Indications, techniques, and role of new minimally invasive benign prostate hyperplasia surgical options

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ABSTRACT

Novel emerging techniques for the surgical treatment of benign prostate hyperplasia (BPH) related to lower urinary tract symptoms are being investigated very seriously to help search for a better method, and the studies are getting their place in the literature. In this review article, UroLift® system, (i)TIND®, Aquablation®, Rezūm® system, and prostatic artery embolization have been discussed according to the literature and both European and American urological guidelines. All related randomized controlled trials are discussed under the appropriate headings. Indications, technique, and the role of these minimally invasive surgical options for BPH are assessed. These methods, which are still being studied, are promising for the future. As the studies get completed, the indications will become clearer, and these techniques will find their respective places as the personalized treatment options.

Keywords: Aquablation; benign prostatic hyperplasia; iTIND; lower urinary tract symptoms; minimally invasive surgical therapy; prostatic artery embolization; rezūm; urolift.

Introduction

Although transurethral resection of prostate (TURP) and open prostatectomy have been historically leading and have been the most preferred techniques in the surgical treatment of benign prostate hyperplasia (BPH) related to lower urinary tract symptoms (LUTS) for many years, with the developing world and the inevitable technology adapted to medical science, many minimally invasive treatment techniques have emerged. These emerging techniques aim to provide sufficient benefits to the patients, such as requiring less anesthesia, while trying to eliminate the adverse events (AEs) related interventions. Therefore, novel ablative and nonablative methods have been developed as an alternative to TURP. Some of them benefit from robotic technologies, whereas others aim to give a new shape to the prostatic urethra by mechanical correction. Some of them achieve their final effects mostly by guiding body's responses such as triggering ischemia or denaturing cell membranes.[1]

In this article, the indications, technical details, and the role of the prostatic urethral lift (PUL), temporary implantable nitinol device (TIND), image-guided robotic waterjet ablation (Aquablation®), convective water vapor energy (WAVE) ablation (The Rezūm® system), and prostatic artery embolization (PAE) will be discussed.

Among BPH treatment options that will be discussed in this article, only PUL has been studied under a separate title, unlike other treatments (TIND, Aquablation, The Rezūm system, and PAE) that are classified as techniques under investigation in the European Association of Urology (EAU) latest guidelines of management of non-neurogenic male LUTS, including benign prostatic obstruction.[1] The American Urological Association (AUA) guideline on surgical management of LUTS attributed to BPH (2018, amended 2019) does not cover TIND and does not recommend PAE as a treatment option owing to the lack of evidence.[2] In this review, urology

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guidelines of EAU and AUA, related randomized controlled trials (RCTs), and review-metanalysis have been discussed.

PUL

Indication

UroLift® system (NeoTract/Teleflex Inc., Pleasanton, CA, USA) should be offered to patients who desire preserving the ejaculatory function (EjF) and are not willing to undergo surgery. The ideal prostate volume (PV) for the PUL candidate was reported as <80 g in the AUA guidelines and <70 mL in the EAU guidelines. Both guidelines recommend PUL for the patients with hyperplastic lateral lobes (HLLs) without an obstructive middle lobe (OML). Both guidelines provide algorithm flowcharts (Figure 1) for the PUL; however, the AUA guidelines indicate PUL as the treatment option for small (<30 g) and moderate (30-80 g) prostates, whereas the EAU guidelines indicate it as the treatment option only for moderate prostates.[1,2]

Although the company (https://www.urolift.com/press-releases/fda-expanded-indication-up-to-100cc) announced on January 7, 2020, that United States Food and Drug Administration (FDA) has granted the company an extension for the use of UroLift® system to treat prostates up to 100 mL, this information has not been included in the guidelines yet.

Another confusion regarding this issue has arisen due to the MedLIFT study.[3] The study showed improvement in LUTS by opening the obstructed bladder neck (BN) and reducing the ball-valve effect due to OML using their described method. However, neither guidelines found this information sufficient and the AUA guidelines recommended an explanation and stated that "the nature of the study was not a randomized trial, it was a nonrandomized cohort."

Based on this information, it is believed that some indication changes will occur in the near future.

Main Points:

- Preservation of sexual functions, especially the ejaculatory function, is a condition in which new methods try to outperform, and all novel methods mentioned in this article have been shown to help in the preservation of ejaculatory functions.
- Do not offer prostatic urethral lift (UroLift® system) or temporary implantable nitinol device (iTIND) to the patients with obstructed middle lobe; but consider MedLIFT study, and follow the innovations closely.
- iTIND, convective water vapor energy (WAVE) ablation (The Rezūm® system), and prostatic artery embolization use the body's natural healing response to achieve the desired prostatic urethral opening.
- Robotically controlled prostate ablation has taken its place with image-guided robotic waterjet ablation-Aquablation®-in the benign prostate hyperplasia surgical treatment.

Technique

The UroLift® system is intended for single use only and comprises two main components and requires an ancillary equipment. The main components are UroLift® delivery device (DD) and UroLift® implant (Figure 2). Each UroLift® DD also includes one UroLift® handle release tool for use in troubleshooting steps.

PUL could be performed under both local and general anesthesia. PUL is a minimally invasive non-ablating technique and aims to alter the prostate anatomy with mechanical compression using permanent nitinol and stainless-steel suture-based implants on the HLLs of the prostate under cystoscopic guidance. The implant consists of a capsular tab connected by a monofilament suture to the urethral end-piece (UEP). The suture is made from polyethylene terephthalate, the capsular tab is made from nitinol (nickel titanium alloy), and the UEP is made from stainless steel. The implants are deployed using the DD to provide sufficient tension to pull the urethral lumen toward the capsule. To obtain the desired urethral opening, it is recommended to place the implants starting from 1.5 cm distal to the BN throughout the length of both HLLs at approximately 1 cm intervals up to the verumontanum in the anterior aspect of the prostate. The position of the DD tip is recommended to be at the 2 to 3 o'clock position on the left side and 9 to 10 o'clock position on the right side. Between and after implants are deployed, it is recommended to perform a cystoscopy to confirm the desired opening.[1,2,4]

Implant invagination into the prostatic urethral wall and epithelialization caused by the injury from the implant were shown in the 12-month cystoscopic view of PUL. No encrustation was found on implants. Histopathological analysis revealed a benign response to implants and no prostate-specific antigen (PSA) changes.[2,4]

Role

In 2004, PUL was first performed on dogs and cadaver models.[5,6] Two initial safety and feasibility studies were published in 2011 and both studies were funded by the NeoTract, Inc. as mentioned in the studies. Chin et al.[7] assessed the 1-year follow-up results, whereas Woo et al.[8] studied the 2-year results. Both studies resulted in significant improvement in patient's International Prostate Symptom Score (IPSS), Quality of Life (QoL), BPH Impact Index (BPHII), and maximum urinary

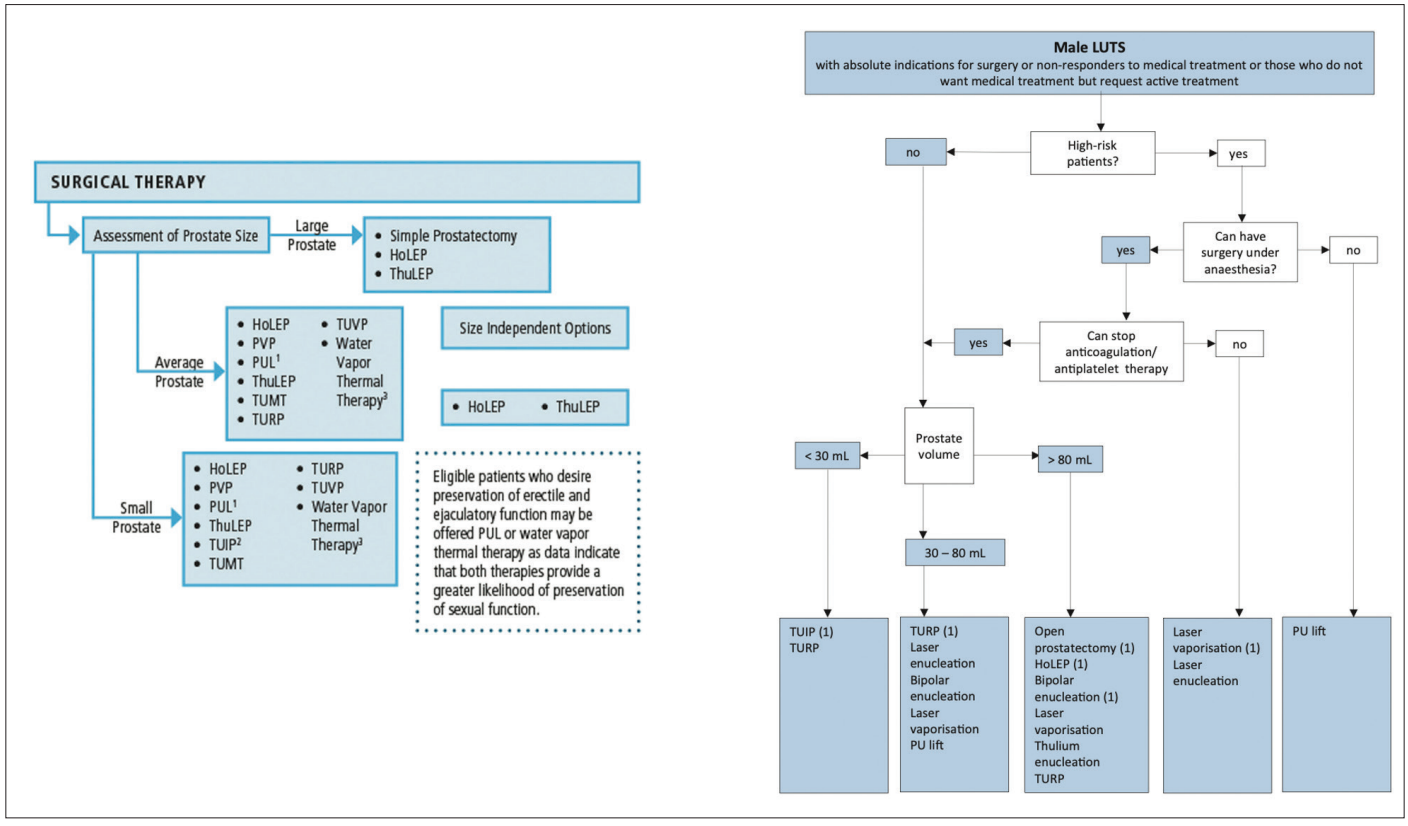

Figure 1. Treatment algorithm flowchart of AUA Guideline (left) and EAU Guideline (right)

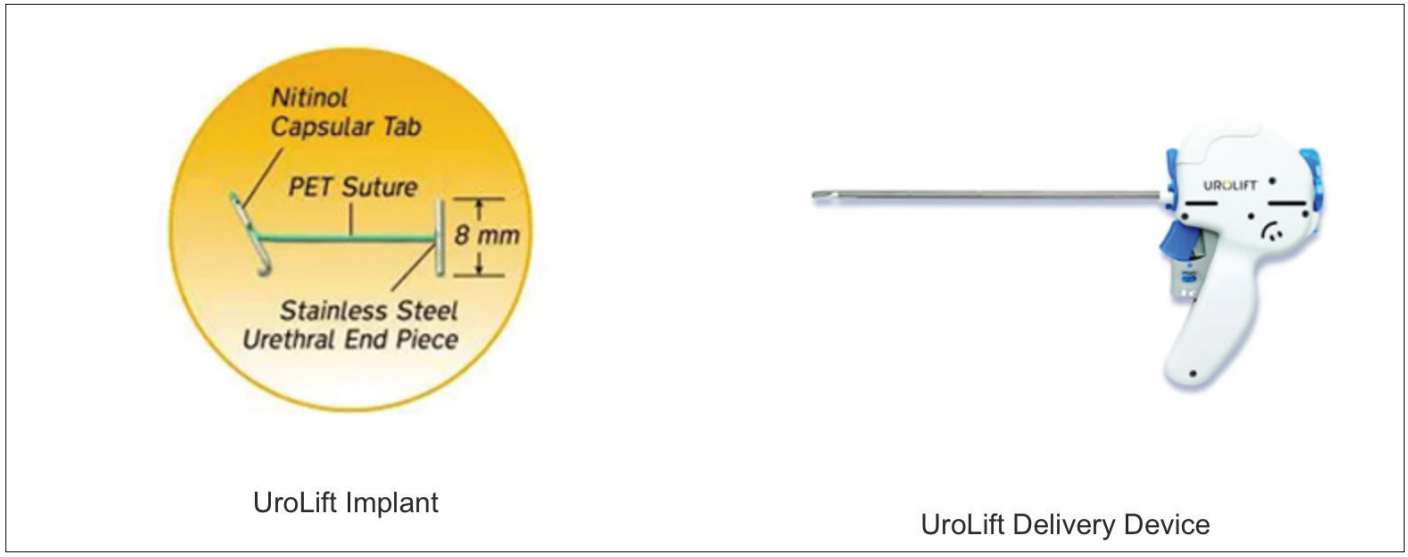

Figure 2. The UroLift® System is comprised of two main components; UroLift® Delivery Device and UroLift Implant

flow rate (Qmax) parameters. These improvements occurred as early as 2 weeks with durable effect of up to 2 years. The most common AEs were hematuria, dysuria, and irritative symptoms, which typically resolved within a week or a month.

Chin et al.[7] also used standardized questionnaires to demonstrate the preservation of sexual function (SxF) after PUL. They used the Male Sexual Health Questionnaire-Ejaculatory (MSHQ-EjD) function and bother parameters for EjF and International Index

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of Erectile Function (IIEF-5) questionnaire for erectile functions (ErF). They reported significant improvements in the MSHQ-EjD bother parameters even up to 2 years after PUL as well as improvements in the IIEF-5 and MSHQ-EjD function scores.

Roehrborn et al. evaluated PUL to provide 1-[4], 3-[9] and 5-[10] year data, which is the longest post-PUL follow-up, comparing PUL (n=140) with sham (n=66) groups. This RCT of the PUL was approved by the FDA, Health Canada, and the Therapeutic Goods Administration of Australia. The procedure for the sham group was conducted to mimic the PUL procedure with visual and auditory stimuli. Improvements in IPSS, QoL, BPHII, and Q_{max} were durable throughout the 5 years. LUTS and QoL were significantly improved by 2 weeks with return to preoperative physical activity within 8.6 days. Surgical retreatment was needed in 19 patients (13.6%) over 5 years. AEs were mild to moderate and transient. The maintenance of IIEF-5 scores and significant improvement in MSHQ-EjD scores showed that SxF was stable over 5 years. No, de novo, sustained erectile or ejaculatory dysfunction was recorded.[4,9,10]

Another RCT was designed at 10 European centers involving 80 males comparing PUL and TURP. The name, BPH6 study, comes from the number of examined subjects; improvement of LUTS, recovery, worsening of ErF and EjF, continence, and safety. The IPSS improvement was better in the TURP group at the 12th month. Preservation of ejaculation and quality of recovery were superior with PUL ($p<0.01$). The PUL group experienced an improvement in the average MSHQ-EjD score from the baseline ($p=0.03$), whereas the TURP group experienced a significant decline ($p<0.0001$). For the BPH6 ejaculatory assessment, the response of the PUL group was 100%, significantly better than the 60.6% response in the TURP group ($p<0.0001$). Surgical recovery from PUL is more rapid and more extensive in the first 3 to 6 months. The PUL group showed faster catheter removal. The average number of days to discharge was significantly lower and the return to preoperative activity levels was significantly faster in PUL patients. Continence preservation was comparable between the groups, and no patient experienced new-onset stress or sphincter incontinence. The Clavien-Dindo classification was used to report complications in this study, and no statistically significant number of AEs was observed between the groups. PUL did not cause any AEs that required surgical intervention or revision (0%) while two patients (6%) in the TURP group required surgical intervention, which was not significant between the groups.[11] Two-year results of the BPH6 study showed significant improvements in IPSS, QoL, BPHII, and Qmax in both arms, but the change in IPSS and Qmax in the TURP arm was superior to the first-year data. The ErF was preserved in both arms. All patients in the PUL arm had preserved EjF, whereas 34% of patients in the TURP group reported that they could not ejaculate at 2 years ($p<0.001$). These results were similar to those obtained from the first-year data.[12] A meta-analysis showed an overall improvement following PUL, including IPSS, Qmax, and QoL. The SxF was preserved with a small improvement estimated at 12 months.[13]

The MedLIFT study was a non-randomized cohort study, designed to understand the efficacy of PUL on patients with OML. Outcomes were compared with a previous LIFT study. At 1, 3, 6, and 12 months, the mean IPSS, Qmax, QoL, and BPHII improved significantly ($p<0.0001$). Compared with a previous study, the MedLIFT study subjects with OML showed improvement in symptoms at every time point ($p\leq0.01$). SxF was same as that in the previous LIFT study. Authors concluded that OML can be safely and effectively treated with PUL.[3]

TIND

Indication

The indications of TIND (Medi-Tate® Ltd., Or Akiva, Israel) are not yet clearly defined, and no precise indications are included in the guidelines. As there is no RCT on this subject and no comparative study with other accepted methods, there seems to be a little more time to determine the indications for this technique. The AUA guidelines have not yet covered this method, whereas the EAU guidelines have put TIND in the techniques under investigation section and evaluated it based on the work led by Porpiglia.[1,14,15] The EAU guidelines state that RCTs comparing (i)TIND®, which is the second-generation TIND, to a reference technique are ongoing.[1]

Based on Porpiglia's studies, TIND appears to be a treatment option for patients with BPH who desire preserving the EjF and do not wish to use a catheter after intervention. First studies of TIND were conducted on the <60 mL (mean PV: 29.5 mL) prostates using the first-generation TIND,[14,15] whereas a recently published studies evaluated the technique on <75 mL (mean PV 40.5 mL) prostates using the second-generation (i)TIND®.[16,17]. In a recent study, only patients with OML were clearly shown to have failed the procedure.[17] Future studies are expected to determine the more satisfying indication criteria for (i)TIND®.

Technique

In this part the information about (i)TIND®, which is the second-generation TIND and currently the only such device available on the market, is described. Similar to first-generation TIND, the second-generation (i)TIND® is a CE-Mark-approved device. TIND has four elongated nitinol struts and an anchoring

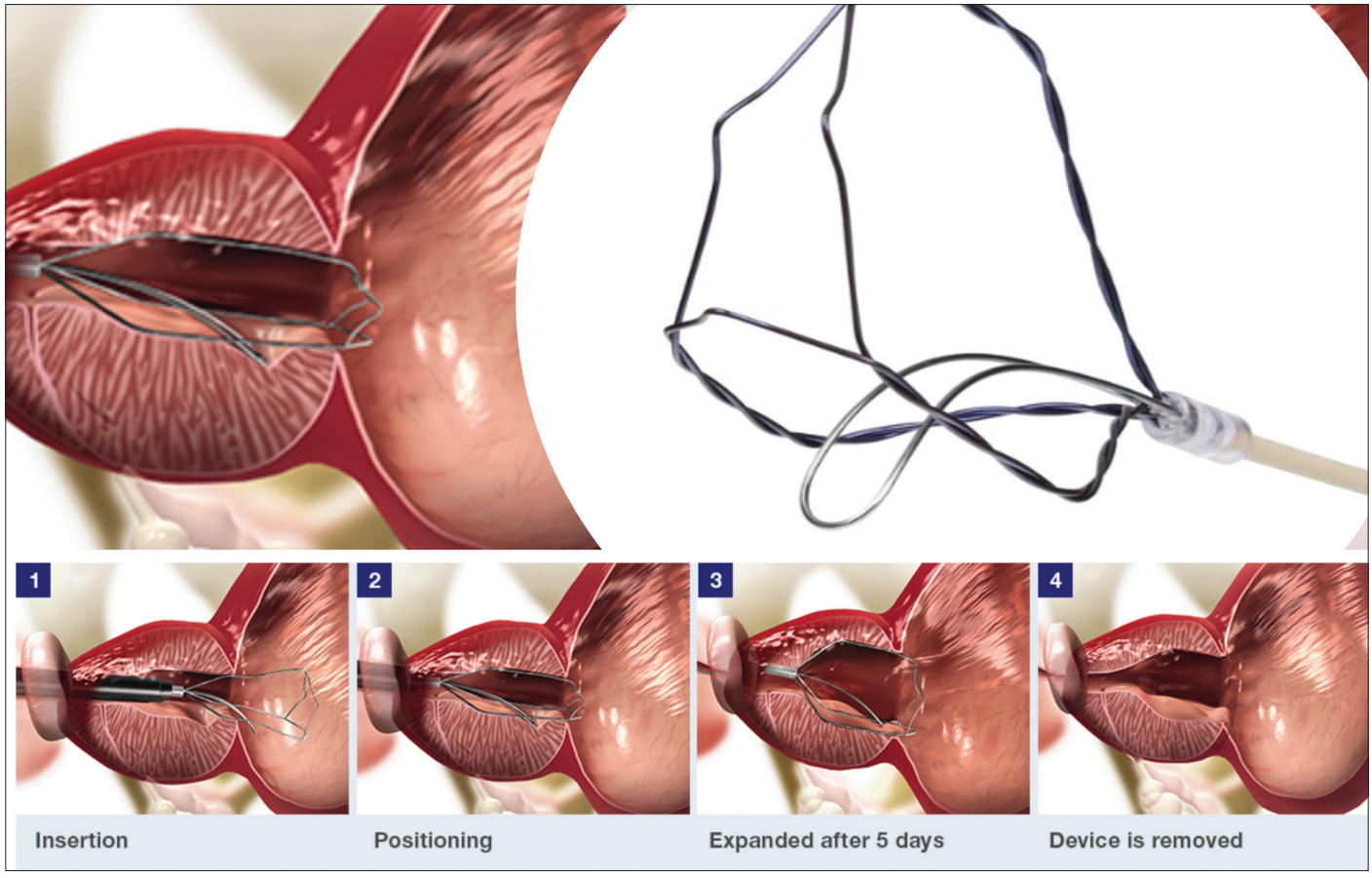

Figure 3. (i)TIND®; demonstrated in animation pictures with its three double intertwined (nitinol braid) struts fixed at the cranial end of the device

nitinol leaflet. The tip of the device is covered by a soft plastic material to avoid any bladder injury. Device has a polyester suture for retrieval at the distal end. To cover the entire length of the prostatic urethra and not to harm the external urethral sphincter, the device has been designed as 50 and 33 mm, in total length and outer diameter, respectively. With the (i)TIND®, two main changes come along:

1) Number of struts: Four single-layer nitinol struts were replaced by three double intertwined (nitinol braid) struts.
2) Design of struts: The fixation of three intertwined wires at the cranial end of the device instead of the distal end to avoid any potential injury to the bladder mucosa and the need for a soft plastic cover as in TIND (Figure 3). [16,18]

Treatment of (i)TIND® is scheduled in two procedural steps at two different dates with a waiting time of 5 to 7 days.

1) (i)TIND® implantation: The procedure for (i)TIND® implantation is performed in a lithotomy position under intravenous sedation and antibiotic prophylaxis. First, a rigid cystoscope sheath of 19 to 22 F is inserted into the meatus and guided up to the urethra until it passes to the BN to perform the standard urethrocystoscopy with the visualization of a 5-mm 30°-optic. (i)TIND® is inserted into the sheath and pushed through until it is deployed into the bladder. The cystoscope sheath is withdrawn and reinserted/guided-back in parallel to (i)TIND® delivery system for visualization. The (i)TIND® device is manipulated to bring the anchoring leaflet into the 6 o'clock position and distal to the BN. The cystoscope is removed after the emptying of the bladder, and the guidewire is cut at its proximal end and removed exposing the retrieval suture. (i)TIND® is left in place where it will remain for 5 to 7 days. No catheterization is required.

When device expands in the prostatic urethra, three cutting struts of the device exert pressure on the prostatic urethra and BN. This circumferential radial forces of the progressive and continuous pressure, creates three deep longitudinal incisions through ischemia and necrosis while

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pushing the obstructive tissue away from the prostatic urethral lumen. After 5 days, the device reaches its complete expansion, allowing for a decrease in BN tension resulting in incisions at the 12, 5, and 7 o'clock positions similar to a Turner-Warwick incision (Figure 3).[1,16]

2) (i)TIND® removal: At 5 to 7 days after placement, (i)TIND® is retrieved in an outpatient setting. The patient is placed in a lithotomy position and 20 mL lidocaine gel is applied to the urethra. After standard cystoscopy, first the retrieval suture is inserted through an open-ended circumferly catheter and advanced until it meets with the (i)TIND,® and the retrieval suture is pulled back while the catheter remains stabilized. (i)TIND® is easily collapsed into the catheter and removed through the urethra.

Role

First, studies were designed using first-generation TIND, which was available at that time. The results of single arm, prospective study were published with the assessment of the first- and third-year feasibility and safety data of 32 patients. The mean PV was 29.5 (7.4) mL. All devices were implanted successfully with no intraoperative complication. The mean total operative time was 5.8 min. Whereas the median postoperative stay was 1 (1-2) day, from the 20th procedure, patients were discharged on the same day as the surgery. All devices were retrieved on the 5th day in an outpatient setting. The change from the baseline in IPSS, QoL, and Qmax was significant at every follow-up. The Qmax showed a 67% and 41% increase, after 12 and 36 months of follow-ups, respectively. The early complications of a mild nature rate in the postoperative period was recorded at 12.5%. With the 36 months of follow-up data, TIND was concluded as a safe, effective, and well-tolerated method for the treatment of BPH.[1,14,15]

Another prospective, multicenter, and single arm study, which started with the launch of the (i)TIND® was published recently with its 2 years' functional results, after the 1-year results were published.[16,17] Follow-up assessments were done at 1, 3, 6, 12, and 24 months. All patients were discharged on the same day of surgery with no intraoperative complication. The largest prostate treated with (i)TIND® was 65 mL (16-65 mL) in this study. The retrieval of the (i)TIND® was 5.9±1.1 days following implantation. No >grade 2 complications were recorded. A significant improvement in the IPSS, QoL, and Qmax were observed ($p<0.0001$) at all assessment points. No subsequent sexual or ejaculatory dysfunction was detected. Only patients with OML were clearly shown to have failed the procedure, with a failure rate of 14% within 12 months and 85.7% between 12 and 24 months.

Image-Guided Robotic Waterjet Ablation: Aquablation®

Indication

Aquablation® is recommended for patients with moderate-to-severe LUTS and prostates between 30 and 80 mL in both EAU and AUA guidelines. The presence of the OML was not reported to be a restrictive situation. Both guidelines stated that this treatment is under investigation and long-term follow-up is necessary for the assessment of the clinical value. Neither guidelines included this technique on the algorithm flowcharts (Figure 1).[1,2] It may be a preferred alternative for patients who want to maintain their SxFs.[19,20]

Technique

Aquablation® (PROCEPT BioRobotics; Redwood Shores, CA, USA) therapy is an ultrasound-guided, robotically controlled waterjet prostate ablation treatment allowing for an individualized prostate resection using autonomous AquaBeam®. AquaBeam® Robotic System components and other required equipments are needed for this complex robot-assisted resection of the prostate (Figure 4).

Once the patient is general anesthetized in the dorsal lithotomy position, the surgeon places the transrectal ultrasound (TRUS) under the transverse plane view. Once the position is taken, TRUS is switched to the sagittal view for the handpiece insertion. The 24-Fr AquaBeam® handpiece is assembled with the reusable cystoscope provided. The tip of the handpiece is inserted into the penis and advanced through the prostatic urethra and into the bladder 1 to 2 cm past the BN, then it is secured with the articulating arm. The live TRUS video is imported and displayed by the conformal planning unit (CPU). Before treatment, the surgeon maps the desired resection areas of the prostate. The sagittal image is used to select the area for the resection. The surgeon can use the images to identify landmarks and determine the depth of three-dimensional planning and begins the treatment by depressing the foot pedal. AquaBeam® uses the principle of hydro-dissection to ablate prostatic parenchyma while sparing collagenous structures such as blood vessels and the surgical capsule without the generation of thermal energy. The CPU displays the real-time ultrasound image and provides the ability to monitor the progress of the procedure. The handpiece delivers high-velocity sterile saline at a 90° angle and works as the cutting mechanism for the ablation of both median and lateral. During the procedure, the ablated tissue is aspirated through a series of ports on the handpiece prob and enables the samples to be used for histological analysis. The handpiece follows the prescribed treatment plan based on the mapping input by the surgeon. At any point during the treatment the surgeon can pause the Aquablation®. The surgeon maintains complete

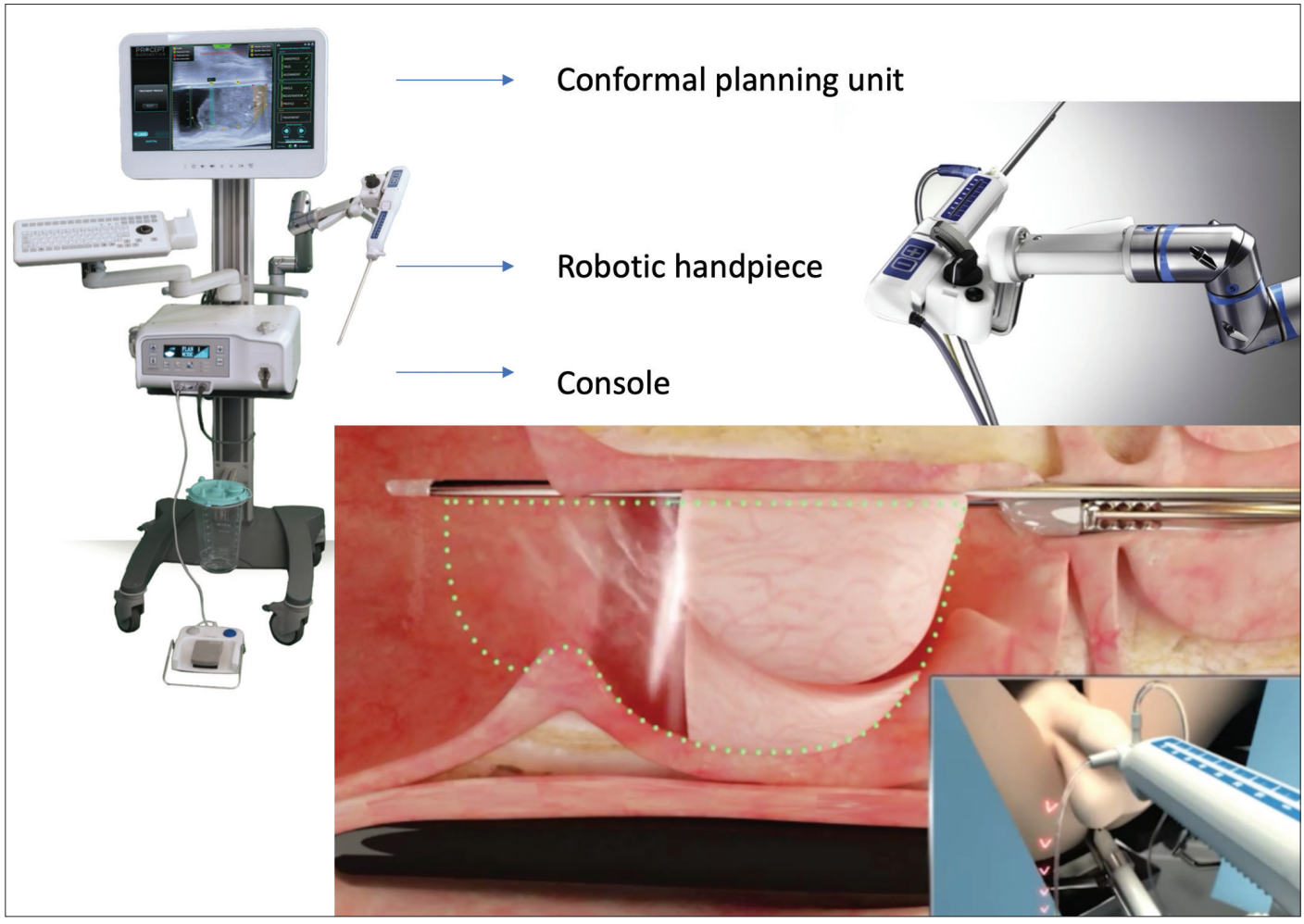

Figure 4. AquaBeam® Robotic System components

cystoscopic visualization during the procedure. The resection is completed in approximately 5 minutes. At this point, the surgeon can perform an endoscopic assessment of the treated prostate. The TRUS images are also available for final assessment. At the completion of the entire procedure, subsequent hemostasis is performed with a Foley balloon catheter on light traction or diathermy or low-powered laser, if necessary.[1,2,20,21]

Role

Gilling et al.[22] designed the Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue (WATER) clinical trial that compared Aquablation® and TURP for the treatment of BPH. A 6-month follow-up assessment was done. The mean PVs for groups were 54.1 (16.2) versus 51.8 (13.8) (p=0.3062). They noted similar mean total operative time between the groups (p=0.2752) but the resection time was lower for Aquablation® (4 vs. 27 min, p<0.0001). The 6th month IPSS results were not significant between the groups (Aquablation -16.9 vs. TURP -15.1, p=0.14). The ejaculation rate was lower in Aquablation® (10% vs. 36%, p=0.0003). They concluded that larger prostates (50-80 mL) demonstrated a more pronounced safety and efficacy benefit. Each group achieved significant symptom relief compared with the baseline with similar rates of Clavien-Dindo 2 or greater complications.[22]

Recently, the 3-year outcomes of WATER trial were published. Over 3 years of treatment, improvements in IPSS, Qmax, and PSA reduction were statistically similar across the groups. The 2-year retreatment rates of Aquablation® versus TURP were 4.3% and 1.5% (p=0.4219), respectively, while no surgical retreatments for BPH beyond 20 months for either Aquablation® or TURP were seen. At all postoperative time points, changes in EjF, as measured by MSHQ-EjD were better in Aquablation® (p=0.0008). Similarly, the MSHQ bother score was higher in the TURP group (p=0.0411). The ErF, as measured by IIEF-15, showed no statistically significant changes in either group and no differences across the groups. One (0.9%) and 4 (6.2%) of Aquablation® and TURP subjects had urethral stricture

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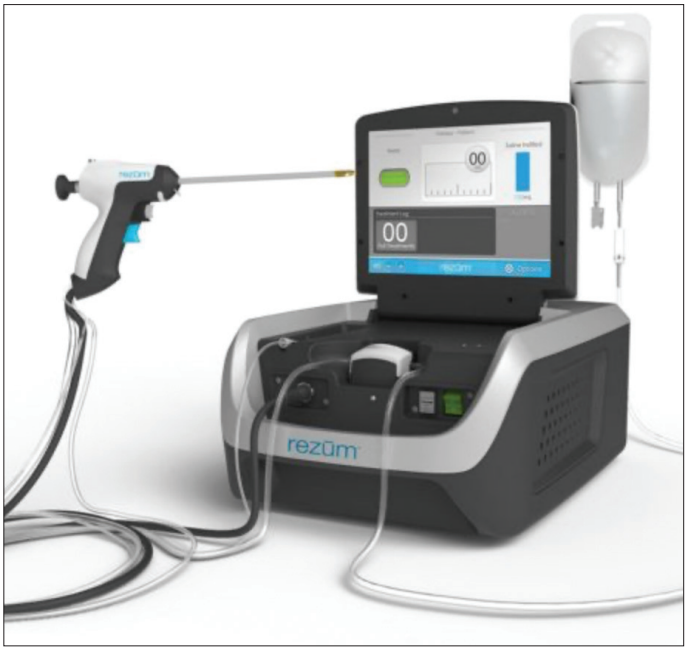

Figure 5. Rezūm® system

(p=0.0567); 3 (2.5%) and 0 (0%) subjects had meatal or submeatal stenosis (p=0.5539). Overall, 3-year retreatment rates were 5/116 (4.3%) in the Aquablation® and 1/65 (1.5%) in the TURP group (p=0.4219).[19,23-25]

Desai et al. designed the WATER-II trial of Aquablation®. The mean PV was 107 mL (80-150 mL). They showed improvement in IPSS, Qmax, PVR, and PSA at 3 and 6 months. The mean length of hospital stay after Aquablation® was 1.6 days (0-6 days). At 6 months, 22% a Clavien-Dindo grade 2, 14% a grade 3, and 5% a grade 4 AEs rates were recorded. Bleeding complications requiring intervention and/or transfusion were needed in eight patients before discharge and in six patients after discharge. Ejaculatory dysfunction occurred in 19% of sexually active men.[26]

Based on a recently published systematic review,[19] the Aquablation® procedure has comparable clinical results at least to the conventional TURP for the PV 30 to 80 mL. High-speed resection time, low complication rate, and SxF preservation make this an effective technique, and it may be used effectively for larger prostates up to 150 mL.

WAVE ablation: The Rezūm® system

Indication

Both EAU and AUA guidelines accept WAVE ablation: The Rezūm® system (Boston Scientific; Marlborough, MA, USA) which is used as a treatment method of LUTS secondary to BPH. The AUA guideline states that Rezūm® may be offered as a treatment method to patients with BPH with PV <80 g (conditional-recommendation; evidence-level: Grade-C) and includes Rezūm® as the treatment option for small (<30 g) and moderate (30-80 g) prostates on the algorithm flowchart; however the EAU guideline hesitates to give statement on this subject, commenting that RCTs against a reference technique are needed to confirm the first promising clinical results and to evaluate mid- and long-term efficacy and safety of Rezūm®. In addition, EAU guidelines do not give any statement on the algorithm flowchart (Figure 1).[1,2]

The AUA guidelines offer Rezūm® to eligible patients who desire preservation of ErF and EjF (conditional-recommendation; evidence-level: Grade-C) [2] and the EAU guidelines support this statement.[1,27] The EUA guidelines do not give any summary of evidence or recommendation about Rezūm® and accept it as the technique under investigation.[1]

The presence of the OML was not reported to be restrictive to Rezūm®, even the treatment technique to be applied in the presence of the OML of prostate has been mentioned in the both AUA and EAU guidelines.[1,2] A recently published review reported that Rezūm® is contraindicated in patients with concurrent artificial urinary sphincter or penile prosthesis implants in place.[6]

Technique

The Rezūm® system (Figure 5) is a novel ablative technique, which uses the stored thermal energy created by radiofrequency (RF) currents in the form of steam to target prostate tissue utilized by a platform technology. The Rezūm® system consists of a RF-power-supply generator, system controls, and a single-use transurethral DD. The hand-held DD is similar in shape and size to a cystoscope and incorporates a standard 4-mm, 30° endoscopic cystoscopy lens. The DD has 12 holes at the tip of an 18-gauge needle. A few drops of sterile water are heated to approximately 103°C, and as the sterile water transforms from liquid into steam or vapor, the volume expands by almost 1,700 times and stores 540 calories of thermal energy for every milliliter. The DD is inserted transurethrally and one to three injections of water vapor are administered to each HLL of the prostate (including one to two injections to OML, if present). Injections last approximately 9 seconds and are delivered at the 3- and 9-o'clock positions. The device delivers the water vapor (103°C) through a retractable needle, and sterile saline flush irrigation is used to enhance the visualization and cool the surface of the urethra. Injections begin at 1 cm distal from the BN and advance every 0.5 to 1.0 cm of the prostatic urethra until the proximal portion of the verumontanum is reached.

During each 9-second treatment, 0.42 mL of heated sterile water vapor is released throughout the targeted prostate tissue when the steam turns back, all the stored energy is released resulting in cell death. Cell membranes are denatured, thereby causing immediate cell death; the vasculature is closed; and there is denervation of the alpha-adrenergic nerves within the treatment zone providing the patient with an efficient, uniform, predictable treatment. Over time, this ablated tissue is reabsorbed by the body's natural healing response, reducing the volume of tissue and allowing the urethra to open the relieving LUTS. Most patients begin to experience symptom relief as soon as 2 weeks, and the maximum benefit will occur within 3 months. The Rezūm® system could be performed safely as an outpatient procedure with only local anesthesia.[1,6,27,28] Reductions of 29% and 38% were reported at 6 months in PVs and targeted transitional zone volumes, respectively. Furthermore, convective thermal lesion sizes are generally reduced by >95% at 6 months after procedure.[28]

Role

Following the FDA clearance in 2015,[6] studies on this issue gained speed. McVary et al. have started working on a multicenter RCT, which they planned to last for 5 years if the primary efficacy endpoint could be passed. They have already published the 4-year results. Objective improvement of LUTS was observed as early as 2 weeks in the first study and remained consistently durable throughout all 4 years.[29-32] IPSS, QoL, Qmax, and BPHII showed significant improvements at 4-year post-procedure. In addition, clinically meaningful improvements of Qmax and IPSS scores were observed for OML when compared with untreated OML. Urinary incontinence scores decreased significantly throughout the 4 years. The 2 years after treatment showed that IIEF and MSHQ-EjD scores remained unchanged. The ejaculatory bother score improved relative to the baseline over 3 years ($p \leq 0.05$).[32] The Rezūm® system related AEs was transient and of mild-to-moderate severity, most of which resolved spontaneously within 3 weeks. Serious procedural AEs were <2% and included extended urinary retention, BN contracture, and urosepsis one from each groups. Catheterization after the procedure was performed in >90% of patients with a mean of 3.4 days. Of these, only 32% actually required catheterization because of unsuccessful void trial before discharge.

McVary et al.[27] showed that the ErF and EjF preserved with convective WAVE treatment. No de novo erectile dysfunction occurred after Rezūm®, related to the treatment or device. IIEF and MSQH-EjD function scores were not different from the control group at 3 months or from the baseline at 1 year. The MSQH-EjD bother score improved by 31% over the baseline ($p=0.0011$). Also, 32% of subjects achieved minimal clinically important differences in ErF scores at 3 months, and 27% at 1 year, including those with moderate-to-severe erectile dysfunction.

Another study reported 12-month follow-up to evaluate clinical experience with the Rezūm® system by multiple community urologists. A total of 131 males with PV ranging from 13 to 183 cm^3 were included in a retrospective analysis. Significant improvement in IPSS, QoL, and PVR was observed throughout 1 year. AEs were mild to moderate in severity, and most of which resolved within a short time. No de novo erectile or ejaculatory dysfunction was reported without using validated questionnaires. Three patients (2%) with obstructing residual tissue or insufficient improvement underwent a TURP 7 to 12 months later; one patient had a second Rezūm® procedure 12 months later.[33]

Retreatment rates of 4.4% after Rezūm® appeared smaller than the rates of 14 to 51% after transurethral needle ablation and 9 to 21% after transurethral microwave thermotherapy. Retreatment rates for the PUL have also been reported at 10.6% at 3 years and 13.6% at 5 years, while that of TURP ranges from 3% to 14.5% after 5 years.[6]

PAE

Indication

PAE, which initially emerged as a method used to control massive hemorrhage after prostatectomy or prostate biopsy, was thought as a BPH treatment method after the reduction in PV in the follow-up of a patient undergoing PAE.[34] Also, an animal study on pigs was established with the significant reduction in PV after embolization, preserving the SxF of the animals.[35] The AUA guidelines do not recommend PAE for the treatment of BPH as an expert opinion owing to the lack of sufficient high level of evidence and low overall quality of currently published studies, and finds PAE as a novel and largely unproven technique because of the deficiencies of included trials.[2]

The EAU guidelines makes a different interpretation. However, the EAU guidelines accept PAE as a technique under investigation. The EAU guidelines find current evidence of safety and efficacy of PAE adequate and give summary of evidence and recommendations on this topic. It is suggested that patient selection should be made by the urologist and radiologist; however, the suitability of the patient for intervention should be investigated by the urologist only. This method should be done in centers where adequate facilities are provided by an interventional radiologist with specific mentored training and expertise in PAE.[1]

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Indications for PAE as a first choice therapy for BPH include patients with special risks regarding surgery or anesthesia, sexually active men, PV >65 mL, permanent bladder catheter, and recurrent bleeding caused by BPH. Patients with malignancy, bladder abnormalities, chronic renal failures, acute urinary tract infection, renal insufficiency (eGFR <60 mL/min), advanced atherosclerosis of the iliac or prostatic arteries, and urethral strictures should be excluded.[36-38] The EAU guidelines state that patients with larger prostates (>80 mL) may have the most to gain from PAE.[1,39] The guidelines and the literature data published so far, show that there is insufficient information for the patient selection and indications for PAE.

Technique

PAE is generally performed under local anesthesia in an outpatient setting. Urinary catheter is recommended as a reference point during PAE. Using computerized tomography (CT) digital subtraction angiography scan (cone-beam CT), the arterial anatomy and the appropriate prostatic arterial supply can be selectively embolized. Various beads, gels, or non-spherical polyvinyl alcohol to infarct prostatic vessels can be used. As a rule, bilateral embolization of the prostate arteries is targeted. Procedure starts with retrograde puncture of the right common femoral artery and insertion of a angiography catheter. The rotation CT angiography scan of the pelvic arteries is acquired, giving the contrast agent above the bifurcation of the common iliac artery. Probing the internal iliac artery, the origin of the prostate artery is identified and superselectively probed. The prostate artery has an average diameter of 0.9 mm and usually originates from the internal pudendal artery or from a common origin with the superior vesical artery. To complete the embolization of the prostate artery, fewer than 0.5mL of microspheres/contrast agent mixture is needed. Flow stop and no reflux should be maintained on both sides. It is believed that PAE reduces the PV due to ischemia in intraprostatic arteries and subsequent inflammation. Decrease in dihydrotestosterone and intraprostatic testosterone following PAE was shown.[37,38]

Role

DeMeritt et al.[40] reported a 76-year-old patient with 305 mL PV who was successfully treated with PAE for his threatening blood loss attacks. Authors noticed reduced PV and PSA levels; PV measured 235 mL, 160 mL, and 190 mL at 2nd, 5th, and 12th months, respectively, and PSA dropped from 40 to 4 ng/mL at fifth month with no sexual impairment. Carnevale et al.[41] published the 18 months' follow-up of two patients and emphasized on the continuous PV and symptom reduction during the follow-up. PAE, which is mainly used for controlling prostate bleeding gave the idea that this method could be an alternative for BPH.

United Kingdom (UK) Register of Prostate Embolization (UK-ROPE) study was a prospective multicenter matched cohort study that enrolled 216 PAE and 89 TURP patients. The study found PAE was a clinically effective method with a median 10-point IPSS improvement that was lower than the median 15-point IPSS improvement of TUR at the 12th month. In 65 closely matched pairs of patients who underwent PAE and TURP, there was no evidence of PAE being non-inferior to TURP in terms of IPSS and QoL. The PAE group showed a statistically significant improvement in Qmax and PV reduction at 12 months. AEs were observed; one had sepsis, one required a blood transfusion; four had local arterial dissection; four had a groin hematoma; and two had penile ulcers in the PAE group. The total reoperation rate for PAE cases was nearly 20%.[42] Also, a systematic review[43] identified up to a 19% failure rate with 15% of patients requiring TURP within the first year after treatment.

A retrospective review of 93 patients with >80 mL enlarged prostates showed significant reduction in PV at 3 and 12 months (141.7 mL to 98.1 and 82.2 mL, respectively, p<0.01). Significant improvements in IPSS, QoL, PVR, and Qmax were also observed.[44] Another RCT was published by Gao et al.[45] and Carnevale et al.[46] Gao et al.[45] showed IPSS, QoL, Qmax, PVR, PSA, and PV improvements after TURP and PAE at all follow-up time points when compared with preoperative values (p=0.001); however, the TURP group showed greater degree of improvement in the IPSS, QoL, Qmax, and PVR at 1 and 3 months, as well as greater reduction in the PSA level and PV at all follow-up time points (p=0.05). The PAE group showed overall more AEs and complications (p=0.029). Similarly, Carnevale et al.[46] showed significant improvement in IPSS, QoL, PV, and Qmax in both groups compared with the baseline, and better Qmax and prostate reduction in the TURP group.

Another RCT compared 48 PAE patients with 51 TURP patients and provided 12 weeks' follow-up results. They noted that PAE was associated with fewer complications than TURP but had disadvantages regarding functional outcomes, which should be considered when selecting patients. Procedural time was shorter for TURP, while bladder catheter indwelling time and duration of hospital stay were shorter in PAE patients.[47] A systemic review and meta-analysis showed QoL, IPSS, PV, PVR, and IIEF improvements were maintained at 3 years.[48] PAE should still be considered as an experimental treatment modality although there is growing evidence of the efficacy and safety of PAE for treatment of BPH.

Conclusion

In this review, five novel treatment methods used in the treatment of LUTS related to BPH are discussed. These methods give the patients optimal benefits, while eliminating side effects. Preservation of SxF is one of the most important issues for male patients, and all these methods claim preserving the SxF, particularly the EjF. These methods, which are still studied, are promising for the future. As the studies get completed, the indications will become clearer, and these techniques will find their place as personalized treatment options.

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