UPDATE – 2022 Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH)

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Introduction

The current document summarizes the state-of-the-art knowledge as it relates to management of male lower urinary tract symptoms (MLUTS) secondary to benign prostatic hyperplasia (BPH) by updating the 2018 Canadian Urological Association (CUA) BPH guideline.¹ The process continues to highlight the essential diagnostic and therapeutic information in a Canadian context. The information included in this document includes that reviewed for the 2010 guideline and further information obtained from an updated MEDLINE search of the English language literature (search terms included BPH, alpha blockers, 5 alpha reductase inhibitor, anti-cholinergic, beta3 agonist, Phosphodiesterase type 5 inhibitor (PDE5I), Transurethral resection of the prostate (TURP), monopolar, bipolar, open simple prostatectomy, enucleation, green light, PVP, aquablation, rezum, urolift, iTiND), as well as review of the most recent American Urological Association (AUA)² and European Urological Association (EAU) guidelines.³ References include those of historical importance, but management recommendations are based on literature published between 2000 and 2021. When information and data is available from multiple sources, the most relevant (usually most recent) article is cited based on committee opinion.

These guidelines are directed toward the typical male patient over 50 years of age, presenting with LUTS and benign prostatic enlargement (BPE) and/or benign prostatic obstruction (BPO). It is recognized that men with LUTS associated with causes other than BPO may require more extensive diagnostic workup and different treatment considerations. We acknowledge that not all patients identify as male. These guidelines should also be applicable to non-binary people, transwomen, and any patients who may have anatomical features of a cis-male genitourinary tract such as a prostate. It is our intent to make these guidelines inclusive to all persons experiencing lower urinary tract symptoms or an enlarged prostate.

In this document, we will address both diagnostic and treatment issues. Diagnostic guidelines are described in the following terms as: mandatory, recommended, optional, or not recommended. The recommendations for diagnostic guidelines and principles of treatment were developed on the basis of clinical principle (widely agreed upon by Canadian urologists) and/or expert opinion (consensus of committee and reviewers). The grade of recommendation will not be offered for diagnostic recommendations. Guidelines for treatment are described using the GRADE approach⁴ for summarizing the evidence and making recommendations

1. Diagnostic guidelines

The committee recommended minor revisions in regard to diagnostic considerations as outlined in the 2018 CUA BPH guideline.¹

1.1. Mandatory

In the initial evaluation of a man presenting with LUTS, the evaluation of symptom severity and bother is essential. Medical history should include relevant prior and current illnesses, as well as prior surgery and trauma. Current medication, including over-the-counter drugs and phytotherapeutic agents, must be reviewed. A focused physical examination, including a digital rectal exam (DRE), is also mandatory. Urinalysis is required to rule out diagnoses other than BPH that may cause LUTS and may require additional diagnostic tests.^{1-3,5,6,7}

- History
- Physical examination including DRE
- Urinalysis

1.2. Recommended

Symptom inventory (should include bother assessment)

A formal symptom inventory (e.g., International Prostate Symptom Score [IPSS] or AUA Symptom Index [AUA-SI]) is recommended for an objective assessment of symptoms at initial consultation, for follow up of symptom evolution for those on watchful waiting, and for evaluation of response to treatment.⁸⁻¹¹

PSA

Testing of prostate-specific antigen (PSA) should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management, as well as those for whom PSA measurement may change the management of their voiding symptoms (ie. estimate for prostate volume which may lead to more precise measurements). Among patients without prostate cancer, serum PSA may also be a useful surrogate marker of prostate size and may also predict risk of BPH progression.^{12,13}

1.3. Optional

In cases where the physician feels diagnostic uncertainty exists, it is reasonable to proceed with one or more of the following:

- Serum creatinine
- Urine cytology
- Uroflowmetry
- Post-void residual (PVR)
- Voiding diary (recommend frequency volume chart for men with suspected nocturnal polyuria)
- Obstructive sleep apnea (OSA) screening for men with nocturia over the age of 50 (STOP BANG questionnaire)
- Sexual function questionnaire

1.4. Not recommended

The following diagnostic modalities are not recommended in the routine initial evaluation of a typical patient with BPH-associated LUTS. **These investigations may be required** in patients with another indication, such as hematuria, diagnostic uncertainty, DRE abnormalities, poor response to medical therapy, or for surgical planning.

- Cytology
- Cystoscopy
- Urodynamics
- Radiological evaluation of upper urinary tract
- Prostate ultrasound
- Prostate biopsy

An algorithm summarizing the appropriate diagnostic steps in the workup of a typical patient with MLUTS/BPH is summarized in Figure 1.

1.5. Further diagnostic considerations for surgery

Indications for surgery

Indications for MLUTS/BPH surgery¹⁻³ include a) recurrent or refractory urinary retention; b) recurrent urinary tract infections (UTIs); c) bladder stones; d) recurrent hematuria; e) renal dysfunction secondary to BPH; f) symptom deterioration despite medical therapy; and g) patient preference. The presence of a bladder diverticulum is not an absolute indication for surgery unless associated with recurrent UTI or progressive bladder dysfunction.

Preoperative testing

Determination of prostate size and extent of median lobe are related to procedure-specific indications (see section on Surgical Treatment). For patients in whom surgery is being considered, cystoscopy should be performed to evaluate prostate size, as well as presence or absence of significant middle/median lobe and/or bladder calculi. Ultrasound (US) (either by transrectal ultrasound [TRUS] or transabdominal US) is recommended to determine the volume of the prostate and the extent of median lobe presence in order to select appropriate modality of surgical therapy. This information can also be obtained from a recent abdominal CT or MRI.

2. Treatment guidelines

2.1 Principles of treatment

Therapeutic decision-making should be guided by the severity of the symptoms, the degree of bother, and patient preference. Information on the risks and benefits of BPH treatment options should be explained to all patients who are bothered enough to consider therapy. Patients should be invited to participate as much as possible using a shared-decision making approach to determine the best treatment selection for them. This can be facilitated with the use of the Canadian Urological Association Surgical BPH Decision Aid.¹⁴ The patient's therapeutic goal of management should be discussed and documented.

Patients with mild symptoms (e.g., IPSS <7) should be counselled about a combination of lifestyle modification and watchful waiting. Patients with mild symptoms and severe bother should undergo further assessment.

Treatment options for patients with bothersome moderate (e.g., IPSS 8–18) and severe (e.g., IPSS 19–35) symptoms of BPH include watchful waiting/lifestyle modification, as well as medical, minimally invasive, or surgical therapies.

Physicians should use baseline age, LUTS severity, and prostate volume to advise patients of their individual risk of symptom progression, acute urinary retention or future need for BPH-related surgery (these risk factors identify patients at risk for progression).

A variety of lifestyle changes may be suggested for patients with non-bothersome symptoms. These can include the following:

- Fluid restriction, particularly prior to bedtime
- Avoidance of caffeinated beverages, alcohol, and spicy foods
- Avoidance/monitoring of some drugs (e.g., diuretics, decongestants, antihistamines, antidepressants)
- Timed or organized voiding (bladder retraining)
- Avoidance or treatment of constipation
- Weight loss and prevention or treatment of conditions associated with metabolic syndrome
- Pelvic floor physical therapy (PFPT) in cases of suspected non-relaxing pelvic floor dysfunction (causing LUTS, pelvic and or genital pain, bowel and sexual dysfunction, etc.) or overactive bladder and/or urinary incontinence (Kegel exercises, urge suppression, etc.)

2.2. Post-treatment followup

Watchful waiting

Patients on watchful waiting should have periodic physician-monitored visits to monitor for any complications associated with their BPO. Physicians should assess either progression of bother i.e. validated questionnaire such as IPSS (subjective) or worsening urinary function i.e. uroflowmetry or post-void residual (objective)

Medical therapy

Patients started on medical therapy should have follow-up visit(s) to assess for efficacy and safety (side effects) of medications. If the patient-directed therapeutic goal is achieved, the patient may be followed by the primary care physician as part of a sharedcare approach. The primary care physician should be counselled with clear instructions on follow-up and re-referral as necessary.

Surgical therapy

Patients who receive prostate surgery for BPH should be reviewed 4–6 weeks after catheter removal to evaluate treatment response (with symptom assessment [e.g., IPSS], and if indicated, uroflowmetry, and PVR volume). Side effects and adverse events should also be screened for. The individual patient's circumstances and type of surgical procedure employed will determine the need for and type of further follow-up required by the urologist and/or primary care physician.

2.3 Medical therapy

The committee recommended few changes in the recommendations for the primary medical management of BPH and MLUTS with alpha-blockers and/or 5-alpha-reductase inhibitors (5ARIs) since 2018. Since the 2018 guideline publication, new evidence is available in regard to other medical therapy, namely beta-3 agonists for the treatment of MLUTS.

2.3.1. Alpha-blockers

Alfuzosin, doxazosin, tamsulosin, terazosin, and silodosin are appropriate treatment options for LUTS secondary to BPH.¹²⁻²³ Doxazosin and terazosin require dose titration and blood pressure monitoring. Alpha-blockers do not alter the natural progression of BPH (little impact on prostate growth, risk of urinary retention or the need for BPH-related surgery). The most common adverse effect associated with alpha-blockers is dizziness (2–10%, with the highest rates for terazosin and doxazosin), while ejaculatory disturbances are most often reported with tamsulosin and silodosin. Floppy iris syndrome has been reported in patients on alpha-blockers, particularly tamsulosin, but this does not appear to be an issue in men with no planned cataract surgery and can be managed by the ophthalmologist, who is aware that the patient is on the medication.²⁴Although there are differences in the adverse event profiles of these agents, all five agents appear to have equal clinical effectiveness. The choice of agent should depend on the patient's comorbidities, side effect profiles, and tolerance.

We recommend alpha-blockers as an excellent first-line therapeutic option for men with symptomatic bother due to BPH who desire treatment (strong recommendation, evidence level A).

2.3.2. 5-ARIs

Several studies have demonstrated that 5-ARI therapy, in addition to improving symptoms and causing a modest (25–30%) shrinkage of the prostate, can alter the natural history of BPH through a reduction in the risk of acute urinary retention (AUR) and the need for surgical intervention.^{25,26} Efficacy is noted in patients with a prostate volume >30 cc (and/or PSA levels >1.5 ng/ml). 5-ARI treatment is associated with erectile dysfunction, decreased libido, ejaculation disorders, and rarely gynecomastia and post-finasteride syndrome.²⁷

We recommend 5-ARIs (dutasteride and finasteride) as appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement (*strong recommendation, evidence level A*).

2.3.3. Combination therapy (alpha-blocker and 5-ARI)

Prognostic factors suggesting the potential for BPH progression risk^{28,29} include: serum PSA >1.4 ng/mL, age >50 years, and gland volume >30 cc. Clinical trial results have shown that combination therapy significantly improves symptom score and peak urinary flow compared with either of the monotherapy options. Combination medical therapy is associated with decreased risk of urinary retention and/or prostate surgery, but also the additive side effects of dual therapy (in particular ejaculatory disturbances).^{30,31}

We recommend that the combination of an alpha-adrenergic receptor blocker and a 5-ARI as an appropriate and effective treatment strategy for patients with symptomatic LUTS associated with prostatic enlargement (> 30 cc) (strong recommendation, evidence level B).

It may be appropriate to consider discontinuing the alpha blockers in patients successfully managed with combination therapy after 6–9 months of combination therapy.^{32,33}

We suggest that patients successfully treated with combination therapy may be given the option of discontinuing the alpha-blocker. If symptoms recur, the alpha-blocker should be restarted (conditional recommendation, evidence level B).

2.3.4. Antimuscarinic and beta-3 agonist medications

Storage symptoms (urgency, frequency, nocturia) are a bothersome component of MLUTS associated with BPH. Antimuscarinics (anticholinergics) and the beta-3 agonist have demonstrated improvements in male storage LUTS (with and without BPH), including reductions in frequency, urgency, and urgency incontinence episodes.^{34,35} Studies of contemporary antimuscarinics, such as tolterodine and fesoterodine and the beta-3 agonist, mirabegron have shown low rates of urinary retention, although caution should be exercised in elderly men and those with significant bladder outlet obstruction (BOO) (with PVR >250–300 cc since there is little evidence of safety in men with high PVRs).

We suggest that antimuscarinics or beta-3 agonists may be useful therapies in predominately storage symptoms and BPH with caution in those with significant BOO and/or an elevated PVR (conditional recommendation, evidence level C).

2.3.5. Antimuscarinic or beta-3 agonist medications in combination with alpha blockers Mixed LUTS (storage and voiding symptoms) can be managed safely with alphablockers in combination with antimuscarinics or beta-3-agonists. Clinical trials studied the following drug combinations: tamsulosin 0.4 mg plus solifenacin 5 mg, tamsulosin plus tolterodine ER 4 mg and tamsulosin 0.4 mg plus mirabegron 50 mg. ³⁶⁻⁴¹ Evidence showed that combination therapies provide significant improvement in storage symptoms without clinical or statistical evidence of decreased maximum flow rate on uroflowmetry (Qmax) or increased risk of retention. Patients with high PVR> 200 ml or previous history of acute urinary retention were excluded.

We suggest that alpha-blocker combination with antimuscarinics or beta-3 agonists may be useful therapies in MLUTS/BPH in men with both voiding and storage symptoms and failure of alpha blocker monotherapy.

(conditional recommendation, evidence level B).

2.3.5. Phosphodiesterase inhibitors

PDE5Is have been shown to not only improve erectile function, but also are an effective treatment for male LUTS. Tadalafil 5 mg daily, due to its longer half-life, is approved for male LUTS. Studies have shown improvements in IPSS, storage and voiding symptoms, and quality of life.⁴² Evidence shows that combination therapy of PDE5I and alphablockers is superior to alpha-blockers alone in men with voiding symptoms and erectile dysfunction. ⁴³

We recommend long-acting PDE5Is as monotherapy for men with MLUTS/BPH, particularly in men with both MLUTS and erectile dysfunction (strong recommendation; evidence level B).

2.3.6. Desmopressin

Nocturnal polyuria (NP) often coexists with MLUTS and BPH, but may not respond to typical BPH pharmacotherapies. NP is a major contributing factor of nocturia and is defined by the International Continence Society (ICS) as an abnormally large volume of urine during sleep. More specifically, 33% of the total daily urine volume occurs at night, while the daily total urine output remains normal. Desmopressin is a synthetic analogue of the antidiuretic hormone, arginine vasopressin (AVP). Desmopressin reduces total nocturnal voids and increases hours of undisturbed sleep by reducing urine production in men with nocturnal polyuria.⁴⁴ While the risk of hyponatremia is low in men with normal baseline serum sodium, sodium must be checked at baseline in all men, and 4–8 days as well as 30 days after initiation of treatment in men taking desmopressin melts or men ≥ 65 years taking 50 µg oral disintegrating tablet. In men whose predominant symptom is

bothersome nocturia and who do not respond to conservative measures or other monotherapies, desmopressin should be considered.

We recommend desmopressin as a therapeutic option in men with MLUTS/BPH with nocturia as result of nocturnal polyuria (*conditional recommendation, evidence level B*).

2.3.7. Phytotherapies

Plant-based herbal preparations may appeal to some patients. Common formulations include Serenoa repens (saw palmetto), Pygeum africanum (African plum bark), and Urtica dioica (stinging nettle). Phytotherapies lack consistent formulation, predictable pharmacokinetics, and regulatory oversight. Numerous studies and Cochrane meta-analyses report no significant difference between phytotherapies and placebo, as measured by AUA-SI, peak flow rates, prostate volume, residual urine volume, PSA, or quality of life.⁴⁵⁻⁴⁸ There are few side effects associated with phytotherapies but there are important potential drug interactions.

We do not recommend phytotherapies as standard treatment for MLUTS/BPH

(strong recommendation, evidence level B).

2.4. Surgical therapy

2.4.1. Transurethral resection of the prostate (TURP)

Monopolar TURP (M-TURP)

M-TURP remains the primary, standard-reference surgical treatment option for moderate to severe LUTS due to BPH in patients with prostate volume $30-80 \text{ cc.}^{49}$ Perioperative mortality has decreased over time and is currently approximately 0.1%, while morbidity is related to prostate volume (particularly >60 cc).⁵⁰ Contemporary series have reported the following complications: bleeding (2–9%), capsule perforation with significant extravasation (2%), TUR syndrome (0.8%), urinary retention (4.5–13%), infection (3–4%; sepsis 1.5%), incontinence (<1%), bladder neck contracture (3–5%), retrograde ejaculation (65%), erectile dysfunction (6.5%), and need for surgical retreatment (2%/year).^{51,52}

We recommend M-TURP as a standard first-line surgical therapy for men with moderate to severe MLUTS/BPH with prostate volume of 30–80 cc (strong recommendation, evidence level A).

Bipolar TURP (B-TURP) (including Bipolar plasma kinetic vaporization) B-TURP offers a resection alternative to M-TURP in men with moderate to- severe LUTS secondary to BPH with similar efficacy, but lower perioperative morbidity.⁵²⁻⁵⁴ The predominant difference between M-TURP and B-TURP is the decreased risk of perioperative bleeding <u>and TUR syndrome</u>. The choice of B-TURP should be based on equipment availability, surgeon experience, and patient preference.

We recommend B-TURP as a standard first-line surgical therapy for men with moderate to severe MLUTS/BPS with prostate volume of 30–80 cc (strong

recommendation, evidence level B).

2.4.2. Open simple prostatectomy (OSP)

OSP is an effective treatment alternative for men with moderate to severe LUTS with substantially enlarged prostates >80 cc and who are significantly bothered by symptoms.⁵⁵ Other indications for OSP include plans for concurrent bladder procedure, such as diverticulectomy or cystolithotomy (for very large bladder calculi) and in men who are unable to be placed in dorsal lithotomy position due to severe hip disease.⁵⁶ OSP is the most invasive surgical method requiring longer hospitalization and catheterization. The estimated transfusion rate has been reported from 7–14%.^{55,56} Complications include transient urinary incontinence (8–10%), bladder neck contracture, and urethral stricture (5-6%).^{55,56}

We recommend OSP as a first-line surgical therapy when anatomic endoscopic enucleation of the prostate (AEEP) (see below) is unavailable, for men with moderate to severe MLUTS/BPS and enlarged prostate volume >80 cc (strong recommendation, evidence level A).

2.4.3. Minimally invasive simple prostatectomy

With the advent of minimally invasive surgery starting with laparoscopy and proceeding to robotic assisted laparoscopy the natural evolution came to the OSP as well. These techniques are still relatively new.

Laparoscopic simple prostatectomy (LSP) and Robot-assisted simple prostatectomy (RASP), like OSP, are indicated in patients with significantly enlarged prostates (>80cc-100cc) and bothersome LUTS. ^{57,58} They are also beneficial when performed due to concomitant pathology such as large bladder stones or bladder diverticulum. There are no randomized control trials comparing LSP and RASP to OSP or to any other enucleation procedure. The largest retrospective series includes both techniques and has shown both to be safe and efficacious. ⁵⁹ A recent systematic review found that RASP showed similar improvements in IPSS, PVR, Qmax, and QoL, while having similar complication rates and EBL to laser vaporization and enucleation of the prostate.⁶⁰ In comparison to OSP, the <u>length of stay (LOS)</u> and EBL are significantly lower for RASP. ⁶¹ Finally, catheterization time and LOS are longer with RASP compared to laser enucleation of the prostate.⁶⁰

We recommend LSP or RASP as an alternative surgical therapy for men with moderate to severe MLUTS/BPS and enlarged prostate volume >80 cc in centers where there are surgeons with high level expertise in robotics or laparoscopy (conditional recommendation, evidence level B).

2.4.4. Anatomic endoscopic enucleation of the prostate (AEEP)

Anatomical endoscopic enucleation of the prostate (AEEP) adopts the principle of open prostatectomy (OP) using different energy sources and instruments. The holmium laser (HoLEP) with or without Moses technology, GreenLight laser (GreenLEP), monopolar enucleation (MonolEP), bipolar enucleation (BipolEP), diode laser (DiLEP), thulium laser (ThuLEP), and thulium fiber laser (ThuFLEP) are among the available energy sources. The efficacy and safety of AEEP, regardless of the energy source utilized, have been widely demonstrated.⁶²

When compared to TURP and OSP, AEEP was associated with greater improvements in IPSS, Qmax, and PVR. AEEP resulted in greater prostate tissue removal, reduced hemoglobin loss, shorter catheterization time, and shorter LOS.⁶³ Recent evidence supports the use of AEEP in patients with BPH on anticoagulant (AC) or antiplatelet (AP) therapy. ⁶⁴⁻⁶⁶ AEEP has demonstrated durable results with a low reoperation rate of 0-3.7% (attributed to adenoma regrowth) on long-term follow-up of up to 18 years.⁶⁷⁻⁷¹ The procedure requires a steep learning curve (estimated >20–50 cases)⁷².

We recommend AEEP as an alternative to TURP or OSP in men with moderate to severe LUTS and any size prostate > 30 cc if performed by an AEEP-trained surgeon. AEEP can be safely performed in patients on AC/AP therapy (strong recommendation, evidence level A).

2.4.5. Photoselective vaporization of the prostate (PVP)

Greenlight-PVP (180W XPS and 120W HPS systems) provides comparable outcomes to TURP in terms of durable improvements in IPSS and Qmax with similar overall complication rate.⁷³ Five-year mid-term durability of XPS reported a 1.1% retreatment rate in prostates with volumes on average of 80 grams.⁷⁴ In the GOLIATH international multicenter RCT study, ^{68,75} comparing the 180W XPS PVP to TURP for prostate volumes 30-80cc, there was a statistically significant difference in early adverse events,

notably bleeding-related within the first 30 days favouring XPS PVP. Compared to TURP, PVP has better perioperative safety, shorter catheterization time, shorter hospitalization.⁷⁶ Multiple studies have demonstrated that PVP is safe and effective for elderly men, with significant medical comorbidities,⁷⁷ large median lobes,⁷⁸ and patients who continue their anticoagulant/ antiplatelet therapy, with negligible transfusion rates.⁷⁹⁻⁸¹ Further to Greenlight safety profile, PVP has been shown to be a cost-effective alternative to TURP in the Canadian setting.⁸² There exists no size or shape limitation to PVP; only surgeon expertise and clinical judgement dictates size limitations.

We recommend PVP as an alternative to M-TURP or B-TURP in men with moderate to severe LUTS (*strong recommendation based on high-quality evidence*). We <u>also</u> suggest Greenlight PVP therapy as an alternate surgical approach in men on anticoagulation or with a high cardiovascular risk (*conditional recommendation*, *evidence level B*).

2.4.4. Transurethral incision of the prostate (TUIP)

TUIP is an appropriate therapy for men with a small prostate size <30 cc without a middle lobe.⁸³ Symptoms and voiding parameters are improved, the risk of retrograde ejaculation and TUR syndrome is reduced (18.2% and 0%) compared to TURP, however, the risk of surgical retreatment for LUTS related to BPH are significantly higher for TUIP (18.4%) than after TURP (7.2%).

We recommend TUIP to treat moderate to severe LUTS in men with prostate volume <30 cc without a middle lobe. Patients should be made aware of the high retreatment rate (strong recommendation, evidence level B).

2.4.5. Minimally invasive techniques

Transurethral microwave therapy (TUMT)

TUMT is an option for elderly patients with significant comorbidities or greater anaesthesia risks as this procedure can be performed under local anesthesia.^{84,85} Although short-term success for LUTS improvement have been reported, the long-term durability of TUMT is limited with five-year cumulative retreatment rates between 42 and 59%.⁸⁶ TUMT should not be performed in patients with a significant median lobe.

We suggest TUMT therapy as a consideration for treatment of carefully selected, well-informed men (*conditional recommendation, evidence level C*).

Prostatic stents

Temporary stents can provide short-term relief from BPO in patients temporarily unfit for surgery.⁸⁷ In general, stents are subject to misplacement, migration, and poor tolerability because of exacerbation of LUTS and encrustation. Given these common side effects, prostatic stents have a limited role in the treatment of moderate to severe LUTS. A newer generation of stents are currently being evaluated and may provide an alternative surgical option for the management of BPH LUTS in the future.

We suggest prostatic stents only as an alternative to catheterization in men unfit for surgery with a functional detrusor (conditional recommendation, evidence level C).

Prostatic urethral lift

The prostatic urethral lift procedure or Urolift[®] (small, permanent, suture-based nitinol tabbed implants compress encroaching lateral lobes delivered under cystoscopic guidance) provides less effective, but adequate and durable improvements in IPSS and QMax compared to TURP while preserving sexual function (no reported retrograde ejaculation observed at 12 months).⁸⁸ Most complications are mild and resolve within four weeks but include dysuria (34%), hematuria (26%), pelvic pain (19%), urge incontinence (7%), and UTI (3%). Surgical retreatment was 13.6% over five years.⁸⁹ A recent study (MedLift study) reported on the use of prostatic urethral lift in patients with a median lobe. For middle lobe deployment, the intravesical tissue is pulled into the prostatic fossa and affixed to either side of the urethra. 44 patients underwent this technique and results are very similar to the pivotal L.I.F.T. trial regarding improved IPSS, and IPSS QoL while preserving ejaculatory function. It should be noted that follow up for this study was only 12 months.⁹⁰

We suggest that prostatic urethral lift (Urolift) may be considered as an alternative treatment for men with LUTS interested in preserving ejaculatory function, with prostates <80 cc. Prostatic urethral lift can be also be offered to patients with a small to moderate median lobe and bothersome LUTS. Patients (with or without a median lobe) should be made aware of the higher retreatment rate at 5 years (conditional recommendation, evidence Level C).

Convective water vapour energy ablation

Ablation using the Rezum[®] system (uses the thermodynamic principle of convective energy transfer), report significant improvement of IPSS and Qmax at three months and sustained until 12 months⁹¹ with preservation of erectile and ejaculatory function.⁹² Recent five -year results have confirmed durability of the positive clinical outcomes with a 57% reduction in IPSS, 45% increase in quality of life and 44% increase in Qmax. Surgical retreatment rate is 4.4% at 5 years.⁹³

We suggest that Rezum system of convective water vapour energy ablation may be considered an alternative treatment for men with LUTS interested in preserving ejaculatory function, with prostates <80 cc, including those with <u>a</u> median lobe (*conditional recommendation, evidence level C*).

Image-guided robotic waterjet ablation

Aquablation (robotic-guided hydrodissection ablates prostatic parenchyma while sparing collagenous structures such as blood vessels and the surgical capsule)⁹⁴ has shown comparable improvements in efficacy and safety compared to TURP in men with <80 cc prostates .⁹⁵ Additional studies have also demonstrated efficacy and safety in glands 80-150 cc . Aquablation preserves erectile and ejaculatory function in nearly 100% and approximately 90% of patients, respectively. Five-year retreatment rates are low (6% at 5 years).

We suggest that Aquablation be offered to men with LUTS interested in preserving ejaculatory function, with prostates < 150 cc, with or without <u>a</u> middle lobe. (conditional recommendation, evidence level C).

Temporary implantable nitinol device (iTind)

iTind is a temporary (five days and then removed under local anaesthetic), mechanical, stent-like device designed to remodel the bladder neck and the prostatic urethra through pressure necrosis.

Three prospective, randomized clinical trials (n=269) have demonstrated IPSS reduction of -45% to -60%, Qmax increase in +50% to +110%, no changes in erectile or ejaculatory function and a retreatment rate of 9% at 3 years.⁹⁶⁻⁹⁸ Long term durability studies are pending.

We recommend that iTind may be offered to men with LUTS interested in preserving ejaculatory function, with prostates 30-80 cc. Patients should be made aware of the higher retreatment rate at 3 years (conditional recommendation, evidence level C).

Prostatic artery embolization (PAE)

PAE is a minimally invasive treatment option exclusively performed by interventional radiologists at specialized centres. PAE results in significant IPSS, Qmax, and PVR improvement compared to baseline at 12 months,⁹⁹ however, inferior outcomes compared to TURP ¹⁰⁰⁻¹⁰² or OSP.¹⁰³ Although PAE has reportedly fewer complications than TURP, non-targeted embolization may lead to rare ischemic complications like transient ischemic proctitis, bladder ischemia, urethral and ureteral stricture, or seminal vesicles

ischemia.¹⁰⁴ Efficacy of PAE may be more advantageous in prostate volumes larger than 80 mL,¹⁰⁵ and can be considered as a treatment for gross hematuria of prostatic origin.¹⁰⁶

At centers with urological and radiological collaboration and technical expertise, highly selected, well-informed patients may be offered PAE if they wish to consider an alternative treatment option. Patients should be informed of lack of long-term durability (conditional recommendation, evidence level C).

Algorithms summarizing the management of a patient with MLUTS/BPH are summarized in Figures 2, 3.

2.5. Special situations

Acute urinary retention (AUR)

Data suggest that in patients with AUR, the use of alpha-blockers (specifically tamsulosin, alfuzosin, and silodosin) during the period of catheterization will increase the chances of successful voiding after catheter removal,^{107,108} while the addition of a 5ARI may decrease the risk of future prostate surgery.^{30,31,109}

We suggest that men with AUR secondary to BPH may be offered alpha-blocker therapy during the period of catheterization (conditional recommendation, evidence level B).

Detrusor underactivity (DU)

There is no effective treatment for DU, defined as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span.¹¹⁰ In primary DU, treatment approach should be to facilitate bladder emptying, identify agents that can decrease bladder contractility, or increase urethral resistance. Behavioural modification, including scheduled voiding and or double voiding, clean intermittent self-catheterization (CIC), or indwelling catheters, are optional strategies.¹¹¹ The data suggests that DU is not necessarily a contraindication for TURP or enucleation.^{112,113}

We have no evidence-based specific recommendation for management of detrusor underactivity.

BPH-related bleeding

A complete assessment, including history and physical examination, urinalysis (routine microscopy, culture and sensitivity, cytology), upper tract radiological assessment and cystoscopy, is necessary to exclude other sources

of bleeding. Finasteride has been reported to reduce the risk of recurrent BPH-related hematuria.¹¹⁴

We suggest that a trial with a 5ARI is appropriate in men with BPH-related hematuria (*conditional recommendation, evidence level C*).

BPH patients with prostate cancer concern

The BPH patient with an elevated serum PSA and negative prostate biopsy may be counselled on the potential benefits of 5ARI therapy (finasteride, dutasteride) for prostate cancer detection risk reduction.^{115,116} The patient must be aware of the possible low absolute increased risk (0.5–0.7%) in incidence of high-grade (Gleason 8–10) cancer with 5ARI use. Most experts believe this phenomenon was observed due to an artifact of prostate glandular cytoreduction, induced by the 5ARI, and it appears there is no demonstrable increase in prostate cancer mortality.¹¹⁷ Patients on 5ARI therapy who experience a rising PSA 6–12 months after PSA nadir is reached should be assessed for the possibility of high-grade prostate cancer.¹¹⁸

We recommend case-to-case patient-specific informed discussion and close PSA follow-up, as indicated in men on 5ARI therapy treatment for BPH (conditional recommendation, evidence level B).

Summary

MLUTS secondary to BPH remains one of the most common age-related disorders afflicting men. As the aging of the Canadian population continues, more men will be seeking advice and looking for guidance from their healthcare providers on the management of their symptoms. The information offered in this guideline document, based on consensus evaluation of the best available evidence, will aid Canadian urologists as they strive to provide state-of-the-art care to their patients.

Competing interests

Dr. Elterman has attended advisory boards for, is a speaker for, and has received grant funding from Allergan, Astellas, Boston Scientific, Ferring, Medtronic, and Pfizer; and has participated in clinical trials supported by Astellas, Medtronic, Meditate and Procept Biorobotics. Dr. Aube-Peterkin is an investigator for clinical Optilume trial supported by Urotronic. Dr. Elmansy has received honoraria from Boston Scientific, Lumenis, and Clarion Medical Technologies. Dr. Zorn has received honoraria from Boston Scientific and as a proctor/lecturer for Greenlight; and participated in the WATER 2 supported by Procept Biorobotics. Dr. Bhojani is a consultant for Boston Scientific, Olympus, and Procept BioRobotics; and has participated in the WATER 2 trial supported by Procept BioRobotics.

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Figures and Tables

Figure 1. Algorithm of appropriate diagnostic steps in the workup of a typical patient with male lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH). PE: physical exam; PSA: prostate-specific antigen; PVR: post-void residual; U/A: urinalysis.

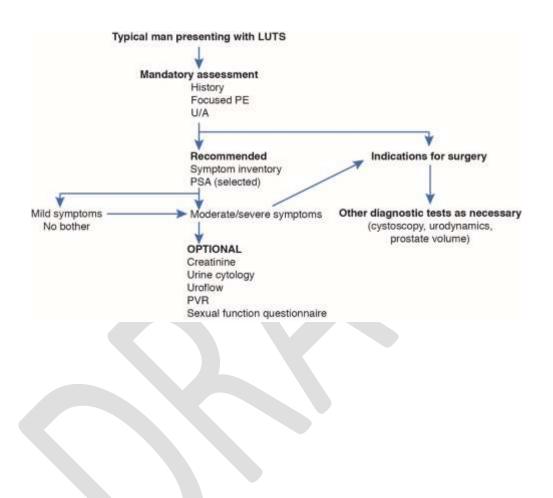


Figure 2. Male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH) management algorithm. ED: erectile dysfunction; PDE5: phosphodiesterase type 5; PSA: prostate-specific antigen.

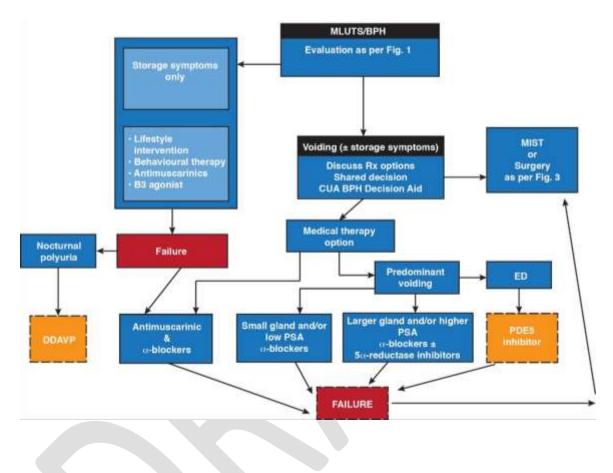


Figure 3. Treatment algorithm of bothersome lower urinary tract symptoms (LUTS) refractory to conservative/medical treatment or in cases of absolute operation indications. The flowchart was stratified by the patient's ability to have anesthesia, cardiovascular risk, and prostate volume. *Current standard/first choice. The alternative treatments are presented in alphabetical order. **Must exclude the presence of a middle lobe. BPH: benign prostatic hyperplasia; B-TURP: bipolar transurethral resection of the prostate; HoLEP: holmium laser enucleation of the prostate; iTIND: temporary implantable nitinol device; M/TURP: monopolar transurethral resection of the prostate; TUIP: transurethral incision of the prostate; TUMT: transurethral microwave therapy.

