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Review Article

Potential benefits of spinal cord stimulation treatment on quality of life for paralyzed patients with spinal cord injury

Xiang-Ling Huang[a,b], Yu-Chen Chen[a,c], Chang-Chih Kuo[d]*, Sheng-Tzung Tsai[a,e]*

[a]Department of Neurosurgery, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan, [b]Department of Nursing, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Tawian, [c]Department of Medical Informatics, Tzu Chi University, Hualien, Taiwan, [d]Department of Physiology and Master Program in Biomedical Sciences, School of Medicine, Tzu Chi University, Hualien, Taiwan, [e]School of Medicine, Tzu Chi University, Hualien, Taiwan

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Abstract

Spinal cord injury (SCI) is a severe central nervous system injury that can cause sensory or motor dysfunction. Although mortality rates for people with spinal cord injuries have dropped dramatically with advances in medicine, chronic long-term sequelae after SCI persist. The most bothersome problems reported by patients include pain, spasticity, urinary dysfunction, and loss of motor function. Thus, quality of life (QoL) is an essential issue in chronic SCI. Spinal cord stimulation (SCS) applies an adjustable, nondamaging electrical pulse that can reduce uncomfortable comorbidities and improve mobility, thus enhancing the QoL of patients with SCI. This review summarizes pivotal breakthroughs from SCS for individual clinical impairment from SCI. We conclude that careful evaluation of SCS can help improve neuropathic pain, spasms, motor symptoms, and voiding dysfunction in patients with SCI, thus improving QoL.

Keywords: *Quality of life, Spinal cord injury, Spinal cord stimulation*

Introduction

Spinal cord injuries (SCIs) are severe central nervous system (CNS) injuries resulting in motor or sensory dysfunction and can cause physiological, psychological, and socioeconomic problems [1]. The incidence rate of traumatic SCI in the United States is 54 per 1 million people [2]. The annual incidence rate of SCI is 17.2 per 1 million people in Taiwan [3]. People with SCI experience significant impairments in many parts of their lives, including impacts on their families, socialization, economic issues, and quality of life (QoL) [4]. SCI-related morbidity and mortality are often caused by complications such as pneumonia, pressure ulcers, or other issues that can lead to increased rates of rehospitalization and decreased QoL [1]. SCI patients usually have several coexisting disabilities, including respiratory dysfunction, cardiovascular complications, neurogenic bladder, impaired autonomic dysregulation, spasticity, and medical refractory neuropathic pain [5-7]. Current treatments for chronic SCI include rehabilitation and limited medications. Therefore, studies exploring the safety and effectiveness of stem cell treatments, functional electrical stimulation, and epidural spinal cord stimulation (SCS) are warranted [8].

SCS is achieved through the use of an adjustable electrical pulse applied by a skilled physician who is trained to avoid inflicting further damage. SCS gives rhythmic electrical current to the spinal cord via electrodes inserted into the epidural space to activate central circuits that mediate locomotion and pain. Thus, epidural stimulation has also been confirmed to modulate medication efficacy for refractory neuropathic pain and improve patients' locomotion [9,10].

These clinical studies suggest that medical advances have improved treatment of SCI. The goal of comprehensive rehabilitation of individuals with SCI is to extend their

***Address for correspondence:** Dr. Sheng-Tzung Tsai,
Department of Neurosurgery, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, 707, Section 3, Chung-Yang Road, Hualien, Taiwan.
E-mail: flydream.tsai@tzuchi.com.tw
Prof. Chang-Chih Kuo,
Department of Physiology, School of Medicine, Tzu Chi University, 701, Chung-Yang Road, Section 3, Hualien, Taiwan.
E-mail: cckuo@mail.tcu.edu.tw

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life expectancy and help patients attain an optimal level of independent living and QoL, which is regarded as a key outcome of SCI [11,12]. In this review, we describe the QoL of patients with SCI and present clinical reports to support the effectiveness of SCS in individual domains of impairment in patients with severe SCI, such as pain, spasticity, urinary dysfunction, and motor impairment.

Quality of life after spinal cord injury

SCI is a devastating condition that commonly causes incomplete or complete loss of motor or sensory function below the level of the injury [13]. Functional impairments associated with SCI and the risk of several progressive secondary health conditions such as neuropathic pain or spasticity can result in restrictions in daily activities and social participation. This can further increase the risk of depression and anxiety and reduce QoL [14,15]. Boakye *et al*. reported that patients with SCI experience decreased QoL, compared to healthy controls and normative data. The most salient symptoms involve pain, deficiencies in physical functioning, and movement disorders [16,17].

Neuralgia and depression are tightly connected; there is evidence that depression often exists simultaneously with pain. Patients with SCI have been reported as having a more depressed mood than healthy individuals [18]. Thus, the association between depressive mood and pain denotes that the presence of pain significantly affects the long-term emotional distress experienced by patients with SCI. In addition, SCI patients with high pain severity have a significantly lower QoL than those with lower pain severity [18,19]. Therefore, managing chronic pain may improve the QoL of these patients.

Pain and spasticity often coexist in patients with SCI [6]; spasticity may additionally lead to musculoskeletal pain. One study found that spasticity indicators were consistently negatively correlated with life satisfaction and QoL [20]. Another QoL study evaluated spasticity severity in patients with SCI, demonstrating adverse effect of spasticity severity on the World Health Organization QoL Instrument assessment scores, especially on parameters assessing physical health and social relation [21].

Regarding motor function, patients with paraplegia had higher QoL scores than those with tetraplegia [22]. Skevington *et al*. reported that higher levels of injury led to decreased whole-body muscle strength and more severe muscle loss, which are strongly associated with lower QoL scores [23]. Moreover, another study found a significant and moderately strong positive relationship between the degree of motor activity and QoL in adults with SCI [24].

Furthermore, voiding dysfunction observed in the most SCI patients has been reported to be associated with increased complications and decreased QoL [25]. Hicken *et al*. reported that patients with poor bowel or bladder control after spinal cord injury (SCI) had a lower QoL than patients who could control their bowel and bladder voluntarily. Such reports indicate that bladder management is an essential part of SCI treatment [26].

Individuals who experience additional symptoms associated with SCI must cope with challenges at the physical, social, environmental, and psychological levels. Many studies have shown that SCS can reduce pain and spasms, improve voiding disorders, and improve motor function, as shown in Table 1. Therefore, improving these uncomfortable symptoms may facilitate the recovery of a good QoL. We discuss how SCS might improve the individually impaired system and disability after chronic SCI below.

Applications of spinal cord stimulation

Spinal cord stimulation for neuropathic pain

The traumatic SCI universal consequences are pain and spasticity. Neuropathic pain was rated as more severe and more intrusive than skeletal pain and was associated with lower QoL scores [6]. Such evidence shows that a complex relationship exists between depression and chronic pain and that symptoms can interact [27]. Therefore, developing a nondrug program to relieve chronic pain and ameliorate the QoL of patients with SCI is worthy of attention. SCS has been shown in many studies to improve various types of pain symptoms and reduce opioid use in patients. SCS is a possible treatment modality that is particularly relevant in light of current opioid addiction and abuse trends [28].

Electrotherapy began to gain traction in 1965 when Melzack and Wall proposed the gate control theory, which paved the way for the development of SCS and supported its underlying mechanisms [29]. The theory is that a mechanism in the dorsal horn of the spinal cord acts like a gate in which nerves that carry painful stimuli, vibrations, and touch terminate. Activation of large myelinated A-fibers inhibits the transmission of pain stimulation to the brain through the spinal integration center [30].

Clinically, electrodes are inserted percutaneously into the epidural space in the thoracic or thoracolumbar region of the spine and then advanced with radiological guidance. The optimal target site which produces paresthesia in the areas of the trunk or lower extremities experiencing pain can be determined during a trial period, with the electrodes externalized and attached to a current generator. After a period of testing time, usually 2–3 days, the optimal site where pain is replaced with paresthesia is determined. The electrodes are then completely internalized or replaced with surgical leads and attached to a subcutaneous internal pulse generator [9].

In a previous study, 30 patients with chronic, intractable pain associated with SCI received SCS to relieve their pain. The best range of stimulation parameters for relieving pain was from 0.5 to 3V, with a 200 s pulse and a frequency of 40–50 Hz. Patients reported the most relief from burning pain originating from damage to the CNS, but chronic bone, joint, and disk pain responses were relatively poor [31]. In a later study, 25 patients with intractable pain from chronic SCI received percutaneous SCS. At the end of the testing, 40.9% of patients reported an average of 65% remission of pain, with the patients experiencing pain spasms or constrictive pain with incomplete chest lesions reporting overall improvement, despite not achieving complete relief [32]. Furthermore, a

Table 1: A summary of clinical studies of spinal cord stimulation for spinal cord injury patients, including patients' injury level, treatment type, and outcome

Author/year	Level of spinal cord injury	ASIA Impairment Scale	Method	Parameters	Treatment type	Outcome
Nashold Jr. and Friedman, 1972 [31]	Lumbar (10) Other (20)	N/A	Bilateral dorsal column stimulation	Intensity: 0.5-3 V Frequency: 40-50 Hz Pulse width: 200 µs	Pain	Relief of the burning pain caused by central nervous system damage
Cioni *et al*, 1995 [32]	C1-7 (5) T1-11 (9) T12-L1 (11)	Complete (6) incomplete (19)	Epidural electrode	Pulse width: 210 µs 85 cycles/s	Pain	Reduced of burning pain (28.6%), painful spasms (75%), constriction (50%), tearing (33%), and allodynia (28.5%)
Levine *et al*, 2017 [33]	Neuropathic pain	N/A	Boston Scientific's Clik electrodes	Intensity: <2 mA Pulse width: 250-700 µs	Pain	Most patients obtained ≥50% pain relief
Cook and Weinstein 1973 [35]	N/A	N/A	Subdural extra arachnoid space electrode	Intensity: 0.4-4 V Frequency: 150-200 Hz Pulse width: 200 µs	Spasticity	Significant modification of abnormal neurological signs and dysfunction
Barola *et al*, 1995 [37]	C4 T7-8	N/A	Medtronic electrode	Intensity: Usually 2-130 Hz	Spasticity	Rapid decrease in spasms in 3 out of 6 patients
Biktimirov *et al*, 2020 [38]	n/a	N/A	SCS was performed in 18 patients, ITB was used in 15 patients	N/A	Spasticity	Improvement in spasticity index in both groups, but the SCS patients had better results
Herman *et al*, 2002 [44]	C5-6	C	5-6-5 specify, medtronic, progressive training	Frequency: 20–60 Hz	Motor	Better stamina, less effort, and lighter legs
Angeli *et al*, 2014 [45]	C7 (2) T5 (2)	A (2) B (2)	5-6-5 specify, medtronic; 6 months local motor training	Intensity: 0.5-7.5 V Frequency: 25 Hz or 30 Hz Pulse width: 450 µs	Motor	Participants' ability to voluntarily move improved
Rejc *et al*, 2015 [46]	C7 (1) T2 (1) T4 (2)	A (2) B (2)	5-6-5 specify, medtronic; stand training (1 h, 5 sessions/ week)	Intensity: 1-5 V Frequency: 5-50 Hz Pulse width: 450 µs	Motor	Two participants were able to stand, using minimal external assistance for hip extension
Walter *et al*, 2018 [51]	C5 (1)	B (1)	5-6-5 specify, medtronic	Intensity: 4-7 V Frequency: 25-45 Hz Pulse width: 300-450 µs	Voiding	Increased external anal sphincter and pelvic floor muscle tone and detrusor pressure
Herrity *et al*, 2018 [52]	C5 (1)	B (1)	5-6-5 specify, medtronic Step and stand training	Intensity: 0.8 V Frequency: 30 Hz Pulse width: 450 µs	Voiding	Improved reflexive voiding
Herrity *et al*, 2021 [53]	C (6) T (4)	A (6) B (4)	5-6-5 specify, medtronic Step and stand training	N/A	Voiding	Experimental group with significant improvement in bladder capacity, 4 participants were able to voluntarily void with intent

C: Cervical, T: Thoracic, ASIA: American Spinal Injury Association grading, SCS: Spinal cord stimulation, NA: Not available, SCI: Spinal cord injury, ITB: Intrathecal baclofen therapy

recent study recruited 15 SCI patients with upper extremity neuropathic pain, who underwent SCS implantation. At a 12-month follow-up, most patients obtained ≥50% pain relief, compared to baseline. They were also able to reduce opioid use and had significantly improved Short Form-36 QoL scores [33].

Spinal cord stimulation for spasticity

Spasticity is a symptom term that includes velocity-dependent increases in muscle tone, increased tendon reflexes, muscle spasms, and clonus. Severe spasticity may cause functional impairment and decreased QoL [6]. Currently, several spasticity management techniques are available, including physiotherapy, pharmacotherapy, and surgical management. Surgical options fall into three major categories: implantation of a device to deliver a steady dose of medication; physically severing nerves; or implantation of electrical stimulation devices [34].

The earliest treatment of SCS for spasticity dates back to 1973, when Cook and Weinstein demonstrated a significant improvement in spasticity in patients with multiple sclerosis who were experimentally treated with SCS for the management of pain [35]. Subsequently, the percutaneous epidural stimulation became a preferred method. Of the initial 166 patients in their study, 99 reported improvements. Others have also tested the efficacy of percutaneous SCS on reducing spasticity, expanding treatment application; however, these studies did not focus on patients with SCI alone [36]. Future efforts should focus on spinal spasticity. Barolat *et al*. found improvements when initially testing 6 patients with SCI implanted with an SCS system; it was found that stimulation rapidly decreased spasms in 3 of the 6 patients. Electrodes are placed below the injury level but do not affect above the injury level function, unaffected by stimulation. Researchers have concluded that this treatment outperforms other invasive techniques in treating incomplete SCI [37]. Further, Biktimirov *et al*. analyzed the surgical treatment report of 66 patients with severe spasticity after SCI. All patients underwent temporary implantation using an SCS system. If SCS improved spasticity, the patients underwent SCS surgery and permanent implantation. Otherwise, patients received intrathecal baclofen therapy. Fifteen patients received intrathecal baclofen. After the first 3 months of observation, the spasticity index improved significantly in both the groups, but the results were better in patients who underwent SCS [38].

Most patients have reported moderate or marked improvement, but there have also been some contradictory results, showing that SCS was not helpful in relieving spasticity. Therefore, it is likely that the frequency of electrical stimulation and the location of the leads are significant in determining patient outcomes and the outcomes of future clinical studies [39].

Spinal cord stimulation for functional motor control

SCI disrupts the communication between the spinal cord neuronal centers and muscles, causing different degrees of paralysis that dramatically affect a person's functional ability and QoL [40]. A study found that physically active individuals with SCI could manage their new lifestyles independently. The study shows that SCS could help patients increase functional independence, autonomy, self-worth, and efficacy. On the other hand, those who were inactive felt that they had little to no choice for self-determination about their lives [41]. Recently, many practices to improve motor function after SCI have been proposed in clinical trials, such as cell-based therapies, pharmacological approaches, electrical stimulation, and rehabilitation [40,42]. Among these techniques, SCS is a new method to directly stimulate muscle activity.

When electrical stimulation is applied to the lumbar spinal cord, the patient can experience brief motor-like lower extremity activity, also known as segmental muscle twitches. These are directly activated as monosynaptic reflexes initiated in large-diameter afferent nerves within the posterior (dorsal) root. Segmental muscle twitches suggest that human spinal cord circuits can generate motor-like activity even when not controlled by the brain, and that externally controlled continuous electrical stimulation of the spinal cord can possibly replace the brain-generated tonic drive [43]. With SCS, it may be possible to specifically place epidural electrodes over the thoracolumbar region to control lower limb spasticity following SCI. Minimally invasive SCS is a promising approach to harness the motor capacity of the lumbar spinal cord. This could help apply tonic stimulation to target spinal cord segments that are important to movement, especially when combined with other complementary interventions to restore sensory and motor function, such as partial weight-bearing therapy [9].

Herman *et al*. It was further evidence that for patients with SCI apart, from exercise rehabilitation, SCS could help them restore the ability to walk on exercise-assisted treadmills. After 1.5 months of continual training, SCS patients report better endurance, less effort, and a feeling of lighter legs. After 4 months of rehabilitation training, participants can walk 270 m [44]. Similar findings were reported in other studies; neuromodulation with a lumbosacral epidural spinal cord stimulator can allow four fully paralyzed individuals to recover lower extremity movement. With daily epidural stimulation and training, the ability of all four participants to voluntarily move their lower extremities improved over time. All participants exercised at the optimal frequency of 25 Hz or 30 Hz. They also received stand or step training. These results suggested that repetitive epidural stimulation and training can improve motor function to promote force production and accuracy, using task-specific learning [45]. Rejc *et al*. showed that the synergistic effects of stand training with lumbosacral SCS improved motor function and standing in four participants with complete paralysis. This study shows that it is possible for people with complete loss of sensory and motor function to recover the ability to stand if both active rehabilitation and personalized epidural stimulation are provided. That not only improves daily functioning but also combats the secondary health consequences of inactivity [46].

Spinal cord stimulation for voiding function

Bowel and bladder dysfunction caused by SCI may affect multiple aspects of QoL. In addition to the physical function being involved, it reduces self-esteem and the ability to maintain social relationships [26]. Two syndromes can distinguish bladder dysfunction after SCI into the lower motor neuron (LMN) and upper motor neuron (UMN) dysfunction. In LMN dysfunction, damage to the anterior horn cells of the sacrum (S2-S4) or their associated axons results in impaired bladder motor output and reduced or absent detrusor contractility, leading to relaxation and incontinence. UMN dysfunction is a performance by breaking off the descending spinal pathways, which affects and changes the input to the sacral voiding center, resulting in increased urethral resistance [47]. Neurogenic bladder additionally leads to a substantial decrease in QoL and can cause urinary tract infections, urinary stones, bladder and renal impairment, and rehospitalization [48].

Methods to manage voiding disorders in SCI patients include the Valsalva and Crede maneuver, intermittent catheterization, indwelling catheterization, medication with alpha-blockers, botulinum toxin injection, urethral stents, transurethral sphincterotomy, bladder augmentation, urinary diversion, posterior sacral rhizotomy, and electrical stimulation [49]. Currently, the application of electrical stimulation in different locations to restore functional bladder control has been investigated, such as the sacral anterior root, sacral nerve, pudendal nerve, and percutaneous tibial nerve [50]. Walter *et al*. showed that SCS adjusted detrusor pressure and external anal sphincter and pelvic floor muscle tone. In addition, the time needed for bowel management was significantly reduced [51].

In addition, Herrity *et al*. used SCS therapy to improve bladder control after SCI in a patient with C5 injury by adjusting electrode voltage, stimulating frequency, and stimulating pulse and step/stand training. After 4 months, bladder function mapping using different electrode configurations during repetitive cystometry showed increased reflex voiding efficiency. Specifically, a high frequency (about 30 Hz) proved to be improved bladder emptying than a lower frequency [52]. The researchers further divided the participants into experimental and control groups in a subsequent study, where the experimental group received epidural stimulation and step/stand training. The experimental group had a significant improvement in bladder capacity, and four participants demonstrated the ability to voluntarily void with intent [53].

Since neurogenic bladder is a common and important issue impacting the QoL of patients with chronic SCI, it is necessary to have a more aggressive attitude toward urinary management after SCI.

Conclusion

Compared with the general population, the QoL of patients with SCI is generally lower because of the sequelae surrounding such injuries. The majority of patients with SCI experience pain and movement disorders, which can even affect their psychology. Thus, QoL is a significant result in SCI practice and research. Recent studies have suggested that SCS might provide benefits for pain, spasticity, motor function, and voiding in patients with SCI. There is also growing evidence that epidural SCS can stimulate parts of damaged neural circuits caused by SCI and promote voluntary control of the lower extremities. In addition, considering the current epidemic of opioid addiction and abuse, SCS is an adjustable and reversible treatment option for patients with neuropathic pain. Although medication and surgery can treat spasticity, these treatments are still suboptimal in practice, providing incomplete relief of symptoms, with side effects. SCS may be an alternative way to physically relieve disabling spasticity.

Epidural stimulation of the lumbosacral spinal cord promotes effective lower extremity movement in paralyzed patients. These patients not only have improved motor function but may also have reduced complications from insufficient activity. Although SCS does not result in a great enough improvement in voiding function to avoid catheterization, voiding function does improve with SCS, which can still reduce the frequency of catheterization. This can provide more flexibility during daily activities and reduce sleep disruption.

However, the SCS procedure has some risks, such as lead migration, lead fracture and malfunction, device-related discomfort, dural damage, infection, and skin erosion [28]. Therefore, careful evaluation is required before its implementation. Furthermore, patients with SCI have different comorbidities, and the parameters of using SCS to treat different symptoms are likewise dissimilar. Thus, it is necessary to develop novel strategies using different SCS stimulating models to improve the clinical treatment.

Based on the consequences of SCI affecting numerous systems, SCS has the potential to improve motor and sensory function as an intervention. In particular, if activity-based rehabilitation is provided in combination with SCS, patients with sensory and motor complete SCI may be able to incorporate standing as part of their daily routine. We can, thus, presume that SCS can effectively improve the QoL of patients with SCI. Therefore, future research should focus on quantifying the improvement of QoL after SCS by multidisciplinary collaborations with clinical experts, neurophysiological, and medical engineers.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sezer N, Akkuş S, Uğurlu FG. Chronic complications of spinal cord injury. World J Orthop 2015;6:24-33.
2. Jain NB, Ayers GD, Peterson EN, Harris MB, Morse L, O'Connor KC, et al. Traumatic spinal cord injury in the United States, 1993-2012. JAMA 2015;313:2236-43.
3. Chen HY, Chiu WT, Chen SS, Lee LS, Hung CI, Hung CL, et al. A nationwide epidemiological study of spinal cord injuries in Taiwan from July 1992 to June 1996. Neurol Res 1997;19:617-22.
4. Squair JW, White BA, Bravo GI, Martin Ginis KA, Krassioukov AV. The economic burden of autonomic dysreflexia during hospitalization for individuals with Spinal cord injury. J Neurotrauma 2016;33:1422-7.
5. Hagen EM, Faerestrand S, Hoff JM, Rekand T, Gronning M. Cardiovascular and urological dysfunction in spinal cord injury. Acta Neurol Scand Suppl 2011;191:71-8.
6. Andresen SR, Biering-Sørensen F, Hagen EM, Nielsen JF, Bach FW, Finnerup NB. Pain, spasticity and quality of life in individuals with traumatic spinal cord injury in Denmark. Spinal Cord 2016;54:973-9.
7. Tollefsen E, Fondenes O. Respiratory complications associated with spinal cord injury. Tidsskr Nor Laegeforen 2012;132:1111-4.
8. Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: From point of injury to rehabilitation. J Spinal Cord Med 2017;40:665-75.
9. Tator CH, Minassian K, Mushahwar VK. Spinal cord stimulation: therapeutic benefits and movement generation after spinal cord injury. Handb Clin Neurol 2012;109:283-96.
10. Falowski S, Celii A, Sharan A. Spinal cord stimulation: An update. Neurotherapeutics 2008;5:86-99.
11. Noreau L, Shephard RJ. Spinal cord injury, exercise and quality of life. Sports Med 1995;20:226-50.
12. Leduc BE, Lepage Y. Health-related quality of life after spinal cord injury. Disabil Rehabil 2002;24:196-202.
13. Hearn JH, Cross A. Mindfulness for pain, depression, anxiety, and quality of life in people with spinal cord injury: A systematic review. BMC Neurol 2020;20:32.
14. Lude P, Kennedy P, Elfström ML, Ballert CS. Quality of life in and after spinal cord injury rehabilitation: A longitudinal multicenter study. Top Spinal Cord Inj Rehabil 2014;20:197-207.
15. Kunz S, Carrard V, Galvis Aparicio M, Scheel-Sailer A, Fekete C, Lude P, et al.. Longitudinal measurement invariance of the international

spinal cord injury quality of life basic data set (SCI-QoL-BDS) during spinal cord injury/disorder inpatient rehabilitation. Qual Life Res 2022;31:1247-56.

16. Boakye M, Leigh BC, Skelly AC. Quality of life in persons with spinal cord injury: Comparisons with other populations. J Neurosurg Spine 2012;17:29-37.
17. Kennedy P, Lude P, Taylor N. Quality of life, social participation, appraisals and coping post spinal cord injury: A review of four community samples. Spinal Cord 2006;44:95-105.
18. Ataoğlu E, Tiftik T, Kara M, Tunç H, Ersöz M, Akkuş S. Effects of chronic pain on quality of life and depression in patients with spinal cord injury. Spinal Cord 2013;51:23-6.
19. Burke D, Lennon O, Fullen BM. Quality of life after spinal cord injury: The impact of pain. Eur J Pain 2018;22:1662-72.
20. Westerkam D, Saunders LL, Krause JS. Association of spasticity and life satisfaction after spinal cord injury. Spinal Cord 2011;49:990-4.
21. Vural M, Yalcinkaya EY, Celik EC, Gunduz B, Bozan A, Erhan B. Assessment of quality of life in relation to spasticity severity and socio-demographic and clinical factors among patients with spinal cord injury. J Spinal Cord Med 2020;43:193-200.
22. Zwecker M, Heled E, Bluvstein V, Catz A, Bloch A, Zeilig G. Assessment of the unmediated relationship between neurological impairment and health-related quality of life following spinal cord injury. J Spinal Cord Med 2022;45:293-300.
23. Skevington SM, Lotfy M, O'Connell KA, WHOQOL Group. The World Health Organization's WHOQOL-BREF quality of life assessment: Psychometric properties and results of the international field trial. A report from the WHOQOL group. Qual Life Res 2004;13:299-310.
24. Stevens SL, Caputo JL, Fuller DK, Morgan DW. Physical activity and quality of life in adults with spinal cord injury. J Spinal Cord Med 2008;31:373-8.
25. Liu CW, Attar KH, Gall A, Shah J, Craggs M. The relationship between bladder management and health-related quality of life in patients with spinal cord injury in the UK. Spinal Cord 2010;48:319-24.
26. Hicken BL, Putzke JD, Richards JS. Bladder management and quality of life after spinal cord injury. Am J Phys Med Rehabil 2001;80:916-22.
27. Ullrich PM, Lincoln RK, Tackett MJ, Miskevics S, Smith BM, Weaver FM. Pain, depression, and health care utilization over time after spinal cord injury. Rehabil Psychol 2013;58:158-65.
28. Huang Q, Duan W, Sivanesan E, Liu S, Yang F, Chen Z, et al.. Spinal cord stimulation for pain treatment after spinal cord injury. Neurosci Bull 2019;35:527-39.
29. Melzack R, Wall PD. Pain mechanisms: A new theory. Science 1965;150:971-9.
30. Melzack R, editor. Gate Control Theory: On the Evolution of Pain Concepts. Pain Forum. London: Elsevier; 1996.
31. Nashold BS Jr., Friedman H. Dorsal column stimulation for control of pain. Preliminary report on 30 patients. J Neurosurg 1972;36:590-7.
32. Cioni B, Meglio M, Pentimalli L, Visocchi M. Spinal cord stimulation in the treatment of paraplegic pain. J Neurosurg 1995;82:35-9.
33. Levine AB, Parrent AG, MacDougall KW. Cervical spinal cord and dorsal nerve root stimulation for neuropathic upper limb pain. Can J Neurol Sci 2017;44:83-9.
34. Hodge JO, Brandmeir CL, Brandmeir NJ. Neuromodulation therapies for spasticity control: Now and beyond. Neurol India 2020;68:S241-8.
35. Cook AW, Weinstein SP. Chronic dorsal column stimulation in multiple sclerosis. Preliminary report. N Y State J Med 1973;73:2868-72.
36. Illis LS, Sedgwick EM. Spinal cord stimulation. In: Harrison MJ, editor. Contemporary Neurology. Ch. 37. Oxford United Kingdom: Butterworth-Heinemann; 1984. p. 301-12.
37. Barolat G, Singh-Sahni K, Staas WE Jr., Shatin D, Ketcik B, Allen K. Epidural spinal cord stimulation in the management of spasms in spinal cord injury: A prospective study. Stereotact Funct Neurosurg 1995;64:153-64.
38. Biktimirov A, Bryukhovetskiy I, Sharma A, Sharma HS. Spinal cord stimulation and intrathecal baclofen therapy for patients with severe spasticity after spinal cord injury. Prog Brain Res 2020;258:79-99.
39. Nagel SJ, Wilson S, Johnson MD, Machado A, Frizon L, Chardon MK, et al.. Spinal cord stimulation for spasticity: Historical approaches, current status, and future directions. Neuromodulation 2017;20:307-21.
40. Gomes-Osman J, Cortes M, Guest J, Pascual-Leone A. A systematic review of experimental strategies aimed at improving motor function after acute and chronic spinal cord injury. J Neurotrauma 2016;33:425-38.
41. Filipcic T, Sember V, Pajek M, Jerman J. Quality of life and physical activity of persons with spinal cord injury. Int J Environ Res Public Health 2021;18:9148.
42. Baptiste DC, Fehlings MG. Update on the treatment of spinal cord injury. Prog Brain Res 2007;161:217-33.
43. Dimitrijevic MR, Gerasimenko Y, Pinter MM. Evidence for a spinal central pattern generator in humans. Ann N Y Acad Sci 1998;860:360-76.
44. Herman R, He J, D'Luzansky S, Willis W, Dilli S. Spinal cord stimulation facilitates functional walking in a chronic, incomplete spinal cord injured. Spinal Cord 2002;40:65-8.
45. Angeli CA, Edgerton VR, Gerasimenko YP, Harkema SJ. Altering spinal cord excitability enables voluntary movements after chronic complete paralysis in humans. Brain 2014;137:1394-409.
46. Rejc E, Angeli C, Harkema S. Effects of lumbosacral spinal cord epidural stimulation for standing after chronic complete paralysis in humans. PLoS One 2015;10:e0133998.
47. Burns AS, Rivas DA, Ditunno JF. The management of neurogenic bladder and sexual dysfunction after spinal cord injury. Spine (Phila Pa 1976) 2001;26:S129-36.
48. Taweel WA, Seyam R. Neurogenic bladder in spinal cord injury patients. Res Rep Urol 2015;7:85-99.
49. Consortium for Spinal Cord Medicine. Bladder management for adults with spinal cord injury: A clinical practice guideline for health-care providers. J Spinal Cord Med 2006;29:527-73.
50. McGee MJ, Amundsen CL, Grill WM. Electrical stimulation for the treatment of lower urinary tract dysfunction after spinal cord injury. J Spinal Cord Med 2015;38:135-46.
51. Walter M, Lee AH, Kavanagh A, Phillips AA, Krassioukov AV. Epidural spinal cord stimulation acutely modulates lower urinary tract and bowel function following spinal cord injury: A case report. Front Physiol 2018;9:1816.
52. Herrity AN, Williams CS, Angeli CA, Harkema SJ, Hubscher CH. Lumbosacral spinal cord epidural stimulation improves voiding function after human spinal cord injury. Sci Rep 2018;8:8688.
53. Herrity AN, Aslan SC, Ugiliweneza B, Mohamed AZ, Hubscher CH, Harkema SJ. Improvements in bladder function following activity-based recovery training with epidural stimulation after chronic spinal cord injury. Front Syst Neurosci 2020;14:614691.