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Advances in Minimally Invasive Treatment of Benign Prostatic Hyperplasia

Hang Xie, Yuanhua Liu, Jiang Zheng*

The First Affiliated Hospital of Yangtze University, Jingzhou, China
Email: *1453620139@qq.com

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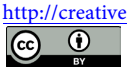

Abstract

Benign prostatic hyperplasia (BPH) is a chronic condition that is more common in older men. BPH most commonly causes symptoms associated with LUTS and bladder outlet obstruction. Lower urinary tract symptoms (LUTS) in men with BPH are a major cause of reduced quality of life in older men. If bladder outlet obstruction persists for a longer period of time, the contractility and voiding capacity of the detrusor muscle will gradually be affected by the obstructive factors, eventually leading to a loss of compensatory phase, characterised by a reduced electrical stimulation response, replacement of bladder muscle tissue by connective tissue, and a possible increase in voiding pressure, but a decrease in contractility of the detrusor muscle. As BOO progresses, it eventually leads to permanent contractile dysfunction of the detrusor muscle. Therefore, early initiation of surgical treatment in patients who are not well controlled by medication can reduce the complications associated with prostate enlargement. With the rise of minimally invasive treatment and the complications of open surgery, minimally invasive treatment of BPH has attracted increasing attention. Various emerging minimally invasive surgical modalities are being developed in clinical practice, and more and more minimally invasive techniques and concepts are focusing on safety, improving quality of life and reducing long-term complications to meet the different needs of different patients. Transurethral resection of the prostate (TURP) is currently the "gold standard" of minimally invasive surgical treatment, but with concerns about post-operative complications, the search for safer and more effective minimally invasive surgical options has become even more important. In recent years, with the increasing clinical application of new minimally invasive techniques such as various lasers, interventional treatments and implantable devices, there are more options for minimally invasive treatment of BPH. This article provides a brief review of research advances in the minimally invasive treatment of benign prostatic hyperplasia, with a view to informing clinical decisions.

*Corresponding author.

Keywords

Benign Prostatic Hyperplasia (BPH), Minimally Invasive Treatments, Therapeutic Efficacy, Security

1. Introduction

BPH can lead to Lower urinary tract symptoms (LUTS) and bladder outlet obstruction (BOO) [1]. Lower urinary tract symptoms (LUTS) caused by urinary dysfunction have become a major cause of reduced quality of life in middle-aged and older men [2]. The pathology of benign prostatic hyperplasia (BPH) is characterised by cellular proliferation of the epithelial and stromal components of the prostate. Studies have shown that the prevalence of prostate enlargement increases with age, with the prevalence of BPH/LUTS ranging from 50% to 75% in men aged 50 years and older and 80% in men aged 70 years and older [3]. As the disease progresses, patients develop further associated complications such as secondary urinary tract infections, bladder stones or kidney damage. Clinically, BPH is characterised by progressive development of lower urinary tract symptoms (LUTS). These symptoms range from nocturia, incomplete voiding, hesitant urination, weak urinary flow, frequency and urgency to the development of acute urinary retention. These symptoms can have a significant negative impact on the quality of life of older men, leading many men to actively seek surgical treatment.

2. Lasers and Their Associated Surgical Modalities

2.1. Holmium Laser

The holmium laser works: The holmium laser penetrates to a depth of approximately 0.40 mm and its energy is rapidly absorbed by water and water-containing tissues. The blasting effect of the holmium laser rapidly separates the enlarged gland along the surgical envelope of the prostate, pushes the separated gland into the bladder and uses a matching tissue crusher to crush the gland and suction it out of the bladder. Holmium laser enucleation is currently the most commonly used procedure in clinical practice. As the use of lasers becomes more widespread, there is increasing clinical evidence that Holmium laser enucleation has replaced TURP as the new gold standard for BPH surgery [4]. Yin *et al.* conducted a systematic evaluation through a clinical study, which showed that Qmax and IPSS were not significantly different between the HoLEP and TURP groups at 1 and 6 months post-treatment, but over time, at 12 months post-operatively, the HoLEP group showed better surgical outcomes in terms of Qmax and IPSS. The results also showed that HoLEP was much better than TURP in terms of bleeding, catheterisation time, length of stay and blood transfusion rate, but in contrast TURP was better than HoLEP in terms of operative time and recurrence of postoperative voiding difficulties [5]. Yuk *et al.*

showed that HoLEP can be performed safely with or without preoperative anticoagulant medication [6]. TURP surgery may pose a higher risk of intraoperative bleeding in patients with coagulation-related dysfunction, but the risk of severe intraoperative bleeding is reduced due to the good cutting and haemostatic properties of the holmium laser. Thus, the risk of severe intraoperative bleeding is reduced, as are the risks associated with other procedures. Mohamed H. *et al.* showed that holmium laser enucleation of the prostate (HoLEP) performed within 6 weeks after transrectal ultrasound (TRUS)-guided prostate biopsy had no negative impact on the outcome of the procedure [7]. A prospective study by El-Hakim and Elhilali showed that HoLEP takes longer to train than standard TURP and has a steeper learning curve. For HoLEP inexperienced doctors can perform HoLEP with proficiency after about 50 cases with results comparable to those of experts [8].

2.2. Green Laser

The first generation of green laser emitters (60 W and 80 W) used potassium titanium oxide phosphate crystals to double the frequency of the Nd: YAG laser, a wavelength at which haemoglobin molecules have a very high absorption coefficient, thus facilitating coagulation of blood vessels and vaporisation of tissue. The new generation of GreenLight XPS can be increased to a maximum power loss of 180 W. As a result, the green laser vaporisation of the prostate (PVP) is widely used in clinical practice. One study showed that the postoperative catheter insertion time and hospital stay were shorter and the risk of blood transfusion was lower in the PVP group compared to TURP, but the risk of dyspareunia and reoperation rates were higher in the PVP group, and there was no difference in the risk of urinary tract infection or risk of postoperative re-catheterisation between the two groups. Whereas in the postoperative follow-up included (IPSS, QoL, Qmax and PVR), the improvement in IPSS after TURP surgery was better than PVP in the early versus mid-term (2-year follow-up results), while QoL and Qmax were not significantly different, and PVR improved better than TURP after PVP surgery, and the 5th year follow-up showed that: the results of IPSS, QoL and Qmax TURP was better after surgery, while PVR was not significantly different between the two groups [9]. Lai *et al.* showed that in perioperative terms (including bleeding-related transfusion, TUR syndrome, perforation of the peritoneum, clot retention, urinary tract infection and acute urinary retention), PVP had a lower incidence of transfusion, RR = 0.14 ($p < 0.01$) and clot retention (RR = 0.14, $p < 0.01$), TUR syndrome (RR = 0.19, $p < 0.01$) and perforation of the peritoneum (RR = 0.09, $p < 0.01$) were lower, but PVP had a higher risk of mild to moderate voiding difficulties (RR = 1.76, 95% CI 1.17 to 2.65, $p < 0.01$), and there was no significant difference between PVP and TURP in terms of long-term complications (including bladder neck contracture, retrograde ejaculation, urethral stricture) [10]. Results of a systematic evaluation of 180 W PVP in 1640 men showed a greater reduction in PSA levels in the 180 W group compared to the 120 W group (54% vs 79% and 34% vs 51% respectively). And

the latter had a shorter running time [11]. Isaac *et al.* showed that: in the perioperative period PVP catheterisation time and hospital stay were shorter and interoperative intervals were longer compared to TURP procedures. Significantly lower likelihood of postoperative complications from blood transfusion and clot retention; no difference in other complications [12]. Hueber *et al.* demonstrated by a comparative analysis of different laser intensities that the procedure time decreased with increasing laser intensity and that tissue ablation was more effective with increasing laser intensity [13]. Overall, the green laser is simple to operate, both vaporises and cuts, causes relatively little thermal damage to surrounding tissue, is faster, has less chance of scar contracture, has relatively few post-operative complications, minimal post-operative wound oedema, uses saline irrigation and has no risk of TURS, but the long-term safety and rates of high power laser systems (180 W) have not been proven and further research into their long-term safety and effectiveness is required.

2.3. Thulium Laser

The thulium laser, also known as the Tm: YAG laser, is similar to the holmium laser in that the wavelength of the thulium laser is close to the absorption peak of water, so its energy is rapidly absorbed by water and tissues containing water, but unlike the holmium laser, the thulium laser is delivered in a continuous wave. This produces a more effective vaporisation effect as well as a shallower penetration depth. It has a much smaller area of thermal damage. The thulium laser does not produce a bursting effect on the prostate tissue, has a better vaporisation and cutting effect with a neat wound and better haemostasis [14]. The thulium laser has a vaporising and cutting effect, so the thulium laser can be used to surgically treat patients with BPH in a variety of ways, such as thulium laser resection of the prostate, thulium laser vaporization of the prostate, thulium laser enucleation of the prostate and thulium laser vaporisation of the prostate. Thulium laser resection of the prostate, Thulium laser vaporization of the prostate, Thulium laser enucleation of the prostate, and Thulium laser vaporization of the prostate (Thu-VEP). Thulium laser vaporization of the prostate is currently the most commonly used procedure in clinical practice. A prospective randomised study by Bozzini showed that compared to HoLEP, ThuLEP showed similar procedure times (63.69 vs 71.66 min, $p = 0.245$), denuded tissue weight (48.84 vs 51.13 g, $p = 0.321$), catheter insertion time (1.9 vs 2.0 days, $p = 0.450$) and hospital (2.2 vs 2.8 days, $p = 0.216$), but resulted in a lesser reduction in haemoglobin (0.45 vs 2.77 g/dL, $p = 0.005$). HoLEP showed a significant increase in the number of patients with acute postoperative urinary retention and stress urinary incontinence. There were no significant differences in PSA, Q max, PVR, IPSS and QoL scores during follow-up [15]. A meta-analysis by Hartung *et al.* showed that no significant differences were observed between ThuLEP and HoLEP in terms of operative time, weight of gland removal, time to catheter insertion or length of hospital stay. hemoglobin decline was significantly lower in ThuLEP (mean difference 0.54 g/dl, 95% confidence interval [CI] 0.93 to

0.15; $p < 0.001$) and Transient urinary incontinence was more common in HoLEP (preponderance ratio 0.56, 95% CI 0.32 - 0.99; $p = 0.045$), and no significant differences were observed in other comorbidities or functional measures and symptom scores [16].

2.4. Diode Laser

The diode laser, also known as the semiconductor laser, has wavelengths that depend on the nature of the semiconductor used, with wavelengths of 940, 980, 1318 and 1470 nm. The role of the semiconductor laser is to vaporise and remove prostate tissue, and the 980 nm semiconductor laser was the first laser used in large numbers in clinical practice. The 980 nm red laser is characterised by selective absorption properties of water and haemoglobin contained in the tissue, providing excellent tissue cutting and haemostasis. Highly efficient vaporisation and cutting of tissue is accompanied by coagulation and haemostasis of blood vessels, which allows for a clear surgical field. In a comparative study between 980-nm semiconductor laser BPH vaporization and TURP, there were significant improvements in QOL, IPSS, Qmax and PVR, with no significant differences [17]. He *et al.* showed better haemostasis with a holmium laser compared to a 980 nm semiconductor laser (980 nm) [18]. Recently, the 1470 nm semiconductor laser has been gradually used in prostate laser surgery. Zhang *et al.* showed that the 1470 nm semiconductor laser was safe and effective in patients with prostate enlargement receiving continuous oral anticoagulants or antiplatelet drugs [19]. The thickness of the coagulation layer of the 100 W 1470 nm diode laser during surgery is thin, only about 2.30 mm, and the thickness of the coagulation layer meets the requirements for haemostasis during prostate surgery without causing damage to the deeper tissues of the prostate. A clinical study comparing 1470 nm diode laser prostate enucleation with plasma electrodesection of the prostate showed similar efficacy and safety of DiLEP and PKRP in relieving obstruction and low urinary tract symptoms. Compared to PKRP, DiLEP reduced the risk of bleeding, operative time, bladder flushing time, catheterisation time and length of hospital stay. However, IPSS, QoL, Qmax and PVR were similar for both procedures at 12 months post-operatively [20]. Thanks to its excellent vaporisation and haemostasis capabilities, the 1470 diode laser can be used to safely perform the procedure without non-stop treatment with anticoagulants.

3. Prostatic artery Embolization (PAE)

Prostatic artery embolization (PAE) is an interventional radiology technique that uses polyvinyl alcohol pellets to block the arteries supplying the prostate through the femoral artery, causing the prostate gland to become ischemic and atrophy, improving urethral obstruction and thus relieving the symptoms of dyspareunia. Pisco *et al.* reported on 255 men with BPH who were difficult to treat surgically and who were treated with PAE, with a success rate of 98% after 10 months of

follow-up and only one serious complication, confirming its efficacy [21]. Jung, J. H. [22] *et al.* showed that short-term follow-up of PAE improved urinary symptom scores and quality of life in the same way as TURP. In terms of sexual function, PAE preserved erectile function similar to TURP, but PAE may reduce ejaculatory disturbances. PUL and PAE have similar clinical efficacy and safety in the treatment of LUTS associated with BPH. A study by Knight *et al.* [23] stated that there was no significant difference between PAE and TURP in terms of changes in International Prostate Symptom Score (IPSS), IPSS Quality of Life (IPSS-QoL), International Index of Erectile Function (IIEF-5) and post-void residual (PVR). PAE was associated with fewer adverse events (AE) (39.0% vs. 77.7%; $p < 0.00001$) and shorter hospital stays (mean difference = −1.94 days; $p < 0.00001$), but longer operative times (mean difference = 51.43 minutes; $p = 0.004$).

4. Prostate Urethral Lift (PUL)

Prostatic Urethral Lift (PUL) is a new, minimally invasive treatment for BPH that involves the placement of a special urethral suspension device to suspend and compress the lateral lobes of the enlarged prostate, thereby widening the urethra, relieving urethral obstruction in the prostate and improving the patient's symptoms. The US Food and Drug Administration and the Institute for Health and Clinical Excellence in the UK have approved PUL as a safe, effective and cost effective treatment for BPH [24]. Roehrborn *et al.* [25], Bozkurt *et al.* [26] and Rukstalis *et al.* [27] showed that IPSS, Qmax and QOL improved significantly after PUL surgery, and at the 5-year postoperative follow-up, IPSS, Qmax and QOL remained improved and sexual function was not significantly affected. In a prospective randomised controlled trial, Souhil *et al.* [28]. studied and compared the results: ejaculate preservation rates of 66% to 91% for modified TURP, 87% to 96% for modified prostatic photovaporization, and 100% versus 34% for prostatic urethral lift (PUL) compared to conventional TURP. Perera *et al.* [29] concluded that PUL has the advantage of requiring less equipment, does not require general anaesthesia and can be done as a day case procedure. However, it is important to note that PUL can only compress both sides of the enlarged gland and is not effective in the treatment of BPH patients with middle lobe prostate enlargement. Therefore, the European Association of Urology guidelines only recommend PUL for the treatment of BPH patients with both sides of lobe enlargement who have a high sexual function requirement and a prostate volume of <70 mL. As PUL requires only local anaesthesia, it may also be considered for patients with BPH who are unable to tolerate general anaesthesia due to their medical condition or underlying disease. The advantages of PUL as a treatment for BPH include easy and rapid improvement of LUTS while preserving erectile and ejaculatory function and improving the patient's quality of life, the ability to perform day surgery with only local anaesthetic, low physical demands on the patient, and the ability to treat patients with

multiple underlying conditions.

5. Temporary Implantable Nitinol Device (TIND)

The temporary implantable nitinol device (TIND) is a nitinol stent implanted into the prostatic urethra and anchored to the bladder neck, causing ischaemic necrosis of the bladder neck and prostate tissue through compression of the stent, thereby reshaping the urinary tract of the bladder neck and prostate and relieving BPH-induced LUTS. Porpiglia *et al.* [30] [31] first reported TIND, showing that all procedures were performed within 10 min without intraoperative complications; patients began to show improvement in clinical symptoms from the third postoperative week onwards; persistent improvement in LUST was found at 3 years postoperative follow-up, with a 41% increase in Q max after 36 months of follow-up (mean 10.1 mL/s) The Q max rose by 41% to (mean 10.1 mL/s) after 36 months of follow-up. There were four early complications (12.5%), including one case of urinary retention (3.1%), one case of transient incontinence due to device displacement (3.1%) and two cases of infection (6.2%). No further complications were recorded during the 36-month follow-up period. However, this is the first published prospective clinical trial in humans and its long-term safety and reliability cannot be clarified, and there is a lack of extensive research around the long-term efficacy and safety of TIND.

6. Transurethral Water Vapor Therapy (TUWVT)

TUWVT is a new prostate ablation technique based on the Rezum System (NxThera, Inc., Maple Grove, MN), which consists of a steam generator and a disposable sheathed transurethral water vapour delivery device combined on a 30 degree standard rigid cystoscope for direct visualisation of the procedure. Water vapour heat is generated by applying radiofrequency current to an induction coil heater, which delivers heat to the prostate tissue via a retractable needle. Patients are placed in a back truncal position for this procedure and a cystoscopy is performed to confirm the contours of the prostate and the planned distribution of thermal injury. The treatment needle is positioned to start approximately one centimetre from the distal bladder neck and is aimed by eye at the transitional and central prostatic adenoma. Each injection of water vapour lasts approximately nine seconds. Steam injections are performed at one centimetre intervals from the initial injection site in the prostatic urethra to the proximal edge of the prostate. A saline flush is used to enhance visualisation and cool the urethral surface, with the resulting tissue temperature of approximately 70˚C resulting in irreversible and near instantaneous cell death [32] [33]. Dixon *et al.* [32] reported in 2016 the results of a 2-year follow-up study after TUWVT: in terms of effectiveness, 72.6% of patients had an IPSS decrease of ≥50% at 3 months after heat therapy. An improvement in IPSS reduction of ≥50% was observed in 60.5% of patients and persisted for 24 months; Q max showed a gradual improvement, increasing significantly from a mean of 8.1 mL/s to 12.7 mL/s at 12 months and remaining at 12 mL/s at 24 months; in terms of safety

regarding the procedure, adverse events included urinary retention, dyspareunia, urgency, haematuria and suspected urinary tract infection (UTI), but all were mild to transient-moderate and resolved within a few days to 4 weeks. Davide *et al.* [34] 2022 reported the results of a multicentre study: A total of 262 patients were followed up for 11 months. No early or late serious adverse events occurred. Early complications occurred in 39.3% of cases, including clot retention in 4 cases and blood transfusion in 1 case. Urge incontinence was reported in 6 patients (2.2%). Treatment failure requiring reintervention occurred in 4 cases (1.5%). The preoperative paraphimosis rate was 56.5%, increasing to 78.2% postoperatively. The QoL increased by ≥1 point in 92.7% of cases. Dean *et al.* [35] 2022 reported on the safety and efficacy of Rezūm therapy in macroglands > 80 mL. At 12 months, patients showed a 59% improvement in IPSS and a 70% improvement in IPSS quality of life scores. Maximum urine flow measurements improved by 59% at 12 months, while erectile and ejaculatory function remained unchanged. TUWVT provides rapid and effective relief of LUTS without significant impairment of sexual function, but the long-term efficacy of TUWVT remains to be validated by additional trial results.

7. Robot-Guided Highenergy Water Ablation (RHWA)

RHWA is a new exploration of the use of high-energy hydrodissection technology for the treatment of BPH. The PROCEPT Aquablation TM system currently consists of 3 components: a transrectal ultrasound probe, a robotic system, and a jet of high velocity salt-containing water. All patients receive general anaesthesia prior to the procedure. A custom 22-F rigid cystoscope was used to enter the bladder via the urethra, a 15 mL balloon was inflated with saline and retracted to hold the handheld piece securely in the prostate, a high velocity sterile saline stream was delivered orthogonally (90˚) at different flow rates depending on the depth of penetration required as measured by the probe, and finally a laser was used to cauterise the wound surface and leave a catheter in place. Gilling *et al.* [36] first evaluated the safety and feasibility of RHWA in a human study in 2015. 15 subjects were used for water ablation treatment in less than 10 minutes, most patients were discharged the day after the procedure and all but one patient had their catheter removed within 24 hours of the procedure. No patient required a blood transfusion and 5 patients required re-catheterisation. Statistically significant improvements were seen in IPSS, Qmax, QoL and PVR at the 6-month post-operative follow-up. A meta-analysis by Manfredi *et al.* [37] showed that Aquablation, Rezūm and iTIND significantly improved functional urinary outcomes; and Aquablation appeared to produce better functional outcomes. Rezūm and iTIND appear to have an excellent safety profile, but Aquablation appears to expose patients to a non-negligible risk of bleeding.

8. Outlook

TURP has long been accepted by urologists as the gold standard in the surgical management of BPH, but this view has been challenged by the increasing availa-

bility of minimally invasive techniques. Laser surgery has demonstrated a degree of excellence in surgical safety, whether it is vaporisation, excision or enucleation, to meet clinical needs to a certain extent, but the problem is that the surgeon needs sufficient surgical experience to accurately identify the anatomical landmarks of prostate enlargement and control the energy output, avoiding complications such as thermal injury and perforation of the pericardium as much as possible. PAE demonstrates a pioneering and multidisciplinary approach to urology and radiology, and shows us a new direction for development. TIND also offers more options for day surgery and for patients requiring only local anaesthesia. As technology continues to develop, more and more established surgical procedures will be used in the management of prostate enlargement. By understanding the patient's goals and desires, and through discussion between the patient and the surgeon, the treatment of prostate enlargement will become more diverse and individualised in the future.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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