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Review – Benign Prostatic Hyperplasia – Editor's Choice

Summary Paper on the 2023 European Association of Urology Guidelines on the Management of Non-neurogenic Male Lower Urinary Tract Symptoms

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Abstract

Context: Lower urinary tract symptoms (LUTS) are common, often bothersome, and have multifactorial aetiology.
Objective: To present a summary of the 2023 version of the European Association of Urology guidelines on the management of male LUTS.
Evidence acquisition: A structured literature search from 1966 to 2021 selected the articles with the highest certainty evidence. The Delphi technique consensus approach was used to develop the recommendations.
Evidence synthesis: The assessment of men with LUTS should be practical. A careful medical history and physical examination are essential. Validated symptom scores, urine test, uroflowmetry, and postvoid urine residual, as well as frequency-volume charts for patients with nocturia or predominately storage symptoms should be used. Prostate-specific antigen should be ordered if a diagnosis of prostate cancer changes the treatment plan. Urodynamics should be performed for selected patients. Men with mild symptoms are candidates for watchful waiting. Behavioural modification should be offered to men with LUTS prior to, or concurrent with, treatment. The choice of medical treatment depends on the assessment findings, predominant type of symptoms, ability of the treatment to change the findings, and the expectations to be met in terms of the speed of onset, efficacy, side effects, and disease progression. Surgery is reserved for men with absolute indications, and for patients who fail or prefer not to receive

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medical therapy. Surgical management has been divided into five sections: resection, enucleation, vaporisation, and alternative ablative and nonablative techniques. The choice of surgical technique depends on patient's characteristics, expectations, and preferences; surgeon's expertise; and availability of modalities.
Conclusions: The guidelines provide an evidence-based approach for the management of male LUTS.
Patient summary: A clinical assessment should identify the cause(s) of symptoms and define the clinical profile and patient's expectations. The treatment should aim to ameliorate symptoms and reduce the risk of complications.

1. Introduction

Lower urinary tract symptoms (LUTS) are common complaints in adult men, are often bothersome, negatively affect quality of life (QoL), and are associated with a substantial economic burden for patients and health care systems [1,2]. As the prevalence of LUTS increases with age, it is expected that the burden of LUTS will increase due to future demographic changes [1,3–5]. Several modifiable factors have been correlated with LUTS, suggesting potential targets for prevention [6].

Herein, we present a summary of the current version of the European Association of Urology (EAU) guidelines on the management of non-neurogenic male LUTS (MLUTS) [7]. The updated version offers practical evidence-based guidance on the assessment and treatment of men aged ≥40 yr with non-neurogenic benign forms of LUTS, including LUTS/benign prostatic obstruction (BPO), detrusor overactivity/overactive bladder (OAB), and nocturnal polyuria. It must be emphasised that although clinical guidelines present the best evidence available to experts, these can never replace clinical expertise, and physicians are advised to consider patients' values and preferences when making treatment decisions [8].

2. Evidence acquisition

The recommendations are based on a literature search on articles published in English on PubMed/Medline, Web of Science, and Cochrane databases between 1966 and May 1, 2021, and included the following search terms: lower urinary tract symptoms, benign prostatic hyperplasia, detrusor overactivity, OAB, nocturia, and nocturnal polyuria, in combination with the various treatment modalities. The detailed search strategies are available at http://www.uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/supplementary-material. A new section on male urinary incontinence has been added in 2022, and a summary has been published previously [9].

The EAU Non-neurogenic Male LUTS Guidelines Panel consists of an international group of experts with urological and clinical epidemiological background. The modified GRADE methodology was used to rate the strength of each recommendation as strong or weak [10]. Additional information can be found online at the EAU website: http://www.uroweb.org/guideline.

3. Evidence synthesis

3.1. Diagnostic evaluation

The objective of clinical assessment is the identification of LUTS aetiology (Fig. 1) and the recognition of patients with an increased risk of disease progression. Suspicious findings, such as haematuria, should be investigated according to the relevant EAU guidelines.

3.1.1. Medical history

Despite the lack of high certainty evidence, medical history represents an integral part of a patient's evaluation. It helps recognise the potential causes of LUTS and review patient comorbidities, medications, lifestyle habits, etc. [11]. It is also crucial for assessing patients' characteristics, expectations, and preferences [11–13].

3.1.2. Symptom score questionnaires

Symptom questionnaires are standard tools for assessing male LUTS, identifying symptom changes and monitoring treatment [14–20]. The International Prostate Symptom Score (IPSS), International Consultation on Incontinence Questionnaire (ICIQ-MLUTS), and Danish Prostate symptom Score (DAN-PSS) are most frequently used. However, these are not specific for disease, gender, or age, and should be validated for the language being used [21]. Compared with ICIQ-MLUTS and DAN-PSS, IPSS lacks assessment of incontinence, postmicturition symptoms, and bother caused by each separate symptom. The novel Visual Prostate Symptom Score may be used in men with limited literacy [22,23].

3.1.3. Frequency-volume chart and bladder diaries

Frequency-volume charts (FVCs) and bladder diaries provide real-time documentation of urinary function and minimise recall bias. The FVC/bladder diary is particularly useful for the assessment of nocturia, which underpins the underlying mechanisms [24–26]. The duration of the FVC/bladder diary needs to be long enough to avoid sampling errors but short enough to minimise noncompliance [27]. A systematic review (SR) recommended that FVCs should continue for ≥3 d [28].

3.1.4. Physical examination and digital rectal examination

Physical examination should evaluate the suprapubic area and the external genitalia. Digital rectal examination can estimate prostate volume but is less accurate than ultrasonography (US) [29,30].

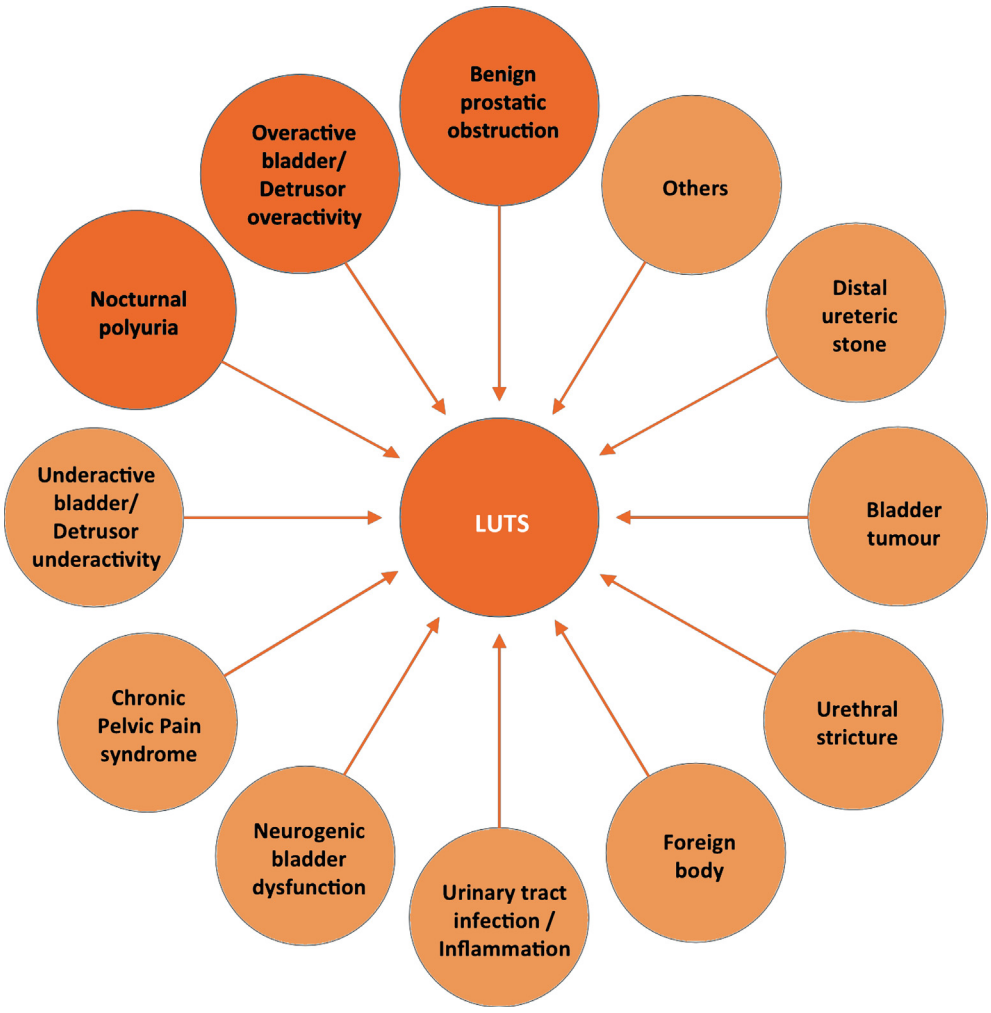

Fig. 1 – Assessment algorithm of LUTS in men aged 40 years or older. Acronyms: *DRE = digital-rectal examination; FVC = frequency volume chart; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PSA = prostate specific antigen; PVR = post-void residual; US = ultrasound.*

3.1.5. Urinalysis

Urine tests can identify urinary tract infections (UTIs), proteinuria, haematuria, or glycosuria, which require further assessment [31–33].

3.1.6. Prostate-specific antigen

Besides its role in the detection of prostate cancer, prostate-specific antigen (PSA) has good predictive value for prostate volume, prostate growth, and the risk of acute urinary retention (AUR) and BPO-related surgery [34–36].

3.1.7. Renal function measurement

Men with LUTS and poor flow are at an increased risk of chronic kidney disease, especially those with hypertension and diabetes [37,38]. Patients with renal insufficiency are at a higher risk of postoperative complications [39].

3.1.8. Postvoid residual urine

Monitoring postvoid urine residual (PVR) allows for the identification of patients at an increased risk of AUR [40,41]. However, PVR is not necessarily associated with bladder outlet obstruction (BOO), since high PVR volumes can be a consequence of obstruction and/or poor detrusor function (detrusor underactivity). At the 50 ml threshold, PVR measurement has a 63% positive predictive value for BOO recognition [40].

3.1.9. Uroflowmetry

Uroflowmetry can be used to correlate symptoms with objective findings and monitor treatment outcomes [42]. The diagnostic accuracy of uroflowmetry for detecting BOO varies considerably and is substantially influenced by threshold values. Specificity can be improved by repeated flow-rate testing.

3.1.10. Imaging

The upper urinary tract can be evaluated using US, especially in men with a large PVR, haematuria, or a history of urolithiasis. In practice, the prostate is assessed using transrectal (or transabdominal) US [43]. The prostate volume is an important criterion for interventional treatment selection. It can also predict the risk of symptom progression and BPO-related complications [44].

3.1.11. Urethrocystoscopy

Patients with LUTS and a history of haematuria, urethral strictures, bladder cancer, or interventional treatments for which the presence of middle lobe is a contraindication should undergo urethrocystoscopy. No correlation between urethrocystoscopic and urodynamic findings has been demonstrated [45].

3.1.12. Urodynamics

The most common invasive urodynamic techniques are filling cystometry and pressure flow studies (PFSs). Video urodynamics uses fluoroscopy and provides additional anatomical and functional information. Studies have described an association between BOO and detrusor overactivity of up to 61% and have been associated with BOO grade and ageing [46,47]. Detrusor underactivity is diagnosed in 11–40% of men with LUTS [48,49]. The UPSTREAM trial investigated whether urodynamics would reduce surgery without increasing urinary symptoms and showed that urodynamics should be used selectively in men with uncomplicated LUTS [50].

To minimise invasiveness and mimic the diagnostic accuracy of PFSs, several tests have been proposed to recognise BOO [51–56]. Data regarding the diagnostic accuracy of these tests are limited by heterogeneity and a small number of studies. Hence, the specificity, sensitivity, positive predictive value, and negative predictive value of noninvasive tests were highly variable.

Recommendations for the diagnostic evaluation of male LUTS are provided in Table 1.

3.2. Disease management

3.2.1. Conservative treatment

Watchful waiting (WW) is an option for men with nonbothersome LUTS, as only a few develop BPO-related complications [57–59]. Men with mild-to-moderate LUTS who are not particularly troubled by their symptoms are also candidates for WW since 85% will remain stable for 1 yr [60–62]. Increasing symptom severity or high PVR volumes are predictors of WW failure. Self-management, as part of WW, is superior to standard care because it reduces symptoms and progression [63]. Self-management includes education, reassurance, periodic monitoring, lifestyle advice, and adequate management of comorbidities, and should be included in the self-care management offered to patients with LUTS [57,62–64].

3.2.2. Pharmacological treatment

3.2.2.1. Alpha-1 adrenoceptor antagonists. Alpha-1 adrenoceptor antagonists (α1-blockers) are the first-line pharmacological treatment for male LUTS, because of their rapid onset of action, good efficacy, and low rate of adverse events (AEs). All α1-blockers have similar efficacy at appropriate doses, and significantly improve urinary symptoms and flow rate compared with placebo, regardless of prostate volume and patient age [65–67]. However, α1-blockers do not prevent AUR or the need for surgery. Data from long-term studies demonstrate that α1-blocker monotherapy is more efficacious in patients with smaller prostates (<40 ml) [34,68–71].

Table 1 – Recommendations for the diagnostic evaluation of MLUTS

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 3 d.	Strong
Perform a physical examination including digital rectal examination in the assessment of male LUTS.	Strong
Urinalysis and prostate-specific antigen	
Use urinalysis (by dipstick or microscopy) 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
Counsel patients about PSA testing and the implications of a raised PSA test.	Strong
Renal function, postvoid 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 postvoid residual in the assessment of male LUTS.	Weak
Perform uroflowmetry in the initial assessment of male LUTS.	Weak
Perform uroflowmetry prior to medical or invasive treatment.	Strong
Imaging and urethrocystoscopy	
Perform ultrasound of the upper urinary tract in men with LUTS.	Weak
Perform imaging of the prostate when considering medical treatment for male LUTS, if it assists in the choice of the appropriate drug.	Weak
Perform imaging of the prostate when considering surgical treatment.	Strong
Perform urethrocystoscopy in men with LUTS prior to minimally invasive/surgical therapies if the findings may change treatment.	Weak
Pressure-flow studies	
Perform PFS only in individual patients for specific indications prior to invasive treatment or when further evaluation of the underlying pathophysiology of LUTS is warranted.	Weak
Perform PFS in men who have had previous unsuccessful (invasive) treatment for LUTS.	Weak
Perform PFS in men considering invasive treatment who cannot void >150 ml.	Weak
Perform PFS when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} >10 ml/s.	Weak
Perform PFS when considering invasive therapy in men with bothersome, predominantly voiding LUTS with a postvoid residual of >300 ml.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS, aged >80 yr.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS, aged <50 yr.	Weak
Noninvasive tests in diagnosing bladder outlet obstruction	
Do not offer noninvasive tests, as an alternative to urodynamics/PFS, for diagnosing bladder outlet obstruction in men.	Strong

LUTS = lower urinary tract symptoms; MLUTS = male LUTS; PFS = pressure-flow study; Qmax = maximum flow rate.

Frequent AEs include asthenia, dizziness, and orthostatic hypotension [72,73]. Alpha-1 blockers do not affect libido, but ejaculatory dysfunction (EjD) is significantly more common than placebo, especially for selective α1-blockers such

as tamsulosin and silodosin. A meta-analysis reported that men on α1-blockers who underwent cataract surgery are at an increased risk of intraoperative floppy iris syndrome [74].

3.2.2.2. 5α-Reductase inhibitors. Two representatives of 5α-reductase inhibitors (5-ARIs) are finasteride and dutasteride. Their clinical effect is slow and is directly related to the baseline prostate size. The 5-ARIs improve IPSS by 15–30%, decrease prostate volume by 18–28%, and increase maximum flow rate (Q_{max}) by 1.5–2.0 ml/s [75–79]. These inhibitors reduce the relative risk of AUR by 57–68% and the need for surgery by 55–64% at 4 yr [34,80–84].

The most common AEs of 5-ARIs are related to sexual function and include reduced libido, erectile dysfunction (ED), and less frequently, ejaculation disorders such as retrograde ejaculation, ejaculation failure, or decreased semen volume. Their effect on PSA should be considered in prostate cancer screening.

3.2.2.3. Muscarinic receptor antagonists. The safety and efficacy of muscarinic receptor antagonist (MRA) monotherapy have been tested in female-only or mixed-population studies involving men with OAB without BOO [85–92]. Monotherapy can significantly improve urgency, urge urinary incontinence (UUI), and daytime frequency. Evidence has shown that men with PSA levels <1.3 ng/ml might benefit more [93]. Frequent AEs include dry mouth, constipation, dizziness, nasopharyngitis, and voiding difficulties including increased PVR; however, AUR is rare in men with a low PVR at baseline (<150 ml) [94,95].

Not all antimuscarinics have been tested in elderly men, and long-term studies on the efficacy of MRAs in men of any age with LUTS are not yet available. In addition, only patients with low PVR volumes at baseline were included in the studies. These drugs should therefore be prescribed with caution, and with regular re-evaluation of IPSS and PVR. Men should be advised to discontinue medication if worsening voiding LUTS or urinary stream is noted after the initiation of therapy.

3.2.2.4. Beta-3 agonists. Mirabegron is the only β3-agonist licensed in Europe for MLUTS management. A meta-analysis of eight randomised controlled trials (RCTs; 27% male) found that mirabegron monotherapy improves frequency, urgency, and UUI episodes compared with placebo or tolterodine [96].

Mirabegron is well tolerated in the elderly and in patients with multiple comorbidities; however, it is contraindicated in patients with severe uncontrolled hypertension [97,98]. The most frequent AEs are hypertension, UTIs, headache, and nasopharyngitis [99–102]. Mirabegron does not affect voiding urodynamic parameters, and the overall change in PVR is small [103]. Long-term data on the efficacy and safety of mirabegron in men of any age with LUTS are not available.

3.2.2.5. Phosphodiesterase 5 inhibitors. Tadalafil 5 mg is the only phosphodiesterase 5 inhibitor (PDE5I) licensed for the treatment of MLUTS. A Cochrane review found that PDE5Is may result in a small reduction in IPSS compared with placebo, whereas there was no difference between PDE5Is and α1-blockers in IPSS [104]. Other meta-analyses have reported improvements in IPSS and International Index of Erectile Function (IIEF) score, but not in Q_{max} [105,106]. A combination of PDE5Is and α1-blockers significantly improves IPSS score (−1.8), IIEF score (+3.6), and Q_{max} (+1.5 ml/s) compared with α1-blocker monotherapy [105].

AEs frequently include flushing, gastro-oesophageal reflux, headache, dyspepsia, back pain, and nasal congestion. Tadalafil is contraindicated in patients using nitrates or guanylate cyclase stimulators and in those with cardiac disease, hypotension, poorly controlled blood pressure, recent stroke (<6 mo), or significant hepatic or renal insufficiency. In addition, it is contraindicated in those who report sudden loss of vision due to anterior ischaemic optic neuropathy after previous use of PDE5Is [107].

3.2.2.6. Plant extracts—phytotherapy. Heterogeneity and a limited regulatory framework characterise the current status of phytotherapeutic agents. The European Medicines Agency has developed the Committee on Herbal Medicinal Products (HMPC). European Union herbal monographs contain HMPC's scientific opinion on safety and efficacy data about herbal substances and their preparations intended for medicinal use. The extracts of the same plant produced by different companies do not necessarily have the same biological or clinical effects; therefore, the effects of one brand cannot be extrapolated to others [108]. Additionally, batches from the same producer may contain different concentrations of active ingredients [109]. According to the HMPC, only hexane-extracted *Serenoa repens* (HESr) is recommended for well-established use.

A large meta-analysis of 30 RCTs with 5222 men included all different brands of *S. repens* and found no benefit of treatment with *S. repens* in comparison with placebo for the relief of LUTS, but a similar improvement in IPSS or Q_{max} to finasteride or tamsulosin. HESr improves Q_{max} and results in fewer voids/night (0.64 [95% confidence interval 0.98–0.31]) than placebo [110,111]. HESr has a favourable safety profile and limited impact on sexual function, with the most frequently reported AE being gastrointestinal upset (mean incidence 3.8%).

3.2.2.7. Alpha-1 adrenoceptor antagonists plus 5-ARI combination therapy. Long-term data from the MTOPS and CombAT studies showed that combination therapy of α1-blockers and 5-ARIs is superior to either monotherapy for symptoms and Q_{max}, as well as superior to α1-blockers alone, in reducing the risk of AUR or the need for surgery [34,68,69].

The MTOPS study reported that combination therapy reduced clinical progression risk by 66% versus placebo, 34% versus finasteride, and 39% versus doxazosin [34]. In the CombAT study, combination therapy reduced the relative risks of AUR by 68%, BPO-related surgery by 71%, and symptom deterioration by 41% compared with tamsulosin at 4 yr [68,69]. To prevent one case of urinary retention and/or surgical treatment, 13 patients needed to be treated for 4 yr with dutasteride and tamsulosin combination

therapy compared with tamsulosin monotherapy, while the absolute risk reduction (risk difference) was 7.7%. Hence, combination therapy should be used only when intended for a long term.

The AEs observed during the combination treatment were typical of α1-blockers and 5-ARIs. Combination therapy is associated with a higher rate of AEs than monotherapy.

3.2.2.8. Apha-1 adrenoceptor antagonists plus antimuscarinic combination therapy. Several studies have investigated the combination of α1-blockers with MRAs in men with OAB and presumed BPO, either as an initial treatment or as a sequential treatment for storage symptoms persisting while on an α1-blocker [112–122]. Combination treatment is superior to α1-blockers or placebo alone in reducing urgency, UUI, voiding frequency, nocturia, IPSS, and QoL [113,122]. Evidence from a meta-analysis showed that combination treatment does not affect voiding function parameters [123]. The effectiveness of therapy is primarily evident in men with moderate-to-severe storage LUTS [124].

AEs of both drug classes were observed with combination treatment using α1-blockers and MRAs. There is a low risk of AUR using α1-blockers and MRAs in men with a PVR of <150 ml [90,125,126]. Most trials were of a short duration and included patients with low PVR volumes at baseline. Therefore, PVR measurements are recommended during combination treatment.

3.2.2.9. Alpha-1 adrenoceptor antagonists plus beta-3 agonist combination therapy. The efficacy and safety of the mirabegron plus tamsulosin combination have been explored in several RCTs [127–129]. Combination treatment results in a mild improvement of urinary frequency and urgency episodes per day compared with α1-blockers alone. The AEs of both drug classes are observed with combined treatment using α1-blockers and mirabegron [127,128,130], and the incidence of AUR is estimated to be 1.7% [128].

Recommendations for the conservative and pharmacological management of MLUTS are provided in Table 2.

Table 2 – Recommendations for the conservative and pharmacological management of MLUTS

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 and self-care information prior to, or concurrent with, treatment.	Strong
Pharmacological management	
Offer α1-blockers to men with moderate-to-severe LUTS.	Strong
Use 5-ARIs in men who have moderate-to-severe LUTS and an increased risk of disease progression (eg, prostate volume >40 ml).	Strong
Counsel patients about the slow onset of action 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 bladder medications in men with a PVR volume of >150 ml.	Weak
Use beta-3 agonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Weak
Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.	Strong
Offer hexane extracted *S. repens* to men with LUTS who want to avoid any potential adverse events especially related to sexual function.	Weak
Inform the patient that the magnitude of efficacy may be modest.	Strong
Offer combination treatment with an α1-blocker and a 5-ARI to men with moderate-to-severe LUTS and an increased risk of disease progression (eg, prostate volume >40 ml).	Strong
Use combination treatment of an α1-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 in men with a PVR volume of >150 ml.	Weak
Use combination treatment of an α1-blocker with mirabegron in patients with persistent storage LUTS after treatment with α1-blocker monotherapy.	Weak

5-ARI = 5α-reductase inhibitor; LUTS = lower urinary tract symptoms; MLUTS = male LUTS; PVR = postvoid residual.

3.2.3. Surgical treatment

Surgery remains the cornerstone of management of LUTS/BPO. As clinical reality is primarily reflected by the surgical approach and not necessarily by a specific technology, surgical management has been divided into five sections: resection, enucleation, vaporisation, alternative ablative techniques, and nonablative techniques.

Some patients value sexual function and perceive higher safety over maximum efficacy; therefore, some patients consciously choose an alternative ablative or nonablative technique despite that it might not be their definitive treatment. In contrast, many urologists are critical of these procedures due to their inferior relief from BOO.

Recommendations for new devices or interventions are included once supported by a minimum level of evidence, as reported previously [131]. To account for evolving evidence, recommendations for some techniques under investigation have been made. These techniques remain under investigation until further studies provide more data on safety and efficacy.

3.2.3.1. Resection of the prostate. Bipolar or monopolar transurethral resection of the prostate (TURP) is the current standard surgical procedure for men with prostate size of 30–80 ml and bothersome moderate-to-severe LUTS secondary to BPO. Monopolar TURP (M-TURP) delivered durable outcomes at follow-up period of 22 yr. Bipolar TURP (B-TURP) achieved short-, mid- and long-term results comparable with those of M-TURP.

The perioperative mortality and morbidity of M-TURP have decreased over time, but remains significant (0.1% and 11.1%, respectively) [132]. B-TURP has a more favourable perioperative safety profile than M-TURP [133–135]. Preoperative use of oral anticoagulants or antiplatelet medications leads to longer catheterisation and hospitalisation times, and higher blood transfusion and re-hospitalisation rates [136]. Comparative evaluations of the effects on overall sexual function, quantified with IIEF-15, showed no differences between B-TURP and M-TURP at 12 mo of

follow-up [137], and the erectile function measured by IIEF-5 appears similar at 12 mo as well [135].

Laser vaporesection of the prostate using thulium: yttrium-aluminium garnet laser (Tm:YAG) vaporesection (ThuVARP) has similar operation, catheterisation, and hospitalisation times to TURP. ThuVARP and TURP are equivalent in terms of IPSS but not Q_{max}, with TURP deemed superior at 12-mo follow-up. ThuVARP and TURP showed similar short-term safety. Mid- to long-term efficacy and safety results compared with TURP are limited.

Transurethral incision of the prostate (TUIP) is performed either by electrocautery or by alternative energy sources such as holmium laser [138]. Efficacy and safety shown by TUIP are similar to those of M-TURP for treating moderate-to-severe LUTS secondary to BPO in men with prostate volume <30 ml; however, the operation time and retrograde ejaculation rate were significantly lower in the conventional TUIP arm, while the reoperation rate was higher after TUIP (18.4%) than after M-TURP (7.2%) [138,139]. The choice between TUIP and TURP should be based on the prostate volume (<30 ml suitable for TUIP).

3.2.3.2. Enucleation of the prostate. Open prostatectomy (OP) is an effective and durable procedure for the treatment of LUTS/BPO, but it is the most invasive surgical method. In the absence of an endourological armamentarium, OP is a reasonable option for men with prostate volume >80 ml. The reintervention rates were 3.0%, 6.0%, and 8.8%, at 1, 5, and 8 yr, respectively [3]. Mortality has decreased significantly (<0.25%), and the estimated transfusion rate is 7–14% [140–143]. Complications include transient urinary incontinence (<10%), bladder neck contracture (BNC), and urethral stricture (6%) [140,143–146].

The efficacy of bipolar transurethral enucleation of the prostate (B-TUEP) is similar to B-TURP and OP in IPSS, QoL score, and Q_{max} at 12- and 36-mo follow-up [147–154]. B-TUEP has a better perioperative safety profile than TURP; yet, the incidence of urethral stricture and BNC is similar [153–155].

Holmium:yttrium-aluminium garnet laser enucleation of the prostate (HoLEP) demonstrates similar mid- to long-term efficacy to M-TURP for smaller prostates (<80 ml) and to B-TURP and OP for larger prostates (>80 ml) [140,144,147,153,156–163]. Several meta-analyses have found that HoLEP has longer operation times, shorter catheterisation and hospitalisation times, reduced blood loss, fewer blood transfusions, and similar urethral strictures (2.6% vs 4.4%) and stress urinary incontinence (1.5% vs 1.5%) rates to those of M-TURP [153,156,158,164,165].

HoLEP can safely be performed in patients taking anticoagulant and/or antiplatelet medications [166,167]; however, robust evidence regarding this practice is lacking. Short- and mid-term erectile function changes were similar between HoLEP and TURP, whereas long-term IIEF scores were significantly better for HoLEP [168,169]. Attempts to maintain ejaculatory function with HoLEP have been successful in up to 46.2% of patients [170].

Enucleation using Tm:YAG laser includes thulium vapoenucleation of the prostate (ThuVEP) and thulium laser enucleation of the prostate (ThuLEP). ThuLEP offers similar efficacy and safety to TURP, B-TUEP, and HoLEP [147,153,171,172]. Scarce evidence for ThuVEP has shown significant improvements in IPSS, Q_{max}, and PVR [173–176]. Comparative studies have reported that ThuVEP is safe in patients with large prostates and in those receiving anticoagulants or antiplatelet medications [174,175]. ThuLEP demonstrates safety similar to TURP/bipolar transurethral (plasmakinetic) enucleation and HoLEP in the short and mid-term [147].

Diode laser enucleation of the prostate (DiLEP) has similar efficacy and safety to B-TURP and B-TUEP, but the evidence is of poor quality. A direct comparison of DiLEP (980 nm) and HoLEP reported comparable perioperative and follow-up outcomes [177]. The retreatment rate should be evaluated in future high-quality RCTs.

Currently, minimal invasive simple prostatectomy (laparoscopic simple prostatectomy and robot-assisted simple prostatectomy) and 532 nm (“GreenLight”) laser enucleation of the prostate are under evaluation due to the lack of high-quality evidence with regard to efficacy and safety [7]. Available data show that minimally invasive simple prostatectomy is feasible in men with prostate volume >80 ml who require surgical treatment; however, more RCTs are needed.

3.2.3.3. Vaporisation of the prostate. Bipolar transurethral vaporisation (B-TUVP) is comparable with TURP in efficacy at 12-mo follow-up [147,157,178]. Regarding the safety profile, B-TUVP has fewer perioperative complications, but the incidences of urethral stricture, ED, and EjD are similar to those of TURP [157,179].

GreenLight laser photoselective vaporisation of the prostate (PVP) uses 80-W potassium titanyl phosphate, 120-W lithium triborate (LBO), and 180-W LBO generator. The efficacy of GreenLight is comparable with that of TURP at 36 mo [147,180]. An RCT comparing PVP with HoLEP, in patients with prostate volume >60 ml, showed comparable symptomatic improvement, but HoLEP provided significantly higher flow rates and lower PVR; furthermore, PVP had a 22% conversion rate to TURP [181]. Although PVP is characterised by a longer operation time, it has shorter catheterisation and hospitalisation times, as well as lower transfusion and clot retention episode rates, and urethral stricture/BNC incidence is similar to that of TURP [157,182]. The 180-W PVP is noninferior to TURP in terms of perioperative complications. The reoperation rate after 180-W XPS laser was comparable with that after TURP but was significantly higher after 120-W HPS laser (11% vs 1.8%; $p = 0.04$) [183,184]. Evidence from case series showed that the 80-, 120-, and 180-W GreenLight lasers are safe in high-risk patients and in those receiving anticoagulation [185–188]. The EjD rate after the GreenLight laser is comparable with that after TURP (49.9% vs 56.7%) [169,189].

Diode laser vaporisation of the prostate remains under investigation due to a lack of strong evidence [190]. Available data show that diode laser vaporisation leads to similar improvements in clinical and symptomatic parameters during short-term follow-up to TURP. In a number of studies, severe postoperative complications such as severe storage

symptoms and persistent incontinence occurred with laser vaporisation of the prostate using 120-W 980-nm diode laser.

3.2.3.4. Alternative ablative techniques. Aquablation is image-guided robotic waterjet ablation therapy (AquaBeam). During mid-term follow-up, aquablation provides noninferior functional outcomes compared with TURP in patients with LUTS and a prostate volume between 30 and 80 ml [191–193]. The retreatment rates were 4.3% and 1.5% for AquaBeam and TURP, respectively; however, the former had fewer complications (26% vs 42%) [191,194]. An SR reported a significant haemoglobin drop (2.06 g/dl), but the need for transfusion was low [195]. However, there are still some concerns about the best methods for achieving post-treatment haemostasis. Among sexually active men, the rate of EjD was lower in the aquablation group than in the TURP group (10% vs 36%).

Prostatic artery embolisation (PAE) can be performed as a day procedure with access to the femoral or radial arteries [196,197]. For both improving symptoms and urodynamic parameters, PAE is inferior to TURP [198–200]. The procedural time and retreatment rate is favourable for TURP, but blood loss, catheterisation, and hospitalisation time are favourable for PAE [199].

A multidisciplinary team approach involving urologists and radiologists is mandatory, and patient selection should be performed by urologists and interventional radiologists. Investigation of patients with LUTS to indicate suitability for invasive techniques should be performed by urologists only. This technically demanding procedure should only be performed by an interventional radiologist with specific mentored training and expertise in PAE [201].

Convective water vapour energy ablation (Rezum system) is an ablative technique currently under investigation. One multicentre RCT compared Rezum with sham treatment [202]. At 3 mo, relief of symptoms, measured by a change in IPSS and Q_{max}, was significantly improved and maintained compared with the sham arm, although only the active treatment arm was followed up to 12 mo. Rezum improves LUTS, preserves sexual function, and is associated with low surgical retreatment rates over 4 yr [203]. More RCTs against a reference technique is needed to confirm the first promising clinical results and to evaluate the mid- and long-term efficacy and safety of water vapour energy treatment.

3.2.3.5. Nonablative techniques. Prostatic urethral lift improves the IPSS, Q_{max}, and QoL; however, these improvements are inferior to those by TURP at 24 mo [204].

Table 3 – Recommendations for the surgical treatment of MLUTS

Recommendations for resection of the prostate	Strength rating
Offer bipolar or monopolar TURP to surgically treat moderate-to-severe LUTS in men with prostate size of 30–80 ml.	Strong
Offer laser resection of the prostate using Tm:YAG laser (ThuVARP) as an alternative to TURP.	Weak
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
Recommendations for enucleation of the prostate	
Offer open prostatectomy in the absence of bipolar transurethral enucleation of the prostate and holmium laser enucleation of the prostate to treat moderate-to-severe LUTS in men with prostate size >80 ml.	Strong
Offer bipolar transurethral (plasmakinetic) enucleation of the prostate to men with moderate-to-severe LUTS as an alternative to TURP.	Weak
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 enucleation of the prostate using the Tm:YAG laser (ThuLEP, ThuVEP) to men with moderate-to-severe LUTS as an alternative to TURP, holmium laser enucleation, or bipolar transurethral (plasmakinetic) enucleation.	Weak
Offer Tm:YAG laser enucleation of the prostate to patients receiving anticoagulant or antiplatelet therapy.	Weak
Offer 120-W 980-, 1318-, or 1470-nm diode laser enucleation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to bipolar transurethral (plasmakinetic) enucleation or bipolar TURP.	Weak
Recommendations for vaporisation of the prostate	
Offer bipolar transurethral vaporisation of the prostate as an alternative to transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with a prostate volume of 30–80 ml.	Weak
Offer 80-W 532-nm 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 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 lasers for the treatment of patients receiving antiplatelet or anticoagulant therapy with a prostate volume of <80 ml.	Weak
Recommendations for alternative ablative techniques	
Offer aquablation * to patients with moderate-to-severe LUTS and a prostate volume of 30–80 ml as an alternative to TURP.	Weak
Inform patients about the risk of bleeding and the lack of long-term follow-up data.	Strong
Offer PAE * to men with moderate-to-severe LUTS who wish to consider minimally invasive treatment options and accept less optimal outcomes than TURP.	Weak
Perform PAE only in units where the work-up and follow-up are performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE-suitable patients.	Strong
Recommendations for nonablative techniques	
Offer prostatic urethral lift (Urolift) to men with LUTS interested in preserving ejaculatory function, with prostate volume <70 ml and no middle lobe.	Strong
Do not offer intraprostatic botulinum toxin-A injection treatment to patients with male LUTS.	Strong

Ho:YAG = holmium:yttrium-aluminium garnet; KTP = potassium titanyl phosphate; LBO = lithium borate; LUTS = lower urinary tract symptoms; MLUTS = male LUTS; PAE = prostatic artery embolisation; ThuLEP = thulium laser enucleation of the prostate; ThuVARP = thulium:yttrium-aluminium garnet laser vaporesection; ThuVEP = thulium vapoenucleation of the prostate; Tm:YAG = thulium:yttrium-aluminium garnet laser; TURP = transurethral resection of the prostate.

Frequent, complications include haematuria, dysuria, pelvic pain, urgency, transient incontinence, and UTIs [205–208]. The retreatment rate was 13.6% over 5 yr. Prostatic urethral lift has a low incidence of sex-related side effects.

Various injectables have been used to improve LUTS, such as botulinum toxin-A (BoNT-A), fexapotidetriflutate (NX-1207), and PRX302 [209]. Results from clinical trials have shown no clinical benefits for BoNT-A compared with placebo for the management of LUTS due to BPO [210,211]. High-quality evidence against reference techniques is lacking. Studies report ambiguous efficacy results; however, safety assessments have reported only a few mild and self-limiting AEs for all injectable drugs [209,212]. An SR and meta-analysis reported low incident rates of procedure-related AEs.

The iTIND is composed of three nitinol-based elongated struts and an anchoring leaflet that remodels the bladder neck and prostatic urethra. Evidence from a multicentre sham-controlled RCT reported that 78.6% of iTIND versus 60% of sham patients showed an IPSS reduction of ≥3 points at 3 mo, while at 12 mo, there were improvements in IPSS (–9.25), Q_{max} (+3.5 ml/s), and QoL score (–1.9)

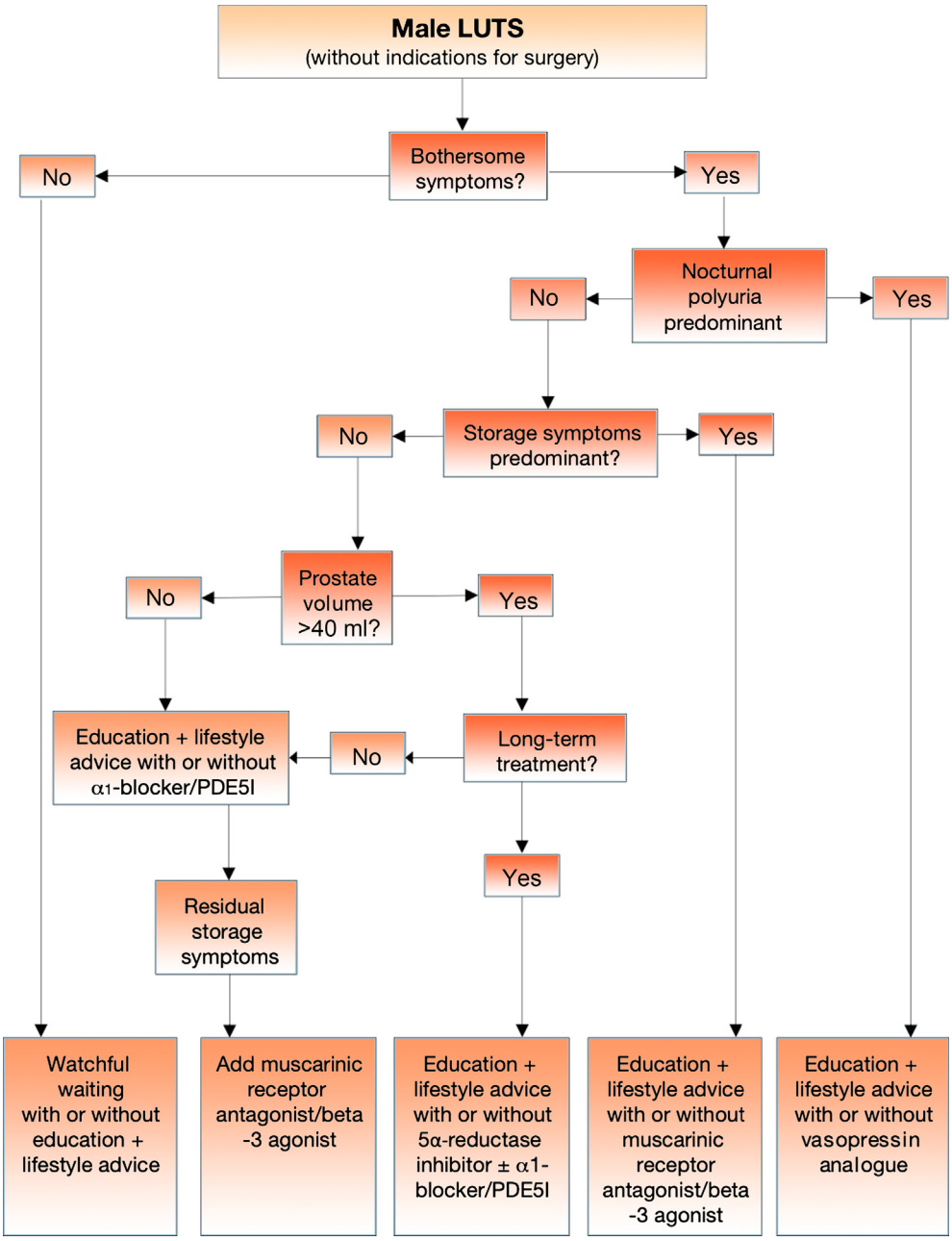

Fig. 2 – Treatment algorithm of male LUTS using medical and/or conservative treatment options. Treatment decisions depend on results assessed during initial evaluation. Note that patients' preferences may result in different treatment decisions. Acronyms: *PDE5I = phosphodiesterase type 5 inhibitors.*

[213]. The device was well tolerated without any new ED or EjD [213].

Recommendations for the surgical treatment of MLUTS are provided in Table 3.

3.3. Patient selection

The choice of treatment depends on the findings of the patient evaluation, ability of the treatment to change the

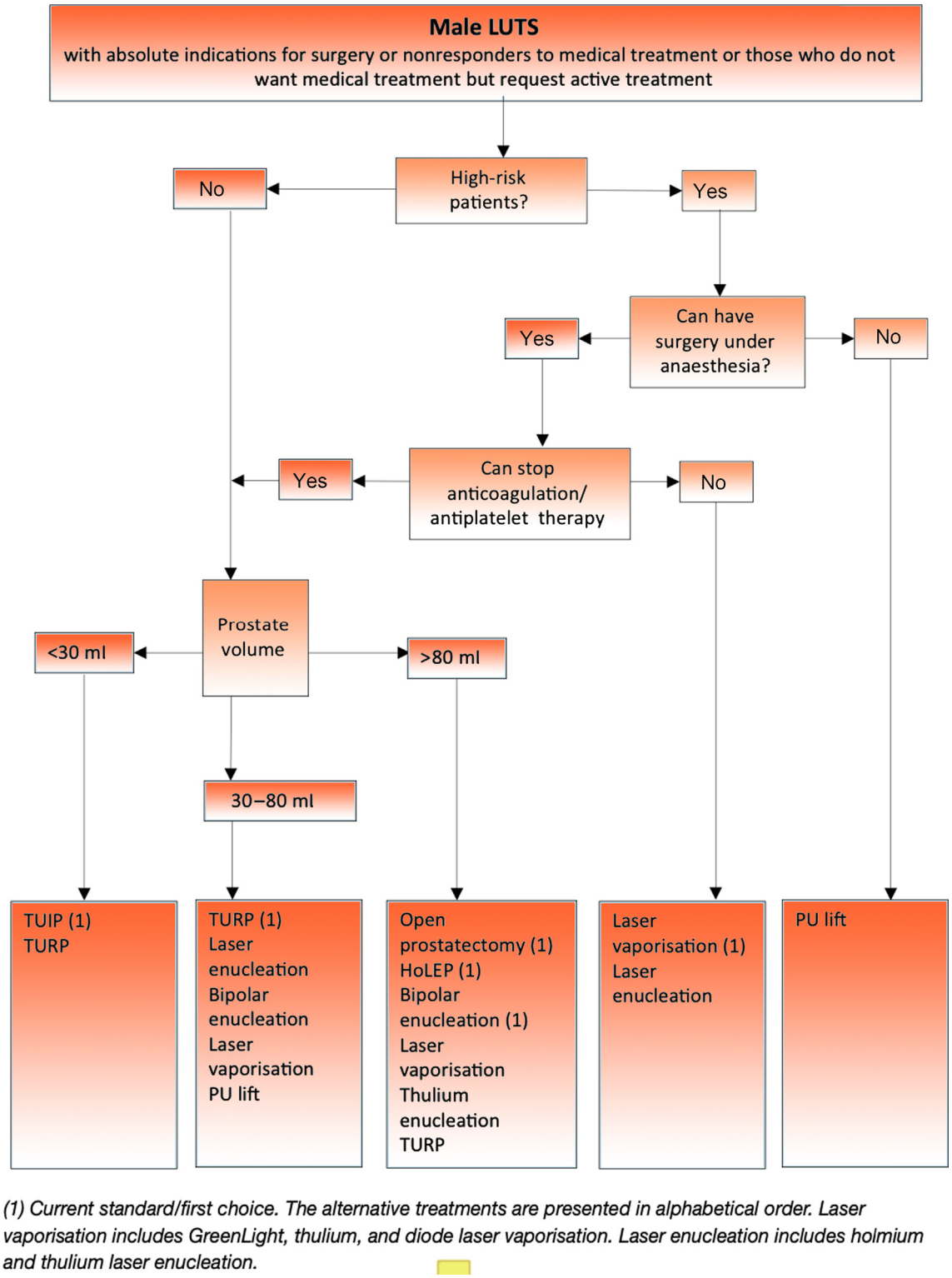

Fig. 3 – Treatment algorithm of bothersome LUTS refractory to conservative/medical treatment or in cases of absolute operation indications. The flowchart is stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size. Acronyms: *(1) Current standard/first choice. The alternative treatments are presented in alphabetical order. 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; PU = prostatic urethral.*

Table 4 – Recommendations for follow-up of MLUTS

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

LUTS = lower urinary tract symptoms; MLUTS = male LUTS.

findings, patient preferences, and expectations to be met in terms of speed of onset, efficacy, side effects, QoL, and disease progression. Behavioural modifications with or without medical treatment are usually the first choice of therapy. Figure 2 provides a flow chart illustrating the medical and conservative treatment choices according to evidence-based medicine and patient profiles.

Surgical treatment is usually required when patients have experienced recurrent or refractory urinary retention, overflow incontinence, recurrent UTIs, bladder stones or diverticula, treatment-resistant macroscopic haematuria due to benign prostatic hyperplasia/benign prostatic enlargement, or dilatation of the upper urinary tract due to BPO with or without renal insufficiency (absolute operation indications and need for surgery). Additionally, surgery is usually needed when patients have not obtained adequate relief from LUTS or PVR using conservative or medical treatment (relative surgical indications). The choice of surgical technique depends on the patient's prostate size, comorbidities, ability to have anaesthesia, patient preference, and willingness to accept surgery-associated specific side effects; availability of the surgical armamentarium; and experience of the surgeon with these surgical techniques. An algorithm for surgical approaches according to evidence-based medicine and patient profiles is shown in Figure 3.

3.4. Follow-up

Follow-up after conservative, medical, or surgical treatment is based on empirical data or theoretical considerations, and is not evidence based. Patients under WW should be reviewed at 6 mo and then annually, provided that there is no deterioration of symptoms. All patients who receive pharmacotherapy should be reviewed 4–6 wk after treatment initiation to determine treatment response. For patients with adequate symptom control without troublesome AEs, the treatment may be continued. Patients should be reviewed at 6 mo and then annually, provided that there is no deterioration of symptoms or development of absolute indications for surgical treatment. Those who receive 5-ARIs should be reviewed after 12 wk and 6 mo to determine their response and AEs. The recommended follow-up tests are history, IPSS, uroflowmetry, and PVR volume. Frequency volume charts should be used in those with OAB or to assess nocturia. PSA should be re-evaluated at 6 mo in those who receive 5-ARIs.

All patients who underwent any type of prostate surgery should be reviewed 4–6 wk after catheter removal to evaluate treatment efficacy and treatment-related complications. If patients have symptomatic relief and are without AEs, no further reassessment is necessary.

Recommendations for follow-up of MLUTS are provided in Table 4.

4. Conclusions

This short version of the EAU guidelines on non-neurogenic MLUTS provides practical guidance for the management of men experiencing LUTS. The full version is available online (https://uroweb.org/guidelines/management-of-non-neurogenic-male-luts).

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Acquisition of data: Schouten.
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