effects of aerobic exercise cannot be over-looked. Running this exercise program as a group class would likely enhance the psychological benefits resulting from the cardiovascular exercise alone. Further, motivation to attend and work intensively during the exercise class would likely be heightened by peer support.

4.5 Future work

This thesis has only begun to explore aerobic training during sub-acute rehabilitation from cervical SCI. A number of further studies are recommended:

- A large before-after study, using a group exercise class, could be done to determine if the effects of this exercise program generalize to other individuals under-going sub-acute rehabilitation from cervical SCI.
- A clinical trial, with an appropriate control group, should be undertaken to determine the effectiveness of aerobic training during sub-acute rehabilitation from cervical SCI.
- A cross-sectional study could be used to assess the correlation between cardiovascular fitness and ability to perform activities of daily living during the sub-acute phase of rehabilitation from cervical SCI.

4.6 Summary

The exercise literature concerning individuals with cervical SCI is limited in quantity. Our systematic review revealed a wide range of VO_2peak values. In general, VO_2peak increased with decreasing severity of injury, while higher intensity training seemed to elicit higher effect sizes for VO_2peak. The case report demonstrated that despite the common complication associated with sub-acute rehabilitation from cervical SCI, aerobic training can be a feasible and beneficial addition to standard therapy.

4.7 References

1. Chen, D., Apple, D. F., Hudson, L. M., and Bode, R. (1999). Medical complications during acute rehabilitation following spinal cord injury—current experience of the model systems. Arch Phys Med Rehabil. **80,** 1397-1401.

2. Kilkens, O. J., Dallmeijer, A. J., Nene, A. V., Post, M. W., and LH. (2005). The longitudinal relation between physical capacity and wheelchair skill performance during inpatient rehabilitation of people with spinal cord injury. Arch Phys Med Rehabil. **86,** 1575-1581.

3. Lasko-McCarthey, P., and Davis, J. A. (1991a). Effect of work rate increment on peak oxygen uptake during wheelchair ergometry in men with quadriplegia. Eur J Appl Physiol Occup Physiol. **63,** 349-353.

4. Lasko-McCarthey, P., and Davis, J. A. (1991b). Protocol dependency of VO2max during arm cycle ergometry in males with quadriplegia. Med Sci Sports Exerc. **23,** 1097-1101.

5. Martin Ginis, K. A., and Hicks, A. L. (2007). Considerations for the development of a physical activity guide for Canadians with physical disabilities. Appl Physiol Nutr Metab. **32,** S135-S147.

Appendix A: Consent form

THE UNIVERSITY OF BRITISH COLUMBIA

Subject Information and Informed Consent Form

The effects of a group exercise program on function in spinal cord injury rehabilitation

Principal Investigator:
Dr. Janice Eng, PhD PT/OT
School of Rehabilitation Sciences, UBC
Rehab Research Lab, GF Strong Rehab Centre
Phone: (604) 714-4108

Study Coordinator:
Amira Tawashy, BSc, MSc Candidate
School of Rehabilitation Sciences, UBC
Rehab Research Lab, GF Strong Rehab
Phone: (604) 714-4109

Contact number for study information and questions: 604-714-4108
Emergency Telephone Number:
You may contact Dr. Janice Eng at (604) 839-7835, 24 hours a day, 7 days a week.

Introduction:
We are investigating the effects of different exercise programs on the function of individuals who have had a spinal cord injury. You have been invited to participate in this study because you are currently participating in rehabilitation at GF Strong Rehab Centre.

Your Participation is Voluntary:
- Your participation is voluntary**;** it is up to you to decide whether or not to take part in this study. This consent form will tell you about the study, why the research is being done, what will happen to you during the study and the possible benefits and risks.
- If you wish to participate, you will be asked to sign this form. If you decide to take part in this study, you are still free to withdraw at any time and without giving any reason.
- If you do not wish to participate you will not lose the benefit of any medical care to which you are entitled or are presently receiving.

Background and purpose:
Heart disease is currently the leading cause of death in individuals with spinal cord injury. One of the most significant risk factors for heart disease is low fitness levels, a condition that is common among those with spinal cord injury. We want to find the best way for people with spinal cord injury to exercise during their rehabilitation so that heart disease can be minimized.

Falls during transfers are a major cause of bone fracture in individuals with spinal cord injury. Balance is one of the main elements of successful transfers. We want to find the best way to increase balance so that falls (and bone fractures) occur less frequently in people with spinal cord injury.

Who can participate in this study?
If you meet the following criteria you are eligible to participate in this study:
- Are an in-patient at GF Strong
- Had a traumatic spinal cord injury
- Are between the ages of 16-50
- Use a manual wheelchair for your daily activities
- Able to push an arm crank cycle

Who should not participate in this study?
If you have any of the following conditions you are not eligible to participate in this study:

- Have a known history of cardiovascular disease (irregular heart beat, chest pains, etc)
- Have respiratory disease, uncontrolled high blood pressure or injuries to muscles, bones, ligaments, tendons or joints
- Have increased pain with arm activities
- Have a brain injury which stops you from understanding the instructions that will be given during the research study

Time Commitment for the Study:
Weekly sessions: 30 minutes X 3 days per week for 6 weeks.
In addition to participating in the exercise classes, you will attend four testing sessions over a two month period. These sessions will take approximately 2 hours and will be done on separate days. Two sessions will be held before you do the exercise class and will consist of: (Day 1) an arm crank cycle test and muscle and sensory testing; and (Day 2) a cardiovascular stress test and balance test. So, the total time required for the study is 17 hours.

What does the study involve?
The study will take place at GF Strong. Thirty people with spinal cord injury will be recruited for this study.

Medical Information:
Your medical records will be looked at, and the following information taken from them: date of injury and ASIA score.

Maximal Cardiovascular Test:
This test, which measures your cardiovascular function (how well your heart works), will be performed on an arm crank cycle in the presence of a medical doctor and a research technician. You will begin to cycle with your arms at a very light intensity, and as the test progresses, the intensity will gradually increase until your arms are tired. The intensity refers to how challenging the arm cycling will be; it will be very easy when you begin and gradually become more difficult. You will have 12 electrodes attached to your chest (they stick to your skin similar to a band-aid, and are painless when on your skin) to measure how well your heart is handling the exercise. You will also be fitted with a face mask to measure the amount of oxygen that you are breathing in. The test will be stopped if any abnormal signals arise from the electrodes monitoring your heart, or if you feel chest discomfort, if you feel dizzy or lightheaded, or if your blood pressure gets too high.

Submaximal Cardiovascular Test:
This assessment is similar to the maximal cardiovascular test. You will cycle for 6 minutes at a somewhat-hard intensity. You will wear a heart rate monitor, and will wear the same face mask as when you do the Maximal Cardiovascular Test.

Balance Test:
You will reach forward as far as you can while sitting. We will be standing beside you to make sure you don't fall and we will measure how far you can reach.

Sit-up Test
We will measure your heart rate and blood pressure while you are lying down. Then, you will sit-up and we will measure your heart rate and blood pressure again.

Blood tests:
We would like to see if your cholesterol levels change after the exercise program. To do this, a registered nurse from Vancouver Coastal Health will take an 8 mL blood sample from you at the beginning and at the end of the exercise program.

Questionnaires and functional level evaluation:
You will be given questionnaires regarding your health. You do not have to respond to any questions you do not feel comfortable answering. Your spasticity level will be measured by bending your joints while you are relaxed and your strength will be measured by you pushing against a lever. We will also measure your level of injury by testing your sensation and muscle strength. To measure your sensation, we will lightly touch your skin with a cotton ball and a small pin to see how well you can feel different patches of skin on your body. To determine your muscle strength, we will measure how well you can move your legs, arms and hands.

Determining which group you will participate in:
Your involvement in the study depends on the group which you are assigned to by chance (like the flip of a coin). You have an equal chance to be in the 'arm program' or 'balance program'.

Description of study programs:
You will receive the usual care provided by the rehabilitation centre that you are attending. In addition, you will receive one of the following programs:

Arm Program:
In the hospital you will be attending your usual sessions with either physiotherapy, occupational therapy or both. In addition, you will attend a 30 minute long exercise class three times per week which will focus on increasing your wheeling ability. This program will last for 6 weeks.

Balance Program:
In the hospital you will be attending your usual sessions with either physiotherapy, occupational therapy or both. In addition, you will attend a 30 minute long session three times per week which will focus on improving your balance skills. This program will last for 6 weeks.

What are the possible risks of participating?
There is a chance you may feel tired or have some muscle soreness when you first start the exercise sessions. This is usually gone in a few days.

There is also a chance that you may feel tired or experience some muscle soreness after the testing sessions. During and immediately following the cardiovascular stress test, you may experience some discomfort (i.e. dry mouth, dizziness from breathing too heavily, muscle soreness). These symptoms can be minimized by drinking 2 cups of water prior to testing, and deep breathing and stretching following the test. In addition, there is a slight chance that the electrodes used to monitor your heart during the stress test may cause skin irritation. During any activities which involve exercise, there is a low risk that you may experience a cardiac event (problems with your heart). Some of the questions you will be asked before the study begins will determine if you are more likely to experience a cardiac event, and if you are, you will not be able to participate in the study. The stress testing will be done with a medical doctor present.

Benefits:

Participants have the potential to improve their efficiency in daily activities, but improvement is not guaranteed by this program.

New Information Available that May Affect Your Decision to Participate:
If there is new information that may affect your willingness to be in the study, you will be advised of this information.

If You Withdraw Your Consent to Participate:

- Your participation in this research is entirely voluntary. You can decide to withdraw at any time without providing any reason. If you decide to enter the study and withdraw, there will be no penalty and your medical care will not be affected.
- The study investigators may decide to stop the study, or withdraw you from the study if they feel that it is in your best interest.
- If you choose to withdraw, all data collected about you will be retained for analysis.

Alternatives to the Study Program:
During the study you will be participating in usual care spinal cord injury rehabilitation.

If Something Goes Wrong:
In case of an emergency, please report to it to the medical staff on your unit. **You do not waive your legal rights by signing the consent form.**

After the Study is Completed:
Once the study is completed and the data are analyzed, you will be sent a report on your arm function. You may be contacted in the future for related studies. At that time you can refuse to participate and your name will be removed from future correspondence. If you decide to participate in future studies, you will be asked to sign another consent form specific to that study.

Confidentiality:
Your confidentiality will be respected. No information that shows your identity will be released or published without your specific consent. Research and medical records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of Health Canada and the UBC Research Ethics Board for the purpose of monitoring the research. No records that identify you by name or initial will be allowed to leave the Investigators' offices.

Contact:
If you have any questions with respect to this study or during participation, you can contact Dr. Janice Eng or one of her associates at (604) 714-4108. If you have any concerns about your rights as a research subject and/or your experiences while participating in this study, contact the Research Subject Information Line in the University of British Columbia Office of Research Services at 604-822-8598.

Consent to Participate:
This is not a contract and I understand that I do not give up any legal rights by signing it. By signing the form I am indicating that:

- I have read and understood the subject information and consent form.
- I have had the opportunity to ask questions and have had satisfactory responses.
- I understand that all the information collected will be kept confidential and that the results will only be used for scientific objectives.
- I understand that my participation in this study is voluntary and I am free to refuse to participate or withdraw at any time without changing the quality of care that I receive.
- I understand I am not waiving any legal rights as a result of signing this consent form.
- I have read this form and I freely consent to participate in this study.
- I have been told that I will receive a dated and signed copy of this form.

☐ Yes, I would like to be contacted for future studies.

☐ No, I would not like to be contacted for future studies.

Printed Name of Subject	Subject Signature	Date
Printed Name of Witness	Witness Signature	Date
Printed Name of Principal Investigator/Designated Representative	Signature of Principal Investigator/Designated Representative	Date

Appendix B: AIS

ASIA IMPAIRMENT SCALE

- ☐ **A = Complete:** No motor or sensory function is preserved in the sacral segments S4-S5.
- ☐ **B = Incomplete:** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.
- ☐ **C = Incomplete:** Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.
- ☐ **D = Incomplete:** Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.
- ☐ **E = Normal:** motor and sensory function are normal

CLINICAL SYNDROMES

- ☐ Central Cord
- ☐ Brown-Sequard
- ☐ Anterior Cord
- ☐ Conus Medullaris
- ☐ Cauda Equina

STANDARD NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

MOTOR

KEY MUSCLES

	R	L	
C2			
C3			
C4			
C5			Elbow flexors
C6			Wrist extensors
C7			Elbow extensors
C8			Finger flexors (distal phalanx of middle finger)
T1			Finger abductors (little finger)
T2			
T3			
T4			
T5			
T6			
T7			
T8			
T9			
T10			
T11			
T12			
L1			
L2			Hip flexors
L3			Knee extensors
L4			Ankle dorsiflexors
L5			Long toe extensors
S1			Ankle plantar flexors
S2			
S3			
S4-5			Voluntary anal contraction (Yes/No)

0 = total paralysis
1 = palpable or visible contraction
2 = active movement, gravity eliminated
3 = active movement, against gravity
4 = active movement, against some resistance
5 = active movement, against full resistance
NT = not testable

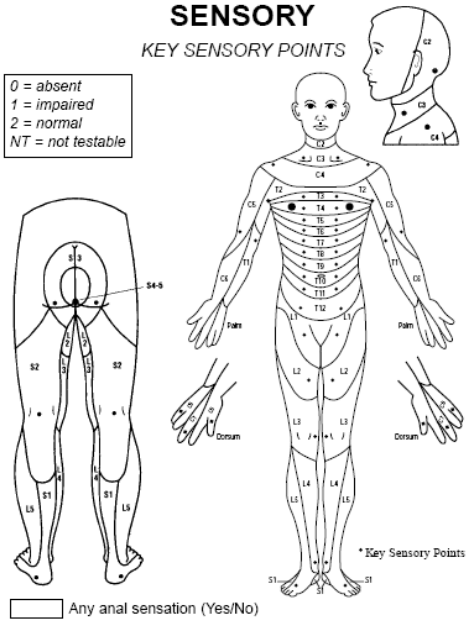
TOTALS ☐ + ☐ = ☐ **MOTOR SCORE**
(MAXIMUM) (50) (50) (100)

SENSORY

	LIGHT TOUCH R	LIGHT TOUCH L	PIN PRICK R	PIN PRICK L
C2				
C3				
C4				
C5				
C6				
C7				
C8				
T1				
T2				
T3				
T4				
T5				
T6				
T7				
T8				
T9				
T10				
T11				
T12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				

KEY SENSORY POINTS

0 = absent
1 = impaired
2 = normal
NT = not testable



☐ Any anal sensation (Yes/No)

TOTALS { ☐ + ☐ = ☐ **PIN PRICK SCORE** (max: 112)
= ☐ **LIGHT TOUCH SCORE** (max: 112)
(MAXIMUM) (56) (56) (56) (56)

NEUROLOGICAL LEVEL *The most caudal segment with normal function*	R	L
SENSORY	☐	☐
MOTOR	☐	☐

COMPLETE OR INCOMPLETE? ☐
Incomplete = Any sensory or motor function in S4-S5

ASIA IMPAIRMENT SCALE ☐

ZONE OF PARTIAL PRESERVATION *Caudal extent of partially innervated segments*	R	L
SENSORY	☐	☐
MOTOR	☐	☐

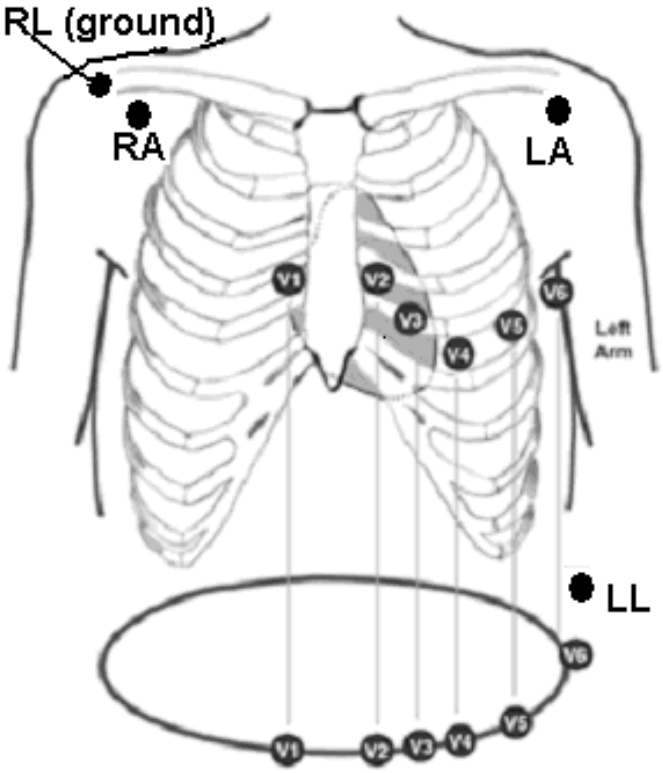
This form may be copied freely but should not be altered without permission from the American Spinal Injury Association.

2000 Rev.

Appendix C: Electrode Placement for ECG leads

Electrode Placement for Limb and Augmented Leads(I, II, II, AVF, AVR, AVL)
RL: Right Leg- (Ground wire) put on the right acromion process
RA: Right Arm- put just inferior the right clavicle
LL: Left Leg- put just superior to the left ASIA
LA: Left Arm- put just inferior to the left clavicle

Electrode Placement for Precordial Leads (V1, V2, V3, V4, V5, V6)
V1 4th intercostal space, right of sternum
V2 4th intercostal space, left of sternum
V3 midway between V2 and V4
V4 5th intercostal space, in the midclavicular line
V5 same level as V4, at anterior axillary line (between V4 and V6)
V6 in 5th intercostal space, in the midaxillary line



ECG Electrode Skin Preparation
1. Shave the skin so it is free of hair.
2. Rub the spot with alcohol until it is red.

Appendix D: VO_2peak protocol

Equipment calibration: The Cosmed $K4b^2$ was used for metabolic measurement. The equipment consists of a soft mask to sample exhaled air, a sensor system to measure ventilation, and oxygen and carbon dioxide analyzers. Respiratory flow was measuredby a turbine fixed to the face mask, and expired gas concentrations were measured using a polarographic electrode for the oxygen fraction and an infrared electrode for the carbon dioxide fraction. The Cosmed $K4b^2$ system was calibrated before each test according to the manufacturer's recommended procedures (operator's manual of $K4b^2$ system). Calibrations included a gas calibration to determine the time delay between expiration and inspiration, and a turbine calibration using a known volume of air.

Positioning: The participant remained seated in his wheelchair (brakes on) for the VO_2peak test. Adjustments were made such that the centre of the crank was level with their shoulder. He was positioned such that during the arm cycling, his elbows did not reach full extension.

Instructions: The participant was given full instructions prior to the beginning of the test. First, he was informed of a short (1-2 minute) warm-up period, where he was able to cycle against zero resistance. He was then told :

'During the test, the resistance, or difficulty of the cycling will start out pretty easy. At the end of each minute, it will get a little bit harder. You might not even notice the first increase. We want you to keep cycling at the same speed for the whole test. Towards the end, it will start to get quite difficult. We will give you lots of encouragement to keep cycling for as long as you can. If you feel any chest pain, lightheadedness, or feel sick to your stomach, please stop the test right away and tell us how you are feeling.'

Protocol: Power output increased at 5W/minute.

Appendix E: BORG RPE Scale

6	
7	**very, very light**
8	
9	**very light**
10	
11	**fairly light**
12	
13	**moderately hard**
14	
15	**hard**
16	
17	**very hard**
18	
19	**very, very hard**
20	

APPENDIX F - Psychometric properties of outcome measures

Outcome Measure	Reliability	Validity
American Spinal Injury Association Impairment Scale (AIS)`	*Motor score*: Intra-rater reliability, intraclass correlation coefficient (ICC) = 0.99, inter-rater reliability ICC = 0.98 *Pin-prick score*: Intra-rater reliability ICC = 0.98, inter-rater reliability ICC = 0.96 *Light-touch score*: Intra-rater reliability ICC = 0.99, inter-rater reliability ICC = 0.96 *Impairment scale*: Intra-rater reliability Kappa = 0.84, inter-rater reliability Kappa = 0.72 (Cohen and Bartko, 1994)	*Motor score*: Criterion validity with cumulative motor score, r = 0.988 (Masry et al., 1996)
VO_2peak Test	Peak VO_2: ICC = 0.82 (SEM = 1.65) (Stewart et al., 2000)	
6-Minute Arm Test (6-MAT)	*Heart rate*: Steady state ICC = 0.90 (SEM = 7.12) *VO_2*: Steady state ICC = 0.81 (SEM = 1.62) (Hol et al., 2007)	Concurrent Validity: Steady state VO_2 and HR relates to VO_2peak (as measured by ACE), r = 0.92 and 0.63, respectively) (Hol et al., 2007)
Sit-up Test	Reliability results not found in the literature	Concurrent Validity: Preservation of palmar sympathetic skin response (SSR) following median nerve stimulation related to changes in MAP following assumtion of the upright posture (r = 0.47, p < 0.01) (Claydon and Krassioukov, 2006)

APPENDIX G - Ethics approval

The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL

PRINCIPAL INVESTIGATOR:	DEPARTMENT:	UBC CREB NUMBER:
Janice Eng	UBC/Medicine, Faculty of/Rehabilitation Sciences	H07-01073

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
Vancouver Coastal Health (VCHRI/VCHA)	GF Strong Rehabilitation Centre

Other locations where the research will be conducted:
N/A

CO-INVESTIGATOR(S):
William C. Miller
Andrei V. Krassioukov
Amira Tawashy

SPONSORING AGENCIES:
N/A

PROJECT TITLE:
The effects of a group exercise program on function in spinal cord injury rehabilitation: A pilot randomized controlled trial.

EXPIRY DATE OF THIS APPROVAL: July 18, 2009

APPROVAL DATE: July 18, 2008

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

Approval of the Clinical Research Ethics Board by: