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SPANISH CONSENSUS DOCUMENT FOR THE DIAGNOSIS, TREATMENT AND MANAGEMENT OF NEUROGENIC BLADDER

Joan Vidal Samsó[1], Manuel Esteban Fuertes[2], María Ángeles Alcaraz Rousselet[2], Carolina María Alemán Sánchez[3], Cruz Almuiña Díaz[4], Juan Carlos Ariza Lahuerta[5], Aníbal Blanco Vivo[6], Francisca Carrión Pérez[7], Juan Casar García[6], Montserrat Cuadrado Rebollares[8], Manuel F. De la Marta García[2], Ana del Pino Santana León[3], Mónica Garrán Díaz[9], Miguel Ángel Gil Agudo[2], Manuel Giner Pascual[10], Carmen Grao Castellote[10], Ricardo Jariod Gaudes[5], María Luisa Jáuregui Abrisqueta[8], Natacha León Álvarez[11], María Luisa López Llano[9], Antonio Montoto Marqués[4], Montserrat Moreno Linares[12], Ariadna Navés Prujá[1], María Isabel Núñez Angulo[10], Carmen Ocaña Fernández[13], Karla Patricia Rojas Cuotto[12], Pilar Sánchez Pérez[2], Fátima Torralba Collados[10], Rocío Veras Cosmo[13] and Inmaculada García Obrero[14].

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CONTRIBUCIONES DE LOS AUTORES: Joan Vidal Samsó y Manuel Esteban han contribuido al estudio como coordinadores del consenso. El resto de los autores han contribuido en la redacción, revisión y toma de decisiones en el estudio de consenso.

Summary.- *OBJECTIVES: The purpose of this document is to establish practical recommendations on neurogenic bladder (NB) management based on scientific evidence and medical and nursing perspective in Spinal Cord Injury (SCI) Units as a first multidisciplinary consensual approach in Spain.*

MATERIALS AND METHODS: This paper reports results from the first modified Delphi consensus building exercise on this procedure. A committee of recognised opinion-makers in rehabilitation and urology with special interest in NB was constituted. A working group formed by rehabilitation doctors, urologists and nursing staff of SCI and Neurorehabilitation Units of a number of Spanish hospitals and specialised centres associated with the panel of NB experts have prepared this document.

Results: This review provided an overview of the main aspects described by the different clinical guidelines al-

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ready available and highlighted the need to focus on recommendations in special priority situations in which there was no consensus. In view of the considerable impact this condition has on quality of life, patients should be offered help to better understand the disorder and they should be taught how to use the treatment techniques to obtain satisfactory results and promote their autonomy.

CONCLUSIONS: This article presents a version of guidelines for patients with NB. The guidelines define the clinical profile of patients to provide the best evidence-based care and also an overview of the current drug and surgical treatments of NB.

Keywords: *Clinical practice guidelines. Epidemiology. Lower urinary tract. Neurogenic bladder. Neurologic event. Therapeutics.*

Resumen.- *OBJETIVO: El objetivo de este documento es establecer recomendaciones prácticas sobre el manejo de la vejiga neurógena (VN) en función de la evidencia científica y las perspectivas médicas y de enfermería en Unidades de Lesionados Medulares (ULM) como un primer enfoque de consenso multidisciplinar en España.*

MATERIALES Y MÉTODOS: En este artículo se presentan los resultados del primer ejercicio de consenso basado en metodología Delphi modificada sobre este procedimiento. Se constituyó un comité del que formaron parte reconocidos expertos en rehabilitación y urología, especializados en el manejo de VN. Este documento ha sido elaborado por un grupo de trabajo formado por médicos especialistas en rehabilitación, urólogos y personal de enfermería de ULM y unidades de Neurorrehabilitación de varios hospitales y centros especializados españoles asociados con el panel de expertos sobre VN. Resultados: Esta revisión ofrece un resumen de los principales aspectos descritos en diversas guías clínicas ya disponibles y destaca la necesidad de centrarse en recomendaciones sobre situaciones especialmente prioritarias sobre las que actualmente no existe consenso. En vista del considerable impacto de esta enfermedad sobre la calidad de vida, los pacientes deben recibir ayuda para que comprendan mejor su enfermedad y también deben recibir formación sobre el uso de técnicas de tratamiento para conseguir resultados satisfactorios y fomentar su autonomía.

CONCLUSIONES: En este artículo se presenta una versión de la guía para el manejo de pacientes con VN. Las guías definen el perfil clínico de los pacientes para ofrecer la mejor asistencia basada en la evidencia y también un resumen de los tratamientos farmacológicos y quirúrgicos actuales para la VN.

Palabras clave: *Guías de práctica clínica. Epidemiología. Tracto urinario inferior. Vejiga neurógena. Evento neurológico. Terapéutica.*

INTRODUCCTION

According to ICS (International Continent Society) (1), Neurogenic bladder (NB) or Neurogenic Lower Urinary tract Disfunction (NLUTD) refers to abnormal or difficult function of the bladder, urethra (and/or prostate in men) in mature individuals in the context of clinically confirmed relevant neurologic disorder. NB involves dysfunction in the voluntary emptying of the bladder that causes sudden unwanted expulsion of urine, or voluntary but incomplete voiding that predisposes to the onset of urinary tract infections (UTIs). Some patients develop urinary retention, leading to high bladder pressure and vesicoureteral reflux (VUR) (2). More serious complications can also occur, such as bladder cancer (3-5) and autonomic dysreflexia, affecting the patient's psychological wellbeing. Although numerous guidelines have been published on the management of NB (6-13), there is no up-to-date document on the diagnosis and treatment of this type of bladder dysfunction that analyses the various diseases that can cause this condition. The purpose of this document is to establish practical recommendations for a standardised approach to diagnosis and treatment for the different specialists involved in the control of bladder function. It aims to be easy to understand and apply, both from a medical and nursing care point of view, to enable appropriate management of NB.

This document is aimed at a wide range of patients with different nervous system disorders (affecting the central nervous system [CNS], peripheral nervous system [PNS] or both), diseases involving the CNS (multiple sclerosis, spinal cord injuries, cerebral palsy [CP], stroke myelomeningocele, diseases of the basal ganglia, e.g. Parkinson's disease, Huntington's disease, or brain tumours), peripheral nerves (peripheral neuropathy, herniated lumbar disc disease pelvic surgery) or both.

MATERIALS AND METHODS

Evidence Acquisition

Modified Delphi protocol is a recognized strategy for consensus building amongst experts. It allows experts to contribute and adjust their opinion anonymously (14).

A multidisciplinary panel of 30 specialists (specialists in physical medicine and rehabilitation,

urologists and nurses) from the Spinal Cord Injury Units and Centres in Spain (2 monographic centres and 10 Spinal Cord Injury Units), all of them experts in the treatment and rehabilitation of spinal cord injuries and specifically in the management of neurogenic bladder, reunited to discuss issues in the assessment, diagnosis, and treatment of adults with neurologic disease or injury and symptoms consistent with NB.

The group met twice (June 2016, Madrid and June 2017, Dublin) during the development of the guideline.

The aim of this exercise was to develop consensus amongst NB experts on a range of practices and principles concerning this procedure following a modified Delphi protocol.

The guideline did not consider general management of the underlying disorder or comorbidities, associated faecal incontinence, sexual dysfunction or psychological problems

Search strategy

We carried out a review of the literature in the Medline, Pubmed and Cochrane databases, using the search strategy guidelines [MeSH Terms] OR consensus document [MeSH Terms] AND neurogenic bladder [MeSH Terms]. Additionally, with the aim of locating local publications in Spain, we consulted Google Scholar. This review provided a resume of the main aspects described by the different clinical guidelines already available and highlighted the need to focus on recommendations in special priority situations in which there was no consensus.

Study eligibility

The working group classified and ordered the level of evidence and grade of recommendation of the information gathered from the scientific literature according to the criteria of the Infectious Diseases Society of America (IDSA) (Table I).

RESULTS

Evidence synthesis

Epidemiology and risk factors

NB has a very varied aetiology which is the result of damage to the neural pathways that control the lower urinary tract.

Table I. Criteria of the Infectious Diseases Society of America (IDSA).

Category	Definition
LEVEL OF EVIDENCE	
I	Evidence from ≥ 1 properly randomised clinical trial.
II	Evidence from ≥ 1 well-designed, non-randomised clinical trial; cohort or case-control studies (preferably involving > 1 site), multiple time series, or important results from uncontrolled trials.
III	Opinions of respected authorities, based on clinical experience, evidence from de-scriptive studies, or reports of expert committees.
GRADE OF RECOMMENDATION	
A	Strong recommendation, high-quality evidence.
B	Strong recommendation, moderate-quality evidence.
C	Strong recommendation, low-quality evidence.
D	Weak recommendation, moderate-quality evidence.
E	Weak recommendation, high-quality evidence.

One of the causes of bladder dysfunction is traumatic SCI, with an overall incidence rate of 2.3 cases per 100,000 population (15). Recent studies show an increase in the incidence of such cases related to accidental falls from the age of 65 onwards (16).

NB is also commonly associated with demyelinating lesions of the CNS such as MS. Among patients with MS, some 50-90% have lower urinary tract disorders after six years of disease progression, while virtually 100% of patients with impaired mobility and walking difficulties have such disorders (17,18).

The development of voiding dysfunction is also associated with cerebrovascular disease (19).

Apart from cognitive problems, urinary incontinence is one of the most important symptoms in patients who suffer from dementia (18).

There are certain diseases and conditions that cause peripheral nerve injury which commonly leads to detrusor areflexia (20). One of the most prominent is diabetes mellitus (DM), in which 75-100% of patients who develop somatic neuropathy experience neurogenic dysfunction of the lower urinary tract, being more frequent in insulin-dependent patients than in those with oral antidiabetic agents (21). Another is radiculopathy derived from or associated with discopathy which leads to voiding symptoms in 28-87% of cases (22). Other less common causes are HIV, herpes zoster and Guillain-Barré syndrome (22). Radical hysterectomy and pelvic radiotherapy have also been linked to bladder disorders. However, over 80% of individuals who undergo radical pelvic surgery recover spontaneously (20).

Lower urinary tract (LUT) function is regulated by a complex system involving the brain, spinal cord and autonomic nerve ganglia, which coordinate the activity of the smooth and striated muscles of the bladder and urethra (23,24).

From a urodynamic point of view, the most practical pathophysiological classification of NB distinguishes three basic categories according to the nerve injury origin, having a characteristic voiding pattern (25).

The consequences will depend on the nerve involved in each case; damage to the pudendal nerve causes underactivity of the external sphincter, damage to the pelvic nerve causes areflexia and/or underactivity of the detrusor, and damage to the hypogastric nerve, internal sphincter incompetence (25).

Diagnosis

Diagnosis of NB involves prior diagnosis of the neurological disorder causing the dysfunction. However, that is often difficult to establish (26).

Evaluation of renal function:

The measurement of glomerular filtrate is the best index of evaluation of renal function, being serum creatinine the most used marker of glomerular filtrate despite being submitted to diverse sources of variability. Therefore, to detect alterations of renal function, creatinine clearance and measurement of glomerular filtrate by nuclear medicine tests are more appropriate (27). Another option to measure renal function is cystatin C. However, its determination is more expensive and presents alterations in serum concentration by different factors than filtrate, so there is currently no evidence to justify the change of measure of renal function of cystatinine by creatinine (28,29).

Imaging diagnosis:

The upper and lower urinary system is usually evaluated by ultrasound and serial mictional cystourethrogrady (CUMS). This exploration determines the capacity and vesical morphology of the bladder and, if existing, the presence of vesicoureteral reflux. In cases of absence of voluntary urination, a retrograde cystography is performed (10).

Ultrasound is also particularly useful for long-term follow-up because it is a non-invasive imaging technique that can inform us of the presence of urinary lithiasis. Ultrasound is also very sensitive to the detection of dilation of the upper urinary tract (28,30).

Other imaging techniques, such as Computer tomography (CT), Magnetic Resonance Imaging (MRI), or nuclear medicine studies are reserved for specific situations (31).

Videourodynamics:

The combination of fill cystomanometry and flow pressure study combined with images, is the reference method for urodynamic investigation of the neurogenic bladder, being able to detect possible pathological findings, along with morphological abnormalities of the lower and upper urinary tract (28).

Medical history

A very thorough medical history must be compiled for the patient, including information about metabolic disorders, frequency of urinary tract infections,

relevant surgical interventions, medication administered, neurological and congenital abnormalities, with special attention to the patient's mental and/or emotional state, presence of neurological symptoms (somatic and sensory) and spasticity or signs of autonomic dysreflexia (32). It must include information about the patient's habits (smoking, alcohol, etc.), quality of life and intestinal and sexual history, as these aspects may be altered by the neurological disorder [III, A].

Table II. Main differential characteristics and applications of the most used urodynamic techniques (22,26,32).

Technique	Parameter(s)	Diagnostic utility	Advantages	Limitations
Uroflowmetry Uroflow rate	Volume of urine voided per unit of time.	- ↓ Vflow. - Intermittent flow. - Difficulty in starting to urinate. - Residual urine.	Simple and non-invasive.	Unreliable.
Cystometry	Pbladder/ Pabdominal/ Pdetrusor (filling phase)	- Detruor overactivity. - Poor detrusor compliance. - Abnormal bladder sensations. - Incontinence. - Incompetent urethra.	Complete and reliable, discriminative for lesions ("ice water test").	Invasive.
	Detrusor leak point pressure (Pdetrusor nec-essary to produce a leak of urine)	- To assess risk in the urinary tract.	Screening test.	Invasive and not determinant.
Pressure-flow study	Pbladder and voiding flow (empty-ing phase)	- Intravesical obstruction. - Detrusor underactivi-ty. - Residual urine. - Urethra not relaxed.	Determinant, can be combined with cystometry.	Invasive.
Electromyography	Bioelectrical potentials of the muscles that control urina-tion.	- Pudendal nerve injury. - External urethral sphincter innervation injury. - Dyssynergia-.	Non-invasive and painless.	
Video urodynamics	Pbladder/ Pabdominal/ Pdetrusor (filling phase) Pbladder and voiding flow (empty-ing phase)	- Morphological abnormalities. Disorders diagnosed by cystometry and pressure-flow study.	Simultaneously displays the urodynamic pa-rameters and radiographic findings of voiding.	Invasive; *use of contrast.
Urethra profile	There is no basic consen-sus on the parameters that indicate pathological findings	Records pressure along the posterior urethra, from bladder neck to external striated sphincter.		Utility very lim-ited.

V: Velocity; P: Pressure.

Data related to LUT function should be collected as well as specific symptoms or signs of the NB dysfunction, such as the voiding pattern, urinary incontinence, bladder sensitivity, the type of urination and the need for catheterisation [III, A].

Physical examination

Physical examination of the patient should include both general and specific examination. The general examination should include an abdominal and rectal examination to detect the possible presence of pelvic masses, a vaginal examination in women to rule out vaginitis, mucosal atrophy, cystocele/rectocele etc. and prolapses, urological examination in men to detect any type of malformation that could be affecting the bladder, as well as stress tests with a full bladder to detect any leaking with abdominal effort (for example, cough or Valsalva manoeuvre) (26) [III, A].

The neuro-urological examination studies the reflex activity at sacral level, testing the cremasteric, patellar, Achilles, bulbocavernosus, bulbo-clitoral, anocutaneous and cough reflexes.

Within neurourological exploration it is necessary to specifically assess bilateral S2-S5 sensitivity, the tone of the anal sphincter and if voluntary contraction of the anal sphincter exists. In the medullary injured patient, the presence of a voluntary contraction of the external anal sphincter indicates that it is about an incomplete motor injury (ASIA C) and can be correlated with better voiding control.

Superficial anal pressure and deep discrimination sensations are also analysed, as vesico-urethral sensitivity, through the desire to void, the feeling that urination is imminent, the sensation of urine passing through the urethra and the sensation of pain (26) [III, A].

Urodynamics

Urodynamic testing is an indispensable tool for the diagnosis of LUT dysfunctions, as it evaluates the functional activity of these pathways in their two phases (filling and emptying) by quantifying intravesical pressure, abdominal pressure and detrusor pressure using a series of techniques depending on the patient's condition (18) (Table II) [III, A].

Among the urodynamic tests, the following should be highlighted (28):

• Flowmetry and residue evaluation: provide guidance on possible mictional dysfunctions, such as difficulty in initiating miction, mictional residue, volume eliminated, etc., and represent a first step before carrying out a complete urodynamic study.

• Filling cystomanometry: assesses bladder and lower urinary tract function during the bladder filling phase. Very useful when combined with bladder pressure parameters during voiding.

• Pressure-flow detrusor study: a test that assesses coordination between the detrusor muscle of the bladder and the urethra or pelvic floor during voiding. The results of hypoactivity or acontractility of the detrusor, vesico-spinterian dyssynergia, are key diagnoses in the management of the neurogenic bladder.

• Electromyography (EMG): a test used to record the activity of the external urethral sphincter, as well as its coordination with the dynamics of the detrusor. It is usually recorded simultaneously with cystomanometry or pressure/flow study, in order to know not only the sphincter activity, but also its synergism.

• Videourodynamics, the combination of fill cystomanometry and pressure-flow study combined with image, is the reference method for the urodynamic study of the neurogenic bladder.

Treatment

The main goal of NB treatment is to prevent deterioration of the upper urinary tract (UUT), preventing complications that compromise the patient's life such as UTIs, urological sepsis or renal failure (33) (Annex 1). The secondary objective is to maintain urinary continence (32), as this also helps to prevent the patient's social isolation (34). Proper treatment should include restoring LUT function, thereby improving quality of life (22).

It is essential to start treatment as soon as possible (22). Early intervention using intermittent catheterisation prevents irreversible deterioration of the upper and lower urinary tracts.

Conservative treatments

Behaviour modification techniques

Regular emptying of the bladder is an essential element for achieving optimal healthcare in patients with NB. Behaviour modification techniques are common, but are particularly useful in patients who have some control of the bladder and have normal bladder sensation (35) [III, A].

Techniques for improving bladder emptying

The Credé and Valsalva manoeuvres can be used, as well as the triggering of the micturition reflex by external stimuli (36) [III, C]. Before recommending bladder emptying through abdominal compression manoeuvres, it must be demonstrated that this is urodynamically safe for the patient. Reflex bladder emptying can only be recommended in patients with intact sacral reflex arc and can be a good alternative after sphincterotomy or injection of botulinum toxin into the sphincter (10). Specialised nursing staff are required to train the patient to perform these techniques correctly (37), and the importance of good adherence must also be emphasized.

Lower urinary tract rehabilitation

The most effective techniques involve magnetic or electrical stimulation of the afferent fibres of the pudendal nerve (22,32) [III, C].

Drug therapy

Antimuscarinics

Antimuscarinics act as antagonists of the muscarinic receptors, reducing the detrusor reflex activity (37), and thereby inhibiting involuntary bladder contractions. They are the first-line treatment in patients with NB hyperreflexia, and provide adequate management of neurogenic detrusor overactivity (38) [I, A]. The different antimuscarinic drugs have very similar efficacy, but there are differences in certain undesirable effects and tolerability (32) (Table III).

These drugs are not always effective in achieving complete continence. A combination of anticholinergic agents may be an alternative for patients with NB refractory to previous antimuscarinic monotherapy, and the use of other more invasive treatments may be deferred (39).

Other drugs with different mechanisms of action

Alpha-blocking drugs have been shown to reduce resistance to the passage of urine, facilitate voiding (40) [II, A] and decrease residual urine (32) [I, A]. Urapidil has been shown to produce a significant decrease in detrusor overactivity (41) and urethral resistance, proportional to the dose administered [I, C]. Alpha-blockers have also been found to improve the symptoms of autonomic dysreflexia in patients with spinal cord injury [II, C]. However, all the studies were carried out in patients who were still able to void.

Table III. Antimuscarinic agents authorised in Spain, posology and associated undesirable effects (38,39,42).

DRUG	POSOLOGY	UNDESIRABLE EFFECTS
Immediate-release oxybutynin	5 mg (2-3 times/day)	Higher incidence of undesirable effects than any of the others, with more severe cognitive undesirable effects
Oxybutynin in transdermal patch	3.9 mg/24 hours.	Skin irritation
Immediate-release tolterodine	2-4 mg/day	Undesirable effects worse with the immediate-release pharmaceutical form
Prolonged-release tolterodine	4 mg/day	
Solifenacin succinate	5 mg/day (can be increased to 10 mg/day)	Higher rate of constipation than any of the others
Prolonged-release fesoterodine	4 mg/day (can be increased to 8 mg/day)	UTIs and urinary retention, especially in elderly men
Immediate-release trospium chloride	40 mg/day	Undesirable effects worse with the immediate-release pharmaceutical form
Prolonged-release trospium chloride	60 mg/day	

Once administered in conjunction with antimuscarinic therapy, they act synergistically by reversibly blocking completely different receptors in the bladder, increasing efficacy and improving the safety profile [II, C].

An additional treatment with desmopressin may improve the efficacy of the treatment (22,42) [III, C]. Approved for treatment of nocturnal enuresis, desmopressin has been shown to reduce the need for intermittent catheterisation (IC) during the night in patients with spinal cord injury and spina bifida.

Thus, it could be used in these patients, ruling out other causes of polyuria such as diuretic treatment, congestive heart failure, etc (43). The use of desmopressin has been better studied to treat nocturia in multiple sclerosis (44). Candidates must have adequate serum creatinine and sodium levels to begin therapy (38). This requires regular monitoring to prevent hyponatremia, especially in patients over 65 years of age.

If the antimuscarinic therapy produces an insufficient effect, β3 receptor agonists can be used as adjuvant therapy (45) [III, C]. β3 receptor agonists cause detrusor relaxation with relatively mild undesirable effects, but they are not recommended in patients with uncontrolled hypertension (38).

Another treatment that has shown activity is baclofen, by decreasing hypertonia and detrusor overactivity at the same time as reducing leakage and increasing the functional capacity of the bladder [III, C].

Tricyclic antidepressants with sedative properties cause relaxation of the detrusor muscle through their muscarinic-receptor agonist action. In patients with refractory incontinence, the triple combination of imipramine, an antimuscarinic agent and an alpha-blocker has been shown to improve maximum detrusor pressure, and bladder capacity and function (42).

Minimally invasive treatments

Intermittent catheterisation (IC)

This is one of the most effective and commonly used methods used in patients with NB who cannot completely empty their bladder (32). Its effectiveness has been confirmed in patients suffering from underactive or acontractile bladder and in patients with overactive bladder if anticholinergic drugs work and overactivity can be controlled (22) [III, A].

Intermittent catheterisation techniques

Traditionally there are two alternatives: sterile technique and clean technique. The sterile technique has the advantage of significantly reducing the risk of UTIs and/or bacteriuria (22,32) [III, A]. However, it is considered a routine procedure only in the sterile conditions associated with the hospital environment. The clean technique is that used by patients or their careers at home (22) [III, A].

New options have been proposed such as the aseptic technique, which allows the insertion of the catheter through a protective cover, sterile gloves or any other guiding mechanism that prevents contact with the surface of the catheter ("no-touch" technique), and only requires prior cleaning of the genital area with disinfectant (46,47). The "no-touch" technique is considered the preferred choice in the guidelines of the European Association of Urology (EAU) (32) and the European Association of Urology Nurses (EAUN), and is recognised as the ideal option among those termed as aseptic techniques (47,48) [III, A].

Catheterisation frequency

Intermittent catheterisation (IC) is the gold standard for the management of neurogenic LUT disorders which involve the presence of residual urine in the bladder. Achieving adequate catheterisation and reducing the associated complications, mainly UTIs, are the fundamental responsibility of specialized nursing staff.

A fluid intake of 1.5 to 2 litres distributed over the course of the day needs to be encouraged to maintain good hydration and adequate diuresis (49).

Personalised plans can help determine the appropriate frequency, according to various parameters (46). The average frequency of catheterisation when the patient is unable to void independently ranges from four to six times a day. Less frequent catheterisation leads to higher catheterisation volumes and an increased risk of urinary tract infection. The number of catheterizations should be determined primarily by the residual volume obtained. Generically speaking, the bladder volume of the catheter should be less than 400 ml, bearing in mind that the bladder capacity is different according to the urodynamic pattern of each patient (10).

The number of catheterisations each day has to be decided on an individual basis in line with the recommendations of the patient's doctor (46). Training from specialized nursing staff is recommended, as they are also able to assess the patient's general

condition, knowledge and understanding the use of the catheter of choice.

Catheter selection

The choice of indwelling or intermittent catheter can be adapted to the needs of the individual with special attention to their personal circumstances, following the classification shown in Figure 1. Nowadays, a wide range of lumens, lengths and materials is available to suit everyone. Adherence to the catheterisation regimen can be improved with adequate training and the right choice of catheter (50).

Long-term indwelling catheter (IDC)

If IC is not possible, an IDC can be used as an alternative. This type of catheter is a suitable alternative during the spinal shock phase resulting from an injury (51) or other similar cases.

The use of silicone catheters (A/B), the use of sterile materials and aseptic technique, and the routine care of the catheter always in the context of closed drainage systems (C/D) are recommended (10).

It is recommended to assess the patency of the catheter and the evacuation circuit periodically with fluid intake as well as the appearance of the urine, in order to detect possible signs of infection (51).

Drugs for intravesical administration

Anticholinergic drugs can also be administered intravesically to decrease detrusor overactivity (32). Although this type of administration is more complicated, there are fewer undesirable effects and a greater concentration of the drug is achieved in the bladder (22) [III, C]. The administration of vanilloids (such as capsaicin or resiniferatoxin) has been shown

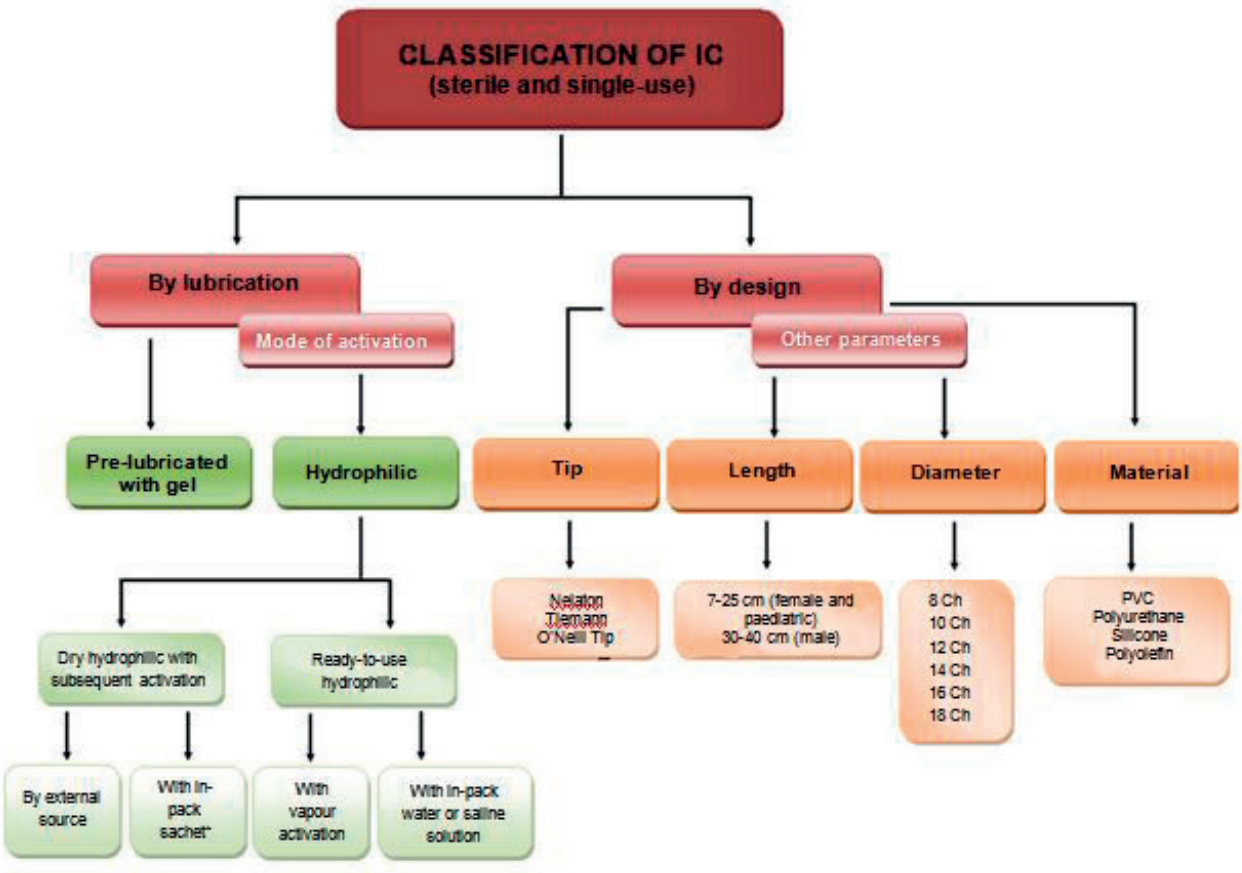

Figure 1. Classification diagram of the main types of IC according to their lubrication and design (adapted from references).

**Some hydrophilic catheters include the source of lubrication in the pack, to prevent risk of the use of contaminated water. In such cases, the contents may be sterile water or a saline solution with or without other additives, contained in a sachet that has to be broken before opening the catheter to activate the hydrophilic coating or activated by water vapour, ready to use, in order to avoid further steps or stains during catheterization.*

to improve neurogenic overactivity of the detrusor associated with MS or spinal cord injury (52) [I, C].

Similarly, injection of botulinum-A toxin into the detrusor has been shown to be effective and safe in the treatment of neurogenic detrusor overactivity, producing long-lasting improvements in urinary incontinence and patient quality of life (32,53) [I, A]. These injections are recommended when antimuscarinic therapy is insufficient or causes many undesirable effects. However, it should be considered that this can temporarily increase the volume of residual urine, generating the need for IC. The development of UTIs is also an undesirable effect associated with this type of intervention, and antibiotic prophylaxis is therefore recommended prior to its administration (54) [II, A].

Botulinum toxin causes a reversible denervation, its effect can last up to 6-9 months. In many cases the injections must be repeated successively.

Techniques for reducing bladder neck and sphincter resistance

To protect the UUT it may be necessary to reduce the resistance of the bladder outlet tract by injecting botulinum-A toxin into the external sphincter. This lowers intravesical pressure during emptying which helps reduce the post-voiding residue and the risk of damage to the UUT [I, A]. A sphincterotomy can also be performed, which can reduce resistance to output of urine while avoiding complete loss of the urethral closure mechanism (22) [III, B]. One of the problems associated with these techniques is urinary incontinence, the impact of which can be minimised by medical devices such as urine catchers or absorbent nappies (22).

Percutaneous posterior tibial nerve stimulation (55).

Posterior tibial nerve stimulation is a minimally invasive neuromodulation technique that intermittently stimulates the posterior tibial nerve at the ankle with a transcutaneously placed electrode (56). Currently included in the ICS, American Urological Association (AUA), and EAU guidelines for treatment of overactive bladder (57). Although it leads to improvement of the clinical and urodynamic parameters (III), its role is not well established in the Neurogenic Lower Urinary Tract Dysfunction (NLUTD) (10).

Surgery

When conservative and minimally invasive treatments fail, surgical interventions are an accepted therapeutic alternative (58).

Neurostimulation of the sacral roots

Sacral anterior root stimulator (SARS) technology has been shown to have a 92% success rate in the treatment of patients with neurogenic detrusor overactivity, with a low incidence of undesirable effects. Although long-term studies have suggested that its efficacy may disappear after 1-4 years, it is a valid alternative to conservative treatment (37) [I, B].

Enterocystoplasty

Bladder augmentation is considered the most effective surgical technique to achieve an adequate reservoir for urine (37) [III, B] in certain refractory cases to other interventions, such as patients with myelomeningocele or spina bifida. However, after the intervention of a large number of patients require a collection device for urine and/or IC; there is also a risk of multiple surgical complications (49).

Sphincterotomy

External sphincterotomy in spinal cord injured (SCI) males is a safe and simple treatment that is commonly employed in patients with detrusor hyperreflexia and autonomic dysreflexia (IIC) (49).

Other surgical procedures

As an alternative to sphincterotomy, ureteral stents can be used as implants through the neck of the bladder. However, they are not recommended in patients with recurrent UTIs due to the risk of postoperative infection (37) [III, C]. The technique of balloon dilation of the external sphincter has shown results at 12 months comparable to sphincterotomy, but follow-up suggests that the results may not be long-term (59) [III, C].

In patients who have urinary incontinence because of an incompetent sphincter but adequate bladder capacity, the implantation of an artificial urinary sphincter device can be considered. If the bladder capacity is insufficient, this procedure should be accompanied by bladder augmentation surgery (37) [III, C].

In patients with incomplete emptying problems who cannot perform intermittent self-catheterisation through the urethra, surgery to create a suprapubic cystostomy may be performed to divert urinary flow. The success rate of this surgical intervention is over 90%, and it can be performed on the wall of the anterior detrusor muscle of the bladder without the need to enlarge it, or on the posterior wall of the bladder in conjunction with such enlargement (37) [III, C].

The following diagram shows the therapeutic algorithm recommended for each case according to the alteration in urinary elimination pattern presented by the patient (Figure 2).

Clinical Progress and Follow-up

The clinical progress of NB is related to the underlying disease and urinary problems generally tend to worsen as the disease progresses. This is particularly relevant in neurodegenerative diseases, such as MS or Parkinson's disease (33).

Regardless of the neurological origin of the problem, progression of the NB leads to a series of consequences with varying degrees complexity, and these include the development of both upper and lower urinary tract infections.

The frequency of check-ups carried out by a specialist is determined by the underlying neurological disease and how well the NB is managed. In general, patients should undergo check-ups annually or every two years. In the case of MS, spinal injuries or warning signs, the frequency should be increased (22) [III, A].

Additional assessment tests should be performed in conjunction with the check-ups. Patients should undergo an annual physical examination and blood analysis. In addition of an annual basis, they should have a kidney and bladder ultrasound with measurement of post-voiding residual urine (22) [III, A]. Urodynamic testing should be performed if neurological changes, complications or signs of risk for UUT appear or whenever a surgical intervention is planned (22) [III, A].

DISCUSSION

This document has been prepared with the objective of establishing practical recommendations on the management of NB. It is based on published scientific evidence obtained from a review and clinical practice of a panel of NB experts made up of a total of 30 specialists (physicians specializing in

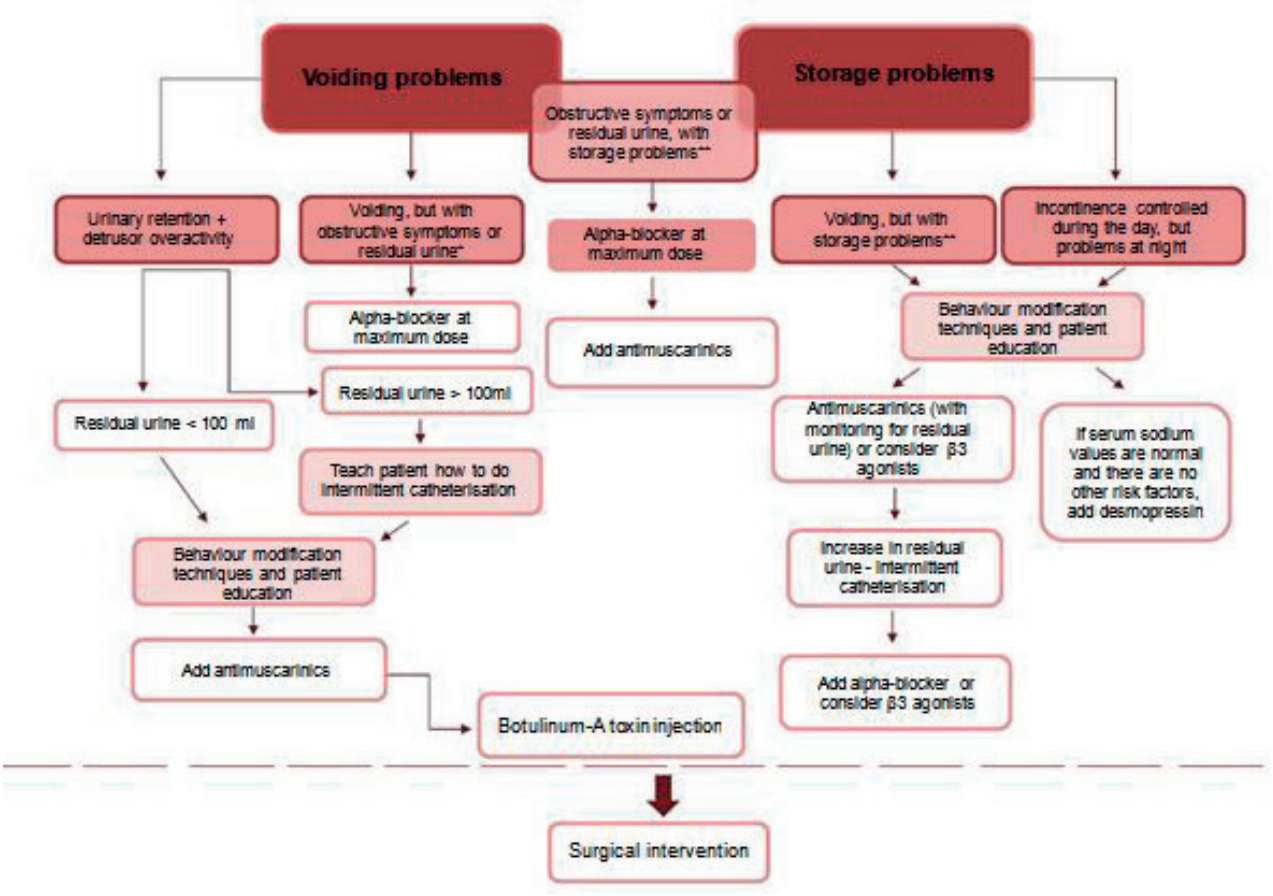

Figure 2. Treatment algorithm for NB according to the alteration in urinary elimination pattern. General strategy. It should be personalised for each patient.

**If residual urine volume is > 100 ml, use intermittent catheterisation.*

** *Storage problems being defined as: urinary urgency, high urinary frequency, urge incontinence and nocturia.*

physical medicine and rehabilitation, urologists and nurses) from the Spinal Cord Injury Units and Centres in Spain, allowing a broader and joint view of the management of this condition from a multidisciplinary perspective.

It´s about the first Spanish consensus drawn up with a committee of experts from all spinal cord injury units that gathers the published evidence into a single global document that can serve as a protocol for the diagnosis and treatment of NB.

This document focuses on a wide variety of patients with different disorders of the nervous system including not only spinal cord injury, but other diseases affecting the CNS such as multiple sclerosis.

Finally, it should be noted that currently there is not enough quality scientific evidence available for many of the recommendations and this means that the level of evidence is limited in some of them. However, the degree of agreement of the experts when assessing them has been very high, which makes these recommendations have great value in daily clinical practice.

CONCLUSIONS AND IMPLEMENTATION

NB is a condition with wide-ranging aetiology that requires an early, complete and specific diagnosis of the underlying disease (26) before personalised treatment can be established.

In view of the considerable impact on quality of life, patients should be offered help to better understand the disorder and they should be taught how to use the treatment techniques properly in order to promote their autonomy. First-line therapeutic approaches include measures such as modification of voiding habits and administration of anticholinergic agents.

These measures are complemented by minimally invasive techniques such as IC. If such options fail, surgical interventions, such as neurostimulation of the sacral nerve or enterocystoplasty, should be considered (37).

Once the treatment is established, patients should be followed up annually or every two years, or more often in the case of MS or spinal cord injuries if alarm symptoms appear (22).

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CONFLICTS OF INTEREST

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ANNEX 1

Protocol for the management of UTIs in patients with intermittent catheterisation (IC)

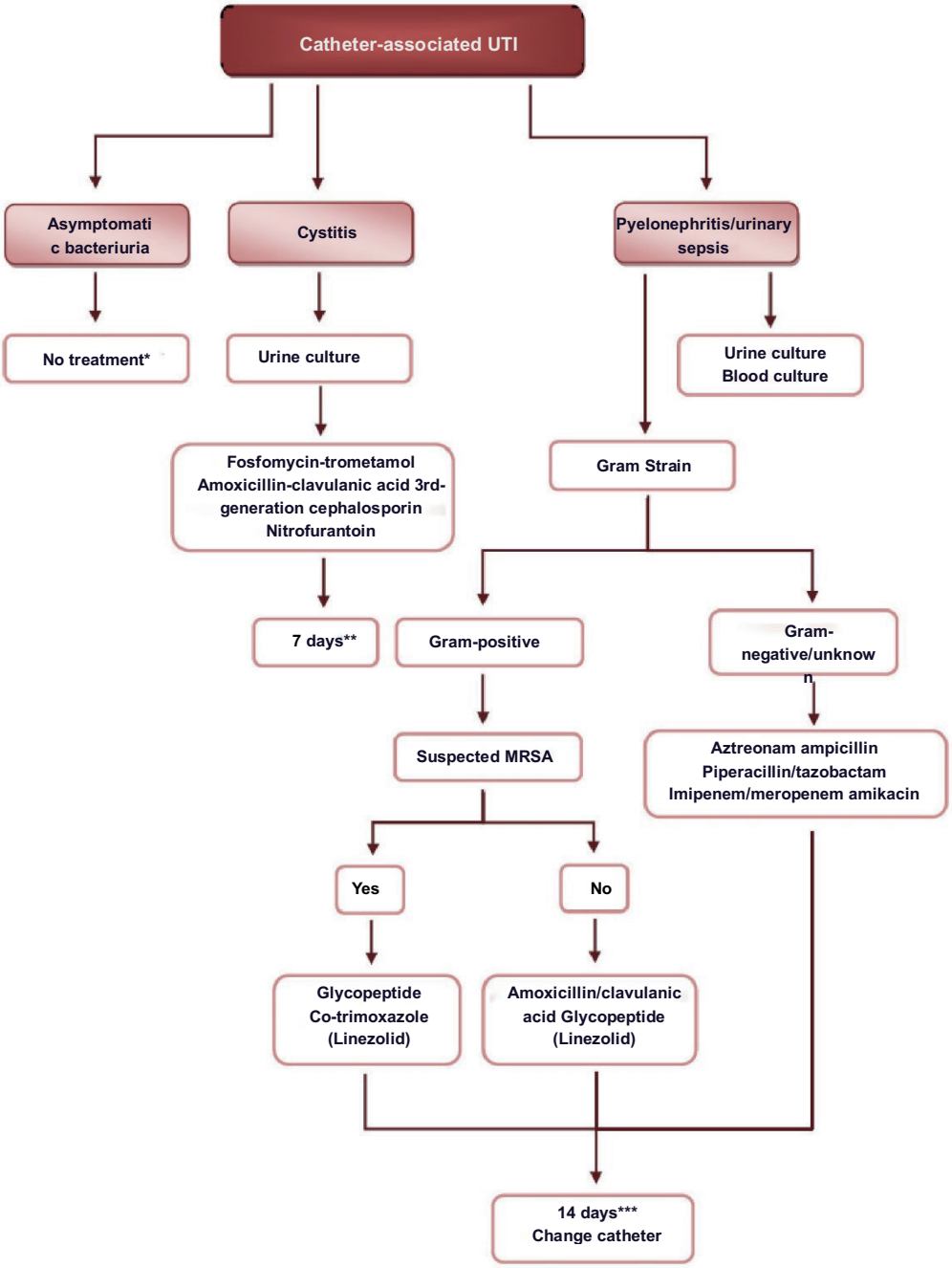
In patients with IC, the device prevents the incomplete emptying of the bladder, leaving residual urine (60), as well as interfering with defence mechanisms and detrusor muscle tone, leading to atrophy of the muscle (61).

UTIs are the most common complication in patients with neurogenic bladder; risk factors predisposing to infections include bladder overdistension, incomplete bladder emptying, elevated bladder pressures, lithiasis, and bladder instrumentation among others. Bladder instrumentation as a method of bladder emptying is considered an important risk factor for UTIs in this population. The initial infection tends to be caused by *E. coli* or other Enterobacteriaceae. Less commonly, *P. aeruginosa*, enterococci, Candida spp. or a multi-resistant microorganism are identified as causative agents (60).

Certain symptoms have been defined in which a urine culture should be requested, such as fever, low-back or hypogastric pain during voiding/catheterisation, urinary incontinence, increased spasticity, autonomic dysreflexia, changes in the smell and appearance of the urine, sensation of malaise, lethargy and restlessness (62).

Only symptomatic UTIs should be treated (63), as the use of antimicrobial prophylaxis has not been shown to decrease the frequency of clinical infections. In fact, it can enhance the selection of resistant strains (62) or even result in the clinical benefit being cancelled out by the undesirable effects of the treatment (64). Therefore, if the patient has increased spasms, spasticity and/or leaks of urine between catheterisations without fever or malaise, the approach should simply be to increase fluid intake and consider inserting an indwelling catheter (IDC) for seven days. However, if the patient presents with fever, antibiotic therapy should be prescribed in addition to the IDC and increase in fluid intake.

The protocol of action against UTIs in patients with IC and the therapeutic strategies of choice in each case, if applicable, are shown in the algorithm below.



Algorithm for action in catheter-associated UTIs.

*MRSA: Methicillin-resistant Staphylococcus aureus. *Except urological surgery, pregnant women, catheter replacement if risk of endocarditis, persistent bacteriuria after removal of catheter. **Consider replacement of catheter. ***If sepsis occurs after manipulation, the duration or the catheter can be shortened to 5-7 days*

ANNEX 2

Summary tables of main recommendations classified according to scope of action

A. DIAGNOSIS	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
1. Comprehensive compilation of data related to the patient's medical history.	III	A
2. Compilation of specific data related to lower urinary tract (LUT) function.	III	A
3. General physical examination that includes abdominal and rectal examination, vaginal examination in women and urological examination in men.	III	A
4. Neuro-urological examination that includes cremasteric, patellar, Achilles, bulbocavernosus, bulbo-clitoral, anocutaneous and cough reflexes, as well as sensation of superficial anal pressure and vesico-urethral sensitivity.	III	A
5. Urodynamic testing quantifying three basic parameters: intravesical pressure, abdominal pressure and detrusor pressure.	III	A

B. CONSERVATIVE TREATMENT	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
1. Behaviour modification techniques, especially in patients who have some control of the bladder and have normal bladder sensation.	III	A
2. Techniques to aid bladder emptying such as the Credé and Valsalva manoeuvres, as well as triggering of the micturition reflex by external stimuli.	III	C
3. Lower urinary tract rehabilitation techniques such as magnetic or electrical stimulation of the afferent fibres of the pudendal nerve.	III	C
4. Oral anticholinergic monotherapy (also called antimuscarinic).	I	A
5. Alpha-blockers:		
• To reduce resistance to the passage of urine and decrease residual urine.	II	A
• To reduce detrusor overactivity and urethral resistance.	I	C
• To improve the symptoms of autonomic dysreflexia in patients with spinal cord injury.	II	C
6. β3-receptor agonists as adjuvant therapy.	III	C
7. Desmopressin as adjuvant therapy.	III	C
8. Tricyclic antidepressants (imipramine).	III	C
9. Gamma-aminobutyric acid type B (GABA-B) receptor agonists (baclofen).	III	C

C. MINIMALLY INVASIVE TREATMENTS	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
1. Intermittent catheterisation (IC), both in patients suffering from underactive or acontractile bladder and in patients with overactive bladder.	III	A
2. Sterile IC if the patient is in hospital.	III	A
3. Clean IC if the patient is at home.	III	A
4. "No-touch" IC technique as mode of choice for aseptic catheterisation.	III	A
5. Intravesical anticholinergic therapy.	III	C
6. Vanilloid drugs.	I	C
7. Intravesical botulinum-A toxin.	I	A
8. Antibiotic prophylaxis associated with the administration of intravesical botulinum-A toxin.	II	A
9. Intersphincteric botulinum-A toxin.	I	A

D. SURGICAL TREATMENTS	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
1. Sacral anterior root stimulator (SARS).	I	B
2. Enterocystoplasty.	III	B
3. Sphincterotomy.	III	B
4. Ureteral stents implanted through the neck of the bladder.	III	C
5. External sphincter balloon dilation technique.	III	C
6. Artificial urinary sphincter implantation technique.	III	B
7. Suprapubic cystostomy.	III	A

E. FOLLOW-UP AND PROGRESS	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
1. Follow-ups:		
a. Annual reviews in patients with spinal cord injury without risk factors for renal impairment.	III	A
b. Check-ups will be performed more frequently if there are complications, risk factors, or changes in bladder behaviour.	III	C
c. In MS, they will also be performed more frequently if, in addition to the above situations, there is progression of the disease.	III	A
2. Annual additional assessment tests: physical examination, blood analysis and kidney and bladder ultrasound with measurement of post-voiding residual urine.	III	A
3. Urodynamic testing if neurological changes, complications or signs of risk for upper urinary tract (UUT) appear or whenever a surgical intervention is planned.	III	A

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