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Neurogenic Lower Urinary Tract Dysfunction: Clinical Management Recommendations of the Neurologic Incontinence Committee of the Fifth International Consultation on Incontinence 2013

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Background: Evidence-based guidelines for the management of neurological disease and lower urinary tract dysfunction have been produced by the International Consultations on Incontinence (ICI). These are comprehensive guidelines, and were developed to have world-wide relevance. **Aims:** To update clinical management of neurogenic bladder dysfunction from the recommendations of the fourth ICI, 2009. **Materials and methods:** A series of evidence reviews and updates were performed by members of the working group. The resulting guidelines were presented at the 2012 meeting of the European Association of Urology for consultation, and consequently amended to deliver evidence-based conclusions and recommendations in 2013. **Results:** The current review is a synthesis of the conclusions and recommendations, including the algorithms for initial and specialized management of neurogenic lower urinary tract dysfunction. The pathophysiology is categorized according to the nature of onset of neurological disease and the part(s) of the nervous system affected. Assessment requires clinical evaluation, general investigations, and specialized testing. Treatment primarily focuses on ensuring safety of the patient and optimizing quality of life. Symptom management covers conservative and interventional measures to aid urine storage and bladder emptying, along with containment of incontinence. A multidisciplinary approach to management is essential. **Discussion:** The review offers a pragmatic review of management in the context of complex pathophysiology and varied evidence base. *Neurourol. Urodynam. 35:657–665, 2016.* © 2016 Wiley Periodicals, Inc.

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INTRODUCTION

Neurogenic lower urinary tract dysfunction (NLUTD) is a general term referring to the diverse effects of neurological disease on urinary tract function. The neurological regulation of the individual organs and their voluntary, and reflex control is complex, and mediated at several levels of the neuraxis. Thus, the potential for lower urinary tract (LUT) dysfunction in someone with neurological disease is substantial, and this may be one of the worst aspects of their condition for the affected individual, in terms of quality of life impact. This clinical guide for neurogenic bladder management sets out the conclusions of the Neurologic Incontinence panel of the fifth International Consultation on Incontinence regarding assessment and treatment of NLUTD.

METHODS

Using the previous review of the Neurologic Incontinence committee from the fourth International Consultation on Incontinence[1,2] as a baseline, an updated literature search of all published research was conducted from January 2008 to August 2012. A pragmatic narrative review of the major

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databases (Medline, Embase, Cochrane Library, Biosis, Science Citation Index), was undertaken with no restriction on date, covering key terms: neuro-urology; neurogenic incontinence; neurogenic bladder; diagnostic tests; therapy; specific conditions. The full reference list is available gratis from the website of the International Consultation on Urological Diseases (http://www.icud.info/incontinence.html). The findings were presented at the annual scientific meeting of the European Association of Urology in 2012 for consultation, and modifications applied for the fifth edition of the ICI scientific report in 2013.[3] Levels of evidence (LOE) and grades of recommendation (GOR) were derived according to the modified Oxford system developed by the International Consultations on Urological Diseases.[4]

PATHOPHYSIOLOGY

With a neurologic lesion, the type of NLUTD that arises depends on the site, extent, and the evolution of the lesion. Key categories include:

1. Time of neurological dysfunction; congenital or perinatal, are considered distinct from those acquired later on, since the former never develop normal LUT function.
2. Likelihood of neurological progression; progressive conditions, contrasting with neurological lesions which are typically stable.
3. Extent of loss of neurological function.
4. Which part(s) of the nervous system is affected[5] (Table I).

a) "Suprapontine," i.e., patients with lesions above the pons (forebrain or midbrain); they usually continue to have reflex contractions of the detrusor, but impaired cerebral regulation, and central inhibition. This may lead to:

- Inappropriate timing of voids.
- Inability to initiate voiding.
- Neurogenic detrusor overactivity (NDO) and NDO-associated incontinence.
- Voiding (where present) is usually synergic, but voluntary sphincter contraction to resist DO may give rise to "pseudo-dyssynergia."

b) Pontine. Brainstem lesions are rarely compatible with more than short-term survival. However, lesions could cause NDO or detrusor underactivity and even detrusor-sphincter-dyssynergia (DSD) according to the location and extent of the lesion.

c) Suprasacral spinal cord.

- NDO and NDO-associated incontinence are common.
- Detrusor-urethral sphincter dyssynergia (DSD) can also occur, often resulting in a significant post void residual (PVR) and "high pressure" bladder.
- Poorly sustained detrusor contractions are often seen and lead to incomplete bladder emptying.
- Detrusor compliance during bladder filling may be impaired.
- Altered function of the sympathetic spinal center in the thoraco–lumbar spinal cord may alter blood pressure control. Lesions above T6 spinal cord level may place the patient at risk of autonomic dysreflexia (AD).
- Altered male ejaculatory function.

d) Sacral spinal cord.

- Detrusor areflexia (loss of parasympathetic function).
- Stress urinary incontinence (SUI) due to sphincter deficiency (loss of Onuf's nuclei).
- Detrusor compliance during bladder filling may be impaired.

e) Subsacral (cauda equina and peripheral nerves). There may be detrusor areflexia and/or SUI. Detrusor compliance can be impaired. In diabetic neuropathy, detrusor overactivity can be seen in combination with the above.

The peripheral nerves and the lower spinal centers are often grouped under the term "lower motor neurones," as severe damage to these structures causes loss of contractile function. However, it is recognized that incomplete damage to peripheral nerves and the lower spinal centers can result in altered reflex activity and symptoms of bladder overactivity.[6] Elsewhere, the neurological lesions are termed "upper motor neuron lesions," where the consequences are impaired co-ordination and reflex function. This is a considerable simplification, and anatomically inexact, so the committee considers categorization into lower versus upper motor neuron lesions should no longer be supported.

Recommendations

- Neural lesions are described according to time of onset, risk of neurological progression, completeness, and neurological level.

TABLE I. Categorization of Neurological Lesions According to Time of Onset, Clinical Course, and CNS Location, With Example Conditions

	Congenital & perinatal lesions	Acquired, stable conditions	Acquired, progressive conditions
Brain and brainstem	Cerebral palsy	Stroke, head injury	Multiple sclerosis,[a] Parkinson's disease, dementia, multiple system atrophy[a]
Suprasacral spinal cord	Hereditary spastic paraparesis, spinal dysraphism[a]	Trauma	Multiple sclerosis,[a] spondylosis with myelopathy
Sacral spinal cord	Spinal dysraphism, sacral agenesis, anorectal anomaly	Conus injury	Tumor
Subsacral	Spinal dysraphism, familial dysautonomia	Cauda equina injury, pelvic nerve injury	Tumor, peripheral neuropathy (e.g. diabetic)

[a]Conditions that can arise in more than one region of the CNS.

- Complete suprasacral spinal cord lesions should describe whether enough sympathetic nucleus function is retained to place the patient at risk of AD.

INITIAL ASSESSMENT

The aim of initial assessment is to ascertain:

1. The nature of the NLUTD, focussing on risk factors for major complications and associated symptoms.
2. Previous management, availability of support, home circumstances, lifestyle factors, quality of life, and desire for treatment.
3. What limitations the neurological disease places on management options, e.g., cognition, mobility, toilet transfer, hand function, and core support.
4. Whether any other factors may contribute to LUT dysfunction, e.g., prostate enlargement or post-obstetric urethral hypermobility.
5. Urinary tract infections (UTIs)/bacteriuria, noting that symptoms may be unclear (especially where neurological disease affects sensory function), and that over-diagnosis is common.
6. Medical, medication, and surgical history, including whether any other co-morbidity may limit therapy options.
7. Whether the neurological disease affects blood pressure control, leading to AD or postural hypotension.
8. Bowel and sexual function.
9. Risk of decubitus ulcers.

An overview of the assessment and treatment is given in Figures 1 and 2.

SPECIALIZED ASSESSMENT

Urodynamic Tests

Urodynamic techniques evaluate multiple functional parameters in NLUTD, aiming to define bladder and outlet function during bladder filling and emptying. Relevant investigations include: voiding diary, urodynamic studies (cystometry, electromyography (EMG), uroflowmetry, pressure-flow study), diagnostic imaging with voiding cystourethrography and ultrasonography. The use of multichannel cystometry and pressure flow studies with synchronous imaging (video-urodynamics) offers suitable testing in most patients.

The International Urodynamic Basic Spinal Cord Injury (SCI) dataset[7] recommends data to be included in the urodynamic evaluation of patients with SCI. Variables included comprise:

- Bladder sensation during filling cystometry.
- Detrusor function and compliance during filling cystometry.
- Sphincter function during bladder filling.
- Detrusor/sphincter function during voiding.
- Detrusor leak point pressure in patients with impaired detrusor compliance.
- Cystometric bladder capacity and post-void residual.

Video-urodynamics (VUDS) offers visualization of bladder and outlet, including pelvic floor support, to provide anatomical and functional information during filling and voiding. Such testing is informative regarding risk factors for upper urinary tract problems, mechanism(s) of incontinence, and mechanism(s) of voiding dysfunction. Without such information, caution is needed in interpreting cystometry and pressure flow study results. The presence of vesico-ureteric reflux and of reflux of X-ray contrast into the prostatic ducts may also be detected during a video-urodynamic assessment.

Filling rate for cystometry should be initiated at a slow rate (e.g., 10 ml/min); medium fill rates can be used in patients who are known to have a normal or high functional bladder capacity where compliance is seen in the early phases of a test to be normal.

- Findings of urodynamic tests can be difficult to anticipate from clinical assessment alone in NLUTD (LOE 2).
- A combination with EMG and/or imaging adds to the diagnostic possibilities (LOE 2).
- Filling rate can influence the outcome of several urodynamic parameters (LOE 2).
- Pressure development in the bladder is one of the important parameters to be studied and a high detrusor leak point pressure is a risk factor for renal deterioration (LOE 2).
- Sensation of filling may be preserved despite spinal abnormality (LOE 2).
- Antibiotic prophylaxis should be considered for invasive urodynamic testing (LOE 2).

Recommendations.

- Urodynamic tests should selectively be employed to supplement clinical assessment in determining management in NLUTD.
- Methods of Urodynamic testing in NLUTD should follow International Continence Society recommendations.[8,9]
- EMG of the urethral sphincter can be considered as a diagnostic method in patients with NLUTD and neurologic urinary incontinence (GOR B).
- There are some arguments that nerve conduction studies can be useful in the further differentiation of the nerve deficits in cases of a suspected neurological cause for bladder dysfunction (GOR C).
- Somatosensory evoked potentials can be of use in the further diagnosis of neurological deficits related to LUT dysfunction (GOR C).
- Sympathetic skin responses seem promising and the further study of them are recommended for the evaluation of the LUT sympathetic innervation (GOR B).

CONSERVATIVE TREATMENT

A range of measures aimed at symptom management or containment can be considered. Some are experimental, and need additional development before they can be recommended for routine practice. Others are no longer recommended, but are included in the current report because patients may have been established on the method previously, and do not wish to convert to an alternative method. Individuals with NLUTD due to SCI often change their method of bladder management during the protracted follow-up necessary, influenced by a range of factors including renal function (LOE 2).[10]

Safety Considerations

Some specific situations require particular attention in NLUTD;

1. AD; acute life-threatening risk can result from severe hypertension in patients with high spinal cord dysfunction

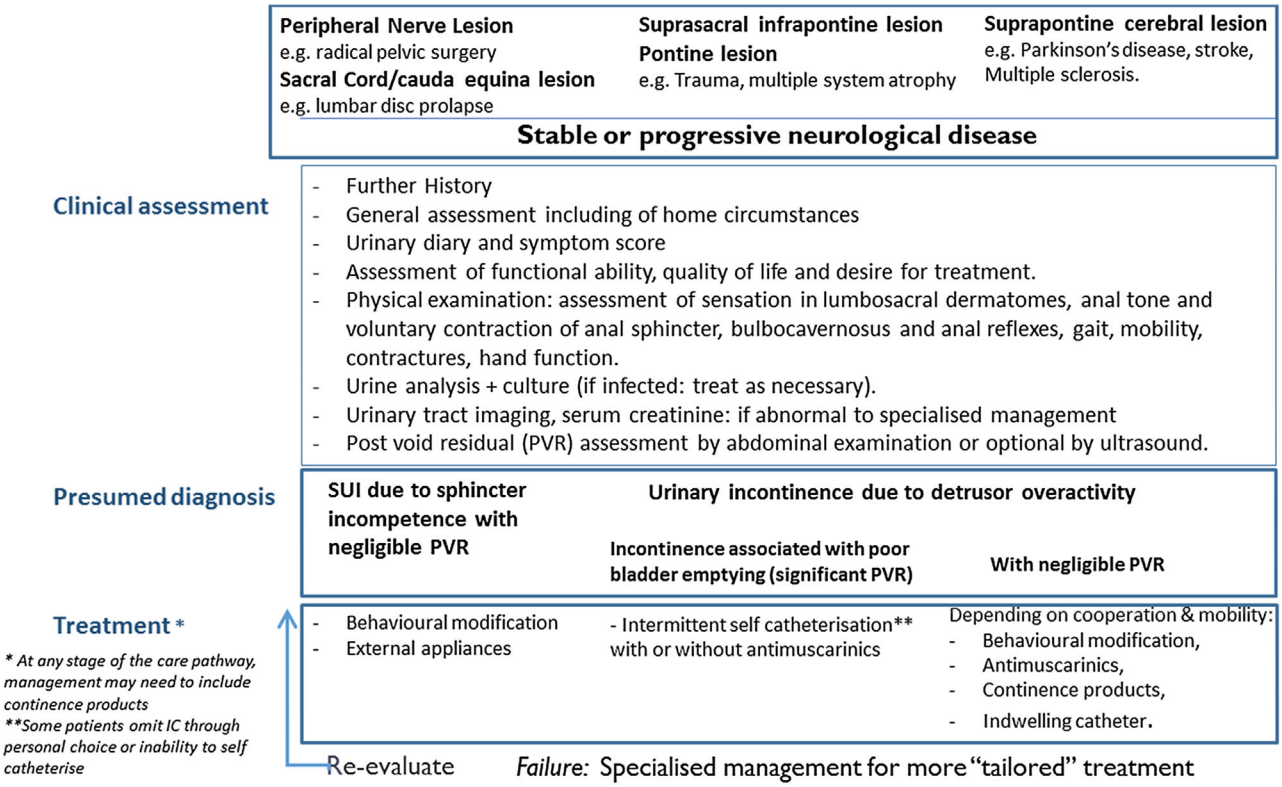

Fig. 1. Initial assessment and therapy of neurogenic lower urinary tract dysfunction.

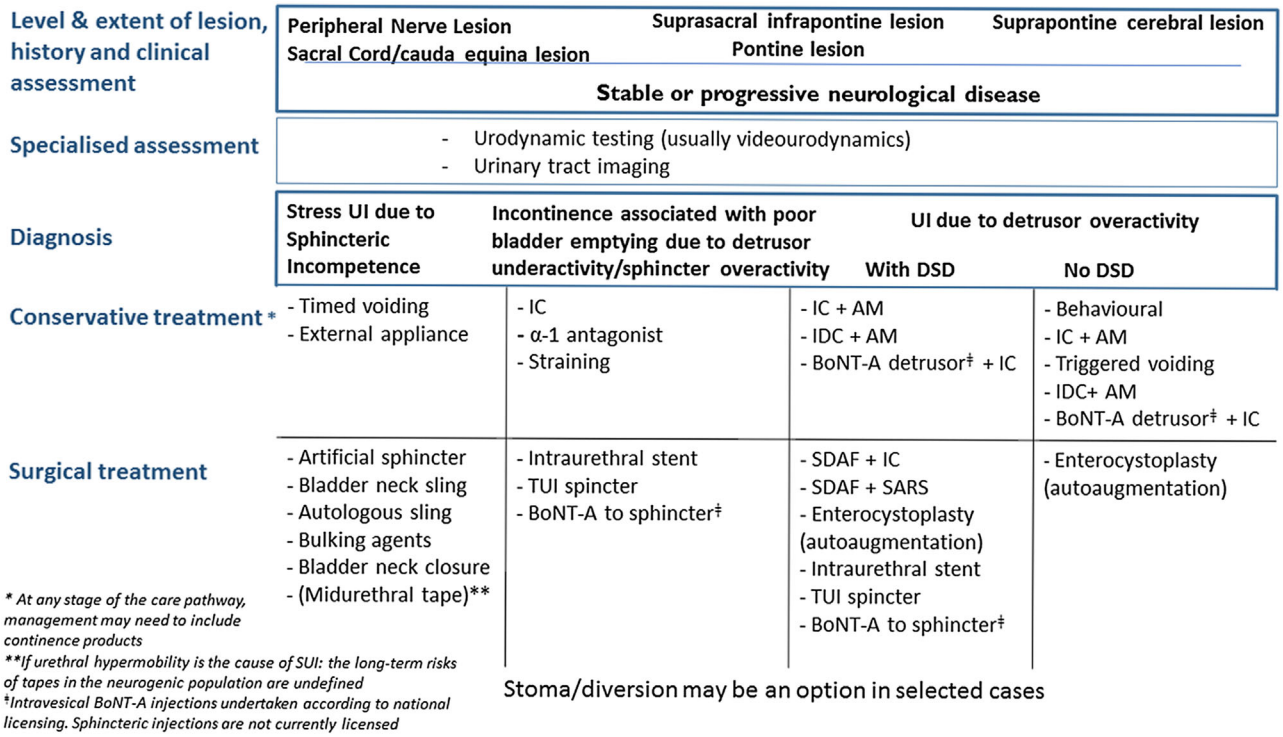

Fig. 2. Specialized assessment and therapy of neurogenic lower urinary tract dysfunction. AM, antimuscarinics; BoNT-A, botulinum neurotoxin-A; DSD, detrusor sphincter dyssynergia; IC, intermittent catheterization; IDC, indwelling catheter; PVR, postvoid residual; SARS, sacral anterior-root stimulator; SDAF, sacral deafferentation; TUI, transurethral incision.

(typically SCI above T6). Various triggers of episodes AD are recognized, including iatrogenic urological procedures. Routine blood pressure monitoring during investigations or invasive therapy is therefore appropriate.
2. Allergy to latex needs appropriate preventive and therapeutic arrangements to be in place in case of anaphylactic reaction.
3. Urodynamic features should be used to gauge potential impact on a patient's renal function as a consequence of NLUTD, in particular; (i) Impaired detrusor compliance with a high detrusor leak point pressure is a high risk situation needing early intervention; (ii) DSD; (iii) Vesico-ureteric reflux.

Exact parameters for acceptable values of urodynamic parameters have not been established.

- Reflex bladder emptying is based on a non-physiological sacral reflex. It is potentially dangerous and has a limited role in managing the NLUTD (LOE 3).
- Bladder emptying using external expression, is hazardous for the urinary tract if there is functional obstruction at the level of the pelvic floor (LOE 3).
- Bladder emptying by abdominal straining is contraindicated if it creates a high intravesical pressure, particularly in association with reflux into the ureters or seminal vesicles. Hernias, pelvic organ prolapse, hemorrhoids, and urethral pathology (strictures) are relative contraindications (LOE 3).
- Bladder expression and abdominal straining may adversely affect a flaccid pelvic floor, potentially exacerbating incontinence (LOE 3).

Recommendation.
- Any unit managing patients with SCI should be appropriately set up to manage acute AD.
- Urological management of patients at risk of AD should consider whether there is risk of inducing an attack of AD. Standard departmental procedures should be in place for monitoring, and for instigating intervention if AD becomes apparent.

Symptom Management

The detrusor and sphincter are often both affected by the neurogenic lesions. In many patients, a storage problem, leading to incontinence, is associated with an emptying problem; therefore both aspects have to be considered. Therapy of neurogenic incontinence is primarily a conservative one. Timed bladder emptying, controlled fluid-intake and avoidance of urinary tract infections are needed for successful treatment. Throughout, all measures to address symptom management need to consider that assessments of safety have been undertaken and necessary safety treatment measures are in place.

In supraspinal lesions, NDO is mostly associated with normal sphincter function; NDO-associated incontinence is the main problem for many patients and antimuscarinic therapy together with behavioral treatment is the method of choice, more so in patients with cognitive impairment.

Spinal lesions mostly cause simultaneous dysfunction of the detrusor and the sphincter. In suprasacral lesions, DO often occurs with an overactive/dyssynergic sphincter. For these patients, spontaneous reflex voiding may be possible, but often emptying is incomplete. The mainstay of treatment in current practice is intermittent catheterization (IC), undertaken by the patient or carer. However, to achieve low pressure LUT urine storage and continence between catheterizations, additional pharmacotherapy may be necessary. If incontinence persists and if operative procedures are not indicated or possible, containment products will be needed. The indwelling catheter remains an option for conservative therapy, and can offer acceptable quality of life outcomes and long-term protection of the upper urinary tract. Most experts regard indwelling catheterization as being associated with significant problems [10]. While suprapubic catheters are generally preferred over urethral, there is little published evidence on which to base practice, but it is very clear that urethral catheters can be associated with severe urethral trauma. Urethral leakage can persist despite continuous drainage with a SPC, so surgical treatment of the stress incontinence, or even bladder neck closure, may need to be considered.

For complete conus lesions, areflexia of the detrusor with areflexia of the sphincter is characteristic. Sphincter incompetence causes neurogenic SUI and may be combined with dribbling incontinence if adequate emptying is not achieved. Penile sheath systems or incontinence pads are often necessary, and consideration of suitability of surgery may be needed.

Sometimes, areflexia of the detrusor may be combined with overactivity of the sphincter, in which case IC may be appropriate, or an indwelling (suprapubic) catheter may be needed. DO with sphincter areflexia can occur in myelomeningoceles; bladder relaxant agents may be trialled, but conservative treatment alone is generally unable to restore continence, so appliances or operative treatment must be considered.

Cauda equina and peripheral nerve lesions are often incomplete. Acontractile detrusor may be combined with a normally functioning external striated sphincter, or the reverse combination, may be present.

Conclusions.
- Behavioral techniques should be used in conjunction with other therapies (pharmacological treatment, catheterization) (LOE 2).
- When appropriate, toileting assistance should be used to improve continence of neurologic impaired patients (LOE 3).
- Prompted voiding may be able to decrease incontinence episodes, and should be considered in patients with cognitive impairment and higher dependency (LOE 2/3).

Recommendations.
- Triggered bladder emptying could be recommended only for patients whose situation has proven to be urodynamically safe and stable, and who can manage reflex incontinence.
- Triggered bladder emptying can be considered for patients after sphincterotomy and/or bladder neck incision and/or alpha-blockers and/or intrasphincteric botulinum toxin injections, in order to improve spontaneous reflex voiding (GOR C).
- Reflex bladder emptying can be recommended only if an adequate follow-up is guaranteed (GOR C).
- Before recommending bladder emptying by abdominal straining, it must be proven that the LUT is urodynamically safe (GOR B).
- Exclude contraindications, such as vesico-ureteric reflux, pelvic organ prolapse, hernias, urethral pathology, and symptomatic UTIs before recommending this type of bladder emptying (GOR B).
- In general, IC should be considered to be the most appropriate means of achieving complete bladder emptying in most patients with neurogenic bladder-sphincter dysfunction and impaired bladder emptying (GOR B).

- Behavioral techniques are a suitable component of the rehabilitation program for each individual (GOR C).
- There are no guidelines or consensus on suitable intervals for bladder emptying. They should ideally be derived from the voiding diary and other related factors (bladder volume, fluid intake, post-void residual urine volume, urodynamic parameters) (GOR C).
- The mental status of a patient must be taken into consideration, and a rehabilitation program realistically tailored to the patient's possibilities (GOR B/C).

Catheters and Appliances

Bladder drainage with a catheter is necessary in a substantial proportion of people with NLUTD. Complications can include:

- Encrustation, which may be predictive of bladder stones. Cystoscopy is the most reliable way to detect bladder stones; CT scanning may be considered, but ultrasound and abdominal x-ray are not a reliable way to diagnose the presence of bladder stones (LOE 3).
- Urethral trauma (traumatic hypospadias in men, patulous urethra in women) from the use of indwelling urethral catheter in patients with NLUTD.
- Urinary tract infection. Urethral flora may be a bacterial source for the development of urinary infection (LOE 3), but low bacterial concentrations in the urine ($<$105 cfu/L) of patients on IC might be due to contamination (LOE 3). Cranberry extract, methenamine hippurate, or phosphorus supplements were not found to be effective in acidifying urine or preventing urinary tract infection (LOE 2). A weekly oral cyclic antibiotic seemed efficacious in preventing UTI (LOE 3). Bladder irrigation was not effective in reducing bacteriuria in persons using indwelling catheterization (LOE 2). In people with spinal cord dysfunction, combined IC during the day time with indwelling catheter at night time showed less urinary infection than IC with incontinence or indwelling catheterization (LOE 3).

Recommendations for IC.

- IC is the first choice treatment for those with inability to empty the bladder adequately and safely in neurogenic voiding dysfunction. It is a valuable tool for achieving continence (GOR A).
- Proper education and teaching are necessary to achieve a good outcome (GOR B).
- To prevent and reduce complications, a non-traumatizing technique (external lubricant or lubricant coated catheters) with complete emptying should be achieved (GOR B), guided by the individual patient clinical assessment to estimate appropriate frequency of catheterization.
- Annual follow-up is needed (GOR B/C), which may require repeat assessment including monitoring of renal and/or urodynamic function.
- It is not currently possible to state whether any IC method is advantageous (GOR D) and further research on the topic is strongly recommended.
- IC can be combined with a treatment that improves bladder storage, like an antimuscarinic medication (GOR A).
- Patients on IC and bladder storage treatment often require long-term urodynamics and upper tract monitoring (GOR A).

Conclusions for IC.

- IC in the neurogenic bladder is effective and safe for short- and long-term use (LOE 1).
- Complications such as UTI are regularly seen and seem to be related to both the catheterization itself and the pre-existing LUT condition (LOE 2).
- Urethral and bladder complications seem to increase in the long-term (LOE 3).
- In order to reduce and prevent complications, appropriate materials and correct techniques should be taught and performed (LOE 3).
- Frequency of IC according to individualized assessment, a non-traumatizing technique, and suitable materials are the key factors for a successful outcome (LOE 2).

Recommendations for indwelling catheters.

- Silicone or hydrogel-coated catheters are preferable (GOR A/B).
- Use sterile materials and aseptic technique, and routine catheter care in the context of a closed drainage system (GOR C/D).
- Catheters should be changed regularly, to try to pre-empt obstruction or infection (GOR C/D).
- Bladder irrigation and antibiotic prophylaxis are not recommended as a routine infection-control measure. Symptomatic UTI should be treated with narrowest spectrum antibiotic possible, according to local microbiology practice (GOR B).
- Patient education on daily cleanliness and hygiene care are mandatory (GOR C).
- Short-term indwelling catheter during the acute phase of neurological injury is a safe management for neurologic patients (GOR B).
- Long-term indwelling catheter may necessitate monitoring of renal function and upper urinary tract imaging (GOR B).
- Consider the use of antimuscarinics in individuals with suprasacral lesions using chronic indwelling catheters (GOR C).
- Patient comfort, convenience, sexuality, and quality of life need to be considered (GOR C).

Conclusions for indwelling catheters.

- Long-term indwelling urethral catheter use in neurologic patients can predispose to complications (LOE 2).
- The catheter chosen should use the largest luminal diameter possible that does not traumatize or damage the urethra (LOE 4).
- All silicone catheters may be a suitable choice, in view of the comparatively large luminal size for some models (LOE 4).
- Five to ten milliliters self-retaining balloons should be used to minimize the pressure effect on the bladder neck (LOE 4).
- Closed drainage systems are associated with lower infection risk (LOE 1).
- Frequency of change largely depends on time to blockage, which is influenced by catheter materials and lumen, patient factors, and infection (LOE 3).
- Suprapubic catheter is preferred to urethral catheter if long-term catheterization is needed, but IC is the first line intervention (LOE 3).
- Suprapubic catheter is generally safe and effective in management of urinary retention (LOE 3).

Recommendations for penile sheath appliances. Skin breakdown is a potential problem for patients using sheaths, because the skin is occluded for most of the day. Clear silicone sheaths allow the condition of the patient's skin to be monitored without removing the sheath. If skin breakdown occurs, the general rule is to remove the sheath, and use an alternative containment approach while healing is achieved.

- Size selection should consider control of leakage, and prevention of penile compressive effects (GOR B).
- Regular bladder emptying with low bladder pressures and low post void residual should be confirmed (GOR B).

Conclusions for penile sheath appliances.

- Penile sheath appliances facilitate urinary containment of incontinence in some male patients with NLUTD (LOE 3).
- Complications may be less if technique, state of the penile skin, hygiene, replacement, and maintenance of low bladder pressures are optimized (LOE 3).

Pharmacotherapy (Oral and Intravesical)

- Antimuscarinic drugs improve storage function (LOE 1).
- Antimuscarinic drugs have a high incidence of side effects (dry mouth, constipation, urinary retention, etc.). Antimuscarinics with longer duration of action and controlled-release formulations have significantly less side effects compared to immediate-release oxybutynin (LOE 1).
- High doses of oxybutynin have been used to treat patients with neurogenic bladder dysfunction (LOE 3).
- Intravesical instillation of oxybutynin may be an alternative route of administration (LOE 4).
- Onabotulinumtoxin-A injection into the detrusor muscle improves clinical and urodynamic parameters (LOE 1), and has been approved as second-line treatment for urinary incontinence associated with NDO in patients with inadequate response to or intolerance of an anticholinergic.
- Repeat intradetrusor injections of Onabotulinumtoxin-A provide sustained clinical benefits (LOE 3).
- Treatment with intradetrusor Onabotulinumtoxin-A is considered overall safe, with increased post-void residual and need for post-treatment IC being the most common adverse event (LOE 1).
- BoNT-A can be considered for the treatment of DSD in spinal cord injury patients (LOE 2). The effect of BoNT-A intrasphincteric injections are short-lived, and therefore the long-term safety and efficacy of the treatment is uncertain. However, on the basis of one LOE 1 study, BoNT-A does not provide significant benefit for the treatment of DSD in MS patients. Further evidence is needed before recommendation for its use is possible.

Recommendations.

- Antimuscarinic drugs should be recommended for the treatment of neurogenic detrusor overactivity (GOR A). Titration of the dosage of these drugs individually should be done for optimal balance of therapeutic and adverse effects. If one drug is not tolerated, another drug should be tried (GOR C/D).
- Onabotulinumtoxin-A should be offered as a treatment option for incontinence associated with NDO (GOR A).
- Further research is needed on long-term outcomes and safety, administration techniques, the bio-equivalence of the various preparations of BoNT-A, the concomitant use of anticholinergic drugs, mechanisms of action, and wider effects (GOR A).
- Vanilloid intravesical therapy is not recommended except within clinical trials (GOR C/D).
- For decreasing outlet resistance in neurogenic bladder alpha-adrenergic antagonists may be used (GOR B/C).
- BoNT-A may be considered for DSD in spinal cord injury patients (GOR B).
- For neurogenic sphincter deficiency, no effective drugs are available up to now; further research is needed (GOR D).
- For detrusor areflexia no effective drugs are available up to now; further research is needed.

Behavioral Therapy

- Triggered reflex bladder emptying.
- Bladder expression (Credé) techniques are no longer recommended due to the high rate of renal complications that are seen with this type of bladder emptying.
- Bladder emptying by abdominal straining (Valsalva).
- Toileting assistance.

INTERVENTIONAL PROCEDURES

Surgery to Treat Neurogenic Detrusor Overactivity

- For severe neurogenic DO, bladder surgery using intestinal segments may be considered. In idiopathic DO/OAB, sacral neuromodulation (SNM) is an alternative to intravesical Onabotulinumtoxin-A treatment, but the role of SNM in NLUTD is not established. Additional research is needed to ascertain the potential contribution of SNM for NLUTD in routine practice.
- Bladder denervation, for example, peripheral nerve blockade, and dorsal rhizotomy, is mainly reserved for those suffering complete spinal cord injuries, and has not achieved consistent results.
- Sacral neuromodulation is not first line treatment for neurogenic DO. There are some limited reports showing that it may be beneficial (LOE 3).
- Percutaneous tibial nerve stimulation gives improved clinical and urodynamic parameters (LOE 3), but its role is not established.

Recommendations.

- Sacral neuromodulation is not routinely recommended in management of neurogenic DO (GOR C/D).
- Ileum, colon, stomach, or ureter may be used for bladder augmentation, but the ileum seems to give the best results in terms of ease of use, risk of complications, and efficacy (GOR B). Limited data is available concerning gastrocystoplasty and ureterocystoplasty in adults (GOR D).
- Patients should be informed that the most frequent and serious complications are bladder calculi and perforation at the bladder/bowel junction, usually caused by over-distension of the bladder (GOR B).
- Bladder augmentation may have sequela such as intestinal transit disorder and patients should be informed of this before surgery (GOR C).
- The body of evidence concerning detrusor myomectomy in neurological patients is controversial. Therefore, detrusor myomectomy should not be recommended in patients with impaired bladder function (GOR D).

Surgery to Treat Poor Bladder Emptying

Outlet dyssynergia. DSD is a characteristic feature of suprasacral and infrapontine lesions.

- The aim of sphincterotomy is to assist bladder emptying using reflex micturition or, in a few patients, abdominal straining, into a penile sheath appliance, thus protecting the upper urinary tract. Endoscopic sphincterotomy has been the technique of choice for patients who cannot or do not want to do IC. It is invasive, irreversible, and the patient has no adaptation period (LOE 3).
- Sphincterotomy or botulinum neurotoxin-A (BoNT-A) may reduce the outflow resistance, but may also induce or increase urinary stress incontinence (LOE 3).
- Prosthetic sphincterotomy using a urethral endoprosthesis (or stent) is an alternative, where available, which can be associated with significant complications (LOE 3).

Recommendations.

- Whatever type of sphincterotomy is chosen (surgical or prosthetic):
  - Patients must think carefully about the different modes of micturition possible for them (GOR A).
  - The few studies reporting long-term results of sphincterotomy demonstrate the vital importance of regular patient monitoring for the recurrence of DSD or blockage (GOR B).
  - This mode of micturition is contraindicated in women, and in men with difficulty in maintaining a condom catheter (GOR B).
  - Men who wish to have children should be warned of the risk of ejaculatory duct obstruction (GOR B).
- For patients who have chosen surgical sphincterotomy:
  - The reference technique involves an elective 11, 12, or 1 o'clock incision of the urethral sphincter (GOR B).
  - Although surgical sphincterotomy is the accepted reference treatment for neurogenic DSD, analysis of the literature highlights the lack of reliable efficacy and reproducibility criteria for the technique (GOR B).
- For patients who have chosen prosthetic sphincterotomy:
  - Careful follow-up is needed when leaving a permanent urethral stent (GOR B).
  - Published data is inadequate to support a recommendation on the use of bladder neck incision in patients with inadequate bladder emptying due to detrusor-bladder neck dyssynergia (DBND).

Surgery to increase voiding strength. Some teams have suggested placing rolled strips of muscle around the bladder. Some authors have also suggested a strip of rectus abdominis muscle. This is easier to perform and may be used essentially for reconstructive surgery, such as in bladder exstrophy (LOE 4).

Recommendations.

- Latissimus dorsi myoplasty on the bladder is a promising technique that needs to be validated further (GOR C).

Stress Urinary Incontinence Due to Sphincteric Incompetence

Patients with lesions of the conus medullaris, the cauda equina, or peripheral sacral nerves are at risk of developing neurogenic SUI. In all forms of NLUTD, direct sphincter injury may result from urethral catheter trauma, or previous interventions such as sphincterotomy or dorsal rhizotomy. In women, SUI may be present for non-neurogenic reasons such as urethral hypermobility due to previous pregnancy and childbirth.

Recommendations.

- Patients with stress incontinence in association with NLUTD require careful assessment in order to plan appropriate management. Video-urodynamic study must be used to evaluate both bladder and sphincter function (GOR C).
- The clinical assessment must also evaluate the degree of patient handicap in order to determine whether they can perform self-catheterization, or whether an alternative means of emptying the bladder will be required (GOR D).
- Patients require careful pre-operative counselling with respect to the benefits and risks of different operative approaches.
- Autologous slings can be used to treat neurogenic stress incontinence (GOR B). The use of synthetic slings and tapes is not supported by an adequate evidence base at present (GOR C).
- Artificial urinary sphincter (AUS) can be used to treat neurogenic stress incontinence (GOR A). AUS infection is a major problem which necessitates removal of the device, and is more likely to occur in patients with NLUTD than in the general population. Some AUS patients undertake IC for bladder emptying; this requires specific training, and could represent a risk factor for AUS complications.
- Bladder neck reconstruction can be used to treat neurogenic stress incontinence (GOR D).
- Bulking agents can be used to treat neurogenic stress incontinence when there is a demand for a minimally invasive treatment (GOR D). The patient should be aware that the technique has a low success rate.
- Bladder neck closure should be offered to patients who have persistent neurogenic stress incontinence where alternative treatments have either failed or are likely to fail (GOR B).

Urinary Diversion

Continent cutaneous diversion.

- The use of a continent catheterizable abdominal channel (CCAC) should be considered in the context of a multidisciplinary evaluation involving the urologist and a neurologist or rehabilitation doctor, as well as stomatherapy nurses or occupational therapists for estimating patient catheterization capabilities (GOR A).
- Use of the appendix to carry out CCAC is the standard method in children, but few long-term data are available in adults (GOR C). The appendix may have a short mesentery, so a reconfigured ileal segment is often needed.
- If the patient has undergone an appendicectomy, the use of a segment of the small intestine can be proposed, with slightly poorer short-term results (GOR C).
- Long-term follow-up after CCAC is needed to enable monitoring of the upper urinary tracts, electrolyte and metabolic abnormalities, and vitamin deficiencies (GOR B), and to have a better idea of the long-term results of the various procedures (GOR C).

Non-continent cutaneous diversion.

- Non-continent urinary diversion is the last resort for patients with neurogenic bladder (GOR A).
- The risks and benefits of carrying out a simultaneous cystectomy should be discussed with the patient because of the risk of later complications from the defunctioned bladder (GOR B).
- It may be indicated for urological dysfunction or in the event of a motor handicap that prevents other modes of LUT management (GOR C).
- Ileal conduit urinary diversion has the best long-term results for non-continent diversion, if the following pre- and peri-operative precautions are taken (GOR B):
  - Pre-operative identification of optimal location for the stoma site, with wheelchair test, if necessary.
  - Avoidance of the use of an unnecessarily long intestinal segment.
  - Minimal dissection of the ureters.
- Patients with an ileal conduit urinary diversion require long-term follow-up to enable monitoring of the upper urinary tracts, electrolyte and metabolic abnormalities, and vitamin deficiencies (GOR B).

- There are several reports of good results for ileovesicostomy, but the medium-term results need to be confirmed in the long-term. Quality-of-life studies should also be performed (GOR C).
- Vesicostomy may be a useful temporary solution, particularly for children (GOR D).
- Cutaneous ureterostomy should not be used for non-continent urinary diversion in adult patients because of the rate of long-term complications (GOR B).

CONCLUSIONS

The pathophysiology of NLUTD is categorized according to the nature of onset of neurological disease, likelihood of progression, and where the nervous system is affected. Assessment requires history and examination, general investigations, and specialized testing. Treatment primarily focusses on ensuring safety of the patient. Symptom management covers conservative and interventional measures to aid urine storage and emptying, with containment, and practical support an essential element in achieving acceptable quality of life and dignity. A multidisciplinary team approach to management is essential.

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