

Guidelines on Neurogenic Lower Urinary Tract Dysfunction

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TABLE OF CONTENTS

PAGE

1.	AIM AND STATUS OF THESE GUIDELINES	4
1.1	Purpose	4
1.2	Standardization	4
1.3	References	4
2.	BACKGROUND	4
2.1	Risk factors and epidemiology	4
2.1.1	Brain tumours	4
2.1.2	Dementia	4
2.1.3	Mental retardation	4
2.1.4	Cerebral palsy	5
2.1.5	Normal pressure hydrocephalus	5
2.1.6	Basal ganglia pathology (Parkinson's disease, Huntington's disease, Shy-Drager syndrome, etc)	5
2.1.7	Cerebrovascular (CVA) pathology	5
2.1.8	Demyelination	5
2.1.9	Spinal cord lesions	5
2.1.10	Disc disease	5
2.1.11	Spinal stenosis and spine surgery	5
2.1.12	Peripheral neuropathy	6
2.1.13	Other conditions (SLE)	6
2.1.14	HIV	6
2.1.15	Regional spinal anaesthesia	6
2.1.16	Iatrogenic	6
2.2	Standardization of terminology	6
2.2.1	Introduction	6
2.2.2	Definitions	7
2.3	Classification	9
2.3.1	Recommendation for clinical practice	10
2.4	Timing of diagnosis and treatment	10
2.5	References	10
3.	DIAGNOSIS	17
3.1	Introduction	17
3.2	History	17
3.2.1	General history	17
3.2.2	Specific history	18
3.2.3	Guidelines for history taking	18
3.3	Physical examination	18
3.3.1	General physical examination	18
3.3.2	Neuro-urological examination	19
3.3.3	Essential investigations	21
3.3.4	Guidelines for physical examination	21
3.4	Urodynamics	21
3.4.1	Introduction	21
3.4.2	Urodynamic tests	21
3.4.3	Specific uro-neurophysiological tests	22
3.4.4	Guidelines for urodynamics and uro-neurophysiology	23
3.5	Typical manifestations of NLUTD	23
3.6	References	23
4.	TREATMENT	25
4.1	Introduction	25
4.2	Non-invasive conservative treatment	26
4.2.1	Assisted bladder emptying	26
4.2.2	Lower urinary tract rehabilitation	26
4.2.3	Drug treatment	26

4.2.4	Electrical neuromodulation	27
4.2.5	External appliances	27
4.2.6	Guidelines for non-invasive conservative treatment	27
4.3	Minimal invasive treatment	28
4.3.1	Catheterization	28
4.3.2	Guidelines for catheterization	28
4.3.3	Intravesical drug treatment	28
4.3.4	Intravesical electrostimulation	28
4.3.5	Botulinum toxin injections in the bladder	28
4.3.6	Bladder neck and urethral procedures	29
4.3.7	Guidelines for minimal invasive treatment	29
4.4	Surgical treatment	29
4.4.1	Urethral and bladder neck procedures	29
4.4.2	Detrusor myectomy (auto-augmentation)	30
4.4.3	Denervation, deafferentation, neurostimulation, neuromodulation	30
4.4.4	Bladder covering by striated muscle	30
4.4.5	Bladder augmentation or substitution	30
4.4.6	Urinary diversion	31
4.5	Guidelines for surgical treatment	31
4.6	References	32
5.	TREATMENT OF VESICO-URETERAL REFLUX	46
5.1	Treatment options	46
5.2	References	46
6.	QUALITY OF LIFE	47
6.1	Introduction	47
6.2	Conclusions and recommendations	48
6.3	References	48
7.	FOLLOW UP	48
7.1	Introduction	48
7.2	Guidelines for follow-up	48
7.3	References	49
8.	CONCLUSIONS	50
9.	ABBREVIATIONS USED IN THE TEXT	51

1. AIM AND STATUS OF THESE GUIDELINES

1.1 Purpose

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.

1.2 Standardization

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).

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2. BACKGROUND

2.1 Risk factors and epidemiology

NLUTD may be caused by various diseases and events affecting the nervous systems controlling the LUT. The resulting lower urinary tract dysfunction (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 realize 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 and therefore the true incidence of incontinence caused by dementia is not known. 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 non-specific NLUTD (8-13). The occurrence of incontinence is reported to be between 23% and 48% (14, 15) in patients with Alzheimer's disease. The onset of incontinence usually correlates with disease progression (16). 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 (17, 18).

2.1.4 Cerebral palsy

LUTD has been described in about 30-40% (19, 20).

2.1.5 Normal pressure hydrocephalus

There have only been case reports of LUTD (21-23).

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

Parkinson's disease is accompanied by NLUTD in 37.9-70% (24-25).

In the rare Shy-Drager syndrome, almost all patients have NLUTD (26), with incontinence found in 73% (27).

Hattori et al. (28) reported that 60% of Parkinson patients had urinary symptoms. However, Gray et al. (29) reported that functional disturbances of the LUT in Parkinson's disease 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 (30-32), or 53% in men and 63% in women using a non-validated questionnaire, which included a urinary incontinence category (32), with all these values being significantly higher than in healthy controls. In most patients, the onset of the bladder dysfunction occurred after the motor disorder had appeared.

2.1.7 Cerebrovascular (CVA) pathology

Cerebrovascular pathology causes hemiplegia with remnant incontinence NLUTD in 20-50% of patients (33-34), with decreasing prevalence in the post-insult period (35). In 1996, 53% of patients with CVA pathology had significant urinary complaints at 3 months (36). Without proper treatment, at 6 months after the CVA, 20-30% of patients still suffered from urinary incontinence (37). The commonest cystometric finding was detrusor overactivity (38-43).

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 (45-46).

2.1.8 Demyelination

Multiple sclerosis causes NLUTD in 50-90% of the patients (47-49).

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 (50). There is almost a 100% chance of having LUT dysfunction 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 (51). LUT dysfunction appears mostly during the 10 years following the diagnosis (52).

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 (53). 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 (54), and in the USA 1 per 1,000 births (55). The incidence of urethrovessical dysfunction in myelomeningocele is not completely known, but most studies suggest it is very high at 90-97% (56). About 50% of these children will have detrusor sphincter dyssynergia (DSD) (57, 58).

2.1.10 Disc disease

This is reported to cause NLUTD in 28-87% of the patients (<20%) (59-60). The incidence of cauda equina syndrome due to central lumbar disc prolapse is relatively rare and is about 1-5% of all prolapsed lumbar discs (60-63, 64-67). There have been case reports of NLUT without cauda equine syndrome (69).

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) (70). These symptoms may be overlooked or attributed to primary urological disorders, with 61-62% affected by LUTD (71, 72). 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 (73, 74).

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 (75, 76). 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 (77).

Alcohol abuse will eventually cause peripheral neuropathy. This has a reported prevalence that varies widely from 5-15% (78) to 64% (79). 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 (79).

Less prevalent peripheral neuropathies include the following:

- Porphyria: bladder dilatation occurs in up to 12% of patients (80).
- Sarcoidosis: NLUTD is rare (81).
- 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% (82, 83). NLUTD is transient in most patients.
- Guillain Barré syndrome: the prevalence of micturition disorders varies from 25% to more than 80% (84,85), but is regressive in most cases (86). The true incidence is uncertain because, during the acute phase, patients are usually managed by indwelling catheter.

2.1.13 *Other conditions (SLE)*

Nervous system involvement occurs in about half of patients with systemic lupus erythematosus (SLE). Symptoms of LUT dysfunction can occur, but data on prevalence are rare and give an incidence of 1% (87, 88).

2.1.14 *HIV*

Voiding problems have been described in 12% of HIV-infected patients, mostly in advanced stages of the disease (89, 90).

2.1.15 *Regional spinal anaesthesia*

This may cause NLUTD but no prevalence figures have been found (91, 92).

2.1.16 *Iatrogenic*

Abdominoperineal resection of rectum has been described as causing NLUTD in up to 50% of patients (93, 94). One study has reported that NLUTD remains a long-term problem in only 10% (95); 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 (96, 97).

NLUTD has been reported following simple hysterectomy (98) and in 8-57% of patients following radical hysterectomy or pelvic irradiation for cervical cancer (99-102). Surgical prevention can be used to prevent it (103). Neurological dysfunction of the pelvic floor has been demonstrated following radical prostatectomy (104).

2.2 **Standardization of terminology**

2.2.1 *Introduction*

Several national or international guidelines have already been published for the care of patients with NLUTD (105-108). The guidelines will evolve as time goes by. The guidelines include definitions of important terms and procedures. The ICS NLUTD standardization report (106) deals specifically with the standardization of terminology and urodynamic investigation in patients with NLUTD. Other relevant definitions are found in the general ICS standardization report (109).

Section 2.2.2 lists the definitions from these references, partly adapted, and other definitions considered useful for clinical practice in NLUTD (Tables 1 and 2). For specific definitions relating to urodynamic investigation, the reader is referred to the appropriate ICS report (106).

2.2.2 Definitions

Table 1: 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
Catheterization, indwelling	Emptying of the bladder by a catheter that is introduced (semi-) permanently
Catheterization, intermittent (IC)	Emptying of the bladder by a catheter that is removed after the procedure, mostly at regular intervals
<ul style="list-style-type: none"> • Aseptic IC 	The catheters remain sterile, the genitals are disinfected, and disinfecting lubricant is used
<ul style="list-style-type: none"> • Clean IC 	Disposable or cleansed re-usable catheters, genitals washed
<ul style="list-style-type: none"> • Sterile IC 	Complete sterile setting, including sterile gloves, forceps, gown and mask
<ul style="list-style-type: none"> • Intermittent self-catheterization (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
<ul style="list-style-type: none"> • Frequency volume chart (FVC) 	Times of micturitions and voided volumes only
<ul style="list-style-type: none"> • Micturition time chart (MTC) 	Times of micturitions only
Filling rate, physiological	Below the predicted maximum: body weight (kg)/ 4 in mL/s (109, 110)
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)	See below under storage phase
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	See below under symptom syndrome
Overactivity, detrusor	See below under storage phase
Rehabilitation, LUT	Non-surgical non-pharmacological treatment for LUT dysfunction
Sign	To verify symptoms and classify them
Sphincter, urethral, non-relaxing	See below under voiding phase
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	See below under storage phase

Table 2: Further definitions useful in clinical practice

Storage phase	
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 (111)
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
<ul style="list-style-type: none"> Stress urinary incontinence 	On effort or exertion, or on sneezing or coughing
<ul style="list-style-type: none"> Urge urinary incontinence 	Accompanied by or immediately preceded by urgency
<ul style="list-style-type: none"> Mixed urinary incontinence 	Associated with urgency and also exertion, effort, sneezing, or coughing
<ul style="list-style-type: none"> Continuous urinary incontinence 	
Bladder sensation	
<i>Normal</i>	
<ul style="list-style-type: none"> Symptom and history 	Awareness of bladder filling and increasing sensation up to a strong desire to void
<ul style="list-style-type: none"> Urodynamics 	First sensation of bladder filling, first desire to void, and strong desire to void at realistic bladder volumes
<i>Increased</i>	
<ul style="list-style-type: none"> Symptom and history 	An early and persistent desire to void
<ul style="list-style-type: none"> Urodynamics 	Any of the three urodynamic parameters mentioned under 'normal' persistently at low bladder volume
<i>Reduced</i>	
<ul style="list-style-type: none"> Symptom and history 	Awareness of bladder filling but no definite desire to void
<ul style="list-style-type: none"> 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	
<ul style="list-style-type: none"> Maximum cystometric capacity 	Bladder volume at strong desire to void
<ul style="list-style-type: none"> 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-anaesthetized condition
Normal detrusor function	Little or no pressure increase during filling; no involuntary phasic contractions despite provocation
Detrusor overactivity	
<ul style="list-style-type: none"> Phasic detrusor overactivity 	Characteristic phasic contraction
<ul style="list-style-type: none"> Terminal detrusor overactivity 	A single contraction at cystometric capacity
<ul style="list-style-type: none"> High pressure detrusor overactivity 	Maximal detrusor pressure > 40 cm H ₂ O (106, 112)
<ul style="list-style-type: none"> Overactivity volume 	Bladder volume at first occurrence of detrusor overactivity
<ul style="list-style-type: none"> Detrusor overactivity incontinence 	Self-explanatory
Leak point pressure	
<ul style="list-style-type: none"> Detrusor leak point pressure (DLPP) 	Lowest value of detrusor pressure at which leakage is observed in the absence of abdominal strain or detrusor contraction

<ul style="list-style-type: none"> 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 (ΔV) and change in detrusor pressure (Δp_{det}): $C = \Delta V / \Delta p_{det}$ (ml/cm H ₂ O)
<ul style="list-style-type: none"> Low detrusor compliance 	$C = \Delta V / \Delta p_{det} < 20$ mL/cm H ₂ 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
Voiding phase	
<ul style="list-style-type: none"> Slow stream 	Reduced urine flow rate
<ul style="list-style-type: none"> Intermittent stream (intermittency) 	Stopping and starting of urine flow during micturition
<ul style="list-style-type: none"> Hesitancy 	Difficulty in initiating micturition
<ul style="list-style-type: none"> Straining 	Muscular effort to initiate, maintain, or improve urinary stream
<ul style="list-style-type: none"> 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 and/or 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
Post-micturition phase	
Feeling of incomplete emptying (symptom only)	
Post-micturition dribble: involuntary leakage of urine shortly after finishing the micturition	
Pain, discomfort or pressure sensation in the lower urinary tract and genitalia that may be related to bladder filling or voiding, may be felt after micturition, or be continuous	
Symptom syndrome: combination of symptoms	
<ul style="list-style-type: none"> Overactive bladder syndrome: urgency with or without urge incontinence, usually with frequency and nocturia Synonyms: Urge syndrome, urgency-frequency syndrome This syndrome is suggestive for LUTD 	

2.3 Classification

The classification of NLUTD helps to facilitate the understanding and management of NLUTD and to provide a standardized terminology of the disease processes. The normal LUT function depends on neural integration at, and between, the peripheral, spinal cord, and central nervous systems. The gross type of NLUTD is dependent on the location and the extent of the lesion: suprapontine or pontine, suprasacral spinal cord, or subsacral and peripheral (53, 107).

The classification systems for NLUTD are based on either the neurological substrate (type and location of the neurological lesion) (113), the neuro-urological substrate (neurological lesion and LUTD) (114-116), the type of LUTD (117, 118), or are strictly functional (107, 109, 119-122). Many descriptive terms were derived from these classification systems. However, they are standardized only within any specific system, have little meaning outside the system, and can sometimes be confusing.

A perfect classification system does not exist. Neurological classification systems, by nature, cannot describe the LUTD completely and vice versa. Individual variations exist in the NLUTD caused by a specific neurological lesion, so that the description of the NLUTD should be individualized for any particular patient.

Madersbacher (107, 122) presented a very simple classification, which basically focused on the therapeutic consequences (Figure 2.1). It is based on the clinical concept that the important differentiation in the diagnosis exists between the situations of high and low detrusor pressure during the filling phase and

urethral sphincter relaxation and non- relaxation or DSD during the voiding phase. A non-relaxed sphincter or DSD will cause high detrusor pressure during the voiding phase. This classification is the easiest one for general use in the clinical diagnosis of NLUTD.

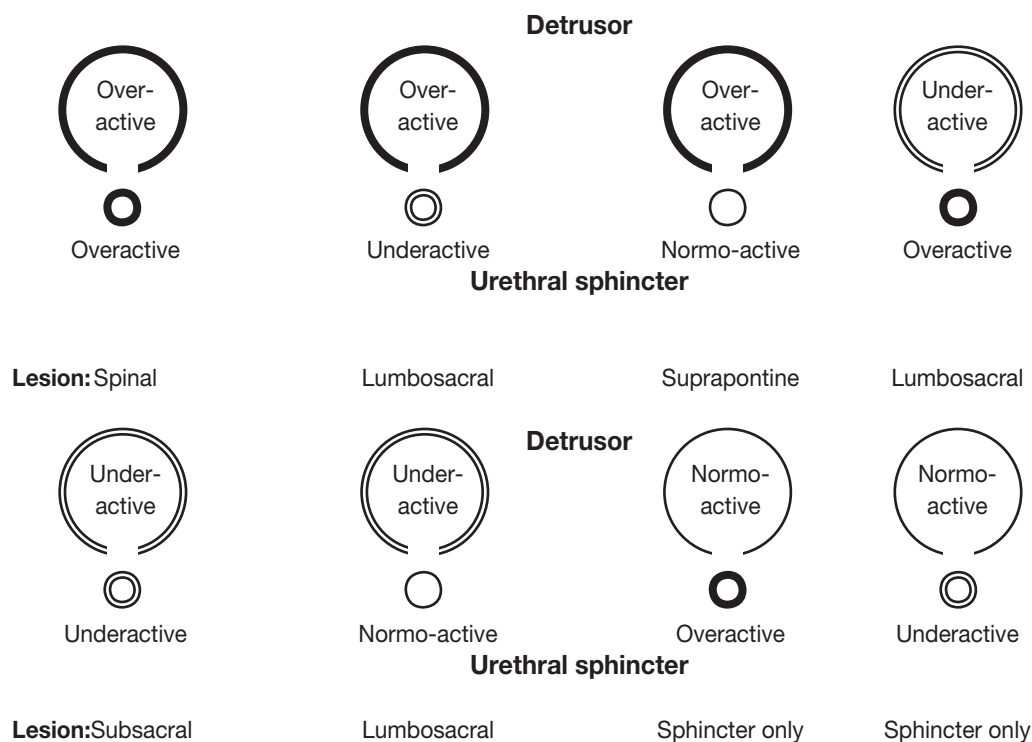


Figure 2.1. Madersbacher classification system (107, 122) with typical neurogenic lesions

2.3.1 Recommendation for clinical practice

The Madersbacher classification system (107, 122) (Figure 2.1) is recommended for clinical practice (Grade of recommendation: B).

2.4 Timing of diagnosis and treatment

Both in congenital and in acquired NLUTD, early diagnosis and treatment is essential as irreversible changes may occur, especially in children with myelomeningocele (123-128), but also in patients with traumatic spinal cord injury (129-131), even if the related neuropathological signs may be normal (132).

It must also be remembered that LUTD by itself may be the presenting symptom for neurological pathology (50, 133).

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3. DIAGNOSIS

3.1 Introduction

Before any functional investigation is planned, an extensive general and specific diagnosis should be performed. Part of this diagnosis is specific for neurogenic pathology and its possible sequelae. The clinical assessment of patients with NLUTD includes and extends that for other LUTD. The latter should consist of a detailed history, bladder diary and a physical examination. In urinary incontinence, leakage should be demonstrated objectively.

These data are indispensable for reliable interpretation of the findings in diagnostic investigations performed subsequently in NLUTD.

3.2 History

3.2.1 General history

The general history should include relevant questions about neurological and congenital abnormalities, social factors and the patient's motivation, any previous occurrences and frequency of urinary infections, and relevant surgery. Information must be obtained on medication with known or possible effects on the lower urinary tract (1-3). The general history should also include the assessment of menstrual, sexual and bowel function, and obstetric history (3).

Hereditary or familial risk factors should be recorded. Symptoms of any metabolic disorder or neurological disease that may induce NLUTD must be checked particularly. Specific signs, such as pain, infection, haematuria, fever, etc, may justify further particular diagnosis.

Items of particular importance include:

- Congenital anomalies with possible neurological impact
- Metabolic disorders with possible neurological impact
- Preceding therapy, including surgical interventions
- Present medication
- Lifestyle factors, such as smoking, alcohol, or addictive drug use

- Infections of the urinary tract
- Quality of life
- Life expectancy.

3.2.2 Specific history

Urinary history: This consists of symptoms related to both the storage and the evacuation functions of the lower urinary tract. The onset and the nature of the NLUTD (acute or insidious) should be determined. Specific symptoms and signs must be assessed in NLUTD and if appropriate should be compared with the patient's condition before the NLUTD developed. The separate diagnostic field items should be diagnosed in as much detail as possible (3):

- LUTS
- Voiding pattern
- Urinary incontinence
- Bladder sensation
- Mode and type of voiding (catheterization).

The urinary (bladder) diary gives (semi-)objective information about the number of voidings, daytime and night-time voiding frequency, volumes voided, and incontinence and urge episodes.

Bowel history: Patients with NLUTD may suffer from a related neurogenic condition of the lower gastrointestinal tract. The bowel history must also address symptoms related to the storage and evacuation functions. Specific symptoms and signs must be compared with the patient's condition before the neurogenic dysfunction developed. Again, the diagnostic items should be detailed (3):

- Ano-rectal symptoms
- Defecation pattern
- Fecal incontinence
- Rectal sensation
- Mode and type of defecation.

Sexual history: Sexual function may also be impaired because of the neurogenic condition. The details of the history will differ of course between men and women (3):

- Genital or sexual dysfunction symptoms
- Sexual function
- Sensation in genital area and for sexual functions
- Erection or arousal
- Orgasm
- Ejaculation.

Neurological history: This should concentrate on the following information:

- Acquired or congenital neurological condition
- Neurological symptoms (somatic and sensory), with onset, evolution, and performed therapy
- Spasticity or autonomic dysreflexia (lesion level above Th6).

Individuals with spinal cord injury (SCI) are often not accurate at knowing whether they have had a urinary tract infection based on their symptoms (4).

3.2.3 GUIDELINES FOR HISTORY TAKING

1. 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.
2. Special attention should be paid to the possible existence of alarm signs, such as pain, infection, haematuria, fever, etc, that warrant further specific diagnosis.
3. A specific history should be taken for each of the four mentioned functions.

3.3 Physical examination

3.3.1 General physical examination

Attention should be paid to the patient's physical and possible mental handicaps. Problems may be caused by impaired mobility, particularly in the hips, or extreme spasticity.

Patients with very high neurological lesions may suffer from a significant drop in blood pressure when moved in a sitting or standing position. Subjective indications of bladder filling sensations may be impossible in

mentally impaired patients.

Inspection of the abdominal wall, prostate palpation or observation of pelvic organ prolapse is mandatory.

3.3.2 Neuro-urological examination

General neurological examination: This investigates the motor and sensory functions of the body, the limbs and hand functions (Figure 3.1). A suprapubic globe should be looked for and the skin condition in the genital and perineal regions should be assessed.

Figure 3.1. Dermatomes of spinal cord levels L2-S4

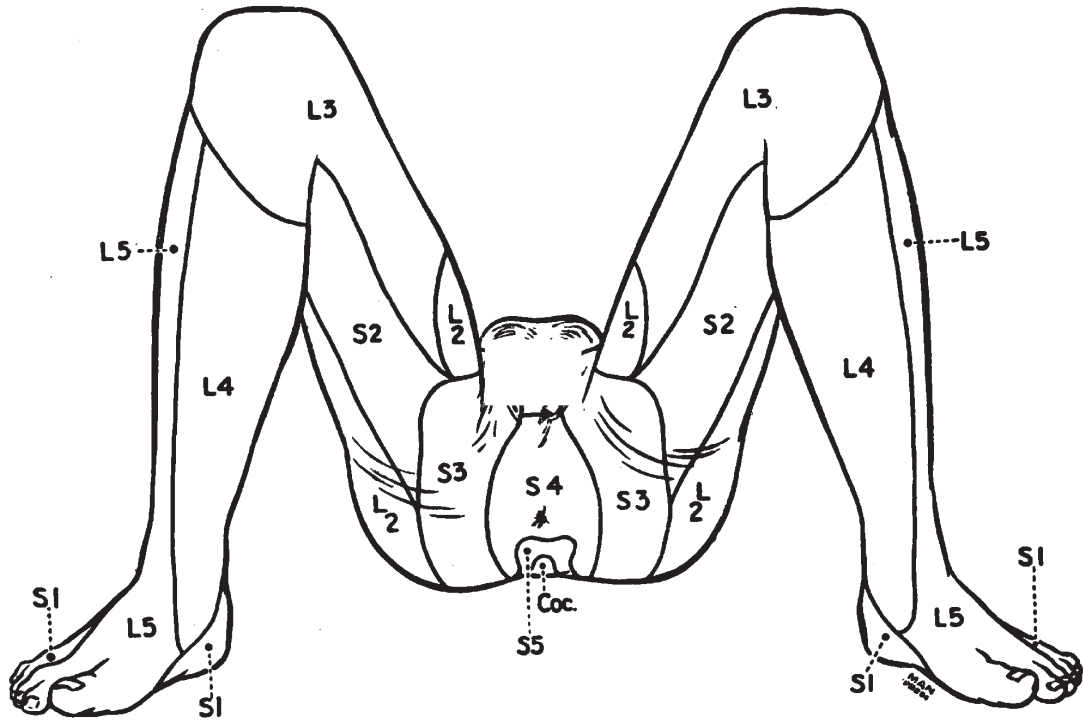


Figure 3.2. Urogenital and other reflexes in lower spinal cord

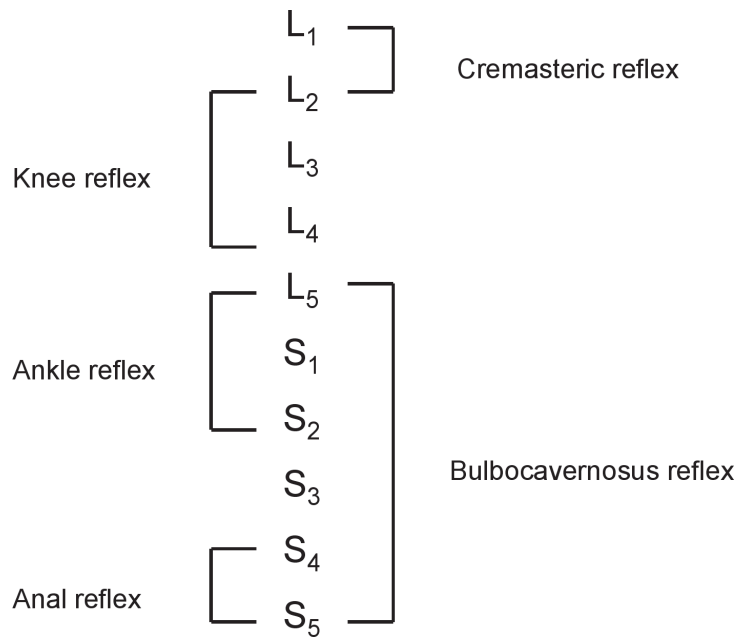


Figure 3.3. Innervation overview of bladder and bowel. Afferent and efferent nerves in the different peripheral nerves and central nervous system are shown

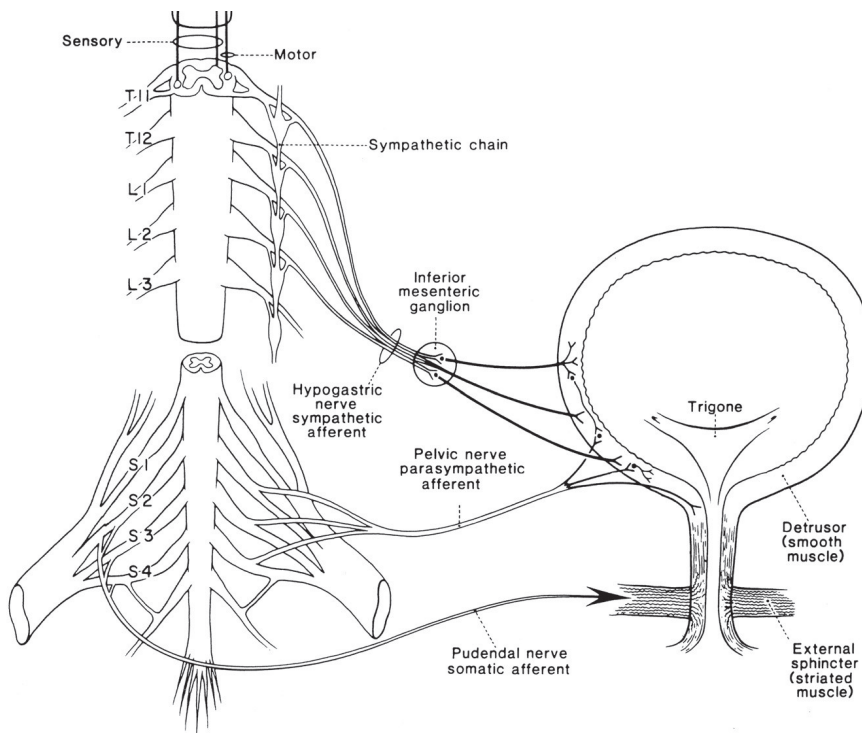
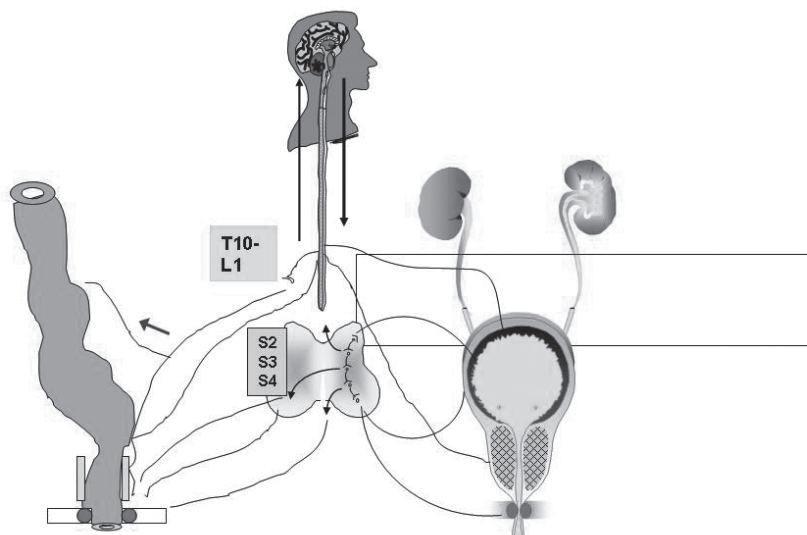


Figure 3.4. Overview of peripheral nerves innervating the lower urinary tract

Innervation lower urinary and bowel tract



Specific neuro-urological examination: This investigation is necessary in patients with NLUTD. It includes several tests for sacral reflex activity and an evaluation of the sensation in the perineal area. Figure 3.1 shows the different dermatomes and Figure 3.2 the associated reflexes in this area.

Specified information should become available on:

- Sensation S₂-S₅ on both sides of the body
- Reflexes
- Anal sphincter tone
- Volitional contraction of anal sphincter and pelvic floor.

A high correlation exists between the clinical neurological findings and NLUTD in some types of neuropathy, but less so in other types (5-10). The correspondence is low, for instance, in myelomeningocele patients (7)

and in combined traumatic spinal cord lesions, but high in single-level traumatic spinal cord lesions (10). In SCI patients with thoracolumbar fractures, neurogenic voiding dysfunction cannot be predicted by the sensory evaluation (11). In SCI patients with thoracolumbar fractures, the presence of a voluntary contraction of the plantar flexors of the toes correlates with active contraction of the external anal/urethral sphincter, but does not enable differentiation of the types of neuropathic voiding disorders (12). A congenital association of lower urinary tract and bowel dysfunction with an abnormal facial expression is named the urofacial (Ochoa) syndrome. (13).

Individuals with SCI were frequently not accurate at predicting whether they had a UTI based on their symptoms (4).

3.3.3 Essential investigations

Essential investigations include (3):

- Urinalysis
- Blood chemistry
- Voiding diary
- Assessment of residual urine, if possible with free flowmetry. Because of natural variations, several assessments (at least 2-3) are necessary (3, 10, 11).
- Quantification of urine loss by pad testing if appropriate
- Urinary tract imaging studies.

3.3.4 GUIDELINES FOR PHYSICAL EXAMINATION

1. Individual patient handicaps should be acknowledged in planning further investigations.
2. The neurological status should be described as completely as possible. Sensations and reflexes in the urogenital area must all be tested.
3. The anal sphincter and pelvic floor functions must be tested extensively.
4. Urinalysis, blood chemistry, voiding diary, residual and free flowmetry, incontinence quantification and urinary tract imaging should be performed.

3.4 Urodynamics

3.4.1 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 detrusor overactivity 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 (12).

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 lower urinary tract 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 (3, 12, 13).

3.4.2 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 (3, 14). 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 (3, 10, 11). 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 (3).

Possible pathological findings include detrusor overactivity, 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 (3, 15). 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 (16). 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 lower urinary tract 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 (17, 18), non-relaxing urethra, or non-relaxing bladder neck (3, 19, 20). 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 (21).

Video-urodynamics: This combination of filling cystometry and pressure flow study with imaging is the gold standard for urodynamic investigation in NLUTD (3, 22, 23). 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 utilizing predominantly natural filling of the urinary tract and reproducing normal subject activity (24).

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) (25-30). 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 (27) and does not seem to be fully discriminative in other patients (28, 29).

It was thought that a positive bethanechol test (31) (detrusor contraction > 25 cm H₂O) 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 (32); this test turned out to be both selective and predictive for successful oral bethanechol treatment.

3.4.3 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.

3.4.4 GUIDELINES FOR URODYNAMICS AND URO-NEUROPHYSIOLOGY

1. Urodynamic investigation is necessary to document the (dys-)function of the LUT (Grade of recommendation: A).
2. The recording of a bladder diary is advisable (Grade of recommendation: B).
3. Non-invasive testing is mandatory before invasive urodynamics is planned (Grade of recommendation: A).
4. 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 (Grade of recommendation: A).
5. A physiological filling rate and body-warm saline must be used (Grade of recommendation: A).
6. Specific uro-neurophysiological tests are elective procedures (Grade of recommendation: C).

3.5 Typical manifestations of NLUTD

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 (33-37).

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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 quality of life.

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 spinal cord-injured 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 quality of life. It is also pivotal in preventing urinary tract infection (6, 7). If complete continence cannot be achieved, methods to attain a socially acceptable control of incontinence can be used.

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

In patients with high detrusor pressure during the filling phase (detrusor overactivity, 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).

4.2.2 Lower urinary tract rehabilitation

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).

Pelvic floor electrostimulation: This technique may help to improve the effect of pelvic floor muscle exercises, or to teach the patient how to contract the pelvic floor, or to improve the patient's compliance with the exercises (11, 22, 23).

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

4.2.3 Drug treatment

A single optimal medical therapy for NLUTD is not yet available. A combination of therapies is currently the best way to maximize outcomes (26-32) (Level of evidence: 1a, Grade of recommendation: A).

Anticholinergic agents are the most useful medications available for neurogenic detrusor overactivity (NDO) (32-36) (Level of evidence: 1a, Grade of recommendation: A). As these drugs bind to muscarinic receptors, they are also termed muscarinic receptor antagonists. Anticholinergic agents are used to reduce detrusor overactivity and to improve bladder compliance (32) (Level of evidence: 1a, Grade of recommendation: A).

Neurogenic patients may need a higher dose of anticholinergics than patients with idiopathic detrusor overactivity (32, 33, 37-39) (Level of evidence: 1b, Grade of recommendation: A). However, this may lead to early discontinuation of therapy because of adverse events (19, 21, 38, 40, 41) (Level of evidence: 1b, Grade of recommendation: A).

Oxybutynin (32) (Level of evidence: 1a, Grade of recommendation: A) (33-36, 39, 40, 42), trospium chloride (32, 37, 38), tolterodine (43) (Level of evidence: 1a, Grade of recommendation: A) and propiverine (32, 40, 44) are established effective medical treatments. These drugs are well tolerated and safe, even during long-term treatment. They have diverse tolerance profiles so that a different anticholinergic agent may be prescribed if a patient experiences adverse effects or if the therapeutic effect is not sufficient.

Recently, darifenacin and solifenacin have been introduced, but as yet no clinical experience with

these drugs in neurogenic bladder overactivity has been published.

Phosphodiesterase inhibitors demonstrated significant effects upon detrusor overactivity in pilot studies and may become a future alternative or adjunct to anticholinergic treatment (45). Additional treatment with desmopressin might improve the efficacy of the treatment (46, 47).

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 parasympathomimetics, specifically when frequent and/or serious possible side effects are taken into account (48) (Level of evidence: 1a, Grade of recommendation: A). Combination therapy with a cholinergic drug and an alpha-blocker appears to be more useful than monotherapy (49). In conclusion, there is no drug with evidence of efficacy for underactive detrusor (11, 50-53) (Level of evidence: 2a, Grade of recommendation: B).

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, 54-58) (Level of evidence: 2a, Grade of recommendation: B).

Increasing bladder outlet resistance: several drugs have shown efficacy in the treatment of selected cases of mild stress urinary incontinence, but there are hardly any publications in patients with NLUTD (11, 59).

Conclusions:

- Long-term efficacy and safety of anticholinergic therapy for NDO is well documented (Level of evidence: 1a, Grade of recommendation: A).
- A combination of therapies is often considered to maximize outcomes for NDO (Level of evidence: 1a, Grade of recommendation: A).
- There is no drug with evidence of efficacy for underactive detrusor (Level of evidence: 2a, Grade of recommendation: B).
- Alpha-blockers have been partly successful for decreasing bladder outlet resistance and autonomic dysreflexia prophylaxis in SCI patients (Level of evidence: 2a, Grade of recommendation: B).
- There is a lack of prospective randomized controlled studies in the medical management of NLUTD.

4.2.4 Electrical neuromodulation

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, 60). 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 (61). This stimulation might then support the restoration of the balance between excitatory and inhibitory inputs at the spinal or supraspinal level (11, 62, 63). It might also imply that patients with incomplete lesions will benefit (11, 63, 64), but patients with complete lesions will not (65).

Although electrical stimulation of the posterior tibial nerve afferents has been used for neurogenic patients (66), there is no current evidence suggesting this therapy has any benefit in NLUTD patients.

4.2.5 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.

4.2.6 GUIDELINES FOR NON-INVASIVE CONSERVATIVE TREATMENT

1. The first aim of any therapy is the protection of the upper urinary tract.
2. The mainstay of treatment for overactive detrusor is anticholinergic drug therapy (Level of evidence: 1, Grade of recommendation: A).
3. Lower urinary tract rehabilitation may be effective in selected cases.
4. A condom catheter or pads may reduce urinary incontinence to a socially acceptable situation.
5. Any method of assisted bladder emptying should be used with the greatest caution (Grade of recommendation: A).

4.3 Minimal invasive treatment

4.3.1 Catheterization

Intermittent self- or third-party catheterization (67, 68) is the gold standard for the management of NLUTD (1, 11). It is effective in patients with:

- Detrusor underactivity or acontractility (1)
- With detrusor overactivity, provided the overactivity can be controlled (1, 11, 26-31).

Sterile IC, as originally proposed by Guttman and Frankel (67), significantly reduces the risk of UTI and/or bacteriuria (1, 11, 69, 70), compared with clean IC introduced by Lapedes et al. (68). However, it cannot be considered a routine procedure (11, 70). Aseptic IC is an alternative (1, 71), which provides a significant benefit in reducing the potential for external contamination of an intermittent urinary catheter (72). Insufficient patient education and the inherent greater risk of UTI in patients with NLUTD are contributing factors (11, 73-77). The average frequency of catheterizations per day is 4-6 times and the catheter size should be 12-14 Fr.

Less frequent catheterization results in higher catheterization volumes and a higher risk of UTI (1, 73-76). More frequent catheterization increases the risk of cross-infections and other complications (1, 73-76). Bladder volume at catheterization should be lower than 400 mL.

The prevalence of complications can be limited by adequate patient education, use of non-traumatizing techniques and adequate precautions to prevent infections (11, 77).

Indwelling transurethral catheterization and, to a lesser extent, suprapubic cystostomy are significant and early risk factors for UTI and other complications (11, 16, 78-87). 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 GUIDELINES FOR CATHETERIZATION

1. Intermittent catheterization is the standard treatment for patients who are unable to empty their bladder (Level of evidence: 2, Grade of recommendation: A).
2. Patients should be well instructed in the technique and risks of IC.
3. Aseptic IC is the method of choice (Level of evidence: 2, Grade of recommendation: B).
4. The catheter size should be 12-14 Fr (Grade of recommendation: B).
5. The frequency of IC is 4-6 times per day (Grade of recommendation: B).
6. The bladder volume should remain below 400 mL (Grade of recommendation: B).
7. Indwelling transurethral and suprapubic catheterization 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. (Grade of recommendation: A).

4.3.3 Intravesical drug treatment

To reduce detrusor overactivity, anticholinergics can also be applied intravesically (88-94). This approach may reduce adverse effects because the anticholinergic drug is metabolized differently (92) and a greater amount is sequestered in the bladder, even more than with electromotive administration (93, 94).

The vanilloids, capsaicin and resiniferatoxin, desensitize the C-fibres and thereby decrease detrusor overactivity for a period of a few months until the sensation of these fibres has been restored (95-100).

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 (100).

4.3.4 Intravesical electrostimulation

Intravesical electrostimulation (101) enhances the sensation for bladder filling and urge to void and may restore the volitional control of the detrusor (11, 102, 103). Daily stimulation sessions of 90 minutes with 10 mA pulses of 2 ms duration at a frequency of 20 Hz (103, 104) are used for at least 1 week (104). 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, 103, 104). Also, the positioning of the stimulating electrodes and bladder filling are important parameters (105). With these precautions, the results in the literature are still not unequivocal: both positive (102, 104, 106, 107) and negative (Level of evidence: 3, Grade of recommendation: C) (108, 109) 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 (110-116). 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 randomized placebo-controlled trial in NLUT (117).

Repeated injections seem to be possible without loss of efficacy (116, 118, 119). Generalized

muscular weakness is an occasional adverse effect (114, 116, 119). Histological studies have not found ultrastructural changes after injection (120).

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 (121-123).

Balloon dilatation: although favourable immediate results were reported (124), 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, 117). The laser technique appears to be advantageous (1, 126).

Sphincterotomy also needs to be repeated at regular intervals in a substantial proportion of patients (127), but is efficient and without severe adverse effects (1, 9, 124-128). Secondary narrowing of the bladder neck may occur, for which combined bladder neck incision might be considered (1, 129).

Bladder neck incision: This is indicated only for secondary changes at the bladder neck (fibrosis) (1, 9, 125, 129). 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 (130, 131), the costs (1) and possible complications or re-interventions (130, 132, 133) 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, 134-138).

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 (139).

4.3.6 GUIDELINES FOR MINIMAL INVASIVE TREATMENT

1. Guidelines for catheterization are listed separately under Section 4.3.2.
2. Botulinum toxin injection in the detrusor is the most effective minimally invasive treatment to reduce neurogenic detrusor overactivity (Level of evidence: 1, Grade of recommendation: A).
3. Sphincterotomy is the standard treatment for DSD (Level of evidence: 2, Grade of recommendation: A).
4. Bladder neck incision is effective in a fibrotic bladder neck (Level of evidence: 3, Grade of recommendation: B).

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 catheterization being performed after the procedure (4).

Urethral sling: Various materials have been used for this procedure with enduring positive results (4, 140-153). 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 (154) for this patient group and the need for revisions (154) has decreased significantly with new generations of devices (146, 156-159).

Functional sphincter augmentation: By transposing the gracilis muscle to the bladder neck (160) or to the proximal urethra (161), the possibility exists for creating a functional autologous sphincter by electrical stimulation (160,161). This would open the possibility of restoring control over the urethral closure.

Bladder neck and urethra reconstruction: The classical Young-Dees-Leadbetter (162) procedure for bladder neck reconstruction in children with bladder exstrophy and the Kropp urethral lengthening (163) improved by Salle (164) are established methods to restore continence provided that intermittent catheterization is practised and/or bladder augmentation is performed (146, 155, 163-174).

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 (175). Since its clinical introduction by Cartwright and Snow (176) in children and by Stöhrer (177) in adults, this procedure for reducing detrusor overactivity 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 quality of life, and because it does not preclude further interventions (1, 4, 176-195).

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, 176, 177). A diverticulum will develop, but this may take 1-2 years in adults (1, 165, 166). A laparoscopic procedure (26, 179, 183, 187), covering of the mucosa at the detrusor defect (transperitoneal) (24, 186, 188, 192), supporting the bladder (176, 192), or simple incision of the detrusor muscle (detrusor myotomy) (194, 195) 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 detrusor overactivity (16, 196-200), but it is used nowadays mostly as an adjuvant to sacral anterior root stimulation (201-212). Alternatives for rhizotomy are sought in this treatment combination (213-215).

Sacral anterior root stimulation (SARS) is aimed at producing a detrusor contraction. The technique was developed by Brindley (216) 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 (201-212). 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 (217). 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 detrusor overactivity (62, 218). 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 (184, 219-223).

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 (224).

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 volitionally, an acontractile bladder could be restored to perform a voiding function. The rectus abdominis (225) and the latissimus dorsi (226) 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 detrusor overactivity. 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, 227-229). 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 must be 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 (182, 184-186, 189-191, 228-231). 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 (190, 232-237).

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 quality of life (4, 238).

Continent diversion: This should be the first choice for diversion. In patients for whom indwelling catheterization or suprapubic catheterization 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 to using the urethra for catheterization (4). The continent stoma is created following various techniques. All of them, however, do show frequent complications, including leakage or stenosis (4, 239). The short-term continence rates are over 80% and good protection of the upper urinary tract is achieved (4, 13, 237-251). For cosmetic reasons, the umbilicus is often used for the stoma site, but this may have a higher risk of stenosis (242, 244, 249).

Incontinent diversion: If catheterization 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 lower urinary tracts, 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, 252-256). 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 (246). The patient must be carefully counselled and must comply meticulously with the instructions (4). Successful undiversion can then be performed (257).

4.5 GUIDELINES FOR SURGICAL TREATMENT

1. 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 (Level of evidence: 2, Grade of recommendation: B).
 - Sacral rhizotomy with SARS in complete lesions and sacral neuromodulation in incomplete lesions are effective treatments in selected patients (Level of evidence: 2, Grade of recommendation: 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 (Level of evidence: 2, Grade of recommendation: B).
 - Underactive
 - SARS with rhizotomy and sacral neuromodulation are effective in selected patients (Level of evidence: 2, Grade of recommendation: B).
 - Restoration of a functional bladder by covering with striated muscle is still experimental (Level of evidence: 4).
2. 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 (Level of evidence: 2, Grade of recommendation: B).

- The artificial urinary sphincter is very effective (Level of evidence: 2, Grade of recommendation: B).
- Transposition of the gracilis muscle is still experimental (Level of evidence: 4).

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5. TREATMENT OF VESICO-URETERAL REFLUX

5.1 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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6. QUALITY OF LIFE

6.1 Introduction

Quality of life (QoL) represents a very important aspect in the global management of neurogenic patients. Restoring QoL as much as possible is one of the aims of therapy. QoL is a reflection of the individual's ability to cope with the new life situation (1). Besides the limitations directly related to the 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, productivity, self-esteem, financial stability, education, physical and social environment (2) (Level of evidence: 3, Grade of recommendation: B). Age, sex, ethnicity and patient's acceptance of the condition should be taken into consideration (3) (Level of evidence: 3, Grade of recommendation: B).

There are no specific QoL questionnaires for neurogenic bladder dysfunction. The only validated tools are a generic Visual Analogue Scale (VAS) for 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 (4, 5) (Level of evidence: 3, Grade of recommendation: B).

The appropriate therapy should manage symptoms, functional abilities, QoL, and avoid secondary complications (5). Changes in NLUTD appear to be the major determinants of a patient's QoL (6, 7) (Level of evidence: 2a, Grade of recommendation: B).

6.2 Conclusions and recommendations

1. Assess QoL to evaluate LUTS in neurogenic patients and during any type of treatment for neurogenic bowel dysfunction (Level of evidence 2a, Grade of recommendation: B).
2. Available tools are: Qualiveen, a specific tool for spinal cord lesion and multiple sclerosis patients, VAS for bother. However, generic (SF-36) or specific tools for incontinence (I-QOL) questionnaires could be used too. (Level of evidence: 2a, Grade of recommendation: B).
3. There is a lack of disease-specific outcome measures assessing health-related QoL in patients with NLUTD.

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7 FOLLOW-UP

7.1 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 spinal cord injury, 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 specialized investigation.

7.2 GUIDELINES FOR FOLLOW-UP

1. Possible UTI checked by the patient (dip stick)
2. Urinalysis every second month
3. Upper urinary tract, bladder morphology, and residual urine every 6 months (ultrasound)
4. Physical examination, blood chemistry, and urine laboratory every year
5. 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.

6. All of the above should be more frequent if the neurological pathology or the NLUTD status demand this.

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8. CONCLUSIONS

NLUTD is a multi-faceted pathology. It requires an extensive and specific diagnosis before we can embark on an individualized 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 all the patient's 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.

9. ABBREVIATIONS USED IN THE TEXT

This list is not comprehensive for the most common abbreviations

CVA	cerebrovascular
DLPP	detrusor leak point pressure
DSD	detrusor sphincter dyssynergia
EMG	electromyography, electromyogram
FVC	frequency volume chart
IC	intermittent catheterization
ISC	intermittent self-catheterization
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

Conflict of interest

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