

EAU GUIDELINES ON NON-NEUROGENIC MALE LUTS INCLUDING BENIGN PROSTATIC OBSTRUCTION

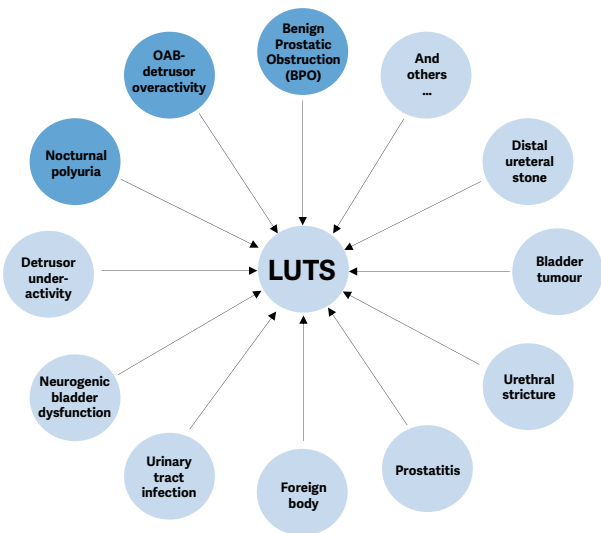
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Introduction

The EAU Guidelines on Male Lower Urinary Tract Symptoms (LUTS) is a symptom-orientated guideline that mainly reviews LUTS secondary to benign prostatic enlargement (BPE) or benign prostatic obstruction (BPO), detrusor overactivity or overactive bladder, and nocturia due to nocturnal polyuria in men \geq 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 mean 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	LE	GR
A medical history must be taken from men with LUTS.	4	A*
A validated symptom score questionnaire with QoL assessment should be used during the assessment of male LUTS and for re-evaluation during and/or after treatment.	3	B
Micturition frequency volume charts or bladder diaries should be used to assess male LUTS with a prominent storage component or nocturia.	3	B
Frequency volume charts should be performed for the duration of at least three days.	2b	B
Physical examination including DRE should be a routine part of the assessment of male LUTS.	3	B
Urinalysis (by dipstick or urinary sediment) must be used in the assessment of male LUTS.	3	A*
PSA measurement should be performed only if a diagnosis of PCa will change the management or if PSA can assist in decision-making in patients at risk of progression of BPE.	1b	A
Renal function assessment must be performed 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.	3	A*
Measurement of post-void residual in male LUTS should be a routine part of the assessment.	3	B
Uroflowmetry in the initial assessment of male LUTS may be performed and should be performed prior to any treatment.	2b	B

Imaging of the upper urinary tract (with US) in men with LUTS should be performed in patients with a large PVR, haematuria or a history of urolithiasis.	3	B
When considering medical treatment for male LUTS, imaging of the prostate (either by TRUS or transabdominal US) should be performed if it assists the choice of the appropriate drug.	3	B
When considering surgical treatment, imaging of the prostate (either by TRUS or transabdominal US) should be performed.	3	B
Urethrocytoscopy should be performed in men with LUTS to exclude suspected bladder or urethral pathology and/or prior to minimally invasive/surgical therapies if the findings may change treatment.	3	B
PFS should be performed only in individual patients for specific indications prior to invasive treatment or when evaluation of the underlying pathophysiology of LUTS is warranted.	3	B
PFS should be performed in men who have had previous unsuccessful (invasive) treatment for LUTS.	3	B
When considering invasive treatment, PFS may be used for patients who cannot void > 150 mL.	3	C
When considering invasive therapy in men with bothersome, predominantly voiding LUTS, PFS may be performed in men with a PVR > 300 mL.	3	C
When considering invasive treatment in men with bothersome, predominantly voiding LUTS, PFS may be performed in men aged > 80 years.	3	C

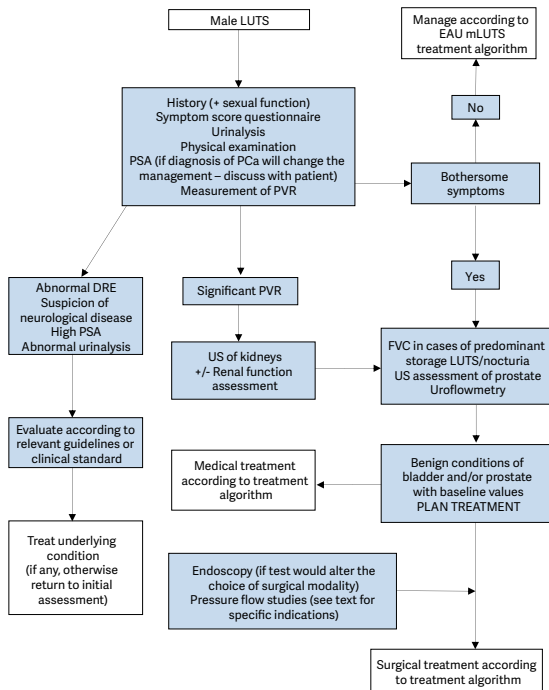
When considering invasive treatment in men with bothersome, predominantly voiding LUTS, PFS should be performed in men aged < 50 years.	3	B
None of the non-invasive tests in diagnosing bladder outlet obstruction in men with LUTS can currently be recommended as an alternative for PFS.	1a	B

**Upgraded based on Panel consensus.*

BPE = Benign prostatic enlargement; DRE = digital-rectal examination; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PFS = pressure flow studies; PSA = prostate specific antigen; PVR = post-void residual; QoL = quality of life; TRUS = transrectal ultrasound; US = ultrasound.

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

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



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.

Treatment

Conservative treatment

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

Pharmacological management

The level of evidence (LE) and the grade of recommendation (GR) for each treatment option are summarised below.

Recommendations for the conservative and pharmacological management of male LUTS.	LE	GR
Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.	1b	A
Offer men with LUTS lifestyle advice prior to or concurrent with treatment.	1b	A
Offer α 1-blockers to men with moderate-to-severe LUTS.	1a	A
Offer 5 α -reductase inhibitors to men who have moderate-to-severe LUTS and an enlarged prostate (>40 mL).	1b	A
5 α -reductase inhibitors can prevent disease progression with regard to acute urinary retention and the need for surgery.	1b	A
Muscarinic receptor antagonists may be used in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	1b	B
Caution is advised in men with a post void residual volume greater than 150 mL.	4	C
PDE5Is may be used in men with moderate-to-severe LUTS with or without erectile dysfunction.	1a	A

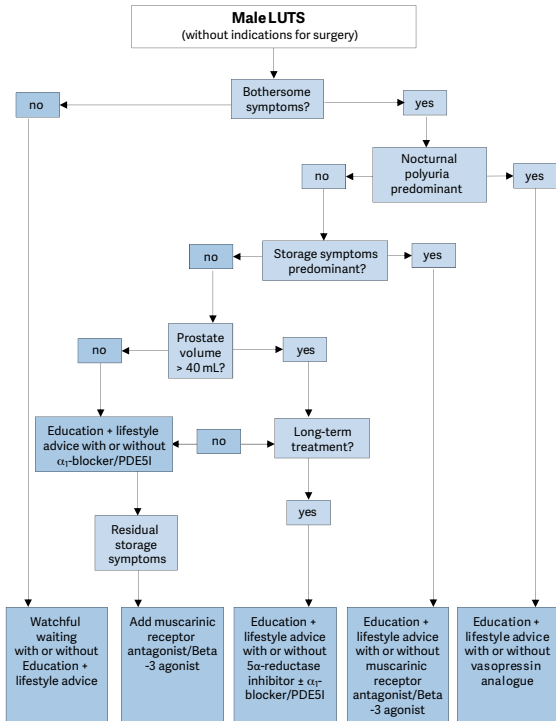
Beta-3 agonists may be used in men with moderate-to-severe LUTS who have predominantly bladder storage symptoms.	1b	B
Offer combination treatment with an α 1-blocker and a 5 α -reductase inhibitor to men with moderate-to-severe LUTS and risk of disease progression (e.g. prostate volume > 40mL).	1b	A
Use combination treatment of an α 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.	1b	B
Prescribe combination treatment with caution in men with a post void residual volume > 150 mL.	2b	B

LUTS = lower urinary tract symptoms; PDE5Is = phosphodiesterase type 5 inhibitors.

Summary conservative and/or medical treatment

First choice of therapy is behavioural modification, with or without medical treatment. A flowchart illustrating conservative and medical 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.



*LUTS = lower urinary tract symptoms;
PDE5I = phosphodiesterase type 5 inhibitor.*

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 macroscopic 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 from LUTS or PVR after conservative or medical treatments (relative operation indications).

Recommendations for surgical treatment of male LUTS	LE	GR
M-TURP is the current surgical standard procedure for men with prostate sizes of 30-80 mL and bothersome moderate-to-severe LUTS secondary of BPO. M-TURP provides subjective and objective improvement rates superior to medical or minimally invasive treatments.	1a	A
The morbidity of M-TURP is higher than for drugs or other minimally invasive procedures.	1a	A
B-TURP achieves short- and mid-term results comparable with M-TURP.	1a	A
B-TURP has a more favourable peri-operative safety profile compared with M-TURP.	1a	A
TUIP is the surgical therapy of choice for men with prostate sizes < 30 mL, without a middle lobe, and bothersome moderate-to-severe LUTS secondary to BPO.	1a	A

OP or EEP such as holmium laser or bipolar enucleation are the first choice of surgical treatment in men with a substantially enlarged prostate (e.g. > 80 mL) and moderate-to-severe LUTS.	1a	A
OP has a high operative morbidity.	1b	A
TUMT achieves symptom improvement comparable with TURP, but TUMT is associated with decreased morbidity and lower flow improvements.	1a	A
Durability is in favour of TURP which has lower re-treatment rates compared to TUMT.	1a	A
TUNA™ is a minimally invasive alternative with decreased morbidity compared to TURP but with less efficacy.	1a	A
Durability is in favour of TURP with lower re-treatment rates compared to TUNA™.	1a	A
HoLEP and 532-nm laser vaporisation of the prostate are alternatives to TURP in men with moderate-to-severe LUTS leading to immediate, objective, and subjective improvements comparable with TURP.	1a	A
The short-term and mid-term functional results of 532-nm laser vaporisation of the prostate are comparable with TURP.	1b	A
The long-term functional results of HoLEP are comparable with TURP or open prostatectomy.	1b	A
Thulium enucleation may be an alternative to TURP and HoLEP in men with moderate-to-severe LUTS leading to immediate and mid-term objective and subjective improvements.	1b	A
Diode laser operations lead to short-term objective and subjective improvement.	1b	B

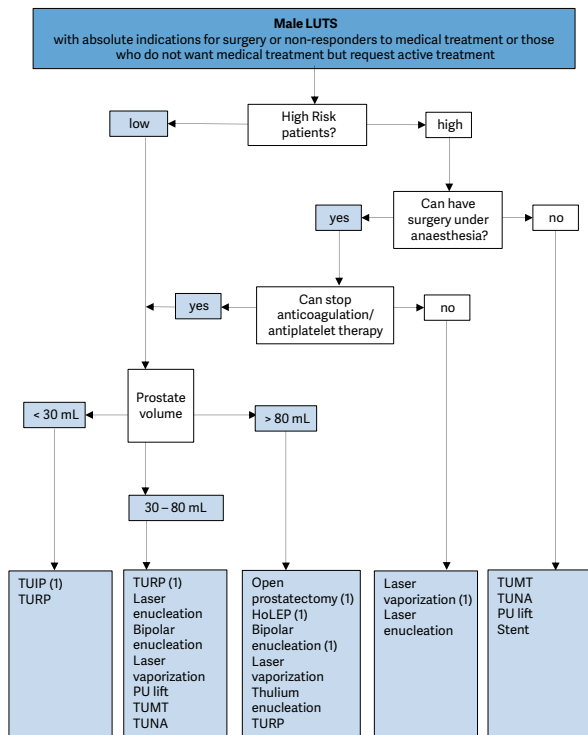
ThuVaRP is an alternative to TURP for small- and medium-size prostates.	1b	A
With regard to intra-operative safety and haemostatic properties, diode and thulium lasers appear to be safe.	3	C
With regard to intra-operative safety, 532-nm laser vaporisation is superior to TURP.	1b	A
532-nm laser vaporisation should be considered in patients receiving anticoagulant medication or with a high cardiovascular risk.	3	B
Offer prostatic stents as an alternative to catheterisation for men unfit for surgery.	3	C
Prostatic urethral lift (Urolift™) leads to objective and subjective short- and mid-term improvements. RCTs with longer follow-up are required.	1a	B
Recommendations for investigational operations		
MISP seems to be feasible in men with prostate sizes > 80 mL needing surgical treatment. Since more data are required, MISP remains under evaluation.	2	B

TURP = transurethral resection of the prostate ; M-TURP = monopolar TURP; LUTS = lower urinary tract symptoms; BPO = benign prostatic obstruction; B-TURP = bipolar TURP; OP = open prostatectomy; EEP = enucleation of the prostate; TUMT = transurethral microwave therapy; TUNA = transurethral needle ablation; HoLEP = holmium laser enucleation; ThuVaRP = Tm:YAG vaporesction; MISP= minimal invasive simple prostatectomy; TUIP = transurethral incision of the prostate; LUTS = lower urinary tract symptoms; RCTs = randomised controlled trails.

Summary surgical treatment

The choice of the surgical technique depends on prostate size, co-morbidities, ability to undergo anaesthesia, and 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 was stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



(1) Current standard/first choice. The alternative treatments are presented in alphabetical order.
 Notice: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

Laser vaporisation includes GreenLight, thulium, and diode lasers vaporisation; Laser enucleation includes holmium and thulium laser enucleation.

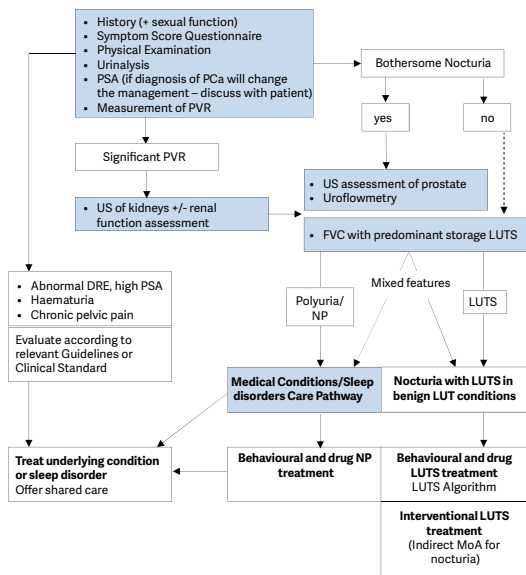
HoLEP = holmium laser enucleation; TUIP = transurethral incision of the prostate; TUMT = transurethral microwave therapy; TUNA = transurethral needle ablation; TURP = transurethral resection of the prostate.

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



Medical conditions and sleep disorders shared care pathway

Figure 6. 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 CONTRIBUTION
<p>Diagnosis of LUTD</p> <ul style="list-style-type: none"> • Urological/LUTS evaluation • Nocturia symptom scores • Bladder diary 		<p>Diagnosis of conditions causing NP</p> <ul style="list-style-type: none"> • Evaluate patient's known conditions • Screening for sleep disorders • Screening for potential causes of polyuria*
<p>Conservative management</p> <p>Behavioural therapy</p> <ul style="list-style-type: none"> • Fluid/sleep habits advice • Drugs for storage LUTS • (Drugs for voiding LUTS) • ISC/catherisation 	<p>Conservative management</p> <ul style="list-style-type: none"> • Antidiuretic • Diuretics • Drugs to aid sleep 	<p>Management</p> <ul style="list-style-type: none"> • Initiation of therapy for new diagnosis • Optimised therapy of known conditions <p>* Potential causes of polyuria</p> <p>NEPHROLOGICAL DISEASE</p> <ul style="list-style-type: none"> • Tubular dysfunction • Global renal dysfunction <p>CARDIOVASCULAR DISEASE</p> <ul style="list-style-type: none"> • Cardiac disease • Vascular disease <p>ENDOCRINE DISEASE</p> <ul style="list-style-type: none"> • Diabetes insipidus/mellitus • Hormones affecting diuresis/natriuresis <p>NEUROLOGICAL DISEASE</p> <ul style="list-style-type: none"> • Pituitary and renal innervation <p>RESPIRATORY DISEASE</p> <ul style="list-style-type: none"> • Obstructive sleep apnoea <p>BIOCHEMICAL</p> <ul style="list-style-type: none"> • Altered blood oncotic pressure
<p>Interventional therapy</p> <ul style="list-style-type: none"> • Therapy of refractory storage LUTS • Therapy of refractory voiding LUTS 		

Treatment for nocturia

Recommendations for treatment of nocturia	LE	GR
Treatment should aim to address underlying causative factors, which may be behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	4	A*
Discuss lifestyle changes to reduce nocturnal urine volume and episodes of nocturia, and improve sleep quality.	3	A*
Desmopressin may be prescribed to decrease nocturia due to nocturnal polyuria in men under the age of 65. Screening for hyponatremia must be undertaken at baseline, during dose titration and during treatment.	1a	A
α 1-adrenergic antagonists may be offered to men with nocturia associated with lower urinary tract symptoms.	1b	B
Anti-muscarinic drugs may be offered to men with nocturia associated with overactive bladder.	1b	B
5 α -reductase inhibitors may be offered to men with nocturia who have moderate-to-severe LUTS and an enlarged prostate (> 40 mL).	1b	C
Do not offer PDE5Is for the treatment of nocturia.	1b	B
A trial of timed diuretic therapy may be offered to men with nocturia due to nocturnal polyuria. Screening for hyponatremia should be undertaken at baseline and during treatment.	1b	C

Agents to promote sleep may be used to aid return to sleep in men with nocturia.	2	C
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*Upgraded based on Panel consensus.

PDE5Is = Phosphodiesterase 5 inhibitors.

Follow-up

Recommended follow-up strategy:

- Patients on watchful waiting should be reviewed at 6 months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving α 1-blockers, muscarinic receptor antagonists, PDE5Is, or a combination should be reviewed 4-6 weeks after drug initiation. If patients gain symptomatic relief, without troublesome side-effects, drug therapy may be continued. Patients should be reviewed at 6 months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving a 5 α -reductase inhibitor should be reviewed after 12 weeks and 6 months to determine their response and adverse events.
- Patients receiving desmopressin: serum sodium concentration should be measured at day 3 and 7 and after 1 month and, if serum sodium concentration has remained normal, every 3 months subsequently; the follow-up sequence should be re-started after dose escalation.
- After prostate surgery patients should be reviewed 4-6 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 of male LUTS	LE	GR
Follow-up for all conservative, medical, or operative treatment modalities is based on empirical data or theoretical considerations, but not on evidence-based studies.	3-4	C

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 978-90-79754-98-4), available to all members of the European Association of Urology at their website, <http://www.uroweb.org>.