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Chapter

Principles of Rehabilitation Strategies in Spinal Cord Injury

Seyed Mansoor Rayegani, Roozbeh Tavanaei and Saeed Oraee-Yazdani

Abstract

Spinal cord injury (SCI) is a debilitating condition that affects millions of people worldwide and results in a remarkable health economic burden imposed on patients and the healthcare system annually. The most common causes of SCI are the trauma caused by falls, traffic accidents, or violence. The course of SCI is associated with several complications that severely impair the patient's quality of life, including sensory and motor dysfunction, pain, neurogenic bladder and bowel, autonomic dysreflexia, cardiovascular and pulmonary dysfunction, spasticity, urinary tract infection, and sexual dysfunction. Despite great strides that have been made in the field of regenerative medicine and neural repair, the treatment of SCI still mostly revolves around rehabilitative strategies to improve patients' quality of life and function. Rehabilitation following the SCI is a multidisciplinary process that requires the involvement of multiple disciplines. Moreover, recent advances in the field of neurorehabilitation following SCI, are changing the face of this field. Therefore, we decided to review various aspects of rehabilitation following the SCI, including the goals and different modalities whereby we could achieve them.

Keywords: spinal cord injury, rehabilitation, paraplegia, restoration of function, quality of life

1. Introduction

Spinal cord injury (SCI) results from damage to the spinal cord, which could lead to significant temporary or permanent functional impairment. As a debilitating condition, SCI affects millions of people worldwide and imposes a considerable economic burden on patients and the healthcare system each year [1, 2]. Traumatic etiologies, such as traffic accidents, falls, and violence constitute the most common causes of SCI [2]. Throughout the course of SCI, various complications could severely impair the patients' quality of life (QoL) and activities of daily living (ADL) over the long term. These complications include sensory and motor dysfunction, pain, neurogenic bladder and bowel, autonomic dysreflexia, cardiovascular and pulmonary dysfunction, spasticity, urinary tract infection, and sexual dysfunction [3].

In recent decades, great strides have been made in the field of neuroregeneration to provide functional recovery through neural repair and axonal regrowth [4].

However, at present, there exists no definitive treatment modality to effectively restore spinal cord structural integrity following SCI with subsequent functional recovery. Therefore, the treatment of SCI still mostly revolves around rehabilitative strategies to improve patients' QoL and function [5, 6]. Rehabilitation following the SCI is a multidisciplinary process that requires the involvement of multiple disciplines, such as physiatrists, nurses, psychologists, dieticians, physical therapists, social workers, occupational therapists, orthotists and speech therapists [6, 7]. The rehabilitation process in SCI mostly centers around restoring the lost functions or augmenting the remaining intact functions while minimizing the associated complications. Holistic approach derived from biopsychosociospiritual model of health is essential for rehabilitation management of SCI. Functional restoration measures including mobility, strength, stretch and coordination training as well as cardiovascular and pulmonary rehabilitation constitute the main aspects of the rehabilitation process following SCI [6, 8].

In addition to current rehabilitation programs, recent advances in the field of neurorehabilitation for functional recovery, are changing the face of this field. Therefore, the focus of this chapter is on the goals of rehabilitation in SCI, current rehabilitative strategies, and recent advances in neurorehabilitation that have opened new horizons for patient management.

2. Goals of rehabilitation in spinal cord injury

The American Spinal Injury Association (ASIA) Impairment Scale (AIS) is a standardized tool for the classification of SCI patients based on injury severity and the level of sensorimotor impairment [9]. The AIS ranges from A (complete injury with no sensorimotor function preserved below the level of injury) to E (a normal sensorimotor function without neurological deficit). **Table 1** demonstrates details of AIS grading. Given its strong correlation with the functional status of the patient, AIS grade is one of the major factors in determining the functional goals of SCI patients following rehabilitation. In this regard, patients with complete SCI have a poorer prognosis for neurological recovery and improvement in functional outcomes compared to those with incomplete injury [10–13].

The neurological level of injury is another factor that affects the prognosis of SCI patients [14, 15]. In terms of motor recovery, patients with the cervical level of injury generally have a higher potential for functional improvement in comparison with those who have thoracic SCI. Moreover, among patients with cervical SCI, those who have an injury at lower cervical levels (C6-C8) show the greatest rehabilitation potential [6]. This is due mostly to remarkable functional impairment in upper cervical injuries and functional independence in many ADLs in thoracolumbar SCI patients, which reduces their potential for recovery. Concerning this, a number of patients with a high cervical level of injury (C3-C4) are ventilator-dependent and almost all of them are dependent to perform their ADLs. Patients with a C5 level of injury, although dependent on assistance for transferability, could perform ADLs, such as nutrition, dressing, and hygiene with assistance, given the preserved strength of elbow flexion in this group. Lower levels of cervical injury are generally associated with enough muscle strength for wrist extension, elbow extension, or finger flexion, which make patients in this group independent in most self-care ADLs and also transferring using assistive devices [6]. Patients with thoracic SCI, however, are totally independent in ADLs and transferability using a manual wheelchair. Thus, the main aim of rehabilitation in this group of patients

Grade A	No sensorimotor function
Grade B	Preserved sensory function with no motor function below the level of injury, which includes S4-S5 level
Grade C	Preserved motor function in more than half of the key muscles below the level of injury with a strength <3/5
Grade D	Preserved motor function in at least half of key muscles below the level of injury with a strength ≥3/5
Grade E	Normal sensorimotor function

Table 1.
The American spinal injury association (ASIA) impairment scale (AIS).

is ambulation. Patients with lower levels of injury (L1 or lower) show complete independence in ADLs and transferability in addition to an adequate degree of ambulation [6].

In addition to neurological recovery, early rehabilitation is necessary to prevent potential long-term complications [6]. As mentioned earlier, various complications affect the QoL in SCI patients, especially over the long term. Many interventions and strategies have been utilized in SCI rehabilitation to reduce the risk of chronic complications in patients with SCI. Recent advances in the field of SCI rehabilitation with the existing evidence have been discussed in the forthcoming paragraphs of this chapter based on different areas of rehabilitation.

3. Rehabilitation interventions

Multidisciplinary team approach is mainstay of SCI rehabilitation. In this model of rehabilitation an organized team including physician with expertise in rehabilitation that is usually a physical medicine and rehabilitation specialist (physiatris) as the team leader, physical therapist, occupational therapist, rehabilitation nurses, social worker, clinical psychologist, orthotists and dietician has the responsibility of planning, executing and follow up of rehabilitation measures. The team benefits from expertise skills of neurospine surgeon and other medical specialties as needed. Followings are more related and mostly used rehabilitation medicine measures that are used in management of SCI.

3.1 Sensorimotor dysfunction

3.1.1 Physical therapy

Physical therapy is one of the major measures of the post-SCI rehabilitation program and begins early in the course of SCI [6, 8, 16]. By targeting various aspects of impairment, such as strength, joint mobility, muscle extensibility, spasticity, pain, and cardiovascular fitness, physical therapy could improve patients' functional independence and prevent long-term complications. Range of motion and stretching exercises could prevent the development of contractures and protect the unwanted tenodesis effect [6]. Moreover, passive muscle stretching exercises could reduce muscle tone and help in maintaining the range of motion and joint mobility, which in turn decrease spasticity-related side effects.

3.1.2 Orthoses and assistive devices

Orthoses could also be used to position the joints and prevent contracture formation [6, 17, 18]. Strengthening exercises for intact regions are of great importance, particularly in patients with complete paraplegia during the early period of rehabilitation, to provide adequate strength for independent mobilization and transferability. Assistive devices, such as a wheelchair, walker, or crutch might also be utilized depending on the functional status of patients for ambulation during the chronic rehabilitation period [6].

3.1.3 Transcranial direct current stimulation

Transcranial direct current stimulation (tDCS) is a noninvasive modality that is used to modify cortical excitability by delivering weak electrical currents (1–2 mA). The tDCS consists of anodal and cathodal electrodes, which following their application, could increase and suppress cortical excitability [19, 20]. The main concept behind the use of tDCS in SCI is modulation of the excitability of residual cortical motor pathways to enhance functional recovery. Previous individual studies have demonstrated promising potential for tDCS combined with various rehabilitative strategies in improving motor cortex excitability and muscle power [21–24]. However, a meta-analysis including six studies and 78 patients with SCI found no significant efficacy for tDCS in increasing muscle strength in comparison with sham tDCS [25]. Moreover, based on their findings, the effect of tDCS on motor functional improvement was marginally significant with a small effect size. In addition, their subgroup analyses failed to demonstrate any significant association between cortical area (hand or leg motor cortex), additional interventions (tDCS alone or tDCS combined with other interventions), or tDCS intensity (1 or 2 mA) the impact of tDCS on outcomes observed in patients. Nevertheless, the limited number of studies, as well as the heterogeneity in methods and protocols among existing investigations have mostly resulted in inconclusive results regarding the efficacy of tDCS in SCI. Therefore, future high-quality studies are highly demanded to show the potential effectiveness of tDCS in improving motor outcomes in SCI patients. Further, some of characteristics, such as non-invasiveness and cost-effectiveness, make tDCS a great potential therapeutic option for SCI.

3.1.4 Repetitive transcranial magnetic stimulation

Transcranial magnetic stimulation (TMS) is another safe and non-invasive cortical stimulation method for modulating neuronal excitability. In this technique, following the passage of the electrical current through a coil, which is placed on the scalp, short magnetic fields are generated. These magnetic fields subsequently induce electrical pulses in neurons, which act as secondary coils [26]. One single TMS pulse over the primary motor cortex elicits action potentials in a group of neurons, which induce motor evoked potential (MEP) in the corresponding muscle group, depending on the topographic area stimulated [26]. Considering this effect, the delivery of several pulses using TMS in a sequential order could exert long-term changes in neuroplasticity-related mechanisms, such as long-term potentiation or depression [27, 28]. This specific TMS modality is known as repetitive TMS (rTMS). Based on stimulation parameters, rTMS could either increase (facilitatory) or decrease (inhibitory) cortical excitability [26]. The therapeutic efficacy of rTMS is well-established in

some psychological disorders, such as depression. Moreover, a huge body of evidence has demonstrated significant effects of rTMS on motor recovery following stroke [29]. With respect to SCI, however, limited evidence exists especially on the effects of rTMS on sensorimotor recovery [30]. Previous investigations have demonstrated significant improvements in lower extremities motor scores following the use of high-frequency rTMS compared with the sham stimulation in patients with SCI [31–35]. One study also demonstrated an average increase of 40–50% in the amplitude of corticospinal responses and magnitude of maximal voluntary contractions in targeted muscles after paired stimulation using both rTMS and peripheral nerve stimulation in patients with SCI [36]. In addition to sensorimotor recovery, the effects of rTMS on SCI-induced spasticity and neuropathic pain have also been evaluated. Two recent meta-analyses and systematic reviews, one including 10 randomized controlled trials (RCTs) and one evaluating 6 RCTs, demonstrated a significant reduction in SCI-induced neuropathic pain intensity in patients who received rTMS compared with the control group [37, 38]. Some prior studies have also reported significant improvements in spasticity following the SCI in patients receiving rTMS [31, 33, 34]. However, as mentioned earlier, given the existing heterogeneity among these studies regarding the rTMS parameters, further evidence is highly demanded.

3.1.5 Deep brain stimulation

Deep brain stimulation (DBS) is a minimally invasive neurosurgical procedure, which includes adjustable stimulation of specific target parts of the brain through implanted electrodes, and is widely implemented for the treatment of movement disorders [39]. Recently, however, DBS has received attention as a potential option for motor functional recovery in SCI. The electrical activation of preserved sublesional descending motor pathways such as the reticulospinal tract forms the rationale behind the potential use of DBS in SCI. In this regard, previous preclinical investigations have demonstrated significant improvement in deficient gait due to SCI and stroke following the stimulation of the mesencephalic locomotor region (MLR) in animal models [40–42]. In a previous study, acute excitatory DBS of the MLR resulted in remarkably improved motor function of the paretic hindlimb in a rat model of chronic incomplete SCI [40]. Moreover, significant improvements in dynamic gait parameters and walking speed have also been reported with high-frequency DBS of the MLR in the rat stroke model [41]. An ongoing clinical trial (NCT03053791) is currently recruiting patients to evaluate the potential effects of MLR-DBS in SCI patients for the first time [43]. This therapeutic modality with its application in SCI is still at its initial stages, and further research is required to elucidate various aspects of it, especially underlying mechanisms, and translate it to the clinical setting.

3.1.6 Epidural spinal cord stimulation

One form of spinal cord stimulation (SCS) is epidural SCS (eSCS), which includes surgical implantation of an array of electrodes over the dorsal surface of the spinal cord in the epidural space with direct stimulation of dorsal nerve roots. Initially, eSCS was evaluated for its impact on chronic pain due to its neuromodulatory effects on nociceptive afferent. Subsequent investigations showed that eSCS could also improve motor functional independence in chronic SCI patients through stimulating dorsal nerve roots and activating interneuronal pathways associated with locomotion [44]. Initial reports demonstrated that eSCS could restore independent standing with

volitional control of lower limb activity and independent stepping in patients with complete SCI [45–47]. In another report including four patients, following multiple sessions of eSCS with gait training, all patients achieved independent standing and trunk stability, and two could walk on the ground [48]. Wagner et al. showed that spatiotemporal stimulation of the lumbosacral spinal cord using an implanted pulse generator in patients with chronic SCI could restore adaptive control of muscles and improve locomotion following rehabilitation [49]. In a recent study, the same research group demonstrated the restoration of a number of activities, including standing, walking, cycling, swimming, and trunk control, in three patients with complete sensorimotor paralysis using eSCS, as part of a clinical trial (NCT02936453) [50]. In this study, the optimal position of the paddle lead was determined using a computational framework to allow for the restoration of various motor activities using different activity-specific programs. In addition, there is preclinical evidence regarding the improvements in upper limb function, such as reaching and grasping following the use of cervical eSCS in cervical SCI [51]. A prior study, including two patients with chronic cervical SCI, also demonstrated improved hand strength and volitional hand control using cervical eSCS [52].

3.1.7 Transcutaneous spinal cord stimulation

Similar to eSCS, transcutaneous spinal cord stimulation (tcSCS) activates spinal motor pathways through stimulating dorsal root afferents, yet in a non-invasive manner [53]. In tcSCS, electrodes are generally placed on the skin overlying lower thoracic or lumbar vertebrae. The increase in excitability of local interneuronal pathways following the use of tcSCS facilitates the activity of previously spared nonfunctional supraspinal pathways [54]. This could lead to significant functional improvement, particularly in combination with other conventional rehabilitation strategies. Some previous reports have indicated improved postural control and ankle motility in patients with complete or incomplete SCI [55, 56]. A previous study showed improvements in weight loading capacity and reduced gait asymmetry in 19 patients who received exoskeleton-based training with tcSCS [57]. There are other studies reporting significantly enhanced volitional lower extremity movement, walking speed, endurance, and symmetry using tcSCS combined with walking and locomotion training [58–60]. In regard to the upper limb, similarly, a number of studies have demonstrated significant durable improvements in upper extremity function, such as grip force and dexterity following tcSCS with training [61, 62]. Based on prior findings, tcSCS results in a functional recovery sustained over periods without stimulation. Therefore, given the speed of acquisition, it has been proposed that tcSCS might be associated with a broader modulatory effect on neuronal pathways compared with eSCS, which merely causes a transient increase in excitability [53]. Despite being non-invasive and inexpensive, tcSCS has a remarkably lower spatiotemporal precision than eSCS. Current literature on the utility of tcSCS in SCI is heterogeneous, especially in terms of stimulation parameters, study design, and outcome measures. Hence, future high-quality clinical trials with larger sample sizes are highly needed in this regard.

3.1.8 Functional electrical stimulation

Functional electrical stimulation (FES) is a widely used neurorehabilitation modality in which electrical stimulation of the paralyzed muscles is performed to achieve functional improvement. During FES sessions, generally, neuromuscular stimulation

is contemporaneous with specific tasks, such as cycling [63]. Previous studies have demonstrated that FES is associated with improved circulation, muscle strength, range of motion, and reduced spasticity [64]. Various activities have been evaluated in previous studies on FES, including cycling, walking, grasping, reaching, and stair climbing [63]. FES-evoked cycling is one of the most frequently used FES training modalities in the clinical setting [64, 65]. In this rehabilitation method, patients with no or reduced volitional lower extremity control can perform cycling using an exercise bicycle. The pedaling motion is produced by computer-generated electrical pulses that are transmitted to leg muscles through surface electrodes. Several benefits have been previously reported for FES cycling, including significant improvements in motor scores, functional independence, spasticity, and cardiopulmonary function in SCI patients [63, 64, 66, 67]. A recent systematic review evaluated 99 studies, including 999 SCI patients, and suggested that FES cycling exercise could improve lower-body muscle health, power output, and aerobic fitness in SCI patients [64]. With respect to the upper limb, prior studies have also reported better recovery in hand function in cervical SCI patients receiving FES, especially when combined with conventional occupational therapy [68, 69]. Electrical pulses in FES are defined mainly based on three parameters, including pulse frequency (typical values, 20–50 Hz), amplitude (typical values, 0–100 mA), and width (typical values, 300–600 μs) [63]. Differences in parameter adjustments significantly change the effects of FES on muscle contraction and fatigue. Therefore, depending on the rehabilitation goals and the patient's functional status, parameters could be individualized.

3.1.9 Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation (TENS) is a non-invasive and safe rehabilitation modality whereby electrical pulses are delivered to the skin to stimulate nerves and reduce pain subsequently. Based on prior findings, a remarkable increase in blood circulation following TENS results in pain improvement [70–73]. Various clinical conditions could be targeted through differences in electrode placement and stimulation parameters, including frequency and intensity [73, 74]. The frequency of stimulation could be high (>50 Hz) or low (<10 Hz). The stimulation intensity is also classified based on the response achieved, which could be sensory or motor. The use of TENS in pain treatment is well-studied and mostly consists of delivering low-frequency electrical pulses to the affected area. A recent meta-analysis, including six RCTs with 165 patients, indicated that visual analog scale (VAS) for pain and short-form McGill pain questionnaire scores were significantly reduced in SCI patients who received TENS compared with the control group [75]. In addition to pain, prior evidence supports the use of TENS in improving spasticity [76]. Regarding this, a previous systematic review and meta-analysis demonstrated a significant association between the TENS applied for more than 30 minutes and reduction in lower limb spasticity in patients with chronic stroke [77]. Similarly, a number of previous studies have reported significant improvements in SCI-induced spasticity using TENS [78–80]. Given its safety profile and low cost as well as effects on pain and spasticity, TENS is regarded as a great adjunct to physical therapy and conventional SCI rehabilitation program.

3.1.10 Robotic-assisted gait training

In addition to reduced functional independence, immobility due to SCI could lead to a variety of secondary problems, including cardiopulmonary complications,

bowel and bladder dysfunction, osteoporosis, pressure ulcers, and obesity [81–83]. Accordingly, recovery of ambulation is of crucial importance in the rehabilitation program of patients with SCI [84]. Locomotor rehabilitation training following the SCI is performed either in a conventional manner, in which the therapist assists manually, or by using rehabilitation robots, which are also known as exoskeletons. In comparison with the former, robotic-assisted gait training is associated with a less physical burden for the therapist while also allowing for quantitative evaluation of the patient's progression [85–92]. Since the introduction of Lokomat, as the first exoskeleton, different types of gait rehabilitation robots have been developed [92, 93]. Many prior studies have evaluated the effects of robotic-assisted gait training in SCI rehabilitation. Several beneficial impacts for this modality have been reported previously, including improvements in musculoskeletal, urinary, cardiopulmonary, somatosensory, and neural plasticity [87, 89, 94, 95]. Based on a previous systematic review, including 13 RCTs, body weight-supported treadmill training and robotic-assisted gait training increase the walking speed no more than overground gait training and other forms of physical therapy in patients with SCI [90]. However, the results were not clear regarding the changes in walking distance. Another systematic review and meta-analysis, including 10 RCTs, found that robotic-assisted gait training results in significantly greater improvement in mobility-related outcomes, such as gait distance, functional level of mobility and independence, and leg strength compared with conventional overground training in incomplete SCI patients [87]. Nevertheless, potential differences in response to therapy between different individuals with SCI should also be considered. Concerning this, patients with incomplete lesions or a recent injury might show a better response to therapy with robotic-assisted gait training than those with complete or chronic injuries [90]. Thus, future trials are warranted to allow for further subgroups analyses in this regard. Furthermore, recently, wearable exoskeletons, as emerging therapeutic devices are receiving much attention since they require active participation from the patient and could also be utilized as assistive devices in the community [92]. Additionally, wearable exoskeletons seem to address limitations associated with grounded exoskeletons by providing more freedom during gait and the ability to perform complex motions and more activities of daily living. However, since there is a paucity of data regarding various aspects of wearable exoskeletons and their effectiveness in patients with SCI, future clinical trials are highly warranted to evaluate the utility of different robots and also compare them with other types of gait therapy in this population [92].

3.1.11 Occupational therapy

One of the important disciplines in rehabilitation team of SCI is occupational therapy.

A person's functional independence has a major impact on their quality of life, and consequential social participation. Some people with a spinal cord injury (SCI) will have the ability to achieve a high level of independence while others, limited by their physical ability, will be able to achieve a level of independence through directing their care and by using technology options. Whilst it is reasonable to expect that the degree of functional independence achievable is dependent on a person's level of injury, a person's neurological level should not be viewed as strictly predictive but rather as indicative of potential function. Adjustment of SCI with post injury functional limitation and activity of daily living (ADL) copping is very essential for victims of SCI. Transfer activities, transportation from and to different environments, home adjustments and

copping to new adjusted work are among professional activities of occupational therapist in rehabilitation team. In addition, neurorehabilitation facilitations techniques such as anti-spasticity manures are carried out by occupational therapists.

3.2 Cardiopulmonary dysfunction

Recent advances in the care and rehabilitation of SCI patients have changed the pattern of SCI morbidity and mortality with a shift from septicemia, pneumonia, and renal failure to cardiovascular complications as one of the major causes of death in this group of patients [96, 97]. Many risk factors for cardiovascular disease are associated with SCI, including physical inactivity due to the non-ambulatory state, extreme fluctuations in blood pressure, dyslipidemia, abnormal glycemic control, and chronic inflammation [98, 99]. With respect to this, a previous survey with a large sample of 60,000 SCI patients showed a significant association between SCI and increased odds of heart disease and stroke [96].

In addition, numerous previous investigations have reported a high prevalence of orthostatic hypotension in SCI [100, 101]. Similar to acute injury, orthostatic hypotension could be persistent throughout the course of chronic SCI and remarkably interfere with the rehabilitation process and patient's QoL [100]. Improvements in orthostatic hypotension have been reported previously through a variety of measures, including pressure interventions (e.g., pressure stockings and abdominal binders), increasing fluid and salt intake (volume augmentation), lower limb FES, exercise, and pharmacotherapy using different agents, such as midodrine, fludrocortisone, ephedrine, dihydroergotamine, and droxidopa [100].

Autonomic dysreflexia is also an urgent cardiovascular condition associated with SCI, which is characterized by acute episodes of hypertension with either bradycardia or tachycardia [102, 103]. Most patients with a T6 level of injury or higher are at risk of autonomic dysreflexia. Various noxious and non-noxious stimuli below the level of injury, such as pressure sores, and bladder or bowel irritation, could lead to autonomic dysreflexia mainly by triggering massive sympathetic discharge. The clinical manifestation of autonomic dysreflexia is variable and ranges from mild discomfort to severe acute hypertension with ominous consequences [102, 103]. Prior reports have shown a significant correlation between the severity of autonomic dysreflexia and the level of injury, as well as the completeness of the SCI with higher and complete injuries are associated with more severe manifestations [102, 104]. Prevention plays a crucial role in the management of autonomic dysreflexia and mainly aims at resolving the underlying triggers through several non-pharmacologic measures, such as regular bladder and bowel care. Depending on the severity, pharmacologic therapy with rapid-onset antihypertensive drugs is also used in acute cases of autonomic dysreflexia [102].

Pulmonary dysfunction also noticeably complicates the course of SCI, particularly in patients with cervical and upper thoracic injuries. Functional impairments in respiratory muscles, including the diaphragm, intercostal, and accessory respiratory muscles, substantially reduce lung capacity and increase respiratory demand. Moreover, atelectasis ensues when the dysfunction of respiratory muscles leads to reduced compliance of the lung and chest wall. Impaired function of expiratory muscles also causes ineffective cough, which in turn negatively affects airway clearance. Consequently, many severe complications could occur as a result of pulmonary dysfunction, such as mucus retention, pleural effusion, pneumonia, and respiratory failure [105, 106]. Therefore, pulmonary rehabilitation is a vital part of the SCI rehabilitation program to prevent respiratory complications in patients [106]. Prior

investigations have shown that respiratory muscle training effectively improves respiratory muscle strength and subsequently reduces respiratory complications in SCI patients [107–113]. Among subgroups of SCI patients, greater improvement in respiratory function following the rehabilitation has been reported in patients with tetraplegia and subacute injury [109]. Respiratory muscle training involves increasing the load on respiratory muscles, and different types of it have been reported previously, such as the use of resistive and threshold trainers, singing training, and normo-capnic hyperpnoea [107].

3.3 Bladder and bowel dysfunction

Bladder and bowel dysfunction involves a significant proportion of patients following SCI and remarkably impairs their QoL. Genitourinary infections constitute the most common cause of re-hospitalization in SCI patients with about 30% of them being hospitalized annually. Moreover, the fifth most common cause of mortality in SCI patients, is genitourinary infection. Bowel dysfunction is the fourth leading cause of re-hospitalization and the second most common complication according to SCI patients [114–116]. Therefore, bladder and bowel care comprise a notable part of the SCI rehabilitation program.

Based on a prior report, about 77% of SCI patients lack the ability to void voluntarily, which makes them dependent on assistance [117]. The most common bladder drainage method for neurogenic bladder management with the lowest risk of complications and urinary tract infection in SCI patients is clean intermittent catheterization [114, 118]. Tetraplegic patients, however, might use indwelling or suprapubic catheters, which could increase the risk of complications, such as infection. Other techniques, such as Credé and Valsalva maneuvers might also be helpful in addition to primary drainage methods. Pharmacological therapy using anticholinergics or beta-3-agonists is also effective in reducing the intravesical pressure in cases with hyper-reflexic detrusor. In refractory cases or patients with renal impairment, a number of procedures, such as intravesical botulinum-A toxin injection, surgical interventions (e.g., bladder reconstruction and diversion procedures), and sacral neuromodulation, might also help in improving the symptoms [114].

According to SCI patients, about 95% of them have chronic constipation, and 75% have experienced fecal incontinence, which could significantly affect various aspects of QoL and the social life of patients. Further, several complications might occur as a result of chronic constipation, including anal fissures, rectal bleeding, hemorrhoids, autonomic dysreflexia, and urinary tract infection [114, 119]. Therefore, SCI rehabilitation should include an individualized bowel management program aimed at regular bowel emptying, maintaining functional continence, and preventing potential complications [114, 119]. Conservative management in neurogenic bowel includes diet, abdominal massage, drinking a warm liquid before bowel care, digital rectal stimulation, and using stimulant suppositories. Further, there might be an additional need for pharmacological therapy using oral or rectal laxatives, especially in older patients or those with longstanding SCI [114, 120, 121]. For maintenance of stool consistency, bulking agents and stool softeners might also be used regularly. In addition, prucalopride is a prokinetic agent, which is used for chronic constipation due to neurogenic bowel [114]. In case of inadequate response to conservative therapy, invasive procedures, such as intestinal diversion (e.g., ileostomy or colostomy), Malone anterograde continence enema could significantly improve the patients' QoL [114, 122].

3.4 Neuropathic pain

Pain is one of the most common disabling complications following the SCI, which could significantly impair the patient's QoL [123–125]. According to prior information, the prevalence of pain among patients with SCI is about 65 to 85%, and approximately one-third of them report severe pain [126]. Based on International Spinal Cord Injury Pain (ISCIP) classification and underlying mechanisms, SCI-related pain is classically divided into nociceptive and neuropathic categories [127]. Nociceptive pain originates from nociceptors with preserved sensory innervation and could be either musculoskeletal or visceral. Analgesics, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids, could significantly improve nociceptive pain [127]. Neuropathic pain, however, is the most common type of pain in SCI patients with no definitive therapy due to its more complex etiology, which is still not well understood [128]. Neuropathic pain mainly arises from the disease of the somatosensory system and could occur either at the level of injury or below it. Relative to the neurological level of injury, the former type is defined as the pain within the distribution of one rostral and three caudal dermatomes. The below-level pain, however, is localized below the three dermatomes caudal to the neurological level of injury. Neuropathic pain might also be associated with sensory phenomena in the painful area, such as allodynia, which is defined as pain triggered by non-noxious stimuli (e.g., light touch), especially in the at-level pain category [127]. Given the complexity of neuropathic pain, many pharmacological and non-pharmacological therapeutic interventions have been utilized previously with variable efficacy and safety profiles. Pharmacological therapy using antiepileptics, tricyclic antidepressants, opioids, and cannabinoids has been reported. In refractory cases, non-pharmacological interventions, such as intrathecal drug administration, nerve blocks, dorsal root entry zone (DREZ) ablation procedures, SCS, tDCS, transcranial electrical stimulation (TES), and TMS might be beneficial [129].

3.5 Spasticity

Spasticity is one of the most common complications following injuries to upper motor neurons, such as SCI. Approximately 65% of SCI patients show symptoms of spasticity following their discharge from the acute rehabilitation program, and about 93% of those in the community are affected [130, 131]. As a sensorimotor control disorder due to upper motor neuron lesion, spasticity is presented as a velocity-dependent increase in tonic stretch reflex with clonus, spasms, and hyperreflexia [18]. About 35% of chronic SCI patients have problematic spasticity, which is defined as spasticity leading to functional limitation or requires antispasticity treatment [131, 132]. SCI-related spasticity shows a gradual course, which begins following the areflexia associated with the spinal shock period. Incomplete SCI and preserved sensorimotor function below the level of injury are associated with severe spasticity. SCI-related spasticity could significantly affect the patient's QoL and limit ADLs. Moreover, poorly treated spasticity results in pain, contractures, and skin breakdown, which interferes with the rehabilitation process and could also prevent neurological recovery [18, 130, 131]. Due mainly to the more diffuse pattern of SCI-induced spasticity in comparison with other pathologies, such as stroke or traumatic brain injury, regional or systemic therapies are preferred in SCI [18, 130]. Initial therapy for SCI-induced spasticity consists of physical therapy and pharmacological treatment. However, often the approaches fail to manage spasticity in SCI patients, or intolerable

side effects due to pharmacological therapy occur, and further treatment modalities might be required. Intrathecal administration of baclofen using an implantable pump has been significantly effective in reducing intractable SCI-induced spasticity. However, this method is associated with some limitations, such as surgical complications, pump failure, and infections [133, 134]. Depending on the status of the patient, other modalities might also be used, such as local chemodenervation using phenol, ethanol, or botulinum toxin. Surgical interventions, such as selective dorsal rhizotomy, tenotomy, tendon lengthening and transfers might also be used in selected severe cases [18, 130].

4. Conclusions

This chapter reviewed different modalities and strategies used in the field of neurorehabilitation for SCI and various aspects of it, specifically. The process of rehabilitation is time-consuming and requires the participation of multiple disciplines as well as the patients and their family. In addition, in many cases, the use of each modality individually might not result in a discernible improvement. Therefore, it is of paramount importance to consider a combinatorial approach to SCI rehabilitation with the aim of improvement in patients' function and QoL using all the available options. Moreover, a notable number of strategies for neurological recovery in SCI were not covered, mainly because they were beyond the scope of this chapter. Recent advances in different fields, such as brain-machine interface, stem cell therapy, tissue engineering, gene therapy, exosomes, and optogenetics, have shown promising results in various aspects of SCI, both preclinically and clinically. However, still, further research is needed to translate these potentially effective modalities into the clinical arena and use them as part of the rehabilitation plan.

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