# **FALIGUIDELINES ON NON-**NEUROGENIC MALE LUTS INCLUDING BENIGN PROSTATIC OBSTRUCTION

(Limited text update March 2020)

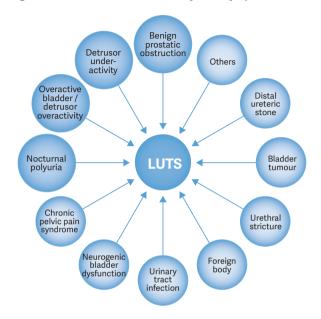
S. Gravas (Chair), J. N. Cornu, M. Gacci, C. Gratzke, T.R.W. Herrmann, C. Mamoulakis, M. Rieken, M.J. Speakman, KAO Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde,

Introduction

V. Sakalis, R. Umbach

The EAU Guidelines on Male Lower Urinary Tract Symptoms (LUTS) is a symptom-orientated guideline that mainly reviews LUTS secondary to benign prostatic obstruction (BPO), detrusor overactivity/overactive bladder (OAB), or nocturnal polyuria in men ≥ 40 years. The multifactorial aetiology of LUTS is illustrated in Figure 1.

Figure 1: Causes of male lower urinary tract symptoms (LUTS)



## **Diagnostic Evaluation**

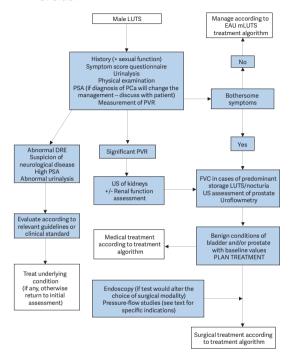
The high prevalence and the underlying multifactorial pathophysiology of male LUTS mean that an accurate assessment of LUTS is critical to provide best evidence-based care. Clinical assessment of LUTS aims to differentially diagnose and to define the clinical profile. A practical algorithm has been developed (Figure 2).

| Recommendations for the diagnostic evaluation of male LUTS  | Strength rating |  |
|---|-----------------|--|
| Take a complete medical history from men with LUTS.   | Strong          |  |
| Use a validated symptom score questionnaire including bother and quality of life assessment during the assessment of male LUTS and for re-evaluation during and/or after treatment.           | Strong          |  |
| Use a bladder diary to assess male LUTS with a prominent storage component or nocturia.   | Strong          |  |
| Tell the patient to complete a bladder diary for at least three days.   | Strong          |  |
| Perform a physical examination including digital rectal examination in the assessment of male LUTS.   | Strong          |  |
| Urinalysis and prostate-specific antigen (PS  | SA)             |  |
| Use urinalysis (by dipstick or urinary sediment) in the assessment of male LUTS.  | Strong          |  |
| Measure PSA if a diagnosis of prostate cancer will change management.   | Strong          |  |
| Measure PSA if it assists in the treatment and/or decision making process.  | Strong          |  |
| Renal function, post-void residual and uroflowmetry   |                 |  |
| Assess renal function if renal impairment is suspected based on history and clinical examination, or in the presence of hydronephrosis, or when considering surgical treatment for male LUTS. | Strong          |  |
| Measure post-void residual in the assessment of male LUTS.  | Weak            |  |

| Perform uroflowmetry in the initial          | Weak   |
|--|--------|
| assessment of male LUTS.                     |        |
| Perform uroflowmetry prior to medical or     | Strong |
| invasive treatment.                          |        |
| Imaging and urethrocystoscopy                |        |
| Perform ultrasound of the upper urinary      | Weak   |
| tract in men with LUTS.                      |        |
| Perform imaging of the prostate when         | Weak   |
| considering medical treatment for male       |        |
| LUTS, if it assists in the choice of the     |        |
| appropriate drug.                            |        |
| Perform imaging of the prostate when         | Strong |
| considering surgical treatment.              |        |
| Perform urethrocystoscopy in men with        | Weak   |
| LUTS prior to minimally invasive/surgical    |        |
| therapies if the findings may change         |        |
| treatment.                                   |        |
| Pressure-flow studies (PFS)                  |        |
| Perform PFS only in individual patients      | Weak   |
| for specific indications prior to invasive   |        |
| treatment or when evaluation of the          |        |
| underlying pathophysiology of LUTS is        |        |
| warranted.                                   |        |
| Perform PFS in men who have had previous     | Weak   |
| unsuccessful (invasive) treatment for LUTS.  |        |
| Perform PFS in men considering invasive      | Weak   |
| treatment who cannot void > 150 mL.          |        |
| Perform PFS when considering surgery         | Weak   |
| in men with bothersome predominantly         |        |
| voiding LUTS and Q <sub>max</sub> > 10 mL/s. |        |
|  |        |

| Perform PFS when considering invasive<br>therapy in men with bothersome,<br>predominantly voiding LUTS with a<br>post-void residual > 300 mL. | Weak   |
|---|--------|
| Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged > 80 years.                           | Weak   |
| Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged < 50 years.                           | Weak   |
| Non-invasive tests in diagnosing bladder outlet obstruction   |        |
| Do not offer non-invasive tests, as an alternative to PFS, for diagnosing bladder outlet obstruction in men.                                  | Strong |

Figure 2: Assessment algorithm of LUTS in men aged 40 years or older



DRE = digital-rectal examination; FVC = frequency volume chart; LUTS = lower urinary tract symptoms;

PCa = prostate cancer; PSA = prostate specific antigen;

PVR = post-void residual; US = ultrasound.

Note: Readers are strongly recommended to read the full text that highlights the current position of each test in detail.

## **Disease Management**

## Conservative and pharmacological treatment

Watchful waiting is suitable for mild-to-moderate uncomplicated LUTS. It includes education, re-assurance, lifestyle advice, and periodic monitoring.

| Recommendations for the conservative and pharmacological management of male LUTS  | Strength rating |
|---|-----------------|
| Conservative management   |                 |
| Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.  | Strong          |
| Offer men with LUTS lifestyle advice prior to, or concurrent with, treatment.   | Strong          |
| Pharmacological management  |                 |
| Offer $\alpha\mbox{1-blockers}$ to men with moderate-to-severe LUTS.  | Strong          |
| Use $5\alpha$ -reductase inhibitors (5-ARIs) in men who have moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL). | Strong          |
| Counsel patients about the onset of action (three to six months) of 5-ARIs.   | Strong          |
| Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.   | Strong          |
| Do not use antimuscarinic overactive<br>bladder medications in men with a post-<br>void residual (PVR) volume > 150 mL.   | Weak            |
| Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.   | Strong          |

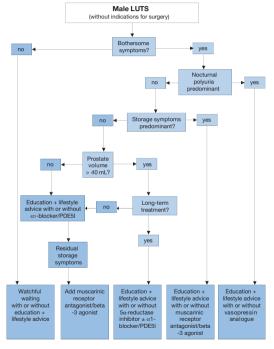
| Use beta-3 agonists in men with moderate-<br>to-severe LUTS who mainly have bladder   | Weak   |
|---|--------|
| storage symptoms.   |        |
| Offer combination treatment with an $\alpha$ 1-blocker and a 5-ARIs to men with moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).                                    | Strong |
| Use combination treatment of a $\alpha$ 1-blocker with a muscarinic receptor antagonist in patients with moderate-to-severe LUTS if relief of storage symptoms has been insufficient with monotherapy with either drug. | Strong |
| Do not prescribe combination treatment of an $\alpha$ 1-blocker with a muscarinic receptor antagonist in men with a PVR volume > 150 mL.  | Weak   |

## Summary conservative and/or medical treatment

First choice of therapy is behavioural modification, with or without pharmacological treatment. A flowchart illustrating conservative and pharmacological treatment choices according to evidence-based medicine and patients' profiles is provided in Figure 3.

Figure 3: Treatment algorithm of male LUTS using medical and/or conservative treatment options.

Treatment decisions depend on results assessed during initial evaluation. Note that patients' preferences may result in different treatment decisions.



PDE5I = phosphodiesterase type 5 inhibitor.

Note: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

## Surgical treatment

Prostate surgery is usually required when patients have experienced recurrent or refractory urinary retention, overflow incontinence, recurrent urinary tract infections, bladder stones or diverticula, treatment-resistant visible haematuria due to BPH/BPE, or dilatation of the upper urinary tract due to BPO, with or without renal insufficiency (absolute operation indications, need for surgery). Surgery is usually needed when patients have had insufficient relief of LUTS or post-void residual after conservative or pharmacological treatments (relative operation indications).

| Recommendations for surgical treatment of male LUTS   | Strength rating |
|---|-----------------|
| Offer transurethral incision of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size < 30 mL, without a middle lobe.                              | Strong          |
| Offer bipolar or monopolar transurethral resection of the prostate (TURP) to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.                    | Strong          |
| Offer bipolar transurethral vaporisation of the prostate as an alternative to monopolar TURP to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL. | Weak            |
| Offer open prostatectomy in the absence of endoscopic enucleation to treat moderate-to-severe LUTS in men with prostate size > 80 mL.   | Strong          |

| Laser treatments of the prostate   |        |
|--|--------|
| Offer laser enucleation of the prostate using Ho:YAG laser (HoLEP) to men with moderate-to-severe LUTS as an alternative to TURP or open prostatectomy.                                  | Strong |
| Offer 80-W 532-nm Potassium-Titanyl-Phosphate (KTP) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP. | Strong |
| Offer 120-W 532-nm Lithium Borat (LBO) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.              | Strong |
| Offer 180-W 532-nm LBO laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.                              | Strong |
| Offer laser vaporisation of the prostate using 80-W KTP, 120 or 180-W LBO for the treatment of patients receiving antiplatelet or anticoagulant therapy with a prostate volume < 80 mL.  | Weak   |
| Offer 120-W 980 nm diode laser vaporisation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to TURP.   | Weak   |
| Offer 120-W 980 nm or 1,318 nm diode laser enucleation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to TURP or bipolar enucleation.                   | Weak   |

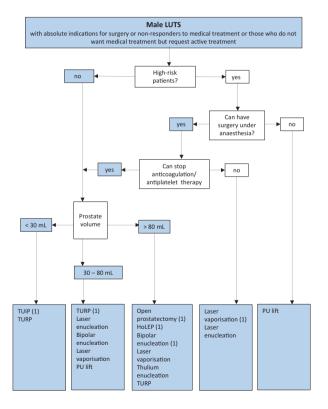
| Offer laser enucleation of the prostate using Tm:YAG vapoenucleation (ThuVEP) and Tm:YAG laser assisted anatomical enucleation (ThuLEP) to men with moderate-to-severe LUTS as alternatives to TURP and HoLEP. | Weak   |  |
|--|--------|--|
| Offer ThuVEP to patients receiving anticoagulant or antiplatelet therapy.  | Weak   |  |
| Offer laser resection of the prostate using Tm:YAG laser (ThuVARP) as an alternative to TURP.  | Strong |  |
| Offer ThuVARP to patients receiving anticoagulant or antiplatelet therapy.   | Weak   |  |
| Prostatic urethral lift  |        |  |
| Offer Prostatic urethral lift (Urolift®) to<br>men with LUTS interested in preserving<br>ejaculatory function, with prostates<br>< 70 mL and no middle lobe.   | Strong |  |
| Intra-prostatic injections   |        |  |
| Do not offer intraprostatic Botulinum toxin-A injection treatment to patients with male LUTS.  | Strong |  |

### **Summary surgical treatment**

The choice of the surgical technique depends on prostate size, co-morbidities, ability to undergo anaesthesia, patient's preference/willingness to accept surgery-associated side effects, availability of the surgical armamentarium, and experience of the surgeon. Figure 4 illustrates surgical treatment choices according to the patient's profile.

Figure 4: Treatment algorithm of bothersome LUTS refractory to conservative/medical treatment or in cases of absolute operation indications.

The flowchart is stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



Laser vaporisation includes GreenLight, thulium, and diode laser vaporisation: Laser enucleation includes holmium and thulium laser enucleation

HoLEP = holmium laser enucleation: TUIP = transurethral incision of the prostate; TURP = transurethral resection of the prostate and PU = prostatic urethral.

## **Techniques Under Investigation**

A recommendation is given for Aquablation and Prostatic Artery Embolisation (PAE); however, these two techniques should still be considered as under investigation in order to better define their position in the armamentarium of invasive therapies for BPO and to better define the subgroups of patients who will benefit most from them.

| Recommendations for techniques under investigation  | Strength rating |
|---|-----------------|
| Offer Aquablation* to patients with moderate-to-severe LUTS and prostates between 30 – 80 mL as an alternative to transurethral resection of the prostate (TURP).                                       | Weak            |
| Inform patients about the risk of bleeding and the lack of long-term follow up data.  | Strong          |
| Offer prostatic artery embolisation (PAE)* to men with moderate-to-severe LUTS who wish to consider minimally invasive treatment options and accept less optimal objective outcomes compared with TURP. | Weak            |
| Perform PAE only in units where the work up and follow up is performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE suitable patients.  | Strong          |

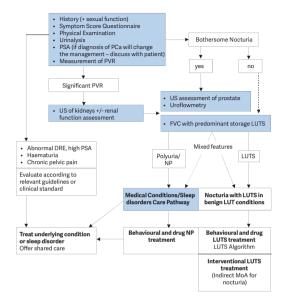
<sup>\*</sup> Technique remains under investigation

## Management of Nocturia in Men with LUTS

## Diagnostic assessment

Evaluation is outlined in Figure 5.

Figure 5: Evaluation of nocturia in non-neurogenic male LUTS



Assessment must establish whether the patient has polyuria. LUTS, sleep disorder or a combination. Therapy may be driven by the bother it causes, but non-bothersome nocturia may warrant assessment with a frequency volume chart. (indicated by the dotted line), depending on history and clinical examination since potential presence of a serious underlying medical condition must be considered. DRE = digital rectal examination: NP = nocturnal polyuria: MoA = mechanism of action: PVR = post-void residual: PSA = prostate-specific antigen: US = ultrasound: FVC = frequency volume chart

## Medical conditions and sleep disorders shared care pathway

Table 1: Shared care pathway for nocturia, highlighting the need to manage potentially complex patients using relevant expertise for the causative factors.

| UROLOGICAL CONTRIBUTION           | SHARED CARE | MEDICAL<br>CONTRIBUTION                 |  |
|-----------------------------------|-------------|---|--|
| Diagnosis of                      |             | Diagnosis of conditions                 |  |
| LUTD                              |             | causing NP                              |  |
| <ul> <li>Urological/</li> </ul>   |             | <ul> <li>Evaluate patient's</li> </ul>  |  |
| LUTS                              |             | known conditions                        |  |
| evaluation                        |             | <ul> <li>Screening for sleep</li> </ul> |  |
| <ul> <li>Nocturia</li> </ul>      |             | disorders                               |  |
| symptom                           |             | Screening for                           |  |
| scores                            |             | potential causes of                     |  |
| <ul> <li>Bladder diary</li> </ul> |             | polyuria*                               |  |

| Conservative |
|--------------|
| management   |
| Behavioural  |

therapy

- Fluid/sleep habits advice
- · Drugs for storage LUTS
- · (Drugs for voiding LUTS)
- ISC/ catherisation

## Interventional therapy

- Therapy of refractory storage LUTS
- Therapy of refractory voiding LUTS

## Conservative management

- Antidiuretic Diuretics
- · Drugs to aid sleep

#### Management

- Initiation of therapy for new diagnosis
- · Optimised therapy of known conditions
- \* Potential causes of polyuria NEPHROLOGICAL DISEASE
- Tubular dysfunction
- Global renal dysfunction CARDIOVASCULAR DISEASE
- Cardiac disease
- Vascular disease
- ENDOCRINE DISEASE
- Diabetes insipidus/mellitus
- · Hormones affecting diuresis/natriuresis

#### NEUROLOGICAL DISEASE

- Pituitary and renal innervation
- Autonomic dysfunction RESPIRATORY DISEASE
- Obstructive sleep apnoea BIOCHEMICAL
- Altered blood oncotic pressure

| Recommendations for treatment of nocturia   | Strength rating |
|---|-----------------|
| Treat underlying causes of nocturia, including behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.   | Weak            |
| Discuss behavioural changes with the patient to reduce nocturnal urine volume and episodes of nocturia, and improve sleep quality.  | Weak            |
| Offer desmopressin to decrease nocturia due to nocturnal polyuria in men < 65 years of age.   | Weak            |
| Offer low dose desmopressin for men > 65 years of age with nocturia at least twice per night due to nocturnal polyuria.   | Weak            |
| Screen for hyponatremia at baseline, day three and day seven, one month after initiating therapy and periodically during treatment. Measure serum sodium more frequently in patients > 65 years of age and in patients at increased risk of hyponatremia. | Strong          |
| Discuss with the patient the potential clinical benefit relative to the associated risks from the use of desmopressin, especially in men > 65 years of age.   | Strong          |
| Offer $\alpha$ 1-adrenergic antagonists for treating nocturia in men who have nocturia associated with LUTS.  | Weak            |

| Offer antimuscarinic drugs for treating nocturia in men who have nocturia associated with overactive bladder.                         | Weak |
|---|------|
| Offer 5α-reductase inhibitors for treating nocturia in men who have nocturia associated with LUTS and an enlarged prostate (> 40 mL). | Weak |
| Do not offer phosphodiesterase type 5 inhibitors for the treatment of nocturia.   | Weak |

### Follow-up

Recommended follow-up strategy:

- Patients managed with watchful waiting should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving α1-blockers, muscarinic receptor antagonists, beta-3 agonists, phospodiesterase 5 inhibitors. or a combination should be reviewed four to six weeks after drug initiation. If patients gain symptomatic relief, without troublesome side effects, drug therapy may be continued. Patients should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving 5α-reductase inhibitors should be reviewed after twelve weeks and six months to determine their response and adverse events.
- Patients receiving desmopressin: serum sodium concentration should be measured at day three and seven and after one month and, if serum sodium concentration has remained normal, every three months subsequently; the follow-up sequence should be restarted after dose escalation

 Patients after prostate surgery should be reviewed four to six weeks after catheter removal to evaluate treatment response and side effects. If patients have symptomatic relief and there are no side effects, further assessment is not necessary.

| Recommendations for follow-up               | Strength rating |
|---|-----------------|
| Follow-up all patients who receive          | Weak            |
| conservative, medical or surgical           |                 |
| management.                                 |                 |
| Define follow-up intervals and examinations | Weak            |
| according to the specific treatment.        |                 |

Readers are strongly recommended to read the full version of the Guidelines where the efficacy, safety and considerations for each treatment are presented.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/quidelines.