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Review Article

## Urodynamic Evaluation of Adult Neurogenic Lower Urinary Tract Dysfunction: A Review - ②

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## ABSTRACT

Disorders of the lower urinary tract can have a significant impact on quality of life. This is especially true in the case of neurogenic lower urinary tract dysfunction also known as the neurogenic bladder. Caused by damage or a disease process of the nervous system, this can lead to dysfunction with bladder storage or emptying or both. Symptoms of neurogenic lower urinary tract dysfunction depend on etiology and location of nervous system disease process. The disorders include spinal cord injuries as well as diseases such as multiple sclerosis, Parkinson's disease, cerebrovascular accidents, or tumors, among others. A comprehensive urodynamic evaluation of each patient with neurogenic lower urinary tract dysfunction should be performed. Each component of the urodynamics is crucial to evaluate a patient with neurogenic lower urinary tract dysfunction. Both non-invasive and invasive urodynamic evaluations are useful. Findings on the urodynamics denote risk factors for upper tract and lower tract urinary deterioration and will help guide treatment decisions.

**Keywords:** Urodynamics; Neurogenic Bladder; Neurogenic Lower Urinary Tract Dysfunction; Urodynamics Test

## ABBREVIATIONS

NLUTD: Neurogenic Lower Urinary Tract Dysfunction; LUT: Lower Urinary Tract; UDS: Urodynamics; MS: Multiple Sclerosis; SCI: Spinal Cord Injury; CVA: Cerebrovascular Accident ; WHO: World Health Organization; PD: Parkinson's Disease; NB: Neurogenic Bladder; AUA: American Urologic Association; UUT: Upper urinary tract; QoL: Quality of Life; PVR: Post-Void Residual; UUTD: Upper Urinary Tract Disease; PFS: Pressure Flow Studies; CMG: Cystometrography; DO: Detrusor Overactivity; VUDS: Videourodynamics; EMG: Electromyography; DESD: Detrusor External Sphincter Dyssynergia; DSD: Detrusor Sphincter Dyssynergia; BOO: Bladder Outlet Obstruction; UTI: Urinary Tract Infection; VCUG: Voiding Cystourethrogram; DLPP: Detrusor Leak-Point Pressure; SNC: Substantia Nigra Pars Compact; Pdet: Detrusor Pressure; V: Volume; P: Pressure

## INTRODUCTION

Neurogenic Lower Urinary Tract Dysfunction (NLUTD), previously called neurogenic bladder, is a disorder of the Lower Urinary Tract (LUT) caused by damage to or diseases of the nervous system. This disorder may include dysfunction of bladder storage and/or bladder emptying. NB/NLUTD may be associated with significant morbidity, such as upper urinary tract deterioration including chronic renal insufficiency, bladder stones, or urosepsis [1]. Several mechanisms of injury and neurological pathology may contribute to the syndrome of NB/NLUTD [2]. As a result, understanding, diagnosing and managing this condition can be challenging.

Urodynamics (UDS) is a collection of tests that can separately or in combination allow for assessment of the LUT by evaluating the transport, storage and evacuation of urine. Objective measurement of the function or dysfunction of the LUT is critically important in patients with NB. The authors in this review present a comprehensive review of the urodynamic evaluation of adult neurogenic lower urinary tract disorders.

## EPIDEMIOLOGY OF NEUROGENIC LOWER URINARY TRACT DYSFUNCTION

In the United States the disease burden of NLUTD is clearly evident: 40% to 90% of Multiple Sclerosis (MS) patients, 37% to 72% of parkinsonism patients, and 15% of patients with stroke suffer from the sequel of NB [2]. These patients may also be at risk for sepsis and renal failure and are associated with higher numbers of clinical office and ED visits annually. Up to one-third of these visits lead to a need for hospitalization [2]. The need to comprehensively reevaluate and take initiative with our understanding of NB is imperative from

a public health perspective. Clinicians managing these patients are challenged to provide comprehensive diagnosis and assessment of bladder dysfunction to guide them to appropriate patient-specific treatment plans [2].

## COMMON ETIOLOGIES OF NLUTD

### Spinal cord injury

In the United States since the 1970s, the estimated prevalence of patients with traumatic Spinal Cord (SCI) exceeds 200,000, with an annual incidence of approximately 12,000 patients [3]. The main causes of SCI are motor vehicle accidents (42.1%) and falls (26.7%) [3]. Among these patients, urinary dysfunction is very common. Approximately 81% of patients with SCI report at least some degree of impaired bladder function within 1 year after injury [2]. The degree and symptoms of bladder dysfunction may potentially be determined by the spinal level at which the SCI occurred [2].

SCI based on the level of injury provides valuable information, but may be insufficient to describe the extent of lower urinary tract dysfunction. It is generally agreed that UDS should be performed to provide a precise diagnosis for each patient [3]. Often times, based on the mechanism of SCI and extent of injury, there can be a mismatch between somatic neurologic signs and urodynamic findings [3]. Detrusor overactivity, loss of compliance, and detrusor-sphincter dyssynergia are the main elements of bladder dysfunction following SCI [4]. Other urologic phenomena are also present in chronic SCI; approximately 7% of patients will develop an initial kidney stone within 10 years after initial injury. The greatest risk occurs during the first 3 months after injury [5].

The time frame of symptom presentation is an important factor to consider when discussing the implications of SCI. Immediately after SCI, spinal shock can occur because of the absence of function below the level of cord injury. Spinal shock may last from 6 to 12 weeks after injury and is variable based on completeness of injury [3]. Spinal shock includes a suppression of autonomic activity as well as somatic activity. The bladder is acontractile and areflexic. As spinal shock proceeds to the recovery stage, recovery of detrusor activity is usually heralded by the recovery of skeletal muscle reflex [3].

The ultimate goals of bladder management in SCI are to preserve upper tract function while maintaining low intravesical pressure through adequate bladder drainage and to maintain urinary continence [3].

### Central nervous system tumors

Primary and metastatic brain tumors may result in NLUTD based on their location. The areas that are most frequently involved

with associated micturition dysfunction are the superior aspects of the frontal lobe. When lower urinary tract dysfunction occurs, it usually consists of detrusor overactivity and urinary incontinence [5]. In addition, urinary retention has also been described in patients with space-occupying lesions of the frontal cortex [5]. Anterior frontal lobe tumors have been observed to cause disturbances in micturition. The typical clinical picture of frontal lobe incontinence is of a patient with severe urgency and frequency of micturition with associated urge incontinence [4].

Uchiyama, et al. [6] investigated the pathophysiology of lower urinary tract dysfunctions in patients with spinal cord tumors. UDS and urinary questionnaires were performed to evaluate the patient population. Patients with cervical-thoracic tumors commonly had voiding symptoms (75%). The main urodynamic features on these patients were detrusor overactivity (39%) and hypocontractile detrusor during voiding (21%) [6]. Patients with epiconus/conus medullaris tumors commonly had voiding symptoms as well (58%). They however were found to have decreased urge to void (50%), detrusor-sphincter dyssynergia (42%), and acontractile detrusor on voiding (32%). Patients with cauda equina tumors commonly had storage symptoms (88%), of which sensory urgency was most common (63%). The authors concluded that spinal cord tumors presented with a greatly unpredictable pattern of detrusor-sphincter-lesion, thus highlighting the importance of urodynamic studies for proper diagnosis [6].

### Cerebrovascular accident

The annual incidence in the United States of Cerebrovascular Accident (CVA) has been cited as approximately 795,000 and 15 million worldwide. The cited prevalence of urinary incontinence ranges from 32% to 79% on hospital admission for CVA, 25% to 28% on discharge, and 12% to 19% several months later. After an initial acute CVA, urinary retention from acontractile detrusor often occurs. The most common long-term expression of LUT dysfunction after CVA is phasic detrusor overactivity [5]. Gariballa, [7] found that urinary incontinence at admission had a hazard ratio of 2.8 as a predictor of stroke death at 3 months. Stroke patients incontinent of urine were malnourished and had an increased risk of infective complications during their hospital course.

Damage to the nervous system will trigger a sequence of events that will induce the body's inherent capacity to undergo structural and functional modification [5]. Neuroplastic changes consist of changes in neural reorganization of the micturition reflex that occur after complete spinal cord transection above the level of S2 and the changes in the peripheral parasympathetic innervation of the LUT [5].

Gelber, et al. [8] prospectively studied bladder function in stroke patients to determine the mechanisms responsible for post-stroke urinary incontinence. Results showed that incontinence was associated with large infarcts, aphasia, cognitive impairment, and functional disability ( $p < 0.05$ ). Urodynamic studies performed on all 19 incontinent patients revealed bladder overactivity in 37%, normal studies in 37%, bladder hypocontractility in 21%, and detrusor-sphincter dyssynergia in 5% [8]. The authors elucidated three major mechanisms responsible for post stroke urinary incontinence.

1. Disruption of the neuro-micturition pathways, resulting in bladder overactivity and urgency incontinence.
2. Incontinence due to stroke-related cognitive and language deficits, with normal bladder function.

3. Concurrent neuropathy or medication use, resulting in bladder hyporeflexia and overflow incontinence [8].

Wein et al coined two possible mechanisms for the incontinence associated with involuntary bladder contractions in patients who have sustained a CVA:

1. Impaired striated sphincter control and
2. Lack of appreciation of bladder filling and impending bladder contraction [5].

Burney, et al. [9] evaluated the correlation of the site of brain injury with urodynamic findings. Complete urodynamic studies on patients were completed within 72 hours of established CVA. The majority of the lesions responsible for detrusor overactivity were from the cerebral cortex and internal capsule. The internal capsule is an area of condensation of various ascending and descending tracts, thus lesions usually mimic frontoparietal lesions. Detrusor acontractility was noted in association with cerebellar infarcts and no effect on the external urethral sphincter. Of all 21 patients with acontractility 81% had hemorrhagic infarcts. The cerebellum derives sensory input from the detrusor and pelvic floor musculature through spinocerebellar tracts. Detrusor-sphincter dyssynergia was related to large focal lesions and combined internal capsule/basal ganglia lesions [9].

### Multiple sclerosis

The World Health Organization (WHO) in 2008 estimated that 2 to 2.5 million people worldwide had Multiple Sclerosis (MS). The age of onset most commonly occurs at 30 to 38 years of age for relapsing, remitting, and progressive phases. The demyelinating process most commonly involves the lateral corticospinal (pyramidal) and reticulospinal columns of the cervical spinal cord, and it is thus not surprising that LUT dysfunction and sphincter dysfunction are so common [5]. The incidence of LUT dysfunction in MS is related to patient-specific disability status, 50% to 90% report voiding symptoms at some time; the prevalence of incontinence is cited as 37% to 72% [5].

Detrusor overactivity is the most common abnormality detected, occurring in 34% to 99% in reported patient series. Striated sphincter dyssynergia coexists with overactivity in 30% to 65% of patients. The prevalence of coexistent impaired detrusor contractility or areflexia ranges from 12% to 38% [5].

Most patients with MS have pathological lesions at multiple central nervous system sites. Therefore, it is difficult to establish a definitive relationship between lesion site and bladder dysfunction [10]. Araki, et al. [10] investigated the relationship of voiding dysfunction type and the lesion site in patients with MS. In their findings, lesions at the cervical level are most susceptible to detrusor-sphincter dyssynergia. In addition, the study showed that detrusor hypocontractility results mainly from lesions at the pons. Litwiller, et al. [11] discussed specific urinary complaints and possible correlating neurologic lesion sites. Detrusor overactivity was associated with a high incidence of cervical and intracranial plaque formation in MS. Detrusor hypocontractility was related to cerebellar plaque involvement, lack of cortical facilitatory input or sacral cord involvement. Detrusor-sphincter dyssynergia highly correlated with cervical plaque formation as well as increased cerebrospinal fluid myelin basic protein.

The wide range of underlying bladder and sphincter abnormalities behooves the urologist to utilize urodynamic evaluation on a regular basis in the individualized bladder management of MS patients [11].

Ciancio, et al. [12] discussed the plasticity of MS in regards to voiding dysfunction and the importance of analyzing urodynamic pattern changes when managing bladder symptoms for MS patients. In their series, 43% of patients with no new urologic symptoms developed a change in the urodynamic pattern or compliance on follow-up examination [12].

### Parkinson's disease

Parkinson's Disease (PD) is a neurodegenerative disorder associated with loss of dopaminergic neurons. Bladder dysfunction is one of the most common autonomic disorders, the incidence estimated at 55-80% [13]. Patients typically present with extrapyramidal neurologic symptoms and urinary dysfunction as a manifestation of autonomic failure [2]. The time from onset of PD to initiation of LUTS in most studies averages 5 years. The most frequent symptoms include nocturia in 86% of patients, followed by frequency in 71% of patients, and urgency in 68% of patients [5].

It has been hypothesized that dopamine modulates the normal micturition reflex; thus, neurogenic degeneration in the nigrostriatal pathway leads to the significant LUT dysfunction associated with PD [5]. The net effect of the basal ganglia on micturition is thought to be inhibitory. The micturition reflex is under the influences of dopamine and GABA [13]. One widely accepted theory of urinary dysfunction in PD involves the D1 receptors and that cell depletion in the SNC in PD results in the loss of D1-mediated inhibition of the micturition reflex and consequently results in detrusor overactivity [14]. The urodynamic diagnosis with involuntary rise in detrusor pressure during filling of the bladder refers to detrusor overactivity [14]. The storage-phase urodynamic abnormalities in PD include reduced bladder capacity together with detrusor over activity [13].

Another potential mechanism of urinary dysfunction in PD is the pharmacological effects of anti parkinsonian medications. Levodopa, a mainstay in PD therapy has been shown to have an unpredictable effect on bladder function [15]. Brusa, et al. [16] evaluated the acute and chronic effects of levodopa on bladder function in PD patients and demonstrated that acute dosing significantly worsened bladder overactivity and bladder capacity. However, the chronic dosing group improved the first sensation of bladder filling and bladder capacity.

Overall, urinary dysfunction, primarily in the form of detrusor overactivity, may arise from direct effects of the disease or through the effects of PD medication therapy [14]. Since maintenance therapy of PD medications is essential to the successful management of PD patients, it is imperative to incorporate urodynamic studies to continually evaluate the oscillating nature of urinary dysfunction in PD patients.

## PATTERNS OF NB

Certain patterns of NB exist as they relate to lesions in particular locations in the central nervous system.

### Above the brainstem

Neurologic lesions above the brainstem that affect micturition typically result in involuntary bladder contractions. Sensation and voluntary striated sphincter function are usually preserved, but sensation may be deficient or delayed. Smooth and striated sphincter synergy is usually maintained [5]. Common symptoms include urinary frequency, urgency, and urge urinary incontinence [2]. In uninhibited neurogenic bladder dysfunction, there is usually reduced

awareness of bladder fullness and a low capacity bladder due to reduction of inhibition of the pontine micturition center by cortical and subcortical structure damage. Urinary incontinence may occur with brain lesions occurring above the pontine micturition center, especially with bilateral lesions [17].

### Brainstem to sacral spinal cord

Suprasacral spinal cord lesions in patients exhibit detrusor overactivity that may lead to urinary incontinence. In addition, detrusor-external sphincter dyssynergia can occur leading to obstructive voiding and incomplete bladder emptying [2]. Lesions between the pontine micturition center and sacral spinal cord produce upper motor neuron bladder [17]. Upper motor neuron bladder dysfunction is characterized by detrusor-sphincter dyssynergia, where simultaneous detrusor and urinary sphincter contractions produce high pressures in the bladder leading to vesicoureteral reflux that can cause renal damage [17]. As the bladder hyper tonicity produces hypertrophy of the detrusor muscle, the normal oblique course of the ureter through the detrusor wall at the ureterovesicular junction is compromised, thus allowing vesicoureteral reflux [17]. Lesions above the T10 level (above the sympathetic autonomic nervous system innervation of the bladder) will cause the bladder and sphincters to be spastic [17].

### Below Sacral Spinal Cord

Trauma or disease below spinal cord level S2, manifests with detrusor areflexia [5]. Depending on the type and extent of neurologic injury, decreased bladder compliance may occur during filling. An open smooth sphincter area may result, but the striated sphincter may exhibit varied types of dysfunction [2]. Several variations of neurogenic bladder may result from damage to the sacral spinal cord. Lesions that damage the detrusor nucleus, but spare the pudendal nucleus produce a Mixed Type A bladder. The Mixed Type A neurogenic bladder renders the detrusor flaccid, while the intact pudendal nucleus is spastic producing a hypertonic external urinary sphincter [17]. Urinary retention will result as the bladder has low pressure with the spastic external sphincter [17]. The Mixed Type B neurogenic bladder results from sacral cord lesions that spare the detrusor nucleus, but damage the pudendal nucleus. A flaccid external urinary sphincter will result due to the pudendal nucleus lesion, while the bladder is spastic due to the disinhibited detrusor nucleus [17]. This pathogenicity will result in urinary incontinence.

## URODYNAMIC STUDIES IN NEUROGENIC BLADDER

Urodynamics (UDS) refers to a group of tests that individually or collectively allow for dynamic assessment of the Lower Urinary Tract (LUT) by evaluating the transport, storage and evacuation of urine. Though widely employed, the clinical utility of UDS is not well defined. UDS offers a more complete evaluation of the LUT through objective measurements of bladder and urethral function, which can assist in diagnosis and guide treatment strategies. There is a paucity of Level-1 evidence defining universal indications for UDS. This is likely because randomized controlled trials would be both dangerous and unethical due to the potentially devastating negative effects of untreated neurogenic dysfunction [18]. Per the most recent published AUA guideline statements on UDS, patients who may benefit from a UDS study include:

1. Those in whom information beyond that obtained by a history, physical examination and basic tests is necessary in order to make an accurate diagnosis and direct therapeutic decisions.
2. Those whose LUT condition may have the potential to cause deleterious and irreversible effects on the upper urinary tracts [19].

Both of these criteria are relevant to patients afflicted by NLUTD. Consequently, UDS, in addition to a thorough history and physical exam, plays an important role in the diagnosis and management of NLUTD.

Patients with NLUTD can be symptomatic or asymptomatic, and symptoms have not been demonstrated to reliably correlate with long-term complications [20]. UDS thus provides an essential opportunity to establish diagnosis and risk stratify patients [18]. If improperly managed, NLUTD can lead to upper urinary tract (UUT) decompensation, which has been attributed to elevated detrusor storage pressures [21]. Timely diagnosis and disease management is of utmost importance in maintaining good quality of life [22]. However, UDS is not without risk, and a proper analysis of potential risks and benefits of this invasive study is warranted.

Before UDS is performed, all patients must have thorough history and physical examination, including the use of a bladder diary for at least 2-3 days. Additionally, while there are currently no validated questionnaires specifically designed for neurourology patients, clinicians should consider the quality of life (QoL) of each patient. In patients with SCI, urodynamic functionality and bladder management strategies were shown to be correlated with changes in QoL [23]. Understanding the effect of management strategies on QoL is essential in designing individualized care plans for patients.

In determining whether or not to use UDS in the evaluation of a patient with suspected NLUTD, many clinicians consider the risk of having prolonged elevations in detrusor pressure (Pdet) during bladder filling or voiding, as this has been shown to be a primary indicator of progression to UUTD [24,25]. High suspicion for chronically elevated Pdet, such as in patients with spinal cord injury or myelomeningocele, is a compelling reason to use UDS for further evaluation and monitoring of treatment efficacy. On the other hand, patients with urgency incontinence after a stroke or women with multiple sclerosis with a low post-void residual (PVR) would generally be considered low risk and may be initially managed without UDS. Of course, there is a category of patients with moderate risk, such as men with Parkinson's disease or multiple sclerosis, where decision-making is not as straightforward [18].

The goal of this discussion is to define the different components of UDS used in the evaluation of patients suffering from NLUTD, to discuss specific urodynamic parameters and findings and to consider possible complications of UDS. Final thoughts will emphasize urodynamic risk factors for urinary tract deterioration and surveillance regimens in these patients.

## COMPONENTS OF URODYNAMIC EVALUATION

UDS is composed of various components that can be interpreted individually or in combination with other components. Recognizing occasional discrepancies in the meaning of urodynamic terms, all terms used in this discussion adhere to the definitions as defined by

the current International Continence Society guidelines [26]. UDS can be divided into non-invasive and invasive tests. Non-invasive UDS are preferred for initial evaluation as they are inexpensive, readily available, and have low associated morbidity [27]. Below, specific urodynamic tests are presented alongside current AUA recommendations in the context of neurogenic bladder.

### Non-Invasive urodynamic tests

**Post-void residual:** The Post-Void Residual (PVR) is an assessment of bladder emptying evaluated either by ultrasound or catheterization. An elevated PVR indicates poor bladder emptying, but not the reason [18]. Per the most recent AUA guidelines, it is suggested that clinicians perform PVR assessment both during the initial evaluation and as part of ongoing follow-up of patients with neurogenic bladder [19]. Given the vast number of possible etiologies of NLUTD, the PVR helps to determine the degree of or absence of significant bladder or outlet dysfunction.

The timing of bladder dysfunction as identified through PVR is important in the context of NLUTD. For example, in cases of spinal shock due to a spinal cord injury, an abrupt change in bladder function occurs and may remain relatively stable after the insult. MS and PD tend to show progressive deterioration of bladder function over time, whereas other conditions such as a CVA may show bladder dysfunction on PVR that is confounded clinically by associated functional voiding issues due to mobility issues [19]. Thus, it is valuable to gather baseline PVR assessments in each patient and to compare these to future measurements, as certain etiologies for NLUTD may cause significant elevations of PVR over time. This finding may lead to an alteration in management (implementation of intermittent catheterization or surgical intervention), as elevated PVR can lead to UTI's, urosepsis, UUTD, and stone disease [19,28-30]. Some experts believe a PVR < 100-200 is an acceptable goal to prevent infections and demonstrates normal detrusor function [31].

**Pressure flow analysis:** Pressure flow studies (PFS) allow for measurement of bladder pressure and urine flow rate, allowing for distinction between bladder outlet obstruction and detrusor hypocontractility/acontractility [32]. One particularly useful application of PFS in patients with NLUTD is in the diagnosis or evaluation of possible coexisting processes such as benign prostatic hyperplasia, incontinence overactive bladder, or diabetes, which may complicate the overall clinical picture [33-35]. According to the AUA panel recommendations, while there is little evidence supporting or refuting the use of PFS for patients with NLUTD, there is a role in providing a reliable identification of the voiding disorder, which can aid in determining management [19].

### Invasive urodynamic tests

**Filling cystometry:** Cystometry (CMG) evaluates pressure/volume relationships of the bladder during filling. CMG can be performed through a variety of catheter types and different methods. A single-channel cystometry records isolated intravesical pressures during filling with a single catheter. Multichannel cystometry incorporates a bladder catheter and a second catheter, usually in the rectum or vagina to approximate intra-abdominal pressure. In general catheters should be 10 French or less in caliber to avoid urethral irritation and obstruction of flow. Four catheter-based manometer systems are used in clinical practice. Water-filled catheters use water as a transduction medium; while air-charged catheters use air as a transduction medium. Fiber-optic and microtip

transducers use electrical transduction mediums [36]. Bladder sensations, compliance, bladder capacity and the presence or absence of detrusor overactivity (DO) can all be determined. Per AUA guidelines, it is recommended to perform a cystometric evaluation during the initial workup (or after period of spinal shock in SCI) of patients with relevant neurological conditions with or without symptoms and as part of ongoing follow-up if appropriate [19]. In patients with meningomyelocele and SCI, CMG provides valuable therapeutic and prognostic information; one of the goals of managing these conditions is to keep intravesical pressures low to prevent UUTD. In other neurologic conditions like MS, PD and CVA, there is a role for CMG to evaluate detrusor function and protect renal function, but it is less defined in these patient populations [19,33,37].

**Videourodynamics:** Videourodynamics (VUDS) combines UDS parameters with radiographic imaging (most commonly C-arm fluoroscopy) of the LUT, providing the most precise evaluation of voiding function/dysfunction [24]. VUDS is widely considered to be the gold standard in the evaluation of NLUTD [1,38]. Concomitant radiographic imaging allows for identification of anatomic and structural abnormalities in the bladder neck or elsewhere, which when interpreted alongside urodynamic parameters, may provide insight on the underlying neuropathology [39,40]. Per AUA guidelines, clinicians are encouraged to perform VUDS in patients with neurologic disease at risk for NLUTD or in patients with other neuropathology with elevated PVR or urinary symptoms [19].

**Electromyography:** Electromyography (EMG) measures striated external urethral and anal sphincters and pelvic floor muscle activity to evaluate for possible abnormal function. EMG can be performed with monopolar needle electrodes or concentric needle electrodes. Concentric needle electrodes have a stable signal and provide a more focal/specific measurement. The monopolar needle electrode has the capability of measuring both normal and denervated muscle activity. Monopolar needles have a larger measuring area (approximately three times that of concentric needles), thus recruiting activity from a larger amount of muscle fibers than concentric needles [41-43]. In patients with NLUTD, this test is especially helpful in determining presence of detrusor external sphincter dyssynergia (DESD) [12,44], and whether or not perineal muscles are coordinated with detrusor contractions [45]. EMG testing is technical difficult to perform and prone to artifact. However, when interpreted alongside VUDS, CMG and PFA, EMG is currently recommended in patients at risk for NLUTD secondary to relevant neuropathology, in patients with elevated PVR, or in patients with urinary symptoms in the context neurologic disease [19]. See table 1 for an overview of AUA recommendations and evidence grading [46].

## URODYNAMIC FINDINGS IN THE NEUROGENIC LOWER URINARY TRACT DYSFUNCTION

### Detrusor sphincter dyssynergia

Detrusor Sphincter Dyssynergia (DSD) is an urodynamic description of BOO resulting from involuntary urethral sphincter activation coupled with detrusor muscle contraction. It can only occur in the presence of neuropathology, and falls into the general category of dysfunctional voiding in the absence of neuropathology [26]. DSD is commonly associated with SCI, MS, spina bifida, and may put patients with NLUTD at increased risk for autonomic dysreflexia, recurrent UTI's, or UUTD if not properly managed [47]. Diagnosis

**Table 1:** AUA/SUFU Guidelines on Urodynamic Evaluation of Neurogenic Lower Urinary Tract Dysfunction [42].

Guideline	Evidence Grade
Perform a PVR assessment during a UDS study or separately during the initial evaluation and continue during follow up when appropriate for patients with relevant neurological conditions	B
Perform a CMG or pressure flow study during the initial evaluation and continue during follow up for patients when appropriate with relevant neurological conditions.	C
Perform a pressure flow analysis in patients in patients with relevant neurological conditions who are at high risk for neurogenic bladder, elevated PVR, or with LUTS	C
Fluoroscopy should be combined with UDS to perform a VUDS for patients with relevant neurologic conditions who are at risk for neurogenic bladder, elevated PVR, or with LUTS.	C
An EMG should be performed in with a CMG +/- a pressure flow study and VUDS for patients with relevant neurologic conditions who are at risk of neurogenic bladder, elevated PVR, or with LUTS.	C

typically involved EMG, VCUG (if available) and urethral pressure profiles. Detailed urodynamic diagnostic criteria characterizing DSD have been described elsewhere [47-49].

### Detrusor overactivity

Detrusor Overactivity (DO) is defined as involuntary detrusor contractions during filling that are unable to be suppressed by the patient. DO is diagnosed during CMG by visualizing uninitiated detrusor contractions during bladder filling, which can lead to urgency/frequency symptoms, incontinence at low storage volumes and elevated pressures [27]. In the context of NLUTD may cause incontinence, potentially leading to embarrassment, depression, social isolation, skin decubiti, urethral erosions and UUTD [50].

### Low bladder compliance

Compliance is defined as the increase in pressure per unit of volume (V/P). The bladder is normally very compliant and can reach high volumes with very little increase in detrusor pressure. Low bladder compliance originates from disease processes within the bladder wall resulting in fibrosis and decreased elasticity [51].

### Abnormal detrusor leak-point pressure

Detrusor Leak-Point Pressure (DLPP) is the lowest detrusor pressure at which urine leakage occurs in the absence of a detrusor contraction or increased abdominal pressure [26]. DLPP testing followed observations of urinary incontinence secondary to impaired bladder compliance in children with MMC. Retrospective evaluation was done in the hope of finding predictive facts for UUTD [24]. Based on the recent recommendations from the ICS, DLPP can discriminate patients at high risk for UUTD, but should not be used as a sole parameter. Previously, a cut-off of 40cm H<sub>2</sub>O was used, but it may have too low a sensitivity to predict UUTD. Other factors that codetermine UUTD risk include bladder compliance, volume where leakage occurs, and detrusor contraction duration and amplitude [52].

## COMPLICATIONS OF URODYNAMICS

UDS is generally well tolerated. However, UDS may be associated with significant morbidity and discomfort. UTI's are a well-studied complication, and one should assure sterile urine prior to UDS. Significant bacteriuria is present in about 1%-4% of women and 2%-

6% of men after UDS [53]. Gross hematuria and urinary retention, while rare in women, may occur in about 3%-4% of men, with obstructed patients at higher risk [54]. Autonomic dysreflexia, an exaggerated sympathetic response to afferent visceral or painful stimuli, can occur and may have life-threatening consequences. Generally, this phenomenon occurs most frequently in patients with SCI at level T6 or above. Common symptoms include flushing, sweating, headaches, bradycardia, and severe hypertension that may necessitate immediate management [19].

### High-risk urodynamic features of the neurogenic bladder

Urinary dysfunction associated with NLUT puts a patient at increased risk of various sequela that can lead to deterioration of both the UUT and LUT. Risk of deterioration is associated with decreased bladder compliance, DSD, elevated detrusor pressure, elevated detrusor leak point pressure, and urinary retention with elevated intravesicular pressures [55]. Of these risk factors, detrusor pressure seems to confer the highest risk of morbidity and mortality in the patient [24,56]. Conditions such as myelodysplasia and suprasacral spinal cord injury place the patient at high-risk for elevated detrusor pressure due to detrusor hyperreflexia and DSD [57-60]. UDS play an important role in the assessment of NLUT in patients that are high-risk for urinary tract deterioration, which are those with myelodysplasia, spinal cord injury, males with MS and anorectal abnormalities [55]. Initial work up in these patients would include imaging as well as full urodynamic study to establish the type and degree of dysfunction [20,57,60]. This could include, but not limited to VUDS, CMG, and EMG. In order to monitor for high-risk sequela, subsequent visits should at least include PVR to assess for the presence of urinary retention and DLPP, as this has been shown to have strong predictive value with regard to progression of specifically UUTD [57].

### Risk factors for upper urinary tract deterioration

The most predictive factor for UUTD in patients with NLUT is detrusor pressure [20]. These patients are at high-risk for upper urinary tract deterioration with 25% progressing to renal failure within 20 years [61]. This increased risk is associated with multiple factors including vesiculoureteral reflux, recurrent pyelonephritis, and recurrent urinary calculi. In conditions with high-risk of persistently elevated detrusor pressures, studies have shown that most, if not all patients will eventually present with vesiculoureteral reflux and resultant hydronephrosis if left untreated [49,62,63]. Recurrent urinary calculi and recurrent pyelonephritis are well-established risk factors for histopathologic changes in the kidney and subsequent renal insufficiency or failure [63]. In NLUT, there may be a persistence of urine stagnation, which predisposes these patients to increased incidence of these recurrent pathologies and subsequent renal failure. Incidence of renal calculi and pyelonephritis in NLUT is 29-55% and 8-22% respectively, with higher incidences in those patients requiring ureteral stents, intermittent catheterization, or suprapubic catheterization [61,64-66].

Considering the high-risk of UUT complications and deterioration in patients with NLUT, surveillance and appropriate intervention plays an important role in decreasing the associated morbidity and mortality. Regular follow-up for and surveillance is warranted in all patients with NLUT, which should include renal ultrasound and PVR. Conditions that are high-risk for UUT complications, as previously stated, may benefit from regular surveillance with UDS [59]. The most effective studies are aimed at assessing detrusor pressure, as this is associated with the highest risk of UUT deterioration. These

studies include bladder storage pressure, detrusor leak point pressure, and bladder compliance with the first two expected to be less than 40mmHg in order to assume minimal risk of UUT deterioration [20,59]. One study showed that a detrusor leak point pressure of up to 75mmHg may actually be permissible and only above this pressure does the patient have a statistically significant risk of deterioration [67].

### Risk factors for lower urinary tract deterioration

LUT deterioration represents a lower percentage of the morbidity and mortality associated with NLUT, though complications can still result in devastating outcomes. Risk factors for LUT complications in these patients include incomplete emptying, elevated intravesicular pressure, and catheter use [68]. Major LUT complications include recurrent UTIs, bladder calculi, and urethral strictures. UTIs are the most common complication with a prevalence of as high as 57% and an incidence of 2.5 episodes per person per year [69]. Incidence of bacteremia in patients with NLUT, specifically in patients with spinal cord injury is 1.3% with 74% of those infections originating from the urinary tract [70]. Mortality associated with bacteremia in these patients is 17%, thus the risk of severe complications originating from a UTI is very high [71].

The role of UDS for regular surveillance of the LUT in NLUT patients remains unclear. The risk factors previously stated could be reliably evaluated through the use of UDS, however the approach to therapy may not be modified based on the findings. The role of prophylactic antibiotics for patients that demonstrate a urodynamic pattern that predisposes to UTIs is currently unclear. Some studies have demonstrated a significant reduction in the incidence of UTIs [68,72-74]. However prophylaxis has also been shown to greatly increase the amount of bacterial resistance, which may outweigh the benefits associated with prophylactic therapy [75]. Further studies are required to determine the efficacy of antibiotic prophylaxis as well as the usefulness of regular urodynamic surveillance.

### Surveillance regimen and frequency of UDS

Surveillance protocols and frequency for NLUT patients with regard to UDS have not yet been clearly defined. UDS are both costly as well as having associated morbidity, which must be considered when determining indications for studies [76]. It is clear that at minimum, high-risk patients with NLUT could benefit from regular UDS, however, it may be the case that all patients with NLUT would stand to benefit. Surveillance should be aimed at risks for renal failure as this poses the largest risk for morbidity and mortality and these patients [49]. To assess for UUT and risk of renal failure, studies should include detrusor pressure, intravesicular pressure, and detrusor leak point pressure [24,55,56]. Symptoms for UUT deterioration to the point of renal insufficiency tend to present late, thus waiting to perform studies with the onset of symptoms is not sufficient for appropriate monitoring [20].

Currently there is a dearth of data with regard to the appropriate frequency of UDS in patients with NLUT. The European Association of Urology recommends that in patients with NLUT, follow-up UDS be employed every 2 years in all patients with frequency being increased to yearly in those with detrusor overactivity and/or low bladder compliance [59]. Alternatively, SCI Think Tank proposed yearly urodynamic surveillance only in NLUT patients considered to be high-risk for complications, which includes those with myelodysplasia, spinal cord injuries, and males with MS, and

anorectal abnormalities [77]. Further studies must be performed to determine the optimal patient populations, regimen and frequency of UDS.

## CONCLUSION

The neurogenic lower urinary tract dysfunction is a complex and heterogeneous condition with potentially devastating consequences if not adequately evaluated and appropriately managed. Early detection of high-risk features (e.g., low detrusor compliance, detrusor sphincter dyssynergia and vesicoureteral reflux) and appropriate management can potentially obviate deterioration of upper urinary tract function. Urodynamics plays an important role in the functional assessment of the lower urinary tract function, specifically identifying high-risk features and by defining baseline parameters to which future measurement can be compared during goal-directed treatment. Future studies are warranted to better define the role of UDS within specific neurourological disease states and to better identify prognostic factors that may change management strategies of adult neurogenic lower urinary tract dysfunction.

## REFERENCES

- Groen J, Pannek J, Castro Diaz D, Del Popolo G, Gross T, Hamid R, et al. Summary of European Association of Urology (EAU) Guidelines on Neuro-Urology. *Eur Urol*. 2016; 69: 324-333. <https://goo.gl/NNcC9e>
- Ginsberg, D. The epidemiology and pathophysiology of neurogenic bladder. *Am J Manag Care*, 2013; 19: 191-196. <https://goo.gl/EhGr7K>
- Jeong SJ, SY Cho, SJ Oh. Spinal cord/brain injury and the neurogenic bladder. *Urol Clin North Am*. 2010; 37: 537-546. <https://goo.gl/HbR6Xt>
- Fowler CJ. Neurological disorders of micturition and their treatment. *Brain*. 1999; 122: 1213-1231. <https://goo.gl/N4Fpd5>
- Scott McDougal W, Alan J Wein, Louis R Kavoussi, Alan W Partin, Craig A. Peter Campbell-Walsh Urology, 11th Edition, AJ Wein, et al. Editors. Elsevier Saunders: Philadelphia; 2016. p. 1761-1795. <https://goo.gl/kpcWKb>
- Uchiyama T, Sakakibara R, Hattori T, Yamanishi T. Lower urinary tract dysfunctions in patients with spinal cord tumors. *Neurourol Urodyn*. 2004; 23: 68-75. <https://goo.gl/hkCn6D>
- Gariballa SE. Potentially treatable causes of poor outcome in acute stroke patients with urinary incontinence. *Acta Neurol Scand*. 2003; 107: 336-40. <https://goo.gl/cWL7hc>
- Gelber DA, Good DC, Laven LJ, Verhulst SJ. Causes of urinary incontinence after acute hemispheric stroke. *Stroke*. 1993; 24: 378-382. <https://goo.gl/JmLdrj>
- Burney TL, Senapati M, Desai S, Choudhary ST, Badlani GH. Acute cerebrovascular accident and lower urinary tract dysfunction: a prospective correlation of the site of brain injury with urodynamic findings. *J Urol*. 1996;156: 1748-1750. <https://goo.gl/qicqgG>
- Araki I, Matsui M, Ozawa K, Takeda M, Kuno S. Relationship of bladder dysfunction to lesion site in multiple sclerosis. *J Urol*. 2003; 169: 1384-1387. <https://goo.gl/ppczSi>
- Litwiler SE, EM Frohman, PE Zimmern. Multiple sclerosis and the urologist. *J Urol*. 1999; 161: 743-757. <https://goo.gl/7KUBtZ>
- Ciancio SJ, Mutchnik SE, Rivera VM, Boone TB. Urodynamic pattern changes in multiple sclerosis. *Urology*. 2001; 57: 239-245. <https://goo.gl/pT2e4T>
- Sakakibara R, Tateno F, Kishi M, Tsuyuzaki Y, Uchiyama T, Yamamoto T. Pathophysiology of bladder dysfunction in Parkinson's disease. *Neurobiol Dis*. 2012; 46: 565-71. <https://goo.gl/kRzyLE>
- Blackett H, R Walker, B Wood. Urinary dysfunction in Parkinson's disease: a review. *Parkinsonism Relat Disord*. 2009. 15: 81-87. <https://goo.gl/51e9cy>
- Yeo L, Singh R, Gundeti M, Barua JM, Masood J. Urinary tract dysfunction in Parkinson's disease: a review. *Int Urol Nephrol*. 2012; 44: 415-424. <https://goo.gl/hyPvaL>
- Brusa L, Petta F, Pisani A, Moschella V, Iani C, Stanzione P, et al. Acute vs chronic effects of L-dopa on bladder function in patients with mild Parkinson disease. *Neurology*. 2007; 68: 1455-1449. <https://goo.gl/soQdVS>
- Dorsher PT, PM McIntosh. Neurogenic bladder. *Advances in Urology*. 2011. 2012: 816274. <https://goo.gl/Z2ru7K>
- Nitti V, B Brucker. *Campbell-Walsh Urology*. 11th Edition. A.J. Wein et al. Editors. Elsevier Saunders: Philadelphia, 2016; 1718-1742.
- Collins CW, Winters JC. AUA/SUFU adult urodynamics guideline: a clinical review. *Urol Clin North Am*. 2014; 41: 353-62. <https://goo.gl/FDoHHK>
- Nosseir M, A Hinkel, J Pannek. Clinical usefulness of urodynamic assessment for maintenance of bladder function in patients with spinal cord injury. *Neurourol Urodyn*. 2007; 26: 228-233. <https://goo.gl/T9dr3w>
- Satar N, Bauer SB, Shefner J, Kelly MD, Darbey MM. The effects of delayed diagnosis and treatment in patients with an occult spinal dysraphism. *J Urol*. 1995; 154: 754-758. <https://goo.gl/yfYvGX>
- Bomalaski MD, JL Teague, B Brooks. The long-term impact of urological management on the quality of life of children with spina bifida. *J Urol*. 1995; 154: 778-781. <https://goo.gl/S9o8SA>
- Pannek J, B Kullik. Does optimizing bladder management equal optimizing quality of life? Correlation between health-related quality of life and urodynamic parameters in patients with spinal cord lesions. *Urology*. 2009; 74: 263-266. <https://goo.gl/qLYBmb>
- McGuire EJ, RD Cespedes, HE O'Connell. Leak-point pressures. *Urol Clin North Am*. 1996; 23: 253-262. <https://goo.gl/TqzoGc>
- Kurzrock EA, S Polse. Renal deterioration in myelodysplastic children: urodynamic evaluation and clinical correlates. *J Urol*. 1998; 159: 1657-1661. <https://goo.gl/YvAQUi>
- Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002; 21: 167-178. <https://goo.gl/sHGL6n>
- Allio BA, AC Peterson. Urodynamic and physiologic patterns associated with the common causes of neurogenic bladder in adults. *Transl Androl Urol*, 2016. 5: 31-38. <https://goo.gl/R7zPd7>
- Fakas M, Souli M, Koratzanis G, Karageorgiou C, Giamarellou H, Kanellakopoulou K. Effects of antimicrobial prophylaxis on asymptomatic bacteriuria and predictors of failure in patients with multiple sclerosis. *J Chemother*. 2010; 22: 36-43. <https://goo.gl/3FHpEC>
- Ito T, Sakakibara R, Yasuda K, Yamamoto T, Uchiyama T, Liu Z, et al. Incomplete emptying and urinary retention in multiple-system atrophy: when does it occur and how do we manage it? *Mov Disord*. 2006; 21: 816-823. <https://goo.gl/pdNnEG>
- Bemelmans BL, Hommes OR, Van Kerrebroeck PE, Lemmens WA, Doesburg WH, Debruyne FM. Evidence for early lower urinary tract dysfunction in clinically silent multiple sclerosis. *J Urol*. 1991; 145: 1219-1224. <https://goo.gl/r7xqYU>
- Vodusek DB, F Boller. Introduction. *Handb Clin Neurol*. 2015; 130: 3-7. <https://goo.gl/uFFsN6>
- Sakakibara R, Fowler CJ, Hattori T, Hussain IF, Swinn MJ, Uchiyama T, et al. Pressure-flow study as an evaluating method of neurogenic urethral relaxation failure. *J Auton Nerv Syst*. 2000; 80: 85-88. <https://goo.gl/Lx1C1N>
- Nitti VW, H Adler, AJ Combs. The role of urodynamics in the evaluation of voiding dysfunction in men after cerebrovascular accident. *J Urol*, 1996. 155: 263-266. <https://goo.gl/h8k71N>
- Kaplan SA, AE Te, JG Blaivas. Urodynamic findings in patients with diabetic cystopathy. *J Urol*. 1995; 153: 342-344. <https://goo.gl/chTqqn>
- Rapidi CA, Karandreas N, Katsifotis C, Benroubi M, Petropoulou K, Theodorou C. A combined urodynamic and electrophysiological study of diabetic cystopathy. *Neurourol Urodyn*. 2006. 25: 32-38. <https://goo.gl/9E5AET>
- Cooper MA, Fletter PC, Zaszczurynski PJ, Damaser MS. Comparison of air-charged and water-filled urodynamic pressure measurement catheters. *Neurourol Urodyn*. 2011; 30: 329-334. <https://goo.gl/Ayb2Mx>



37. Myers DL, LA Arya, JH Friedman. Is urinary incontinence different in women with Parkinson's disease? *Int Urogynecol J Pelvic Floor Dysfunct.* 1999; 10: 188-191. <https://goo.gl/btV7KF>
38. Stöhrer M, Goepel M, Kondo A, Kramer G, Madersbacher H, Millard R, et al. The standardization of terminology in neurogenic lower urinary tract dysfunction: with suggestions for diagnostic procedures. International Continence Society Standardization Committee. *Neurourol Urodyn.* 1999; 18: 139-158. <https://goo.gl/MjWDPa>
39. Sakakibara R, Hattori T, Uchiyama T, Yamanishi T. Videourodynamic and sphincter motor unit potential analyses in Parkinson's disease and multiple system atrophy. *J Neurol Neurosurg Psychiatry.* 2001. 71: 600-606. <https://goo.gl/ng78Vq>
40. Light JK, Beric A, Petronic I. Detrusor function with lesions of the cauda equina, with special emphasis on the bladder neck. *J Urol.* 1993; 149: 539-42. <https://goo.gl/E3oZ1Y>
41. Joynet RL. The selection of electromyographic needle electrodes. *Arch Phys Med Rehabil.* 1994. 75: 251-258. <https://goo.gl/RuSNY2>
42. Joynet RL. The concentric versus the monopolar needle electrode. The case for monopolar needles. *Muscle Nerve.* 1998; 21: 1804-1806; discussion 1809. <https://goo.gl/tgGQw2>
43. Trojaborg W. The concentric versus the monopolar needle electrode. The case for concentric needles. *Muscle Nerve.* 1998; 21: 1806-1808. <https://goo.gl/L28QbB>
44. Schurch B, Schmid DM, Karsenty G, Reitz A. Can neurologic examination predict type of detrusor sphincter-dyssynergia in patients with spinal cord injury? *Urology.* 2005; 65: 243-246. <https://goo.gl/cAkK4z>
45. Carlson KV, S Rome, VW Nitti. Dysfunctional voiding in women. *J Urol.* 2001; 165: 143-147. discussion 147-148.
46. JC Winters, Roger RD, Howard BG, CD Anthony Herndon, Kathleen CK, Stephen RK, et al. Urodynamic studies in adults: AUA/SUFU guideline. *J Urol.* 2012; 188: 2464-2672. <https://goo.gl/BqNtXL>
47. Stoffel JT. Detrusor sphincter dyssynergia: a review of physiology, diagnosis, and treatment strategies. *Transl Androl Urol.* 2016; 5: 127-135. <https://goo.gl/Bto5af>
48. Blaivas JG, Sinha HP, Zayed AA, Labib KB. Detrusor-external sphincter dyssynergia: a detailed electromyographic study. *J Urol.* 1981; 125: 545-548. <https://goo.gl/vZMku9>
49. Weld KJ, Wall BM, Mangold TA, Steere EL, Dmochowski RR. Influences on renal function in chronic spinal cord injured patients. *J Urol.* 2000; 164: 1490-1493. <https://goo.gl/kYBpRg>
50. O'Leary M, M Dierich. Botulinum toxin type A for the treatment of urinary tract dysfunction in neurological disorders. *Urol Nurs.* 2010; 30: 228-234. <https://goo.gl/E3kbe2>
51. Toppercer A, Tetreault JP. Tetreault, Compliance of the bladder: an attempt to establish normal values. *Urology.* 1979; 14: 204-5. <https://goo.gl/wjWguQ>
52. Tarcan T, Demirkesen O, Plata M, Castro-Diaz D. ICS teaching module: Detrusor leak point pressures in patients with relevant neurological abnormalities. *Neurourol Urodyn.* 2017; 36: 259-262. <https://goo.gl/fRL7ez>
53. Gomes CM, Arap S, Trigo-Rocha FE. Voiding dysfunction and urodynamic abnormalities in elderly patients. *Rev Hosp Clin Fac Med Sao Paulo.* 2004; 59: 206-15. <https://goo.gl/bG3Ffe>
54. Klingler HC, Madersbacher S, Djavan B, Schatzl G, Marberger M, Schmidbauer CP. Morbidity of the evaluation of the lower urinary tract with transurethral multichannel pressure-flow studies. *J Urol.* 1998; 159: 191-4. <https://goo.gl/M7juEF>
55. Campbell-Walsh *Urology.* 10<sup>th</sup> ed. AJ Wein, et al. 2012, Philadelphia, PA: Elsevier Saunders. <https://goo.gl/4Vre3P>
56. Shin JC, Lee Y, Yang H, Kim DH. Clinical significance of urodynamic study parameters in maintenance of renal function in spinal cord injury patients. *Ann Rehabil Med.* 2014; 38: 353-9. <https://goo.gl/hZEXsN>
57. Elliott DS, Boone TB. Boone, Recent advances in the management of the neurogenic bladder. *Urology.* 2000; 56: 76-81. <https://goo.gl/E5SiQs>
58. Kotkin L, Milam DF. Milam, Evaluation and management of the urologic consequences of neurologic disease. *Tech Urol.* 1996; 2: 210-9. <https://goo.gl/8S4jdQ>
59. Stöhrer M, Blok B, Castro-Diaz D, Chartier-Kastler E, Del Popolo G, Kramer G, et al. EAU guidelines on neurogenic lower urinary tract dysfunction. *Eur Urol.* 2009; 56: 81-8. <https://goo.gl/YGCBu8>
60. Zhang Z, Liao L. Risk factors predicting upper urinary tract deterioration in patients with spinal cord injury: a prospective study. *Spinal Cord.* 2014; 52: 468-71. <https://goo.gl/Zqz3ch>
61. Weld KJ, Dmochowski RR. Effect of bladder management on urological complications in spinal cord injured patients. *J Urol.* 2000; 163: 768-72. <https://goo.gl/es7NJB>
62. McGuire EJ, Woodside JR, Borden TA. Upper urinary tract deterioration in patients with myelodysplasia and detrusor hypertonia: a followup study. *J Urol.* 1983; 129: 823-6. <https://goo.gl/PeH6dF>
63. El-Khatib, MT, GJ Becker, PS Kincaid-Smith. Reflux nephropathy and primary vesicoureteric reflux in adults. *Q J Med.* 1990; 77: 1241-1253.
64. Maimoun L, Fattal C, Micallef JP, Peruchon E, Rabischong P. Bone loss in spinal cord-injured patients: from physiopathology to therapy. *Spinal Cord.* 2006; 44: 203-10. <https://goo.gl/HxQLDE>
65. Larsen LD, Chamberlin DA, Khonsari F, Ahlering TE. Retrospective analysis of urologic complications in male patients with spinal cord injury managed with and without indwelling urinary catheters. *Urology.* 1997; 50: 418-22. <https://goo.gl/bXURfz>
66. Bakke A, Vollset SE. Risk factors for bacteriuria and clinical urinary tract infection in patients treated with clean intermittent catheterization. *J Urol.* 1993; 149: 527-31. <https://goo.gl/72n9B5>
67. Ozkan B, Demirkesen O, Durak H, Uygun N, Ismailoglu V, Cetinel B. Which factors predict upper urinary tract deterioration in overactive neurogenic bladder dysfunction? *Urology.* 2005; 66: 99-104. <https://goo.gl/qf8Qpa>
68. Esclarín De Ruz A, García Leoni E, Herruzo Cabrera R. Garcia Leoni and R. Herruzo Cabrera, Epidemiology and risk factors for urinary tract infection in patients with spinal cord injury. *J Urol.* 2000; 64: 1285-9. <https://goo.gl/Lr3qbG>
69. Esclarín De Ruz A1, García Leoni E, Herruzo Cabrera R. Epidemiology and risk factors for urinary tract infection following spinal cord injury. *J Urol.* 2000; 164: 1285-9. <https://goo.gl/FMysAQ>
70. Waites KB, Canupp KC, Chen Y, DeVivo MJ, Moser SA. Bacteremia after spinal cord injury in initial versus subsequent hospitalizations. *J Spinal Cord Med.* 2001; 24: 96-100. <https://goo.gl/RA9sdN>
71. Bhatt K, Cid E, Maiman D. Maiman, Bacteremia in the spinal cord injury population. *J Am Paraplegia Soc.* 1987; 10: 11-4. <https://goo.gl/fcchU6>
72. Reid G, Howard L. Effect on uropathogens of prophylaxis for urinary tract infection in spinal cord injured patients: preliminary study. *Spinal Cord.* 1997; 35: 605-7. <https://goo.gl/8SHR88>
73. Kuhlemeier KV, Stover SL, Lloyd LK. Prophylactic antibacterial therapy for preventing urinary tract infections in spinal cord injury patients. *J Urol.* 1985; 134: 514-7. <https://goo.gl/ppr4z9>
74. Gribble MJ, Puterman ML. Prophylaxis of urinary tract infection in persons with recent spinal cord injury: a prospective, randomized, double-blind, placebo-controlled study of trimethoprim-sulfamethoxazole. *Am J Med.* 1993; 95: 141-52. <https://goo.gl/W4CrcC>
75. Siroky MB. Pathogenesis of bacteriuria and infection in the spinal cord injured patient. *Am J Med.* 2002; 113: 67S-79S. <https://goo.gl/GyrXco>
76. Anders K, Cardozo L, Ashman O, Khullar V. Morbidity after ambulatory urodynamics. *Neurourol Urodyn.* 2002; 21: 461-3. <https://goo.gl/3HUXsu>
77. Abrams P, Agarwal M, Drake M, El-Masri W, Fulford S, Reid S, et al. A proposed guideline for the urological management of patients with spinal cord injury. *BJU Int.* 2008; 101: 989-94. <https://goo.gl/21zAJD>