Functional Electrical Stimulation in Neuro-urologic Disorders

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Jürgen Pannek and Jens Wöllner

Main tasks of the lower urinary tract (LUT) are to store and voluntarily evacuate the urine. To fulfil these tasks, complex regulation mechanisms at different levels of the nervous system are involved. Any neurologic disorder may lead to a neurogenic lower urinary tract dysfunction (NLUTD). Clinical symptoms do not correlate with the type and severity of the dysfunction. Therefore, an exact diagnosis of NLUTD by video-urodynamic examination is important. Depending on the type of NLUTD, an adequate therapy is essential to preserve renal function and to sustain the best possible quality of life (QoL).

By video-urodynamic examination, risk factors for the upper urinary tract can be evaluated. If risk factors are present, treatment should be based on these objective parameters to protect renal function. If no risk factors are present, bladder management can be based on symptoms, e.g. urgency, frequency, incontinence, difficulty to void, or urinary tract infections.

Neuromodulation for the treatment of neurogenic lower urinary tract dysfunction (NLUTD) in patients with SCI is under rapid development.

Functional electrical stimulation (FES) of the LUT can be applied via peripheral nerves (vaginal/rectal/genital), tibial nerve stimulation, by intravesical stimulation, and by magnetic or electrical stimulation of the spinal cord. Although especially the spinal cord stimulations are at an experimental stage, they carry the potential to become treatment options in the future. In addition, neuromodulation may even be suited to prevent NLUTD instead of just treating it, which will significantly improve the quality of life of the affected persons.

15.1 Physiology and Pathophysiology of the Lower Urinary Tract

Main tasks of the lower urinary tract (LUT) are to store and voluntarily evacuate the urine. To fulfil these tasks, complex regulation mechanisms at different levels of the nervous system are involved. Supraspinal centres such as the frontal cortex, the pontine micturition centre and the insula are responsible for the voluntary control of micturition [1, 2]. The spinal cord is essential for the transmission of information originating from the LUT to the supraspinal neural networks. Together with descending efferent fibres from the cortical micturition centres to the lowest sacral segments, they form a closed-loop system to control urine storage and voiding. The integrity of the connections between cortical, supraspinal centres and spinal neurons is essential and must therefore be preserved. As a consequence, any neurologic disorder may lead to a neurogenic lower urinary tract dysfunction (NLUTD).

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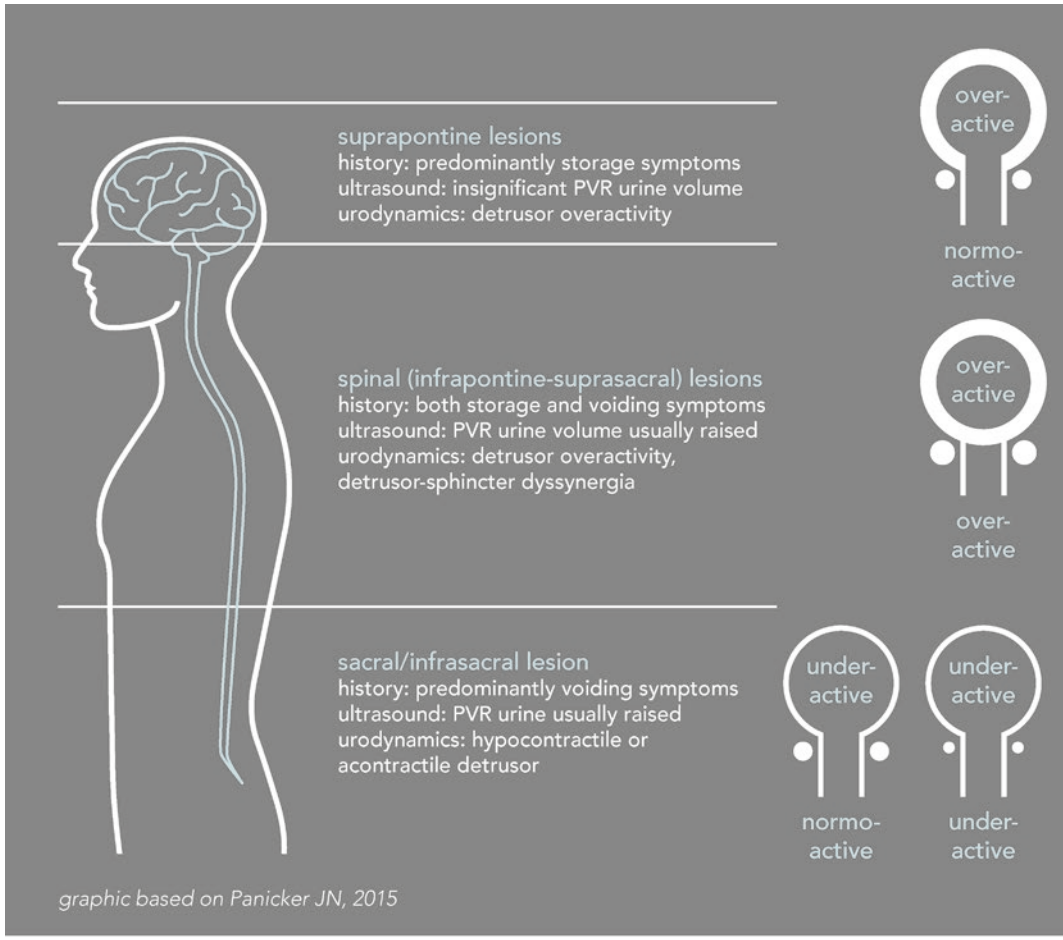


Fig. 15.1 Neurogenic lower urinary tract dysfunction (NLUTD) based on the level of lesion

Treatment of NLUTD is not mainly based on the type of neurogenic disorder, but on the resulting type of lower urinary tract dysfunction in the storage and voiding phase. Depending on the level and completeness of the neurogenic lesion, different clinical manifestations of NLUTD can occur [3]. Basically, cortical or subcortical lesions above the pontine micturition centre (e.g. stroke, traumatic brain injury) leads to a loss of inhibition of detrusor activity. As a consequence, neurogenic detrusor overactivity (NDO), an unvoluntary contraction of the detrusor, is frequent in these patients, leading to elevated pressure in the bladder during the storage phase and may result in urgency and/or urinary incontinence. An infrapontine, suprasacral spinal lesion carries the highest risk for renal function. In these types of lesion, often the coordination between the detrusor muscle and the urethral sphincter is affected. Thus, simultaneous contractions of the bladder and the sphincter occur, leading to elevated intravesical pressure due to functional obstruction during bladder contraction. This phenomenon, referred to as detrusor-sphincter dyssynergia (DSD), can have detrimental consequences for renal function by either reflux or obstruction of the upper urinary tract. In addition, it can lead to incomplete voiding and elevated post-void residual urine, often leading to recurrent urinary tract infections (UTI) [4]. Subsacral spinal lesions or peripheral nerve lesions typically result in an acontractile bladder with insufficient or incomplete drainage. In addition, a flaccid urethral sphincter can cause stress urinary incontinence.

Unfortunately, clinical symptoms do not correlate with the type and severity of dysfunction. Up to 70% of patients with spinal cord injury (SCI) representing the group with a worsening of the pattern of the NLUTD and would require treatment, do not show additional symptoms [5]. It is of utmost importance to know that in one-third of the affected patients, the type of NLUTD is different from the prediction based on the level of lesion [3] (Fig. 15.1). Therefore, an accurate diagnosis of NLUTD by video-urodynamic examination is essential.

Depending on the type of NLUTD, an adequate therapy is essential to preserve renal function and to sustain the best possible quality of life (QoL). In the management of NLUTD, the general status, motor impairments, patient compliance, cognition, and social circumstances must be taken into account. Basically, as the type of NLUTD can change over time, a life-long follow-up is mandatory in these patients.

Summary
Neurological disorders can affect the integrity of the lower urinary tract. Depending on the underlying disease, extent of the lesion and the location of the lesion (central, peripheral), various dysfunctions of the storage and voiding phase can occur. NLUTD can affect the function of the upper urinary tract and can impair renal function. Furthermore, symptoms like urinary incontinence and voiding difficulties can have a negative impact on patients' quality of life.

15.2 Examination

The most important instrument to evaluate the function of the lower urinary tract is the (video)-urodynamic examination/study ([V]UDS). During this examination, the storage and voiding phase of the urinary bladder are evaluated. This is established by the insertion of a small transurethral double-lumened catheter. Via one channel of the catheter, the bladder is filled with sterile body-warm fluid at a defined filling speed. In urodynamic studies, saline is used. For video-urodynamic studies, a mixture of contrast media and saline is instilled. The second channel of the catheter is used for a permanent recording of the intravesical pressure. This allows to permanently record intravesical pressure and volume. The sphincter EMG is measured with surface electrodes. In video-urodynamics, measurement is combined with fluoroscopy. By filling the bladder with contrast media, structural alterations of the lower urinary tract and potential risk factors for renal function (e.g. vesico-ureteral-renal reflux) can be detected. In persons with SCI, the examination is most frequently performed in the sitting or lying position.

By video-urodynamic examination, risk factors for the upper urinary tract, e.g. detrusor overactivity during the storage phase exceeding 40 cm , H_2O, DSD, vesico-renal reflux, or loss of elasticity (low compliance) can be evaluated. If risk factors are present, treatment should be based on these objective parameters to protect renal function. If no risk factors are present, bladder management can be based on symptoms. The most common symptoms are:

- Urgency.
- Frequency.
- Incontinence.
- Difficulty to void/feeling of incomplete voiding.
- Recurrent urinary tract infections (UTI).

15.3 FES Techniques in NLUTD

As neuromodulation is regulated via afferent nerves, an at least partially preserved sacral reflex arch is a prerequisite for any neuromodulatory technique, including peripheral electrical stimulation [6]. Therefore, electrical stimulation does not seem to be indicated in persons with complete spinal cord injury but for cortical lesions like multiple sclerosis, stroke and traumatic brain injury.

15.3.1 Intravesical Stimulation

Intravesical electrical stimulation (IVES), first introduced by Katona [7], aims at activating

detrusor contractions to improve voiding in patients with neurogenic non-obstructive urine retention. Usually, a monopolar active electrode is inserted in the bladder via a catheter using monophasic rectangular impulses with a frequency between 10 and 20 Hz. To either manifest or prove the failure of this treatment, 3 weeks of daily 1-h IVES sessions seem to be sufficient. The largest single-centre study in patients with chronic retention requiring intermittent catheterization demonstrated a minimum reduction of 50% both in the number of daily catheterizations and residual urine in 38 of these 102 patients (37.2%). After 8–15 months, these parameters returned to baseline, but a second IVES cycle led to similar improvements as the first ones [8]. Due to the low success rate and the short duration of the effect, IVES seems to be merely useful for a limited, well-selected group of patients.

15.3.2 Nervus Pudendus Stimulation

Temporary peripheral electrical stimulation**.**

This therapeutic approach offers a non-invasive alternative to medical therapy for detrusor overactivity in patients with neurogenic disorders. Due to the non-invasive approach and the easy handling, it can be used as home therapy, which increases patients' acceptance and compliance.

15.3.2.1 Vaginal/Rectal Electrical Stimulation

Detrusor overactivity can be suppressed by afferent stimulation of the pudendal nerve and suppression of pelvic nerve activity by activation of central inhibition. Frequencies between 5 and 10 Hz were most successful in animal experiments and clinical studies [9, 10].

Electrical Stimulation

Transcutaneous electrical nerve stimulation can be applied by various routes. Whereas stimulation in non-neurogenic patients is frequently performed via rectal or vaginal electrodes (Fig. 15.2), hardly any data regarding this method can be found in persons with SCI. There are few studies

Fig. 15.2 Rectal or vaginal electrodes

examining persons with neurogenic OAB due to various neurologic disorders, predominantly multiple sclerosis, pointing out that this stimulation may improve detrusor overactivity by daily stimulation at home. Whereas one study found a long-term effect [11], other studies described an effect duration of about 2 months in patients with MS [12]. In the study of Pannek et al., stimulation was applied twice a day for 20 min, using vaginal probes for women and rectal probes for men, with a frequency of 8 Hz and a pulse width of 400 μs over a period of 3 months. On the contrary, Primus et al. performed 15 20-min sessions over 3 weeks, with a pulse width of 1 ms and a frequency of 20 Hz. In both studies, the maximum tolerable stimulus was chosen by slowly increasing the intensity. The significant differences in both, stimulation frequency and stimulation parameters, may at least partially explain the different results.

15.3.2.2 Genital Electrical Stimulation

The pudendal nerve originates in the nerve roots of S2–S4. It innervates the pelvic floor and external sphincter. The dorsal penile and clitoral nerves are the most superficial and exclusively afferent branches of the pudendal nerve. These branches have frequently been used for electrical stimulation, as they are inhibitory to the micturition reflex. In animal and human studies,

spontaneous bladder contractions could be inhibited with stimulation of pudendal nerves. In persons with SCI, genital (penile/clitoral) stimulation is used more frequently than electrical stimulation with vaginal or rectal probes. Most frequently, 200 microsecond width square waves at a frequency of 25 Hz and a mean stimulus amplitude of 26 mA are applied. Both, acute continuous or conditional stimulation, lead to an increase in bladder capacity [13] and to an improvement of urodynamic parameters [14]. Data on chronic genital electrical stimulation in persons with SCI, however, is rather scarce. Lee et al. demonstrated an improvement in bladder capacity and detrusor overactivity in five out of six participants 2–4 weeks after a stimulation period of 14–28 days [15]. In the most recent study, five participants with chronic SCI used penile stimulation for seven days, which led to an improvement in continence, bladder capacity, and detrusor overactivity [16]. A retained sensation seems to be a prerequisite for treatment success. Genital stimulation is either used constantly or conditionally (event-driven). Both techniques can result in an inhibition of detrusor contractions and lead to an increase in functional bladder capacity [17], but both techniques require constantly wearing genital electrodes. This belongs to the apparent drawbacks of this type of stimulation.

15.3.2.3 Sacral Stimulation

Sacral neuromodulation by implantable electrodes is an established therapy for the treatment of overactive bladder and non-obstructive urinary retention and constipation. Non-invasive procedures, such as transcutaneous stimulation, are an option for patients who do not want to undergo surgery, even if it is minimally invasive. With surface electrodes placed above the sacral foramina S2 and S3, symptoms of overactive bladder can resolve. Different stimulation parameters are reported in the literature, applying a frequency of 10 to 50 Hz and pulse duration of 100 to 500 µs. Also, the stimulation duration (twice daily to 12 h for 3 months) is not clearly defined. As some studies and case series show a therapeutic effect of percutaneous sacral stimulation, this technique might be an alternative option in patients who reject invasive sacral neuromodulation [18].

15.4 Tibial Nerve Stimulation (TNS)

Electrical stimulation of the tibial nerve, which proximally enters the sciatic nerve and the L4/5-S3 roots, is believed to modulate spinal cord and/or brain reflexes to exert its clinical effect on detrusor overactivity in persons with SCI (Fig. 15.3) [19]. Electrical percutaneous neuromodulation therapy (PTN) has been delivered transcutaneously, percutaneously, and via implanted electrodes. As the latter is a minimally invasive procedure, this paragraph will focus on the former techniques.

Percutaneous tibial nerve stimulation (PTNS) involves the placement of a needle electrode and usually requires weekly visits to the clinic for at least 12 weeks for stimulation, followed by monthly visits to maintain the effect [20]. In a study using PTNS utilizing the schedule mentioned above, including a monthly maintenance stimulation, the authors demonstrated a significant improvement in patients with neurogenic as in idiopathic detrusor overactivity for a period of 4 years [20]. The majority of studies is related to tibial nerve stimulation and neurogenic bladder dysfunction has been performed in persons with multiple sclerosis. In this group of patients, several researchers reported clinical as well as urodynamic improvements in detrusor overactivity/overactive bladder [21, 22].

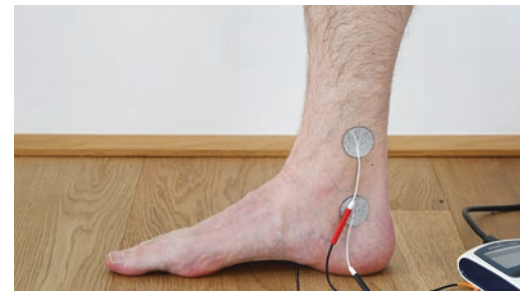


Fig. 15.3 Tibial nerve electrode placement for detrusor overactivity

Transcutaneous tibial nerve stimulation (TTNS) is applied through skin electrodes and can be performed by the individuals themselves continuously or on demand [19]. Thus, TTNS is easier to perform and can be used by the patients themselves at home. Results, however, are conflicting. In a randomized study, TTNS was not effective in treating idiopathic or neurogenic detrusor overactivity [23]. In the study using TTNS specifically in persons with SCI, the authors applied this technique in the acute phase, and found deterioration in neurogenic bladder dysfunction in those without TTNS, but not in the TTNS group. Thus, they concluded that the method may be useful for preventing neurogenic bladder dysfunction in SCI [24]. This study, however, comprised of 19 patients only. To further explore this subject, a multicentred, prospective, randomized, sham-controlled study for TTNs in persons with acute SCI has started recently [25].

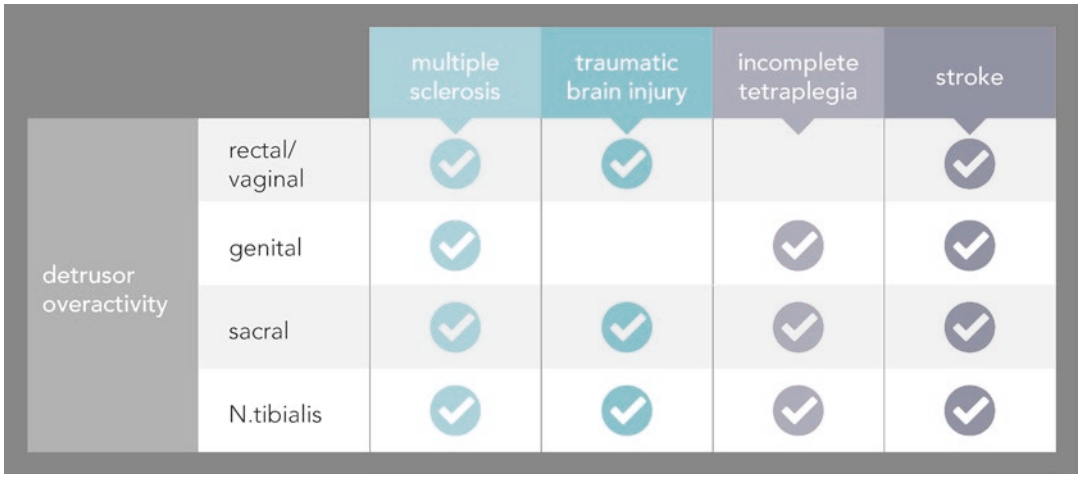
15.5 Spinal Cord Stimulation (SCS)

Case reports described mixed results of lumbosacral spinal cord epidural electrical stimulation (SCEES) on bladder function after SCI. SCEES was performed via an epidural spinal cord stimulator and a 16-electrode array that was surgically placed at the spinal segments L1-S1, 3.3 years after traumatic SCI. The individual may turn the stimulator on and off and may select programs. The stimulation needs to be individualized. SCEES may function by increasing central excitability involving activation of spared supraspinal pathways to neural networks and modulating spinal reflexes [26]. Further research in optimizing electrode location and stimulation parameters is needed, which may lead to programs for storage and voiding at low pressures. A more developed system may have an effect on other autonomic functions including the cardiovascular system and bowel, Nevertheless, this might as well imply challenges since several programs would coexist. Currently, there is no experience with long-term SCEES.

Transcutaneous electrical spinal cord stimulation (TESCS) may reduce detrusor overactivity, increase bladder capacity, and lessen detrusor-sphincter-dyssynergia by transforming the automaticity of the spinal neural circuits into a more physiological functioning by activating the spinal micturition centre. Using a non-invasive transcutaneous electrical spinal cord stimulator with electrodes placed over the interspinous ligaments of Th11 and L1 and the iliac crest individualized stimulation parameters were applied [27]. TESCS is non-invasive but requires thorough evaluation and meticulous individualized urodynamic evaluation of the optimal stimulation parameters. It can be utilized in persons with chronic SCI. The initial results of the existing case combined with small studies that can be performed in larger trials may lead to a long-term solution for TESCS as a tool before implanting SCEES. The effects of transcutaneous magnetic spinal cord stimulation on the lower urinary tract were evaluated in a proof-of-concept study in five patients, using a figure-8 coil at vertebra L1 in the midline to allow the magnetic field to be parallel to the spinal cord [28]. Applying magnetic stimulation once a week for 16 weeks, demonstrated an increase in bladder capacity and a decrease in number of self-catheterizations. Yet, the stimulation must be individualized and repeated weekly to maintain this effect [28]. As anticipated for electrical stimulation, magnetic stimulation may facilitate the coordination of the activity in the spinal micturition circuits, but with a lower risk of painful stimulation [28].

In all mentioned spinal cord stimulations, hardly any case reports or small case series exist, pointing out that further studies are required before these techniques can be used in clinical practice (Table 15.1).

Table 15.1 Different stimulation sites in detrusor overactivity in different neurological diseases



15.6 Perspective

Non-invasive neuromodulatory therapies are available for patients with underlying neurological disorders. In patients with neurogenic overactive bladder (OAB), this therapy can be an option. Due to the non-invasive character, it may serve as an alternative to medical treatment in a well-defined group of patients without risk factors for renal damage. Nevertheless, the evidence for non-invasive neuromodulation in patients with neurogenic lower urinary tract dysfunction is low. There is a lack of prospective, sham-controlled trials. Especially stimulation parameters, duration, and intensity are based on expert experience. Therefore, this therapy should be further elucidated by clinical trials.

Neuromodulation for the treatment of neurogenic lower urinary tract dysfunction (NLUTD) in patients with SCI is developing rapidly. For a long period of time, the treatment of NLUTD was based on the prevention of secondary complications. Oral medication, onabotulinum toxin detrusor injections and bladder augmentation are all qualified to treat NLUTD, but they are not able to restore both storage and voiding function. The sacral deafferentation and anterior root stimulation lead to safe detrusor storage pressures, voluntary voiding in physiologic intervals and continence in patients with complete SCI. This resembles the natural bladder cycle more closely than any other procedure, yet this process is invasive and irreversible. Current research aims at overcoming these obstacles by using external devices. Although these treatments are at an experimental stage, they carry the potential to become common options in the future. In addition, neuromodulation may even be suited to prevent NLUTD instead of only treating it, which will significantly improve the quality of life of the affected persons (Table 15.2).

- The treatment of a neurogenic lower urinary tract dysfunction due to a spinal cord injury is complex, challenging, and crucial. The aim is to preserve kidney function, continence, and to improve patient's quality of life. Especially for tibial nerve neuromodulation in MS patients, there are initial data sets that prove its effectiveness. As FES is usually well tolerated, it is a therapy option for selected patients with neurogenic lower urinary tract dysfunction with no immediate risk for the upper urinary tract.

Table 15.2 Recommended stimulation parameters for electrical stimulation at different stimulation sites

		frequency (Hz)	pulse width (μs)	duration/ session (min)	sessions per week	total period (weeks)
stimulation parameters	rectal/ vaginal	5-20	200-400	20	7	8
	genital	5-20	200-400	20	7	8
	sacral	5-20	200-400	20	7	8
	N.tibialis	5-20	200-400	20	7	8

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