Modern best practice in the management of benign prostatic hyperplasia in the elderly

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Abstract: Benign prostatic hyperplasia (BPH), with its associated lower urinary tract symptoms (LUTS), can be a debilitating disease in the elderly male. Transurethral resection of the prostate (TURP) remains the gold standard; however, many patients will choose to avoid surgery if possible. Medical therapy is an effective alternative, however, new studies are showing that there may be more side effects than previously realized in the elderly male. Newer, novel minimally invasive techniques, including UroLift® and Rezūm™, are gaining favor as alternative office-based procedural techniques that do not require general anesthesia and may better preserve ejaculatory function. Though promising, at this point, these techniques are not approved for all patients. With a range of medical, procedural, and surgical options for treatment of BPH with LUTS, it is important to have a discussion with your patient regarding the short- and long-term risks and benefits, as well as alternatives, before deciding on a treatment plan for your patient with BPH.

Keywords: benign prostatic hyperplasia, elderly, medical therapy, ambulatory procedures, surgery

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Introduction

Benign prostatic hyperplasia (BPH) is a common disease in men, with the prevalence of histologically diagnosed BPH increasing from 8% in men aged 31–40 years, to over 80% in men older than age 80.1 BPH is characterized as progressive enlargement of the prostate gland from nonmalignant proliferation of smooth muscle and epithelial cells. The enlargement manifests clinically as lower urinary tract symptoms (LUTS) such as nocturia, urgency, frequency, urinary retention, straining to urinate, and a weak urinary stream. Without treatment, a significant number of men will suffer from worsening voiding and storage symptoms as they continue to age, with potential progression to acute urinary retention requiring Foley catheter placement.

An association exists between age and disease burden of BPH. Although most men will exhibit some degree of prostate enlargement throughout the course of their lifetime, not all of these men will develop manifestations of LUTS. However, age is likely the most significant contributor to the prevalence of LUTS in BPH patients, with reports showing that the prevalence of LUTS increases to 80% in men at 70 years of age.2 Without treatment, many of these men will suffer from worsening voiding and storage symptoms as they continue to age.3 The gold standard for the management of BPH is surgical treatment by transurethral resection of the prostate (TURP). However, in older adults, medical therapy is preferred to surgical intervention when possible. While medical therapy for BPH has historically been thought to be both safe and effective, newer studies have shown that some of these medications can have unwanted side effects, particularly for the elderly population. Additionally, emerging ambulatory, minimally invasive options, along with novel inpatient techniques, have been developed over the past decade that show promise for those that have failed medical therapy and are either not healthy enough or do not want the untoward side effects...
of TURP. This paper reviews different options for treatment of BPH, including medical therapy, minimally invasive therapy, and surgical therapy as it relates to the elderly male.

**Medical therapy**

**Alpha blockers**

It is important to evaluate the use of alpha-adrenergic antagonists as they are one of the most common classes of medications prescribed for BPH. The smooth muscle of the prostate and bladder neck contain alpha-1a receptors. Alpha-adrenergic antagonists relax the smooth muscle of the prostate and bladder neck to relieve bladder outlet obstruction. There exist both selective and non-selective alpha-blockers, and their side effect profiles are variable. The non-selective alpha-blockers are alfuzosin (Uroxatral), terazosin (Hytrin), and doxazosin (Cardura), whereas tamsulosin (Flomax) and silodosin (Rapaflo) are selective alpha-1a antagonists. Silodosin is the most novel alpha-blocker and has the highest relative selectivity to the prostatic alpha receptors. Silodosin is the most novel alpha-blocker and has the highest relative selectivity to the prostatic alpha receptors. Common side effects of these medications include dizziness, orthostatic hypotension, retrograde ejaculation, and rhinitis. Dizziness and orthostatic hypotension are of increased concern in the elderly population as they can lead to significant morbidity, such as falls and subsequent injuries. Intraoperative floppy iris syndrome (IFIS), a sudden intraoperative iris prolapse and pupil constriction, is also a major concern for patients on these medications. IFIS can increase the risk of complications during cataract surgery. Although increased age has not been found to be associated with increased risk of IFIS, it is important to screen patients who potentially will be undergoing cataract surgery. It is recommended that they consult an ophthalmologist before starting alpha-blockers so as to avoid any surgical complications.

Concerns have emerged regarding the risk of development of dementia in patients who are taking alpha-blockers. As alpha 1-a receptors are present in the brain as well as the prostate, there is a possibility of adverse central nervous system effects while using these antagonists. In order to explore the relationship between risk of dementia with tamsulosin use and other medical therapies for BPH, Duan et al. conducted a cohort study in over 250,000 males. Included patients were >65 years of age with a diagnosis of BPH in Medicare data from 2006 to 2012, based on patient charts with ICD-9 diagnostic codes for dementia. With a mean follow up of 19.8 months, the risk of dementia was found to be significantly higher in older men with BPH taking tamsulosin in comparison with men who did not take any other BPH medications or to those who take doxazosin, terazosin, alfuzosin, dutasteride, or finasteride. However, a recent article by Tae et al. disputes this study. Using the National Health Insurance Service database from Korea, 59,263 patients >70 years old with BPH were studied to compare those taking tamsulosin with those taking doxazosin, terazosin, alfuzosin, and no medication with the incidence of dementia. After a mean follow up of 1580 days (about 52.6 months), no significant difference was seen in the incidence of dementia in the tamsulosin cohort compared with doxazosin, alfuzosin, or no medication. This remained true after propensity score matching for the drug cohorts, and, thus, the authors concluded that BPH medication is not associated with risk of dementia.

Introduced in 2008, the Fit fOR The Aged (FORTA) classification is a system created to assist physicians in the screening process for harmful or inappropriate medications in older patients. Involving over 200 medications and 25 experts, the classification system labels medications from class A to D, with A being “Absolutely,” B being “Beneficial,” C being “Caution,” and D being “Don’t or Avoid” for men over 65 years old based on available research information. In the FORTA classification system for medications in older adults, silodosin and tamsulosin were labeled “Caution.” These alpha blockers were placed in this category because there was no data on efficacy and safety in older adults. Additionally, there are risks of hypotension, especially in the setting of other antihypertensive medications. FORTA also labeled alfuzosin, doxazosin, and terazosin as “Avoid” secondary to the increased risk for orthostatic hypotension, syncope, vasodilatory effects, and cardiac arrhythmias.

**5-alpha reductase inhibitors**

The benefit of 5-alpha reductase inhibitors (5-ARIs) is unclear for older patients. The mechanism of action of 5-alpha reductase is by conversion of testosterone to dihydrotestosterone. The inhibition of these enzymes suppress androgen synthesis, which, in turn, leads to decreased prostate volume and reduced bladder outlet obstruction over time. Two medications in this class,
finasteride (Proscar) and dutasteride (Avodart), have different specificities for type I and type II 5-alpha reductase. Finasteride inhibits 5-alpha reductase type II, whereas dutasteride inhibits both type I and type II. There is no demonstrable clinical difference between the two. Side effects of both medications include gynecomastia, impotence, and decreased libido and ejaculate volume. In the FORTA classification system, both finasteride and dutasteride are “beneficial” in older persons as they are considered to be efficacious and have no geriatrically adverse effects for the elderly male.6

However, there is growing concern that there may be more long-term risk of taking these medications than was originally thought. As 5-ARIs reduce the synthesis of several neuroactive steroids, the modulation of the neuroendocrine stress response may lead to depression. A population-based, retrospective, propensity matched Canadian cohort study by Welk et al. of 93,000 men >66 years old on 5-ARIs for a median duration of 1.57 years and found that depression risk was elevated during the initial 18 months after starting a 5-ARI and remained elevated, though to a lesser extent, throughout the remainder of the study period. Risk of self-harm was also elevated significantly during the initial 18 months on a 5-ARI, though there was no increased risk of suicide.7

Phosphodiesterase inhibitors
Phosphodiesterase inhibitors (PDE5I) are now approved for BPH in daily use along with their well-known approval for erectile dysfunction (ED). PDE5I works by blocking the breakdown of cGMP to GMP by phosphodiesterase. The prostate contains PDE 4, 5, and 11, and cross-reactivity from PDE5I leads to vasodilation and improvement in LUTS. Tadalafil (Cialis) has shown improvement in BPH quality of life (QoL), and can be used for men that have both LUTS and ED. Side effects from PDE5-I include headaches, flushing, and dyspepsia. In patients taking nitrates, PDE5I are contraindicated as they might potentiate the effect of nitrates and cause life-threatening hypotension. In a systematic review, Tadalafil improved LUTS and International Prostate Symptom Score (IPSS) scores more than placebo with a dose-dependent effect.8 However, this effect might not hold true in the elderly population. In a study by Oelke et al. focused specifically on elderly men, an integrated analysis of 12 phase II–III randomized trials compared the efficacy and safety of 5mg tadalafil in men <75 years of age with that in men >75 years of age, and found that tadalafil was not statistically significantly better than placebo for men >75 years old. The authors attributed this finding to the presence of more co-morbidities in older men, who have more concomitant diseases, with the subsequent use of more medication in older men postulated to lead to reduced efficacy. There was also a concern with the use of PDE5-I as there was a higher rate of diarrhea and dizziness in men older than 75.9 Due to its cardiovascular contraindications, tadalafil is rated as “Caution” in the FORTA classification.6

Anticholinergics
Another class of medications that is important in the context of BPH medical management in the elderly population are anticholinergics. In terms of mechanism of action, they reduce detrusor muscle contractions by inhibiting muscarinic receptors in the bladder wall. Decreased contractions, in turn, decrease the symptoms of detrusor over activity (DO) that could result from outlet obstruction from BPH. Anticholinergics demonstrate efficacy by decreasing urgency, incontinence episodes, and bothersome storage symptoms from BPH with overactive bladder (OAB). Most commonly reported adverse side effects include constipation, dry mouth, and dry eyes or blurry vision. As these medications relax the bladder, urinary retention is a major concern for patients on anticholinergics. There is also a risk of neuro-cognitive deficit in patients on this class of medications, given that the cholinergic system plays an important role in cognitive function. Muscarinic receptors are abundant in the central nervous system, and non-selective anticholinergics may exacerbate symptoms of dementia.

The 2015 Beers Criteria, an updated list by the American Geriatric Society that aims to catalogue medications that may cause side effects in the older adult population due to physiological effects of aging based on evidence-based methodology, recommended than many of the anticholinergics used to treat OAB be avoided in older adults. There is an increased the risk of confusion due to decreased clearance of the medication over time.10 A large longitudinal study by Risacher et al. also concurred with the Beers Criteria’s concerns.11
Their study followed 52 older adult patients with a mean age of 73.3 (standard deviation 6.6 years) that were on an anticholinergic medication as determined by pharmacy dispensing data. This prospective population-based cohort was followed starting from 1994 every 2 years. Their study found that the use of an anticholinergic was associated with increased brain atrophy and clinical cognitive decline, with a 10-year cumulative dose-dependent statistically significant relationship between these medications and the diagnosis of dementia and Alzheimer’s disease (p < 0.001). Furthermore, a prospective population-based cohort study by Gray et al. looked at 3434 patients over 65 with no dementia over a mean follow up of 7.3 years. At the start of the study, 668 participants (19.5%) were taking an anticholinergic for bladder or BPH related disease; 797 participants (23.3%) developed dementia (79.9% of whom developed Alzheimer’s disease). Again, a 10-year cumulative dose-response relationship of anticholinergic intake was observed for dementia and Alzheimer’s disease (test for trend, p < 0.001), showing that higher cumulative anticholinergic use is associated with increased risk of dementia.

Fesoterodine (Toviaz), an anticholinergic with a high affinity for M3 receptors, which are predominantly found in the bladder, was the only medication in this class to receive a “Beneficial” FORTA classification. One study by Wagg et al. compared fesoterodine with placebo in 794 patients aged 65 and older with OAB. Patients who were on fesoterodine experienced statistically significant improvements in urgency episodes (p < 0.001), total voids (p < 0.001), nocturnal voids (p = 0.003), and incontinence pad use (p = 0.01), as measured by bladder diary and an OAB questionnaire. There was no difference found in change in the Mini Mental Status Exam (MMSE) in either groups. The other anticholinergics, solifenacin (Vesicare), darifenacin (Enablex), and toleridene (Detro), were rated as FORTA classification “Caution” because of their cardiovascular effects (heat intolerance, increased heart rate, and decreased ability to sweat) and potential adverse effect on cognitive function.

**Beta-3 agonist**

Beta3-adrenoceptor agonist medications, such as mirabegron, may help to circumvent the need for anticholinergics in older patients with OAB. Mirabegron is a specific agonist of the beta3-adrenoceptor in the human detrusor muscle, in which stimulation leads to active relaxation of the detrusor during the storage phase and increases bladder capacity without an effect on voiding. Many clinical studies have shown the safety, tolerability, and efficacy of once daily mirabegron for patients with OAB. Wagg et al. performed a pooled analysis of three randomized, placebo-controlled, phase III clinical trials on the effect of mirabegron on a subgroup of patients that were >65 years old and >75 years old. Over the 12-week study periods, mirabegron reduced the mean number of incontinence episodes and voids in 24 h from baseline to final visit in both subgroups. At 12 weeks and 1 year after onset of medication, the medication with well tolerated, with hypertension and urinary tract infection the most common adverse events. When compared with a group taking toleridene, an anticholinergic, the incidence of dry mouth was sixfold lower in this group of older patients. Mirabegron is rated as FORTA classification “Caution” at this time as it is a relatively newer medication with cardiovascular risk of hypertension, and in which cognitive effects have not yet been properly studied. A note was made that rating may change to FORTA classification “Beneficial” if studies with proper evaluation of elderly are provided in the future. Currently, mirabegron is approved for treating the symptoms of urgency, increased micturition frequency, and urinary urge incontinence in patients with OAB. There is limited data on the use of mirabegron as monotherapy specifically for patients with OAB due to BPH, but studies exist showing its utility in combination therapy (see below).

**Combination therapy**

Multiple large-scale clinical trials have shown benefits of combination therapy for the treatment of BPH associated LUTS; however, none of these studies focused exclusively on the elderly population. The Medical Therapy of Prostate Symptoms (MTOPS) trial studied the combination of finasteride with doxazosin in 3000 men with average age 62.6 years (SD 7.3 years), and found that the combination improved voiding symptoms and maximum urinary flow rate more than either agent alone. Additionally, this study also showed that combination therapy prevented progression of BPH better than either agent alone, and reduced the long-term risk of acute urinary retention and need for invasive therapy. These results were confirmed in the CombAT (Combination of Avodart and Tamsulosin) trial, where 58% of...
patients were over 65 years old. Combination therapy had greater risk reduction in acute urinary retention or BPH-related surgery, and greater reduction in the relative risk of clinical progression than either monotherapy. Current American Urological Association (AUA) guidelines recommend combination alpha-blocker and 5-alpha reductase inhibitor therapy for men with moderate-severe LUTS symptoms, advanced age, and prostate size larger than 40 g.

Other combination therapies have also been studied. Singh et al. performed a randomized, prospective study in 133 men with average age 61.6 years (standard deviation 6.89 years, 51.1% of the population was over the age of 60) with LUTS secondary to BPH. They compared combination tamsulosin and tadalafil with either medication alone in patients with LUTS. Combination therapy improved IPSS score, Qmax, post-void residual (PVR), and International Index of Erectile Function 5 (IIEF5) score more than either therapy alone. Casabe et al. performed a randomized, double-blind study in 696 men with average age 63.7 years old (41.6% over 65 years old, 7.9% over 75 years old), and found that combination therapy of tadalafil with finasteride improved IPSS score and erectile function more than finasteride alone, with few adverse effects.

More studies evaluated combination therapies. In 2006, the TIMES trial was a randomized, double-blind, placebo controlled trial of 879 men aged 40–92 that looked at the combination of alpha-blockers with anticholinergics as compared with either alone or placebo for the treatment of LUTS with OAB symptoms and found that combination therapy resulted in an improved number of nocturia episodes, daytime frequency, and urgency episodes (as measured by bladder diary) after 12 weeks of treatment. In the more recent NEPTUNE II extension study reported by Drake et al., 1066 men (mean age 65.1) with both storage and voiding LUTS were given a fixed-dose combination therapy of solifenacin and tamsulosin and followed for 52 weeks. Over the study period, the mean total IPSS score was reduced and maintained by 9.0 points. Additionally, the number of micturitions, urgency episodes, and incontinence episodes were reduced. Unfortunately, 46.8% of patients experienced a treatment-based adverse effect, with the most common being dry mouth, constipation, and dyspepsia. In 1.1% of the patients, acute urinary retention occurred. A limitation of both studies is that neither evaluated cognitive effects, which is a major consideration for older patients taking anticholinergic medication.

More recently, mirabegron has been evaluated for efficacy as combination therapy for patients with BPH and OAB. In the recently published MATCH study by Kalkizaki et al., mirabegron add-on therapy with tamsulosin was compared with placebo in patients with LUTS and OAB. Mirabegron add-on therapy was found to have superior outcomes in terms of change in mean number of micturition/24h at 12 weeks, mean volume voided/micturition, OAB symptom score, and IPSS score. No major safety concerns were noted with mirabegron. Published more recently, the PLUS trial was a phase IV, randomized, double-blind trial in which patients with documented LUTS due to BPH and OAB were given an initial 4-week period of tamsulosin and then were given either mirabegron or placebo as add-on therapy. With 56% of patients >65 years old, it gave good insight into the use of this combination therapy in elderly patients. Tamsulosin with mirabegron was statistically superior to tamsulosin with placebo in reducing mean number of micturitions/day ($p=0.039$), mean volume voided/micturition, and urgency episodes/day. PVR and Qmax rate were not statistically different between the two groups, and urinary retention rates were higher in the mirabegron group.

In summary, while we know that medical therapy for the treatment is effective and should be attempted prior to consideration of surgical therapy, side effects do exist that can be debilitating to the older male. Major trials studying the efficacy of these medications were limited as they did not focus specifically on the elderly and did not have a long follow up in order to make meaningful conclusions regarding long-term side effects. It is important to counsel patients accordingly on their efficacy and side effects prior to starting a medical therapy, have a discussion on duration of medical therapy, and when to proceed to procedural or surgical options.

**Alternative minimally invasive/surgical procedures to TURP**

For patients that have failed medical therapy or were unable to handle the side effects, historically the next step would be to undergo TURP. However, TURP requires general anesthesia and has been associated with unwanted side effects of retrograde ejaculation and ED. In the past decade,
there has been a push for minimally invasive, office-based procedures that do not require general anesthesia or hospital stay, and do not have the side effects associated with TURP. New surgical therapies have also been designed in the hopes of similar efficacy with decreased side effects and retreatment rates.

Overall, surgical therapy is recommended in patients with recurrent urinary tract infections secondary to BPH, renal insufficiency secondary to BPH, recurrent bladder stones or gross hematuria from bladder outlet obstruction due to BPH, refractory urinary retention secondary to BPH, and/or patients with LUTS that have failed or those who are unwilling to consider other therapies. Prior to starting any procedural or surgical therapy, clinicians should obtain a PVR, assess prostate size using either ultrasound (abdominal or transrectal), pre-existing cross-sectional imaging, or cystoscopy, and should consider uroflow or pressure flow studies in the appropriate patient.

Prostatic UroLift®

The Prostatic Urethral Lift is an endoscopic therapy for resolving prostate-related bladder outlet obstruction by creating an open urethral channel from the bladder neck to the prostatic apex. A rigid cystoscope is used to place small, permanent transprostatic UroLift® Implants (Neotrac®, INC, Pleasanton, CA, USA), that are positioned in the anterior and lateral aspects of the prostatic urethral lumen. The implants tether the compressed tissue to the prostatic capsule, establishing an open lumen in the prostatic urethra. The UroLift® was approved by the United States Food and Drug Administration (FDA) in 2013 following a prospective, sham-controlled, double-blind study by Roehrborn et al. in which 206 men were randomized in 2:1 fashion to receive either the urethral lift or the sham control. Inclusion criteria were men >50 years old with an American Urological Association Symptom Index (AUASI) >13, a maximum flow rate of 12 ml/s, and a prostate of 30–80 g as measured by prostatic ultrasound. Men were excluded if they had median lobe obstruction, retention, a PVR >250 ml, or active infection, among others. With a mean age of 67 for the UroLift® cohort and 65 for the sham cohort, the results showed that prostatic urethral lift and sham AUASI was reduced by 11.1 ± 7.67 and 5.9 ± 7.66, respectively, with a statistically significant \( p<0.001 \) for the UroLift® cohort. In 2017, the 5-year results were published with improvement in IPSS, QOL, BPHII, and Qmax of 36%, 50%, 52%, and 44%, respectively. The surgical retreatment rate was 13.6% over the 5 years, corresponding with a 2–3% retreatment rate per year. Adverse effects were mild and transient, and sexual function was stable over the 5 years with no new or sustained erectile or ejaculatory dysfunction.

The BPH6 study was a prospective, randomized controlled trial at 10 European centers involving 80 men that were randomized to undergo UroLift® or TURP for management of their BPH symptoms. Inclusion criteria were men >50 years old, IPSS >12, Qmax <15, PVR <350, and prostate volume <60 cc, with men excluded if they had an obstructive median lobe, urinary retention, previous surgery, severe cardiac comorbidities, or anticoagulants within 3 days of procedure. Changes in IPSS and Qmax were superior in the TURP arm to the UroLift® arm; however, UroLift® resulted in superior QoL, ejaculatory function preservation, and performance on the composite BPH6 index. Throughout the 2-year follow up, six (13.6%) PUL patients and two (5.7%) TURP patients had secondary intervention for refractory LUTS.

Given the available evidence, the AUA have proposed guidelines for the use of Prostatic UroLift®. The AUA guidelines states that patients can consider UroLift® “as an option for patients with LUTS attributed to BPH, provided the prostate volume is less than 80 g and there is a verified absence of an obstructive middle lobe, and may be offered to eligible patients concerned with erectile and ejaculatory function for the treatment of LUTS attributed to BPH. Patients should be informed that symptom reduction and flow rate improvement is less significant compared with TURP.”

Rezūm™

Using a transurethral needle ablation technique, Rezūm works by injecting sterile water vapor into the adenoma of BPH. The heat from the water vapor disrupts prostate cell membranes, with eventual cell death. Like UroLift®, Rezūm can be performed under local anesthesia in the outpatient setting. Unlike UroLift®, Rezūm has the added benefit of acceptable use on patients that have a large median lobe. A randomized, multicenter controlled study by McVary et al. studied 197 men...
over the age of 50 with IPSS scores of 13 or greater, maximal flow rate of 15ml/s and prostate size of 30–80g compared Rezūm therapy with a sham control.28 In the initial 2016 1-year follow-up report, IPSS was reduced by 11.2 ± 7.6 in the Rezūm group and 4.3 ± 6.9 in the control group at 1 year (p < 0.0001). The peak flow rate of the Rezūm cohort increased by 6.2ml/s at 3 months and was sustained throughout 12 months (p < 0.0001). At 1 year, no new ED was reported, with all adverse events being mild to moderate.28 In the recently published 4-year results, symptom improvement remained durable throughout 4 years based on IPSS, QoL, and maximal flow rate. Surgical retreatment rate was 4.4% over the 4-year follow up.29

A retrospective analysis by Darson et al. in 2017 looked at 131 patients with moderate-to-severe LUTS with a median age of 71.3 (range 47.4–96.4) at 1 year post Rezūm therapy. Notably, there was no upper limit prostate size in the inclusion criteria, and this study did include some patients with prostate larger than 80g. At 1 year, mean IPSS decreased from baseline 19.4–10.1 and mean Qmax had a 1.5 ml/s increase from baseline, with improvement seen in all size prostates.30

At this time, the AUA recommendations for Rezūm state that it “may be offered to patients with LUTS attributed to BPH provided prostate volume <80g; however, patients should be counseled regarding efficacy and retreatment rates.”17

Aquablation

Using a robotic-assisted, high-velocity waterjet with transrectal ultrasound guidance, Aquablation (AquaBeam, PROCEPT BioRobotics Inc., Redwood Shores, CA, USA) is a novel transurethral surgical therapy for BPH. The water stream allows resection of tissue without using thermal energy. Aquablation does require general anesthesia and a hospital setting, so for the elderly population similar concerns as from TURP from an anesthesia perspective do still exist, and patients are routinely admitted overnight for monitoring. In a prospective, non-randomized, single-center trial of 15 men aged 50–80 with moderate to severe LUTS, with mean prostate size of 54 g (range 27–85 g), Gilling et al. showed a mean IPSS score improvement from 23.1 at baseline to 86 at 6 months (p < 0.001) with Qmax increased from 8.6 ml/s at baseline to 18.6 ml/s at the same time period (p < 0.001).31 Mean prostate size was reduced by 31% from baseline at 6 months. Patients were admitted overnight, with most discharged on postoperative day 1. The most common side effects were dysuria, hematuria, urinary retention, and bladder spasms, with no severe 30 day adverse effects and no reports of urinary incontinence or ED.31

The WATER study was a double-blind, randomized, multicenter, prospective, controlled trial of 181 men with moderate-to-severe LUTS with mean age 66 years old, prostate volume range 30–80g, IPSS >12, and Qmax <15, comparing Aquablation with TURP. After 6 months, Aquablation was shown to be noninferior when compared with TURP for symptom relief, with a mean decrease from baseline IPSS score by 16.9 points in the Aquablation cohort versus 15.1 points in the TURP cohort (noninferiority p < 0.0001, superiority p = 0.1347). Postoperative hemoglobin decrease was significantly higher in the Aquablation cohort, and mean resection time was significantly lower in the Aquablation cohort. Mean hospital stay in both cohorts was 1.4 days, with most patients having their catheter removed on postoperative day 1 in both groups.32 In the recently published 2-year data, mean IPSS score and Qmax were similar in both groups. Surgical retreatment rates after 12 months for Aquablation were 1.7% and 0% for TURP. Over 2 years, surgical BPH retreatment rates were 4.3% and 1.5% (p = 0.4219), respectively.33

At this time, AUA guidelines state that Aquablation should be “offered to patients with LUTS attributed to BPH that have prostate size 30–80g; however, patients should be notified that long term evidence of efficacy and retreatment rates remains limited.”17

Photoselective vaporization and enucleation of prostate

GreenLight™ Laser PVP (Boston Scientific, Malborough, MA, USA) utilizes a laser at a wavelength of 532nm. At this wavelength, the laser energy is absorbed by hemoglobin resulting in vaporization of highly vascular tissues such as the prostate. Enucleation of the prostate utilizes various laser technologies [Holmium-LEP (HoLEP), Thulium-LEP (ThuLEP), Greenlight-LEP (GreenLEP) and Diode-LEP (DiLEP)] to transurethrally enucleate the adenoma to allow for its removal from the capsule. In a recent meta-analysis that compared various laser
enucleation, resection, and vaporization techniques with monopolar and bipolar TURP in 13,676 patients, Huang et al. found, for Qmax at 12 months after treatment, the best three methods compared with monopolar TURP were bipolar enucleation [mean difference 2.42 ml/s (95% confidence interval 1.11–3.73)], diode laser enucleation [1.86 (–0.17 to 3.88)], and holmium laser enucleation [1.07 (0.07 to 2.08)].34 The worst performing method was diode laser vaporization [–1.90 (–5.07 to 1.27)]. IPSS at 12 months after treatment showed similar results. The best three methods, versus monopolar TURP, were diode laser enucleation [mean difference –1.00 (–2.41 to 0.40)], bipolar enucleation (0.87 (–1.80 to 0.07)), and holmium laser enucleation (–0.84 (–1.51 to 0.58)). All methods studied were shown to have better control of bleeding when compared with TURP.34 This is in line with current AUA guidelines, which recommend HoLEP, PVP, and ThuLEP be considered in medically complicated patients with a higher risk of bleeding, such as those on anticoagulation therapy.17

Prostatic artery embolization

Prostate artery embolization (PAE) is a minimally invasive interventional radiology technique that was first developed to stop otherwise controllable prostatic bleeding, but was later offered for the treatment of BPH when some patients who underwent the procedure for bleeding also reported a reduction in LUTS. The procedure is typically performed by an interventional radiologist who peripherally inserts a catheter, navigates to the prostatic artery under fluoroscopic guidance, then identifies the prostatic arteries and branches with an IV contrast agent. Microparticles are then injected to achieve targeted ischemia of the prostate gland. A prospective, randomized, and controlled clinical trial by Gao et al. compared improvement of IPSS, QoL, peak urinary flow, PVR urine volume, prostate-specific antigen (PSA) level, and prostate volume at 1-, 3-, 6-, 12-, and 24-month follow up in 57 men who underwent PAE with 57 men who underwent TURP.37 Whereas both techniques showed an improvement in the six functional outcomes assessed (p = 0.001), the TURP group showed greater degrees of improvement in the IPSS, QOL, peak urinary flow, and PVR urine volume at 1 and 3 months, as well as greater reductions in the PSA level and prostate volume at all follow-up time points, when compared with the PAE group (p < 0.05). The PAE group showed more overall adverse events and complications (p = 0.029), mostly related to acute urinary retention (25.9%), postembolization syndrome (11.1%), and treatment failures (5.3% technical, 9.4% clinical).37

There is an unfortunate lack of long-term, robust data on the efficacy of prostatic stents and in comparison with other methods of treatment for BPH, which may be due to the different types of stents that exist, and high attrition rate in patients that use the stents. As a result, the AUA does not mention prostatic stents as a treatment option for patients with BPH. The EAU guidelines recommend the use of prostatic stents “as an alternative to catheterization in men unfit for invasive procedures that require spinal or general anesthesia.”38 It should be noted that a host of new types of prostatic stents are currently in clinical trials and, if approved, will add to our therapeutic armamentarium.

Prostatic stenting

As stents are a common way of maintaining luminal patency in many areas of medicine, including cardiovascular and gastrointestinal, many thought a prostatic stent may be a good method of maintaining urethral patency in patients with BPH and as an alternative to indwelling catheterization. Different varieties of prostatic stents exist, with the main distinction being permanent versus temporary. Of the temporary types, prostatic stents may be biodegradable or nonabsorbable and prevent tissue epithelialization, which allows for easy removal. Prostatic stent insertions are performed under local or regional anesthesia on an outpatient basis, and as a result are meant as an alternative form of treatment for high-risk, frail patients who may or may not be in urinary retention and are unable to undergo general or spinal anesthesia. According to a review of prostatic stents by Lam et al. in 2001, relative contraindications for prostatic urethral stenting include meatal or urethral strictures, presence of an active urinary tract infection, bladder stones, neurogenic bladder dysfunction, prostatic urethra less than 2 cm long, large median lobe, and presence of bladder neck contracture.35 Complications of the permanent stent types include encrustation, urinary tract infection, and chronic pain. Of the temporary stent types, migration, urinary tract infection, and encrustation are the common complications.
Pisco et al. found PAE to be technically successful in 250 patients (97.9%). Mean follow up, in 238 patients, was 10 months (range 1–36). Cumulative rates of clinical success, defined as improvements in symptoms and QoL measured with IPSS, QoL, IIEF5), uroflowmetry, PSA and volume, were 81.9%, 80.7%, 77.9%, 75.2%, 72.0%, 72.0%, 72.0%, and 72.0% at 1, 3, 6, 12, 18, 24, 30, and 36 months, respectively.

At this time, the AUA does not recommend PAE for the treatment of LUTS attributed to BPH outside the context of a clinical trial. In part, this is because of concerns of the rigor of the aforementioned clinical trials and concerns about short- and long-term safety, including radiation exposure, post-embolization syndrome, and vascular access.

**Conclusion**

BPH is an increasingly common disease in our ever-aging population, and subsequent LUTS can be debilitating for the elderly male. While TURP remains the gold standard for treatment, medical therapy still shows promising results for treatment and avoidance of surgery. However, one must be conscious of the newly recognized side effects that these medications can have in the elderly male, especially over a long period of time. Novel minimally invasive techniques have shown promise for the elderly male who has failed medical therapy and is not a surgical candidate or wants to avoid surgery, though they are not for every patient. As with any disease, it is important to have a discussion with your patient regarding the risks, benefits, side effects, and alternatives before deciding on a treatment plan for your patient with BPH.

**Conflict of interest statement**

The authors declare that there is no conflict of interest.

**Ethics statement**

Approval of an ethics committee was not required as this was a review of other published works.

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