High versus moderate intensity arm-crank exercise for improving oxygen uptake and cardiovascular risk factors in spinal cord injured

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Master Thesis in Clinical Health Science,

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Trondheim, January 2014

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Acknowledgements

This master thesis is a part of my Master Degree in Clinical Health Science at the Norwegian University of Science and technology (NTNU) in Trondheim. The study was conducted at The Department of Spinal Cord Injuries, at St Olavs hospital, Trondheim, in cooperation with the Department of Circulation and Medical Imaging (ISB) at the Faculty of Medicine, NTNU.

First I would like to thank my supervisor Post doc Arnt Erik Tjønna (ISB, NTNU) for being supportive and help me with practical and theoretical challenges. I would also like to thank my secondary supervisor Phd Berit Brurok (Department of spinal cord injuries) for giving me this opportunity to start a project at the Department of Spinal Cord Injuries, thank you for all your motivation, the knowledge you have cheered and time spent on me the last year.

The Department of Spinal cord injuries have given me the opportunity to write this master thesis, thanks to the leaders letting me start this study, and thanks to all good colleagues, and especially thanks to physiotherapist Bodil Sørhøy for helping me conduct the intervention, and for our valuable discussions.

Most of all I would like to thank the participants who have dutifully attended this project, and made it possible to write this thesis.

Finally, I would also like to thank my husband and children for been kind and supportive to me.

Trude Flatås Sæter

Trondheim, January 2014

Abstract

Background/Aim: Spinal cord injury (SCI) is a debilitating condition which leads to loss of sensory and/or motor function of varying degrees below the level of injury. Physical inactivity is a major risk factor for developing cardiovascular disease and early death. Physical inactivity is highly prevalent in SCI population. Maximal oxygen uptake is a predictor for cardiovascular health. In studies with able-bodied, aerobic high intensity training has been found superior compared to moderate intensity, in terms of increasing oxygen uptake and reducing risk factors for CVD. Only a limited amount of studies have investigated the role of intensity of training during arm-crank exercise (ACE) in terms of effect on aerobic capacity and prevention of cardiovascular risk factors in individuals with a SCI. Therefore the primary aim of this study was to compare the effect from high-intensity ACE (i.e. 85-95% of peak heart rate) in 4 x 4 minute intervals, with isocaloric moderate intensity ACE (i.e.70% of peak heart rate) on peak oxygen uptake for individuals with chronic traumatic SCI. Secondary aims were to compare the effect from high- versus moderate intensity ACE on lipid profile, fasting glucose, hypertension and resting heart rate. **Methods**: 10 traumatic SCI participants volunteered for 8 weeks of ACE with 3 exercise bouts per week. The participants were randomized into two groups, high intensity ACE (85-95%HR_{peak}), (N=5), and moderate intensity ACE (70 %HR_{peak}), (N=5). A pre-test posttest design was used, and the participants were tested for VO_{2peak}, lipid profile, insulin resistance, blood pressure and resting heart rate at pre- and posttest. **Results**: No significant difference between the high- and moderate intensity ACE in terms of VO_{2peak} was found. Although not significant there was a favorable trend towards a higher increase in mean VO_{2peak} in the high intensity group compared to the moderate intensity (high intensity group mean increase 8. 9% (l/min), while the moderate intensity group had a minor mean decrease of 2. 1% (l/min)) No significant difference in the blood glucose levels, blood pressure, lipid profile and resting heart rate was found between the two groups after 8 weeks of ACE. **Conclusions**: No significant differences were found between the high and moderate intensity groups after 8 weeks of ACE. Individual differences affect our results. Our findings indicates that eight weeks of high intensity ACE may improve the aerobic capacity for chronic SCI individuals more than moderate intensity ACE. The cardiovascular risk factors such as the lipid profile seem to be improved by exercise for SCI people, but we cannot say if the intensity is the dependent factor.

Keywords: Spinal cord injury, arm crank exercise, aerobic exercise, cardiovascular disease, lipid profile.

Abbreviations

ACE	Arm crank exercise
AD	Autonomic dysreflexia
AIS	American Spinal Injury Association Impairment Scale
ASIA	American Spinal Injury Association
BMI	Body mass index
BORG	Borg scale
CAD	Coronary artery disease
CI	Confidence interval
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
FES	Functional electric stimulation
HDL	High-density lipoprotein cholesterol
HI	High intensity training
HR	Heart rate
HRpeak	Peak heart rate
HRR	Heart rate reserve
HRrest	Resting heart rate
IDF	The international diabetes federation
IR	Insulin resistance
ISNCSCI	International standards for neurological classification of Spinal cord injury
La^{bl-1}	Blood lactate concentration
LDL	Low-density lipoprotein cholesterol
MO	Moderate intensity
N	Participants
P	Probability value
Q	Cardiac output
R	Respiratory exchange ratio
SBP	Systolic blood pressure
SCI	Spinal cord injury
SD	Standard deviation
SNS	Sympathetic nervous system
SV	Stroke volume
TC	Total cholesterol
TG	Triglycerides
TSI	Time since injury
V'E	Total pulmonary ventilation
VO_{2max}	Maximal oxygen uptake
VO_{2peak}	Peak oxygen uptake
WCE	Wheelchair exercise

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1 Background

1.1 Spinal cord injury

The spinal cord is the main connection for motor and sensory information between the brain and the body (1). A traumatic spinal cord injury (SCI) is a condition where the spinal cord is partially or completely injured as a consequence of for example traffic accidents, falls, violence and sport injuries (44). The reported incidence of SCI varies worldwide. The prevalence of traumatic SCI in Europe is reported to be an average of 252 per one million inhabitants (43), while the prevalence in the USA is reported to be 1800 per million inhabitants (42). In Norway, Hagen et al performed a retrospective population-based epidemiology study, and found a total prevalence of 36.5 per 100000 inhabitants with traumatic SCI in Western Norway (45). The wide variation in reported incidence and prevalence of SCI may be explained by differences in definitions of a SCI, inclusion criteria, and identification worldwide (42). There is need for a more uniform registration of SCI in many parts of the world (43).

SCI is divided into high (cervical) and low anatomical damage (thoracic, lumbal and sacral) (1). The term `tetraplegia` refers to cervical damage, and results in impairment of function in all four extremities as well as in the trunk and the pelvic organs (1). `Paraplegia` is used as a term for impairment in the thoracic, lumbar or sacral segments. Arm function is spared with paraplegia, but depending on level of injury there is loss of function (motor and/or sensory) in trunk, legs and pelvic organs (1). The neurological level and severity of injury is classified according to International standard for neurological classification of Spinal Cord Injury (ISNCSCI) (1) American Spinal Injury Association (ASIA) Impairment Scale (AIS) A-E, where A is complete loss of motor and sensory function in the sacral segments (S4-S5) and E is normal sensory and motor function (2). A traumatic SCI is by definition an acute injury of the spinal cord resulting in varying degrees of disturbance and paresis (3).
In a historical perspective, complications of pulmonary conditions and renal function have been the main causes of mortality in the SCI population (6). However, in the last decades, as a consequence of improved medical treatment, the survival rate after a SCI has increased significantly (5).Over the last three decades; there has been a 40% decline in mortality during the first two critical years after contracting a SCI (72). Recent studies have found that

respiratory problems, cardiovascular disease and suicide are now the leading causes of mortality in both acute and chronic stages of a SCI (41). In a study conducted with individuals with a chronic SCI, a mortality rate of 18.9% due to cardiovascular disease (CVD) was found (86). Morbidity from cardiovascular causes, especially coronary artery disease (CAD), tends to occur earlier in persons with a SCI compared to able-bodied individuals (6). Physical inactivity is highly prevalent in people with SCI (13). The reduced amount of muscle mass in SCI lowers the daily energy expenditure, and may be 10-50% lower compared to able-bodied (73). Dallmeijer et al. found an evident relationship between the physical dimensions of health related functional status and lesion level for people with SCI (50). Furthermore, inactivity in the SCI population may also be related to lack of access and fewer opportunities to participate in physical activity (6).

Body composition, hormone regulation and metabolism change over time after a SCI. These changes increase the risk of obesity, cardiovascular disease and type II diabetes. Loss of muscle mass and increased fat mass may be the basis for impaired glucose tolerance, insulin resistance, and also changes in fat hormones and abnormal lipid values (8). Changes in metabolism over time are likely related to inactivity due to level and extent of injury, and to dysfunction of the autonomic nervous system (8).
The autonomic nervous system is important for cardiovascular control. Both blood pressure and heart rate get impulses from the autonomic nervous system (sympathetic and parasympathetic) (7). Disturbances in the autonomic nervous system are factors that together with varying degrees of active muscle mass, changes in metabolic and vascular function limit exercise capacity after a SCI (47). One of many SCI related complications is autonomic dysreflexia (AD). AD is a very serious condition which may be life threatening (40). AD occur as a vascular complication in persons with SCI above thoracic level 6(TH6), and is characterized as a sudden uncontrolled sympathetic response to noxious stimuli below the level of SCI resulting in a sudden rise in blood pressure (40). This sudden rise in blood pressure lies between 20-40 mmHg above baseline values (19).

Physical activity is defined as*: "Any bodily movement produced by skeletal muscles that require energy expenditure"* (9). World health organization (WHO) has declared that physical inactivity is identified as the fourth leading risk factor for global mortality causing an estimated 3.2 million deaths globally. And compared to others with a functional disability or to the population as a whole, people with SCI have been described amongst the most

physically inactive segments in society (11). Physical inactivity is a major risk factor for cardiovascular disease and early death (12). And it is likely that the low level of physical activity partly explain the increased risk of cardiovascular disease in the SCI population (14). In fact, a 3-5 times higher risk of developing type 2-diabetes and a 60% higher incidence of heart attack has been found in people with SCI compared to able-bodied (10). Individuals with a SCI have a low aerobic capacity, and low values of high-density lipoprotein (HDL) cholesterol (15). A low aerobic capacity is further associated with high values of low-density lipoprotein (LDL) cholesterol, triglycerides, and total cholesterol, obesity and glucose values (15).

1.2 Limitations to aerobic capacity in SCI

Maximal oxygen uptake (VO_{2max}) is the main determinant of aerobic capacity. And cardio respiratory exercise testing is considered the gold standard for assessing maximal aerobic capacity (35). The three most important factors determining cardio respiratory endurance performance are; VO_{2max}, lactate threshold and work economy (71). The physiological characteristics for VO_{2max} is described according the Fick`s principle:
(VO_{2max}= cardiac output x arterio-venous O_2 difference) (17). Peak oxygen consumption (VO_{2peak}) is used when the maximal test performance is limited by local muscular factors rather than central circulatory dynamics; hence a demand limitation (17). Lactate threshold is defined as the highest exercise intensity, working dynamically with large muscle groups, where production and clearance of lactate acid is about the same (87). Work economy is the oxygen cost at a standardized workload and it refers to ratio between work output and energy input (71).
In able-bodied persons there is redistribution of blood from inactive tissue to supply the working muscles (19). The reliance on upper body exercise and lack of active muscle mass during exercise limit the possibilities to achieve a high aerobic capacity as a result of exercise training in individuals with a SCI (49). Furthermore, VO_{2peak} is limited by factors like hemodynamic, hormonal and metabolic disturbances related to level and extent of SCI (19). An increase in cardiac output (Q) is a result of an increase in stroke volume (SV) and heart rate (HR). This vasoregulation is controlled by the sympathetic nervous system (SNS) (19). In individuals with a SCI, arm exercise capacity is reduced because of loss of autonomic control below the level of injury (47). The SNS is completely or partially absent in relation to the level of injury for people with SCI (19). This results in a reduced HR response as well as

myocardial contractility, which gives a limited maximal Q and SV. For those with injuries below Th6, the splanchnic-vascular bed is innervated, and a limited or no haemodynamic response is triggered (53). There are different physical responses in arm exercise compared with leg exercise. Circulatory responses to exercise are different in SCI people, compared to able bodied because of disturbed redistribution of blood (65). Smaller muscle groups are involved in arm crank exercise, compared with leg exercise (19). Fatigue in peripheral system will develop before maximum work capacity in the cardiovascular system when arm crank exercising (64). Studies comparing treadmill and arm ergometry exercise concludes a difference for about 58% of $VO_{2peak,}$ between lower and upper body exercise (64). Al-Rahamneh et al studied the validity of using VO_{2peak} in paraplegic, and their results show that that VO_{2peak} may be predicted with reasonable accuracy (48). Also Schrieks et al show in their research that arm crank exercise (ACE) is a valid mean for predicting VO_{2peak} for people unable to perform lower body ergonometry (70).

1.3 Cardiovascular risk factors in SCI

Dyslipidemia is defined as an "*abnormal concentration of blood lipids that confers elevated risk for developing CVD"* (24). Dyslipidemia and obesity are more common among individuals with SCI compared to able-bodied (25). Liang et al. (74) found that men with SCI had a higher risk for reduced HDL (OR=1.76; 95%CI 1.06-2.94) compared to their able-bodied counterparts (74).

High concentrations of total cholesterol (TC), triglycerides, (TG), low-density lipoprotein (LDL) and low concentration of high-density lipoprotein (HDL), induces a higher risk for CVD (54). Compared to able-bodied persons there is a tendency towards an elevated low density lipoprotein cholesterol (LDL) and total cholesterol level as well as a lower high density lipoprotein cholesterol level (HDL), after a SCI (13). The degree of dyslipidemia is more associated with time since injury than to diet (26). The metabolic changes and physical inactivity together may influence the prevalence of dyslipidemia in this population (6). One study has shown that body mass index (BMI) increased significantly during a 5 year period after contracting the injury, but at the same time lipid profiles remained stable (25). Bostom et al (28) studied the relationship between VO_{2peak} and lipid and lipoprotein profiles in SCI men, and found a significant correlation between VO_{2peak}, total cholesterol and high density lipoprotein (28). This study indicates that there is a relationship between aerobic fitness and lipid profile for mid-to-low thoracic SCI as it is for able-bodied (28).

Insulin resistance, glucose intolerance and type II diabetes mellitus is a result of disorders in the carbohydrate metabolism, and is also more prevalent in SCI- compared to the able-bodied population (13). Inactivity is associated with development of insulin resistance and type II diabetes (29). As a consequence of a SCI, skeletal muscle atrophy and fiber-type proportions change towards more type II high fatigue muscle fibers (57). This together with the volume of paralyzed muscles and the neurological level of injury may explain the glucose intolerance in people with a SCI (57). Skeletal muscle is the main area for glucose transport, and exercise leads to activation of glucose transport (58).

There is limited population-based information referring to people with SCI and diabetes (30). There are studies which have found that insulin resistance, type II diabetes mellitus and glucose intolerance seems to be more prevalent in people with SCI (31). Studies also show that those complications appear at younger age for people with SCI than for able-bodied (31). Manns et al. (56) found a significant relationship between lower activity levels and higher fasting glucoses level in paraplegic men. Bauman et al have reported an association between insulin sensitivity and aerobic capacity in individuals with SCI (55).

Blood pressure is positively related to the risks of death from vascular disease not only among individuals who might be considered hypertensive, but also among those who would usually be considered normotensive (at least down to usual blood pressure levels of 115/75 mm Hg) (78). Arterial blood pressure is low in persons with SCI because of an impaired activity of the sympathetic nervous system below the level of injury (27). Resting blood pressure is lower in the cervical injuries than the thoracic injuries (77). There is a known inverse relationship between level of injury and resting blood pressure for people with a SCI (33). Those with a cervical and high thoracic injury level, have the highest prevalence of cardiovascular disease (32). When the spinal cord is injured, sympathetic activity is impaired below the level of injury, and results in sympathetic hypoactivity (7). This cause a low resting blood pressure, disturbed reflex control and the inability to regular blood pressure during exercise is impaired (7). Studies of exercise and hypertensive able bodied patients, indicates that the intensity of exercise is a dependent factor to reduce the blood pressure (79).

Resting heart rate is an independent predictor of cardiovascular risk (80). Epidemiologic studies of asymptomatic working men during a 23 year follow up; show that the heart-rate profile during exercise and recovery is a predictor of sudden death in this population (81).

1.4 Exercise to improve aerobic capacity and risk factors for CVD in SCI

The ability to achieve higher values of VO_{2peak} in the SCI population is mainly by the means of arm/upper body exercise (19). The most common modes of upper body exercise are arm-crank and wheelchair- exercise (ACE and WCE respectively) (51).Studies have found improvements in VO_{2peak} for individuals with SCI paraplegia in the range between 1.10 l/ min- 2.51 l/min after arm exercise (51). Although there are studies that suggest exercise can improve aerobic capacity in people with SCI, there is insufficient evidence to make conclusions about the recommended intensity (25). There is strong evidence that aerobic exercise 2-3 times/week >70% of maximal heart rate increases aerobic capacity for persons with chronic SCI (50). Improvements in aerobic capacity after arm exercise training in the range of 20-30% have been found in individuals with SCI. Most of these studies have evaluated the effectiveness of moderate (40–59% heart rate reserve (HRR) or 55–69% of maximum HR) to vigorous (60– 84% HRR or 70–89% of maximum HR) (34). De Groot et al (n=6)(15) performed an arm-crank exercise study in recently injured tetraplegic and paraplegic individuals. The intensity of exercise in this study varies from 40-80% max HRR, and they found a significant improvement in VO_{2peak}. De Groot et al reported that eight weeks of high intensity ACE exercise training significantly increased VO_{2peak} more compared to low intensity; the improvements in high interval group were 150% while the low intensity group improved 117% (15). There are, however no established guidelines that prescribe exercise for this population (50).

Studies involving use of functional electric stimulation (FES) to improve aerobic capacity for SCI individuals, found a significant increase in VO_{2peak} using high intensity training in a combination of ACE and FES. The effect of using FES can be related to level of injury, and not only FES training (53).

Physical activity is an important tool for prevention of cardiovascular disease. According to the findings of Keteyian et al, (75) $V0_{2peak}$ remains a strong predictor of all-cause death in able bodied population. 1 $mL \cdot kg^{-1} \cdot min^{-1}$ increase in $V0_{2peak}$ is associated with an approximate 15% decrease in risk of death (75). Several studies of high intensity versus moderate intensity for improving aerobic capacity have been conducted. A study of healthy nonsmoking male university student's, found that high intensity training (90-95%HR_{max}) increased VO_{2max} significantly more compared to moderate and low intensity. No significant improvement in VO_{2max}were found in the groups training at 70% and 85% of HR_{max} (59).

Rognmo et al. performed a study of persons with metabolic syndrome exercising in high and moderate intensity (20). The result concludes that intensity is an important factor to improve aerobic capacity. The intensity of the training is important in terms of reducing the risk for metabolic syndrome (20).

2 Introduction

Spinal cord injury (SCI) is a permanent serious condition, which leads to loss of motor and/or sensory function (1). SCI are divided into high (cervical) and low (thoracic, lumbal and sacral) injuries, and is referred to as `tetraplegia` and `paraplegia` (1).Today the survival rate the first two critical years after a SCI has increased significantly due to improved medical care (5). The most common causes of traumatic SCI are traffic accidents, falls, violence, and sport injuries (44). The prevalence of traumatic SCI in Europe is reported to be average 252 per million inhabitants (43).

Previous research has found that physical activity is a tool to prevent CVD (75). Maximal oxygen uptake is the main determinant of cardio respiratory endurance performance (35). An improvement of maximal oxygen uptake is easier to achieve from high intensity aerobic training compared to moderate intensity levels (20, 59, 75). In the SCI population there are few studies that have focused on the intensity of training for improving aerobic capacity (15, 23). However studies conducted with able-bodied have found significant improvements in the risk factors for CVD after high intensity exercise (20, 59). High intensity exercise has been found superior compared to moderate intensity exercise (20, 59). To our knowledge only two studies have assessed the effect from different intensity of exercise during arm-crank ergometry in individuals with SCI. (De Groot et al. 2003 (N = 6) and Hooker et al (N = 11)) Both studies report greater improvements in aerobic capacity from high intensity (70-80%HRR) compared to low intensity (40-50 %HRR) arm-crank exercise. These studies include both tetraplegic and paraplegic persons (15, 23). Furthermore, a limited number of studies (15, 23, and 82) have assessed the effect from arm-crank exercise on cardiovascular risk factors such as LDL, HDL, glucose, resting heart rate and blood pressure in people with a chronic SCI.

Individuals with a SCI have a generally low aerobic exercise capacity. This is likely related to a sedentary lifestyle, level and extent of injury, medical complications, social barriers and low participation in sports (76). The relationship between increased physical activity and health status of SCI has not been studied adequately (34).

The primary aim of this study was to compare the effect from high-intensity (i.e. 85-95% of peak heart rate) in 4 x 4 minute intervals with isocaloric moderate intensity arm-crank

exercise (i.e.70% of peak heart rate) on peak oxygen uptake for individuals with chronic spinal cord injury paraplegia.

Secondary aims were to compare the effect from high-intensity versus moderate intensity arm-crank exercise on cardiovascular risk factors like hypertension, resting heart rate, fasting glucose and lipid profile.

3 Hypothesis

Our primary hypothesis is that eight weeks of high-intensity arm- crank exercise three times per week will increase peak oxygen uptake more compared to isocaloric moderate intensity arm-crank exercise for people with chronic paraplegia.

Our secondary hypotheses is that eight weeks of high-intensity arm-crank exercise three times per week will reduce the cardiovascular risk factors lipid profile, fasting glucose, blood pressure and resting heart rate more compared to isocaloric moderate intensity arm-crank exercise for people with chronic paraplegia.

4 Methods

4.1 Participants

16 participants (13 male, 3 female) were included. The participants were adults with a traumatic SCI recruited from the Department of spinal cord injuries, Clinic for Physical Medicine & Rehabilitation at St Olav's Hospital, Norway. Oral and written informed consent was given and the regional medical ethics committee (REK) accepted all experimental procedures. The study was conducted in accordance with the Declaration of Helsinki.

4.2 Inclusion and exclusion criteria

Inclusion criteria were paraplegia (injury level Th2 or lower), women and men, traumatic injury or myelomeningocele and myelitis, injury> 1 year. The exclusion criteria were spinal cord injury level at Th2 or higher, non-traumatic injury except myelomeningocele and myelitis, cardiovascular disease, diabetes type I and injury <1 year

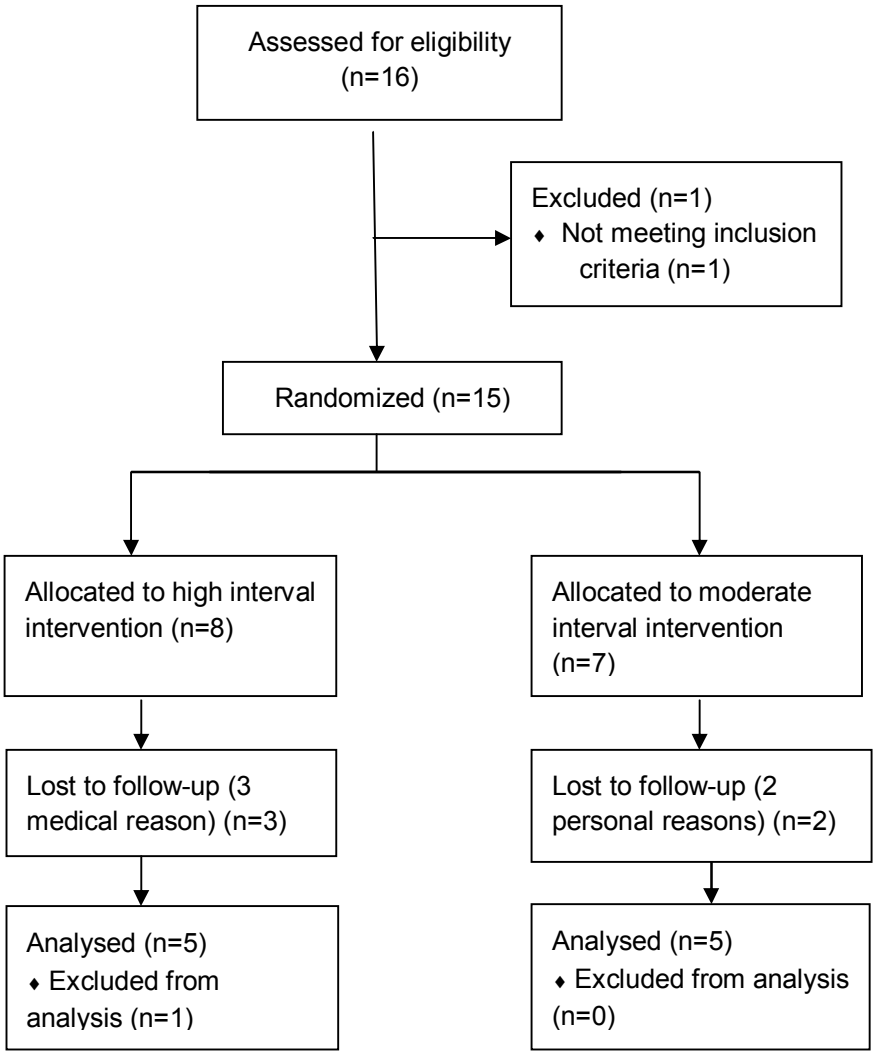


Figure 1, *flow chart*

The participants were randomized into two groups, Group A (high intensity training 85-95% of peak HR) and Group B (moderate intensity training at 70% of peak HR) (figure 1, flow chart). The participants followed a systematic training program using arm-crank ergometer for eight weeks with three workouts per week. The high intensity group performed 4 times 4 minutes intervals at 85-95% of highest measured heart rate with three minutes of active break between the intervals at 70% of highest measured heart rate. To equalize training volumes to similar amounts of kcal/session in the two groups, the moderate intensity group had to perform 49-min at 70% of HR_{max} each exercise session, representing the same total training load as the high intensity aerobic exercise group

4.3 Design

A randomized clinical trial with two intervention groups in a pretest-posttest design. Randomization was done by, the Unit for Applied Clinical Research, NTNU, to make sure that all randomization was blinded. Randomization was stratified by age, younger than 50 years and older than 50 years.

4.4 Measurements

4.4.1 Measurement of peak oxygen uptake

For the VO_{2peak} tests, measurements were performed using a portable MetamaxII Cortex ergo spirometry system (Cortex Biophysics GmbH, Leipzig, Germany). This system measure all oxygen and carbon dioxide exchange, ventilation, ambient temperature and pressure. The Metamax II was calibrated at the beginning of every test day, and no more than three tests were conducted before calibrating again. Calibration was performed using a 3-l standardized calibration syringe (Hans Rudolph Jager, GmbH, Germany). The gas concentration was calibrated with ambient air and chemically standardized two-point calibration gas. (15%O_2 and 5%CO_2). The highest average over 30 seconds was determined as VO_{2peak}.

The test was performed using an Ergomed 840L (Siemens, Germany). This is a modified arm-crank ergometer with an electric brake system that ensures the watts indicated on the screen are the actual watt the participant produces. Prior to each test day the arm-crank ergometer was calibrated by bringing the ergometer to 90 RPM before applying a braking force and ensuring that the time required to decline to a given RPM was correct (35RPM in 40 seconds with a 0 watt braking load, and 0 RPM in 18 seconds with a 25 Watt braking load, Siemens ErgoMed Operation Manual, 1985).

4.4.2 Test Protocol

Prior to the ACE peak test a standardized warm up period of 5 minutes at low intensity was conducted. During the peak test the participants were told to keep a speed of 70 revolutions per minute (RPM). Work rate increments during ACE increased by 10-20 watts each minute until the participants reached volitional fatigue. ACE peak workload was determined by the highest watt kept for the last minute of the test. Ratings of perceived exertion were assessed immediately after terminating the test using the BORG 6-20 scale (84). Peak heart rate (HR_{peak}) was determined to be the highest recorded HR in the last minute of the peak cardiopulmonary exercise test, and blood lactate was measured immediately after each test. Determination criteria for reaching VO_{2peak} was an increase in minute ventilation (VE) (L • min^{-1}), a respiratory exchange ratio (R)> 1.05 and lactate> 7 mmol and Borg scale between 17-19.

4.4.3 Exercise protocol

Exercises were performed in the facilities at the spinal cord unit. They exercised on an arm-crank ergometer for eight weeks with three workouts per week. Each workout started with 10 minutes of warm-ups on the arm-crank ergometer. Group A exercised in 4 x 4 minutes high-intensity intervals at 85-95% of peak heart rate with 3 minutes of active break between each interval (at approximately 70 % of peak heart rate) and group B exercised in 47 minutes at moderate intensity (70% of peak heart rate). To estimate the length of the session, it was isocaloric calculated.

Each participant kept their own training diary. The participants in the high intensity group recorded date of workout and mean heart rate for the last fifteen seconds of each interval. The moderate group documented date of workout and heart rate at twenty minutes, thirty minutes and forty-seven minutes.

Figure 2: *Arm crank exercise (Picture used with permission)*

4.4.4 Lactate measurement

Blood lactate concentration was measured by the hemolytic blood sample taken from the participants' fingertips with the portable Lactate Pro Analyzer LT-1710, (Arkray factory inc, KDK corp., Japan). This instrument has been approved by the FDA in USA and has shown a coefficient of variation of 3%. Blood lactate concentration was measured immediately after all VO_{2peak} tests.

4.4.5 Borg Scale

To assess subjective rating of perceived exertion (RPE) the BORG scale (6-20) was used (Appendix 1) (84).

4.4.6 Weight

Body mass in kilograms was obtained using a Seca 959 digital chair scale (Hamburg, Germany), calibrated for seated weighing, according to 90/384 CEE Directive, III Class calibration.

4.5 Heart rate

Heart rate was measured every minute during all tests with Polar ® Accurex watches (Polar Electro, Oy, Finland). The accuracy of heart rate readings obtained by the Polar ® Accurex was ± 1 heartbeat (Polar Electro, Oy Finland, 1997).

4.6 Blood sample analysis

All blood analyses were performed with standardized local procedures for St Olavs Hospital, University Hospital Trondheim.

Blood samples for lipid profile (HDL, LDL, total cholesterol and triglycerides)were taken fasting (minimum12 hours before the tests) and the participants had to refrain from alcohol the day before the tests were taken. They had to sit in their wheelchair and rest for fifteen minutes before the tests were taken (37). Glucose intolerance and diabetes was measured with blood fasting glucose (P-glucose). Limit of diabetes and impaired glucose tolerance was defined on the basis of reference values defined by the international diabetes federation (IDF) guidelines 2011 (38).

4.7 Blood pressure and resting heart rate

Blood pressure was measured on the left arm with a calibrated Casmed 740 apparatus, after 15 minutes of rest in a sitting position in a wheelchair. Hypertension was defined as blood pressure> 140mmHg systolic and / or 90 mmHg diastolic, according to guidelines (39) and / or ongoing treatment for hypertension. Resting heart rate was measured in a sitting position after 15 minutes rest.

4.8 Statistical analysis

Statistical analyses were performed using IBM SPSS statistics software version 21 for Windows. (SPSS Inc. Chicago, IL., USA)

A Shaphiro Wilks test was used to test for normal distribution of data. Assumptions of normal distribution were not met, and therefore non- parametric tests were used for analysis. The Wilcoxon signed rank test was used to calculate within group differences and the Kruskal-Wallis test was used to calculate differences between groups. $P \leq 0.05$ was considered statistically significant. Excel software (Microsoft Office for windows, version 2010) was used to create the tables and figures.

The use of non- parametric tests do usually present results in sum of ranks. In the present study the results are presented as mean and standard deviation to make them comparable to other studies.

5 Results

5.1 Participant characteristics

Individual characteristics are presented in Table I. In both groups there was only one person with level of injury at thoracic level four (Th4) which is above the critical level for autonomic dysreflexia (AD) (40). Height was significantly higher in the moderate intensity group ($p < 0.05$) ($P=0.046$) compared to the high intensity group. The participants self-evaluated their activity level before starting the intervention period, just to give an overview of their exercise experience. In both groups there was variation in activity level before the intervention, and three of the participants had performed high intensity training after contracting their injury, however not for a long while. In both groups some of the participants self-evaluated that they never had exercised systematically after contracting their injury. All participants were independent in activities of daily life (ADL). There were no significant differences between the groups in neither aerobic capacity nor cardiovascular risk factors at pretest.

Table I. Participant characteristics

Participants	**HI intensity N=5**	**MO intensity N=5**
Gender (m/f)	(4/1)	(5/0)
Age, years (mean±SD)	45(±6)	42(±14)
AIS(level of injuries)	Th4	Th4
	Th8	Th8
	Th8	Th8
	Th9	Th12
	Th11	L2
TSI, years (mean±SD)	15.2(±13.5)	15.0(±11.3)
Height, cm (mean±SD)	175.4(±8.5)	185.9(±6.5)

HI: High intensity MO: moderate intensity.. N: Participants SD: Standard deviation, AIS: American Spinal Injury Association Impairment Scale, TSI: Time since injury.

5.2 Aerobic Capacity

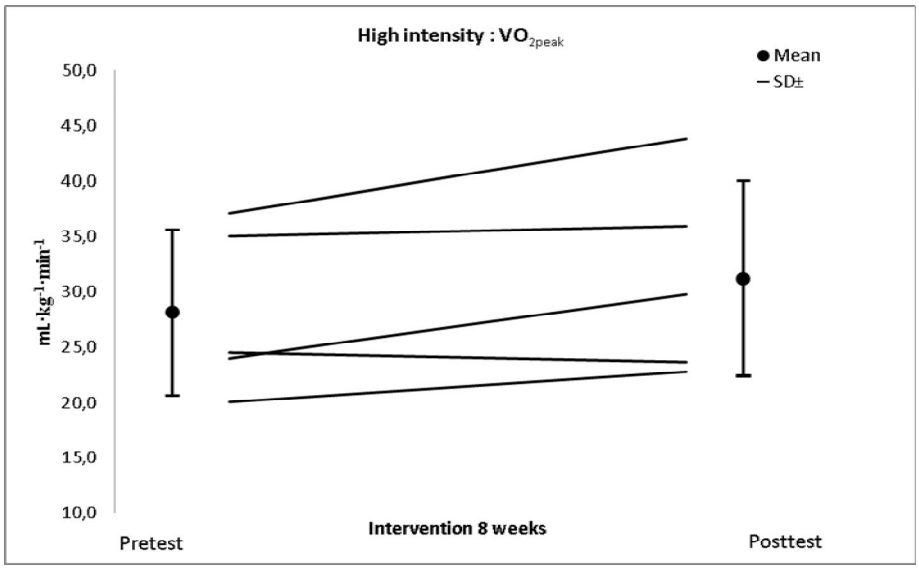
Table II. Aerobic capacity.

Variables	HI-pretest N=6	HI-posttest N=5	MO-pretest N=5	MO-posttest N=5	P-value Between groups	P-value HI-group Pre-post	P-value MO-group Pre-post
Weight, kg	77.00(±11,42)	75.13±(11,97)	92.13(±22,08)	89.84(±22,21)	0.917	0.068	0.500
HR_{max}(Beats/min)	169(±10)	172(±5)	169(±27)	170(±21)	0.346	0.273	0.498
La(mmol/l)	11.40(±1.63)	11.46(±3.64)	10.44(±2.02)	9.62(±1.40)	0.754	0.854	0.225
V02(l/min)	2.13(±0.55)	2.32(±0.70)	2.40(±0.66)	2.35(±0.61)	0.075	0.225	0.343
R	1.17(±0.07)	1.18(±0.03)	1.15(±0.07)	1.15(±0.20)	0.834	0.893	0.713
Borg	18(±1)	19(±1)	18(±1)	19(±1)			
V'E(l/min)	86.83(±24.48)	96.71(±28,57)	94.23(±42.31)	96.86(±39.48)	0.347	0.138	0.893

HI: High intensity. MO: Moderate intensity. N: Participants. SD: Standard deviation, HRmax: Heart rate max, La: Blood lactate concentration, VO2: Oxygen consumption, V'E: Total pulmonary ventilation, R: respiratory exchange ratio, BORG: Borgs scale.
Data is presented as mean and standard deviation for each variable.

The high intensity group increased their mean VO_{2peak} with 8. 9 %(l/min), while the moderate intensity group had a minor mean decrease of 2. 1 %(l/min). There were not significant differences between the groups. Maximal workload (Watt) in high intensity group were not significant different from moderate intensity group. (High intensity group mean (±SD) 111±20.7 pretest and 142±34.9 posttest, moderate intensity group 106±36.5 pretest and 120±43 posttest).

The results of the maximal aerobic capacity test are presented as $mL \cdot kg^{-1} \cdot min^{-1}$ in figure 3.



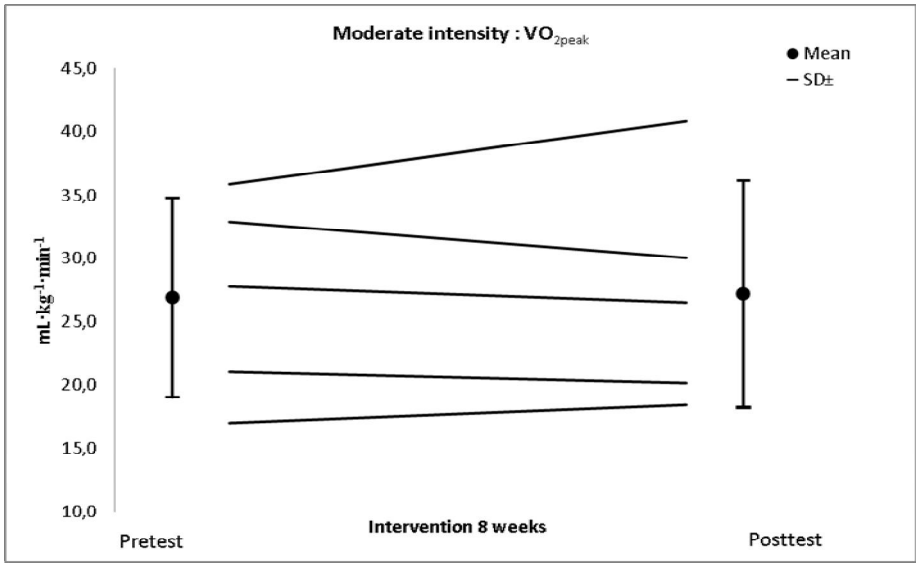


Figure 3: The results are presented in one figure for each of the intervention groups, to show the individual differences within the groups.

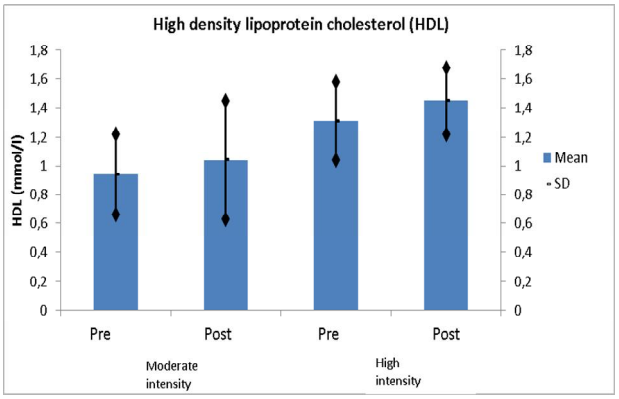
5.3 Cardiovascular risk factors

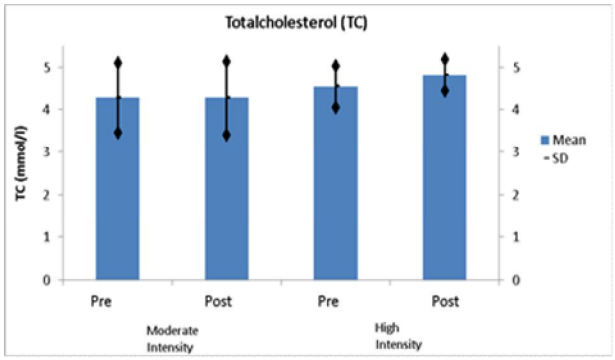
The results of the lipid profile are presented in table III, and the data on lipid profiles are presented in figure 4. High intensity training for eight weeks decreased the fasting glucose with 5.9%, while moderate intensity training decreased the fasting glucose 6. 7%, (table III). The results of systolic and diastolic blood pressure are presented in table III. There are no significant differences between pre and posttest.

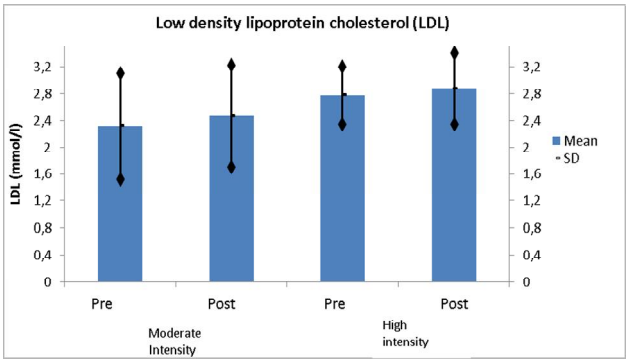
Table III. Pretest values (mean, SD) and posttest values (mean, SD) after the intervention

Variables	HI-pretest N=6	HI-posttest N=5	MO-pretest N=5	MO-posttest N=5	P-value Between groups	P-value HI-group Pre-post	P-value MO-group Pre-post
S-HDL(mmol/l)	1.31(±0.27)	1.45(±0.23)	0.94(±0.28)	1.04(±0.41)	1.000	0.138	0.138
S-LDL(mmol/l)	2.78(±0.43)	2.88(±0.53)	2.32(±0.79)	2.47(±0.76)	0.675	0.405	0.345
S-TC(mmol/l)	4.54(±0.49)	4.82(±0.38)	4.28(±0,83)	4.28(±0.96)	0.343	0.273	0.891
S-TG(mmol/l)	0.98(±0.34)	1.08(±0.25)	2.26(±1.45)	1.70(±1.04)	0.076	0.686	0.225
P-glucose(mmol/l)	5.1(±0.62)	4.8(±0.52)	6.0(±2.60)	5.6(±1.81)	0.596	0.066	0.336
SBP (mmHg)	127(±11)	127(±11)	129(±31)	133(±24)	0.675	0.786	0.500
DBP(mmHg)	83(±13)	84(±13)	81(±18)	84(±11)	0.753	0.786	0.892
HRrest(Beats/min)	67(±14)	68(±7)	82(±14)	87(±7)	0.530	0.786	0.465

HI: High intensity. MO: Moderate intensity. N: Participants. SD: Standard deviation, S-HDL: Serum high-density lipoprotein cholesterol, S-LDL: Serum low-density lipoprotein cholesterol, S-TC: Serum total cholesterol S-TG: Serum triglycerides, P-glucose: Blood fasting glucose, SBP: Systolic blood pressure, DSB: Diastolic blood pressure, HRrest: Heart rate resting,







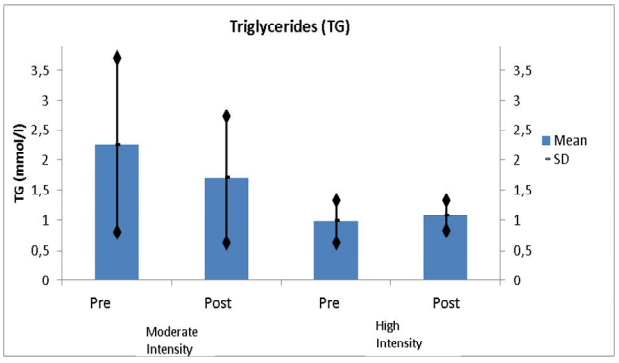


Figure 4: *lipidprofiles mean(±SD):*

6 Discussion

The main finding in the present study was that we did not observe any significant difference in VO_{2peak} between the high and moderate intensity training groups after eight weeks of arm-crank exercise three times per week. This is in contrast with our primary hypothesis. Although not significant, there was a favorable trend towards a higher improvement in VO_{2peak} for the high intensity group compared to the moderate intensity group (8. 9% (l/min) versus 2. 1% (l/min) respectively).

Our findings are in contrast with De Groot et al. (15), who found that 8 weeks of arm-crank exercise at high intensity (70-80%HRR) improved VO_{2peak} more compared to low intensity (40-50 %HRR). A likely explanation to the different findings might be related to the methodological diversities in terms of time since injury and lesion level. Our study included individuals with chronic SCI paraplegia, whereas De Groot et al. (15) included both paraplegic and tetraplegic individuals, injured for less than a year (acute stage). In the present study mean time since injury were about fifteen years in both groups and all were individuals with SCI paraplegia. Creating homogenous groups within the SCI population is a challenge; however the physiological differences between the acute and chronic stages of a SCI, especially in terms of peak oxygen uptake, should be considered when designing a training intervention. This may be supported in the study by Haisma et al. (61); they investigated differences in peak aerobic capacity in individuals with a SCI at start of active primary rehabilitation, at three months, at discharge and one year after discharge. They found a significant difference in wheelchair treadmill test VO_{2peak} between primary rehabilitation; three months and one year after discharge (61). In a follow up study they found no significant changes in VO_{2peak} between one year and five years after discharge (47). Haisma et al detected that VO_{2peak} improved with 24% for SCI people by wheelchair treadmill test during primary rehabilitation and up to one year after discharge (61). The findings from the study by De Groot et al. (15) are in accordance to these findings in early rehabilitation. Both of these studies took place during the first year after injury and included both paraplegic and tetraplegics.

The findings in the present study are also in contrast to studies conducted with able-bodied. In a study by Helgerud et al.(59) , they studied healthy moderately trained males, and found that high aerobic intensity training is significantly more effective compared to moderate and low intensity training in terms of improving peak aerobic capacity (59).Studies of people with metabolic syndrome (20) also support the findings of Helgerud et al. (59).

The small sample size and the variation within the group may explain our findings. In our study there were only five participants in each of our groups. According to the self-reported training diary it seems like the ones with the smallest improvements in VO_{2peak} between pre- and post-testing in the high intensity group also trained at the lowest intensity during their workouts. Hence, those with the smallest improvement exercised at an intensity of 85% HR_{max} while the ones with highest improvements exercised at intensity between 90-95% HR_{max} for longer periods of the intervals. In the high intensity group three of the participants increased their VO_{2peak} between 2.7-6.7 $mL \cdot kg^{-1} \cdot min^{-1}$ after eight weeks of high interval training 85-95%HR_{max}. These observations are in line with Moholdt et al. (85), who found that the individuals who exercised in the high end of the prescribed intensity zone (>92%) improved their VO_{2peak} significantly more compared to those exercising at the low end of the prescribed intensity zone (<88% and 88-92%) (85).

As a qualitative observation in the moderate intensity group, two of the participants reported shoulder pain during pre- and post- testing of VO_{2peak}. Hence, it is likely that they did not reach their true VO_{2peak}.This might result in lower effect of their work outs in the intervention period, because they didn't reach their HR_{peak} level during the pretest. But it's likely to believe that these participants also had the same challenges during posttest trying to reach fatigue.

In the moderate group one participant had a weight loss of 8.5 kg body mass. This participant increased VO_{2peak} by 4.9 $mL \cdot kg^{-1} \cdot min^{-1}$ between pre- and post-test. This may bias the results for VO_{2peak} in the moderate intensity group.

The secondary aims in the present study were to compare the effect from high-intensity versus moderate intensity arm-crank exercise on hypertension, resting heart rate, insulin resistance and lipid profile. There were no significant changes between the two groups in the analyzed cardiovascular risk factors between pre- and post-test.

The high-density lipoprotein cholesterol (HDL) values were not significantly changed after eight weeks of arm-crank exercise in high and moderate intensity. The HDL values did increase in both high and moderate intensity groups (10.7 % high intensity group and 10. 6% moderate intensity group).The mean HDL level was lower in the moderate intensity group after eight weeks of exercise, than the HDL mean level before starting exercise in the high intensity group, but there were no significant differences. Before starting exercise, both groups had rather low mean HDL values. (1.31 mmol/l in the high intensity group and

0.94mmol/l in the moderate intensity group) Low levels of HDL are associated with a major cardiovascular risk factor (66). Both Hooker and Wells (23) and de Groot et al. (15) investigated changes in lipid profiles in their arm crank exercise studies. Hooker and Wells found a significant increase in mean serum HDL from training at moderate intensity (70-80%HRR), whereas no significant increase in HDL from training at low intensity (40-50%HRR) was found (23,15). Hooker and Wells` study involved both paraplegic and tetraplegic, while our study excluded the tetraplegics. Persons with tetraplegia tend to have a higher prevalence of lipid disorders compared to individuals with paraplegia, (6) and therefore it might be differences between the effects of intensity and increase in serum HDL when comparing the results in those two studies. De Groot et al (15) found no significant differences in the values for serum HDL between the high and low intensity groups after their training intervention, however they did see a positive trend towards a higher increase in HDL in the high intensity group (15). In our study, serum HDL increased in both groups, but there were not significant increases. It may seem like the exercise itself can affect the serum HDL levels. In the study of De Groot et al. the participants were in the acute stage of SCI (15), and lipid profiles favorable change during first year of rehabilitation, with an increase of HDL (22). These changes are related to level and extent of SCI, and likely not as an effect from training. Low levels of HDL in individuals with a SCI are often related to physical inactivity (67). Mean time since injury for the participants in our study was about fifteen years in both groups, and the self-reported activity level of the participants varied. The small sample size in the present study and the relatively low activity level before starting the training intervention probably influenced the results for serum HDL in both groups. This is in line with results of Kraus et al. (69), who compared sedentary overweight people with mid- to moderate dyslipidemia in three different intensity levels (high-amount-high intensity, low-amount-high intensity and high-amount low intensity). The improvements in this study were related to the amount of activity, not to the intensity of exercise or improvement in fitness (69).

None of the results of the blood samples of lipid profiles changed significantly after the arm crank exercise intervention. A stronger predictor to cardiovascular risk than serum HDL alone, are serum HDL and serum total cholesterol (TC). The participants in the high intensity group increased the mean TC level after eight weeks of arm-crank exercise with 6. 2%, while in the moderate intensity group the mean TC levels did not change at all from pre- to post testing. There were no significant differences between the two intensity groups. In a study by

Hooker et al. (23), they found a decrease in TC from moderate intensity group, however no significant increase in TC was found in the low intensity group (23).

Low density lipoprotein cholesterol (LDL) increased in both groups, but there were no significant increases in neither the high or moderate intensity group (3, 6% increase in high and 6, 5% increase in moderate intensity group). Both groups had low mean levels of LDL before starting the intervention (2.78 mmol/l and 2.32 mmol/l). The results of LDL were in the normal ranges (1, 4-4,7mmol/l) (37).

There were no significant changes in triglycerides (TG) after eight weeks of arm-crank exercise in SCI individuals (P= 0.076). The mean triglycerides in the high interval group increased with 10. 2% while the mean triglycerides in the moderate interval group decreased 24. 8%. The findings indicate that there is a favorable tendency towards differences between the low and high intensity groups. Hooker and Wells found a significant decrease in triglycerides in the moderate intensity group (70-80%HRR) and no significant decrease in the low intensity group (50-60%HRR) (23). The large standard deviation in the moderate group and the individual variation influence the results and the significance level in our study.

In our study, the fasting blood glucose did not change significantly. There was a decrease in both groups of intensity with about 6% after the intervention period. In the moderate intensity group there were individual variances and the standard deviation was much higher than it was in the high intensity group (Table III) because of the individual differences and the small sample size. One of the participants in the moderate group was medicated for diabetes mellitus type II, and this participant had a decrease of 21, 8% in the fasting blood glucose values, this is a qualitative observation that influence the group result. In this study, we can see a positive trend between exercise and decreased fasting glucose. An inverse relationship was found between fasting glucose and physical activity when Manns et al. (56) investigated if they could determine a relationship between peak aerobic capacity and components of the metabolic syndrome in men with paraplegia (56). There was found a significant difference in fasting glucose between the intensity groups when Tjønna et al compared people with metabolic syndrome at different exercise intensity levels. High intensity training for sixteen weeks significantly reduced fasting glucose levels (20). These findings are in contrast to the findings in the present study.

Blood pressure and resting heart rate did not significantly change in any of the groups after eight weeks of arm crank exercise. There were minor but not significant increase in both

blood pressure and resting heart rate results after the intervention in both intensity groups. Two participants in the moderate group were on medication for hyperlipidemia, and as we can see by the results in table III, the standard deviation is much higher at pretest compared to posttest in both groups. It seems like the decrease in standard deviation indicates a positive effect between exercise and reduction of blood pressure and resting heart rate. The study of Tjønna et al found that moderate and high intensity training both reduced blood pressure (20).

7 Study limitations

At the Spinal Cord unit at St Olavs hospital, there are about thirty new patients registered with a SCI each year (according to registration of new patients at the Spinal Cord unit, St Olavs hospital). Those patients represent the middle and northern parts of Norway. The SCI population in Norway is small, and the recruitment of participants for this study was rather limited because the participants had to come to the Spinal cord unit at St Olavs hospital for testing and exercising. The sample size of both intervention groups were low, and the power of the tests thus rather low. People with a SCI encounter many challenges and is exposed to many potential complications related to for example urine infections, spasticity, pain and many more. In our study we unfortunately had a high level of dropouts (37. 5%). The large size of drop out might be a picture of the complexness of SCI. Three of the subjects got fractures that forced them to drop out. Also some of the subjects that conducted the study had their challenges with urinary infections. This is complications that most of people with a SCI have to deal with, and it complicates their opportunity to perform daily exercise. If the participants got the chance to try a maximal aerobic capacity test in time before the pretest, the result might have been different. Most of the participants had never tried a maximal aerobic capacity test before, and if they had the chance to get used to the mask and how much they could pressure themselves, they might have reached a higher result in the pretest, and then got a higher maximal heart rate, which was the basis for calculating the intensity level in the intervention period**.**

8 Conclusion

The present study is too small to draw conclusions, because of the number of participants. Our findings indicates that eight weeks of high intensity arm crank exercise can improve the aerobic capacity for paraplegics more than moderate intensity arm crank exercise. Even thou we did not find significant changes in VO_{2peak} l/min (P=0.075), we can see a favorable trend towards better improvements. The lipid profile seem to be improved by exercise in individuals with a SCI, however it is difficult to conclude whether the intensity is the dependent factor. People with SCI are often inactive so the effect might be a result of a higher activity level. The glucose levels were improved in both groups after arm crank exercise, while the blood pressure and resting heart rate did not change in any of the groups.

9 Perspectives

It is important to focus on cardiovascular health and a healthy lifestyle in the SCI population. Both in acute and chronic phase there are cardiovascular challenges. Our study had a small sample size, and maybe in a larger sample size, the results would have been stronger, and not so affected by individual differences. A multicenter study would have included more participants, and further research to confirm effects would be of interest. It is important to use the results of research to inform about the beneficial effects of arm crank exercise to SCI people. Guidelines for spinal cord injured and exercise should be established. The spinal cord units or other rehabilitation units or fitness centers, should offer chronic SCI individuals the opportunity to use locations and equipment to perform exercise. The lack of access to exercise equipment should not be a limiting factor for increased activity for people with SCI.

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Appendix 1 Borgs

Exercise in Medicine

Circulation and Medical Imaging

NTNU

HVOR TUNG ER BELASTNINGEN?

6	
7	Meget, meget lett
8	
9	Meget lett
10	
11	Ganske lett
12	
13	Litt anstrengende
14	
15	Anstrengende
16	
17	Meget anstrengende
18	
19	Svært anstrengende
20	

Norsk versjon av Borgs skala:

Borg GA. **Perceived Exertion.** *Exerc Sport Sci Rev.* 1974;2:131-53.