Cardiovascular complications of spinal cord injury

Summary

Background. The aim of this paper is to provide an overview of the autonomic innervation of the cardiovascular system and the cardiovascular complications of spinal cord injury.

Method. A literature search was conducted in the PubMed database using the search terms «traumatic spinal cord injury»/«traumatic spinal cord injuries» combined with the search terms «autonomic dysfunction», «autonomic dysreflexia» and «cardiovascular disease».

Results. The most important cardiovascular complications in the acute phase are bradyarrhythmia, hypotension, increased vasovagal reflexes, supraventricular/ventricular ectopic beats, vasodilation and venous stasis. Important in the chronic phase are orthostatic hypotension and impaired regulation of blood pressure, blood volume and body temperature. Tetraplegia is frequently accompanied by autonomic dysreflexia, reduced transmission of cardiac pain, loss of muscle mass in the left ventricle and pseudoinfarction. Patients with injuries above the sixth thoracic vertebra have a predisposition to autonomic dysreflexia. This is a condition characterised by sudden, uncontrolled sympathetic response accompanied by a rise in blood pressure. Autonomic dysreflexia usually causes headaches and erythema on the upper chest. The condition may cause cerebral haemorrhage and is potentially life-threatening. Patients with spinal cord injury have an increased risk of atherosclerotic disease due to overweight, lipid disorders, metabolic syndrome and diabetes. They are predisposed to thromboembolism due to venous stasis and hypercoagulopathy, especially immediately after the injury.

Interpretation. Knowledge and assessment of cardiovascular complications after spinal cord injury are important for correct diagnostics, planning of preventive measures and optimal therapy.

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Traumatic spinal cord injury is defined as an acute injury of the spinal cord which results in a varying degree of paralysis and/or sensory disorder (1). Injury to the cauda equina is included in the definition, but other isolated injuries to nerve roots are excluded (2).

Injuries to the autonomic nervous system are the cause of many of the cardiovascular complications following a spinal cord injury. Cardiovascular dysfunction in patients with cervical and high thoracic spinal cord injury may be life-threatening and may exacerbate the neurological impairment due to the spinal cord injury. Patients have higher morbidity and mortality as a result of the autonomic dysfunction.

In this overview we provide a brief outline of the autonomic innervation of the cardiovascular system. Various aspects of cardiovascular dysfunction following spinal cord injury are then discussed.

Method

A literature search was conducted in the PubMed database using the search terms «traumatic spinal cord injury»/«traumatic spinal cord injuries» combined with the search terms «autonomic dysfunction», «autonomic dysreflexia» and «cardiovascular disease».

The search was limited to articles published before 1 April 2011, but was not limited backward in time. There was no restriction with respect to language, patient's age at the time of the injury or the design of the studies, but the articles had to be available in full text via either online or via the Bergen University Library. Relevant articles were selected and the data extracted by the first author (EMH).

The autonomic nervous system – anatomy

The parasympathetic preganglionic neurons are located in the nuclei of the four cranial nerves n. oculomotorius (III), n. facialis (VII), n. glossopharyngeus (IX) and n. vagus (X) in the brain stem. Most of the internal organs of the body are supplied with parasympathetic innervation by the n. vagus. The exceptions are the genitals, bladder, distal intestine and anus, which are supplied by the parasympathetic sacral nerves S2–4 (3). Peripheral blood vessels have no parasympathetic innervation, with the exception of the vessels that supply the pelvic organs (3).

The sympathetic preganglionic neurons are located in the intermediolateral cell column laterally in the grey matter of the spinal column at level T1–L2 (3).

Depending on the level of the SCI, the various parts of the sympathetic nervous system will be disconnected from supraspinal control, which will result in altered sympathetic activity below the level of the injury (4). Because the parasympathetic preganglionic neurons of the heart extend from the cranial nerve nuclei in the brain stem, the parasympathetic innervation of the heart will be intact in the event of an injury to the spinal cord. Because the bladder, genitals and lower portion of the intestine are innervated by the sacral portion of the spinal column (S2–S4), their parasympathetic inn-

Main points

- Cardiovascular complications are common after spinal cord injury and result in increased morbidity and mortality
- The most important complications are arrhythmia, hypotension and altered vasovagal reflexes
- Autonomic dysreflexia is a potentially life-threatening condition that requires immediate treatment
- Persons with SCI are at increased risk of thromboembolism in both the acute and the chronic phase

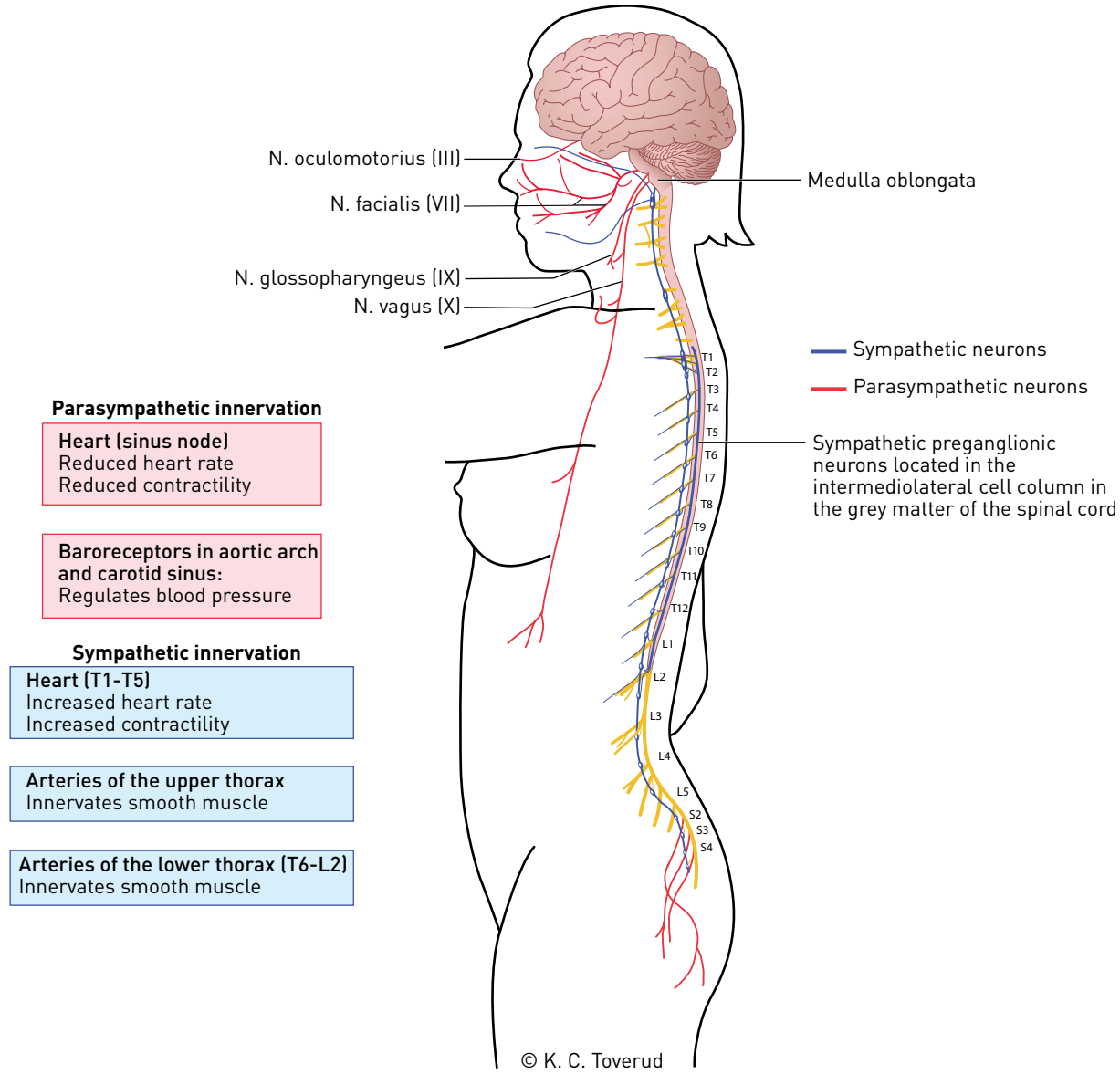


Figure 1 *The parasympathetic and sympathetic innervation of the heart will respectively reduce and increase the heart rate. Sympathetic neurons in the upper thoracic part of the spinal cord innervate the cardiovascular system of the upper thorax. The sinus node receives sympathetic innervation from T3–T4 and parasympathetic innervation from the vagal nerve. Parasympathetic afferent nerves from baroreceptors in the aortic arch and carotid sinus go to the medulla oblongata via the cranial nerves n. glossopharyngeus and n. vagus.*

ervation will be disconnected from supraspinal control in the event of injuries at the level of the conus medullaris (S2–S4) or above (Fig. 1).

Parasympathetic activity reduces the heart frequency and contractility, while sympathetic activity has a stimulating effect on the heart. The distribution of the sympathetic and parasympathetic activity that controls the heart is determined by information from the baroreceptors in the aortic arch, the carotid sinus and the coronary arteries and chemoreceptors in the carotid sinus (3).

Effect on the cardiovascular system

Disruptions of cardiovascular control following spinal cord injury are directly related to the level and degree of the injury.

In the event of a complete cervical injury, the connection between the upper autonomic centres in the brain and the intermediolateral cell column at level T1–L2 of the spinal cord will be destroyed. Patients with cervical injuries have a higher risk of bradycardia (29 %), sudden unprovoked cardiac arrest (16 %) and conduction system disturbances, particularly in the first few weeks after the injury (5). Sudden death is not unusual either (6).

Immediately after a spinal cord injury, there is in almost all patients a sudden loss of the autonomic effect of the smooth muscle in the walls of the blood vessels, and as a result vasodilation occurs. The acute loss of sympathetic stimulation results in bradycardia (7). During the acute phase, the arterial hypotension (neurogenic shock) may be misinterpreted as loss of volume.

The vagus nerve is hypersensitive immediately after an injury. This normally lasts for 2–3 weeks. Sometimes it lasts longer, and in some cases implantation of a temporary or permanent pacemaker is required. During this period, it is important to avoid activating the n. vagus to avoid reinforcing the vagal reflexes. Atropine should be available. Hypoxia increases vagal activity, so hypoventilation should be avoided. All forms of tube in the nose/mouth and throat may cause bradycardia and increased vagal reflexes (8). This can be a life-long problem in patients with high, complete injuries, whereas in patients with lower and/or incomplete injuries the situation may normalise after 4–5 weeks (6). Common cardiovascular complications are summarised in Box 1 (8).

Autonomic dysreflexia

Autonomic dysreflexia occurs in patients with an injury at T6 level or above. The con-

dition is induced by sensory stimulation below the level of the injury, and is characterised by sudden, uncontrolled response in the sympathetic nervous system. This results in episodes of paroxysmal hypertension, frequently accompanied by baroreflex-mediated bradycardia (9, 10). Systolic blood pressure of 250–300 mm Hg and diastolic blood pressure of 200–220 mm Hg have been recorded with autonomic dysreflexia (11).

Autonomic dysreflexia most frequently develops during the first 2–4 months after the injury (12) and affects 10 % during the first year (13). The lifetime frequency among persons with spinal cord injury is 19–70 %. The condition occurs more frequently in patients with cervical lesions and complete injuries (14).

In 85 % of the cases, autonomic dysreflexia is due to a full urinary bladder as a result of retention or catheter blockage (14). Other triggering factors may be distension of the intestine due to obstipation, anal fissures, urinary tract infection, urological and endoscopic procedures, cystoliths, pressure ulcers, ingrown toenails, pregnancy, childbirth, sexual activity and painful stimuli.

The symptoms are an intense, pulsing headache, blurred vision, anxiety, agitation, shortness of breath, nasal congestion, hot flushes, facial flushing, paradoxical sweating above the level of the injury, cold, clammy skin, goose pimples and nausea (14). A rise in systolic pressure of 20–40 mm Hg above the normal level in adults and more than 15 mm Hg in children may in itself be a sign of autonomic dysreflexia.

Some patients only develop mild symptoms, for example if they have a full bladder or intestine, as a signal that the intestine or bladder must be evacuated (15). Some disabled athletes induce mild dysreflexia and thereby higher blood pressure in order to improve their performance (16).

If untreated, autonomic dysreflexia may potentially be life-threatening by causing hypertensive cerebral haemorrhage (17). In one case history, cerebral haemorrhage had occurred at a blood pressure of 180/90 (18). When patients undergo surgery (appendectomy, Caesarean section etc.) it is important that they have adequate anaesthesia in order to avoid autonomic dysreflexia (19).

In cases of autonomic dysreflexia, it is of primary importance to prevent, identify and eliminate triggering factors. Patients receive thorough training in recognising the symptoms.

If the condition is suspected, tight clothing should be loosened and other possible external causes checked. The patient's head should be raised and his or her legs lowered to reduce the intracranial pressure and reduce the risk of cerebral haemorrhage. Blood pressure should be measured and treated, if necessary medically with anti-hypertensive drugs which act rapidly and for a short period of time. The aim of the treatment is to normalise pulse and blood pressure and eliminate the patient's symptoms. Fig. 2 shows our proposed treatment algorithm, based on treatment algorithms developed in other countries (8, 20, 21).

Nitroglycerine is the first-choice drug, but there are no studies of the effectiveness and safety of using nitrates in patients with SCI. Nifedipine (calcium channel blocker) can be useful (19). Preliminary findings indicate that captopril (ACE inhibitor) is effective (22). There is limited documentation on the use of selective α1-antagonists (19, 23).

Common cardiovascular complications after the acute phase

The most important complications after the acute phase (4–5 weeks after the injury) are autonomic dysreflexia, orthostatic hypotension (also in sitting position), reduced cardiovascular reflexes (which regulate blood pressure, blood volume and body temperature) and the absence of cardiac pain. Secondary cardiac changes in connection with tetraplegia are loss of muscle mass in the left ventricle and pseudoinfarction – a rise in troponin with or without ECG changes (8, 24).

Reaction to physical stress

Work physiology stress tests of patients with SCI show that patients with complete tetraplegia can seldom raise their heart rate to more than 125 per minute with maximum loading (25, 26). Autonomic failure occurs to a varying extent, also with incomplete cervical injuries, and may cause patients to become pale and feel unwell in connection with physical exertion.

There is also exercise-related vasodilation in working muscles. Patients with SCI lack compensatory vasoconstriction in other muscles and organs below the level of injury. This results in an exercise-induced fall in blood pressure leading to critically low perfusion pressure in the working muscle and thereby to physical exhaustion (26). During physical work, heat accumulates to a greater extent in these patients than in functionally healthy individuals. Under physical stress they may therefore develop a paradoxical fall in blood pressure and rise in body temperature (27). The heart rate of patients with a high thoracic injury may increase to normal maximum frequency and they will then have fewer problems due to fall in blood pressure when they are exhausted (15, 26, 28). However, they do not have the same rise in blood pressure in connection with physical exertion as functionally healthy persons. Patients with injuries below T10 have a normal blood pressure response to physical stress. Figure 3 shows functional ability in relation to level of injury and autonomic control (8).

Cardiovascular disease

Lack of physical activity, reduced muscle mass and the development of metabolic syndromes increase the risk of coronary disease after SCI (29–31). Most risk factors for cardiovascular disease occur more frequently in this patient group than in others. A higher prevalence of overweight, lipid disorders, metabolic syndromes and diabetes has been found (32).

The risk of developing cardiovascular disease is associated with both the level of the SCI and clinical findings, and increases with increasing age, increasing rostral level of injury and the severity of the SCI (complete vs incomplete) (33).

Patients with SCI may additionally have cardiac diseases that are not related to the injury (8). In patients with SCI above T4 and a pacemaker, a lead fracture may result in autonomic dysreflexia (34).

A clinical study of 47 persons with SCI and without symptoms of coronary disease demonstrated that during pharmacological stress testing 84.6 % of the patients with complete tetraplegia showed signs of myocardial ischaemia measured with single photon emission computed tomography (SPECT). So did 64 % of those with incomplete tetraplegia, 55 % of those with complete paraplegia and 50 % of those with incomplete paraplegia (35, 36).

Box 1

Common cardiovascular complications following spinal cord injury in both acute and chronic phase, based on an article by Phillips et al. (8)

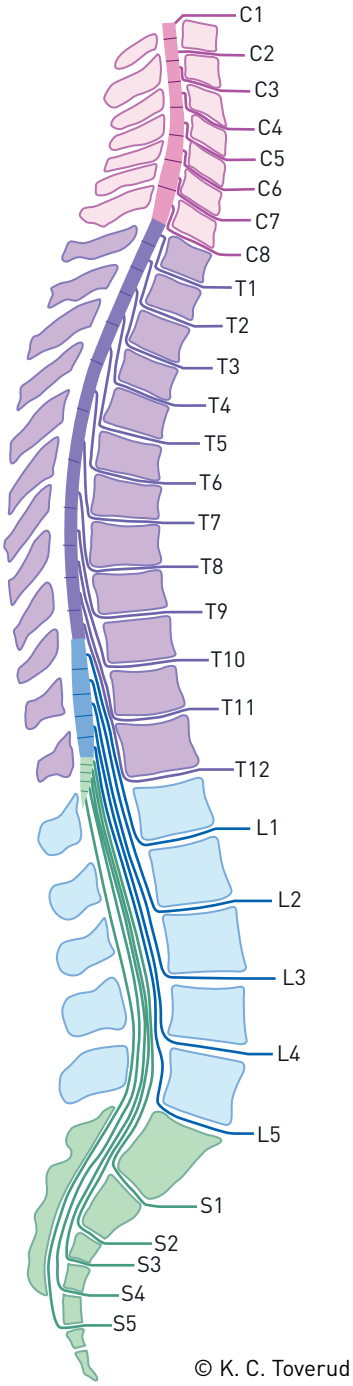
- Acute phase:
  - Sinus bradycardia
  - Loss of vascular tone
  - Bradyarrhythmia with compensatory rhythm
  - Supraventricular/ventricular ectopic beats
  - Arterial hypotension
  - Orthostatic hypotension
  - Enhanced vasovagal reflexes
  - Vasodilation and venous stasis
- Chronic phase:
  - Orthostatic hypotension
  - Impaired cardiovascular reflexes
  - Autonomic dysreflexia (lesions above T6)
  - Impaired transmission of cardiac pain (lesions above T4) resulting in impaired perception of chest pain
  - Loss of reflex changes in the heart (lesions T1–T4)
  - Atrophy of the heart with tetraplegia: loss of muscle mass in left ventricle
  - Pseudo-myocardial infarction: rise in troponin with or without ECG changes without demonstrable cardiovascular cause

Autonomic control

Cranial nerves
Parasympathetic control
- Heart
- Gastrointestinal

T1 – L5
Sympathetic control
- Cardiovascular
- Lungs
- Gastrointestinal
- Kidneys
- Sweat glands

L5 – S3
Parasympathetic control
- Bowel
- Bladder



Functional ability

C3 – C6
- Voluntary movement limited to Diaphragm and partial triceps only
- No grip function but may be able to performed limited arm cranking with hand/wrist straps
- Torso support necessary for stability in wheelchair

C5 – C8
- All or most triceps functions present
- Wrist flexion and extension present
- Most/all finger flexion and extension present permitting grasp mad release functions
- Are able to perform arm crank exercise with/without wrist/hand straps
- Torso support necessary for stability in wheelchair

T1 – L5
- Some upper extremity and back muscle function present
- Able to perform arm cranking with no wrist/hand straps
- Little or no abdominal muscle function
- Torso support may be necessary for stability in wheelchair

T6 – T10
- Most or all upper extremity and back muscle functions present
- Good muscle upper abdominal muscles
- Greater power output possible due to increased contribution of trunk musculature
- Good or normal stability in wheelchair

T11-T12
- Good abdominal and spinal extensor function
- Some hip flexor and adductor function
- Trunk musculature and increased "bracing" from hip flexors and adductors contributes to increased arm crank power output
- Good or normal stability in wheelchair

L1– S2
- Good/fair lower limb function
- Some walking possible
- Little or no physiological limitation on arm crank power output
- Normal stability in wheelchair

Figure 3 *Functional ability and autonomic control in relation to level of injury. The figure is modified after that of Phillips et al. (8) and reproduced with the permission of Elsevier*

Temperature regulation

Abnormal temperature control is another well-known clinical phenomenon after SCI. This is largely due to reduced sensory input to thermo-regulating centres and the loss of sympathetic control of temperature and sweat regulation below the level of injury (3). Patients with cervical and high thoracic injuries are particularly susceptible.

A number of temperature regulation disorders following SCI have been described. Some patients have poikilothermia – an inability to maintain a constant core temperature irrespective of the ambient temperature. Injuries above T8 are often associated with fluctuating temperature, hypothermia and hyperthermia (8).

Sweat secretion

The sweat glands are largely sympathetically innervated in the upper part of the body from T1–T5 and in the lower part of the body from T6–L2. Supraspinal control of sweat excretion is located in regions of the hypothalamus and amygdala (3).

Changes in sweat secretion often occur after SCI, and excessive sweating (hyperhidrosis), absence of sweating (anhidrosis) and diminished sweating (hypohidrosis) may all occur.

Excessive sweating is a common problem in persons with SCI (4, 12). In most individuals, episodic hyperhidrosis is usually associated with other autonomic dysfunctions such as autonomic dysreflexia and orthostatic hypotension, or with post-traumatic syringomyelia. Profuse sweating above the level of injury and minimal or no sweating below the level of injury is the most common. The cause is a compensatory increase in sweat secretion above the level of injury due to the loss of sympathetic stimulation below the level of injury, which results in reduced sweat production (37).

Sweating may also occur exclusively below the level of injury. This type of sweat is

reflex sweating, and is usually a symptom of a massive autonomic response that occurs particularly with cervical and high thoracic injuries (above T8–T10).

Thromboembolism

Patients with SCI have a higher risk of coagulation disorders and venous stasis due to physical inactivity, altered haemostasis with reduced fibrinolytic activity and increased factor VIII activity (38). They are therefore predisposed to thromboembolism (39, 40). The incidences of deep vein thrombosis and pulmonary embolism are estimated to be 15 % and 5 %, respectively, the first year after SCI, with a mortality rate of 1 %, largely among patients with pulmonary embolism (41). Studies have found a bimodal curve where the incidence is highest 2–3 weeks after the injury, followed by a small peak three months after the injury (42). During the chronic phase, the incidence of clinically significant thromboembolism is less than 2 % (38).

The Consortium for Spinal Cord Medicine has prepared guidelines for the prevention of thromboembolism (38). Compression stockings are recommended as a prophylactic measure (38). Prophylactic anticoagulation with low-molecular heparin should be started within 72 hours of injury, provided that there is no ongoing haemorrhage or coagulopathy (39). Patients with incomplete injuries should continue treatment until they are ambulatory. We recommend prophylactic treatment with low-molecular heparin for three months after injury in the case of complete injury. Patients with both complete and incomplete injuries who are additionally at risk of thromboembolism should continue treatment until discharge.

Early mobilisation and training should start as soon as the patient is medically stable (38). This should be maintained both at the hospital and after discharge.

Cardiovascular evaluation

The American Spinal Injury Association (ASIA) and the International Spinal Cord Society (ISCoS) recommend that patients be evaluated systematically with respect to neurogenic shock, cardiac rhythm disorders, orthostatic hypotension, autonomic dysreflexia, temperature regulation disorders and hyperhidrosis as part of their rehabilitation (7). Because all patients with SCI are at increased risk of cardiovascular disorders, they should all be evaluated.

The recommended evaluation includes physiological, biochemical and pharmacological tests (43). The physiological tests include recording of blood pressure, pulse, ECG and respiration in supine, sitting and standing position, during 60° tilt, isometric testing (of muscle strength), deep inspiration and expiration, cold test (cold pressor on the hand), arithmetic test (calculations), Valsalva's manoeuvre, hyperventilation, 24-hour blood pressure measurement, meal test and stress test (ergometer test with arm cycle). The physiological tests are described in Table 1 (44–54). Biochemical tests include catecholamines taken in supine and standing position, while the pharmacological tests include stimulation with adrenaline, noradrenaline, clonidine and atropine. The choice of tests depends on the patient's symptoms.

All patients should have their blood pressure and pulse measured in supine, sitting and standing position and have an ECG. These tests are carried out today at the spinal units. All patients should also undergo physical stress tests with simultaneous measurement of pulse, blood pressure and ECG.

Testing of blood pressure, pulse, ECG and respiration during 60° tilt test, isometric testing (of muscle strength), cold test (cold pressor on hand), arithmetic test (calculations) deep inspiration and expiration, hyperventilation, 24-hour blood pressure measurement, meal test and stress test (ergometer test with arm cycle) should preferably be carried out at a laboratory that focuses on and has special equipment for autonomic dysfunctions, and in teamwork involving several specialists: clinical neurophysiology and cardiology as well as departments that treat patients with SCI.

Arrhythmias, orthostatic hypotension and autonomic dysreflexia can all be treated medically. Preventive measures should also be implemented. Detection and prevention of autonomic disorders will give patients a better quality of life and an increased life expectancy (7).

Conclusion

Patients with SCI have a higher risk of cardiovascular complications and long-term effects as well as thromboembolism and autonomic dysreflexia. The recommended evaluation of cardiovascular dysfunction includes physiological, biochemical and pharmacological tests. Knowledge and assessment of cardiovascular complications following spinal cord injury are important for correct diagnosis and optimal therapy.

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References

1. Kraus JF, Franti CE, Riggins RS et al. Incidence of traumatic spinal cord lesions. J Chronic Dis 1975; 28: 471–92.
2. Maynard FM jr, Bracken MB, Creasey G et al. International standards for neurological and functional classification of spinal cord injury. Spinal Cord 1997; 35: 266–74.
3. Alexander MS, Biering-Sorensen F, Bodner D et al. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord 2009; 47: 36–43.
4. Wallin BG, Stjernberg L. Sympathetic activity in man after spinal cord injury. Outflow to skin below the lesion. Brain 1984; 107: 183–98.
5. Lehmann KG, Lane JG, Piepmeier JM et al. Cardiovascular abnormalities accompanying acute spinal cord injury in humans: incidence, time course and severity. J Am Coll Cardiol 1987; 10: 46–52.
6. Frankel HL, Mathias CJ, Spalding JM. Mechanisms of reflex cardiac arrest in tetraplegic patients. Lancet 1975; 2: 1183–5.
7. Krassioukov AV, Karlsson AK, Wecht JM et al. Assessment of autonomic dysfunction following spinal cord injury: rationale for additions to International Standards for Neurological Assessment. J Rehabil Res Dev 2007; 44: 103–12.
8. Phillips WT, Kiratli BJ, Sarkarati M et al. Effect of spinal cord injury on the heart and cardiovascular fitness. Curr Probl Cardiol 1998; 23: 641–716.
9. Gao SA, Ambring A, Lambert G et al. Autonomic control of the heart and renal vascular bed during autonomic dysreflexia in high spinal cord injury. Clin Auton Res 2002; 12: 457–64.
10. Hjeltnes N, Gjone R. [Autonomic dysreflexia in medullary section lesions]. Tidsskr Nor Lægeforen 1983; 103: 1933–6.
11. Karlsson AK. Autonomic dysreflexia. Spinal Cord 1999; 37: 383–91.
12. Karlsson AK. Autonomic dysfunction in spinal cord injury: clinical presentation of symptoms and signs. Prog Brain Res 2006; 152: 1–8.
13. Johnson RL, Gerhart KA, McCray J et al. Secondary conditions following spinal cord injury in a population-based sample. Spinal Cord 1998; 36: 45–50.
14. Shergill IS, Arya M, Hamid R et al. The importance of autonomic dysreflexia to the urologist. BJU Int 2004; 93: 923–6.
15. Teasell RW, Arnold JM, Krassioukov A et al. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil 2000; 81: 506–16.

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16. Bhambhani Y, Mactavish J, Warren S et al. Boosting in athletes with high-level spinal cord injury: knowledge, incidence and attitudes of athletes in paralympic sport. Disabil Rehabil 2010; 32: 2172–90.
17. Bycroft J, Shergill IS, Chung EA et al. Autonomic dysreflexia: a medical emergency. Postgrad Med J 2005; 81: 232–5.
18. Eltorai I, Kim R, Vulpe M et al. Fatal cerebral hemorrhage due to autonomic dysreflexia in a tetraplegic patient: case report and review. Paraplegia 1992; 30: 355–60.
19. Krassioukov A, Warburton DE, Teasell R et al. A systematic review of the management of autonomic dysreflexia after spinal cord injury. Vancouver : Spinal Cord Injury Rehabilitation Evidence, 2010: 1–33. www.scireproject.com/book/export/html/3.(22.1.12).
20. Middleton J. Treatment of autonomic dysreflexia for adults with spinal cord injuries. A medical emergency targeting health professionals. Rural Spinal Cord Injury Project. www.rah.sa.gov.au/hampstead/downloads/Auto_Dysreflexia2.pdf (17.1.2012).
21. Jackson CR, Acland R. Knowledge of autonomic dysreflexia in the emergency department. Emerg Med J 2011; 28: 866–9.
22. Esmail Z, Shalansky KF, Sunderji R et al. Evaluation of captopril for the management of hypertension in autonomic dysreflexia: a pilot study. Arch Phys Med Rehabil 2002; 83: 604–8.
23. Krassioukov A, Eng JJ, Warburton DE et al. A systematic review of the management of orthostatic hypotension after spinal cord injury. Arch Phys Med Rehabil 2009; 90: 876–85.
24. Lehmann KG, Shandling AH, Yusi AU et al. Altered ventricular repolarization in central sympathetic dysfunction associated with spinal cord injury. Am J Cardiol 1989; 63: 1498–504.
25. Dallmeijer AJ, Hopman MT, van As HH et al. Physical capacity and physical strain in persons with tetraplegia; the role of sport activity. Spinal Cord 1996; 34: 729–35.
26. Hjeltnes N. Cardiorespiratory capacity in tetra- and paraplegia shortly after injury. Scand J Rehabil Med 1986; 18: 65–70.
27. Sawka MN. Physiology of upper body exercise. Exerc Sport Sci Rev 1986; 14: 175–211.
28. Nash MS, Bilsker MS, Kearney HM et al. Effects of electrically-stimulated exercise and passive motion on echocardiographically-derived wall motion and cardiodynamic function in tetraplegic persons. Paraplegia 1995; 33: 80–9.
29. Lee CS, Lu YH, Lee ST et al. Evaluating the prevalence of silent coronary artery disease in asymptomatic patients with spinal cord injury. Int Heart J 2006; 47: 325–30.
30. Bauman WA, Spungen AM. Coronary heart disease in individuals with spinal cord injury: assessment of risk factors. Spinal Cord 2008; 46: 466–76.
31. Myers J, Lee M, Kiratli J. Cardiovascular disease in spinal cord injury: an overview of prevalence, risk, evaluation, and management. Am J Phys Med Rehabil 2007; 86: 142–52.
32. Groah SL, Weitzenkamp D, Sett P et al. The relationship between neurological level of injury and symptomatic cardiovascular disease risk in the aging spinal injured. Spinal Cord 2001; 39: 310–7.
33. Furlan JC, Fehlings MG. Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis, and management. Neurosurg Focus 2008; 25: E13.
34. Garshick E, Kelley A, Cohen SA et al. A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord 2005; 43: 408–16.
35. List CF, Pimenta AD. Sweat secretion in man. VI: Spinal reflex sweating. Arch Neurol Psychiatry 1944; 51: 501–7.
36. Silver JR, Randall WC, Guttmann L. Spinal mediation of thermally induced sweating. J Neurol Neurosurg Psychiatry 1991; 54: 297–304.
37. Yaggie JA, Niemi TJ, Buono MJ. Adaptive sweat gland response after spinal cord injury. Arch Phys Med Rehabil 2002; 83: 802–5.
38. Consortium for Spinal Cord Medicine. Prevention of thromboembolism in spinal cord injury. 2.utg. Washington, DC: Paralyzed Veterans of America, 1999. www.metrohealth.org/documents/patient%20services/norscis/DVTPrevention.pdf (17.1.2012).
39. Ploumis A, Ponnappan RK, Maltenfort MG et al. Thromboprophylaxis in patients with acute spinal injuries: an evidence-based analysis. J Bone Joint Surg Am 2009; 91: 2568–76.
40. Waring WP, Karunas RS. Acute spinal cord injuries and the incidence of clinically occurring thromboembolic disease. Paraplegia 1991; 29: 8–16.
41. Merli GJ, Crabbe S, Paluzzi RG et al. Etiology, incidence, and prevention of deep vein thrombosis in acute spinal cord injury. Arch Phys Med Rehabil 1993; 74: 1199–205.
42. Lamb GC, Tomski MA, Kaufman J et al. Is chronic spinal cord injury associated with increased risk of venous thromboembolism? J Am Paraplegia Soc 1993; 16: 153–6.
43. Mathias CJ. Diseases of the autonomic nervous system. I: Warrell DA, Cox TM, Firth JD, red. Oxford Textbook of Medicine. 5. utg. Oxford: Oxford University Press, 2010: 5055–68.
44. Claydon VE, Steeves JD, Krassioukov A. Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord 2006; 44: 341–51.
45. Ogata H, Nakahara M, Sato T et al. Hyperventilation during orthostatic challenge in spinal cord-injured humans. Clin Auton Res 2009; 19: 327–34.
46. Bluvshtein V, Korczyn AD, Akselrod S et al. Hemodynamic responses to head-up tilt after spinal cord injury support a role for the mid-thoracic spinal cord in cardiovascular regulation. Spinal Cord 2011; 49: 251–6.
47. Prévinaire JG, Mathias CJ, El Masri W et al. The isolated sympathetic spinal cord: Cardiovascular and sudomotor assessment in spinal cord injury patients: A literature survey. Ann Phys Rehabil Med 2010; 53: 520–32.
48. Yamamoto M, Tajima F, Okawa H et al. Static exercise-induced increase in blood pressure in individuals with cervical spinal cord injury. Arch Phys Med Rehabil 1999; 80: 288–93.
49. Coutts KD, Rhodes EC, McKenzie DC. Maximal exercise responses of tetraplegics and paraplegics. J Appl Physiol 1983; 55: 479–82.
50. Catz A, Bluvshtein V, Pinhas I et al. Cold pressor test in tetraplegia and paraplegia suggests an independent role of the thoracic spinal cord in the hemodynamic responses to cold. Spinal Cord 2008; 46: 33–8.
51. Curt A, Nitsche B, Rodic B et al. Assessment of autonomic dysreflexia in patients with spinal cord injury. J Neurol Neurosurg Psychiatry 1997; 62: 473–7.
52. Krassioukov A. Autonomic function following cervical spinal cord injury. Respir Physiol Neurobiol 2009; 169: 157–64.
53. Catz A, Bluvshtein V, Pinhas I et al. Hemodynamic effects of liquid food ingestion in mid-thoracic paraplegia: is supine postprandial hypotension related to thoracic spinal cord damage? Spinal Cord 2007; 45: 96–103.
54. Claydon VE, Hol AT, Eng JJ et al. Cardiovascular responses and postexercise hypotension after arm cycling exercise in subjects with spinal cord injury. Arch Phys Med Rehabil 2006; 87: 1106–14.

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