Benign Prostatic Hyperplasia

David R. Paolone, MD

The histologic entity of benign prostatic hyperplasia (BPH) has, unfortunately, become synonymous with the clinical entity of voiding dysfunction in older men who do not have obvious abnormalities such as multiple sclerosis (Table 1). Perhaps, because of that reason, the urologic community has moved away from using BPH in the generic sense to the term lower urinary tract symptomatology (LUTS) to describe voiding dysfunction in older men. This article reviews the epidemiology of BPH, evaluation of the patient with LUTS, and the management (medical and surgical) for these patients.

EPIDEMIOLOGY

The problems of BPH may be reviewed in the context of histology or clinical symptomatology. The prostate gland is composed of glandular and stromal tissue, and hyperplasia of the periurethral tissue defines this process. Histologically, autopsy studies have revealed that BPH essentially never occurs before age 30 years1 and then progressively increases until it reaches almost 90% for men in their 80s. These numbers have been found consistently across the globe.2–4

Clinically, the situation is much more complex in that the old term prostatism (now LUTS)5 applies to several different phenomena: glandular enlargement, symptomatology, and obstruction.

Glandular enlargement, as described earlier, progressively increases with age; at least population averages do. If on the other hand one looks at individuals, the scatter plot shows all sizes at all ages (Timothy Moon, personal data, 2009).6 Many studies of total prostate volume have been performed.6–8 Most studies have used transrectal ultrasound measurements. Although the total prostatic volume measurements show some variation across studies and continents, measurements of transitions on volumes have shown remarkable consistency. Overall, total prostatic volume measurements have averaged from approximately 25 cm³ for patients aged in their 30s increasing to 45 cm³ for men in their 70s. Transitional zone measurements have

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shown remarkable similarity between United States and European studies averaging 15 cm³ for men in their 40s to 25 cm³ for men in their 70s.7–9

Other Causative Relationships

Although age is an obvious causal factor for BPH, many other causal attributes have been sought for its development. Links have been evaluated for religion, socioeconomic factors, sexual activity, hypertension, smoking, liver cirrhosis, and body mass index (calculated as weight in kilograms divided by the square of height in meters). Studies of religion and socioeconomic factors have not reported any evidence of an association.9 Sexual activity per se does not seem to be causally related. However, a large multinational study has suggested the reverse in that men with increasing LUTS have increasing sexual and ejaculatory disturbances.10 Studies of hypertension and smoking are less than compelling.9 Alcohol through its effect on reducing plasma testosterone has been found to have an increasing association with BPH.

A recent study evaluating metabolic syndrome and LUTS showed a statistical association between metabolic syndrome and LUTS. In this context, the components of diabetes and hypertension were most associated. Further, these data only applied to men less than 60 years old.11

Symptoms

Urinary symptoms have been measured by a variety of questionnaires. However, in the 1990s, under the auspices of the American Urologic Association (AUA), the AUA symptom index (AUASI) was developed, tested, and validated.1 This 7-question assessment has a point score from 0 to 35. A score of 0 to 7 is considered minimally symptomatic, 8 to 19 moderately symptomatic, and 20 to 35 severely symptomatic. International studies have found wide variation in prevalence but all show an increasing prevalence with age. A study in the United States found moderate to severe symptom prevalences of 45% for men in their 50s increasing to 62% for men in their 70s.12 More important, however, than symptoms is the issue of bother, that is, how much do the symptoms affect one’s lifestyle? For most men with mild to moderate symptoms, treatment is optional and generally should be driven by bother rather than “just because we can.”13

Obstruction

Measurements of obstruction can only be made by invasive measurements. This entails a pressure flow study, which requires not only that the man be catheterized

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**Table 1**

<table>
<thead>
<tr>
<th>Age (Decade)</th>
<th>Histologic Prevalence (%)</th>
<th>Clinical Prevalence (%)</th>
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<tbody>
<tr>
<td>30s</td>
<td>0</td>
<td>5–10 (not directly associated with BPH)</td>
</tr>
<tr>
<td>50s</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>70s</td>
<td>80</td>
<td>62</td>
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**Natural history**
- Urinary retention: 0.6–1.8/100 person-years
- UTI: Not directly caused by BPH/LUTS
- Hematuria: 2.5%
- Symptom progression: 3.6/100 person-years
- Socially unacceptable incontinence: 0.3/100 person-years
for pressure measurements and fluid installation but also requires a rectal balloon catheter to measure bowel pressure as a surrogate abdominal pressure. Urine free flow rates provide an indirect measure of obstruction that is less than perfect. However, peak flow rates less than 10 ml/s are highly correlated with obstruction, whereas flow rates in excess of 20 ml/s are rarely associated with obstruction. In the Olmsted County population study, peak flow rates decreased from 20 ml/s for men in their 40s to 14 ml/s for men in their 70s. However, if the graphs of individual studies are reviewed, the spread is much greater than the differences between decades.

**Natural History**

Evaluation of the natural history includes symptom changes and changes in the overall medical condition as a sequela of LUTS/BPH. Symptoms, as noted earlier, have been shown to increase with age. Direct consequences of BPH/LUTS that have a direct effect on the patient’s medical condition include urinary retention, azotemia (from upper tract obstruction), urinary tract infection, and hematuria. Urinary retention has been evaluated in the placebo arm of the Proscar Long-Term Efficacy and Safety Study (PLESS) at 1.8/100 person-years and in the same arm of the Medical Therapy of Prostate Symptoms (MTOPS) trial at 0.6/100 person-years for a cumulative incidence of 2% at 4 years. This same study found no renal insufficiency. However, patients were followed throughout the study and would not have been eligible at the entry point if this had been a serious potential issue. Symptom progression during this period (≥ 4 point change on the AUA symptom score) was 3.6/100 person-years for a cumulative incidence of 14% at 4 years.

Urinary tract infection in general is not considered the direct consequence of BPH/LUTS but for patients with poor emptying and large postvoid residual urine, persistent/recurrent urinary tract infections may become an indication for treatment. Likewise, persistent hematuria is an indication for therapy. Little data exist on its prevalence but 1 study reported a rate of 2.5%.

**PATIENT EVALUATION**

The first objective in evaluating patients with LUTS is in separating those patients with other medical conditions likely to develop urinary symptomatology from those without such comorbidities. To the extent that congestive heart failure and diabetes are so prevalent in the older population, evaluation of urinary symptomatology, in the context of the general medical history, is extremely important. After the medical history, a detailed evaluation of urinary symptomatology is required. The current recommendation would be use of the International Prostate Symptom Score (IPSS) (identical to the AUASI) although any evaluation of irritative symptoms (frequency, nocturia, urgency), obstructive symptoms (hesitancy, poor flow, intermittency, and feeling of incomplete emptying) as well as bother will reasonably suffice. A history of hematuria should always be sought. In addition, questions about diabetes and congestive heart failure may account for frequency/nocturia, whereas a history of trauma/sexually transmitted diseases might raise the possibility of a urethral stricture.

**Physical Examination**

The physical examination evaluates the patient for abnormalities that might affect urination and for other diseases that also might affect LUTS. Thus, the abdominal examination might detect a full bladder, and the external genitalia examination might detect meatal stenosis or severe phimosis. A rectal examination detects prostatic abnormalities, most importantly the possibility of prostate cancer.
<table>
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<th>Table 2: AUA symptom score</th>
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<tr>
<td><strong>Not at All</strong></td>
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<tr>
<td>-------------------</td>
</tr>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?</td>
</tr>
<tr>
<td>3. Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
</tr>
<tr>
<td>4. Over the past month, how often have you found it difficult to postpone urination?</td>
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<tr>
<td>5. Over the past month, how often have you had a weak urinary stream?</td>
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<tr>
<td>6. Over the past month, how often have you had to push or strain to begin urination?</td>
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<tr>
<td>7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
</tr>
<tr>
<td><strong>BOTHER QUESTION</strong></td>
</tr>
<tr>
<td>8. If you were to spend the rest of your life with your urinary condition just the way it is now, how would you think/believe about that?</td>
</tr>
<tr>
<td><strong>Total symptom score:</strong></td>
</tr>
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</table>

Laboratory Evaluation

Although there is no Level I evidence to support it, the AUA\textsuperscript{13} and European Association of Urology (EAU)\textsuperscript{18} support urinalysis as a simple, effective, and cheap test to evaluate for hematuria, inflammation, and infection. It might also help identify the patient consuming large fluid volumes by reason of a very low specific gravity. The presence of hematuria is obviously important as that immediately moves the evaluation to that of hematuria rather than LUTS. The presence of microscopic hematuria requires an evaluation of the complete urinary system for its cause.\textsuperscript{19} Unless the patient has findings suggestive of medical renal disease (proteinuria, red cell casts, or dysmorphic red cells) the current recommendations would be for a computed tomography urogram and cystoscopy. The best practice policy recommendations\textsuperscript{19} recommend this evaluation for all high-risk patients. As this includes patients more than 40 years old and those with urologic disorders (BPH/LUTS), it effectively includes all patients presenting with LUTS. In addition, for these patients and patients with predominantly irritative symptoms but without hematuria, voided urine for cytology is indicated. This is especially so for patients with a history of smoking.

Measurement of serum creatinine level is recommended by the EAU but not the AUA. The EAU’s rationale is that it is cheap and a few patients present with upper tract sequelae. The AUA’s position is that renal function was not identified merely as a result of symptoms and when other sequelae (such as a large postvoid residual) were absent. A review of BPH clinical trial databases showed renal sufficiency in less than 1% of patients.

Measurement of serum prostate-specific antigen (PSA) level is recommended by the AUA\textsuperscript{13} and EAU.\textsuperscript{18} More specifically, the AUA recommends measurement for men with a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management. Both associations recommend measurement when the result would change management plans. Conversely, as a more general statement about screening, rather than specifically in the context of LUTS, the United States Preventative Services Task Force has recommended that PSA screening be discontinued at age 75 years. Population survival tables generate a survival likelihood of approximately 10 years around this age.\textsuperscript{20} Responses to this statement have questioned a chronologic cutoff but would rather place it in the context of biologic/functional age instead.\textsuperscript{21} In addition, when an elderly man (≥75 years of age) presents to his physician with significant LUTS, a clinical knowledge of whether he has carcinoma of the prostate or not remains relevant as the treatment of his LUTS might be the treatment of his prostate cancer.

With the possible exception of ultrasound bladder volume measurement equipment, any additional testing would be beyond the scope of the gerontologist. Essentially, for patients with a less than clear-cut diagnosis or when the symptomatology is likely to be affected by known comorbidities such as urologic disease, then more complex evaluation of the urinary tract function may be required. The simplest tests would be to have a patient complete a 24-hour voiding diary. As most people do not really know how often or how much they urinate, this information can be instructive to the patient as well as the physician. For more complex patients, formal urodynamic evaluation might be necessary. Generally this would involve the placement of a double lumen urethral catheter and a rectal catheter to measure bowel pressure as a surrogate for intraabdominal pressure. Clearly these tests are invasive and fairly uncomfortable for the patient and are obviously beyond the scope of the gerontologists. Such patients require referral to a urologist.
TREATMENT

For most patients, the need for treatment is predicated on bother. Patients with an AUA symptom score of less than 8 do not normally warrant treatment. Patients with a score between 8 and 19 may warrant treatment if the patients’ lifestyle is sufficiently affected (bothered) by the symptoms. Most of these patients are successfully treated with medical therapy. Patients with severe symptoms can be successfully treated with medical therapy, but may require more invasive therapies.

In addition, there are several situations when therapy should be recommended, even if the patient is not bothered (Box 1).

WATCHFUL WAITING

Watchful waiting is appropriate for men with mild symptoms; men with moderate to severe symptoms who do not yet have any medical complications from BPH are also candidates for watchful waiting. Behavioral strategies such as minimizing evening fluid intake, decreasing alcohol intake, and avoiding caffeinated or carbonated beverages can be helpful for symptom relief.

Patients are reassessed subjectively at various intervals with symptom score and measure of bother. Objective factors such as serum PSA value, maximum urinary flow rate, postvoid residual measurement, and measurement of prostate volume can also be checked on some patients as discussed earlier. Progression in subjective or objective measures of BPH may then prompt medical or surgical intervention. A symptom score change of 4 points is usually detectable by patients.

MEDICAL THERAPY

Medications used for treatment of BPH include phytotherapeutic agents and supplements, $\alpha_1$-adrenergic receptor-blocking agents, $5\alpha$-reductase inhibitors (5ARIs), and antimuscarinic agents. Phosphodiesterase type 5 (PDE-5) inhibitors have also been studied for their potential benefit in treating LUTS in addition to erectile dysfunction. Combination therapy using different medication classes also has a role in treating BPH.

Phytotherapy

Phytotherapeutic agents and supplements are more widely used in Europe, but many formulations are available and heavily advertised in the United States. The AUA Guidelines do not recommend use of phytotherapeutic agents or dietary supplements for treatment of BPH at this time because of lack of evidence of efficacy. Sources of

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<table>
<thead>
<tr>
<th>Box 1</th>
<th>Indications for treatment</th>
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<tr>
<td>Elective</td>
<td>Bothersome symptoms</td>
</tr>
<tr>
<td>Absolute</td>
<td>Renal failure from outlet obstruction</td>
</tr>
<tr>
<td></td>
<td>Recurrent urinary retention</td>
</tr>
<tr>
<td></td>
<td>Persistent hematuria</td>
</tr>
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<td></td>
<td>Bladder calculi from outlet obstruction</td>
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phytotherapeutic agents used for treatment of BPH include saw palmetto (*Serenoa repens*) fruit, African plum tree (*Pygeum africanum*) bark, and stinging nettle (*Urtica dioica*) roots; β-sitosterol represents 1 such agent. Proposed mechanisms of action of phytotherapeutic agents include antiandrogenic effect, antiestrogenic effect, inhibition of 5α-reductase, α-adrenergic receptor antagonism, antiinflammatory effect, and inhibition of prostatic cell proliferation.

A prospective, randomized, clinical trial comparing saw palmetto to placebo found no significant difference in AUA symptom scores, maximal urinary flow rate, prostate size, residual volume after voiding, quality of life, or PSA values after 1 year of treatment. However, a meta-analysis of trials treating with pygeum reveals a significant, but modest, improvement in LUTS compared with placebo, although these studies are of small size and short duration. β-Sitosterol has been shown to have some benefit in treating LUTS compared with placebo, and this effect was maintained for 18 months. In the future, prospective double-blinded studies comparing these agents with standard medical treatments for BPH would be critical to establish a legitimate role in treating LUTS and to provide the ability to make accurate comparisons of the relative risks of side effects with benefit achieved. Problematically, because herbals have no patent protection, large double-blind studies will only be performed by groups such as government agencies.

**α-Adrenergic Receptor Blockers**

α-Adrenergic receptor blockers have been used for the management of BPH since the late 1980s. The rationale behind their use relates to the presence of α1-adrenergic receptors in the smooth muscle of the prostate stroma, urethra, and bladder neck. Smooth muscle tension at these locations is believed to play a role in a dynamic component of BPH symptoms. Antagonism of these receptors should theoretically reduce resistance to the flow of urine and hence provide some measure of symptom relief.

There are 3 subtypes of the α1-adrenergic receptor, the α1a-, α1b-, and α1d-receptors. The α1a-receptor subtype is the most dominant in the prostate. The α1b-receptor subtype has minimal expression in prostate stroma, and because of its expression elsewhere throughout the body may have more significance in causing side effects. The α1d-receptor subtype predominates within the spinal cord and bladder body musculature. The clinical efficacy and side effect profile of α1-adrenergic receptors based on subtype specificity is not entirely clear.

α1-adrenergic receptor blockers used for treatment of BPH include alfuzosin, doxazosin, silodosin, tamsulosin, and terazosin. The efficacy of these medications in terms of symptom and flow rate improvement is believed to be similar. Patients can be expected to achieve a reduction in their AUASI of approximately 4 to 6 points, and this is usually felt to be meaningful with regard to patient perception.

Doxazosin and terazosin require dose titration to minimize side effects, but efficacy is also dose-dependent for these α-adrenergic receptor blockers. Safety and efficacy have been shown for doses up to 8 mg of doxazosin and 10 mg of terazosin. Tamsulosin and alfuzosin also have excellent clinical efficacy without significant blood pressure effects or the need for dose titration.

Side effects from treatment with α1-adrenergic receptor blockers include orthostatic hypotension, dizziness, asthenia, ejaculatory problems, and nasal congestion. Doxazosin has been associated with a higher incidence of congestive heart failure in men with hypertension and cardiac risk factors when used as a single first-line therapy for hypertension. This does not seem to have any consequences for its use in treating BPH in normotensive men.
A unique side effect of these medications is intraoperative floppy iris syndrome, which is characterized by miosis, iris billowing, and prolapse in patients undergoing cataract surgery who have taken or are currently taking \(\alpha\)1-adrenergic receptor blockers. This phenomenon is particularly common in patients taking tamsulosin.\(^{37}\) However, it is critical for all patients taking \(\alpha\)1-receptor blockers to alert their ophthalmologist to that fact if they are contemplating cataract surgery.\(^{38}\)

### 5\(\alpha\)-Reductase Inhibitors

The recognition that men suffering from a lack of 5\(\alpha\)-reductase have a hypoplastic prostate provides the rationale for treating BPH with 5ARIs.\(^{39,40}\) 5\(\alpha\)-Reductase converts testosterone to dihydrotestosterone (DHT). There are 2 isoenzymes of 5\(\alpha\)-reductase. Type I is present primarily in extraprostatic tissues such as skin and liver, although type II is found within the prostate.\(^{41}\) DHT binds to androgen receptors in prostate cell nuclei and promotes proliferation. A reduction of DHT should therefore inhibit prostate growth and instead lead to apoptosis and a reduction in prostate size. By creating this reduction in DHT, 5ARIs can address the physical (anatomic) component of BPH leading to LUTS.

There are 2 5ARIs available for treating BPH. Finasteride is an inhibitor of type II 5\(\alpha\)-reductase, and dutasteride is an inhibitor of types I and II. Finasteride can be expected to improve the AUASI score by 3 to 4 points and improve maximum urinary flow rate by 2 ml/s.\(^{13}\) A reduction in the prostate volume of men taking finasteride of 15% to 25% can be achieved with this medication. This reduction in prostate volume results in a decrease in the risk of acute urinary retention and BPH-related surgery by approximately 50%.\(^{15}\) Dutasteride has a similar clinical effect.\(^{42}\) Hence, 5ARIs can be regarded as arresting the disease process of BPH rather than simply providing symptom relief. The symptom relief from 5ARIs is most pronounced in larger glands (>40 cm\(^3\)), and the AUA Guidelines do not recommend them for men who do not have evidence of prostate enlargement.\(^{13}\)

Sexual side effects are the most common effects noted with 5ARIs. These include decreased libido, erectile dysfunction, and ejaculatory disorder. Rarely, some men note breast tenderness in association with use of these medications. These medications are contraindicated in children and pregnant women. They should not even be handled by pregnant women because of the risk of absorption and subsequent risk to a male fetus. 5ARIs may reduce a patient’s PSA level approximately 50% after taking them for 6 months or more, and doubling of the PSA value of men on these medications is necessary to preserve the usefulness of PSA in screening for prostate cancer.\(^{43,44}\)

5ARIs may have a significant benefit beyond treatment of LUTS secondary to BPH. Chemoprevention of prostate cancer through these medications may be feasible. The Prostate Cancer Prevention Trial (PCPT) revealed a relative risk reduction of 24.8% after 7 years of follow-up in men taking finasteride.\(^{45}\) Dutasteride is also being evaluated for the potential to decrease the risk of prostate cancer in the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial.\(^{46}\) However, few urologists are currently aggressively using these medications for primary prostate cancer prevention in men not suffering from BPH.

### \(\alpha\)-Adrenergic Receptor Blockers and 5ARIs

Combination therapy with \(\alpha\)1-adrenergic receptor blockers and 5ARIs has been proposed in the treatment of BPH. The Veteran Affairs Cooperative Study No. 359 reported in 1996 on the results of men randomized to placebo, finasteride, terazosin, and the combination of these 2 medications.\(^{47}\) The mean changes from baseline in

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symptom scores at 1 year for the patients in these groups were decreases of 2.6, 3.2, 6.1, and 6.2 points, respectively. The mean changes at 1 year in the peak urinary flow rates were increases of 1.4, 1.6, 2.7, and 3.2 ml/s, respectively. This study concluded that terazosin was effective therapy for BPH, and the combination of finasteride and terazosin was no more effect than terazosin alone. One criticism of this trial was that the mean size of prostates in the trial may not have been large enough to appreciate benefit from finasteride.

Subsequent trials have renewed enthusiasm for combination therapy. The Medical Therapy of Prostate Symptoms (MTOPS) trial compared use of finasteride, doxazosin, combination of both, and placebo. This trial used progression as its primary end point, with symptomatic worsening, retention of urine, urinary tract infection, deterioration of renal function, or incontinence constituting progression. The combination therapy was superior to either single medication in the primary end point. Combination therapy was also shown to be more effective in relieving symptoms and improving peak urinary flow rate, secondary end points of the study. For example, the 4-year mean reduction in symptom score was 4.9 in the placebo group, 6.6 in the doxazosin group, 5.6 in the finasteride group, and 7.4 in the group on doxazosin and finasteride. Maximum urinary flow rate improvements were 2.8, 4.0, 3.2, and 5.1 ml/s, respectively. However, there was a higher incidence of side effects in the combination group.

Combination therapy with tamsulosin and dutasteride has been similarly assessed in the Combination of Dutasteride and Tamsulosin (CombAT) study. This trial demonstrated superior improvement in symptom relief for the combination of tamsulosin and dutasteride over either medication alone. At 2 years, the mean decreases in IPSS from baseline were 6.2 for combination therapy, 4.9 for dutasteride, and 4.3 for tamsulosin. Significant increases in peak urinary flow rates for the combination groups were also seen from 6 months to 24 months versus either monotherapy. As in MTOPS, the combination therapy group in the CombAT study had an increased incidence of drug-related adverse events. Nonetheless, the MTOPS and CombAT trials suggest that the combination of an $\alpha_1$-adrenergic receptor blocker and 5ARI in men with LUTS and prostate enlargement may have benefit over monotherapy in preventing progression and relieving symptoms. As with 5ARI monotherapy, the benefits from combination therapy are limited to men with prostate enlargement and should not be used for men with prostates less than 25 cm$^3$ in volume.

**Antimuscarinic Medications**

Because many of the symptoms associated with BPH are the same as those caused by overactive bladder (OAB), attempts at addressing these symptoms with antimuscarinic medications have been pursued. Traditionally, it was felt that using this class of medication to treat men with BPH would carry a high risk of causing urinary retention and was therefore discouraged. However, the following recent studies have shown the safety and efficacy of this approach.

Lee and colleagues reported a trial comparing doxazosin with or without tolterodine in men with documented bladder outlet obstruction and OAB based on urodynamics studies. Only 35% of these men noted improvement on doxazosin alone; the addition of tolterodine to doxazosin resulted in improvement of symptoms in 73% of the remaining men. The risk of urinary retention was low (3.3%) in those men treated with the combination.

A trial reported by Kaplan and colleagues randomized men to placebo, tamsulosin, extended-release tolterodine, or a combination of the 2. The men eligible for this study had to have an IPSS of 12 or higher and documented urinary frequency and urgency on a bladder diary. Patient perception of treatment benefit was the primary
end point, and this was only significant versus placebo in the combination group. The
group on combination therapy also showed significant improvement in bladder diary
variables and IPSS compared with placebo, and the clinical conclusion from the study
was that men with documented LUTS including symptoms of OAB do better on an \( \alpha_1 \)-
adrenergic receptor blocker and antimuscarinic medication rather than either 1 alone.
A low incidence of acute urinary retention was seen in all 4 treatment groups.

**PDE-5 Inhibitors**

The potential use of PDE-5 inhibitors to treat erectile dysfunction and LUTS has been
assessed in several recent studies. Daily sildenafil use was found to have significant
benefit for erectile function and demonstrated improvement in the IPSS of 6.32 points
versus 1.93 for placebo.\(^{51}\) Tadalafil has also been similarly studied for this effect, and
its daily use was also found to significantly improve IPSS versus placebo with
a decrease of 7.1 versus 4.5.\(^{52}\) In these 2 studies, neither sildenafil nor tadalafil signif-
ically improved peak urinary flow rate versus placebo despite the documented
benefit for symptom relief.

The combination of an \( \alpha \)-adrenergic receptor blocker and PDE-5 inhibitor has also
been assessed for the potential of an additive effect. In a study comparing alfuzosin 10
mg daily, sildenafil 25 mg daily, and a combination of both, the patients in the combi-
nation group saw the greatest benefit in IPSS, maximum urinary flow rate, and erectile
dysfunction scores.\(^{53}\)

Proposed mechanisms for the ability of PDE-5 inhibitors to improve LUTS include
prostatic smooth muscle relaxation, antiproliferative effects, improved pelvic blood
flow, and an effect on afferent sensory nerve signaling from the prostate or bladder.\(^{52}\)

**MINIMALLY INVASIVE THERAPY**

The goal of minimally invasive therapy for BPH is the heating and subsequent destruc-
tion of prostate tissue surrounding the prostatic urethra. The regression or sloughing
of this tissue then results in a theoretic decrease in bladder outlet obstruction and
symptomatic improvement in LUTS. For tissue necrosis to occur, tissue temperatures
of greater than 45\(^\circ\)C must be achieved.\(^{54}\) These therapies hope to yield results
comparable with more invasive surgical procedures while minimizing morbidity and
allowing office-based treatment with minimal anesthetic requirements. According to
the AUA guidelines, transurethral microwave heat therapy and transurethral needle
ablation are minimally invasive options for treating BPH.\(^{13}\)

**Transurethral Microwave Therapy**

Transurethral microwave therapy (TUMT) delivers heat to the prostate through
a urethral catheter. Simultaneous cooling of the rectal and urethral surface is often per-
formed to help prevent damage to these structures. Approved TUMT devices include
Prostatron, Targis, CoreTherm, and TherMatrx.\(^{13}\) There is no evidence from direct
comparator studies to suggest superiority of one device over another.\(^{13}\) Results
from treatment with these devices are likely to be better than that achieved with
medical therapy but not as great as that with surgery. Long-term durability of the
results of TUMT is also questionable. A systematic review of studies with patients
randomized to either TUMT or transurethral resection of the prostate (TURP) found
that the pooled mean maximum urinary flow rate increased from 8.6 to 18.7 ml/s after
TURP but only 7.9 to 13.5 ml/s after TUMT.\(^{55}\) In only 2 of the studies examined in this
review did the mean maximum flow rate achieve 15 ml/s or greater. This review also
concluded that fewer men required retreatment after TURP than after TUMT.
Potential risks of TUMT include urinary retention and prolonged irritative voiding symptoms. Extended urethral catheterization is sometimes needed. The Food and Drug Administration recommends that patients being considered for TUMT meet the device’s indications, including the criteria for eligible prostate size for the device being considered.\textsuperscript{56} Patients with a history of radiation to the pelvic area are at increased risk of fistula formation.\textsuperscript{56}

**Transurethral Needle Ablation**

Transurethral needle ablation (TUNA) uses radiofrequency (RF) waves (490 kHz) to heat prostatic tissue. The RF energy is administered through 2 18-gauge needles at the tip of a TUNA device. This device is similar in appearance to a rigid cystoscope. It is inserted using a lens that guides placement in the urethra under direct vision, and, once positioned, the needles are inserted into the prostate parenchyma by penetrating the urethra. Tissue in the lateral prostatic lobes is heated to about 100°C to produce coagulation necrosis. Both needles have insulating sheaths to protect the urethral mucosa from heating. The AUA guidelines state that, like TUMT, TUNA may provide better symptom relief than medications but is inferior to TURP.\textsuperscript{13} A meta-analysis of studies examining TUNA found that it typically halved mean IPSS scores at 1 year and maximum flow rates increased by 70% from baseline to 1 year.\textsuperscript{57} Side effects of TUNA include prolonged irritative symptoms and temporary urinary retention.

**SURGERY**

The surgical options available for treatment of BPH include TURP, transurethral incision of the prostate (TUIP), open prostatectomy, and laser procedures. Patients may elect to pursue surgery initially if they have bothersome symptoms, or they may defer surgical treatment until they have failed less invasive forms of therapy or have developed complications of BPH such as acute urinary retention, bladder calculi, recurrent gross hematuria, recurrent urinary tract infections, or renal insufficiency. The choice of surgical approach should be based on the patient’s prostate size, the surgeon’s judgment, and the patient’s comorbidities.\textsuperscript{13}

**TURP**

TURP is the gold standard surgical treatment of BPH given its long-term efficacy established in clinical trials. TURP is performed by placing a working sheath in the urethra through which a working element with an electrified loop is placed to resect prostate tissue and cauterize sites of bleeding. The procedure may be performed under spinal or general anesthesia. A hospital stay is required, and continuous bladder irrigation is often used postoperatively to control bleeding and prevent clot retention.

As noted earlier, TURP has well-established efficacy. The AUA Guidelines describe symptom score reduction of approximately 15 points with TURP at greater than 10 months. Mean change in urinary flow rates was 8 ml/s more than 16 months after surgery.\textsuperscript{13}

Although highly effective in treating BPH, TURP has several potential drawbacks. Significant intraoperative and postoperative bleeding may occur, potentially requiring blood transfusion. Absorption of irrigating fluid may result in transurethral resection (TUR) syndrome, a potentially serious dilutional hyponatremia. Bladder neck contracture and urethral stricture may occur, and sexual side effects such as erectile dysfunction and retrograde ejaculation are possible side effects. Risk of urinary incontinence is approximately 1% according to the Veteran Affairs Cooperative Study.\textsuperscript{58}
One potential advantage of TURP over other treatments that do not remove tissue is the ability to assess the resected specimen for the presence of prostate cancer. However, in the era of aggressive PSA screening for prostate cancer, this may not be a critical factor for most patients in deciding on the most appropriate treatment of BPH.

**TUIP**

An alternative to surgically removing obstructing prostate tissue, TUIP is performed by using an electocautery blade to divide the bladder neck fibers and prostate capsule at 1 or 2 locations. This procedure is suited for patients with only minimal prostate enlargement (<30 cm³) and younger men. Improvement in symptom scores and flow rates from TUIP performed in this group of appropriately selected patients can be expected to be excellent. However, a meta-analysis of studies comparing TURP and TUIP found that there is a slightly better chance of symptom improvement in patients treated with TURP, and the degree of improvement is slightly greater.

Side effects from TUIP include those seen with TURP. There is a lower risk of TUR syndrome caused by shorter operative times, and the incidence of retrograde ejaculation is reportedly lower.

**Open Prostatectomy**

This procedure is reserved for patients with a very large prostate (>75 cm³) in whom satisfactory results are unlikely to be achieved with a single transurethral procedure. Lower retreatment rates, more complete removal of the prostate adenoma under direct vision, and lack of risk of TUR syndrome are potential advantages for open prostatectomy in this group of patients compared with TURP or other endoscopic procedures. Potential disadvantages of the open prostatectomy include the need for a lower abdominal incision, longer hospitalization, longer postoperative recovery time, and the risk of greater perioperative hemorrhage.

Open prostatectomy is performed through either a retropubic or suprapubic approach under general or regional anesthesia. In either approach, the inner core of the prostate representing the transition zone is shelled out. The peripheral zone is left behind, and open prostatectomy is only an adequate procedure for treating BPH, not prostate cancer. In the retropubic approach, the adenoma is removed through a direct incision in the anterior prostatic capsule. The suprapubic approach is performed through a transvesicle incision. Suprapubic prostatectomy is particularly useful when bladder calculi or bladder diverticula are present and can be treated at the same time. Compared with retropubic prostatectomy, the suprapubic approach may be better suited for managing an enlarged prostate that includes a prominent intravesical median lobe. Open prostatectomy has excellent results with regard to improvement in LUTS and urinary flow rates.

Open prostatectomy has the surgical risks one would expect for a procedure involving an abdominal incision and general anesthesia. Bleeding may be significant and may result in transfusion. Other specific risks include urinary incontinence, erectile dysfunction, retrograde ejaculation, urethral stricture, bladder neck contracture, and urinary tract infection. Laparoscopic simple prostatectomy has proved to be feasible and may reduce the morbidity associated with this treatment of BPH.

**Laser Procedures**

There are several ways laser energy can be applied to the prostate endoscopically. Goals of this application include coagulation, vaporization, and resection of prostate tissue. Laser coagulation of the prostate, done either in an interstitial or transurethral
approach, has met with limited results and is not commonly done. However, laser vaporization of the prostate and laser enucleation of the prostate are well-established treatment options with growing evidence of long-term benefit in treatment of BPH.

Laser Vaporization of the Prostate

Transurethral laser vaporization of the prostate can be accomplished with either a potassium-titanyl-phosphate (KTP) laser or holmium laser and is facilitated with the use of a right-angle laser fiber. The procedure can be done under general or spinal anesthesia, typically in an outpatient setting. Vaporization of the prostate tissue creates a TURP-like defect within the transition zone of the prostate. Because coagulation occurs simultaneously with vaporization, this procedure can be done on patients taking anticoagulant medication. Symptom relief and improvement in flow rates have been similar to those achieved by TURP.13

Malek and colleagues64 reported on long-term results for photoselective vaporization of the prostate using a KTP laser. Mean improvement in symptom scores at 1, 2, 3, and 5 years ranged from 83% to 88%. After surgery percentage changes in maximum flow rates ranged from 170% to 252%.

Laser vaporization of the prostate potentially carries a lower risk of bleeding, erectile dysfunction, retrograde ejaculation, and hospital stay compared with TURP. TUR syndrome is much less likely because isotonic solution is used for irrigation during the procedure.

Laser Enucleation of the Prostate

A large section of the prostate adenoma is surgically excised with a holmium laser during laser enucleation of the prostate (HoLEP). The enucleated tissue is then morcel-lated in the bladder to aid in removal. Success rates with this procedure are comparable to TURP, and for larger glands may even match results obtained with open prostatectomy.13 Elzayat and Ehiliali65 have reported on their series of HoLEP patients with mean follow-up of 49 months. In this group, mean maximum flow rates increased from 6.3 to 16.2 ml/s, and mean IPSS improved from 17.3 to 5.6. Potential drawbacks to this promising treatment of BPH include relatively long operative times and a long learning curve to achieve technical expertise in this procedure.

SUMMARY

The number of men suffering from BPH and LUTS in the coming years can be expected to increase as the demographics of the American population change. This article summarizes the goals of evaluation and management of these men. The treatment of men in the geriatric population with BPH will ultimately depend on the distress caused by their symptoms as well as potential medical complications from BPH such as urinary retention. Whether a man chooses medical management only, palliative measures such as long-term urethral catheterization, or intermittent catheterization, or aggressive measures such as surgery, will need to be based on the therapeutic goals, ability to tolerate a given therapy, and a thorough understanding of the potential risks and benefits of any intervention.

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REFERENCES


