

# Guidelines on Neurogenic Lower Urinary Tract Dysfunction

J. Pannek (chair), M. Stöhrer (vice-chair), B. Blok,  
D. Castro-Diaz, G. Del Popolo, G. Kramer, P. Radziszewski,  
A. Reitz, J-J. Wyndaele

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# 1. BACKGROUND

## 1.1 Aims and objectives

The purpose of these clinical guidelines is to provide useful information for clinical practitioners on the incidence, definitions, diagnosis, therapy, and follow-up observation of the condition of neurogenic lower urinary tract dysfunction (NLUTD). These guidelines reflect the current opinion of the experts in this specific pathology and thus represent a state-of-the-art reference for all clinicians, as of the date of its presentation to the European Association of Urology (EAU).

The EAU Guidelines panel consists of an international multidisciplinary group of experts, including urologists specialised in the care of spinal cord injured (SCI) patients, as well as a specialist in the field of urodynamic technologies.

The terminology used and the diagnostic procedures advised throughout these guidelines follow the recommendations for investigations on the lower urinary tract (LUT) as published by the International Continence Society (ICS) (1-3).

## 1.2 Methodology

### 1.2.1 Data identification

Literature searches were carried out for all sections of the Neurogenic Lower Urinary Tract Dysfunction guidelines. Focus of all searches was identification of all level 1 scientific papers (systematic reviews and meta-analyses of randomised controlled trials) in accordance with EAU methodology. In case sufficient data was identified to answer the clinical question, the search was not expanded to include lower level literature. The search was limited to English language publications, animal studies were excluded. Additionally, the guidelines panel have included scientific material from foreign language publications and textbooks.

### 1.2.2 Evidence sources

Searches were carried out in Medline and Embase on the Dialog-Datastar platform. The searches used the controlled terminology of the respective databases. Both Mesh and Emtree were analysed for relevant terms. In many cases the use of free text ensured the sensitivity of the searches.

Randomised controlled trial (RCT) strategies used were based on Scottish Intercollegiate Guidelines Network (SIGN) and Modified McMaster/Health Information Research Unit (HIRU) filters for RCTs, systematic reviews and practice guidelines on the OVID platform and then translated into Datastar syntax.

### 1.2.3 Level of evidence and grade of recommendation

References used in the text have been assessed according to their level of scientific evidence (Table 1), and guideline recommendations have been graded (Table 2) according to the Oxford Centre for Evidence-based Medicine Levels of Evidence (4). The aim of grading recommendations is to provide transparency between the underlying evidence and the recommendation given.

**Table 1: Level of evidence (LE)\***

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised trials
1b	Evidence obtained from at least one randomised trial
2a	Evidence obtained from one well-designed controlled study without randomisation
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study
3	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

\* Modified from Sackett, et al. (4).

It should be noted that when recommendations are graded, the link between the level of evidence and grade of recommendation is not directly linear. Availability of RCTs may not necessarily translate into a grade A recommendation where there are methodological limitations or disparity in published results.

Alternatively, absence of high level evidence does not necessarily preclude a grade A recommendation, if there

is overwhelming clinical experience and consensus. In addition, there may be exceptional situations where corroborating studies cannot be performed, perhaps for ethical or other reasons and in this case unequivocal recommendations are considered helpful for the reader. The quality of the underlying scientific evidence – although a very important factor – has to be balanced against benefits and burdens, values and preferences and costs when a grade is assigned (5-7).

The EAU Guidelines Office, do not perform cost assessments, nor can they address local/national preferences in a systematic fashion. But whenever this data is available, the expert panels will include the information.

**Table 2: Grade of recommendation (GR)\***

Grade	Nature of recommendations
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial
B	Based on well-conducted clinical studies, but without randomised clinical trials
C	Made despite the absence of directly applicable clinical studies of good quality

\*Modified from Sackett, et al. (4).

#### 1.2.4 **Publication history**

The current guidelines present a limited update of the 2008 publication. The EAU published the first guidelines on Neurogenic LUTS 2003 with an update in 2008. A review paper was published in the scientific journal of the association in 2009 (8).

A quick reference document presenting the main findings of the Neurogenic LUTS guidelines is available. All texts can be viewed and downloaded for personal use at the EAU website:

<http://www.uroweb.org/guidelines/online-guidelines/>.

There is a need for ongoing re-evaluation of the information presented in the current guidelines by an expert panel. It must be emphasised that clinical guidelines present the best evidence available to the experts but following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions – also taking personal values and preferences/individual circumstances of patients into account.

#### **Summary of updated information**

An updated literature search was done covering the chapters on Epidemiology, Diagnosis and assessment, Medical Treatment, Sexuality/Fertility and Quality of life. New additions are the Introduction in this chapter 1, Bladder rehabilitation and the chapters on Infections, Sexual Dysfunction and Fertility. Chapter 2 “Epidemiology” has been updated and chapter 3 “Diagnosis” completely renewed.

Readers are advised to consult the other EAU guidelines which may address different aspects of the topics discussed in this document.

### **1.3 Introduction**

The function of the lower urinary tract (LUT) is mainly storage and voiding of urine, which is regulated by a neural control system in the brain and spinal cord that coordinates the activity of the urinary bladder and bladder outlet. Therefore, any disturbance of the nervous systems that control the LUT, including the peripheral nerves in the pelvis, can result in neurogenic lower urinary tract dysfunction (NLUTD). Depending on the extent and location of the disturbance, a variety of different NLUTDs might occur, which can be symptomatic or asymptomatic. Moreover, NLUTD can cause a variety of long-term complications; the most dangerous being damage of renal function. As symptoms and long-term complications do not correlate (9), it is important to identify patients with NLUTD, and establish if they have a low or high risk of subsequent complications.

According to current knowledge, elevated storage pressure in the bladder, either alone or combined with vesicoureteric reflux, is the most important risk factor for renal damage (10). Sustained elevated storage pressure in the bladder is mainly due to a combination of increased detrusor activity during the storage phase (detrusor overactivity (DO) or low compliance), combined with detrusor-sphincter-dyssynergia (DSD). The combination of these two findings is mainly caused by suprasacral infrapontine spinal lesions. Furthermore, elevated detrusor leak point pressure has been demonstrated to be a risk factor for renal deterioration in patients with meningomyelocele (11). Therefore, renal failure has been the leading cause of death in patients with spinal cord injury for a long time (12). Even today, 26% of patients with meningomyelocele who do not

undergo urological treatment develop renal damage. Detrusor leak point pressure  $\geq 40$  cm H<sub>2</sub>O and low bladder compliance are the main risk factors for renal damage (13).

In recent years, adequate diagnosis and treatment of NLUTD in patients with spinal cord lesions have improved the situation of these patients. Nowadays, respiratory diseases are the most frequent (21%) cause of death in patients with SCI (14).

In all other patients with NLUTD, the risk of renal damage is significantly lower. However, in Multiple Sclerosis (MS), urodynamics and clinical symptoms do not correlate, which means that asymptomatic patients can present with abnormal urodynamic findings (15). LUT symptoms do not always lead to urological evaluation in patients with MS, even if the symptoms are troublesome (16). Therefore, urological assessment is important in MS patients (17), although respiratory diseases are currently the leading cause of death for patients with MS, as well those with SCI (18).

In Parkinson disease (PD), NLUTD has not been mentioned as a significant cause of death. Moreover, patients with PD commonly suffer from overactive bladder without DSD (19), which does not seem to be as threatening to the upper urinary tract as DO with DSD. In patients with PD, urodynamic diagnosis of DO correlates well with diagnosis made by questionnaires (20). For these reasons, regular urodynamic follow-up might be less important in PD patients compared with patients suffering from MS or SCI. The same is true for type 2 diabetes, which frequently leads to NLUTD (21), but cardiovascular diseases are the main cause of death in these patients (22).

In summary, treatment and intensity of follow-up examinations are based on the type of NLUTD and the underlying cause.

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## 2. RISK FACTORS AND EPIDEMIOLOGY

### 2.1 Introduction

Neurogenic lower urinary tract dysfunction may be caused by various diseases and events affecting the nervous systems controlling the LUT.

The resulting LUTD depends grossly on the location and the extent of the neurological lesion (see also Section 2.3).

There are no figures on the overall prevalence of NLUTD in the general population, but data are available on the prevalence of the underlying conditions and the relative risk of those for the development of NLUTD. It is important to realise that most of these data show a very wide range of prevalence figures because of the low level of evidence in most published data and smaller sample sizes.

#### 2.1.1 Brain tumours

Brain tumours can cause LUTD in 24% of patients (1). More recently, mostly case reports to small series have been published (2-3). In a series of patients with brain tumours, voiding difficulty was reported in 46/152 (30%) of patients with tumours in the posterior fossa, while urinary incontinence occurred in only three (1.9%) patients (4). Urinary retention was found in 12/17 (71%) children with pontine glioma (5).

#### 2.1.2 Dementia

It is not easy to distinguish dementia-associated LUTD from LUTD caused by age-related changes of the bladder and other concomitant diseases. Therefore, the true incidence of incontinence caused by dementia



is unknown. However, it has been shown that incontinence is much more frequent in geriatric patients with dementia than in patients without dementia (6,7).

Alzheimer, Lewy body dementia, Binswanger, Nasu-Hakola and Pick diseases frequently cause NLUTD (8-13). The occurrence of incontinence is reported to be between 23% and 48% (14,15) in patients with Alzheimer's disease. In Lewy body dementia, 92% of NLUTD is attributed to DO and 53% to incontinence (16). The onset of incontinence usually correlates with disease progression (17). A male-to-female ratio of dementia-related incontinence was found to be 1:15.

### **2.1.3 Mental retardation**

In mental retardation, depending on the grade of the disorder, 12-65% of LUTD was described (18,19).

### **2.1.4 Cerebral palsy**

Lower urinary tract dysfunction has been described in about 30-40% (20,21).

### **2.1.5 Normal pressure hydrocephalus**

There have only been case reports of LUTD (22-24).

### **2.1.6 Basal ganglia pathology (Parkinson disease, Huntington's disease, Shy-Drager syndrome, etc.)**

Parkinson disease is accompanied by NLUTD in 37.9-70% (25-27).

In the rare Shy-Drager syndrome, almost all patients have NLUTD (27), with incontinence found in 73% (28).

Hattori, et al. (29) reported that 60% of Parkinson patients had urinary symptoms. However, Gray et al. (30) reported that functional disturbances of the LUT in PD were not disease-specific and were correlated only with age. Recent, control-based studies have given the prevalence of LUT symptoms as 27-63.9% using validated questionnaires (31-33), or 53% in men and 63.9% in women using a validated questionnaire, which included a urinary incontinence category (33), with all these values being significantly higher than in healthy controls. Ransmayr reported a prevalence of urge episodes and urge incontinence in 53% Lewy body patients, whereas this was observed in 27% of the PD study population, of which 46% were also diagnosed with DO (34).

In most patients, the onset of the bladder dysfunction occurred after the motor disorder had appeared.

### **2.1.7 Cerebrovascular pathology**

Cerebrovascular (CVA) pathology causes hemiplegia with remnant incontinence NLUTD in 20-50% of patients (35,36), with decreasing prevalence in the post-insult period (37). In 1996, 53% of patients with CVA pathology had significant urinary complaints at 3 months (38). Without proper treatment, at 6 months after the CVA, 20-30% of patients still suffered from urinary incontinence (39). The commonest cystometric finding was DO (40-45).

In 39 patients who had brainstem strokes, urinary symptoms were present in almost 50%, nocturia and voiding difficulty in 28%, urinary retention in 21%, and urinary incontinence in 8%. Several case histories have been published presenting difficulties with micturition in the presence of various brainstem pathologies (46-48).

### **2.1.8 Demyelination**

Multiple sclerosis causes NLUTD in 50-90% of the patients (49-51).

The reported incidence of voiding dysfunction in multiple sclerosis is 33-52% in patients sampled consecutively, regardless of urinary symptoms. This incidence is related to the disability status of the patient (52). There is almost a 100% chance of having LUTD once these patients experience difficulties with walking. NLUTD is the presenting symptom in 2-12% of patients, with this finding being as high as 34% in some studies (53). LUTD appears mostly during the 10 years following the diagnosis (54).

### **2.1.9 Spinal cord lesions**

Spinal cord lesions can be traumatic, vascular, medical or congenital. An incidence of 30-40 new cases per million population is the accepted average for the USA. Most of these patients will develop NLUTD (55). The prevalence of spina bifida and other congenital nerve tube defects in the UK is 8-9 per 10,000 aged 10-69 years, with the greatest prevalence in the age group 25-29 years (56), and in the USA 1 per 1,000 births (57). The incidence of urethrovessical dysfunction in myelomeningocele is not completely known, but most studies suggest it is very high at 90-97% (58). About 50% of these children will have DSD (59,60).

In a large review specific data have been given for intradural metastasis from renal carcinoma with 22% of patients presenting with NLUTD (61).

Central cord syndrome is an incomplete SCI. A case series (n = 50) presented NLUTD in 42% of patients at admission, 12 % had residual disturbance during follow up, but most of the 12% related to patients > 70 years old (60% of that age bracket) (62).

In a hereditary spastic paraplegia series, 38 (77.6%) out of 49 patients presented with NLUTD (63).

Caudal Regression Syndrome (CRS): In a case series 61% of patients diagnosed with CRS presented with NLUTD (n = 69). 20% of these CRS patients presented with one kidney (64).

Special attention is to be paid to the combination of traumatic SCI and brain injuries: the incidence of traumatic SCI with clinical concomitant brain injury has increased over the passed 50 years. These findings have consequences for the diagnosis and treatment of NLUTD (65).

In 25% of children with high anorectal malformation, innate NLUTD is present (66).

#### 2.1.10 **Disc disease**

This is reported to cause NLUTD in 28-87% of the patients (< 20%) (67,68). The incidence of cauda equine syndrome due to central lumbar disc prolapse is relatively rare and is about 1-5% of all prolapsed lumbar discs (68-75). There have been case reports of NLUTD without cauda equine syndrome (76) and small series with 90% cure of incontinence (77).

#### 2.1.11 **Spinal stenosis and spine surgery**

About 50% of patients seeking help for intractable leg pain due to spinal stenosis report symptoms of LUTD, such as a sense of incomplete bladder emptying, urinary hesitancy, incontinence, nocturia or urinary tract infections (UTIs) (78). These symptoms may be overlooked or attributed to primary urological disorders, with 61-62% affected by LUTD (79,80). The prevalence of neurological bladder is more significantly associated with the anteroposterior diameter of the dural sac than with its cross-sectional area. Spinal surgery is related to LUTD in 38-60% of patients (81,82). In a series with sacrectomy for sacral chordoma's NLUTD was found in 74% (83).

#### 2.1.12 **Peripheral neuropathy**

Diabetes: This common metabolic disorder has a prevalence of about 2.5% in the American population, but the disease may be subclinical for many years. No specific criteria exist for secondary neuropathy in this condition, but it is generally accepted that 50% of patients will develop somatic neuropathy, with 75-100% of these patients developing NLUTD (84,85). Diabetic patients suffer from various polyneuropathies, with 'diabetic cystopathy' reported in 43-87% of insulin-dependent diabetics without gender or age differences. It is also described in about 25% of type 2 diabetic patients on oral hypoglycaemic treatment (86).

The prevalence of NLUTD in type 2 diabetes gets higher with increasing severity of cardiac autonomic neuropathy (87).

*Alcohol abuse* will eventually cause peripheral neuropathy. This has a reported prevalence that varies widely from 5-15% (88) to 64% (89). NLUTD is probably more likely to be present in patients with liver cirrhosis. The parasympathetic nervous system is attacked more than the sympathetic nervous system (89).

*Less prevalent peripheral neuropathies* include the following:

- Porphyria: bladder dilatation occurs in up to 12% of patients (90).
- Sarcoidosis: NLUTD is rare (91).
- Lumbosacral zone and genital herpes: incidence of LUT dysfunction is as high as 28% when only lumbosacral dermatome-involved patients are considered. The overall incidence is 4% (92,93). NLUTD is transient in most patients.
- Guillain Barré syndrome: the prevalence of micturition disorders varies from 25% to more than 80% (94,95), but is regressive in most cases (96). The true incidence is uncertain because, during the acute phase, patients are usually managed by indwelling catheter.

#### 2.1.13 **Other conditions (systemic lupus erythematosus)**

Nervous system involvement occurs in about half of patients with systemic lupus erythematosus (SLE). Symptoms of LUTD can occur, but data on prevalence are rare and give an incidence of 1% (97,98).

In familial amyloidotic polyneuropathy (FAP) approx. 50% of patients present with NLUTD (99).

### 2.1.14 **Human immunodeficiency virus**

Voiding problems have been described in 12% of HIV-infected patients, mostly in advanced stages of the disease (100,101).

### 2.1.15 **Regional spinal anaesthesia**

This may cause NLUTD but no prevalence figures have been found (102,103).

NLUTD have been described after image guided transforaminal lumbar spine epidural steroid injection (104), and intrathecal methotrexate injection (105).

### 2.1.16 **Iatrogenic**

Abdominoperineal resection of the rectum has been described as causing NLUTD in up to 50% of patients (106,107).

One study has reported that NLUTD remains a long-term problem in only 10% (108); however, the study was not clear whether this was because the neurological lesion was cured or bladder rehabilitation was successful. Surgical prevention with nerve preservation was shown to be important (109,110).

NLUTD has been reported following simple hysterectomy (111) and in 8-57% of patients following radical hysterectomy or pelvic irradiation for cervical cancer (112-115). Surgical prevention can be used to prevent it (116). Neurological dysfunction of the pelvic floor has been demonstrated following radical prostatectomy (117).

## 2.2 **Standardisation of terminology**

### 2.2.1 **Introduction**

Several national or international guidelines have already been published for the care of patients with NLUTD (118-121). The guidelines will evolve as time goes by. The guidelines include definitions of important terms and procedures. The ICS NLUTD standardisation report (119) deals specifically with the standardisation of terminology and urodynamic investigation in patients with NLUTD. Other relevant definitions are found in the general ICS standardisation report (122).

Section 2.2.2 lists the definitions from these references, partly adapted, and other definitions considered useful for clinical practice in NLUTD (Tables 3 and 4). For specific definitions relating to urodynamic investigation, the reader is referred to the appropriate ICS report (119).

### 2.2.2 **Definitions**

**Table 3: Definitions useful in clinical practice**

Acontractility, detrusor	See below under voiding phase
Acontractility, urethral sphincter	See below under storage phase
Autonomic dysreflexia	Increase of sympathetic reflex due to noxious stimuli with symptoms or signs of headache, hypertension, flushing face and perspiration
Capacity	See below under storage phase
Catheterisation, indwelling	Emptying of the bladder by a catheter that is introduced (semi-) permanently
Catheterisation, intermittent (IC)	Emptying of the bladder by a catheter that is removed after the procedure, mostly at regular intervals
• Aseptic IC	The catheters remain sterile, the genitals are disinfected, and disinfecting lubricant is used
• Clean IC	Disposable or cleansed re-usable catheters, genitals washed
• Sterile IC	Complete sterile setting, including sterile gloves, forceps, gown and mask
• Intermittent self-catheterisation (ISC)	IC performed by the patient
Compliance, detrusor	See below under storage phase
Condition	Evidence of relevant pathological processes

Diary, urinary	Record of times of micturitions and voided volumes, incontinence episodes, pad usage, and other relevant information
• Frequency volume chart (FVC)	Times of micturitions and voided volumes only
• Micturition time chart (MTC)	Times of micturitions only
Filling rate, physiological	Below the predicted maximum: body weight (kg) / 4 in mL/s (122,123)
Hesitancy	Difficulty in initiating micturition; delay in the onset of micturition after the individual is ready to pass urine
Intermittency	Urine flow stops and starts on one or more occasions during voiding
Leak point pressure (LPP)	<i>See below under storage phase</i>
Lower motor neuron lesion (LMNL)	Lesion at or below the S1-S2 spinal cord level
Neurogenic lower urinary tract dysfunction (NLUTD)	Lower urinary tract dysfunction secondary to confirmed pathology of the nervous supply
Observation, specific	Observation made during specific diagnostic procedure
Overactivity, bladder	<i>See below under symptom syndrome</i>
Overactivity, detrusor	<i>See below under storage phase</i>
Rehabilitation, LUT	Non-surgical non-pharmacological treatment for LUT dysfunction
Sign	To verify symptoms and classify them
Sphincter, urethral, non-relaxing	<i>See below under voiding phase</i>
Symptom	Subjective indicator of a disease or change in condition, as perceived by the patient, carer, or partner that may lead the patient to seek help from healthcare professionals
Upper motor neuron lesion (UMNL)	Lesion above the S1-S2 spinal cord level
Voiding, balanced: In patients with NLUTD (< 80 mL or < 20% of bladder volume)	Voiding with physiological detrusor pressure and low residual
Voiding, triggered	Voiding initiated by manoeuvres to elicit reflex detrusor contraction by exteroceptive stimuli
Volume, overactivity	<i>See below under storage phase</i>

**Table 4: Further definitions useful in clinical practice**

<b>Storage phase</b>	
Maximum anaesthetic bladder capacity	Maximum bladder filling volume under deep general or spinal anaesthesia
Increased daytime frequency	Self-explanatory; the normal frequency can be estimated at about 8 times per day (124)
Nocturia	Waking at night one or more times to void
Urgency	The symptom of a sudden compelling desire to pass urine that is difficult to defer
Urinary incontinence	Any involuntary leakage of urine
• Stress urinary incontinence	On effort or exertion, or on sneezing or coughing
• Urge urinary incontinence	Accompanied by or immediately preceded by urgency
• Mixed urinary incontinence	Associated with urgency and also exertion, effort, sneezing, or coughing
• Continuous urinary incontinence	
Bladder sensation	

<i>Normal</i>	
• Symptom and history	Awareness of bladder filling and increasing sensation up to a strong desire to void
• Urodynamics	First sensation of bladder filling, first desire to void, and strong desire to void at realistic bladder volumes
<i>Increased</i>	
• Symptom and history	An early and persistent desire to void
• Urodynamics	Any of the three urodynamic parameters mentioned under 'normal' persistently at low bladder volume
<i>Reduced</i>	
• Symptom and history	Awareness of bladder filling but no definite desire to void
• Urodynamics	Diminished sensation throughout bladder filling
<i>Absent</i>	No sensation of bladder filling or desire to void
Non-specific	Perception of bladder filling as abdominal fullness, vegetative symptoms, or spasticity
<i>Definitions valid after urodynamic confirmation only</i>	
Cystometric capacity	Bladder volume at the end of the filling cystometry
• Maximum cystometric capacity	Bladder volume at strong desire to void
• High-capacity bladder	Bladder volume at cystometric capacity far over the mean voided volume, estimated from the bladder diary, with no significant increase in detrusor pressure under non-anaesthetised condition
Normal detrusor function	Little or no pressure increase during filling: no involuntary phasic contractions despite provocation
Detrusor overactivity	Involuntary detrusor contractions during filling; spontaneous or provoked
• Phasic DO	Characteristic phasic contraction
• Terminal DO	A single contraction at cystometric capacity
• High pressure DO	Maximal detrusor pressure > 40 cm H <sub>2</sub> O (119,125)
• Overactivity volume	Bladder volume at first occurrence of DO
• Detrusor overactivity incontinence	Self-explanatory
Leak point pressure	
• Detrusor leak point pressure (DLPP)	Lowest value of detrusor pressure at which leakage is observed in the absence of abdominal strain or detrusor contraction
• Abdominal leak point pressure	Lowest value of intentionally increased intravesical pressure that provokes leakage in the absence of a detrusor contraction
Detrusor compliance	Relationship between change in bladder volume ( $\Delta V$ ) and change in detrusor pressure ( $\Delta p_{det}$ ): $C = \Delta V / \Delta p_{det}$ (mL/cmH <sub>2</sub> O)
• Low detrusor	compliance $C = \Delta V / \Delta p_{det} < 20$ mL/cm H <sub>2</sub> O (106)
Break volume	Bladder volume after which a sudden significant decrease in detrusor compliance is observed
Urethral sphincter acontractility	No evidence of sphincter contraction during filling, particularly at higher bladder volumes, or during abdominal pressure increase
<b>Voiding phase</b>	
• Slow stream	Reduced urine flow rate
• Intermittent stream (intermittency)	Stopping and starting of urine flow during micturition

• Hesitancy	Difficulty in initiating micturition
• Straining	Muscular effort to initiate, maintain, or improve urinary stream
• Terminal dribble	Prolonged final part of micturition when the flow has slowed to a trickle/dribble
<i>Definitions valid after urodynamic confirmation only</i>	
Normal detrusor function	Voluntarily initiated detrusor contraction that causes complete bladder emptying within a normal time span
Detrusor underactivity	Contraction of reduced strength / duration
Acontractile detrusor	Absent contraction
Non-relaxing urethral sphincter	Self-explanatory
Detrusor sphincter dyssynergia (DSD)	Detrusor contraction concurrent with an involuntary contraction of the urethra and/or periurethral striated musculature
<p><b>Post-micturition phase</b></p> <p>Feeling of incomplete emptying (symptom only)</p> <p>Post-micturition dribble: involuntary leakage of urine shortly after finishing the micturition</p> <p>Pain, discomfort or pressure sensation in the LUT and genitalia that may be related to bladder filling or voiding, may be felt after micturition, or be continuous</p> <p>Symptom syndrome: combination of symptoms</p> <ul style="list-style-type: none"> <li>• Overactive bladder syndrome: urgency with or without urge incontinence, usually with frequency and nocturia</li> <li>• Synonyms: urge syndrome, urgency-frequency syndrome</li> <li>• This syndrome is suggestive for LUTD</li> </ul>	

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## 3. DIAGNOSIS

### 3.1 Introduction

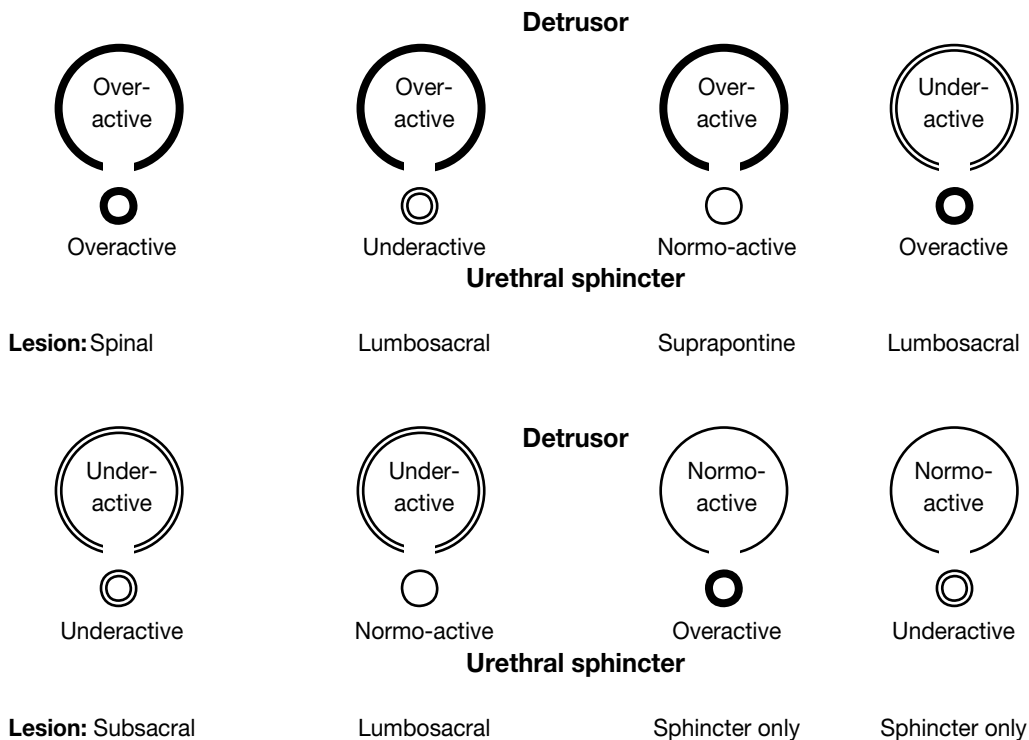
A thorough medical history and physical examination is mandatory, before any additional diagnostic investigations are planned. The clinical assessment of patients with NLUTD includes a detailed history, a

patient voiding diary and systematic physical examination. The initial evaluation is essential to determine the therapeutic scheme for long-term treatment and follow-up.

### 3.2 Classification

The NLUTD classification provides a standardised terminology. Several classification systems have been proposed. A simple classification focused on therapeutic consequences has been proposed by Madersbacher (1) (LE: 4). This classification describes several NLUTD symptoms on the basis of the contraction state of the bladder and external urethral sphincter during voiding and filling phase (Figure 1).

**Figure 1: Madersbacher classification system with typical neurogenic lesions [1]**



### 3.3 Timing of diagnosis and treatment

Early diagnosis and treatment are essential in both congenital and acquired NLUTD. Irreversible changes within the LUT may occur, even with normal neurological reflexes (2,3) (LE: 3). Additionally, NLUTD can be the presenting feature of neurological pathology (4,5) (LE: 3). Early intervention, e.g. intermittent catheterisation (IC), can prevent irreversible deterioration of the lower and upper urinary tract (6) (LE: 3).

### 3.4 Patient history

History taking is the cornerstone of evaluation and should include past and present symptoms and disorders. The patient's past history should be taken in detail, particularly in cases of non-traumatic neurological bladder dysfunction with a slow insidious onset. Occasionally, this is traceable to childhood or adolescence (7) (LE: 4). Urinary history consists of symptoms related to both storage and evacuation functions of the LUT.

Bowel history is important since patients with NLUTD may suffer from a related neurogenic condition of the lower gastrointestinal tract. This may reflect the neurological condition of the urinary bladder (7) (LE: 4). Sexual function may also be impaired because of the neurogenic condition.

Table 5 gives an overview of the items that should be assessed. These items are important to guide the decision process of diagnostic investigations and treatment options.

Special attention should be paid to possible warning signs and symptoms (e.g. pain, infection, haematuria and fever) that warrant further investigation. However, it is usually difficult for patients with SCI to report accurately symptoms related to urinary tract infections (8-10) (LE: 3).

<b>Table 5: History examination in neurogenic lower urinary tract dysfunction*</b>	
<b>Past history</b>	
	Childhood – adolescence – adult
	Hereditary or familial risk factors
	Menarche (age); <i>may suggest metabolic disorder</i>
	Obstetric history
	History of diabetes; <i>in some cases correction will resolve the neurological problem</i>
	Diseases, e.g. <i>syphilis, Parkinsonism, multiple sclerosis, encephalitis</i>
	Accidents and operations, <i>especially those involving the spine and central nervous system</i>
<b>Present history</b>	
	Present medication
	Lifestyle (smoking, alcohol and drugs); <i>may influence bowel and urinary function</i>
	Quality of life
	Life expectancy
<b>Specific urinary history</b>	
	Onset urological history
	Relief after voiding; <i>to detect the extent of a neurological lesion in the absence of obstructive uropathy</i>
	Bladder sensation
	Initiation of micturition ( <i>normal, precipitate, reflex, strain, Credé</i> )
	Interruption of micturition ( <i>normal, paradoxical, passive</i> )
	Enuresis
	Mode and type of voiding (catheterisation)
	Urinary diary; <i>(semi)objective information about number of voids, day- and night-time voiding frequency, volumes voided, incontinence, urge episodes</i>
<b>Bowel history</b>	
	Frequency and faecal incontinence
	Desire to defecate
	Defecation pattern
	Rectal sensation
	Initiation of defecation ( <i>digital rectal stimulation</i> )
<b>Sexual history</b>	
	Genital or sexual dysfunction symptoms
	Sensation in genital area
	Specific male: erection, (lack of) orgasm, ejaculation
	Specific female: dyspareunia, (lack of) orgasm
<b>Neurological history</b>	
	Acquired or congenital neurological condition
	Mental status and comprehension
	Neurological symptoms (somatic and sensory), with onset, evolution and any treatment
	Spasticity or autonomic dysreflexia (lesion above level Th 6)
	Mobility and hand function

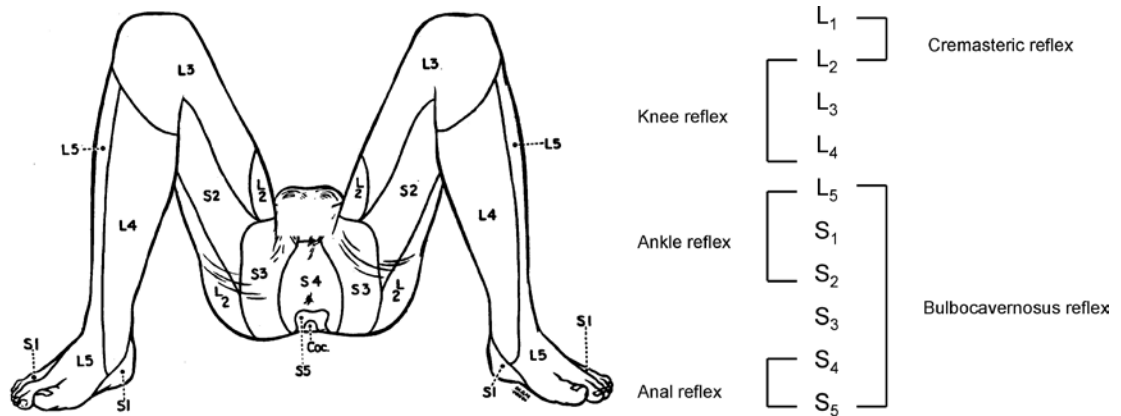
\* Extracted from Bors and Turner ([7] (LE: 4; GR: C) and Stöhrer, et al. [11] (LE: 4; GR: C).

Voiding diaries offer information on the number of voids, volumes voided, incontinence, and urge episodes. A 24-hour voiding diary was shown to be reliable in women with urinary incontinence (12,13) (LE: 3). However, no such information is available in patients with neurological incontinence. The voiding diary is also useful in patients performing intermittent catheterisation (11) (LE: 4).

### 3.5 Physical examination

In addition to a detailed patient history and a general examination, attention should be paid to possible physical and mental handicaps with respect to the planned investigation.

Neurological status should be described as completely as possible (Table 4). Patients with very high neurological lesions may suffer from a significant drop in blood pressure when moved in a sitting or standing position. All sensations and reflexes in the urogenital area must be tested. Furthermore, detailed testing of the anal sphincter and pelvic floor functions must be performed (Figure 2). Availability of this clinical information is essential for the reliable interpretation of subsequent diagnostic investigations.



**Figure 2: The neurological status of a patient with neurogenic lower urinary tract dysfunction (NLUTD) must be described as completely as possible: (a) dermatomes of spinal cord levels L2-S4; (b) urogenital and other reflexes in the lower spinal cord**

**Table 6: Neuro-urological items to be specified\***

Sensations S2-S5 (both sides)	
	Presence (increased/normal/reduced/absent)
	Type (sharp/blunt)
	Afflicted segments
Reflexes (increased/normal/reduced/absent)	
	Bulbocavernous reflex
	Perianal reflex
	Knee and ankle reflexes
	Plantar responses (Babinski)
Anal sphincter tone	
	Presence (increased/normal/reduced/absent)
	Voluntary contractions of anal sphincter and pelvic muscles (increased/normal/reduced/absent)
Prostate palpation	
Descensus (prolapse) of pelvic organs	

\*From Stöhrer, et al. [11] (LE: 4; GR: C).

#### Caution

Autonomic dysreflexia (AD) is a sudden and exaggerated autonomic response to stimuli in patients with spinal cord injuries or dysfunction above level Th 5–Th 6. Hypertension is a relatively common manifestation of AD and can have life-threatening results if not properly managed (14-16) (LE: 3; GR: C).

### 3.5.1 Recommendations for history taking and physical examination\*

History taking	GR
An extensive general history is mandatory, concentrating on past and present symptoms and conditions for urinary, bowel, sexual, and neurological functions, and on general conditions that might impair any of these.	A
Special attention should be paid to the possible existence of alarm signs, such as pain, infection, haematuria, fever, etc, that warrant further specific diagnosis.	A
A specific history should be taken for each of the four mentioned	A
Physical examination	A
Individual patient handicaps should be acknowledged in planning further investigations.	A
The neurological status should be described as completely as possible. Sensations and reflexes in the urogenital area must all be tested.	A
The anal sphincter and pelvic floor functions must be tested extensively.	A
Urinalysis, blood chemistry, voiding diary, residual and free flowmetry, incontinence quantification and urinary tract imaging should be performed.	A

\* All grade A recommendations based on panel consensus.

## 3.6 Urodynamics

### 3.6.1 Introduction

Urodynamic investigation is the only method that can objectively assess the (dys-)function of the LUT. It is essential to describe the LUT status in patients with NLUTD.

In these patients, particularly when DO might be present, the invasive urodynamic investigation is even more provocative than in other patients. Any technical source of artefacts must be critically considered. The quality of the urodynamic recording and its interpretation must be ensured (17).

In patients at risk for autonomic dysreflexia, it is advisable to measure blood pressure during the urodynamic study.

In many patients with NLUTD, it may be helpful to assess the maximum anaesthetic bladder capacity. The rectal ampulla should be empty of stool before the start of the investigation. Drugs that influence the LUT function should be stopped at least 48 hours before the investigation (if feasible) or otherwise be considered when interpreting the data obtained.

All urodynamic findings must be reported in detail and performed according to the ICS technical recommendations and standards (17-19).

### 3.6.2 Urodynamic tests

A bladder diary is a semi-objective qualification of the LUT. It is a highly advisable diagnostic tool. For reliable interpretation, it should be recorded over at least 2-3 days (18,20). Possible pathological findings: high voiding frequency, very low or very high voided volumes, nocturnal voidings, urgency, incontinence.

*Free uroflowmetry and assessment of residual urine* gives a first impression of the voiding function. It is mandatory before planning any invasive urodynamics. For reliable information, it should be repeated at least 2-3 times (18,21,22). Possible pathological findings: low flow rate, low voided volume, intermittent flow, hesitancy, residual urine.

Care must be taken when assessing the results in patients who are not able to void in a normal position. Both the flow pattern and the flow rate may be modified by inappropriate positions and by any constructions to divert the flow.

*Filling cystometry*: The only method to quantify the filling function has limited significance as a solitary procedure. It is much more powerful if combined with bladder pressure measurement during micturition and even more in video-urodynamics. This investigation is necessary to document the status of the LUT function during the filling phase. The bladder should be empty at the start of filling. A physiological filling rate should be used with body-warm saline, as fast filling and room-temperature saline are provocative (18).

Possible pathological findings include DO, low detrusor compliance, abnormal bladder and other sensations, incontinence, incompetent or relaxing urethra.

*Detrusor leak point pressure (DLPP)*: This specific investigation may estimate the risk for the upper urinary tract or for secondary bladder damage (18,23). The DLPP is a screening test only, because it gives no impression of



the duration of the high pressure during the filling phase, which can be expected to have even more impact on the upper urinary tract (24). A high DLPP thus warrants further testing by video-urodynamics.

*Pressure flow study:* This measurement reflects the co-ordination between detrusor and urethra or pelvic floor during the voiding phase. It is even more powerful in combination with filling cystometry and with video urodynamics. It is necessary to document the function of the LUT function during the voiding phase. Possible pathological findings: Detrusor underactivity/acontractility, DSD, non-relaxing urethra, residual urine.

Most types of obstruction caused by NLUTD are due to DSD (25,26), non-relaxing urethra, or nonrelaxing bladder neck (18,27,28). Pressure-flow analysis mostly assesses the amount of mechanical obstruction caused by the urethra's inherent mechanical and anatomical properties and has limited value in patients with NLUTD.

*Electromyography (EMG):* Registration of the activity of the external urethral sphincter, the peri-urethral striated musculature, the anal sphincter, or the striated pelvic floor muscles. The correct interpretation may be difficult due to artefacts introduced by other equipment used. In the urodynamic setting an EMG is useful as a gross indication of the patient's ability to control the pelvic floor. Possible pathological findings: Inadequate recruitment on specific stimuli (bladder filling, hyperreflexive contractions, onset of voiding, coughing, Valsalva, etc.). More detailed analysis (motor unit potentials, single-fibre EMG) is only possible as part of a neurophysiological investigation.

*Urethral pressure measurement:* This investigation has only a very limited place in NLUTD. There exists no basic consensus on parameters indicating pathological findings (29).

*Video-urodynamics:* This combination of filling cystometry and pressure flow study with imaging is the gold standard for urodynamic investigation in NLUTD (18,30,31). Possible pathological findings: All as described under cystometry and pressure flow study, plus morphological pathology of the LUT and the upper urinary tract.

*Ambulatory urodynamics:* Functional investigation of the urinary tract utilising predominantly natural filling of the urinary tract and reproducing normal subject activity (32).

This type of study should be considered when office urodynamics do not reproduce the patient's symptoms and complaints. Possible pathological findings include those found under filling cystometry and pressure flow study, provided the flow is measured also. It should be kept in mind that during this study the actual bladder volume is unknown.

*Provocative tests during urodynamics:* The LUT function can be provoked by coughing, triggered voiding, or anal stretch.

Fast-filling cystometry with cooled saline (the 'ice water test') is considered a discriminative test between upper motor neuron lesion (UMNL) and lower motor neuron lesion (LMNL) (33-38). Patients with UMNL will develop a detrusor contraction if the detrusor muscle is intact, while patients with lower lesions will not. The test gives false-positive results in young children (35) and does not seem to be fully discriminative in other patients (36,37).

It was thought that a positive bethanechol test (39) (detrusor contraction > 25 cm H<sub>2</sub>O) provided proof of a detrusor denervation hypersensitivity and the muscular integrity of an acontractile detrusor; however, in practice, the test has given equivocal results. Recently, a variation of this method was reported using intravesical electromotive administration of the bethanechol (40); this test turned out to be both selective and predictive for successful oral bethanechol treatment.

### 3.6.3 **Specific uro-neurophysiological tests**

These tests are advised as part of the neurological work-up of the patient. They comprise:

- EMG (in a neurophysiological setting) of pelvic floor muscles, urethral sphincter and/or anal sphincter;
- nerve conduction studies of pudendal nerve;
- reflex latency measurements of bulbocavernosus and anal reflex arcs;
- evoked responses from clitoris or glans penis;
- sensory testing on bladder and urethra.

Other elective tests may be asked for specific conditions that became obvious during patient work-up and urodynamic investigations. Possible pathological findings are dependent on the type of the test.

### 3.6.4 Recommendations for urodynamics and uro-neurophysiology

Recommendations	GR
Urodynamic investigation is necessary to document the (dys-)function of the LUT.	A
The recording of a bladder diary is advisable.	B
Non-invasive testing is mandatory before invasive urodynamics is planned.	A
Video-urodynamics is the gold standard for invasive urodynamics in patients with NLUTD. If this is available, then a filling cystometry continuing into a pressure flow study should be performed.	A
A physiological filling rate and body-warm saline must be used.	A
Specific uro-neurophysiological tests are elective procedures.	C

### 3.7 Typical manifestations of neurogenic lower urinary tract dysfunction

Typical findings in NLUTD are listed below:

#### Filling phase

- hyposensitivity or hypersensitivity;
- vegetative sensations;
- low compliance;
- high capacity bladder;
- detrusor overactivity, spontaneous or provoked;
- sphincter acontractility.

#### Voiding phase

- detrusor acontractility;
- dsd;
- non-relaxing urethra;
- non-relaxing bladder neck.

These signs warrant further neurological evaluation, as LUTD may be the presenting symptom of NLUTD (41-45).

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## 4. TREATMENT

### 4.1 Introduction

The primary aims for treatment of NLUTD and their priorities are (1-4):

1. Protection of the upper urinary tract;
2. Improvement of urinary continence;
3. Restoration of (parts of) the LUT function;
4. Improvement of the patient's QoL.

Further considerations are the patient's disability, cost-effectiveness, technical complexity, and possible complications (4).

Preservation of the upper tract function is of paramount importance (1-7). Renal failure was the main factor for mortality in the SCI patient surviving the trauma (5-7). This has led to the golden rule in treatment of NLUTD: ensure that the detrusor pressure remains within safe limits during both the filling phase and the voiding phase (1-4). This approach has indeed significantly reduced the mortality from urological causes in this patient group (8).

The therapy of urinary incontinence is important for social rehabilitation of the patient and thus contributes substantially to the QoL. It is also pivotal in preventing UTI (6,7). If complete continence cannot be achieved, methods to attain a socially acceptable control of incontinence can be used.

The patient's QoL is an essential part of any treatment decision.

In patients with high detrusor pressure during the filling phase (DO, low detrusor compliance) or during the voiding phase (DSD, other causes of bladder outlet obstruction), treatment is aimed primarily at 'conversion of an active, aggressive high-pressure bladder into a passive low-pressure reservoir' despite the resulting residual urine (1).

### 4.2 Non-invasive conservative treatment

#### 4.2.1 Assisted bladder emptying

Incomplete bladder emptying is a serious risk factor for UTI, developing a high intravesical pressure during the filling phase, and incontinence. Methods to improve the voiding process are practised in patients with NLUTD.

*Third party bladder expression (Credé):* Regretfully, this method is still applied, foremost in infants and young children with myelomeningocele and sometimes in tetraplegics. Because of the high pressures that may be created during this procedure, it is potentially hazardous for the urinary tract (9).

*Voiding by abdominal straining (Valsalva):* The considerations mentioned under Credé above also apply to the Valsalva manoeuvre (1,9-11). For both methods of emptying, long-term complications are hardly avoidable (9,10) and the already weak pelvic floor function may be further impaired, thus exacerbating the existing incontinence (11).

*Triggered reflex voiding:* Stimulation of the sacral or lumbar dermatomes in patients with UMNL can elicit reflex contraction of the detrusor (1,11). Morbidity occurs more often during the first decades of treatment (12-16). Strict urodynamic control is therefore required (1,11).

*Behavioural modification techniques:* These are used to improve continence and include prompted voiding, timed voiding (bladder training), and lifestyle modification (17-20).

*Pelvic floor muscle exercises:* These aim to improve continence. They may be helpful in selected patients with NLUTD (21-23).

*Biofeedback:* This method can be used for supporting the voiding pattern modification (24,25).

#### 4.2.2 Lower urinary tract rehabilitation

##### 4.2.2.1 Bladder rehabilitation including electrical stimulation

###### 4.2.2.1.1 Introduction

The term bladder rehabilitation summarises treatment options that aim to re-establish bladder function in patients with NLUTD. Regaining voluntary control over LUTD has been described in individuals with non-neurogenic bladder dysfunction, using behavioural treatment in patients with urge incontinence and biofeedback training for stress urinary incontinence. However, evidence for bladder rehabilitation using electrical stimulation in neurogenic patients is lacking and mainly based on pilot studies with small patient numbers.

A strong contraction of the urethral sphincter and/or pelvic floor, but also anal dilatation, manipulation of the genital region, and physical activity reflexly inhibit the micturition (11,26). Whereas the first mechanism is affected by activation of efferent fibres, the latter ones are produced by activation of afferents (14). Electrical stimulation of the pudendal nerve afferents produces a strong inhibition of the micturition reflex and of the detrusor contraction (27). This stimulation might then support the restoration of the balance between excitatory and inhibitory inputs at the spinal or supraspinal level (11,28,29). It might also imply that patients with incomplete lesions will benefit (11,29,30), but patients with complete lesions will not (31).

#### 4.2.2.1.2 Peripheral temporary electrostimulation

Posterior tibial nerve stimulation and external temporary electrical stimulation (e.g. penile/clitoral or intracavitary) suppress neurogenic DO during acute stimulation (32). Both techniques have also demonstrated sustained prolonged effects (3 months and 1 year, respectively) in patients with neurogenic bladder dysfunction due to MS (33,34).

In MS patients, combining active neuromuscular electrical stimulation with pelvic floor muscle training and electromyography biofeedback achieved a substantial reduction of LUTD (35). Furthermore, this treatment combination was significantly superior ( $p = 0.0028$ ) to electrostimulation alone.

*Biofeedback:* This method can be used for supporting the voiding pattern modification (24,25).

#### 4.2.2.1.3 Intravesical electrostimulation

Intravesical electrostimulation can increase bladder capacity, improve bladder compliance as well as the sensation of bladder filling in patients with incomplete SCI or meningocele (36). In patients with neurogenic detrusor hypocontractility, intravesical electrostimulation may also improve voiding and reduce residual urine volume (37).

#### 4.2.2.1.4 Chronic peripheral pudendal stimulation

The results of a pilot study showed that chronic peripheral pudendal stimulation (chronic, defined as a period of 2 weeks) in patients with incomplete SCI produced significant neuromodulatory effects in the brain which led to changes in urodynamic parameters (38).

#### 4.2.2.1.5 Repetitive transcranial magnetic stimulation

Although repetitive transcranial magnetic stimulation improved voiding symptoms in patients with PD or MS, the duration of the effect, stimulation parameters and the appropriate patient selection are still under investigation (39,40).

#### 4.2.2.1.6 Summary

To date, bladder rehabilitation techniques are mainly based on electrical or magnetic stimulation. However, there is a lack of well-designed studies for all techniques. The different techniques of external temporary electrostimulation, possibly combined with biofeedback training, may be useful, especially in patients with MS or incomplete spinal cord injury. Further studies are necessary to evaluate the usefulness of these techniques.

### 4.2.3 **Drug treatment**

A single, optimal, medical therapy for NLUTD is not yet available. Currently, a combination of therapies is the best way to maximise outcomes (41-50) (LE: 1a).

#### 4.2.3.1 *Antimuscarinic drugs*

Antimuscarinic drugs are the first-line choice for treating NLUTD. They are the most useful medications available for NLUTD and provide an established approach to managing neurogenic detrusor overactivity (NDO) (41-47, 51-53) (LE: 1a). Previously, these drugs were known as 'anticholinergic', but they are now described as muscarinic receptor antagonists because of their action in binding to muscarinic receptors. Antimuscarinic drugs are used to stabilise the detrusor muscle, which reduces its overactivity and makes it moderately refractory to parasympathetic stimulation. This results in improved bladder compliance and reduced symptoms of overactive bladder (47,51), which in turn helps to prevent renal and bladder damage and potentially improve long-term outcomes (54) (LE: 1a).

Neurogenic patients may need a higher dose of antimuscarinic agents than patients with idiopathic DO (47,48,55-57) (LE: 1b). However, adverse events due to the higher dosage may lead to early discontinuation of therapy (19,21,56,58,59) (LE: 1b).

#### 4.2.3.1.1 Choice of antimuscarinic agent

Oxybutynin chloride (47) (LE: 1a) (48-51,57-59), trospium chloride (47,55,56,60), tolterodine tartrate (61-63) and propiverine (47,58,64,65) (LE: 1a) are established, effective, medical treatments. These antimuscarinic agents are known to be well tolerated and safe, even during long-term treatment. They have diverse tolerance profiles, so that a different antimuscarinic agent may be prescribed if a patient experiences adverse effects or if the therapeutic effect is not sufficient (66).

Darifenacin has recently been evaluated in neurogenic overactive bladder secondary to MS (67,68), with results similar to other muscarinic drugs. Solifenacin has also been introduced, even though to date there has been no published clinical evidence of the use of solifenacin in NDO. Data is awaited from an ongoing trial.

#### 4.2.3.1.1.1 Side effects

Antimuscarinic agents have some minor side-effects, e.g. dry mouth. It has been suggested that different ways of administration may help to reduce side effects. In a selected group of patients, transdermal oxybutynin was found to be well tolerated and effective (69,70), while intravesical oxybutynin led to abolishment of the bladder-cooling reflex (71). However, further research is needed into the use of alternative methods of administration, particularly long-term results (LE: 2a).

#### 4.2.3.2 Other agents

##### 4.2.3.2.1 Phosphodiesterase inhibitors (PDE5I)

These have demonstrated significant effects upon DO in pilot studies and in the future may become an alternative or adjunct to antimuscarinic treatment (72).

##### 4.2.3.3 Adjunct desmopressin

Additional treatment with desmopressin might improve the efficacy of treatment (73-75) (LE: 3).

#### 4.2.3.4 Drugs with different mechanisms of action

##### 4.2.3.4.1 Detrusor underactivity

Cholinergic drugs, such as bethanechol chloride and distigmine bromide, have been considered to enhance detrusor contractility and promote bladder emptying, but are not routinely used in clinical practice. The available studies do not support the use of parasympathomimetic agents, especially when frequent and/or serious possible side-effects are considered (76) (LE: 1a).

Combination therapy with an antimuscarinic drug and alpha-blocker appears to be more useful than monotherapy with either agent (77). In conclusion, there is no drug with evidence of efficacy for underactive detrusor (11,78-81) (LE: 2a).

##### 4.2.3.4.2 Decreasing bladder outlet resistance

Alpha-blockers (non-selective and selective) have been partially successful for decreasing bladder outlet resistance, residual urine and autonomic dysreflexia (11,82-86) (LE: 2a).

##### 4.2.3.4.3 Increasing bladder outlet resistance

Several drugs have shown efficacy in selected cases of mild stress urinary incontinence, but there have been very few publications in patients with NLUTD (11,87).

##### 4.2.3.4.4 Conclusions and recommendations on drug treatments

Conclusions	LE
Long-term efficacy and safety of antimuscarinic therapy for NDO is well documented.	1a
A combination of antimuscarinic agents is now used more frequently and is often considered to maximise outcomes for NDO.	1a
Alternative ways of administration of antimuscarinic agents, such as transdermally and intravesically, should now be considered.	2a
There is no drug with evidence of efficacy for underactive detrusor.	2a
Alpha-blockers have been partly successful in decreasing bladder outlet resistance and autonomic dysreflexia prophylaxis in spinal cord injury.	2a
There is a lack of prospective, randomised, controlled studies in the medical management of NLUTD.	

Recommendations on drug treatments	GR
Antimuscarinic therapy for NDO is effective and safe to use, including long term.	A
Outcomes for NDO can be maximised by considering a combination of antimuscarinic agents.	A
Alternative ways of administration of antimuscarinic agents, such as transdermally and intravesically, should be considered with the aim of reducing side effects.	B
Alpha-blockers may help to decrease bladder outlet resistance and may be a preventive measure in spinal cord injury to prevent autonomic dysreflexia.	B

#### 4.2.4 External appliances

As an ultimate remedy, social continence may be achieved by collecting urine during incontinence (1,11). Condom catheters with urine collection devices are a practical method for men. Otherwise, incontinence pads may offer a reliable solution. In both cases, the infection risk must be closely observed (11). Because of the risk of developing high intravesical pressure, the penile clamp is absolutely contraindicated.

#### 4.2.5 Statements & guidelines on non-invasive conservative treatment

Statements	LE
The first aim of any therapy is the protection of the upper urinary tract.	1
A condom catheter or pads may reduce urinary incontinence to a socially acceptable situation.	

Recommendations	GR
The mainstay of treatment for overactive detrusor is anticholinergic drug therapy.	A
Lower urinary tract rehabilitation may be effective in selected cases (patients that do not suffer from a complete spinal cord lesion).	
Any method of assisted bladder emptying should be used with the greatest caution.	A

### 4.3 Minimal invasive treatment

#### 4.3.1 Catheterisation

Intermittent self- or third-party catheterisation (88,89) is the gold standard for the management of NLUTD (1,11). It is effective in patients with:

- Detrusor underactivity or acontractility (1).
- With DO, provided the overactivity can be controlled (1,11,90-95).

Sterile IC, as originally proposed by Guttmann and Frankel (67), significantly reduces the risk of UTI and/or bacteriuria (1,11,96,97), compared with clean IC introduced by Lapedes, et al. (89). However, it cannot be considered a routine procedure (11,97). Aseptic IC is an alternative (1,98), which provides a significant benefit in reducing the potential for external contamination of an intermittent urinary catheter (99). Insufficient patient education and the inherent greater risk of UTI in patients with NLUTD are contributing factors (11,100-104).

The average frequency of catheterisations per day is 4-6 times and the catheter size should be 12-14 Fr.

Less frequent catheterisation results in higher catheterisation volumes and a higher risk of UTI (1,100-103). More frequent catheterisation increases the risk of cross-infections and other complications (1,100-103).

Bladder volume at catheterisation should be lower than 400 mL.

The prevalence of complications can be limited by adequate patient education, use of nontraumatising techniques and adequate precautions to prevent infections (11,104).

Indwelling transurethral catheterisation and, to a lesser extent, suprapubic cystostomy are significant and early risk factors for UTI and other complications (11,16,105-114). Silicone catheters are preferred because they are less susceptible to encrustation and because of the high incidence of latex allergy in the NLUTD population.



#### 4.3.2 Recommendations for catheterisation

Recommendations	GR
Intermittent catheterisation is the standard treatment for patients who are unable to empty their bladder.	A
Patients should be well instructed in the technique and risks of IC.	
Aseptic IC is the method of choice.	B
The catheter size should be 12-14 Fr.	B
The frequency of IC is 4-6 times per day.	B
The bladder volume should remain below 400.	B
Indwelling transurethral and suprapubic catheterisation should be used only exceptionally, under close control, and the catheter should be changed frequently. Silicone catheters are preferred and should be changed every 2-4 weeks, while (coated) latex catheters need to be changed every 1-2 weeks.	A

#### 4.3.3 Intravesical drug treatment

To reduce DO, anticholinergics can also be applied intravesically (115-121). This approach may reduce adverse effects because the anticholinergic drug is metabolised differently (119) and a greater amount is sequestered in the bladder, even more than with electromotive administration (120,121).

The vanilloids, capsaicin and resiniferatoxin, desensitise the C-fibres and thereby decrease DO for a period of a few months until the sensation of these fibres has been restored (122-127).

The dosage is 1-2 mMol capsaicin in 100 mL 30% alcohol, or 10-100 nMol resiniferatoxin in 100 mL 10% alcohol for 30 minutes. Resiniferatoxin has about a 1,000-fold potency compared to capsaicin, with less pain during the instillation, and is effective in patients refractory to capsaicin. Clinical studies have shown that resiniferatoxin has limited clinical efficacy compared to botulinum toxin A injections in the detrusor (127).

#### 4.3.4 Intravesical electrostimulation

Intravesical electrostimulation (128) enhances the sensation for bladder filling and urge to void and may restore the volitional control of the detrusor (11,129,130). Daily stimulation sessions of 90 minutes with 10 mApulses of 2 ms duration at a frequency of 20 Hz (130,131) are used for at least 1 week (131). It appears that patients with peripheral lesions are the best candidates, that the detrusor muscle must be intact, and that at least some afferent connection between the detrusor and the brain must still be present (11,130,131). Also, the positioning of the stimulating electrodes and bladder filling are important parameters (132). With these precautions, the results in the literature are still not unequivocal: both positive (129,131,133,134) and negative (LE: 3) (135,136) results have been reported.

#### 4.3.5 Botulinum toxin injections in the bladder

Botulinum toxin causes a long-lasting but reversible chemical denervation that lasts for about 9 months (137-143). The toxin injections are mapped over the detrusor in a dosage that depends on the preparation used. Botulinum toxin A has been proven effective in a randomised placebo-controlled trial in NLUTD (144). Repeated injections seem to be possible without loss of efficacy (143,145,146). Generalised muscular weakness is an occasional adverse effect (141,143,146). Histological studies have not found ultrastructural changes after injection (147).

#### 4.3.6 Bladder neck and urethral procedures

Reduction of the bladder outlet resistance may be necessary to protect the upper urinary tract. This can be achieved by surgical interventions (bladder neck or sphincter incision or urethral stent) or by chemical denervation of the sphincter. Incontinence may result and can be managed by external devices (see Section 4.2.5).

*Botulinum toxin sphincter injection* can be used to treat detrusor sphincter dyssynergia effectively by injection in a dosage that depends on the preparation used. The dyssynergia is abolished for a few months, necessitating repeat injections. The efficacy of this treatment is high and there are few adverse effects (148-150).

*Balloon dilatation*: although favourable immediate results were reported (151), no further reports since 1994 have been found. Consequently, this method is no longer recommended.

*Sphincterotomy*: by staged incision, bladder outlet resistance can be reduced without completely losing the closure function of the urethra (1,11,144). The laser technique appears to be advantageous (1,152).

Sphincterotomy also needs to be repeated at regular intervals in a substantial proportion of patients (153), but is efficient and without severe adverse effects (1,9,151-154). Secondary narrowing of the bladder neck may occur, for which combined bladder neck incision might be considered (1,155).

*Bladder neck incision*: This is indicated only for secondary changes at the bladder neck (fibrosis) (1,9,152,155). When the detrusor is hypertrophied and causes thickening of the bladder neck, this procedure makes no sense (1).

*Stents*: Implantation of urethral stents causes the continence to be dependent on the adequate closure of the bladder neck only (1,4). Although the results are comparable with sphincterotomy and the stenting procedure has a shorter surgery time and reduced hospital stay (156,157), the costs (1) and possible complications or re-interventions (156,158,159) are limiting factors in its use.

*Increasing bladder outlet resistance*: This can improve the continence condition. Despite early positive results with urethral bulking agents, a relative early loss of continence is reported in patients with NLUTD (4,16,160-164).

*Urethral inserts*: Urethral plugs or valves for management of (female) stress incontinence have not been applied in patients with NLUTD. The experience with active pumping urethral prosthesis for treatment of the underactive or acontractile detrusor was disappointing (165).

#### 4.3.7 **Recommendations for minimal invasive treatment\***

Recommendations	GR
Botulinum toxin injection in the detrusor is the most effective minimally invasive treatment to reduce neurogenic detrusor overactivity.	A
Sphincterotomy is the standard treatment for DSD.	A
Bladder neck incision is effective in a fibrotic bladder neck.	B

\*Guidelines for catheterisation are listed separately under Section 4.3.2.

## 4.4 **Surgical treatment**

### 4.4.1 **Urethral and bladder neck procedures**

Increasing the bladder outlet resistance has the inherent risk of causing high intravesical pressure during the filling, which may become even higher during the voiding phase. Procedures to treat sphincteric incontinence are suitable only when the detrusor activity is, or can be, controlled, when no significant reflux is present.

Moreover, these procedures require the urethra and bladder neck to be in good condition and mostly result in intermittent catheterisation being performed after the procedure (4).

*Urethral sling*: Various materials have been used for this procedure with enduring positive results (4,166-179). The procedure is established in women; for men, the artificial sphincter is obviously the first choice (4).

*Artificial urinary sphincter*: This device has stood the test of time in patients with NLUTD (4). It was introduced by Light and Scott (180) for this patient group and the need for revisions (181) has decreased significantly with new generations of devices (172,182-185).

*Functional sphincter augmentation*: By transposing the gracilis muscle to the bladder neck (186) or to the proximal urethra (187), the possibility exists for creating a functional autologous sphincter by electrical stimulation (186,187). This would open the possibility of restoring control over the urethral closure.

*Bladder neck and urethra reconstruction*: The classical Young-Dees-Leadbetter (188) procedure for bladder neck reconstruction in children with bladder exstrophy and the Kropp urethral lengthening (189) improved by Salle (190) are established methods to restore continence provided that intermittent catheterisation is practiced and/or bladder augmentation is performed (172,181,189-200).

### 4.4.2 **Detrusor myectomy (auto-augmentation)**

The idea of enlarging a shrunken bladder by removing lateral detrusor tissue to free the entrapped ureter in a non-functional fibrotic detrusor was put forward by Couvelaire (201). Since its clinical introduction by

Cartwright and Snow (202) in children and by Stöhrer (203) in adults, this procedure for reducing DO or improving low detrusor compliance has gained popularity because of its acceptable long-term results, its low surgical burden, its low rate of long-term adverse effects, its positive effect on the patient's QoL, and because it does not preclude further interventions (1,4,202-221).

The procedure is performed extraperitoneally under general anaesthesia and consists of the dissection of about 20% of the detrusor tissue around the umbilicus, leaving the mucosa intact (1,202,203). A diverticulum will develop, but this may take 1-2 years in adults (1,191,192). A laparoscopic procedure (205,209,213,222), covering of the mucosa at the detrusor defect (transperitoneal) (24,212,214,218), supporting the bladder (202,218), or simple incision of the detrusor muscle (detrusor myotomy) (220,221) are proposed variations of the procedure but offer no essential advantages.

#### **4.4.3 Denervation, deafferentation, neurostimulation, neuromodulation**

Various procedures estimated to destroy the peripheral detrusor innervation have been abandoned because of poor long-term results and severe complications (4). These procedures include bladder distension, cystolysis, transvaginal denervation (Ingelman-Sundberg procedure) and subtrigonal phenol injections.

Sacral rhizotomy, also known as sacral deafferentation (SDAF), has achieved some success in reducing DO (16,223-227), but it is used nowadays mostly as an adjuvant to sacral anterior root stimulation (228-239). Alternatives for rhizotomy are sought in this treatment combination (240-242).

Sacral anterior root stimulation (SARS) is aimed at producing a detrusor contraction. The technique was developed by Brindley (243) and is applicable only in complete lesions above the implant location because of its stimulation amplitude over the pain threshold. The urethral sphincter efferents are also stimulated, but as the striated muscle relaxes faster than the smooth muscle of the detrusor, a so-called 'post-stimulus voiding' will occur. This approach has been successful in highly selected patients (228-239). By changing the stimulation parameters, this method can also induce defecation or erection.

The sacral nerve stimulation or sacral neuromodulation is based on the research by Schmidt and Tanagho (244). This technique stimulates the afferents and thereby probably restores the correct balance between excitatory and inhibitory impulses from and to the pelvic organs at a sacral and supra-sacral level, thus reducing the DO (28,245). It is used either as a temporary procedure using foramen electrodes with an external stimulator, with the expectation that the changes will persevere after treatment, or as a chronic procedure with an implanted stimulator. In the latter case, a test procedure, the percutaneous nerve evaluation (PNE), with an external stimulator is performed before the implant to judge the patient's response. This procedure also has considerable success in selected patients (210,246-250).

On the basis of the successful application of these systems, future developments towards a device that may be more integrated in the body are under research (251).

#### **4.4.4 Bladder covering by striated muscle**

When the bladder is covered by a (part of) striated muscle that can be stimulated electrically, or ideally could be contracted voluntarily, an acontractile bladder could be restored to perform a voiding function. The rectus abdominis (252) and the latissimus dorsi (253) have been used successfully in patients with NLUTD.

#### **4.4.5 Bladder augmentation or substitution**

Replacing or expanding the bladder by intestine or other passive expandable coverage will reduce detrusor compliance and at least reduce the pressure effect of DO. The inherent complications associated with these procedures include recurrent infection, stone building, perforation or diverticula, possible malignant changes, and for intestine metabolic abnormality, mucus production and impaired bowel function (4,254-256). Since the age of the NLUTD patient population, when the surgery is performed, is generally much lower than that of patients with bladder malignancy, who are elected for this surgery, it is important that any possible, very long-term, complications in particular are appraised. Thus, the procedures should be used with caution in NLUTD patients, but may become necessary if all less-invasive treatment methods have failed.

Bladder augmentation, by procedures such as clam cystoplasty, is a valid option to decrease detrusor pressure and increase bladder capacity, whenever more conservative approaches have failed. A number of different techniques have been published. The results of the various procedures are very good and comparable (208,210-212,215-217,255-258). Bladder substitution to create a low pressure reservoir may be indicated in patients with severely thick and fibrotic bladder wall. Scaffolds, probably of tissue-engineered material for bladder augmentation or substitution or alternative techniques, are promising future options (216,259-264).

#### **4.4.6 Urinary diversion**

When no other therapy has been successful urinary diversion must be considered for the protection of the upper tract and for the patient's QoL (4,265).

*Continent diversion:* This should be the first choice for diversion. In patients for whom indwelling catheterisation or suprapubic catheterisation is the only feasible treatment option, change to a continent stoma may be a better prospect (4). Some patients with limited dexterity prefer a stoma using the urethra for catheterisation (4). The continent stoma is created following various techniques. All of them, however, do show frequent complications, including leakage or stenosis (4,266). The short-term continence rates are over 80% and good protection of the upper urinary tract is achieved (4,13,264-278). For cosmetic reasons, the umbilicus is often used for the stoma site, but this may have a higher risk of stenosis (269,271,276).

*Incontinent diversion:* If catheterisation is impossible, incontinent diversion with a urine collecting device is indicated. Fortunately, nowadays, this indication is seldom because many appropriate alternatives can be offered (4). Ultimately, it could be considered in patients who are wheelchair bound or bed-ridden with intractable and untreatable incontinence, in devastated LUTs, when the upper urinary tract is severely compromised, and in patients who refuse other therapy (4). An ileal segment is used for the deviation in most cases (4,279-283). The rather poor long-term results and the expected complications warrant a permanent follow-up (4).

*Undiversion:* Long-standing diversions may be successfully undiverted or an incontinent diversion changed to a continent one with the emergence of new and better techniques for control of the detrusor pressure and the incontinence (4). Also, in young patients, body image may play a role (273). The patient must be carefully counselled and must comply meticulously with the instructions (4). Successful undiversion can then be performed (284).

#### 4.5 Recommendations for surgical treatment

Recommendations			GR
Detrusor	Overactive	Detrusor myectomy is an acceptable option for the treatment of overactive bladder when more conservative approaches have failed. It is limited invasive and has minimal morbidity	B
		Sacral rhizotomy with SARS in complete lesions and sacral neuromodulation in incomplete lesions are effective treatments in selected patients	B
		Bladder augmentation is an acceptable option for decreasing detrusor pressure whenever less invasive procedures have failed. For the treatment of a severely thick or fibrotic bladder wall, a bladder substitution might be considered	B
	Underactive	SARS with rhizotomy and sacral neuromodulation are effective in selected patients	B
		Restoration of a functional bladder by covering with striated muscle is still experimental	
Urethra	Overactive (DSD)	refer to guidelines for minimal invasive treatment (see Section 4.3.6)	
	Underactive	The placement of a urethral sling is an established procedure	B
		The artificial urinary sphincter is very effective	B
		Transposition of the gracilis muscle is still experimental	

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## 5. URINARY TRACT INFECTION IN NEUROGENIC LOWER URINARY TRACT DYSFUNCTION

### 5.1 Introduction

Complicated UTI is the name given to urinary tract infection (UTI) in neurogenic lower urinary tract dysfunction (NLUTD). A detailed discussion of the clinical presentation, diagnosis, microbiological considerations and treatment strategies of complicated UTI can be found in the *EAU Guidelines on Urological Infections* (1). As stated in these guidelines, bacteriuria in patients with SCI should not be treated, even in cases of intermittent catheterisation. Generally, most knowledge concerning UTI in neurogenic patients comes from studies of patients with SCI and is therefore not directly transferable to other populations, such as MS, stroke, or PD.

### 5.2 Recurrent urinary tract infection in neurogenic patients

Recurrent UTI in patients with NLUTD may indicate a suboptimal management of the underlying functional problem, e.g. high bladder pressure during storage and voiding, incomplete voiding or bladder stones. The improvement of bladder function and the removal of bladder stones or other direct supporting factors are mandatory. Additionally, UTI prevention strategies can be applied (1).

### 5.3 Prevention

It is generally agreed that the best prevention of UTI in neurogenic patients is a well-balanced management of the LUTD, including low-pressure urine storage, maintaining a periodical, low resistance and ensuring complete voiding. If clean, intermittent catheterisation (CIC) is used for emptying, aseptic technique and sterile lubricated (2) or hydrophilic catheters (3,4) should be used. Regular voiding and a minimal daily fluid intake of 30 mL/kg body weight are considered to be supportive factors in UTI prevention.

Various approaches have been tried to minimise UTIs in neurogenic bladder. Randomised controlled trials have shown that cranberry extracts have no benefit (5-7). Research has also shown that both methenamine hippurate (8) and bladder irrigation are ineffective (9). Although urine acidification therapy using drugs, such as L-methionine, is widely used in neurogenic patients in an attempt to prevent UTIs, there is little scientific evidence to support its use. Low-dose, long-term, antibiotic prophylaxis may be an option for patients with recurrent UTI (10), but has the disadvantage of possibly increasing bacterial resistance (11). Vaccination therapy for UTI prevention has not been tested in neurogenic patients.

#### 5.3.1 Recommendations for the treatment of urinary tract infection

Recommendations	GR
Bacteriuria in patients with spinal cord injury (SCI) should not be treated, even in cases of intermittent catheterisation.	
As in the general population, the use of long term antibiotics in recurrent UTIs may cause bacterial resistance and caution is advised.	
Protection of the urinary tract is the main focus.	

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## 6. TREATMENT OF VESICO-URETERAL REFLUX

### 6.1 Treatment options

The treatment options for vesico-ureteral reflux in patients with NLUTD do not differ essentially from those in other reflux patients. They become necessary when the high intravesical pressure during the filling phase or during the voiding phase have been treated successfully, but where the reflux did not resolve (1-4). Subtrigonal injections with bulking agents or ureteral re-implantation are the standard procedures.

*Subtrigonal injections of bulking agents:* This minimal invasive procedure has a relatively good effect with complete success in about 65% of patients (5-12). It can also be easily repeated if not effective and thereby the success rate can be increased to about 75% after the second or third session.

*Ureteral re-implantation:* This technique has an immediate and long-lasting result in over 90% of the patients (11-13). In deciding which procedure will be offered to the patient, the relative risks of more invasive surgery and of less successful therapy should be considered.

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## 7. SEXUAL (DYS)FUNCTION AND FERTILITY

### 7.1 Spinal cord injury and sexuality - introduction

Neurological diseases and injuries have a distinct impact on sexual health, but guidelines for their management are still lacking (1). Periodical check-ups using validated questionnaires will help to assess and therefore improve sexual rehabilitation and response (2) (LE: 3).

### 7.2 Male erectile dysfunction

#### 7.2.1 Medical treatment - Phosphodiesterase type 5 inhibitors

Phosphodiesterase type 5 inhibitors (PDE5Is) are recommended as first-line treatment in men with SCI and ED. They are safe and effective for long-term use. The most common side-effects in men with SCI are headache and flushing, while men with tetraplegia or high-level paraplegia may have postural hypotension for several

hours after using a PDE5I.

Phosphodiesterase type 5 inhibitors are currently the first-line treatment option for ED in patients with SCI because of their high efficacy and safety rates (3-5) (LE: 1b). However, little is known about the effect on erectile function in neurological patients. Tadalafil and sildenafil citrate are effective and safe long-term treatments for patients with MS and PD, respectively (8-11) (LE: 1b).

The great majority of neurogenic patients require long-term therapy for ED. However, some patients have a low compliance rate or they stop therapy because of side-effects (3). In addition, some patients with severe neurological damage may be resistant to PDE5Is (12).

### 7.2.2 Mechanical devices

Mechanical devices (vacuum tumescence devices and penile rings) may be effective but are less popular (6,7).

### 7.2.3 Intracavernosal injections

Patients not responding to oral drugs may be offered intracavernosal injections. Intracavernosal penile injectable medications (ICI) are very effective for the treatment of ED in men with SCI, but their use requires careful dose titration and some precautions. The reported complications of intracavernous drugs include priapism and corpora cavernosa fibrosis.

An intracavernosal injection of vasoactive medication is the first therapeutic option to consider in patients taking nitrate medications, for whom there are concerns about drug interactions with PDE5Is, or in patients for whom PDE5Is are ineffective.

Topical agents for penile smooth muscle relaxation (prostaglandin) or intraurethral preparation of prostaglandin E1 (MUSE) were found to be less effective in SCI patients suffering from ED (13).

### 7.2.4 Penile prostheses

Penile prostheses may be effective for treatment of ED in men with SCI and should be offered when all conservative treatments have failed. Serious complications, including infection and prosthesis perforation, may occur in about 10% of patients, depending on implant type (14-16).

### 7.2.5 Recommendations sexual dysfunction

Recommendations	GR
Oral PDE5Is are the first-line treatment for erectile dysfunction in men with SCI.	A
Intracavernosal injections of vasoactive drugs (alone or in combination) are the second-line treatment when oral medications have failed.	A
Mechanical devices such as vacuum devices and rings may be effective but are not as popular.	C
Surgical prostheses should be reserved for selected patients who have not responded to conservative therapies.	B

## 7.3 Male fertility

Reproductive dysfunction in men with SCI is a common condition and is due to a combination of ED, ejaculatory failure, and abnormal semen parameters, even if the definitive causal mechanism is unknown (17) (LE: 3). Assisted reproductive technologies may be needed.

Pregnancy rates are lower than in the general population. But since the advent of intracytoplasmic sperm injection (ICSI) men with SCI now have a good chance of becoming biological fathers (18-20).

In men with retrograde ejaculation, the use of a balloon catheter to obstruct the bladder neck may be effective in obtaining antegrade ejaculation (21). More comparative trials are needed to evaluate the impact of intracavernosal injections on ejaculation and orgasmic function, their early use for increasing the recovery rate of a spontaneous erection, and their effectiveness and tolerability in the long-term (3). Prostatic massage is a safe and easy method to use for obtaining semen in men with lesions above T10 (22).

The two most commonly used methods of sperm retrieval are vibrostimulation (VS) and transrectal electroejaculation (EEJ) (23-25). Semen retrieval is more likely with VS in men with lesions above T10 (26-28).

Midodrine may be combined with VS in men not responding to VS alone. However, EEJ is the second choice for sperm retrieval when repeated tries at VS have failed (29).

Surgical procedures, such as epididymal (MESA) or testicular (TESE) sperm retrieval, may be used if VS and EEJ are not successful (30,31).

### 7.3.1 **Sperm quality and motility**

The following has been reported about sperm quality and motility:

- Vibratory stimulation produces samples with better sperm motility than electrostimulation (24,32).
- Antegrade samples have better sperm motility than retrograde samples.
- EEJ with interrupted current produces better sperm motility than does continuous current (33).
- Bladder management with clean intermittent catheterisation may improve semen quality compared to indwelling catheterisation, reflex voiding or bladder expression (34).
- Sperm quality in patients with SCI is enhanced by processing in able-bodied seminal plasma (35).

There are no relevant publications about fertility in other neurological pathologies.

## 7.4 **Female sexuality**

Studies have shown that most women (65–80%) continue to be sexually active after SCI, but to a much lesser extent than before injury. In addition, about 25% of women with an SCI report a decreased satisfaction with their sexual life (37-39).

Studies show that the greatest physical barrier to sexual activity is urinary leakage. Problems with positioning and spasticity affect mainly tetraplegics. Peer support may help to optimise the sexual adjustment of women with SCI in achieving a more positive self-image, self-esteem and feelings of being attractive to themselves and others (40-43).

The use of specific drugs for sexual dysfunctions is indicated to treat inadequate lubrication. Sildenafil may partially reverse subjective sexual arousal difficulties, while manual and vibratory clitoral stimulation may increase genital responsiveness (44,45).

Neurophysiological studies have shown that women with the ability to perceive T11-L2 pinprick sensations may have psychogenic genital vasocongestion, while reflex lubrication and orgasm is more prevalent in women with SCI who have preserved the sacral reflex arc (S2-S5). These findings are true, even when it has not been shown in an individual woman that a specific level and degree of lesion is the cause of a particular sexual dysfunction. In SCI women with a complete lesion of the sacral reflex, arousal and orgasm may be evoked through stimulation of other erogenous zones above the level of lesions (46-48).

Studies have reported dissatisfaction with the quality and quantity of sexuality related rehabilitation services for women with SCI and that affected women were less likely to receive sexual information than men (48-50).

## 7.5 **Female fertility**

The reproductive capacity of women with SCI is only temporarily affected by SCI with cessation of menstruation for approximately 6 months post-SCI (51). About 70% of sexually active women use some form of contraception after injury, but fewer women use the birth control pill compared to before their injury (52).

Although pregnancy is usually normal, women with SCI are more likely to suffer complications during pregnancy, labour and delivery compared to able-bodied women. Complications of labour and delivery include bladder problems, spasticity, pressure sores, and anaemia autonomic dysreflexia (53,54). Obstetric outcomes include higher rates of caesarean sections and an increased incidence of low birth-weight babies (55).

Epidural anaesthesia is chosen and effective for most patients with autonomic dysreflexia during labour and delivery (56,57).

There is very little published data on women's experience of the menopause following an SCI (58). There are no relevant publications about sexuality and fertility in other neurological pathologies.



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## 8. QUALITY OF LIFE

### 8.1 Introduction

Quality of life (QoL) is a very important aspect of the global management of NLUTD patients (1). The type of bladder management may influence the health-related QoL (HRQoL) in patients with SCI (2). The effectiveness of urological treatment and the urodynamic functionality of the neurogenic bladder have become increasingly determinant of patient QoL (3). QoL is a reflection of the individual's ability to cope with the new life situation (4). Despite the limitations associated with neurological pathology, adequate treatment is possible in most patients and should not interfere with social independence. QoL can be influenced by several factors including family support, adjustment and coping ability, productivity, self-esteem, financial stability, education, and the physical and social environment (5) (LE: 3). Age, sex, ethnicity, and the patient's acceptance of the condition should also be taken into consideration when assessing QoL (6) (LE: 3).

### 8.2 Quality of life assessment

There are no specific QoL questionnaires for neurogenic bladder dysfunction or NLUTD. The only validated tools are a generic Visual Analogue Scale (VAS) for symptom bother, and Qualiveen® which is a specific tool for QoL in spinal cord lesion and multiple sclerosis patients. Qualiveen appears to be a discriminative evaluation instrument (3,7-9) and a short form is now available (10).

More commonly, QoL is assessed secondarily by generic HRQL questionnaires such as the Incontinence Quality of Life Instrument (I-QOL), King's Health Questionnaire (KHQ), Short Form 36 Health Survey Questionnaire (SF-36), Euro Quality of Life-5 Domains (EQ-5D), Short Form 6D Health Survey Questionnaire (SF-6D), or the Health Utilities Index (HUI).

Furthermore, the quality-adjusted life year (QALY) metric quantifies patient outcomes, by weighting years of life spent in a specified health state by a factor representing the value that society or patients place on that health state (11) (LE: 3).

### 8.3 Therapy influence on quality of life

Appropriate therapies should manage symptoms, improve urodynamic parameters, functional abilities and QoL, and avoid secondary complications (8,12). Changes in NLUTD appear to be a major determinant of patient QoL (13,14) (LE: 2a).

### 8.4 Conclusions and recommendations

Conclusions	LE
One of the main aims of therapy is to improve quality of life.	1
There is a lack of disease-specific outcome measures assessing HRQoL in patients with NLUTD.	

Recommendations	GR
Quality of life should be assessed when evaluating lower urinary tract symptoms in neurogenic patients and when treating neurogenic bowel dysfunction.	B
The available validated tools are Qualiveen, a specific long- and short-form tool for spinal cord lesion and multiple sclerosis patients and VAS for symptom bother. In addition, generic (SF-36) or specific tools for incontinence (I-QOL) questionnaires can be used.	B

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## 9. FOLLOW-UP

### 9.1 Introduction

NLUTD is an unstable condition and can vary considerably, even within a relatively short period. Meticulous follow-up and regular checks are necessary (1-20). Depending on the type of the underlying neurological pathology and on the current stability of the NLUTD, the interval between the detailed investigations should not exceed 1-2 years. In patients with multiple sclerosis and in acute SCI, this interval is of course much smaller. Urine dip sticks should be available for the patient and urinalysis should be performed at least every second month. The upper urinary tract, the bladder shape, and residual urine should be checked every 6 months. Physical examination and blood and urine laboratory should take place every year. Any sign indicating a risk factor warrants specialised investigation.

## 9.2 Guidelines for follow-up

Possible UTI checked by the patient (dip stick).
Urinalysis every second month.
Upper urinary tract, bladder morphology, and residual urine every 6 months (ultrasound).
Physical examination, blood chemistry, and urine laboratory every year.
Detailed specialistic investigation every 1-2 years and on demand when risk factors emerge. The investigation is specified according to the patient's actual risk profile, but should in any case include a video-urodynamic investigation and should be performed in a leading neuro-urological centre.
All of the above should be more frequent if the neurological pathology or the NLUTD status demand this.

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## 10. CONCLUSIONS

NLUTD is a multi-faceted pathology. It requires an extensive and specific diagnosis before we can embark on an individualised therapy, which takes into account the medical and physical condition of the patient and the patient's expectations about his future social and physical situation with respect to the NLUTD.

The urologist or paediatric urologist can select from a wealth of therapeutical options, each with its own pros and cons. Notwithstanding the success of any therapy embarked upon, a close surveillance is necessary for the patient's entire life.

With these guidelines, we offer you expert advice on how to define the patient's NLUTD condition as precisely as possible and how to select, together with the patient, the appropriate therapy. This last choice, as always, is governed by the golden rule: as effective as needed, as less invasive as possible.

## 11. ABBREVIATIONS USED IN THE TEXT

*This list is not comprehensive for the most common abbreviations*

CVA	cerebrovascular
DLPP	detrusor leak point pressure
DO	detrusor overactivity
DSD	detrusor sphincter dyssynergia
EMG	electromyography, electromyogram
FVC	frequency volume chart
HIV	human immunodeficiency virus
HRQoL	health-related quality of life
IC	intermittent catheterisation
ISC	intermittent self-catheterisation
ICS	international Continence Society
LPP	leak point pressure
LMNL	lower motor neuron lesion
LUT	lower urinary tract
LUTD	lower urinary tract dysfunction
LUTS	lower urinary tract symptoms
MTC	micturition time chart
NDO	neurogenic detrusor overactivity
NLUTD	neurogenic lower urinary tract dysfunction
PNE	percutaneous nerve evaluation test
QoL	quality of life
SARS	sacral anterior root stimulation
SCI	spinal cord injury
SDAF	sacral deafferentation
SLE	systemic lupus erythematosus
UMNL	upper motor neuron lesion
UTI	urinary tract infection
VAS	visual analogue scale
VS	vibrostimulation

### **Conflict of interest**

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