Thesis for doctoral degree (Ph.D.) 2010

Cardiovascular Disease Prevention after Spinal Cord Injury - a new Challenge

Kerstin Wahman

Karolinska Institutet

200 1810 – 2010 Years

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From Department of Neurobiology, Care Sciences and Society

Karolinska Institutet, Stockholm, Sweden

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``And let it be noted that there is no
more delicate matter to take in hand,
nor more dangerous to conduct,
nor more doubtful in its success,
than to set up as the leader in the
introduction of changes.

For he who innovates will have for his enemies
all those who are well off under the existing order of things,
and only lukewarm supporters in those who
might be better off under the new."

Niccolò Machiavelli 1469 - 1527
The Prince
N. H. Thomson, translator

ABSTRACT

Spinal cord injury (SCI) typically leads to permanent infralesional motor and sensory functional losses, pathophysiological aberrations in most organ systems and a lasting vulnerability for a variety of complicating conditions. Improvements in acute and rehabilitative management during the last decades have increased long term survival after SCI. Additionally, older persons now sustain and survive SCI. Thus, aging-related issues after SCI have arisen for the first time in history.

One such issue is cardiovascular disease (CVD), which now has emerged as a leading cause of morbidity and mortality in subjects with chronic SCI. However, it is not clear whether this reflects persons with SCI constituting a true high-risk population for CVD, or whether the epidemiological shifts merely reflect a "normalization" of the morbidity and mortality pattern due to the current increasingly effective management of previous "SCI-specific" causes of disease and death in this patient population. The overall aim of the thesis was to assess and explore the need for CVD prevention after SCI, and also to compare CVD risk in this population with that of the general population.

One hundred thirty-five participants (88 % of the total regional cohort), with traumatic wheelchair dependent paraplegia were assessed regarding CVD risk and was also compared with that of the general population (papers II-IV). Additionally, persons with paraplegia (n=8/16) and tetraplegia (n=8/16) were interviewed for the purpose of identifying facilitating factors for physical activity after SCI.

Wheelchair-dependent persons with traumatic paraplegia had an 8,5-fold increased prevalence of myocardial infarction as well as increased prevalence of dyslipidemia (83.1 %), hypertension (39.3%) and diabetes mellitus/impaired fasting glucose (10%). Further, 66-75% of subjects were overweight according adjusted BMI scores. An extensive clustering of cardiovascular risk factors according to authority guidelines was found. From a future intervention perspective, among others the following promoting factors to increase physical activity were identified; to gain and maintain independence, accepting assistance, finding environmental solutions, learning to live with narrower margins. Further, to have a role model and to be a role model was also important.

Conclusions:

- There is a *high and increased CVD risk* in persons with chronic wheelchair dependent paraplegia.
- Thus, regular *CVD screening* is indicated.
- *CVD prevention* including therapeutic lifestyle intervention needs to be developed, evaluated and then systematically implemented.
- *Lifestyle interventions need to be tailored* to the specific needs of this patient group.

Key words: Spinal cord injury, traumatic paraplegia, cardiovascular decease, lifestyle, cardiovascular decease prevention.

LIST OF PUBLICATIONS

I. Kerstin Wahman, Gabriele Biguet, Richard Levi. What promotes physical activity after spinal cord injury? An interview study from a patient perspective. Disabil Rehabil, April 2006; 28(8): 481 – 488

II. Kerstin Wahman, Mark S. Nash, Ninni Westgren, John E. Lewis, Åke Seiger, Richard Levi. Cardiovascular disease risk factors in persons with paraplegia: The Stockholm Spinal Cord Injury Study. J Rehabil Med 2010; 42: 272–278.

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IV. Kerstin Wahman, Mark S. Nash, John E. Lewis, Åke Seiger, Richard Levi. Need for Cardiovascular Disease Intervention after Paraplegia as Assessed by Multifactorial Risk Models: The Stockholm Spinal Cord Injury Study. Submitted to J Rehabil Med January 2010.

CONTENTS

LIST OF ABBREVIATIONS

CHD	Coronary Heart Disease
CVD	Cardiovascular Disease
DL	Dyslipidemia
DM	Diabetes Mellitus
HDL	High Density Lipoprotein
HRV	Heart Rate Variability
HTN	Hypertension
IFG	Impaired Fasting Glucose
LDL	Low Density Lipoprotein
MI	Myocardial Infarction
NRG	Nordic Risk Group
NSCIC	Nordic Spinal Cord Injury Council
SCI	Spinal Cord Injury
SCORE	Systematic Coronary Risk Evaluation
TC	Total Cholesterol
TC/HDL ratio	Total Cholesterol/High Density Lipoprotein Ratio
TLC	Therapeutic Lifestyle Changes
UTI	Urinary Tract Infection
VA	Veterans Administration
WHO	World Health Organization

1 FOREWORD

I first came across the field of spinal cord injury (SCI) and physical activity in the year of 1981. Many questions arose, questions about how it is to live with SCI, questions about physical activity barriers and possibilities, and many more.

During the years that followed and through contact with the patient organization "Rekryteringsgruppen för aktiv rehabilitering" it became easy to understand and support the idea of using physical activity and sports as means to reach an independent life. Even though Sweden as a society already at this time had abandoned the tradition of gathering persons with disabilities in institutions, and focused on integration instead, it still wasn't unusual for young persons with SCI to end up in geriatric long-term care institutions. Technical aids were not very developed, for example manual wheelchairs were big, heavy and difficult to maneuver. Personal assistance was yet not invented as a social support. The paradigm shift from a society with an invisible disabled population stowed away in institutions, to integrated subpopulations with special needs but with similar rights, was just starting.

Empowerment became the catchword, and role models were used to encourage newly injured persons. Physical activity was in this way a tool to get back into society again. No one at that time discussed aging and the specific challenges that come with a chronic physical disorder decades after injury.

Now, 2010, integration has finally become a reality (at least theoretically), and technical aids have developed tremendously. Improved acute care at special SCI units and evidence based guidelines has contributed to a decreased mortality early after injury. "Traditional" medical complications after SCI have decreased significantly. Moreover, persons with SCI now have a life expectancy approaching that of the general population. "Cure", however, is still not in sight, and aging related issues have become a palpable reality. This situation indicates yet another paradigm shift which now needs to address aging issues. One of several aging related topics that demands to be scientifically explored is the cardiovascular disease prevention.

My interest in lifestyle issues as they relate to sustainable long-term health after SCI has grown over the years and has been my focus during this project. About thirty years after my first contact with the field I'm grateful to have had the opportunity to put some of my everyday clinical concerns into a scientific framework. This work is now concluded and comprises my thesis. Hopefully, these insights will now feed back into our practical work for the benefit of our patients.

2 BACKGROUND

2.1 INTRODUCTION

Spinal cord injury (SCI) encompasses several chronic conditions and secondary complications, e.g. paralysis, immobilization, pressure ulcers and urinary tract infections (UTIs). Afflictions like respiratory disorders, septicemia, and UTIs have historically been major causes of premature death after SCI (1-3). Since the development of modern, comprehensive, evidence-based rehabilitation and medical care, persons with SCI generally live longer and thus age with their disability. Survival after SCI is dependent on access to adequate care and rehabilitation and differs substantially between countries (4). The increased long-term survival in the SCI population as a whole requires us to consider both new challenges during the post acute rehabilitation phase and during life-long follow-up. Age-related issues in persons with SCI are still not sufficiently elucidated. Cardiovascular disease (CVD) is one of those issues.

A longer lifespan after SCI has changed the morbidity and mortality panorama towards that of the general population, with an increased prevalence of CVD and cancer. However, respiratory disorders still remain major causes of morbidity and mortality after SCI, especially after tetraplegia (3, 5). All-cause CVD currently represents a frequent cause of death amongst persons surviving over 30 years after SCI, as well as in persons with SCI over 60 years of age (1). It is also noteworthy that CVD morbidity and mortality seem to debut in younger ages and with more accelerated progression than in able-bodied individuals.

However, it has not yet been conclusively established that CVD risk is *increased* (rather than just high, as in the general population) in the SCI population. Some reports (3) support such a notion, whereas others (6-8) do not.

To date, the CVD risks after SCI have primarily been studied in American and, more precisely, within U.S. Veteran populations (9, 10), but also recently in Norwegian and Australian SCI cohorts (11, 12). Such findings may, of cause, not necessarily be representative worldwide for all sub-populations of persons with SCI. CVD risks are known to differ between countries (13). They may also differ over time in the same population (14). Our previous broad survey of a regional SCI population 15 years ago did find several

problematic health issues that distinguished this population from the general population (8). At that time, however, CVD risk was not among those distinguishing issues. Nevertheless, the ageing trend that has emerged in the ensuing years, the concurrent trend of traumatic SCI occurring in older age groups, as well as the conflicting and, as of yet, inconclusive results of studies on this topic, encouraged us to revisit the CVD issue in the present thesis.

2.2 SPINAL CORD INJURY

A SCI typically affects neurotransmission between the brain and spinal cord segments below the level of injury, resulting in paralysis and sensory loss. Among major medical consequences and secondary complications we find: respiratory complications with pneumonia as a common sequel, pressure ulcers, bladder and bowel dysfunction with incontinence and frequent UTIs, and septicaemia (12, 15). Further, cardiac arrhythmias, sexual dysfunction, spasticity and neuropathic (16, 17) as well as musculoskeletal pain (18) are also all-too-common. Depression, psychological distress and drug used for this conditions (19) and low quality of life (20) are also prevalent.

A recent epidemiologic study from our center reported that falls now constitute the most common cause of injury (47%) followed by transportation related accidents (23%) and sports-related injuries (17%) (21). Swedish data have indicated an incidence as low as 10 new cases per million inhabitants/year, data from 1997 - 2002 (22), and a prevalence of about 5 000 persons living with SCI in a population of about 9 million citizens (23).

A standardised classification system for SCI have been developed and revised by the American Spinal Cord Injury Association (ASIA) (24). It is based on clinical examinations of motor and sensory functions. The following key terminology and definitions have been suggested by ASIA;

Tetraplegia; Loss of motor and/or sensory function due to damage of neural elements in cervical spinal cord segments. Tetraplegia results in functional impairment in the arms as well as in the trunk, legs and pelvic organs.

Paraplegia; Loss of motor and/or sensory function in the thoracic, lumbar or sacral (but not cervical) segments of the spinal cord, secondary to damage of neural elements within the sub-cervical spinal canal. With paraplegia, arm function is spared, but, depending on the level of injury, the trunk, legs and/or pelvic organs will be affected.

Neurological level; The most caudal segment of the spinal cord with both normal sensory and motor function bilaterally.

Sensory level; The most caudal segment of the spinal cord with normal sensory function bilaterally.

Motor level; The most caudal segment of the spinal cord with normal motor function bilaterally.

Incomplete injury; Lesion with partial preservation of sensory and/or motor function present below the neurological level *and* including the lowest sacral segments.

Complete Injury; Absence of sensory and motor function in the lowest sacral segments.

AIS- (ASIA – Impairment Scale) comprises five categories, and is aimed to classify degree of sublesional impairment after SCI.

AIS - A – Complete	No sensory or motor function is preserved in the sacral segments.
AIS- B – Incomplete	Sensory, but not motor, function is at least partially preserved below the neurological level including the sacral segments.
AIS - C - Incomplete	Motor function is partially preserved below the neurological level, and more than half of key muscles below the neurological level have a power grade less than 3.
AIS - D – Incomplete	Motor function is partially preserved below the neurological level, and at least half of key muscles below the neurological level have a power grade greater than or equal to 3.
AIS - E – Normal	Sensory and motor functions have returned to normal.

Table I. AIS- (ASIA-Impairment Scale)

2.3 CARDIOVASCULAR DISEASE (CVD) AND ITS RISK FACTORS

CVD and its risk factors constitute the main focus of this thesis. Categorization and definition of CVD is an extensive and complex topic. CVD includes disorders affecting the heart and/or the peripheral blood vessels (25). The causes of CVD are protean, but atherosclerosis, an inflammatory process in the vessel walls, is the most common cause. Manifestations of the atherosclerotic process is clinically classified in several discrete topographical diagnoses, e.g. coronary heart disease (CHD), cerebral stroke, renal artery stenosis, atherosclerotic disease of the aorta or vessels supplying the lower extremities, intestinal ischemia et cetera. Even atherosclerotic CVD per se has multi-factorial causes. Factors promoting the atherosclerotic process can be sub classified into *non-modifiable* factors, such as age, gender, and family history of premature CVD and *modifiable* factors, such as physical activity, smoking, eating habits, overweight/obesity, stress and depression (25). Further, conditions such as diabetes mellitus (DM), dyslipidemia (DL), and hypertension (HTN), comprise diagnoses in their own right as well as constitute biomarkers indicating an accelerated atherosclerotic process (Figure 1.) (26).

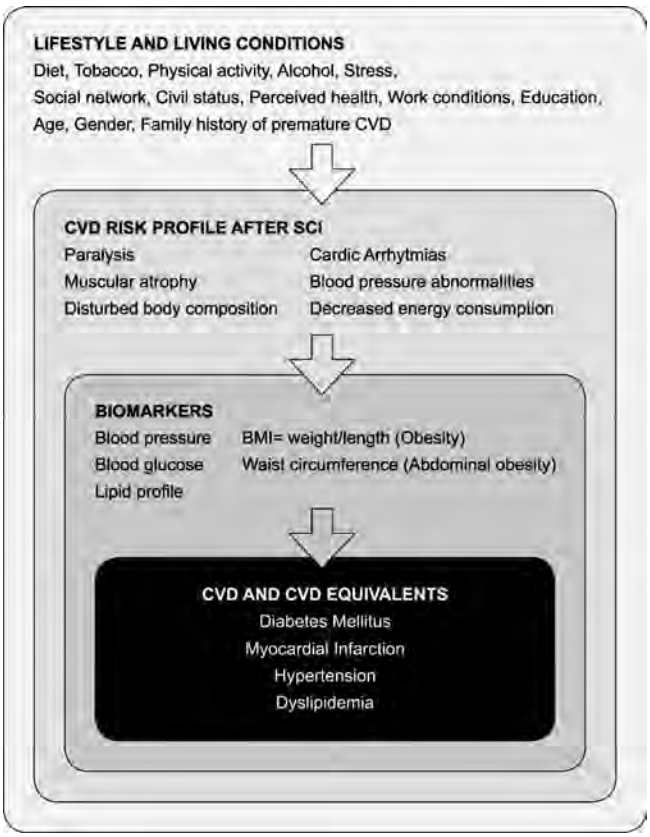

Figure 1. Lifestyle, Living conditions (outer circle), SCI- specific CVD risk profile and biomarkers of relevance for CVD risk.

The studies included in the thesis do not cover the full spectrum of CVD. Neither do they cover the full spectrum of CVD risk factors. Rather, a number of key CVD diagnoses and CVD risk factors have been selected as indicators of the need for CVD related prevention. The CVD related diagnoses thus included are: myocardial infarction (MI), HTN, DL and DM. Additionally, the modifiable CVD risk factors smoking and overweight, the non-modifiable risk factors: age, gender and family history (of premature CVD) were included.

CVD is the most common overall cause of death in western countries and so also in Sweden. In the year 2005, 42% of all deaths were attributed to CVD in Sweden (27).

2.4 CVD RISK PROFILE AFTER SCI

In order to elucidate the specific CVD risk profile of persons with SCI, a simplified theoretical model has been constructed (Figure. 2). It includes direct consequences of the injury, such as paralysis of skeletal musculature, muscular atrophy, reduction in total body and intracellular water, decreased energy consumption and abnormal body composition. It also includes the indirect consequences of immobilization and a low physical activity level and/or a positive energy balance leading to overweight/obesity (28-33). Finally, the model includes several "traditional" or generic risk factors, modifiable as well as non-modifiable.

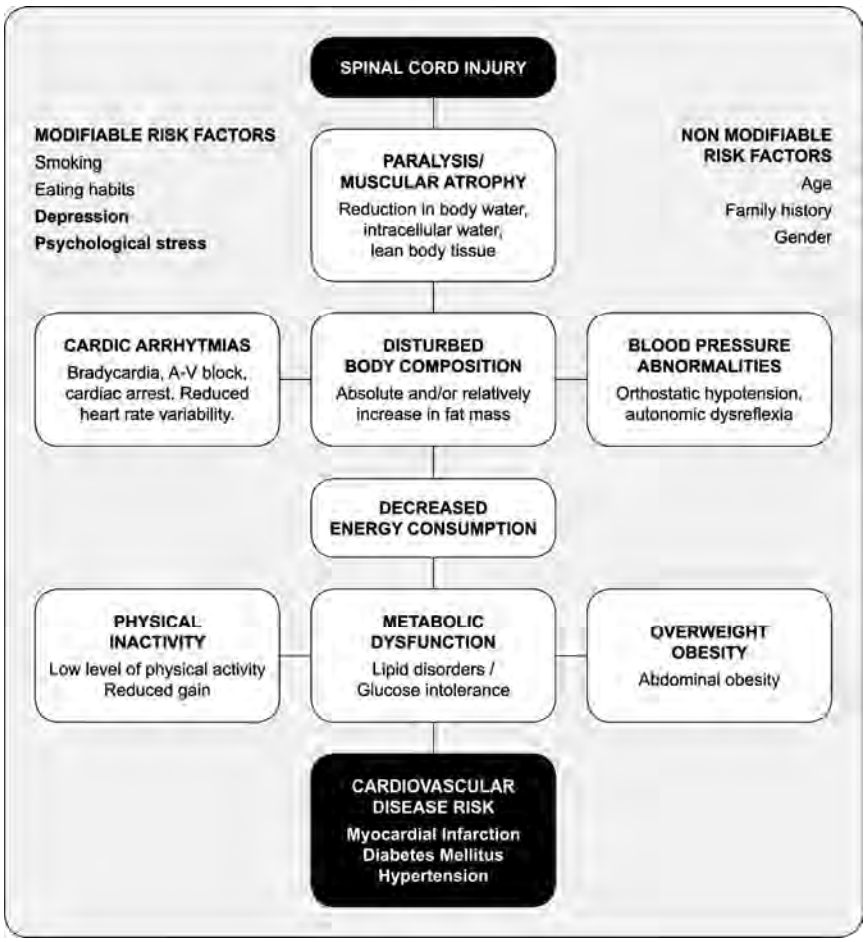

Figure 2. Simplified theoretical model of cardiovascular disease risk profile after spinal cord injury

Several major CVD risk factors in the general population are commonly reported to occur with an even higher prevalence in persons with SCI, and have by some authors been causally linked to an accelerated course of CVD in this population (28, 30). Nevertheless, as mentioned earlier, there are contradicting views on the issue whether there is in fact an *increased* risk for CVD after SCI or not.

2.4.1 Paralysis/muscular atrophy

Studies have shown a variable degree of loss of lean body mass and/or increase in fat mass after SCI (31). It has furthermore been shown that the level of lesion correlates with changes in total body water, intracellular water, lean body mass and fat mass. Additionally, as a result of the muscular atrophy, the energy expenditure will be decreased proportionally to the level of injury (32) (Figure 3).

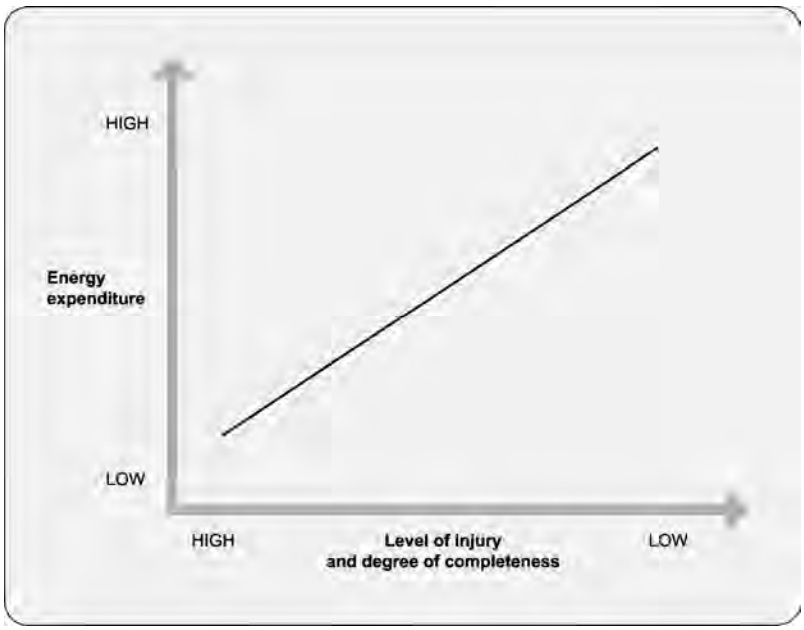

Figure 3. Schematic model of the relationship between level and completeness of spinal cord injury and energy expenditure.

2.4.2 Body composition

Profound body composition changes due to paralysis and immobilization are found in many persons with SCI. Decreased lean body mass and decreased infralesional bone mineral density, as well as increased fat mass, are all more or less pronounced in the SCI population (34). An abnormal body composition with increased fat mass (35, 36), and increased visceral obesity (37) is thus often found in persons with SCI.

2.4.3 Overweight/obesity

Body mass index (BMI) is often used in the clinical setting to estimate body fat and to diagnose overweight and obesity. Increased BMI in the normal population is considered a risk factor for CVD (38). However, a "normal" BMI value (i.e. 18, 5 – 24, 9) due to World Health Organization (WHO) standards typically underestimates body fat in persons with SCI (35). Thus, BMI cut scores used for the general population are questionable for the SCI population. This is because the losses of lean body mass after SCI may mask an absolute or relative increase in fat mass in the BMI equation.

2.4.4 Metabolic dysfunction

Lipid disorders. Abnormal lipid profiles have been reported to be frequent in persons with chronic SCI (39, 40). The most consistent finding is a depressed plasma concentration of high-density lipoprotein cholesterol (HDL) (28, 37, 41), whose physiological functions include protection against development of vascular disease (42). In a recent report, more than fourty percent of young persons with SCI were found to have deficient HDL levels (9).

Diabetes mellitus (DM) and impaired fasting glucose (IFG). The prevalence of DM has been reported to be three times higher in SCI veterans than in the general US population (43, 44). However, in a recent meta analysis, Wilt and colleagues stated that "current evidence is insufficient" to determine if these differences are due to lifestyle and other co-morbidity factors, or specific SCI-dependent ones (45). This conclusion was drawn based on the fact that studies included data mostly from the Veterans Administration (VA) and when comparing DM in VA SCI individuals with VA subjects without SCI no significant difference were found.

It is noteworthy that persons with SCI and DM also reported a higher frequency of CHD, MI and stroke. Also HTN and high cholesterol levels were more common compared with

SCI subjects without DM (46). Another complication in the diabetic SCI group was slow-healing foot sores.

2.4.5 Physical inactivity

A physically active lifestyle is recommended as an important health-promoting factor for sustained health in the general population (47). Among the several salutogenic effects of physical activity, reduced risk of CVD is one. Underlying beneficial factors include normalization of blood lipids, blood glucose and blood pressure as well as a normalization of body weight, with a more healthy body composition in terms of fat/muscle ratios (48, 49). Further, physical activity is known to improve mood, with decreased prevalence of depression (50). Physical inactivity, on the other hand, represents a major risk factor for metabolic disorder that increases the CVD risk (51).

Physical activation after SCI has, in concord with such findings, also been reported to affect CVD risk in a positive way by decreasing; HTN, DM, abnormal BMI and waist circumference and by contributing to healthier body composition (52). However, persons with SCI meet many barriers for physical activity; not only paralysis per se, but also other factors associated with chronic physical impairment, such as; environmental barriers (53-55), lack of social support (54), negative attitudes from others; and low self-confidence (56). Thus, it is not surprising that physical inactivity is commonly reported in the SCI population (28, 57, 58). As an inevitable consequence of combined muscular atrophy and physical inactivity, poor physical fitness often will ensue (59).

2.4.6 Hypertension

The prevalence of HTN has been shown to be increased in the SCI population (5, 60). HTN can, among other and more common causes, also be caused by renal disease (previously a major issue in the SCI population), but the high prevalence of HTN in persons with SCI as a consequence of renal pathology has been challenged (60). SCI above the level of Th 6 is associated with dysfunction in the autonomic nervous system which causes an abnormal blood pressure regulation. This has been stated to increase the all-cause CVD risk especially in persons with high lesion levels (61). Due to the disturbed homeostasis, however, persons with tetraplegic SCI commonly do not experience hypertension, but *hypo*tension.

2.4.7 Smoking

Cigarette smoking in persons with SCI has, as in the general population, been shown to increase the risk of premature death (5). CVD morbidity after SCI has been reported to increase with 3,1 % per year of cigarette smoking (62). Alcohol consumption increases the negative effect of smoking (62).

2.4.8 Arrhythmias

Various cardiac arrhythmias have been reported after SCI, especially in persons with high lesion levels (63). Examples of such arrhythmias are bradycardia, A-V block and cardiac arrest, all of which most often are seen in the acute phase. Additionally, abnormal heart rate variability (HRV) has been reported also in the chronic phase (30). In non-SCI populations, abnormal HRV has been confirmed to be a significant predictor for severe arrhythmias and sudden death. Further, abnormal HRV has been shown to be more prevalent in the SCI population as compared to the normal population (33).

2.4.9 Depression

Depression, which is an established risk factor for CVD, has been shown to be prevalent after SCI, although not necessarily as a consequence of the injury as such (64). Depending on definition, the prevalence has been reported to be between 10% and 60%, with major depressive symptoms in about 20% of the SCI population. Compared to the general population, depression in persons with SCI is about four times more prevalent. The high prevalence of suicide after SCI as compared with the general population may reflect the high prevalence of depression (12).

2.5 CVD – GUIDELINES AND SCREENING

2.5.1 National and international guidelines

So-called authority guidelines for CVD prevention are available both on a national and an international level (65-67). A common way to characterize CVD prevention is to distinguish primary from secondary prevention (68). Primary prevention comprises those measures aiming to minimize the risk for developing and/or delay occurrence of the disease. Secondary preventions, on the other hand, comprise those measures indicated once disease is already present, and the goals at that stage aim to decrease symptoms and/or minimize risk of relapse.

2.5.2 Screening

In order to detect risk for CVD or manifest CVD, various screening tools are used. Risk factors are used in isolation or in risk equations, the latter of which now often are recommended for clinical use (66, 67). Screening can be done using several strategies; population based, opportunistic screening, or directed screening for persons belonging to specific risk categories. Population based, as well as age indicated, CVD screening is typically not recommended. Opportunistic screening, i.e. screening of persons that are in contact with caregivers for any reason, may be justifiable if the person is informed about the consequences of screening and that consent in this context is given. The presence of single risk factors as abdominal obesity, DM, smoking and family history of premature CVD can also be used as indicators for further screening and health dialogue (65).

Under all circumstances, CVD screening is a delicate matter. The atherosclerotic process is, by itself, silent, and progresses over many years before becoming clinically manifest. Even though there are provided “cut points” aimed to indicate the need to commence treatment of a given risk factor, the risk in reality constitutes a continuum and concurrent risks may potentiate each other. Yet another issue is that most (in absolute numbers) CVD related deaths do in fact appear in persons with *low* risk as compared to those with high risk, the so called “Rose Paradox” (66).

Nevertheless, when screening is deemed indicated according to guidelines, a multifactorial model is recommended, and in Sweden the Systematic Coronary Risk Evaluation (SCORE) system is advised (66). Data for the SCORE equation was extracted from 12 European studies, and includes five core variables; age, gender, systolic blood pressure, smoking and TC and/or TC/HDL ratio. SCORE screens for the risk for CVD

related death within 10 years and a ≥5 % risk is classified as “increased”, indicating therapeutic lifestyle changes (TLC) and/or medication, while a <5% risk is classified as “low” risk.

The limitation of currently available CVD screening equations is that they exclude: i) physical activity level; ii) measures indicating overweight/obesity and/or abdominal obesity; iii) measures of depression or of psycho-social stress; and/or iv) family history of premature CVD events. Such variables have all been shown to be risk factors (or protecting factors) for CVD. Thus, in order to estimate a total CVD risk, also these issues should ideally be taken into account.

2.5.3 Primary and secondary prevention of CVD

Primary as well as secondary prevention strategies on CVD and CVD risk factors in able-bodied persons are based on TLC regardless of whether additional measures (e.g. medication) are deemed to be indicated or not (65-67, 69), (Table II, III and IV).

PRIMARY LIFESTYLE BASED CVD PREVENTION

Physical activity;	Minimum of 30 – 60 minutes "moderate" intensity/day
Healthy food choices	
Eat more of;	Vegetables, pulses and root vegetables
	Fruit and berries
	Bread, pasta, rice and fiber-rich grain
	Fish and lean meat
Eat/drink less of;	Fatty cheese, cream and fatty desserts
	Regular margarines and butter (rich in saturated fat) should be replaced by rapeseed or olive oil (rich in monosaturated fatty acids), and low cholesterol margarines.
	Fatty and processed meat
	"Snacks" i.e. crisps
	Sweet drinks (i.e. sugar-rich)
	Sweet products as confectionary (i.e. sugar-rich)
	Salt
Smoking	Give up smoking or maintain a tobacco free lifestyle
Weight	Energy-balance if currently normal body weight.
	Reduced calorie intake and increased physical activity if overweight
Alcohol	No more than a moderate alcohol intake is recommended,
	Definitions; *Men*: maximum two "standard glasses" /day
	Women: maximum just over one "standard glass"/day
	(Beer, wine or spirits)
	A standard glass = 12 g alcohol, equivalent to 15 cl wine, 33 cl beer (5%), 8 cl strong wine or barely 4 cl spirits.

SECONDARY LIFESTYLE BASED CVD PREVENTION

Individual counseling regarding therapeutic lifestyle changes

Lifestyle habits	
Physical activity;	Increased level of physical activity
Healthy food choices;	Increased intake of fruit and vegetables
	Bread and pasta with fiber
	Unsaturated fatty acids, (i.e. olive oil)
Weight	Weight reduction (if needed)
Smoking	No smoking

BIOMARKERS AND TREATMENT TARGETS

Blood pressure < 140/90 mmHg

Lipid profile; TC <5,0 mmol/L, LDL-C < 3,0 mmol/L

Diabetes Mellitus; adequate glucose control

Overweight/Obesity

BMI	BMI ≥ 30 Obese		Weight reduction indicated
	BMI 25 – 29.9 Overweight		Weight reduction indicated
	BMI < 25 Normal weight		Maintain healthy weight
	Suggested SCI adjusted BMI scores		
	BMI ≥ 23		Weight reduction indicated
	BMI < 22 or < 23		Maintain healthy weight
Waist circumference	*Men*	> 102 cm	Weight reduction indicated
		94 – 102 cm	Do not increase weight
		< 94 cm	Maintain healthy weight
	Women	> 88 cm	Weight reduction indicated
		80 – 88 cm	Do not increase weight
		< 80 cm	Maintain healthy weight

Table II. Primary Lifestyle based CVD prevention
Table III. Secondary Lifestyle based CVD prevention
Table IV. Biomarkers and treatment targets for CVD prevention

2.6 PEDAGOGICAL MODELS FOR LIFESTYLE MODIFICATION

Two alternative pedagogical models often used for lifestyle modification, the so-called Transtheoretical model (70) and so-called Motivational interviewing (71).

2.6.1 Transtheoretical model

The *Transtheoretical model* (70), also known as "Stages of change", describes generic stages that persons go through during behavioral change processes (Figure 4). A person can go "up", but also "down", a so called relapse, in stages, and the time spent at each level is variable. The stages are: *Precontemplation*, in which the person is not yet aware that he/she has a lifestyle related problem, or denies it. *Contemplation*, a phase where a lifestyle issue is recognized, and both the pros and cons of lifestyle changes are being considered, i.e. a period when ambivalence often exists. *Preparation*, where the decision for change is taken preceded by preparations, both mental and practical, for a change. *Action*, in which stage the plans for lifestyle changes are actually realized. *Maintenance*, which phase requires effort aiming at maintaining the desired lifestyle and reducing the risk of relapse. *Relapse*, finally, is present if the person falls back to previous (undesirable) lifestyle habits.

2.6.2 Motivational interviewing

Motivational interviewing (71) is a counseling method aiming to identify where in the process a person is, and then to implement the appropriate motivational tools for that stage. The method is based on a non-confrontational approach. Open questions are often aiming to let the client describe the situation, earlier experiences, thoughts about the future and "self-change-talk", which means that the client tells about the changes that he/she wants to accomplish. Important when using motivational interviewing is to: i) assess *where* in the process the person is; ii) estimate *how important* the change is and the degree of *self-efficacy*; iii) *give relevant information* that can increase the feeling of importance for the person (if needed) and support further development of self-efficacy; iv) give guidance through feelings and thoughts of ambivalence towards *decision-making*; and v) realistic *goal setting* - short and long term.

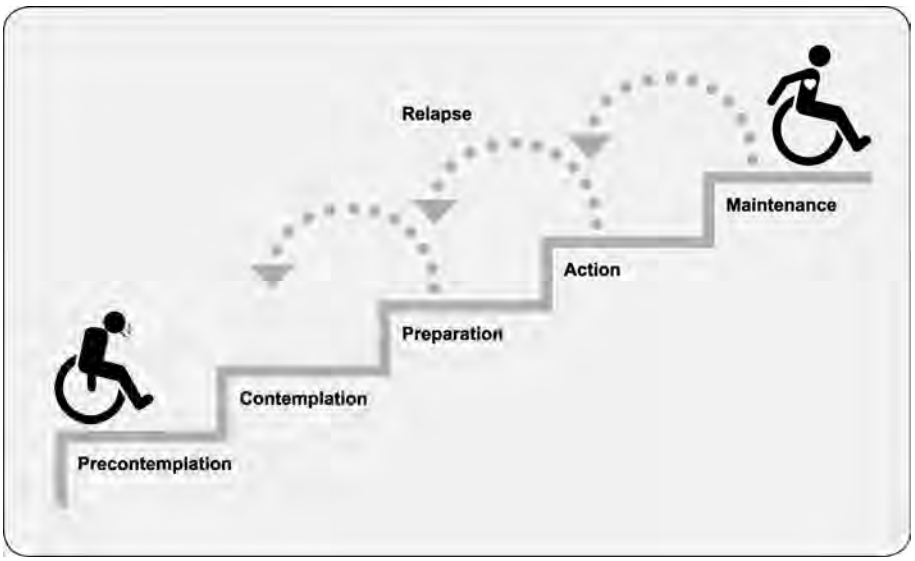

Figure 4. Transtheoretical model

2.7 CVD PREVENTION AFTER SCI

2.7.1 Need of CVD prevention

Studies are indicating that adapted CVD care guidelines are needed (33), and that lifestyle information and counseling should be introduced in the rehabilitation process after SCI (10, 72). Such measures may include information about *how* lifestyle choices can increase or decrease the particular medical health risks that are associated with a chronic SCI (62). Risk assessment and CVD prevention programs for persons with SCI are proposed to include physical activity, diet, weight control, alcohol consumption, as well as smoking cessation sessions (30, 62). Early detection and intervention on CVD is essential if individuals with SCI are to sustain their fullest potential activity and function throughout their lifespan.

However, an earlier report from all six major SCI units in Sweden illustrate an unfulfilled need for screening tools and systematic screening for health habits among health care professionals. Further, prevention programs and pedagogical strategies to support lifestyle changes after SCI were also found to be needed (73).

2.7.2 Screening

Screening; The recommendation is still to use those risk factors present in the general population (45). No other cut scores for intervention than those used in regular CVD guidelines have so far been advised. However, for overweight when using BMI, there are data to suggest that a lower cut level of BMI (BMI 22 – 23) better reflects a healthy weight in the SCI population (34, 74). Recently, study results have suggested that waist circumference might be a better indicator for abdominal obesity and should be implemented in SCI care (75, 76).

2.7.3 Lifestyle based prevention and SCI specific concerns

Physical activity might be *the* lifestyle indicator that has been most frequently scientifically evaluated for persons with SCI. Physical activity has been shown to have many positive effects on CVD related risks. These include; normalization of lipid values (77, 78) and blood glucose (79), and decreasing depressive symptoms (80). Moreover, circuit resistance training, with a combination of strength training and dynamic cardio exercise, has been reported to increase strength and cardiovascular fitness (78). Finally, a compendium has recently been published with energy expenditure for a number of physical activities and for given level of injury (81).

The multitude of consequences and secondary complications which follow SCI result in a need for customized personal and specified considerations vis-à-vis advise on TLC, i.e. physical activity, weight control and/or dietary habits. Recommendations on physical activity after SCI have been suggested in national and international literature (82, 83). Some of the specific considerations that need to be taken into account include; increased risk for pressure ulcers, bladder and bowel incontinence, joint contractures, musculoskeletal and joint injuries and pain, autonomic dysreflexia (AD), and overuse syndromes (82, 83).

Once comprehensive and specific lifestyle based CVD prevention programs for persons with SCI have been developed there are many further aspects to be considered. Persons with SCI have a plethora of health-related issues, from decreased physical margins (and sometimes also decreased psychological resources), over patophysiological dysfunction and decreased reserve capacity in most organ systems, to the fact that activities of daily-life often require much more time than before. All this must be considered, together with an insight into the limited resources extant in the discipline of clinical rehabilitation medicine. In order to create positive conditions of motivation for lifestyle programs after SCI, beneficial short- as well as long-term effects of lifestyle habits have to be addressed, and programs have to be time- and resource-efficient.

2.7.4 Synergies of preventions

However, CVD prevention by lifestyle change on one hand and secondary prevention in general of SCI-specific medical complications on the other, are likely to act synergistically towards desired goals. “Win-win” situations are important to recognize and communicate. Figure 5 illustrates that in the intersection between the two different prevention foci, lifestyle based CVD prevention and prevention aiming to reduce SCI secondary complications, there is a potential that positive synergies occur that can contribute to a sustainable lifestyle for persons with SCI. To achieve simultaneous optimal effect of both preventions requires that the special nature of the injury is taken into account. Thus, the model consists of three components: i) *SCI prevention* includes measures targeting to reduce the risk of secondary complications due to SCI such as: e.g. respiratory disorders, pressure ulcers, UTI, pain, and septicaemia. Also interventions tailoring optimal independency and mood adjustment are represented; ii) *CVD prevention* includes lifestyle-oriented interventions aming to reduce CVD risk e.g.

give up smoking, increase physical activity, healthy food choice, and stress management; iii) *Special SCI considerations* comprises the need for attention to the particular circumstances that must be taken into account when lifestyle prevention is implanted in a SCI population e.g. risk for musculoskeletal pain and joint injuries, bladder and bowel incontinence, joint contractures, autonomic dysreflexia (AD), and overuse syndromes as well as increased risk for pressure ulcers. Moreover, the consequences of loss of motor and sensory function as well as decreased daily energy consumption are important to take into account when considering CVD related lifestyle change. Furthermore, also the need for special and adapted equipments and/or assistance fits this category.

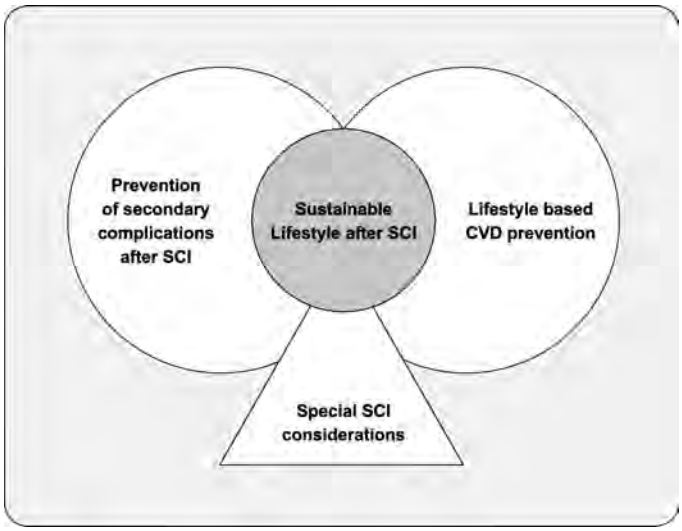

Figure 5. The schematic model of a sustainable lifestyle after SCI includes; prevention of secondary complications after SCI, Lifestyle based CVD prevention, and special SCI considerations vis-à-vis prevention

Some examples of evidence based cross-over benefits that can arise between lifestyle focused CVD prevention and prevention to decrease SCI secondary complications are:

Respiratory morbidity; the risk of respiratory morbidity is associated with level of injury, but also with number of cigarettes smoked per day (62). Persons with tetraplegia have a near 70 % higher risk of respiratory disorders than do persons with paraplegia. Every cigarette smoked per day increases the risk for a respiratory disease by 4.3% (62).

Excess alcohol consumption has also been reported to increase the risk for respiratory morbidity.

Urinary tract infection; In addition to lesion level, lifestyle-related factors such as smoking have been shown to be associated with the occurrence of UTIs (62). For each cigarette smoked per day the risk of UTI increases by about 5%.

Prevalence of *pressure ulcers* has been shown to be associated with cigarettes smoked per day (84).

Pain is frequently reported after SCI. Smoking might aggravate neuropathic pain (85). Moreover, *pain* can be reduced by physical activity (80).

Physical activity has been shown to counteract *depression* and improve *quality of life* after SCI (64, 80), both of which may decrease CVD risk. Among underlying mechanisms a reduction in *pain and stress* has been proposed, which as such is a risk factor for CVD.

Independence and autonomy in an aging SCI population has been shown to be inversely correlated to the presence of overweight (86). Conversely, physical fitness and improved strength have been reported to increase functional ability, especially in persons with high-level SCI (57).

Thus, *if* the SCI population is found to justifiably be considered a high-risk population for CVD, then vigorous intervention will *also* be warranted in light of the "overlaps" between CVD risks on one hand and both short – and long term SCI-specific health – and functional issues on the other, as has been examplified above. Conversely, if the CVD risk only is merely "normalized" as a spin-off of a successful management of a previously high SCI-specific morbidity and mortality it would be unethical to put further burden to this already psychologically heavily taxed patient population by overambitious preventative programs. Thus, it seems of paramount importance to clarify the true need for prevention regarding CVD among persons with SCI. This, in a nutshell is the present thesis.

3 AIMS

The overall aims of this thesis are to assess and explore the need for CVD intervention after SCI in a regional Swedish SCI population: i) in itself; and ii) in comparison with a relevant reference population.

7.1 Key questions

- As SCI by default will hamper a person's ability to be physically active, and as physical activity has been convincingly shown to decrease the overall risk of CVD, which factors may promote participation in physical activities? (Paper I)
- How large proportion of persons with wheelchair-dependent paraplegia is eligible for intervention against CVD risks according to authority guidelines? (Paper II)
- Is there a true increased CVD risk in this population, as compared to the general population? (Paper III)
- Is the conception of SCI as a high-risk diagnosis for CVD in the long-term also corroborated by multifactorial risk scores and assessment of overweight? (Paper IV)

4 METHOD AND MATERIAL

4.1 STUDY DESIGN

The thesis is comprised of two main projects, where the result of the first project is presented in paper I and the results of the second is reported in papers II, III and IV. The thesis utilizes both quantitative and qualitative study designs. In paper I, a qualitative multiple case study design was used. Papers II-IV tap the source of a common data base being analyzed from different perspectives. Paper II and IV both utilizes a cross-sectional study design, while paper III uses a cross-sectional comparative study design.

4.2 PAPER I

4.2.1 Study population

In order to ensure that participants had some experience of practicing physical activity (necessary in order to meaningfully respond to the key questions of this study) we asked persons who had completed a program at our center targeting physical activity and that were at least one year post injury. Seventeen persons met the inclusion criteria, out of which one participant dropped out due to hospitalisation. Thus, 16 persons with SCI were finally included (Table V).

Table V. Participant characteristics; N=16

		N
Injury level	Paraplegia	8
	Tetraplagia	8
Gender	Female	4
	Male	12
Age	21 – 61 (MD 36 years; SD 10.6)	
Duration of injury	2 - 41 years (MD 8.6; SD 9.8)	
Marital status	Married/ living with a partner	6
	Single	6
Employment	Employed or student	9
	Disability pension/sick leave	7
Education	Upper secondary education	12
	University or university colleges	4

4.2.2 Data collection

Data were collected by semi-structured interviews. For data analysis, a cross-case method was chosen (87). In accordance with this method, each interview comprised a case study by itself. In order to detect themes in the total material, all interviews were subsequently cross-compared.

A study-specific interview guide was developed and tested. The results of initial pilot interviews contributed to slight rephrasings of the original interview guide before "sharp" data collection commenced. For the purpose of the study, the concept *"physical activity"*, which was under study, was operationally defined as 'any bodily movement produced by skeletal muscles resulting in energy expenditure' (88).

4.2.3 Data analysis

Subsequent data analysis was conducted in six steps (Figure 6): i) Transcription and reading of interviews aiming to gain a general picture of the material; ii) Preliminary categorization of relevant statements; iii) Further detection of patterns and similarities. Statements were grouped into themes according to content. Content comprising each theme was defined and described and then cross-checked repeatedly against the verbatim transcribed interviews; iv) Themes were scrutinised to avoid overlap; v) Each theme was given a heading reflecting its content; vi) To further elucidate each theme, content specific quotations were chosen and stated.

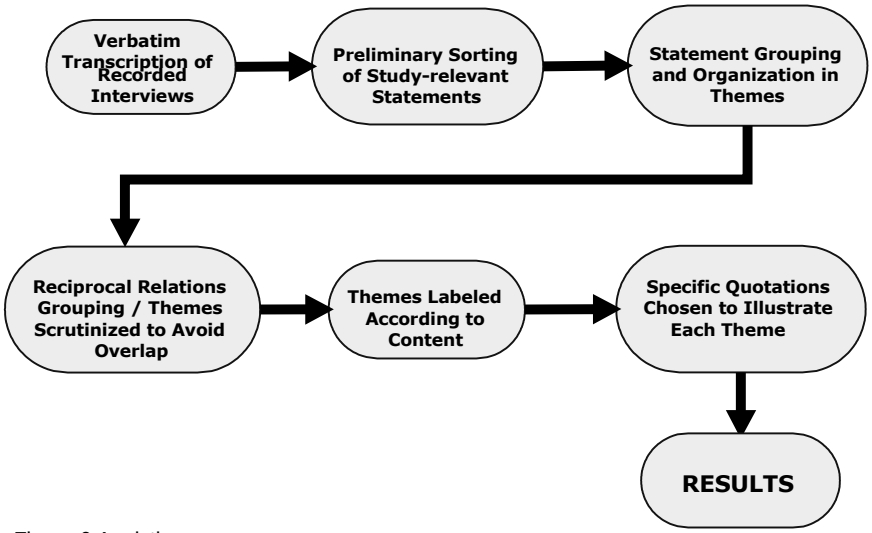

Figure 6 Analytic process

4.3 PAPERS II – IV

4.3.1 Study population

Participants eligible were: i) men and women with *"wheelchair-dependent"* traumatic paraplegia, operationally defined as "exclusive or predominant ambulation by wheelchair" (as opposed to walking); ii) a neurological lesion level (due to traumatic SCI) at or below T1, and an ASIA Impairment Scale grade A, B, or C for at least one year; iii) residence in the greater Stockholm area; iv) registered for medical follow-up at the regional SCI outpatient center (covering over 95% of the total regional prevalence population); and v) age over 18 years.

One hundred and fifty-three persons fulfilled criteria and were asked to participate in the study, as they consecutively were due for annual check-up at the center. One hundred and thirty-five persons (88%) consented to participate. The study was then conducted between November 2006 and December 2007.

Injury level	ASIA			
	A	B	C	Total
Th 1 – 6	39	4	2	45
Th 7 – 12	56	5	5	66
L 1 – 4	14	4	6	24
Total	109	13	13	135

Table IV. Distribution of ASIA grade and level of injury (paper II – IV)

Table VII. Descriptive characteristics of the study participants in project II. (Papers II-IV)

	Mean	S.D.	Range
Age (years)	47.8	13.7	19-79
Injury Duration (years)	18.4	12.3	1-48
Injury Levels	n/135	%	
T1-T6	45/135	33%	
T7-T12	66/135	49%	
L1-L4	24/135	18%	
Marital Status			
Single		69/135	51%
Married		54/135	40%
Committed Partner		12/135	9%
Education			
Completed primary school (i.e., through grade 9)		20/135	15%
Primary school plus 3 years of public education		54/135	40%
Technical training		12/135	9%
>1 year of university education		49/135	36%
Employment Status			
Unemployed		50/135	37%
Full-time		22/135	16%
Part-time		45/135	33%
Retired		15/135	11%
Students		3/135	<3%

4.3.2 Data collection

Data were collected through participant interviews and clinical physical/neurological examinations. Interviews included pre-defined questions relating to: i) smoking habits; ii) history of MI, HTN, DM and DL; iii) current medication for these disorders; and iv) body height. The self reported data were confirmed by scrutinizing medical records. The clinical examination included: i) *Blood pressure,* which was measured after 30 minutes of rest according to standard technique on the left arm with the participant seated; ii) *Body weight,* measured in kilograms on a calibrated scale; *iii) Blood chemistry* for fasting lipid profile (TC, LDL, HDL, TG) and fasting glucose.

BMI was computed as body weight (kg) divided by the square of body height (m).

Neurological status according to ASIA standards was obtained from medical records, based on a neurological exam made by a SCI specialist physician.

4.4 PAPER II

4.4.1 Operational definitions

"Dyslipidemia" (DL), was operationalized as: i) ongoing drug treatment for this disorders; and/or ii) blood chemistry showing pathological lipid levels according to current standards (65). The "cut scores" utilized were: TC ≥ 5 mmol/l (> 200 mg/dL), LDL ≥3mmol/l (> 130 mg/dl), HDL men ≤ 1 mmol/l (< 40 mg/dl), HDL female ≤ 1.3 mmol/l (< 50mg/dl)), and TC:HDL ratio ≥ 4.5.The values within parentheses are cut points for required TLC and/or drug therapy according to US guidelines (67).

"Diabetes mellitus" (DM) was operationalized as: i) ongoing drug therapy for this disorder; and/or ii) blood chemistry showing a fasting blood glucose ≥ 6.1 mmol/L (≥ 110 mg/dl) (65). The values within parentheses are cut points for required TLC and/or drug therapy according to American guidelines (67).

"Overweight" was operationalized as BMI ≥ 25 (38).

"Hypertension" (HTN), was operationalized as: i) ongoing drug therapy for this disorder; and/or ii) systolic blood pressure ≥ 140 mmHg; and/or iii) diastolic blood pressure ≥ 90 mmHg (89). In the presence of multiple risk factors, the cut score used was instead ≥130 mmHg and ≥ 85 mmHg.

Smoking was operationalized as: i) current daily tobacco smoking; or ii) smoking cessation less than one month prior to the study.

4.5 PAPERS II AND IV

4.5.1 Clustering of risk factors

Clustering was assessed three ways. *First*, by individual risk factors according to guidelines, adding the number of factors present. *Second*, by two internationally recommended multifactorial risk models. Those were SCORE (66) and the Framingham risk equation (FRE) (90). In these models, each risk factor has multiplier depending on its relative contributing effect on CVD.

4.6 PAPER III

4.6.1 Comparison between the SCI cohort and the general population

In order to compare CVD risk in the SCI group under study with that of the general population, a subset of self-reported data was used. The comparison group comprised an age, gender and regionally matched cohort from a data base of Swedish Statistics; the *Swedish Annual Level-of-Living Survey*, was utilized (91). This comparison group included 1 488 persons from the Stockholm region between the years 2003 and 2005, i.e. from the same time period as that of the SCI study.

5 RESULTS

5.1 PAPER I

Four main themes of promoting factors for physical activity after SCI emerged. These themes were; *Using cognitive and behavioral strategies; Finding environmental solutions, Exploring motivation post injury; Capturing new frames of reference* (Figure 7). Analysis of the interviews confirmed consistency. The themes were interconnected and together offered a template for promoting the process to become physically active after SCI. We did not find indications that the promoting factors could be ranked hierarchically or chronologically. Interpretation of data implied reorientation and adaptation of values, attitudes, priorities and behaviors.

5.1.1 Using cognitive and behavioral strategies

This theme included the following main promoting factors: finding a role model; creating routines; setting goals; acquiring new knowledge; recalling previous experiences; and to exposure and accepting assistance. A common denominator was that these factors comprise cognitive and behavioural strategies that are used in order to facilitate the intention to participate in physical activity.

5.1.2 Finding environmental solutions

This theme included the following main promoting factors: increasing sufficient accessibility; social supporting; and arrange equipment and funding. “Environment” here relates to the totality of the personals external milieu that may promote physical activity. Such environmental factors include living conditions, outdoor climate, accessibility, legislation, geographical distance and social network.

5.1.3 Exploring motivation post injury

This theme comprised; gaining and maintaining independence; experiencing health and improving physical appearance; becoming a role model; becoming competitive; establishing a self-image as physically active; experiencing pleasure; and becoming part of a social network and being needed. This theme included factors providing motivational drive for the individual to embark on a physically active lifestyle. Characteristically, a person experiences a problem which is troublesome and which is considered to be possible to

change to the better. In the tension between how it is and how it could be the motivational drive arises. Motives may and will change over time.

5.1.4 Capturing new frames of reference

This theme included: learning to live with narrower physical margins; learning to "read" the body; and acquisition of new physical strategies. The consequences of SCI with motor and sensory dysfunction obviously affect possibilities to practice physical activities. To learn how to understand and act with these physical limitations is a long process and requires regular practice. Further, evaluation of bodily reactions after physical activities is carried out in order to adjust the future performance and minimize the negative effects and optimize the positive ones. Participants described the process to keep the balance between too much and too little physical activity as very important but also very difficult, and something that required substantial effort. To perform physical activity after SCI requires new skills that take both time and effort to learn.

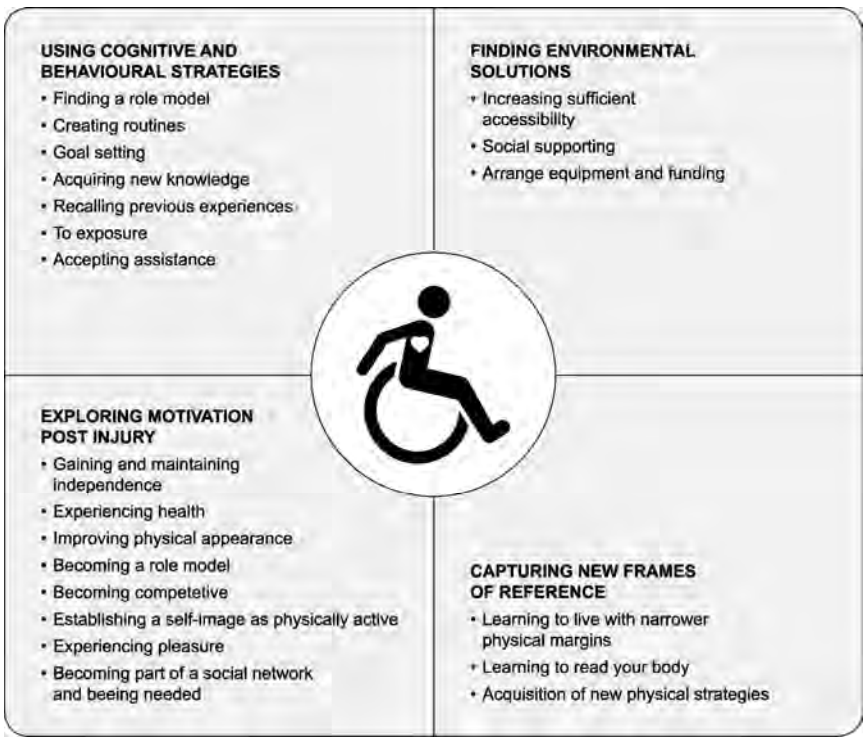

Figure 7. Themes of factors that promotes participation in physical activity after spinal cord injury

5.2 PAPERS II

Prevalence of CVD - related risk factors according to authority guidelines.

5.2.1 Dyslipidemia

The prevalence of DL was high. Increased LDL values were most frequent (57%), followed by increased TC (49%) and decreased HDL (43%) (Figure 8). Additionally, 41% had a TC:HDL ratio above the recommended level. A large majority of the cohort had DL (83.1%).

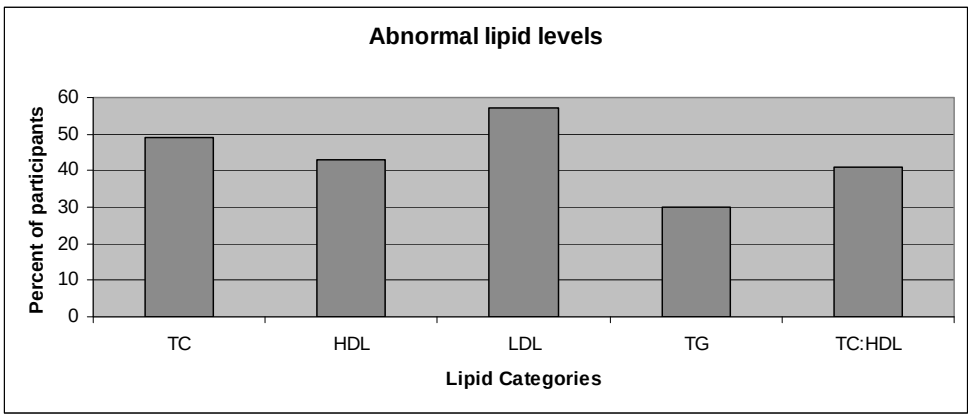

Figure 8. Distribution of abnormal lipid levels

5.2.2 Smoking

The prevalence of smoking was 16 % (N=22).

5.2.3 Glucose

Eight participants were already on medication for DM at the time of the study. An additionally six participants had glucose values that corresponded with the definition of IFG. Thus, the prevalence of DM/IFG was 10% (N=14).

5.2.4 Hypertension

HTN was common with 39%. HTN included; HTN Stage 1, 2 and participants on HTN drug therapy but with a blood pressure in desirable range (Figure 9). Further, Pre-HTN values were present among and additional 17% of participants.

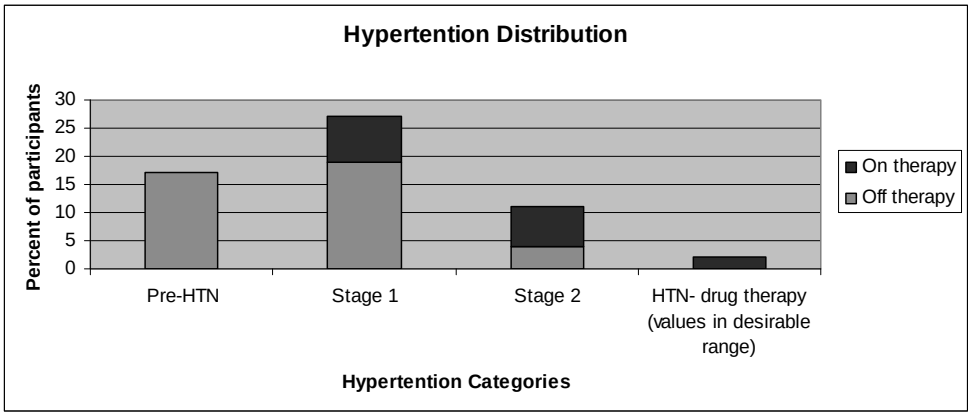

Figure. 9. Distribution of hypertension and use of drug therapy

5.2.5 Overweight

Forty-two percent of participants had a BMI value of 25 or more, i.e. equivalent to the diagnosis of overweight in the general population. Further, when lower (and possibly more relevant for the SCI population) BMI values were also taken into account, the proportion of overweight participants increased substantially. Over half of the sample thus had a BMI ≥ 24, 66% had a BMI equal to or greater than the cut-off point 23, and over 75% had a BMI value ≥ 22. In other words, fewer than 25% of the cohort had a BMI under 22, making the problem of overweight after SCI potentially very extensive (Figure10).

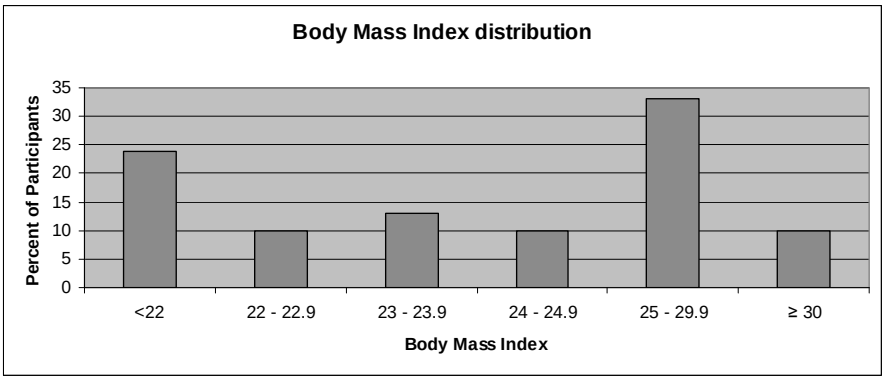

Figure 10. Distribution of body mass index

5.2.6 Pharmacotherapy

Many subjects eligible for drug therapy lacked such measures at the time of the study. Furthermore, pharmacotherapy, when in use, frequently failed to reach recommended therapeutic goals (Table VIII).

Risk Factors	Prevalence	On Therapy	On Therapy Values outside desirable range	Off Therapy
Diabetes Mellitus	14/135	8/135	7/8	6/135
Dyslipidemia	115/135	15/135	9/15	100/135
Hypertension	53/135	19/135	16/19	34/135

Table VIII. Prevalence of CVD risk factors and pharmacotherapy use

5.3 PAPER III

5.3.1 Comparisons between populations

In comparison between the paraplegic cohort and the reference population we could confirm an increased prevalence of the following CVD – related risk factors among persons with paraplegia: i) DM (5.9% versus 2.7% in the general population, P < 0.0001); ii) DL (11.1% versus 1.8% in the general population, P<0.0001); and iii) HTN (14.1% versus 8.7% in the general population, P 0.04). Further, and most noteworthy, history of MI was reported in 5.9% of the paraplegic group versus 0.7% in the comparison group (P< 0.0001) (Figure 11).

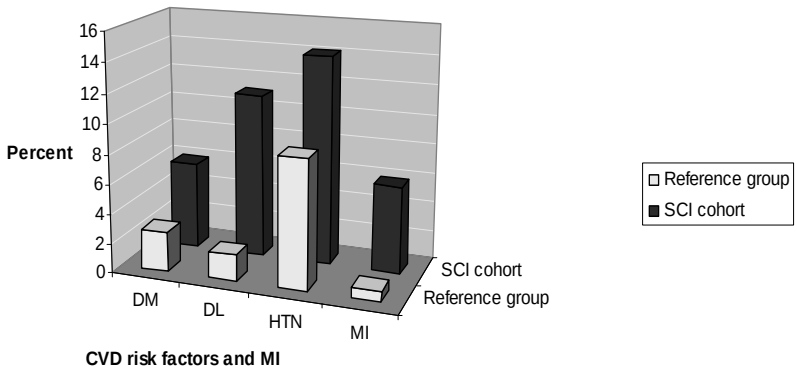

Figure 11. Comparison of prevalence of CVD risk factors and MI between SCI –cohort and reference group.

5.4 PAPER II AND IV

5.4.1 Risk clustering

Clustering of CVD- related risk factors in the study group was common (Figure 1 in paper II*).* Only 4% of the study group had no risk factors at all, while at the other extreme over 20 % had five concurrent CVD risk factors. According to both SCORE and FRE, about one-third of the study group was eligible for intervention. (Figure 1 - 3 in paper IV) Further, when the low-risk groups were additionally assessed regarding BMI, the number of participants in need of intervention further substantially increased, the proportion depending on which BMI cut-off that was used (Table II and III in paper IV).

6 DISCUSSION

This is the first SCI- population based study in Sweden focusing on the need for CVD- prevention. We have explored this topic from four perspectives; *first*, from a patient perspective; *second* by assessing single CVD risk factors; *third* by clustering of CVD risks according to authority guidelines; and *fourth*, by comparison with the general population.

The main findings were a high prevalence of CVD related risk factors according to authority guidelines, including DL (83.1%), HTN (39.3%), and DM/IFG (10%) (Paper II). These findings are in agreement with some previous studies such as; DL and especially decreased HDL (39, 41), HTN (5, 60), and DM (92).

BMI was used to define overweight: The BMI cut score (BMI ≥25) for overweight (38) is too high for the SCI population (35). Previous studies have suggested a "healthy" BMI level of 23 (34) or even at 22 (74) in the chronic phase of SCI. Thus, in this thesis we have reported different levels of BMI to reflect the prevalence of overweight. Under any of these preconditions, overweight was common, and if accepting the proposed adjusted BMI cut scores (22 and 23) overweight was more common in the paraplegia cohort than in the reference population. Our finding of an increased need for prevention of overweight in the SCI population is corroborated by other authors (93, 94). A complicating factor regarding the SCI population is the initial posttraumatic catabolic state in the acute phase. Consequently, the caregiver focuses after severe trauma to support the patient to counteract the catabolic state by promoting a high caloric intake (95). Knowing that energy consumption in the chronic stages SCI is decreased (32), the physical activity level low (59) and an increased BMI correlates with an abnormal lipid profile, there is a challenge for primary prevention to switch strategy once the catabolic phase is over for adequate weight management after SCI (96). When the body weight starts to increase post injury the calculation of the relevant target weight depending on level and extent of injury, will be pedagogically important both for patient and caregiver. Further, for the best effect of prevention, also other caregivers around the patient should be involved like family members and/or personal assistants.

Age was found to be positively correlated with increasing CVD risk in the SCI group. Aging being a risk for developing CVD is already well documented also in the SCI population (39, 97). Perhaps surprisingly, DL did not fit this pattern, something which may be a result of an early development of DL after injury. Hypothetically, the profound and rapid changes in body composition that typically occurs after injury might be sufficient to derange lipid metabolism already in the short-term perspective.

Clustering of CVD risk factors have been reported to increase the risk for developing CVD and for premature death (98). We found that clustering of CVD risks were prevalent both when adding individual risk factors, and when assessing the need for intervention by multifactorial risk models. When also overweight was considered, the need for intervention increased drastically, depending on the BMI cut score used. Our results regarding clustering of CVD risk factors are in agreement with some previous studies (9, 99).

A high percentage of the studied individuals at risk were untreated or treated but not reaching targets according to authority guidelines. This was especially the case for DL and HTN (paper II). This state of affairs may have several causes: *first*, from a clinical perspective, SCI individuals are afflicted by many secondary complications e.g. pressure ulcers, UTIs and respiratory disorders (15), and the preoccupation with these conditions may detract the focus on other, more "invisible" diagnoses, like risk factors for CVD. *Second*, persons with SCI in Sweden are consulting both at the SCI unit and at their general practitioner in parallel, something which may contribute to "responsibility gaps". *Third*, CVD has traditionally not been considered of special relevance when treating subjects with SCI (8) and has therefore not been prioritized in the SCI follow-up programs (100). *Fourth*, drug therapy for CVD related diagnoses might not have the same effect in persons with SCI as compared to that in able bodied persons. *Fifth*, risk factors have a silent progression that in most cases is not directly perceived until the disorder is advanced (101). *Sixth*, untreated risk factors for CVD have also been reported in the general population (102).

In comparison with the reference population, our SCI cohort showed an increased prevalence of MI, DL, HTN, and DM. Our results thus contradict a recent meta analysis which concluded that risk of MI, DL and DM after SCI is equal to that of the general population (45). On the other hand, our results are consistent with some other reviews on this topic (10, 30). It has to be remembered that we are talking about a "moving target". Thus, historical studies may reflect an epidemiological situation that since then has changed. This is a likely explanation since we 15 years ago, in a study conducted in the same region as this present study, did *not* find indications of an increased CVD risk in our SCI population. Since then, our cohort has aged 15 years, and the mortality and incidence pattern has furthermore shifted our population in the direction of aging with SCI. Thus, by the combination of more effective long-term management and a larger proportion of older persons sustaining and surviving SCI, CVD has emerged as a new challenge to address.

It is well-established that physical activity has protective effects against CVD and associated conditions in persons with SCI (52). However, with the multitude of extensive barriers limiting physical activity after SCI (103), it is not surprising that the reported level of physical activating is low (59). This matter of fact provides the rationale behind our inclusion of a study focusing on factors that may support a physically active lifestyle after SCI. The pattern of facilitating factors identified by our study should be readily translatable into practical intervention strategies as to promote physical activity post SCI. Recently a study by Kehn and colleague (103) confirmed our findings that cognitive and behavioural strategies and motivating factors post injury in combination with the ability to find environmental solutions may contribute to a physical active lifestyle. This occurs probably in a complex pattern which is yet not totally explored. Further, they reported, in agreement with our results, that a key motivational factor was to be as independent as possible and stay healthy.

6.1 STUDY PARTICIPANTS

In order to define a reasonably large but still homogeneous subgroup of persons with SCI (project II), we chose to include persons with traumatic paraplegia that were "wheel-chair" dependent. Reliable analysis of subgroups within this cohort was precluded by the relatively small sample size. However, other authors have shown that all CVD, defined as; cardiovascular heart disease, hypertension,

cerebrovascular disease, valvular disease and dysrhythmia, increase with level and severity of SCI (as well as with age) (61). Also, Bauman and colleagues reported that a higher level of injury and completeness increase the risk to develop diabetes (104). Persons with tetraplegia have lower levels of HDL than persons with paraplegia and complete injuries correlate with more depressed HDL values (105). HTN has been reported to be of concern in the paraplegia cohort (5, 60). One the other hand hypotension is prevalent in persons with tetraplegia. However, hypotension does not seem to be "protective" against CVD in general, since persons with tetraplegia show an increased risk for all cause CVD compared to the paraplegia subpopulation (61). This finding seems to suggest that hypotension cannot "compensate" for other CVD risks in SCI. Yet another possibility that has been proposed is that adrenergic receptors below the level of lesion re-establish a new set-point after cervical SCI that makes pressures of 90/60 the norm, and that higher pressures represent a relative hypertension. Yet another disadvantage of tetraplegia, despite the lower blood pressure, might be a yet more pronounced immobilization due to a very limited residual muscle mass with which to exercise and fewer exercise options.

6.2 SCREENING

Screening for CVD is recommended both for the general population (66) as well as, in follow-up programs after SCI (30, 99). Nevertheless, screening as such is a complex phenomenon and has to be discussed also from an ethical perspective. In particular, it has been discussed whether screening is adequate when it will yield a large part of the population defined as being "at risk" (106). The Nordic risk group (NRG) argues that it is important to reflect over when and to whom screening is offered and how it is carried out. They also underscore the importance of not only discussing the beneficial effects but also what potential harm screening can cause. Further, they highlight that a fragmentary view of human health, often the case in screening, does not necessarily contribute to a positive situation that can stimulate empowerment and quality of life. Some important ethical considerations in the context of medical screening are important to point out. Thus, before screening is implemented the following issues need to be secured: i) provide as complete information as possible regarding consequences of screening; ii) screening needs to be consented by the person screened; iii) screening results must be amendable to

evaluation and it is also of importance to define target values for all variables including lifestyle habits; and iv) to work with a holistic-approach where the medical problem oriented screening with biomarkers is balanced by methods focusing on human recourses in a way that strengthens empowerment.

Despite the fact that a need for SCI-specific CVD screening now is indicated, it is far form clear which caregiver should take this responsibility. One consequence of our results might be to further probe this issue. Regarding follow-up after SCI in Sweden (and some other Nordic countries) a dataset called the Nordic Spinal Cord Injury Registry (NSCIR) is used(100). One of several focus areas included is "circulation and metabolism" which currently includes; blood pressure, weight and height, lipid profile and fasting glucose. However, this panel is not included in the so-called "core data set" i.e. the "mandatory" subset of data to be collected. The issue regarding how CVD screening and prevention after SCI should be done, and by whom, needs to be further discussed both from a clinical and a scientific perspective.

6.3 CVD PREVENTION WITH LIFESTYLE PROGRAMS

CVD risk is multifactorial and lifestyle dependent in the general population(107). Hence, both lifestyle change and drug therapy are included in the recommended preventions in various authority driven guidelines (67, 69). Programs for lifestyle intervention on CVD risk for the general population has been studied in the context of the Swedish primary healthcare system for the general population (102). It showed that lifestyle interventions including exercise and diet can reduce risk for CVD (108-110).

To our knowledge no comprehensive lifestyle intervention with diet and exercise has ever been scientifically evaluated in persons with SCI. However, various studies have explored individual CVD protective factors. By physical exercise it has been shown to be possible for persons with SCI to decrease CVD risk with normalization of lipid profiles, (78, 111, 112). Exercise intervention has furthermore been reported to decrease the risk for depression (80). We have only found one study reporting on weight-reduction programs after SCI (113). The results of a holistic wellness program tested on a SCI cohort showed improved

health behaviours and self-efficacy (114), which may be of importance when lifestyle changes are required.

The introduction of health promotion programs for the SCI population has been requested (115). However, it has been questioned whether it is possible to make generic exercise prescriptions for persons with SCI (103). Regardless, several attempts have been made to prescribe physical training after SCI (83, 116, 117). These recommendations might be further developed if they were to consider the specific facilitating factors for physical activity after SCI which have been identified (103). Comprehensive lifestyle programs also need to be put in a pedagogical context, where well-tested concepts for lifestyle changes as the Transtheoretical model (118) and Motivating interviewing (119) can be used.

6.4 LIMITATIONS AND STRENGTHS

Some limitations of the studies included in this thesis should be mentioned: i) assessments were obtained once only, whereas clinical diagnosis typically warrants repeated measures prior to establishing the presence of disease; ii) regardless of the fact that nearly 90 percent of the regional paraplegia population was included, 135 subjects is a small population when studying CVD risk factors; iii) BMI with the given cut scores is not a validated CVD risk indicator in the SCI population. Waist circumference might be a better CVD predictor, but further studies are needed in the SCI population (75, 76); and iv) in order to adequately elucidate the true need for CVD intervention, also other risk factors prevalent in the SCI population have to considered; e.g. physical inactivity, depression and psychosocial stress, perceived health and alcohol over-consumption (66, 120).

Among strengths of the studies included in this thesis we wish to mention: i) the study group comprised a relatively homogeneous group of persons with traumatic SCI; ii) almost 90% of subjects meeting the inclusion criteria participated in the study; iii) all three studies (paper II – IV) showed consistent results; and iv) all data were collected by one investigator (KW).

7 CONCLUSIONS

1. The majority of a regional Swedish paraplegic population display several risk factors for CVD.
2. Eighty-six percent had *multiple risk factors*, and 21 % as many as five risk factors present.
3. The prevalence of *MI was 8.5 times higher in the paraplegic cohort* than in the reference population.
4. CVD risk factors such as; *DL, HTN, DM and overweight were also more prevalent* in the paraplegic cohort.
5. Regular *CVD screening* and assessment according to guidelines is thus, clearly indicated.
6. *CVD prevention* including therapeutic lifestyle intervention needs to be developed, evaluated and then systematically implemented.
7. *Lifestyle interventions need to be tailored to the specific needs* of this patient group.

8 FUTURE STUDIES

There are several potential future studies related to the research field *aging with SCI* and more specifically, *CVD prevention after SCI*. However, our findings suggest that the highest priority now should be focusing on intervention studies. Whereas causes of CVD are as such multifactoriel and in combination with SCI-specific considerations the prevention approach focusing on lifestyle needs to be multifaceted and adapted. Thus, we suggest development and evaluation of effective and SCI-safe prevention programs that are multifactoriel and targeting both the reduction of CVD risks as well as SCI secondary complications.

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