

Minimally invasive interventions for lower urinary tract symptoms: What sits between medical therapy and transurethral resection of the prostate



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Background

There are a variety of medical and surgical treatment options available today for the management of lower urinary tract symptoms (LUTS) secondary to bladder outlet obstruction due to benign prostatic hyperplasia (BPH).

Objective

The aim of this paper is to highlight the various treatment options available for the management of bladder outlet obstruction secondary to BPH and discuss the benefits and potential drawbacks of each.

Discussion

Lifestyle and dietary modification and medical therapies, such as an alpha-1 blocker as monotherapy, should be considered as first-line when initially counselling a patient for LUTS secondary to bladder outlet obstruction due to BPH. If bothersome LUTS persist despite medical management, or if medical management is not suitable or preferable, then surgical interventions can be considered. The mainstay of surgical intervention has traditionally been transurethral resection of the prostate (TURP); however, the treatment landscape is rapidly evolving with the development of minimally invasive procedures.

MALE LOWER URINARY TRACT SYMPTOMS

(LUTS) secondary to bladder outlet obstruction due to benign prostatic hyperplasia (BPH) represents a significant burden of disease in men globally, afflicting an estimated 30% of men aged >50 years.¹ In Australia, LUTS due to BPH affects at least one in every five Australian men aged between 35 and 80 years.² It is well known that LUTS such as urinary frequency, urgency, urinary incontinence and nocturia are associated with reduced quality of life and depression.^{3,4}

Initial management involves medical therapy; however, up to one-quarter of men discontinue or are non-compliant with their medications due to inadequate relief or side effects.⁵ In those who fail medical management, there are various surgical options available.

Aim

The aim of this paper is to highlight the various treatment options available today for management of bladder outlet obstruction secondary to BPH and discuss the benefits and potential drawbacks of each.

Lifestyle modification and medical therapy

The European Association of Urology (EAU) guidelines recommend lifestyle

and dietary modification as first-line when initially consulting a patient for LUTS.⁶ Lifestyle advice includes reducing fluid intake during periods when urinary frequency is most inconvenient, such as while asleep or out in public; avoiding diuretic irritants such as caffeine or alcohol and rationalising medications to reduce the urinary side effect profile. Techniques such as relaxation and double voiding techniques are recommended, aimed at relaxing the perineum, improving the posture of the pelvis and taking the time necessary to complete urination.

In men with moderate-to-severe LUTS, alpha 1-adrenoceptor antagonists (α 1-blockers) can be offered as first-line medical therapy. Alpha 1-blockers aim to inhibit the effect of endogenously released noradrenaline on smooth muscle cells in the prostate and thereby reduce prostate tone and bladder outlet obstruction.⁷ Clinical trials have demonstrated an improvement in both storage and voiding LUTS of at least 25% in the majority of patients, and an increase in the maximum flow rate (Qmax) by 20–30%.^{8,9} The most widely used α 1-blockers currently in Australia are tamsulosin and silodosin. The most frequent adverse side effects of α 1-blockers are orthostatic hypotension and retrograde ejaculation; however, they are generally well tolerated.

5-Alpha reductase inhibitors (5-ARIs) can provide additional benefit for patients with a significantly enlarged prostate. They are often used in combination with an α 1-blocker (eg Duodart). Long-term studies have demonstrated that combination therapy is superior to α 1-blocker or 5-ARI monotherapy in improving symptoms and Qmax.¹⁰ The 5-ARIs inhibit the action of dihydrotestosterone and induce involution and apoptosis of the prostatic epithelium, leading to prostate size reduction.¹¹ It takes 6–12 months for 5-ARIs to exert their full effect. Studies have demonstrated that 5-ARIs can decrease prostate volume, improve urinary symptoms based on the patient's International Prostate Symptom Score (IPSS) by approximately 15–30%, and increase Qmax by 1.5–2.0 mL/s after two to four years of treatment.^{10,12,13} Patients most likely to benefit from 5-ARI have a prostate volume of \geq 40 cc or greater (normal range 20–25 cc).¹⁴ The potential sexual side effects (reduced libido, erectile and ejaculatory dysfunction) are a deterrent for some patients. An alternative pharmacological option for treating male LUTS is low-dose phosphodiesterase-5 inhibitor (tadalafil). This can be a good option for patients with concurrent erectile dysfunction, or those wanting to avoid side sexual side effects of other medications.

Patients with BPH might present with mixed symptoms, often due to secondary bladder changes that lead to symptoms of detrusor overactivity. Pharmacological options to treat these symptoms include anticholinergics such as oxybutynin and beta-3 agonists such as mirabegron. A detailed discussion of the indication and risks associated with these medications is outside the scope of this article.

Transurethral resection of the prostate

Transurethral resection of the prostate (TURP) removes obstructive prostatic tissue from the transitional zone through the urethra by electrocautery and has been considered as the reference mainstay technique for the surgical management of symptomatic BPH due to its widespread availability and high efficacy. There are two modalities; monopolar or bipolar. Monopolar TURP uses a single active electrode (the loop) at the site of surgery, which transmits energy into the prostatic tissue through the patient's

body to the return electrode pad on the skin surface. This circuit requires a non-conductive hypo-osmolar irrigation medium. In contrast, bipolar TURP is locally confined at the operative site between an active electrode (resection loop) and a return electrode situated on the resectoscope tip. This uses a conductive and physiological irrigation medium such as normal saline, and is favoured by some surgeons as it avoids the risk of transurethral resection (TUR) syndrome, characterised by dilutional hyponatraemia, which can occur in monopolar TURP due to its use of hypo-osmolar irrigation.^{15,16}

In a meta-analysis of 20 randomised controlled trials with a maximum follow-up of five years, monopolar TURP resulted in a significant reduction in IPSS and post void residual volume (–77%) and improvement in Qmax (+162%).¹⁷ Both monopolar and bipolar TURP can adversely affect sexual function in men, such as erectile dysfunction and/or retrograde ejaculation, which are linked to worse psychological health outcomes and poorer quality of life.¹⁸

Minimally invasive procedures

Various alternatives to TURP have emerged for the surgical management of LUTS secondary to BPH. The major benefits are that many, such as prostatic urethral lift (UroLift), convective water vapor energy (Rezium) and prostatic arterial embolisation (PAE), can be performed with local anaesthesia within the outpatient office setting.¹⁹ Although the literature currently suggests that minimally invasive procedures (MIPs) are associated with more modest improvements to LUTS and urinary flow, and higher rates of clinical failure requiring secondary intervention, there is growing popularity in favour of these interventions as they avoid adverse side effects to erectile and ejaculatory function, which can occur with medical therapy and TURP.^{20,21} Table 1 summarises the mechanism of action, patient selection criteria and potential side effects of each MIP.

Holmium laser enucleation of the prostate (HoLEP) uses a laser to resect the transitional zone of the prostate from the verumontanum to the bladder neck using anatomical planes. This is followed by morcellation or grinding of this tissue inside the bladder to enable endoscopic tissue extraction for histopathological analysis.

HoLEP has great versatility in the size of prostate that can be treated. Previously, patients with prostates >100–150 cc would need open simple prostatectomy to treat their massive BPH. HoLEP provides a minimally invasive alternative for glands as large as 200–300 cc.²² HoLEP offers a lower risk of bleeding and shorter hospital stay;¹⁹ however, there is a slightly higher risk of urinary incontinence compared with TURP.

Photoselective vaporisation of the prostate (PVP) (or GreenLight laser Prostatectomy) uses a laser fibre to deliver high-energy green light and rapidly vaporise the prostatic adenoma. Efficacy outcomes comparing HoLEP to PVP in randomised trials were comparable.^{23,24}

Prostatic urethral lift (PUL; UroLift®, Teleflex Inc., Pleasanton, CA, USA) involves deploying non-absorbable implants, which act to compress BPH to establish a large calibre urethral channel (Figure 1). Depending on the size and shape of the prostate, a variable number of implants (typically two in each side of the prostate) are used. UroLift® can be performed under local anaesthesia in an office. It is associated with a faster recovery time and preservation of sexual function.

Water vapour thermal therapy (Rezum System, Boston Scientific, MXG, Massachusetts) uses radiofrequency to generate convective water vapour energy, which is delivered to obstructive adenomatous tissue to induce prostatic necrosis (Figure 2). Injections of vapour are delivered transurethrally.²⁵ It can be performed under local anaesthetic in the outpatient setting. The Rezum System is popular for its preservation of sexual function.²⁶ Its drawback is that patients need to have a urethral catheter after surgery, often for up to a week.

Aquablation uses the principle of hydro-dissection to resect prostatic parenchyma using a high velocity waterjet under real-time transrectal ultrasound guidance, without the need to generate thermal energy. Haemostasis is achieved with a Foley balloon catheter on light traction, diathermy or low-powered laser. It is an effective treatment for prostates >100 cc.^{27,28}

Prostatic arterial embolisation (PAE) can be performed as a day procedure with local anaesthesia and involves femoral or radial artery puncture guided by digital subtraction angiography.²⁹ The appropriate prostatic artery is selectively embolised to induce

tissue necrosis. PAE has longer procedural time and is less effective than TURP at improving symptoms and urodynamic parameters such as flow rate.³⁰ However, PAE might be associated with fewer adverse events and shorter length of postoperative hospital stay compared with TURP.³¹ It is particularly well suited to patients who would not otherwise be fit for surgery.

The decision to undergo TURP or a MIP can be guided by the balance of benefits and harms based on patients' values and preferences. Although men prefer a quick relief with stable, long-term results, many are mindful of the risks of opting for surgical intervention such as disturbance to sexual and urinary function.³² Although the literature is in favour of MIPs in terms of fewer adverse

side effects to sexual and urinary function, many studies to date have limitations in their internal validity and generalisability. GPs can optimise care to patients suffering from symptomatic BPH through shared decision making, taking into consideration their preferences and values³² and prescribing medical therapy or referring to a urologist for surgical intervention where appropriate.

Table 1. Properties of each minimally invasive procedure

Technique	Mechanism of action	Indications and patient selection criteria	Side effects	Availability in Australia
Holmium laser enucleation of the prostate (HoLEP)	Pulsed solid-state laser to resect the transitional zone of the prostate using anatomical planes, then morcellation of this tissue inside the bladder to enable endoscopic extraction	BPH of any size including prostate size >200 cc, which previously needed open surgery ^{22,33}	Longer operation times, no significant differences in urethral strictures and stress urinary incontinence rates with TURP ^{34,35}	Private hospitals and some tertiary public hospitals
Photoselective vaporisation of the prostate (PVP)	Deliver high-energy green light energy to rapidly vaporise the prostatic adenoma	Suitable for men with prostate size <100 cc. Promising in patients at high risk of bleeding such as those on anticoagulation ¹⁷	Side effect profile on urinary and sexual function comparable to TURP ¹⁷	Private hospitals and some tertiary public hospitals
Prostatic urethral lift (UroLift®)	Involves placement of several retractors into the prostatic lobes to increase the urethral opening, without the use of electrocautery or dissection	Men with LUTS interested in preserving ejaculatory function, with prostate size <70 cc and no middle lobe Can be performed in an office setting under local anaesthesia and provide rapid relief of LUTS	Favourable safety profile; minimal perioperative morbidity; preservation of antegrade ejaculation and erectile function, and minimal long-term complications ^{17,18}	Private hospitals and few public hospitals
Water vapour therapy (Rezum)	Uses thermal energy in water vapour created by radiofrequency to trigger prostatic necrosis. Injections of water vapour are administered using a treatment needle via cystoscopy	Indicated for men with a prostate volume of ≥30 cc and enlargement of central zone and/or median lobe	Favourable safety profile; minimal perioperative morbidity; preservation of antegrade ejaculation and erectile function, and minimal long-term complications ³⁶	Private hospitals and few public hospitals
Aquablation	Resects prostatic parenchyma using a high velocity waterjet using ultrasound guidance	Effective in men with prostate size >100 cc ²⁸	Risk of postoperative bleeding is lower than TURP, but slightly higher than HoLEP; preservation of antegrade ejaculation and erectile function ²⁸	Not currently available
Prostate artery embolisation (PAE)	Selective embolisation of appropriate prostatic artery to induce tissue necrosis	Patients with moderate-to-severe LUTS Those willing to accept less optimal outcomes compared with TURP	Post-PAE syndrome; urinary retention, transient rectal bleeding, pain, haematuria and UTI Inadvertent embolisation of the bladder, corpus cavernosum, or anus, leading to ischaemia	Private and public hospitals with interventional radiology

BPH, benign prostatic hyperplasia; LUTS, lower urinary tract symptoms; PAE, prostatic arterial embolisation; TURP, transurethral resection of the prostate; UTI, urinary tract infection.

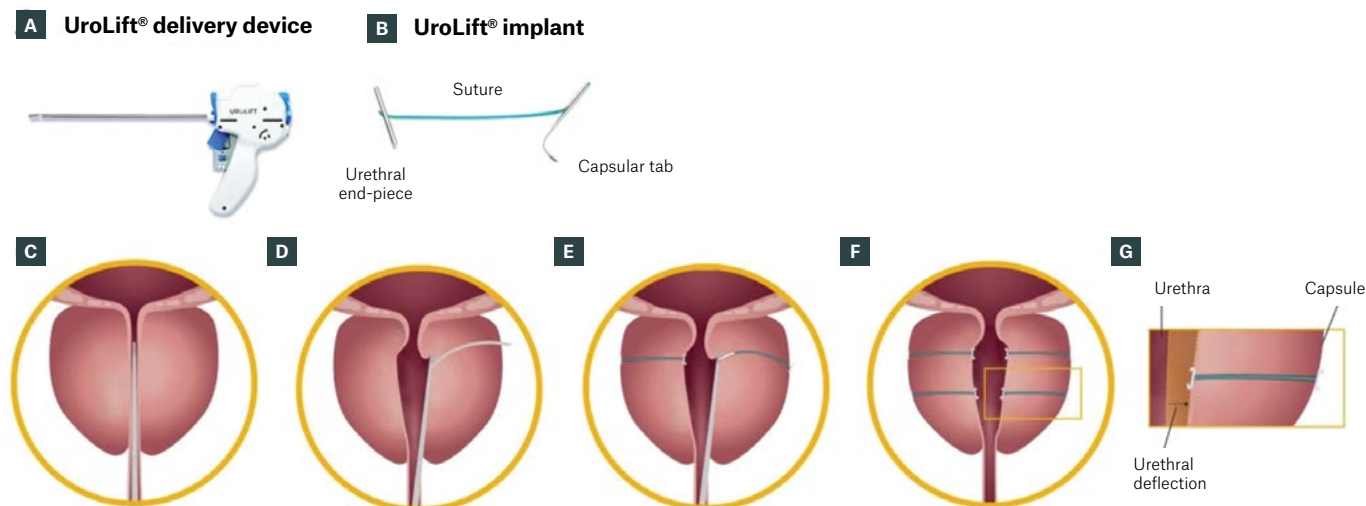


Figure 1. The UroLift System is comprised of two main components: (A) the UroLift delivery device and (B) the UroLift implant. The delivery device is designed to access the prostatic urethra and deliver one implant through the lobes of the prostate. The implant consists of a capsular tab (CT), made from nitinol (nickel titanium alloy), connected by a monofilament polyethylene terephthalate suture to the urethral end-piece (UE), made from stainless steel. The materials used in the implant are made of chemically and biologically inactive materials, commonly used in other implants. Details of the prostatic urethral lift procedure are as follows: (C) under cystoscopic guidance, the delivery device is introduced

through the sheath and is used to compress the prostate lobe. (D) A 19-gauge needle that houses the implant is deployed through the prostatic lobe and capsule. Upon retraction of the needle, the CT is deposited with a suture under tension. (E) The implant is secured by deployment of the UE and excess suture is cut. (F) Additional implants are delivered as required. (G) The glandular stromal tissue of the prostate is compliant and more easily compressed outwardly resulting in the opening of the prostatic urethra.

Reproduced from Roehrborn CG, Chin PT, Woo HH. The UroLift implant: Mechanism behind rapid and durable relief from prostatic obstruction. *Prostate Cancer Prostatic Dis* 2022;25(1), with permission from the Nature Publishing Group.³⁷

Conclusion

There are various options available today for managing LUTS secondary to bladder outlet obstruction due to BPH, ranging from lifestyle modification, medical therapies and surgical interventions, including TURP and MIPs. Although not as effective in the long term in dramatically improving a patient's LUTS compared with TURP, MIPs are proving to be popular due to their low side effect profile and ability to be performed as a day case procedure in an office setting. GPs should follow a stepwise pattern of management, commencing with lifestyle modification advice and consider a medical agent that is appropriate for the age, preferences and sexual habits of the patient. A referral to a urologist is recommended for persisting bothersome symptoms despite medical therapy, for consideration of surgical intervention. An awareness of the various MIPs available today can be helpful when counselling patients on treatment options for LUTS due to bladder outlet obstruction.



Figure 2. Rezum system delivery device and needle.

Reproduced from Woo HH, Gonzalez RR. Perspective on the Rezūm® System: A minimally invasive treatment strategy for benign prostatic hyperplasia using convective radiofrequency water vapor thermal therapy. *Med Devices (Auckl)* 2017;10, with permission from Dovepress.³⁸

Key points

- LUTS, due to BPH, globally affects 30% of men aged >50 years, and in Australia, affects one-in-five men aged between 35 and 80 years, leading to reduced quality of life and depression.
- Lifestyle modifications and α -1-blockers are initially recommended, with 5-ARIs offering additional benefit for patients with a significantly enlarged prostate (with potential sexual side effects).
- Referral to a urologist is recommended for consideration of surgical intervention in men with persisting bothersome symptoms despite medical therapy, or who do not adhere with medical therapy.
- TURP remains the standard of surgical intervention, demonstrating significant improvement in urinary symptoms, but with potential adverse effects on sexual function.
- Emerging minimally invasive options including UroLift[®], Rezum and PAE offer alternatives to TURP, and are proving to be popular due to their low side effect profile, shorter inpatient stay and ability to be performed on co-morbid populations.

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Competing interests: None.

Funding: None.

Provenance and peer review: Commissioned, externally peer reviewed.

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