Benign prostatic hyperplasia: what are the benefits and harms of various surgical management options?

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Benign prostatic hyperplasia (BPH) is characterised by stromal and epithelial prostatic cell hyperplasia. The enlarged prostate may be associated with voiding and storage lower urinary tract symptoms (LUTS). These have been predominantly attributed to bladder outlet obstruction (BOO), assumed to be due to the increased size of the prostate (benign prostatic obstruction; BPO), although recently this assumption has been reconsidered. These troublesome symptoms progress with age and adversely affect the quality of life (QoL), warranting adequate treatment options.

LUTS secondary to BPO (LUTS / BPO) range from mild to severe. Treatment is required for every man with bothersome symptoms and / or impaired QoL. Some patients may require immediate surgical treatment; however conservative options present a feasible option for some patients with LUTS / BPO. All men should receive reassurance, behavioural and dietary advice, as well as optimisation of other related co-morbid conditions. Management with pharmacological agents is applicable if treatment is sought for moderate-to-severe LUTS (International Prostate Symptom Score; IPSS: 8-35) [1].

For many patients the symptoms of LUTS / BPO can remain stable for years either by watchful waiting or with medical management. However, some patients experience progression of their symptoms or develop complications. Complications may include recurrent episodes of haematuria, recurrent urinary tract infections or recurrent episodes of urinary retention, bladder stones, large bladder diverticula or renal impairment secondary to BPO and these will necessitate further treatment when they occur. Surgical treatment is indicated for patients requiring active treatment but who are unwilling to have medical treatment, for non-responders to medical treatment, or for patients with absolute surgical indications (i.e. presenting with the complications mentioned above). In this review we have summarised surgical treatments for LUTS / BPO.

Monopolar transurethral resection and transurethral incision of the prostate

Monopolar transurethral resection of the prostate (M-TURP) has been regarded as the 'gold standard' surgical treatment for LUTS / BPO for several decades. The technique involves resection of the adenoma from the transitional zone. Transurethral incision of the prostate (TUIP) involves incising the bladder outlet without tissue removal. There are several studies, including randomised controlled trials (RCTs) and RCT-based meta-analyses that confirm the effectiveness and durability of M-TURP. However, morbidity remains considerable. Serious bleeding warranting blood transfusion, clot retention, TUR syndrome, acute urinary retention, urethral strictures (US) or bladder neck contracture (BNC), urinary incontinence, retrograde ejaculation and de novo erectile dysfunction may follow. According to the European Association of Urology (EAU) Guidelines, M-TURP and TUIP are strongly recommended surgical treatment options for men with moderate-to-severe LUTS / BPO, with prostate volumes of <30mL without a middle lobe and 30-80mL respectively, but the upper volume limit remains rather subjective [1].

Bipolar transurethral resection of the prostate

This modification of the conventional M-TURP addresses a major limitation of its progenitor by allowing performance (resection of the adenoma from the transitional zone) in normal saline solution rather than in a hypo-osmolar environment necessary for M-TURP, eliminating dilution hyponatraemia. Contrary to M-TURP, in B-TURP systems, the energy does not travel through the patient's body. The energy is transmitted from the resection loop to the normal saline solution, resulting in excitation of sodium ions to form plasma; molecules are then cleaved under relatively low voltage enabling resection. B-TURP can be classified as either 'true' or 'quasi' bipolar systems, based upon how the energy circuit is completed. In the former systems, the current travels from the resection loop (active pole) to a passive pole located at the resectoscope tip. In the latter systems, the bipolar circuit closes between the resection loop and a passive pole located at the resectoscope sheath.

B-TURP is the most widely investigated alternative to M-TURP. During the last two decades, data from 59 RCTs has been reported [2]. Data from these trials has been pooled in high quality meta-analyses concluding that no clinically relevant differences exist between B-TURP and M-TURP in short-term efficacy (IPSS, QoL score and Qmax) [2-4]; this remains durable in the mid- and long-term (up to 60 months) [1,5]. Based on this data no differences exist in short-term US / BNC rates, but B-TURP is preferable due to a more favourable peri-operative safety profile (TUR-syndrome elimination; lower clot retention / blood transfusion rates; shorter irrigation, catheterisation, hospitalisation duration) [2-4]. According to the EAU Guidelines, B-TURP is strongly recommended as an alternative treatment to M-TURP for men with moderate-to-severe LUTS / BPO with prostate volumes of 30-80mL but the upper volume limit is rather subjective, and the choice should be based on the availability of equipment, the experience of the surgeon, and the preference of the patient [1].

Bipolar transurethral vapourisation of the prostate

Bipolar transurethral vapourisation of the prostate (B-TUVP) has evolved from B-TURP (plasmakinetic B-TUVP). It utilises high frequency generators and special bipolar electrodes of various geometry. Recently, the 'plasma' B-TUVP system with the 'mushroom or button-like' electrode has attracted scientific and clinical attention (plasma B-TUVP). These electrodes generate a constant plasma effect that is able to vapourise prostatic adenoma with minimal direct contact, and simultaneously coagulate a thin tissue layer (<2mm), ultimately leaving behind a TURP-like cavity. B-TUVP has been evaluated in a few RCTs as an M-TURP alternative for treating moderate-to-severe LUTS in men with a prostate volume of

<80mL, showing similar short-term efficacy. Plasmakinetic B-TUVP, in particular, has a favourable peri-operative profile, similar mid-term safety, but inferior mid-term efficacy. Plasma B-TUVP, has a lower short-term major morbidity rate. According to the EAU Guidelines, plasma B-TUVP is strongly recommended as an alternative treatment to M-TURP for men with moderate-to-severe LUTS / BPO with prostate volumes of 30-80mL [1]. Nevertheless, RCTs of higher quality and longer follow-up are still needed.

Open prostatectomy

Large obstructive adenomas (>80-100mL) are enucleated with the index finger either trans-vesically or retro-pubically (Freyer's or Millin's open prostatectomy (OP) procedure, respectively). OP is an effective and durable procedure, but it is considered the most invasive one. For this reason, it has been recently compared with minimally invasive options (endoscopic enucleation of the prostate; EEP) for treating patients with large glands, using bipolar circuity (bipolar enucleation of the prostate; BEP) or lasers (see below). Based on the available evidence, OP has similar short-term and mid-term efficacy but EEP shows a more favourable peri-operative safety profile. Although the operation time is longer, EEP is associated with lower transfusion rates, shorter catheterisation and reduced hospital stay. According to the EAU Guidelines, OP is strongly recommended in the absence of a holmium laser or a bipolar system as an alternative treatment for men with moderate-to-severe LUTS / BPO with prostate volumes >80mL [1].

Laser technologies

Holmium:yttrium-aluminium garnet (Ho:YAG; wavelength 2140nm) is a pulsed laser absorbed by water with a limited penetration depth of 3mm to 4mm. This has gained space in the surgical treatment armamentarium for the management of LUTS / BPO, mainly in the form of holmium enucleation of the prostate (HoLEP). Based on the available literature, HoLEP shows comparable long-term efficacy to OP with a more favourable safety profile compared to both TURP and OP (better haemostatic capability / intra-operative safety, shorter catheterisation and hospitalisation time). Nevertheless, mentorship programmes are advised since HoLEP is hindered by a steep learning curve and the high-level endoscopic skills needed. According to the EAU Guidelines, HoLEP is strongly recommended for men with moderate-to-severe LUTS / BPO presenting with prostate volumes >80mL [1].

Greenlight is a continuous laser (wavelength 532nm), absorbed by haemoglobin, with a limited penetration depth (8mm), leading to immediate prostatic adenoma vapourisation. The initial system (80-W potassium-titanyl-phosphate; KTP) has been substituted by the 120W HPS lithium triborate (LBO) and recently by the 180W XPS, which is the current standard generator for performing the Greenlight procedure (photoselective vapourisation of the prostate; PVP). However, the vast majority of evidence is derived from studies on the previous systems and their number / quality is low, especially for large glands (>100mL), with no long-term follow-up. According to the EAU Guidelines, Greenlight (performed with all three systems) is strongly recommended as an alternative to TURP for men with moderate-to-severe LUTS / BPO presenting with prostate volumes 30-80mL, and weakly recommended (KTP / LBO systems) for the specific patient population on antiplatelet / anticoagulant therapy with a prostate volume <80mL [1].

Another laser option for surgically treating LUTS / BPO is thulium:yttrium-aluminium-garnet (Tm:YAG). It operates in a continuous form from 1940-2013nm allowing for vapourisation, resection or enucleation. The potential of this modality has been demonstrated by a few RCTs. Since the number of RCTs is limited with only a few presenting long-term follow-up to support Tm:YAG efficacy, ongoing investigation of the technique is still needed.

Finally, diode lasers which function at various wavelengths and have little high-level evidence have been introduced as an alternative to the aforementioned laser technologies for either enucleation or vapourisation. The limited and poor quality RCT data to date suggests that this modality requires further evaluation. The EAU Guidelines level of recommendation for the use of both Tm:YAG and diode lasers (120W 980, or 1318nm) for prostate adenoma vapourisation and / or enucleation in men with moderate-to-severe LUTS / BPO is weak [1].

Prostatic urethral lift

The prostatic urethral lift (PUL; Urolift®) is a relatively new option for treating LUTS / BPO which is conducted cystoscopically by local or general anaesthesia. It entails insertion of small permanent sutures through the lateral prostatic lobes, which are compressed laterally to create a wider prostatic urethra. PUL has been evaluated in two multicentre RCTs (versus sham treatment and versus TURP with a five-year and a two-year follow-up, respectively) [6,7]. It has been shown to result in functional improvement inferior to TURP at two years, and to bear a low incidence of sexual side-effects. However, patients should know that long-term effects including the re-treatment risk are unknown. According to the EAU Guidelines, PUL is strongly recommended for men with moderate-to-severe LUTS / BPO interested in ejaculatory function preservation, with prostate volumes <70mL without a middle lobe [1].

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Techniques under investigation

During the last couple of decades, numerous minimally invasive techniques have emerged as potential surgical treatments of LUTS / BPO. Often these were prematurely implemented into clinical practice but not continued because they were over-promoted before data with adequate certainty of evidence was available. Acknowledging this fact, the EAU Non-neurogenic Male LUTS Guidelines Panel has made recommendations about the adequate certainty of evidence that should exist before future widespread implementation of novel minimal invasive techniques takes place [8]. According to these recommendations, supporting data should be provided by proof of concept studies, RCTs on efficacy / safety and cohort studies with broad inclusion / exclusion criteria to confirm the reproducibility and generalisability of the benefits and harms. This evidence must also provide adequate follow-up before recommendations are made in high-quality guidelines, allowing for adequate patient information prior to any treatment choice.

In this context, several techniques are currently under investigation, including the minimal invasive simple prostatectomy (MISP); the temporarily implanted nitinol device (iTind®, Medi-Tate Ltd); Aquablation – image guided robotic waterjet ablation (AquaBeam®, Procept BioRobotics); convective water vapour energy (WAVE) ablation (Rezūm system™, Boston Scientific; and prostatic artery embolisation (PAE)) [1].

MISP performed either laparoscopically or robotically-assisted, is a rising alternative to OP. It entails enucleation of prostatic adenoma transvesically or retropubically

using either an extraperitoneal or a transperitoneal approach. Contemporary data reveals significant improvement in Qmax, prostate volume reduction, QoL, IPSS and prostate specific antigen (PSA) reduction; favouring MISP compared to OP in respect to catheterisation time, hospital stay and haemorrhage, compensating for prolonged operation time. All available forms of MISP appear to be equally effective and safe in expert hands but most data is of retrospective nature. High quality studies with long-term follow-up are lacking and learning curve / cost should also be evaluated [1].

The iTIND is a nitinol device that is expanded in the prostatic urethra in a triangular manner for five days. Following exertion of pressure at crucial points (12, 5 and 7 o'clock), it generates ischaemic changes that cause necrosis / scarring, creating deep channels allowing urination. Recent data from a prospective study evaluating the feasibility and safety of the procedure showed a substantial improvement in IPSS, Qmax and QoL, remaining durable at 36 months with low incidence of complications (urinary incontinence, retention and urinary tract infection). No RCTs comparing this device to a reference technique have been published to date but are currently ongoing [1].

The AquaBeam is an innovative technique that ablates the prostatic adenoma using a high velocity saline stream while sparing collagenous structures (hydrodissection) under real-time transrectal ultrasound visualisation of the gland. Initial RCT data versus TURP demonstrates symptom benefit particularly in patients with larger prostates; low operation time (four minutes) and a non-inferior safety profile [9]. Nevertheless, further high quality RCTs are needed with long-term follow-up data [1].

The Rezūm system uses radiofrequency energy delivered via injections in several points of the gland to create water vapour, which releases thermal energy when the steam is liquefied upon cell contact causing necrosis. It can be performed as an office-based procedure. A multicentre RCT versus sham treatment reported durable positive outcomes at four years [10] but confirmatory RCTs against a reference technique are still needed [1].

PAE is another technique performed with access through femoral arteries as a day-case procedure under local anaesthesia. Digital subtraction prostatic angiography is used to display anatomy so that appropriate arteries are selectively embolided. PAE is a technically demanding procedure that impacts the entire prostate without the option for focused / controlled action on BPO. Various techniques have been used. Patient selection criteria that will identify individuals who can benefit needs to be defined. High quality RCTs with long-term follow-up by a multidisciplinary base of urologists / radiologists are needed [1].

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TAKE HOME MESSAGE

- Appropriate surgical treatment for LUTS / BPO should be tailored to individual patient's profile / preference, surgeon's experience, equipment availability and cost-effectiveness.
- TUIP, M-TURP, B-TURP, B-TUVP, OP, HoLEP, Greenlight laser vapourisation, Tm:YAG / Diode laser enucleation and / or vapourisation and PUL constitute our current established armamentarium of surgical treatment for LUTS / BPO.
- Several surgical techniques are currently under investigation for treating LUTS / BPO, including MISP; iTind; AquaBeam; Rezūm and PAE.
- Adequate certainty of evidence should exist before widespread implementation of any novel surgical technique for the treatment of LUTS / BPO.

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