Guidelines

EAU Guidelines on Neurogenic Lower Urinary Tract Dysfunction

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Abstract

Context: Most patients with neurogenic lower urinary tract dysfunction (NLUTD) require life-long care to maintain their quality of life (QoL) and to maximise life expectancy.

Objective: To provide a summary of the 2008 version of the European Association of Urology (EAU) guidelines on NLUTD and to assess the effectiveness of currently available diagnostic tools, particularly ultrasound imaging and urodynamics.

Evidence acquisition: The recommendations provided in the 2008 EAU guidelines on NLUTD are based on a review of the literature, using online searches of Medline and other source documents published between 2004 and 2007. A level of evidence and/or a grade of recommendation have been assigned to the guidelines where possible.

Evidence synthesis: NLUTD encompasses a wide spectrum of pathologies, and patients often require life-long, intensive medical care to maximise their life-expectancy and to maintain their QoL. Treatment must be tailored to the needs of the individual patient and, in many cases, involves a multidisciplinary team of experts. Timely diagnosis and treatment are essential if irreversible deterioration of both the upper and lower urinary tracts are to be avoided. Therapeutic decisions are made on the basis of a comprehensive medical assessment, including urodynamics to identify the type of dysfunction. Advances in investigative technologies have facilitated the noninvasive and conservative management of patients who have NLUTD.

Conclusions: The diagnosis and treatment of NLUTD, which is a highly specialised and complex field involving both urology and medicine, requires up-to-date expert advice to be readily available. The current guidelines are designed to fulfil this need.

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1. **Introduction**

Before the 1980s, considerable morbidity was associated with renal failure in patients with neurogenic lower urinary tract dysfunction (NLUTD) [1,2]. Most patients with NLUTD require life-long care to maintain their quality of life (QoL) and to maximise life expectancy. Significant technologic developments that have occurred over the last 30 yr have helped to achieve these goals.

The European Association of Urology (EAU) Guidelines Working Panel for NLUTD prepared this overview of the 2008 EAU guidelines on NLUTD, presented at the 23rd Annual EAU Congress [3], to enable urologists to incorporate evidence-based management of NLUTD into their clinical practice.

2. **Evidence acquisition**

A detailed literature search for high-quality data published between 2004 and 2007 was carried out using Medline and other source documents (eg, textbooks and medical and scientific Web sites).

Where possible, the panel has used a three-tier system (A–C) [4] to grade treatment recommendations to assist clinicians in determining the validity of a recommendation.

No data on the prevalence of NLUTD in the general population are available. Data are available, however, on the prevalence of underlying causative conditions and the risk that these conditions pose for the development of NLUTD, although generally this information comes from studies involving only small sample sizes.

The limited availability of randomised, controlled trials plus the fact that a considerable number of treatment options involve surgical intervention were further drawbacks. In areas in which conclusive data are lacking, this paper presents a consensus view. Because no consistent level of evidence (LE) is available for most of the diagnostic procedures, grades of recommendations (GRs) are provided based on expert opinion.

The terminology used and the diagnostic procedures outlined in these guidelines follow the recommendations for the investigation of the lower urinary tract (LUT) published by the International Continence Society (ICS) [5,6] (Table 1).

3. **Evidence synthesis**

3.1. **Risk factors and epidemiology**

All central and peripheral neurologic disorders carry a high risk of causing functional disturbances of the urinary tract.

3.2. **Classification**

Several classification systems have been proposed for NLUTD. The recommendations for a functional classification for motor function are based on urodynamic and clinical findings [7] (Fig. 1).

3.3. **Timing of diagnosis and treatment**

In both congenital and acquired NLUTD, early diagnosis and treatment are essential because irreversible changes within the LUT may occur, even when the related neuropathologic signs are normal [8,9]. Additionally, NLUTD can, by itself, be the presenting feature of neurologic pathology [10,11].

3.4. **Diagnosis**

Diagnosis of NLUTD should be based on a comprehensive assessment of neurologic and non-neurologic conditions. Initial patient assessment should include a detailed history, physical examination, and urinalysis.

<table>
<thead>
<tr>
<th>Table 1 – Definitions useful in clinical practice*</th>
<th>Emptying of the bladder by a catheter that is introduced (semi-)permanently</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheterisation, indwelling</td>
<td>Emptying of the bladder by a catheter that is removed after the procedure, mostly at regular intervals.</td>
</tr>
<tr>
<td>Intermittent catheterisation (IC)</td>
<td>The catheters remain sterile, the genitals are disinfected, and (disinfecting) lubricant is used.</td>
</tr>
<tr>
<td>Aseptic IC</td>
<td>Disposable or cleansed reusable catheters, genitals washed.</td>
</tr>
<tr>
<td>Clean IC</td>
<td>Complete sterile setting, including sterile gloves, forceps, gown, and mask.</td>
</tr>
<tr>
<td>Sterile IC</td>
<td>Performed by the patient.</td>
</tr>
<tr>
<td>Intermittent self-catheterisation</td>
<td>Below the predicted maximum calculated as body weight kilograms/4 in millilitres per second.</td>
</tr>
<tr>
<td>Filling rate, physiologic</td>
<td>Lesion at or below the S1–S2 spinal cord level.</td>
</tr>
<tr>
<td>Lower motor neuron lesion</td>
<td>Nonsurgical nonpharmacologic treatment for LUT dysfunction.</td>
</tr>
<tr>
<td>Rehabilitation, LUT</td>
<td>Lesion above the S1–S2 spinal cord level.</td>
</tr>
<tr>
<td>Upper motor neuron lesion</td>
<td>Voiding with physiological detrusor pressure and low postvoid residual.</td>
</tr>
<tr>
<td>Voiding, balanced: in patients with NLUTD (postvoid residual &lt;80 ml or &lt;20% of bladder volume)</td>
<td>Voiding initiated by manoeuvres to elicit reflex detrusor contraction by exteroceptive stimuli.</td>
</tr>
<tr>
<td>Voiding, triggered</td>
<td>Lowest value of detrusor pressure at which leakage is observed in the absence of abdominal strain or detrusor contraction.</td>
</tr>
</tbody>
</table>

* Modified from Abrams et al [6].

LUT = lower urinary tract; NLUTD = neurogenic lower urinary tract dysfunction.
3.4.1. Patient history
An extensive general and specific history is mandatory and should concentrate on past and present symptoms and disorders of the urinary tract and bowel and on sexual and neurologic function. Special attention should be paid to possible warning signs and symptoms (e.g., pain, infection, haematuria, and fever) that warrant further investigation.

The history should include the following items:

- Acquired or congenital neurologic conditions
- Neurologic symptoms (somatic and sensory), including their onset, evolution, and any treatment
- Spasticity or autonomic dysreflexia (lesion above thoracic sixth vertebra)
- Mental status and comprehension
- Prior surgery
- Medications
- Mobility and hand function
- Socioeconomic situation.

3.4.2. Physical examination
In addition to a detailed patient history and a general examination, neurologic status should be described as completely as possible. All sensations and reflexes in the urogenital area must be tested, and detailed testing of the anal sphincter and pelvic floor functions must be performed (Fig. 2). Availability of this clinical information is essential for the reliable interpretation of subsequent diagnostic investigations.

3.4.3. Urodynamic tests
A bladder diary should be recorded for at least 2–3 d [5]. Possible pathologic findings include high voiding frequency, very small or very large voided volumes, nocturnal voiding, urgency, and incontinence.

Uroflowmetry and ultrasound assessment of postvoid residual should be repeated at least two or three times in patients who are able to void [5]. Possible pathologic findings include low urine flow rate, low voided volumes, intermittent flow, hesitancy, and large postvoid residual.

3.4.4. Invasive urodynamic studies
Invasive urodynamic studies use mandatory assessment tools to determine the exact type of NLUTD (Table 2). Although referred to as invasive, these studies are generally associated with low complication rates [12].

Filling cystometry is the only procedure that quantifies the filling function of the bladder; however, when filling cystometry is used alone, the results have limited significance. Possible pathologic findings include detrusor overactivity, low bladder compliance, detrusor/sphincter dyssynergia (DSD), abnormal bladder sensation and other sensations (e.g., autonomic dysreflexia), and incontinence.

Measurement of detrusor leak-point pressure (DLPP) has limited diagnostic value; it is not recommended as a stand-alone test. A high DLPP warrants further investigation with video-urodynamics.

Pressure–flow studies used to test the function of the LUT must also be made during the voiding phase
whenever possible. Possible pathologic findings include detrusor underactivity or acontractility, DSD, an incompetent urethral closure mechanism, nonrelaxing urethral sphincter obstruction, and increased postvoid residual.

Video-urodynamics combine filling cystometry and pressure–flow studies with radiologic imaging. Possible pathologic findings include all of the conditions described above under filling cystometry and pressure–flow studies plus morphologic abnormalities of the urinary tract. Special attention is given to demonstrable vesico-ureteral reflux. Currently, video-urodynamics are considered to provide the most comprehensive information for evaluating NLUTD [5].

Electromyography (EMG) is a semiquantitative measure of pelvic-floor activity that can be used to detect DSD and pelvic-floor relaxation disorders.

3.4.5. Specific uroneurophysiologic tests

Specific uroneurophysiologic tests form part of the neurologic work-up (Table 3) and include the following items:

- Electromyogram of pelvic-floor muscles, urethral sphincter, and/or anal sphincter
- Nerve-conduction studies of the pudendal nerve
- Reflex latency measurements of bulbocavernosus and anal reflex arcs
- Evoked responses from clitoris or glans penis
- Sensory testing of the bladder and urethra.

Table 3 – Characteristic findings in neurogenic lower urinary tract dysfunction

<table>
<thead>
<tr>
<th>Phase</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filling phase</td>
<td>Increased, decreased, or absent bladder sensation</td>
</tr>
<tr>
<td></td>
<td>Vegetative nonspecific sensations</td>
</tr>
<tr>
<td></td>
<td>Low level of bladder compliance</td>
</tr>
<tr>
<td></td>
<td>Detrusor overactivity, spontaneous or provoked</td>
</tr>
<tr>
<td></td>
<td>Incompetent urethral closure mechanism</td>
</tr>
<tr>
<td>Voiding phase</td>
<td>Incompetent/contractile or underactive detrusor</td>
</tr>
<tr>
<td></td>
<td>Bladder-outlet obstruction</td>
</tr>
<tr>
<td></td>
<td>Detrusor/sphincter dyssynergia</td>
</tr>
<tr>
<td></td>
<td>Nonrelaxing urethral sphincter obstruction</td>
</tr>
</tbody>
</table>

** These signs warrant further neurologic evaluation because lower urinary tract dysfunction may be the presenting symptom of a neurologic disease [8].

3.5. Treatment

Treatment of NLUTD aims to protect the upper urinary tract and to improve continence, QoL, and, whenever possible, LUT function. In patients with NLUTD, preservation of upper urinary tract function is essential [2,13]. In patients with a high detrusor pressure in the filling phase, the principal aim of treatment is conversion of an overactive, high-pressure bladder into a low-pressure reservoir, even if this should result in a high postvoid residual [13]. Other considerations when planning treatment of NLUTD should include the patient’s condition, potential complications, technical aspects, and cost effectiveness [13]. The patient’s QoL is a prime consideration when making any treatment decision.

3.5.1. Conservative treatment

There are few prospective, randomised, controlled studies of the medical management of NLUTD.

3.5.1.1. Drug treatment for neurogenic detrusor overactivity. A single optimal medical therapy for neurogenic detrusor overactivity (NDO) is not yet available. Antimuscarinic agents are currently the most widely used treatment, although most of the available drugs have not been registered for the treatment of this patient population (Table 4). Patients with a neurogenic bladder disorder usually need a higher dose of antimuscarinics than patients with idiopathic detrusor overactivity [14] (LE: 1b; GR: A); however, higher doses are associated with a higher rate of side-effects [15]. Antimuscarinic agents can also be given intravesically [16] (Table 4).

3.5.1.2. Drug treatment for neurogenic detrusor underactivity. There is no evidence of effective drug treatment for neurogenic detrusor underactivity [13] (LE: 2a; GR: B).

3.5.1.3. Drug treatment to decrease bladder-outlet resistance. Selective and nonselective α-blockers have been partially successful in decreasing bladder-outlet resistance, residual urine, and autonomic dysreflexia [13] (LE: 2a; GR: B).

3.5.1.4. Catheterisation. Intermittent catheterisation (IC) (ie, self-catheterisation or third-party catheterisation) [17] is the gold standard for the management of NLUTD [13]. Sterile IC significantly reduces the risk of urinary tract infection (UTI) and/or bacteriuria [13,17,18] compared with
clean IC. Sterile IC, however, cannot be used routinely; aseptic or clean IC are feasible alternatives [19,20]. Compared with clean IC, aseptic IC provides significant benefit in reducing the potential for contamination [19]. Inadequate education and the inherently greater risk of UTI in patients with NLUTD contribute to the risk of infection [13,20]. On average, for catheterisation, a 12–14 French catheter is needed four to six times per day. Less frequent catheterisation results in higher bladder-storage volumes and an increased risk of UTI [20]. More frequent catheterisations increase the risk of cross-infection [20].

Indwelling transurethral catheterisation and, to a lesser extent, suprapubic cystostomy should be avoided because they are risk factors for UTI and for significant long-term complications [13,21–23]. If indwelling catheters have to be used, empirical evidence and expert opinion suggest that silicone catheters have advantages over latex catheters [24].

3.5.1.5. Assisted bladder emptying. Triggered reflex voiding is not recommended because there is a risk of pathologically elevated bladder pressures. Only in the case of absence of this reflex or in the case of a reflex reduced as a result of surgery should outlet obstruction be an option [13].

Bladder compression techniques to expel urine (Crede) and voiding by abdominal straining (Valsalva manoeuvre) create high pressures and are potentially hazardous, and their use should be discouraged [13].

3.5.1.6. Rehabilitation. LUT rehabilitation includes prompted voiding, timed voiding (bladder training), and lifestyle modification [14]. In selected patients, pelvic-floor muscle exercises, pelvic-floor electrostimulation, and biofeedback might be beneficial [25].

3.5.1.7. External appliances. External appliances may be the most effective remedy for some patients. Social continence for the incontinent patient can be achieved using an appropriate method of urine collection [13]. Condom catheters or pads can offer a reliable solution. In both cases, the patient must be monitored closely because there is a risk of infection [13]. Because penile clamp is associated with high pressure on the urethral tissue and will reduce penile blood flow, it should not be used routinely [26].

3.5.2. Minimally invasive treatment

3.5.2.1. Botulinum toxin A injections in the bladder. Botulinum toxin A causes a long-lasting (up to 9 mo), reversible, chemical denervation [27,28]. Botulinum toxin A has been proven to be effective in small, randomised, placebo-controlled trials in NLUTD [29,30]. Repeated injections can be given without loss of efficacy [28,31]. Generalised muscle weakness is an occasional adverse effect [28,31]. Histologic studies have not found ultrastructural changes in bladder muscle after injection [32]. Botulinum toxin A is currently only available on a named-patient basis in every European country except Switzerland, where it has regulatory approval.

3.5.2.2. Intravesical vanilloid treatment. The vanilloids, capsaicin, and resiniferatoxin desensitise the C-fibres, thus temporarily decreasing detrusor overactivity. Resiniferatoxin and capsaicin, however, have limited clinical efficacy compared to botulinum toxin A injections into the detrusor [33,34].

3.5.2.3. Bladder-neck and urethral procedures (see section 3.5.3.3). Reduction of the bladder-outlet resistance to protect the upper urinary tract can be achieved by sphincterotomy [35] or by chemical denervation of the sphincter using botulinum toxin A [36]. Incontinence may result and can be managed using external devices. Insertion of urethral stents is not recommended because this procedure is associated with substantial complication and reintervention rates [37]. Increasing bladder-outlet resistance using bulking agents, urethral inserts, or alternative appliances is not recommended for long-term treatment [38] (LE: 2a; GR: B).

3.5.2.4. Neurogenic detrusor overactivity and reflux. Vesico-ureteral reflux should be managed by lowering intravesical pressure. If reflux is persistent, intervention using bulking agents, ureteral reimplantation can be considered [39,40].

3.5.3. Surgical treatment

3.5.3.1. Overactive detrusor. Bladder augmentation (eg, clam cystoplasty) is indicated for an overactive detrusor when less invasive procedures have failed [41,42] (Fig. 3).

<table>
<thead>
<tr>
<th>Drug</th>
<th>References</th>
<th>Comment</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin</td>
<td>Block et al [38], Granata et al [39]</td>
<td>–</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Trospium chloride</td>
<td>Dykstra and Sidi [36], Wilson et al [37]</td>
<td>–</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Tolterodine</td>
<td>Dykstra and Sidi [36], Ströher and Pannik [42]</td>
<td>–</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Propiverine</td>
<td>Granata et al [39], Ströher et al [43]</td>
<td>–</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>–</td>
<td>No data as yet</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>–</td>
<td>No data as yet</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>–</td>
<td>No data as yet</td>
<td>–</td>
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</tbody>
</table>

LE = level of evidence; GR = grade of recommendation.
Alternative options include autoaugmentation (myomec-
tomy) [43]; dorsal rhizotomy, with or without sacral
anterior root stimulation (SARS) (complete lesions); and
neuromodulation (incomplete lesions) [44,45]. Substitution
with either continent [46] or incontinent diversion [47] is
indicated for the small, contracted, noncompliant bladder
[46].

3.5.3.2. **Underactive detrusor.** SARS (complete lesions) and
sacral neuromodulation (incomplete lesions) [44,45] are
effective in selected patients (LE: 2; GR: B).

3.5.3.3. **Sphincter insufficiency (underactive urethra).** The artificial
urinary sphincter is the preferred treatment for patients
with NLUTD [48] (LE: 2; GR: B). Alternative procedures are
the placement of a bladder-neck sling or a midurethral sling
[49,50] (LE: 3; GR: B). Various materials have been used for a
midurethral sling [51].

Procedures to treat sphincter incompetence are suitable
only when the detrusor activity is, or can be, controlled and
there is no significant associated vesico-ureteral reflux.
Simultaneous bladder augmentation and artificial sphincter
implantation is an option in patients with neurogenic
disorders [52].

3.6. **Quality of life**

QoL is a very important aspect of the global management of a
patient who has NLUTD. Restoration and maintenance of the
patient’s QoL, as much as possible, should be one of the major
aims of treatment. QoL should be integral to the evaluation
of LUT symptoms in patients with NLUTD and also when
considering any type of treatment for neurogenic bladder
dysfunction [53] (LE: 2a; GR: B). QoL can be assessed using
Qualiveen, a specific tool for patients with spinal cord lesions
and those suffering from multiple sclerosis and visual
an analogue scale (VAS) [54]. Generic short-form health survey
(SF-36) tools or specific questionnaires like the Urinary
Incontinence Quality of Life Scale (I-QOL) to assess incon-
tinence can also be used [55] (LE: 2a; GR: B). Currently, there
are no disease-specific outcome measures for the assessment
of health-related QoL in patients with NLUTD.

3.7. **Follow-up**

NLUTD is an unstable condition which manifests itself with
considerable variability, even within a relatively short time
frame. Meticulous, regular follow-up is essential [42].
Individualised patient follow-up is imperative to safeguard
QoL and life expectancy. The underlying pathology and the
state of the urinary tract dictate the frequency of follow-up
required. Minimum follow-up is outlined in Table 5.

4. **Conclusions**

NLUTD is a multifaceted pathology. Extensive investigation
and a precise diagnosis are required before the clinician can
initiate individualised therapy. Treatment must take into
account the patient’s medical and physical condition and
expectations with regard to his or her future social, physical,
and medical situation.

This paper provides a summary of the 2008 European
Association of Urology (EAU) guidelines on neurogenic
lower urinary tract dysfunction (NLUTD). More detailed
information and a complete reference list are available in
the full-text version of the guidelines, which can be found
on the Web site of the EAU (http://www.uroweb.org/nc/
professional-resources/guidelines/online/). The full text
version of the NLUTD guideline is also available on the
EAU’s Web site (http://www.uroweb.org/nc/professional-
resources/guidelines/online/).

**Author contributions:** Manfred Stoéhrer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Analysis and interpretation of data:** Stoéhrer, Blok, Castro-Diaz, Chartier-Kastler, Del Popolo, Kramer, Pannek, Radziszewski, Wyndaele.

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**Critical revision of the manuscript for important intellectual content:** Stoéhrer, Blok, Castro-Diaz, Chartier-Kastler, Del Popolo, Kramer, Pannek, Radziszewski, Wyndaele.

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References


