Egyptian Urological Guidelines on Neuro-Urology

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Published by the Egyptian Society for Urologic Researches (ESURS).

For information and orders: ESURS Office 12 Botros Ghaly Street, 7th Floor Roxy, Cairo, Egypt

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Funding.

– *No Fundig sources*

List of Abbreviations.

ANLUTD	*Adult Neurogenic Lower Urinary Tract Dysfunction*
AUDS	*Ambulatory Urodynamics*
AUA	*American Urological Association*
AUS	*Artificial urinary sphincter*
AD	*Autonomic Dysreflexia*
BPO	*Benign Prostatic Obstruction*
BP	*Blood Pressure*
BM	*Bowel Management*
BCR	*Bulbocavernosus Reflex*
CVS	*Cerebrovascular Stroke*
CIC	*Clean Intermittent Catheterization*
DSD	*Detrusor Sphincter Dyssynergia*
DUA	*Detrusor Underactivity*
DM	*Diabetes Mellitus*
DRE	*Digital Rectal Examination*
DMSA	*Dimercaptosuccinic acid*
ED	*Erectile Dysfunction*
EAU	*European Association of Urology*
EMG	*Electromyography*
FDA	*Food and Drug Administration*
FVC-BD	*Frequency-Volume Chart Bladder Diary*
GFR	*Glomerular Filtration Rate*
IPD	*Idiopathic Parkinson's Disease*
ICI	*International Consultation on Incontinence*
ICS	*International Continence Society*
IPSS	*International Prostate Symptom Score*
I-QoL	*Incontinence Quality of Life*
IC	*Intermittent Catheterization*
IIEF-15	*The 15-question International Index of Erectile Function*
LUT	*Lower Urinary Tract*
LUTS	*Lower Urinary Tract Symptoms*
LMNL	*Lower Motor Neuron Lesions*

MAG3 *Mercaptoacetyltriglicine*

MESA. *Microsurgical Epididymal Sperm Aspiration*

MS *Multiple Sclerosis*

MSA *Multiple System Atrophy*

MMC *Myelomeningocele*

NB *Neurogenic Bladder*

NBSS *Neurogenic Bladder Symptom Score*

NLUTD *Neurogenic Lower Urinary Tract Disease*

NICE *National Institute for Health and Care Excellence*

NDO. *Neurogenic Detrusor Overactivity*

OAB *Overactive Bladder*

PS *Parkinsonian Syndrome*

PDE5Is. *Phosphodiesterase Type 5 Inhibitors*

PMC *Pontine Micturition Center*

PD. *Parkinson's disease*

PVR. *Postvoid Residual*

RCTs. *Randomized Controlled Trials*

SB *Spina Bifida*

SCI. *Spinal Cord Injury*

TESE *Testicular Sperm Extraction*

TENS *Transcutaneous Electrical Nerve Stimulation*

TURP *Transurethral Resection of The Prostate*

TOT *Trans obturator Tape*

TVT *Transvaginal Tension Free Vaginal Tape*

UUT *Upper Urinary Tract*

UPP *Urethral Pressure Profile*

UI *Urinary Incontinence*

UTI *Urinary Tract Infection*

UMNL *Upper Motor Neuron Lesions*

UDS *Urodynamics*

VUR *Vesico-Ureteral Reflux*

VUDS *Video-Urodynamics*

VCUG *Voiding Cystourethrogram*

Glossary.

1. ***Neurogenic bladder:*** *Lower urinary tract dysfunction that has occurred likely as a result of a neurological injury or disease, which may be in the central, autonomic or peripheral nervous systems.*
2. ***Adult neurogenic lower urinary tract dysfunction (ANLUTD):*** *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.*
3. ***Autonomic dysreflexia (AD):*** *A sudden and exaggerated autonomic response to various noxious stimuli in patients with SCI or spinal dysfunction at or above level of T6.*
4. ***Assisted bladder emptying:*** *These are techniques used by tetraplegic patients who cannot perform clean intermittent catheterization. These include Credé manoeuvre, Valsalva manoeuvre and triggered reflex voiding.*

Executive Summary.

Scope of the guidelines.

These guidelines deals with the diagnosis and management of patients with NLUTD. Extensive history taking, thorough examination together with laboratory, radiological and urodynamic investigations should be done in every NLUTD patient. Accordingly, tailoring and individualizing the plan of management follows.

Recommendations.

1. *Take extensive general history focusing on past and present symptoms, with special emphasis on four main domains: urinary, sexual, bowel and neurological functions (**STRONG**)*
2. *Assess Quality of life with validated QoL questionnaires for neuro-urological patients (**STRONG**)*
3. *Drug, family, past and present history of neurologic and non-neurologic diseases along with history of external and iatrogenic trauma should be properly taken from patients with NLUTD (**STRONG**)*
4. *Special attention should be paid to warning signs such as fever, hematuria, dysuria, leaking around catheter and autonomic dysreflexia, which could alter/change diagnosis and thus affect the current management (**STRONG**)*
5. *Perineal and genital examination should be performed, including motor and sensory assessment beside specific lumbosacral reflexes (**STRONG**)*
6. *The anal sphincter activity and pelvic floor muscles should be tested (**STRONG**)*
7. *Urine analysis should be performed in the initial evaluation of NLUTD as it has a role in exclusion of UTI in NB patients. It can be also used for following up after antibiotic treatment(**STRONG**)*
8. *Assessment of renal functions is essential in diagnosis and follow-up of NLUTD patients. GFR can be best measured by Cystatin-C based GFR for assessment of renal function (STRONG)*
9. *Renal ultrasound should be done in primary assessment of NLUTD to evaluate UUT anatomy (**STRONG**)*
10. *Perform bladder ultrasound with PVR measurement in the primary evaluation of NLUTD patients (**STRONG**)*
11. *VCUG is recommended in neuro-urological patients to assess the bladder capacity, detect VUR if present and estimate PVR (**STRONG**)*
12. *Perform uroflowmetry in NLUTD patients who can void (**STRONG**)*
13. *Perform a urodynamic investigation to detect and specify LUTD, use same session repeat measurement. Use body-warmed saline, 6 Fr. double lumen urodynamic urethral catheter and filling rate starting at 10 ml/min. If there is no rise in the Pdet, this can be increased to 20 ml/min (**STRONG**)*
14. *Use VUDS in neuro-urological patients. if not, pressure-flow study may be used instead with VCUG(**STRONG**)*
15. *EMG, with surface perineal electrodes, could be used if DSD is suspected in NB patients (**CONDITIONAL**)*
16. *Do not perform assisted bladder emptying techniques (Crede, Valsalva or triggered reflex voiding) as they are hazardous to the upper tract EXCEPT in patients with absent or surgically removed outlet resistance (**STRONG**)*

17. *Do not offer penile clamps as they are absolutely contraindicated in cases of NDO or low bladder compliance because of the risk of developing high intravesical pressure and pressure sores/necrosis in cases of altered/absent sensations (**STRONG**)*
18. *Prescribe anticholinergics as the first-line medical therapy for NDO (**STRONG**)*
19. *Offer combination therapy of antimuscarinics and Beta 3 agonists to maximise outcomes for NDO (**STRONG**)*
20. *Prescribe a-blockers to decrease bladder outlet resistance in NLUTD, putting into consideration their off -label in patients with DSD (CONDITIONAL)*
21. *Use CIC as a standard treatment for patients who are unable to empty their bladder. The average catheterisation schedule is four to six times per day. Use catheter size of 12-16 Fr. Bladder volume should not exceed 400-500 mL at catheterization time (**STRONG**)*
22. *Do not use Foley catheters because of the high incidence of latex allergy in the neuro-urological patient population. Use silicone catheters instead (**STRONG**)*
23. *Avoid use of indwelling transurethral and suprapubic catheterisation whenever possible (**STRONG**)*
24. *Offer intradetrusor botulinum toxin injection to reduce NDO when antimuscarinic therapy fails. The recommended dose of intradetrusal botulinum toxin injection in neurogenic bladder is 200 IU, in 30 sites in the bladder, with exclusion of the trigone, for theoretical prevention of VUR (**STRONG**)*
25. *Offer bladder neck incision in a fibrotic sclerotic bladder neck (**STRONG**)*
26. *Offer botulinum toxin A 100 IU intrasphincteric in cases of DSD (**STRONG**)*
27. *Offer pubovaginal sling in neuro-urological females with decreased outlet resistance who can do self-catheterization (**STRONG**)*
28. *Offer TOT and TVT to neuro-urological females with decreased outlet resistance(**STRONG**)*
29. *Insert an AUS in male patients with neurogenic stress urinary incontinence (**STRONG**)*
30. *Offer bladder augmentation as an alternative to treat refractory NDO and/or impaired bladder compliance (**STRONG**)*
31. *Recommend urinary diversion when no other therapy is successful for NDO and/or impaired bladder compliance (**STRONG**)*
32. *Do not perform screening for asymptomatic bacteriuria nor treat it in NLUTD patients (**STRONG**)*
33. *Avoid the prescription of long-term antibiotics for recurrent UTIs (**STRONG**)*
34. *Prescribe oral PDE5I as first-line medical treatment in neurogenic ED(**STRONG**)*
35. *Offer intracavernous injections of vasoactive drugs as second-line medical treatment in neurogenic ED (**STRONG**)*
36. *Offer penile prostheses for selected NLUTD patients when all other treatments have failed (**STRONG**)*
37. *Perform vibrostimulation and transrectal electroejaculation for sperm retrieval in men with SCI (**STRONG**)*
38. *Do not offer medical therapy for the treatment of neurogenic sexual dysfunction in women (**STRONG**)*
39. *Assess the upper urinary tract every six months in high-risk patients (those with high Pdet/hypocompliant bladders/DSD) by ultrasonography (**STRONG**)*
40. *Perform a physical examination and urine analysis and culture every year in high-risk patients (those with high Pdet/hypocompliant bladders/DSD) (**STRONG**)*
41. *Perform UDS as a mandatory baseline diagnostic intervention. It is recommended yearly in high-risk group, otherwise could be done every two years (**STRONG**)*

Main body.

Introduction, purpose, scope and audience

Introduction.

Neurological diseases are vast, and they may have adverse consequences on the urinary system. The extent and site of the neurological insult will determine the type of neurogenic lower urinary tract disease (NLUTD).

The term "neurogenic bladder" describes lower urinary tract dysfunction that has occurred likely as a result of a neurological injury or disease (1) which may be in the central, autonomic or peripheral nervous systems.

The International Continence Society (ICS) defines "Adult neurogenic lower urinary tract dysfunction" (ANLUTD) as 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 (2).

Neuro-urological disorders are classified according to Panicker et al. into (3):

i. Suprapontine and pontine lesions (Upper motor neuron lesions = UMNL)
ii. Spinal (Infrapontine and suprasacral) lesions (UMNL)
iii. Sacral and infrasacral lesions (Lower motor neuron lesions = LMNL)

The current classification systems serve as a framework since it is not possible to map all lesions and its consequences in every patient in a single classification (4). Most of these systems are of no use today such as: Lapides (1970), Bors and Comarr (1971)& Wein functional classification (1981).

More recently, other classification systems were described according to pattern of clinical urological and urodynamic manifestations and aimed to predict site of neurologic affection. The most commonly used are The Madersbacher system and the system described by Panicker et al.

The worst complication of NLUTD is upper urinary tract (UUT) deterioration, which is the leading cause of morbidity and mortality in this subset of patients. UUT deterioration is more with spinal cord injury (SCI) and spine bifida (SB) patients. It is very crucial to stratify NLUTD patients into high and low risk groups and their lesions according into upper and lower motor neuron lesions, to individualize the plan of management and follow up thus preventing further deterioration and complications. Therefore, early diagnosis (Figure 1), treatment (Figure 2) and follow-up of these patients are crucial.

The main goals of management for NLUTD are satisfaction and avoidance of adverse outcomes which includes (5,6):

- *Protecting upper urinary tract from sustained high filling and voiding pressures (Pdet >40 cmH2O).*
- *Achieving regular bladder emptying, avoiding stasis and bladder over distension, and minimizing PVR to less than 100mls.*
- *Preventing and treating complications such as UTIs, stones, strictures and AD*
- *Achievement (or maintenance) of urinary continence (Social goal).*
- *Restoration of LUT function (Adequate storage and emptying at low intravesical pressure).*
- *Improvement of the patient's QoL.*

The time interval between initial investigations and control diagnostics should not exceed one to two years. In high-risk neuro-urological patients, this interval should be much shorter.

Purpose.

The Urologic Egyptian Guidelines on Neuro-Urology aim to help and guide clinical practitioners to have knowledge of the incidence, standard definitions, diagnosis, therapy, and follow-up of NLUTD. This document integrates recent international guidelines with local experts' opinions based on Egyptian healthcare and socioeconomic circumstances. It also reflects the opinions of experts in Neuro-Urology and represents state-of-the art references for all clinicians, as of the publication date

Target Audience.

- ***Urologists***
- ***Gynecologists***
- ***Neurologists and Neurosurgeons***
- ***General Practitioners***

Methods.

A comprehensive search for guidelines was undertaken to identify the most relevant guidelines to consider for adaptation.

Inclusion/exclusion criteria followed in the search and retrieval of guidelines to be adapted:

- *Selecting only evidence-based guidelines (guideline must include a report on systematic literature searches and explicit links between individual recommendations and their supporting evidence)*
- *Selecting only national and/or international guidelines*
- *Specific range of dates for publication (using Guidelines published or updated 2015 and later)*
- *Selecting peer reviewed publications only*
- *Selecting guidelines written in English language*
- *Excluding guidelines written by a single author not on behalf of an organization in order to be valid and comprehensive, a guideline ideally requires multidisciplinary input*
- *Excluding guidelines published without references as the panel needs to know whether a thorough literature review was conducted and whether current evidence was used in the preparation of the recommendations*

The following characteristics of the retrieved guidelines were summarized in a table:

- *Developing organisation/authors*
- *Date of publication, posting, and release*
- *Country/language of publication*
- *Date of posting and/or release*
- *Dates of the search used by the source guideline developers*

All retrieved Guidelines were screened and appraised using AGREE II instrument (www.agreetrust.org) by at least two members. the panel decided a cut-off point or rank the guidelines (any guideline scoring above 50% on the rigour dimension was retained) (2,7,8)

Evidence assessment.

According to WHO handbook for Guidelines we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations (9,10). GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations. Detailed information on GRADE is available on the following sites:

■ *GRADE working group: http://www.gradeworkingroup.org*

■ *GRADE online training modules: http://cebgrade.mcmaster.ca/*

■ *GRADE profile software: http://ims.cochrane.org/revman/gradepro*

Table 1 Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

Table 2 Significance of the four levels of evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Table 3 Factors that determine How to upgrade or downgrade the quality of evidence

Downgrade in presence of	Upgrade in presence of
Study limitations -1 Serious limitations -2 Very serious limitations	Dose-response gradient +1 Evidence of a dose-response gradient
Consistency -1 Important inconsistency	Direction of plausible bias +1 All plausible confounders would have reduced the effect
Directness -1 Some uncertainty -2 Major uncertainty	Magnitude of the effect +1 Strong, no plausible confounders, consistent and direct evidence
Precision -1 Imprecise data	+2 Very strong, no major threats to validity and direct evidence
Reporting bias -1 High probability of reporting bias	

The strength of the recommendation.

The strength of a recommendation communicates the importance of adherence to the recommendation.

Strong recommendations.

With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional recommendations.

These are made when there is greater uncertainty about the four factors above or if local adaptation has to account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

When not to make recommendations.

When there is lack of evidence on the effectiveness of an intervention, it may be appropriate not to make a recommendation.

Databases searched *included Medline, Cochrane Libraries, European Association of Urology (EAU) guidelines, ICS recommendations, 6th International consultation on incontinence (ICI) recommendations, American Urological Association (AUA) and NICE guidelines, in the period from January 2018 and September 2022.*

Adaptation of the Egyptian cultural aspects, the level of urologists' capabilities and the availability of well equipped hospitals were considered in the methodology of diagnosis and different treatment modalities.

Recommendations.

Table 4: Recommendations for investigations of NB

Recommendations	GRADE Level of certainty	Strength Rating
1. Take extensive general history focusing on past and present symptoms, with special emphasis on four main domains: urinary, sexual, bowel and neurological functions	High (11-17)	Strong
2. Assess Quality of life with validated QoL questionnaires for neuro-urological patients	Moderate (18-26)	Strong
3. Drug, family, past and present history of neurologic and non-neurologic diseases along with history of external and iatrogenic trauma should be properly taken from patients with NLUTD	High(11,14,16)	Strong
4. Special attention should be paid to warning signs such as fever, hematuria, dysuria, leaking around catheter and autonomic dysreflexia, which could alter/change diagnosis and thus affect the current management	High (27,28)	Strong
5. Perineal and genital examination should be performed, including motor and sensory assessment beside specific lumbosacral reflexes	High (29,30)	Strong
6. The anal sphincter activity and pelvic floor muscles should be tested	Moderate(31)	Strong
7. Urine analysis should be performed in the initial evaluation of NLUTD as it has a role in exclusion of UTI in NB patients. It can be also used for following up after antibiotic treatment	High (32,33)	Strong
8. Assessment of renal functions is essential in diagnosis and follow-up of NLUTD patients. GFR can be best measured by Cystatin-C based GFR for assessment of renal function.	Moderate (32,33-35)	Strong
9. Renal ultrasound should be done in primary assessment of NLUTD to evaluate UUT anatomy	Moderate (32,33)	Strong
10. Perform bladder ultrasound with PVR measurement in the primary evaluation of NLUTD patients	High (32,33)	Strong
11. VCUG is recommended in neuro-urological patients to assess the bladder capacity, detect VUR if present and estimate PVR	Moderate (32,33)	Strong
12. Perform uroflowmetry in NLUTD patients who can void	High (36,37)	Strong
13. Perform a urodynamic investigation to detect and specify LUTD, use same session repeat measurement. Use body-warmed saline, 6 Fr. double lumen urodynamic urethral catheter and filling rate starting at 10 ml/min. If there is no rise in the Pdet, this can be increased to 20 ml/min.	Moderate (12,36-39)	Strong
14. Use VUDS in neuro-urological patients. if not, pressure-flow study may be used instead with VCUG	Moderate (40,41)	Strong
15. EMG, with surface perineal electrodes, could be used if DSD is suspected in NB patients	Low (42)	Conditional

Table 5:Recommendations for treatment of NB

Recommendations	GRADE Level of certainty	Strength Rating
1. Do not perform assisted bladder emptying techniques (Crede, Valsalva or triggered reflex voiding) as they are hazardous to the upper tract EXCEPT in patients with absent or surgically removed outlet resistance	Moderate (43-46)	Strong
2. Do not offer penile clamps as they are absolutely contraindicated in cases of NDO or low bladder compliance because of the risk of developing high intravesical pressure and pressure sores/necrosis in cases of altered/absent sensations	High (43)	Strong
3. Prescribe anticholinergics as the first-line medical therapy for NDO	High (46-52)	Strong
4. Offer combination therapy of antimuscarinics and Beta 3 agonists to maximise outcomes for NDO	High (53-62)	Strong
5. Prescribe a-blockers to decrease bladder outlet resistance in NLUTD, putting into consideration their off -label in patients with DSD	Low (63-65)	Conditional

6. *Use CIC as a standard treatment for patients who are unable to empty their bladder. The average catheterisation schedule is four to six times per day. Use catheter size most of 12-16 Fr. Bladder volume should not exceed 400-500 mL at catheterization time*	*Moderate (43, 66-69)*	*Strong*
7. *Do not use Foley catheters because of the high incidence of latex allergy in the neuro-urological patient population. Use silicone catheters instead*	*Moderate (70)*	*Strong*
8. *Avoid use of indwelling transurethral and suprapubic catheterisation whenever possible*	*Moderate (71-74)*	*Strong*
9. *Offer intradetrusor botulinum toxin injection to reduce NDO when antimuscarinic therapy fails. The recommended dose of intradetrusal botulinum toxin injection in neurogenic bladder is 200 IU, in 30 sites in the bladder, with exclusion of the trigone, for theoretical prevention of VUR*	*High(75-82)*	*Strong*
10. *Offer bladder neck incision in a fibrotic sclerotic bladder neck*	*High (83-85)*	*Strong*
11. *Offer botulinum toxin A 100 IU intrasphincteric in cases of DSD*	*Moderate(86-89)*	*Strong*
12. *Offer pubovaginal sling in neuro-urological females with decreased outlet resistance who can do self-catheterization*	*Moderate (90-93)*	*Strong*
13. *Offer TOT and TVT to neuro-urological females with decreased outlet resistance*	*High (94-96)*	*Strong*
14. *Insert an AUS in male patients with neurogenic stress urinary incontinence (SUI)*	*Moderate (97-99)*	*Strong*
15. *Offer bladder augmentation as an alternative to treat refractory NDO and/or impaired bladder compliance*	*Moderate (100-104)*	*Strong*
16. *Recommend urinary diversion when no other therapy is successful for NDO and/or impaired bladder compliance*	*Moderate(105-107)*	*Strong*
17. *Do not perform screening for asymptomatic bacteriuria nor treat it in NLUTD patients*	*High (108-110)*	*Strong*
18. *Avoid the prescription of long-term antibiotics for recurrent UTIs*	*High (111-113)*	*Strong*
19. *Prescribe oral PDE5I as first-line medical treatment in neurogenic ED*	*High (114-117)*	*Strong*
20. *Offer intracavernous injections of vasoactive drugs as second-line medical treatment in neurogenic ED*	*Moderate (118-120)*	*Strong*
21. *Offer penile prostheses for selected NLUTD patients when all other treatments have failed*	*Hig (115, 121,122)*	*Strong*
22. *Perform vibrostimulation and transrectal electroejaculation for sperm retrieval in men with SCI*	*Moderate(123-126)*	*Strong*
23. *Do not offer medical therapy for the treatment of neurogenic sexual dysfunction in women*	*Moderate(115, 127,128)*	*Strong*
24. *Assess the upper urinary tract every six months in high-risk patients (those with high Pdet/hypocompliance/DSD) by ultrasonography*	*Moderate(32,129-131)*	*Strong*
25. *Perform a physical examination and urine analysis and culture every year in high-risk patients (those with high Pdet/hypocompliance/DSD)*	*Moderate(32,129-131)*	*Strong*
26. *Perform UDS as a mandatory baseline diagnostic intervention. It is recommended yearly in high-risk group, otherwise could be done every two years*	*Moderate(32,129-131)*	*Strong*

Clinical indicators for monitoring.

1. ***Renal function tests (urea, creatinine)***
2. ***Urine analysis and urine culture and sensitivity***
3. ***Cystatin-based GFR***
4. ***Uroflowmetry***
5. ***Pressure-flow study***
6. ***Ultrasound abdomen and pelvis***

Update of guidelines.

These guidelines will be updated whenever there is new evidence.

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Annexes

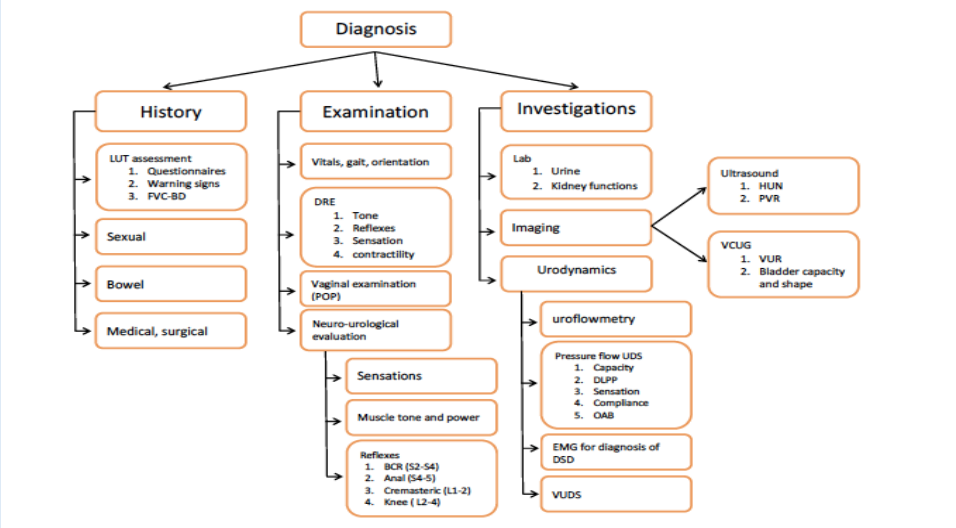

Figure 1. Diagnosis of NLUTD

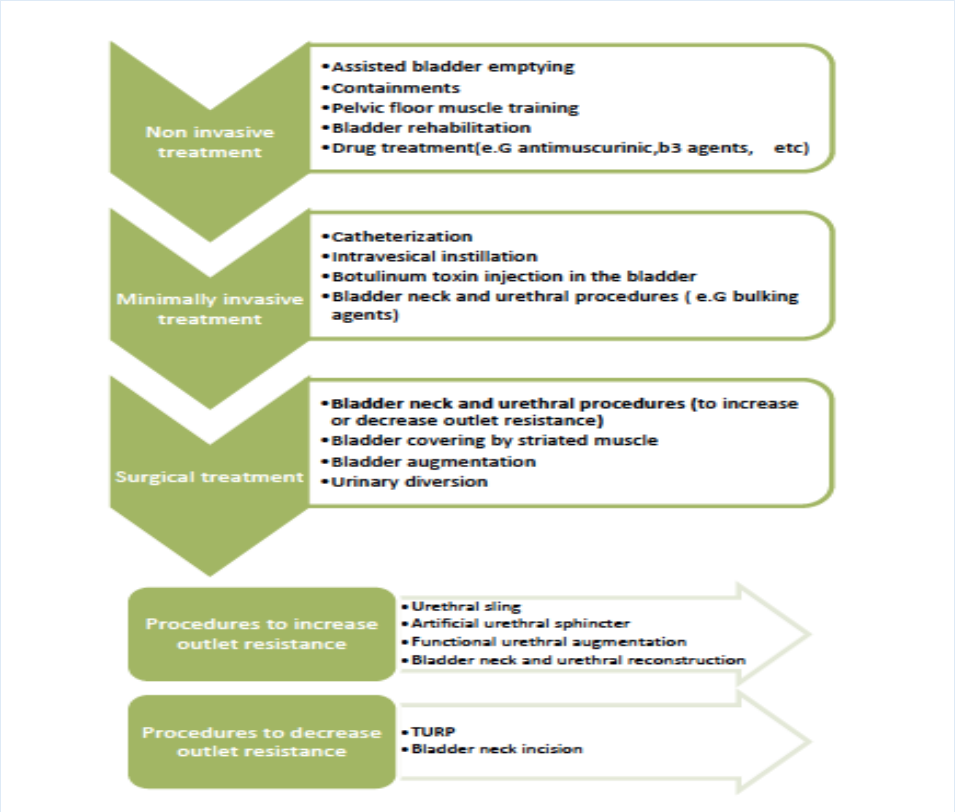

Figure 2. Treatment algorithm of NLUTD