Pharmacophore

ISSN-2229-5402

Journal home page: http://www.pharmacophorejournal.com

RISK FACTORS AND PREVENTION OF CARDIOVASCULAR DYSFUNCTIONS AFTER SPINAL CORD INJURIES. A LITERATURE REVIEW

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ARTICLE INFO

Received:
02 Mar 2023
Received in revised form:
25 May 2023
Accepted:
01 Jun 2023
Available online:
28 Jun 2023

Keywords: Spinal cord injury, Cardiovascular dysfunctions, Risk factors, Prevention

ABSTRACT

This paper aims to analyze the potentially increased cardiovascular risk factors after spinal cord injury (SCI). Taking into account the pathophysiological mechanism of SCI, clinical presentation, and short- and long-term effects, this paper evaluates the prevalence of cardiovascular disorders. Reduced physical activity, low HDL cholesterol, an increase in body fat percentage, poor glucose tolerance, insulin resistance, psychosocial factors, and the hypothesised impacts of SCI on emerging risk factors are all potential increased cardiovascular risk factors following SCI. Nutritional counselling and intervention are especially crucial because people with SCI frequently eat less than is ideal. Screening for risk factors and a worldwide assessment of the risk of coronary heart disease are the first steps in prevention. People with chronic SCI are more likely to have poor glucose tolerance, insulin resistance, and hyperinsulinemia, according to reports. Important therapies for these patients include weight management, dietary adjustments, exercise, and glycemic control. Successful prevention to lower the risk of cardiovascular disease requires both patient and physician motivation.

To Cite This Article: Fodor R, Voiță-Mekeres F, Indrieș M, Beiușanu C, Andreescu G, Voiță IB, et al. Risk Factors and Prevention of Cardiovascular Dysfunctions After Spinal Cord Injuries. A Literature Review. Pharmacophore. 2023;14(3):47-54. https://doi.org/10.51847/iae3qqAG4f

Introduction

Generalities about Spinal Cord Injury

Major sensory, motor, and autonomic dysfunction are all symptoms of spinal cord injury (SCI), a pathological disease that is destructive [1, 2]. Both the acute and long-term phases of care for SCI are accompanied by life-threatening consequences [3]. According to statistics, there are 12,500 spinal cord injuries recorded each year in the USA [4] and 133,000 to 226,000 instances worldwide [5]. SCI carries a hefty price tag; estimates of the average lifetime cost for direct care range from $1.5 million to $4.7 million. The biggest cause of injuries worldwide is traffic accidents, which are becoming increasingly prevalent

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in emerging nations. Although the demographics of SCI patients have changed over time, 80% of newly diagnosed SCI patients are still men [5].

Local spine deformation, such as from direct compression, is the primary cause of primary SCI. After an initial injury, there is a risk of secondary spinal cord damage, which is characterised by a cascade of biochemical and cellular events, including electrolyte abnormalities, free radical generation, edoema, ischemia, and inflammation [6]. Acute, subacute, and chronic phases make up secondary SCI injuries. Haemorrhage and ischemia trigger inflammation, excitotoxicity, and disruption of the ion balance during the acute phase (up to 48 hours after the initial damage). A phagocytic response and reactive proliferation of astrocytes occur in the subacute period (up to two weeks after the initial damage), and this results in glial scarring in the chronic phase. Because scarring hinders axonal regrowth, it is believed to be a crucial factor in persistent impairment. If not, axons may regenerate, but their development is prevented. However, this idea has been refuted, and some researchers have even made the argument that astrocyte scarring might promote regeneration [7]. The healing process is finished during the chronic phase, which lasts longer than six months [2]. In particular, those at or above the sixth thoracic vertebral level (T6) frequently experience inadequate control of sympathetic vasoconstriction of the peripheral vasculature and splanchnic circulation, as well as decreased control of heart rate and cardiac output, due to SCI's impairment of the synchronous functioning of the autonomic nervous system [8, 9].

Notions of the Physiopathology of SCI

Orthostatic hypotension is the main underlying problem that develops as a result of SCI. It lacks reflex vasoconstriction that is sympathetically mediated, especially in the vast arterial beds that supply the splanchnic area and skeletal muscle. Blood pressure drops as a result of the gravitational effects of venous pooling in the lower extremities and the absence of compensatory adjustments in other vascular beds [10, 11].

A lower end-diastolic volume of the heart results from the decline in venous return, which raises the risk of an ischemic stroke. While tachycardia may happen as a result of reflex vagal inhibition, it is insufficient to make up for the diminished sympathetic response [12]. In cervical lesions compared to thoracic lesions, orthostatic hypotension is more common and is present to a greater extent. Some occurrences of orthostatic hypotension following SCI may also be caused by low plasma volume, hyponatremia, and cardiovascular deconditioning. Following traumatic SCI, compared to nontraumatic SCI, orthostatic hypotension has been observed to be more prevalent. Often, but not always, it has been demonstrated that orthostatic hypotension gets better with time. The equilibrium of blood pressure may be aided by compensatory alterations in other vascular beds. The renin-angiotensin-aldosterone pathway can be stimulated by reduced blood supply to the kidney, which can cause glomerular dilatation and activation [13].

Even though there is evidence of a postural decrease in blood pressure in upright posture, tolerance to the symptoms of orthostatic hypotension frequently develops over time. According to certain theories, adaptation to orthostatic hypotension is primarily mediated through autoregulation of cerebral blood flow, which may be more significant than systolic blood pressure regulation. Low blood pressure, orthostatic hypotension, bradycardia, arrhythmias, cardiac arrest, autonomic dysreflexia, decreased cardiovascular capacity, altered exercise capacity, and venous thromboembolism are all cardiovascular problems in SCI [14, 15].

Clinical Signs of Cardiovascular Dysfunctions in SCI

Cerebral hypoperfusion is the cause of many of the major orthostatic hypotension symptoms. Vertigo, unconsciousness, and visual problems such as scotomas, tunnel vision, darkening, and color deficiencies are a few of these. There may also be other symptoms such as pallor, hearing loss, generalized weakness, and lethargic behavior. Overheating may take place above the site of the injury. Uncontrolled blood pressure can have an impact on one's prognosis and quality of life [16, 17].

Due to the emergence of symptoms during mobilization therapy and the perception of orthostatic symptoms as restricting treatment in 43% of a consecutive sample of patients with acute SCI in a single report, orthostatic hypotension may be a barrier to participation in rehabilitation therapies. According to preliminary research, prolonged hypotension in SCI patients may be linked to cognitive dysfunction, including memory, attention, and processing speed problems [18].

Several causes, many of which are reversible, can affect postural hypotension. These include extended recumbency and abrupt changes in posture. When you first get up in the morning, hypotension could be more noticeable. The decline in blood pressure brought on by the blood being pumped into the postprandial splanchnic circulation may be made worse by large meals. By encouraging vasodilation, physical activity, alcohol use, or a warm atmosphere, hypotension might occur. Dehydration and sepsis can make symptoms worse. A number of medications can cause or exacerbate postural hypotension. Orthostatic hypotension may be triggered by tricyclic antidepressants, antihypertensives, diuretics, vasodilators, and narcotic analgesics [19, 20].

An analysis of the potential elevated cardiovascular risk factors following spinal cord injury is the focus of this paper.

Risk Factors and Prevention Strategies of Cardiovascular Dysfunctions in SCI

Numerous studies have been conducted, and the general population's risk factors for atherosclerosis and coronary heart disease have been thoroughly described. The development of these determinants has been the subject of extensive epidemiological investigations, including the Framingham study [21-23]. Increasing age, male sex, and a family history of coronary heart disease are all non-modifiable risk factors. First-degree relatives with a history of early-onset coronary artery disease are

particularly noteworthy, and patients with this history should be carefully recognized and tested for the condition. Where interventions are effective, hypertension, smoking, lipid abnormalities (high LDL, low HDL), physical inactivity, obesity, and diabetes or impaired glucose tolerance are the key modifiable risk factors [23].
Numerous emergent risk factors are being researched in addition to known risk factors. People with SCI may have a higher prevalence of various risk factors **(Table 1)** [24]. Traditional risk assessment methods may underestimate the cardiovascular risk in individuals with chronic SCI, according to some research [25, 26].

Table 1. Potentially increased cardiovascular risk factors after SCI

Decreased physical activity
Low HDL cholesterol
Increase in the proportion of body fat
Impaired glucose tolerance, insulin resistance
Psychosocial factors (depression, social isolation)
Hypothesized effects of SCI on emerging risk factors (inflammation, platelet function)

Motivation from both patients and doctors is necessary for effective prevention to lower the risk of coronary heart disease. The first steps in prevention involve identifying risk variables and estimating the overall risk of coronary heart disease. **Table 2** provides a summary of the major preventative objectives.

Table 2. Key prevention goals for coronary heart disease

Quitting smoking
Lipid management to the target level
Blood pressure control
Weight management
Physical activity
Diabetes management
Additional components of secondary prevention with known coronary heart disease
Antiplatelet agents (aspirin), anticoagulants
Blockers of the renin-angiotensin-aldosterone system
Beta-blockers

Hypertension
Blood pressure (BP) levels and cardiovascular disease are continuously and consistently linked, and there is evidence that treating hypertension lowers heart disease morbidity and death [17]. Lower blood pressure is more prevalent than high blood pressure in patients with SCI, particularly those who have total tetraplegia or high-level paraplegia. However, some research claims that these patients have a notably high rate of hypertension. Although in some instances it might be, this hypertension is frequently idiopathic and unrelated to kidney disease. Based on research population variables such as age, sex, ethnicity, veteran status, and SCI features such as damage severity, complexity, and aetiology, the reported prevalence of hypertension differs significantly between studies [27]. Tetraplegics are said to have a lower prevalence of hypertension than paraplegics, especially those with low paraplegia (T7 and below). After taking into account the available SCI variables, including age, demography, and comorbidities, those with nontraumatic SCI were more likely to develop hypertension compared to those with traumatic SCI. When SCI is caused by aortic disease or complications following a single aorta repair, hypertension is very prevalent. Blood pressure variability caused by autonomic instability and postural factors should both be taken into account when diagnosing hypertension in patients with SCI. People with SCI, particularly those with quadriplegia, may experience blood pressure changes due to their posture [28]. If the quadriplegic person is seated when blood pressure is taken, the presence of supine hypertension may go undetected. Due to autonomic instability, people with SCI frequently experience significant blood pressure variability. Particularly in people with quadriplegia, coexisting illnesses such as autonomic dysreflexia and orthostatic hypotension may make a diagnosis difficult to make. By way of presentation, course, and episodic character, autonomic dysreflexia is clinically separated from essential hypertension. The accuracy of identifying hypertension after SCI may be improved by taking numerous blood pressure readings over time, both supine and seated. Salt limitation, alcohol abstinence, increased physical activity, and healthy weight management are crucial lifestyle changes for those with hypertension [29]. Maintaining compliance is key to effective medication management. When blood pressure is 130/80 mmHg or higher, lifestyle adjustments should be taken into account. Although other objectives may be taken into consideration in some people and subpopulations, for the majority of adults, a threshold of 140/90 mmHg is suitable for the start of pharmacological treatment. It is not yet clear if target blood pressure ranges for patients with SCI should differ from those used in the general population. The selection of medication may be influenced by SCI-related factors. For instance, because of the concomitant diuresis, thiazide diuretics, which are advised as first-line alternatives for the general population [29], may not be practicable for people undergoing intermittent catheterization for bladder control.

Smoking

It is commonly known that smoking causes coronary heart disease. Shortly after quitting smoking, there is a considerable reduction in the risk of myocardial infarction. It is essential to identify every smoker in a methodical manner. Regular one-on-one intervention sessions or a variety of support groups are necessary for quitting smoking.
It is very important that smoking cessation is established once and for all and that patients continue to visit counseling groups. Every time they see a patient, doctors should inquire about smoking habits, encourage smokers to stop, offer counselling and help them create a quitting plan, and consider referring them to special programs and/or pharmacotherapy, such as nicotine and bupropion. Using nicotine gum or patches is one option. As alternatives, there are nicotine sprays, lozenges, and inhalers. Clinicians should be prepared to seek out smokers and contact those who have relapsed in order to discuss options for new pharmaceutical techniques and additional counselling resources [30]. This is because nicotine dependency can be characterized by relapses and remissions. It should be urged to limit exposure to secondhand smoke at home and at work.

Lipid Abnormalities
A known risk factor for coronary heart disease is elevated LDL. Significant LDL reduction significantly slows the progression of coronary artery disease, according to strong evidence. High HDL levels are inversely linked to the risk of coronary heart disease. HDL is a powerful preventive factor. There is evidence to imply that chronic SCI patients have lower HDL levels than the overall population [31]. In comparison to only 10% of the general population, 24% to 40% of people with SCI had an HDL value of less than 35 mg/dL [32].
Assessing the patient's level of risk is the first step in choosing the best course of treatment for lipid disorders [27]. Although there is no universal consensus on optimal screening guidelines, there is agreement that screening recommendations should be based on determining overall cardiovascular disease risk [33, 34]. While the results of studies in able-bodied adults cannot necessarily be fully extrapolated to those with SCI due to physiological differences. A fasting lipid profile should be performed on people with SCI at least every five years, and more frequently in those who are at higher risk or whenever signs of dyslipidemia are seen [32].
Diabetes, hypothyroidism, and specific drugs like anabolic steroids are examples of secondary dyslipidemia causes that should be ruled out in patients who have aberrant findings. The level of risk-reducing therapy should be adapted to the absolute risk of each patient. Effective lifestyle changes are essential for HDL intervention at this time because there is no widespread agreement on the best medication treatments for low HDL. These include giving up smoking, losing weight in overweight individuals, and getting more active in people who are sedentary. Everyone should be urged to live a heart-healthy lifestyle. Although niacin has been reported to increase HDL, including in a study in people with SCI, it is no longer recommended either as monotherapy or as an adjunct to statin therapy due to a lack of demonstrated benefit on mortality or clinical outcomes of cardiovascular and has a higher frequency of adverse reactions with its use [30].
The medication of choice for lowering LDL and cholesterol is statins [35]. In addition to decreasing levels of triglycerides and total and LDL cholesterol, statins are a class of lipid-lowering medications that may also have anti-inflammatory and plaque-stabilizing properties.
Strong evidence is reported by the American College of Cardiology/American Heart Association (ACC/AHA) to support the use of statins for secondary prevention in individuals with clinically atherosclerotic cardiovascular disease, primary prevention in people with primary elevations of LDL ≥ 190 mg/dL, primary prevention in individuals with diabetes aged 40 to 75 years old who have LDL between 70 and 189 mg/dL, and primary prevention in individuals without diabetes and with an estimated 10-year risk of developing the disease. The ACC/AHA recommends fixed-dosage statin therapy using either a high-intensity regimen (daily dose lowers LDL by approximately 50% or more) or a moderate regimen (daily dose reduces LDL levels by about 30% to <50%) [27]. This is preferable to treating a specific LDL-C target [36, 37].
The recommendations state that creatine kinase testing should only be done in cases of muscle complaints such as weakness, soreness, tenderness, cramps, or stiffness in persons taking statins. Given the limitations in assessing these symptoms in those with SCI, this guideline may not necessarily apply and there may be a case for increased surveillance in CK monitoring in this patient population. But there isn't enough proof to back up targeted monitoring. Despite the fact that the majority of research examining the use of statins was conducted in the non-SCI population, a retrospective analysis of a relatively small sample of people with chronic SCI also revealed lower mortality in those receiving statin treatment [35].

Physical Activity
Strong evidence exists that sedentary behavior increases the risk of coronary heart disease on its own [23]. Physical activity has been linked to a number of possible advantages. Improvements in endothelial function, a decrease in systemic inflammation, an increase in insulin sensitivity, improved endothelial function, a greater ability of the heart to use oxygen more effectively, a reduction in blood pressure, and favorable effects on platelet stickiness and blood viscosity are just a few of these [21].
Due to poor mobility, access issues, a lack of options for exercise, and the stress of musculoskeletal injuries, people with SCI frequently lead sedentary lives. In addition, because of muscle loss and altered autonomic function, they have a different physiological reaction to exercise [37]. Cardiovascular fitness cannot be achieved by normal everyday activity and movement with SCI.
Aerobic exercise can help people with SCI increase their work capacity and cardiovascular fitness, but there is a lack of information on the best ways to promote cardiovascular fitness and the effects of exercise on cardiovascular risk in SCI.

Exercises that are readily available and suited to their needs and capabilities, such as upper body aerobic exercise, strengthening exercises, arm or wheelchair ergometry, swimming, and electrically stimulated exercise options like cycling, rowing, and electrically assisted arm ergometry, should be encouraged for people with SCI [35].
Exercise tolerance, endurance, and cardiovascular fitness can all be improved by training. The Department of Health and Human Services, which tracks Americans' physical activity levels, advises adults with disabilities to engage in at least 150 minutes of moderate-intensity exercise per week, 75 minutes of vigorous exercise per week, or an equivalent amount of moderate-intensity exercise plus intense aerobic exercise. It is recommended to spread out aerobic exercise throughout the course of the week in bursts of at least 10 minutes [38]. Additionally, 2 or more days per week should be dedicated to moderate-to-vigorous muscle-strengthening exercises that target all major muscle groups. These exercises provide additional health advantages. They should avoid inactivity and engage in regular physical activity to the best of their abilities if these suggestions cannot be followed. People with impairments should speak with their doctor about the appropriate amount and kind of exercise for them [39].

Obesity and Overweight
Obesity has a negative impact on cardiac function, enhances the risk factors for coronary heart disease, and is a standalone risk factor for cardiovascular disease. In general, individuals with SCI consume less energy than the general population when the acute phase of the damage is over [39]. So it's not unusual for people to gain a lot of weight.
Low muscle mass and a higher body fat percentage are found in those with persistent quadriplegia. Increased risk of coronary heart disease and insulin resistance are associated with excess body fat [40]. Due to the loss of muscle mass and the existence of a higher percentage of body fat after SCI, conventional measurements of obesity (such as weight or BMI) may not be accurate [41]. It is therefore challenging to determine the prevalence of obesity in SCI. A decrease in calorie intake is advised because energy needs decline with chronic damage.
Nutritional counselling and management are particularly crucial since people with SCI frequently consume diets that are inadequate. Depending on the severity of the damage, it has been suggested that basal energy requirements should be decreased from those calculated for healthy individuals by a factor ranging from 10% for those with low paraplegia to 25% for those with high quadriplegia. Depending on the severity of SCI, the optimal body weight may be 10–20 kg lower than what is advised for the general population due to decreased muscle mass [42].

Diabetes Mellitus, Impaired Glucose Tolerance, and Hyperinsulinemia
People with diabetes mellitus (DM) are at an especially high risk for coronary heart disease. Although lipid problems account for a large portion of this risk, other elements, including insulin and blood sugar levels, also seem to play a separate role [43]. Insulin levels and the risk of developing cardiovascular disease are positively correlated. Abdominal obesity, atherogenic dyslipidemia, high blood pressure, insulin resistance, and prothrombotic and proinflammatory states are among the risk factors that make up the metabolic syndrome. In comparison to those without diabetes, SCI patients with DM had a greater rate of coronary heart disease, myocardial infarction, and other comorbidities [43]. Although statistics are conflicting and prevalence is greatly influenced by the study population's demographics, it has been shown that people with chronic SCI are more likely to have impaired glucose tolerance, insulin resistance, and hyperinsulinemia. According to one study, veterans with SCI had DM rates that were higher than those in the general population, but these rates were comparable to those of other veterans [43], indicating that demographic factors other than SCI may be responsible for this finding.
The risk of insulin resistance may be increased by factors such as age, race, ethnicity, military service, and family history. Important therapies for these patients include weight control, dietary modifications, exercise, and glycemic control. A population with SCI and DM benefits significantly when diabetic measures are given special attention [44].

Psychosocial Factors
Psychosocial factors may increase the risk of coronary heart disease, according to the available research [45]. Depression, social isolation, and ongoing stress from daily life are a few of the elements that have been discovered and for which there is strong evidence. Epidemiological research has shown a graded correlation between depression severity and the likelihood of coronary events. Acute myocardial infarction or unstable angina can be caused by depression, which is an independent risk factor for mortality [46-48].
Evidence of platelet dysfunction caused by depression and the stimulation of atherogenesis by hormonal changes, such as elevated cortisol, are two proposed causes. The absence of family, friends, or group activities as a regular component of someone's life is a measure of social isolation. After a myocardial infarction, a considerable risk of recurrent cardiac attacks has been linked to social isolation or a lack of emotional support [45].
There is evidence that people with SCI are more likely than the general population to experience depression and social isolation, although prevalence estimates vary [45]. Following appropriate medical and psychological therapies, monitoring of these patients' depression symptomatology and social support network should be a regular component of the process.

Emerging Risk Factors
Studies have revealed a wide range of other potential risk factors for coronary heart disease in addition to known risk factors, although many of these have not yet been the subject of adequate research to draw firm conclusions on their importance or

treatment options. Oxidants, platelet activators, increased plasma homocysteine, lipoproteins, apolipoprotein B, prothrombotic factors, and proinflammatory factors, including high-sensitivity C-reactive protein (CRP), are a few of these variables [49]. Although there are a few findings specifically mentioning the SCI community, the majority of studies reported on coronary artery disease refer to the general population. According to some findings, platelet abnormalities in SCI may include anomalies in aggregation and resistance to prostacyclin inhibition [40]. The importance of these findings is not yet evident. In the SCI group, several investigations have found higher CRP levels. However, inflammatory markers can be elevated in SCI patients for a variety of reasons, such as the presence of UT infections or pressure injuries, and it is unclear how these indicators relate to the risk of cardiovascular disease in SCI [50].

Conclusion

Males are more likely to have spinal cord injuries, and those injuries are more severe. The likelihood of cervical spinal cord injury increases with age, with people over 65 being the most susceptible. Transverse sections of the spinal cord show effects on the cardiovascular system, by lowering both mean blood pressure and heart rate. People with chronic SCI are more likely to have poor glucose tolerance, insulin resistance, and hyperinsulinemia, according to reports. Important therapies for these patients include weight management, dietary adjustments, exercise, and glycemic control. Successful prevention to lower the risk of coronary heart disease requires both patient and physician motivation.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

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