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# Benign prostatic hyperplasia: Now we can begin to tailor treatment

## ABSTRACT

Our treatment strategies for benign prostatic hyperplasia (BPH) have changed, with new insights into the pathophysiology of the disease, new clinical trials, and surgical advances. We present an update on treatment options and a diagnostic and treatment algorithm for this condition.

## KEY POINTS

The serum prostate-specific antigen (PSA) concentration is part of the routine workup for most patients with BPH.

The most effective medical therapy, in appropriately selected patients, is a combination of an alpha-blocker and a 5-alpha-reductase inhibitor.

Patients with a small prostate and a serum PSA concentration less than 2.0 ng/mL can be started on an alpha-blocker; those with a higher risk of clinical progression (prostate larger than 40 g and PSA level greater than 4.0 ng/mL) and with no suspicion of prostate cancer can start with a 5-alpha-reductase inhibitor alone or with an alpha-blocker.

Many new minimally invasive surgical treatments can be performed in the doctor's office with local anesthesia, but transurethral resection of the prostate (TURP) remains the most effective treatment for BPH in terms of reducing symptoms.

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**T**HE MEDICAL MANAGEMENT of benign prostatic hyperplasia (BPH) has improved considerably in recent years as we have gained understanding about its symptoms, risk factors, and rate of clinical progression. Now, treatment can be tailored on the basis of how bothersome the patient's symptoms are, the size of the prostate, and the patient's preference.

Two types of medical therapies—alpha-blockers and 5-alpha-reductase inhibitors—have different mechanisms of action and can be used in combination for greater effect. And several new and less-invasive surgical procedures can be performed in the urologist's office and show good results.

This article reviews the pathophysiology of BPH, provides an algorithm to diagnose it, and discusses its management, including medications, surgery, and new minimally invasive procedures.

## BPH INCREASES WITH AGE

Although most precisely a histologic diagnosis, the term *benign prostatic hyperplasia* describes a benign enlargement of the prostate gland that commonly occurs in older men and is often accompanied by lower urinary tract symptoms.

In the United States, approximately 14 million men suffer from BPH, and the estimated annual cost of treatment is \$4 billion.<sup>1</sup> Prevalence increases with age: 25% of men older than 40 years experience some BPH symptoms, increasing to one third of men older than 65.<sup>2</sup> The prevalence of moderate to severe symptoms increases from 13% in men in their 40s to 28% in those older than 70.<sup>3</sup>

TABLE 1

### American Urological Association symptom index for benign prostatic hyperplasia

Answer each question as:

- 0 (not at all)
- 1 (less than 1 time in 5)
- 2 (less than half the time)
- 3 (about half the time)
- 4 (more than half the time)
- 5 (almost always)

In the last month or so, how often have you:

- \_\_\_\_\_ 1 ...had a sensation of not emptying your bladder completely after you finished urinating?
- \_\_\_\_\_ 2 ...had to urinate again less than 2 hours after you finished urinating?
- \_\_\_\_\_ 3 ...found you stopped and started again several times when you urinated?
- \_\_\_\_\_ 4 ...found it difficult to postpone urination?
- \_\_\_\_\_ 5 ...had a weak urinary stream?
- \_\_\_\_\_ 6 ...had to push or strain to begin urination?
- \_\_\_\_\_ 7 In the past month or so, how many times per night have you typically had to get up to urinate from the time you went to bed at night until you got up in the morning? (answer 0-none, 1-once per night, 2-two times per night, 3-three times per night, 4-four times per night, 5-five times per night)
- \_\_\_\_\_ **Total score\***

\*0–7 = mild, 8–19 = moderate, 20–35 = severe

ADAPTED FROM AUA PRACTICE GUIDELINES COMMITTEE. AUA GUIDELINE ON MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA (2003). CHAPTER 1: DIAGNOSIS AND TREATMENT RECOMMENDATIONS. J UROL 2003; 170:530–547.

**One third of men older than 65 years have some BPH symptoms**

Besides older age, other risk factors for BPH are normal androgenic function and a positive family history. Possible risk factors include race, geographic location, cigarette smoking, and male pattern baldness.<sup>4,5</sup>

#### ■ LARGER PROSTATE = MORE SYMPTOMS, USUALLY

In general, the larger the prostate, the worse the symptoms and the risk of acute urinary retention. In a longitudinal study, men in their 60s with moderate symptoms were found to have a 13% 10-year cumulative risk of developing acute urinary retention. Prostate volumes greater than 30 cm<sup>3</sup> were associated with a threefold risk of acute urinary retention, and flow rates less than 12 mL/second were associated with a fourfold risk.<sup>6,7</sup>

However, the relationship between lower urinary tract symptoms and BPH is complex.

Only half of men with a histologic diagnosis of BPH have moderate-to-severe lower urinary tract symptoms,<sup>8</sup> and some men with symptoms do not have enlarged prostate glands. Moreover, some men who are treated despite a small prostate have improvement of their symptoms.<sup>9</sup>

#### ■ THREE COMPONENTS: PROSTATE, URETHRA, BLADDER

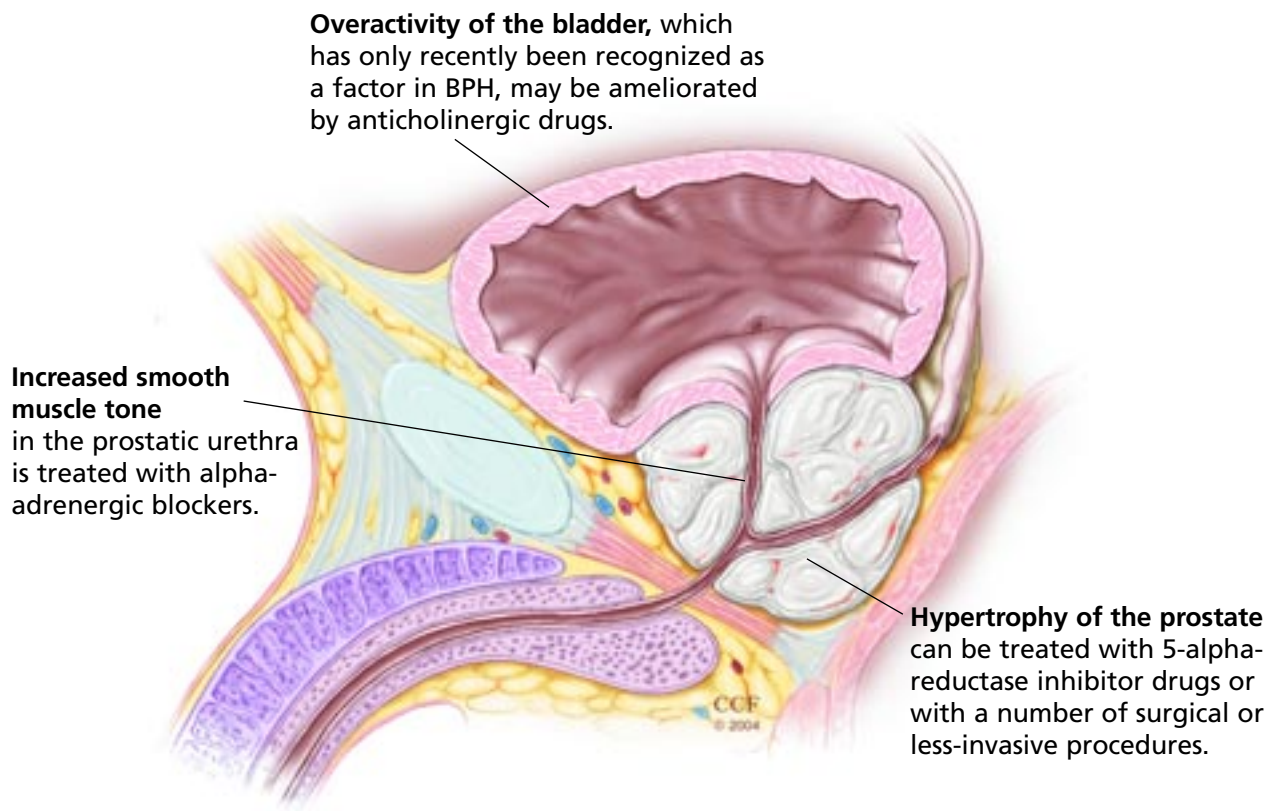
A three-component theory explains how BPH causes lower urinary tract symptoms and why medical therapy works (FIGURE 1).

A static component is the enlarged prostate itself, which obstructs urine flow. Prostates grow in response to androgen exposure over time, causing worsening symptoms with age. Growth can be controlled with 5-alpha-reductase inhibitors, which block the conversion of testosterone to dihydrotestos-



## ■ Benign prostatic hyperplasia: The three-component model

Symptoms of benign prostatic hyperplasia (BPH) such as urgency, frequency, and a weak urinary flow may actually be due to three separate components.



**FIGURE 1**

terone, the main androgen responsible for prostate growth.

There is also a dynamic component: increased smooth muscle tone in the prostatic urethra. This mechanism may account for approximately 40% of the obstruction in BPH.<sup>10</sup> In the 1980s, Lepor et al<sup>11</sup> recognized that prostatic smooth muscle tension was mediated by alpha-1 adrenoceptors, and this discovery led to the development of alpha blockade to treat lower urinary tract symptoms.

A third component, more recently appreciated, is overactivity of the bladder. Prostatic obstruction may accelerate age-related changes in bladder function, contributing to lower urinary tract symptoms.<sup>4</sup> Urodynamic

testing shows that more than half of patients with BPH have detrusor hyperactivity (an overactive bladder). A multicenter trial is under way to evaluate an anticholinergic medication that relaxes the detrusors in men with BPH.

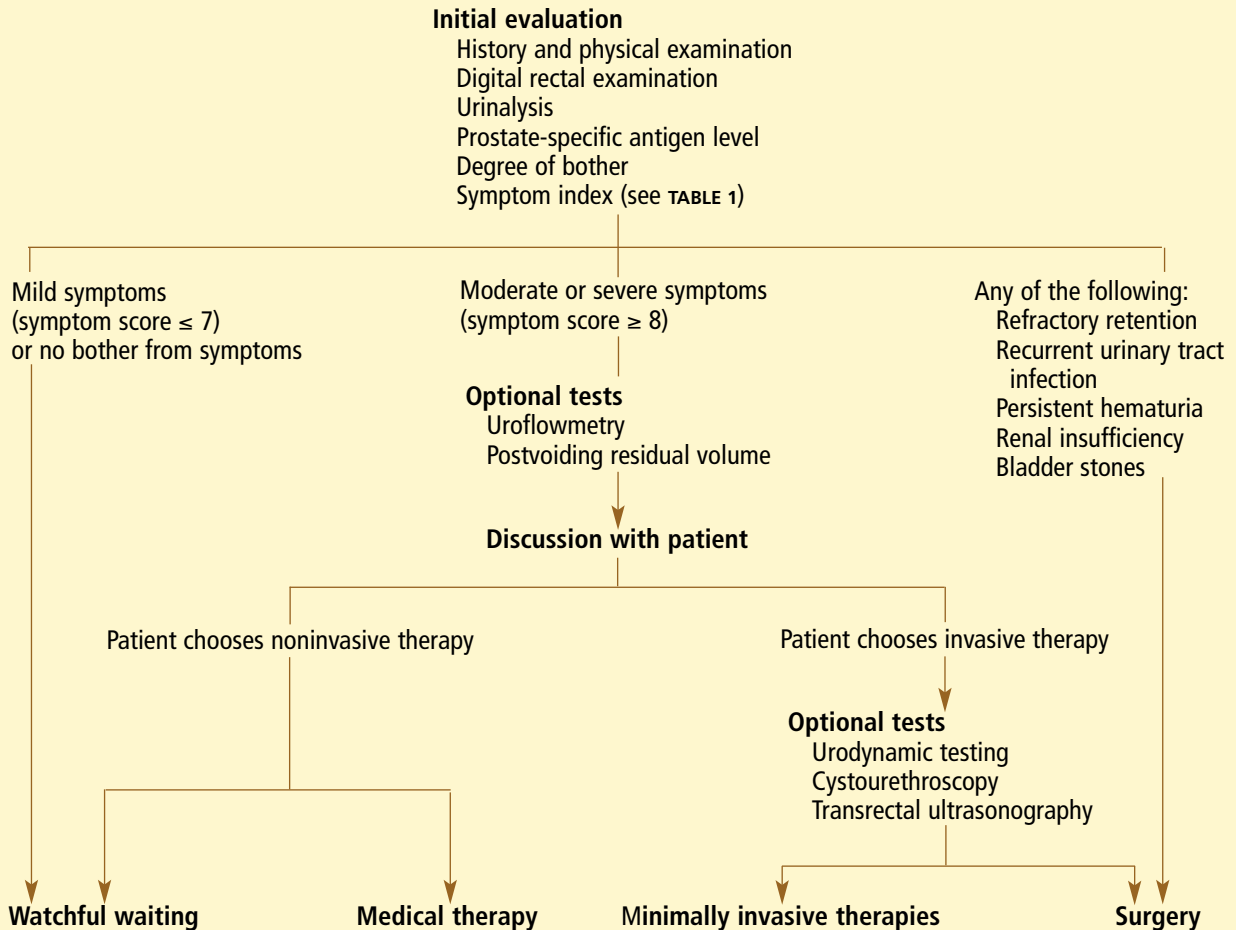
### ■ CLINICAL EVALUATION

BPH can usually be diagnosed clinically.

#### **History**

A brief history should determine the degree of bother caused by the patient's urinary symptoms and any health-related quality-of-life issues.

## American Urological Association guidelines for diagnosing and treating benign prostatic hyperplasia



ADAPTED FROM AUA PRACTICE GUIDELINES COMMITTEE. AUA GUIDELINE ON MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA (2003). CHAPTER 1: DIAGNOSIS AND TREATMENT RECOMMENDATIONS. J UROL 2003; 170:530-547.

**FIGURE 2**

**Typical complaints** include:

- Frequency
- Urgency
- Hesitancy
- Nocturia
- A sensation of incomplete emptying
- A weak urinary stream
- Postvoid dribbling.

**Symptom score.** Patients should complete a symptom index such as the American Urological Association (AUA) Symptom Score or the nearly identical International Prostate Symptom Score.<sup>12</sup> In the AUA

symptom index (TABLE 1), the patient rates seven symptoms on a scale of 0 (not a problem) to 5 (almost always a problem). A total score of 0 to 7 is classified as mild, 8 to 19 as moderate, and 20 to 35 as severe. Changes over time can be used to track disease progression and response to treatment—most patients perceive a decrease of 3 points as a noticeable improvement.<sup>13</sup>

**Family history.** Patients should be asked about family history of BPH and prostate cancer, and the physical examination should include a digital rectal examination.



## Laboratory tests

Urinalysis is recommended to look for hematuria and evidence of infection.

**Prostate-specific antigen (PSA).** The AUA Practice Guidelines Committee recommends measuring the serum PSA concentration only if the patient's life expectancy is at least 10 years (the approximate cutoff for considering treatment if prostate cancer is discovered) and to establish a baseline level in those who may be treated with a 5-alpha-reductase inhibitor, which will lower the PSA level.

PSA is a useful surrogate marker for prostate size and can be used to predict future prostate growth and the risk for urinary retention or surgery<sup>4,14</sup>: patients with a PSA level higher than 3.2 ng/mL have a 20% risk of urinary retention or surgery within 4 years.<sup>15</sup>

**Serum creatinine is no longer routinely measured** in patients with lower urinary tract symptoms. Multiple long-term, placebo-controlled trials have shown that the incidence of renal insufficiency in men with BPH is the same as in the general population.

## Who should undergo further testing?

An algorithm adapted from AUA guidelines for BPH management (**FIGURE 2**) can help guide diagnosis and treatment. Certain patients require a more extensive evaluation: eg, those with polyuria, underlying neurologic disease, or prior lower urinary tract disease, or who are younger than 40 years and have voiding dysfunction.<sup>12</sup> However, most patients can begin medical therapy, if they so choose, after the initial evaluation without any further testing.

Although a primary care physician may perform the initial evaluation and begin medical therapy without further testing, we recommend a urologic consultation for all patients with lower urinary tract symptoms. A urologist can provide more extensive testing, as well as counseling regarding surgical options.

**Uroflowmetry** is a noninvasive measurement of the maximal rate of urinary flow. If the flow rate is normal, the patient's symptoms are more likely due to a problem other than BPH and are less likely to respond to medical or surgical treatment for BPH than if the flow rate is

**TABLE 2**

## Benefit of therapies for benign prostatic hypertrophy

THERAPY	ESTIMATED CHANGE*	
	AUA SYMPTOM SCORE†	PEAK FLOW RATE (ML/SEC)
<b>Watchful waiting</b>	-0.50	2.16
<b>Medications</b>		
Alpha-blockers	-6.38	2.26
Finasteride	-3.40	1.66
Doxazosin plus finasteride	-6.53	3.38
Placebo	-2.33	0.48
<b>Minimally invasive procedures</b>		
Transurethral needle ablation	-9.32	4.25
Transurethral microwave	-10.21	4.21
Visual laser ablation	-20.20	10.97
<b>Surgical procedures</b>		
Transurethral resection (TURP)	-14.80	10.77
Transurethral vaporization	-15.75	12.52
Open prostatectomy	-10.11	11.50

\*After 10 to 16 months of follow-up, except for open prostatectomy (> 16 months follow-up). Adapted from pooled data from multiple studies between 1991 and 2000. Not all trials were randomized, and direct comparisons of treatments should not be made.

†See **TABLE 1**.

ADAPTED FROM AUA PRACTICE GUIDELINES COMMITTEE. AUA GUIDELINE ON MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA (2003). CHAPTER 1: DIAGNOSIS AND TREATMENT RECOMMENDATIONS. J UROL 2003; 170:530-547.

low. A low flow rate does not, however, help differentiate whether the symptoms are due to obstruction or weak bladder contractions.

**Residual volume** after voiding can be measured by ultrasonography or catheterization. Because some patients have large residual volumes without bothersome symptoms, recurrent infections, or renal insufficiency, there is no residual volume above which treatment is mandatory. However, a large residual volume predicts that watchful waiting as a treatment option is likely to fail.<sup>16</sup>

Neither of these tests is mandatory, but they can provide objective information in addition to the symptom score that can be helpful in choosing treatments and measuring treatment responses.

**Cystourethroscopy** and **transrectal prostate ultrasonography** provide anatomic information to guide selection of minimally



invasive or surgical procedures.

**Urodynamic (pressure-flow) studies** measure bladder pressures and perineal muscle activity during mechanical filling of the bladder and during voiding. They are useful for patients for whom surgery is contemplated or whose symptoms persist after a procedure. Surgical outcomes are better for patients whose diagnosis of bladder outlet obstruction is first verified by urodynamic studies.<sup>4,12</sup> Some urologists routinely recommend urodynamic studies for patients starting therapy for lower urinary tract symptoms,<sup>17</sup> although AUA practice guidelines do not.

### ■ WHEN IS TREATMENT NEEDED?

The impact of the symptoms on the patient's quality of life is the primary consideration when deciding whether therapy for BPH is needed. Thus, the patient himself should be the one to decide.

Patients with only mild or moderate symptoms may choose watchful waiting and simple measures such as regulating fluid intake, restricting liquids after dinner, and limiting alcohol and caffeine.

### ■ MEDICATIONS OR SURGERY?

Although surgical treatment with transurethral resection of the prostate (TURP) remains the gold standard, nearly all patients who eventually undergo surgery have had a trial of medical therapy first. Up to 83% of men who elect medical or minimally invasive treatment rather than TURP are pleased with their choice after 1 year.<sup>18</sup> Nevertheless, some men may choose TURP as their initial treatment.

**TABLE 2** lists different treatments for BPH—medical, minimally invasive, and surgical—with estimated improvements in symptom indices and flow rates. The numbers represent averaged data pooled from multiple studies between 1991 and 2000 that formed the basis for the AUA's 2003 guidelines.<sup>12</sup> Not all of the trials were randomized, and since these are pooled data, we cannot use them to compare the different treatments directly. This table should give a general idea, however, of the magnitude of benefit one might expect from each type of treatment.

## ■ MEDICAL TREATMENTS

### Alpha-blockers

Four alpha-blockers are approved by the US Food and Drug Administration (FDA) to treat lower urinary tract symptoms: doxazosin (Cardura), terazosin (Hytrin), tamsulosin (Flomax), and alfuzosin (Uroxatral). The AUA guidelines committee believes that all four are equally effective, reducing the symptom score by 4 to 6 points on average, which most patients perceive as a meaningful change.<sup>12</sup>

Side effects of these medications differ slightly but generally include orthostatic hypotension, dizziness, weakness, nasal congestion, and abnormal or retrograde ejaculation.<sup>10,19</sup>

Doxazosin and terazosin, the original two agents, must be titrated to an effective dose. Tamsulosin, on the other hand, does not need to be titrated, and it targets the alpha-1A adrenoceptor subtype, making it in theory more prostate-specific than doxazosin and terazosin. Alpha-1A receptors account for 70% of alpha-1 adrenoceptors in the prostate, but are also found in extraprostatic tissues. Tamsulosin is 13 times more specific for the prostate than for the urethra, and is 10 times more specific for the prostate than for vascular adrenoceptors.<sup>19</sup> Orthostatic hypotension is rarely a side effect of tamsulosin, although dizziness and retrograde ejaculation can occur.

Alfuzosin has a slightly different side effect profile compared with tamsulosin, with a lower rate of ejaculatory dysfunction and a higher rate of cardiovascular side effects.<sup>10,19</sup>

### 5-alpha-reductase inhibitors for larger prostates

Finasteride (Proscar) and dutasteride (Avodart) inhibit the enzymatic conversion of testosterone to dihydrotestosterone by 5-alpha-reductase, which decreases dihydrotestosterone levels, although not to levels observed after castration. As the primary hormonal stimulus for prostate growth is removed, the prostate shrinks and symptoms diminish.

Unlike alpha-blockers, the effects of which are felt within days, finasteride must be taken for 3 to 4 months before symptoms

**There is no residual volume above which BPH treatment is mandatory**

improve. The average AUA symptom score decreases by 3 points.

Patients with prostates weighing more than 40 g (measured by transrectal ultrasonography) or with PSA levels higher than 3.0 ng/mL (a marker of prostate size), or both, benefit more than patients with smaller prostates, although patients with PSA levels as low as 2.0 ng/mL also respond.<sup>20</sup>

On average, finasteride reduces prostate volume by 20% and serum PSA by 50%.<sup>4</sup> It also decreases bleeding and can be used<sup>2</sup> to treat BPH-associated hematuria and reduce perioperative bleeding when given before TURP; the mechanism is thought to be through interactions with vascular endothelial growth factor.<sup>4</sup>

Side effects include ejaculatory dysfunction, erectile dysfunction, and decreased libido. These effects are reversible and are generally uncommon after the first year of treatment.

**Therapy changes BPH progression.** 5-alpha-reductase inhibition was the first therapy shown to alter the course of BPH. In the landmark Proscar Long-term Efficacy and Safety Study (PLESS), which followed more than 3,000 men for 4 years, finasteride reduced the need for BPH-related surgery by 55% compared with placebo, and also reduced the incidence of acute urinary retention by 57%.<sup>20</sup>

**Does finasteride prevent prostate cancer?** The Prostate Cancer Prevention Trial<sup>22</sup> randomized nearly 19,000 men to receive either finasteride or placebo. After 7 years, prostate cancer had been detected in 24.4% of controls vs 18.4% of treated patients, but the proportion of medium-grade and high-grade tumors was greater in the finasteride group.

These data sparked a flurry of discussion about whether men should take finasteride to prevent prostate cancer, or alternatively, whether they should stop taking it because of the increased risk for high-grade tumors. The answer may come from ascertaining if men who develop prostate cancer while taking finasteride fare differently than men who develop cancer who did not take finasteride.

**Dutasteride** is a new drug that inhibits both type 1 and type 2 5-alpha-reductase isoenzymes. Dutasteride suppresses dihy-

drotestosterone by 90%; in comparison, finasteride suppresses it by 70%, although symptom scores, flow rates, and side effects are comparable with either drug. Thus far, no head-to-head trials of the drugs have been published.<sup>12,23</sup>

### Combination therapy:

#### Superior to monotherapy over the long term

Findings from initial studies that combined an alpha-blocker and a 5-alpha-reductase inhibitor to see if additional benefit could be gained were not promising. The Veterans Affairs Cooperative Group study,<sup>24</sup> published in 1996, found that 1 year of combination therapy was no more effective than monotherapy in improving symptoms or flow rates and was substantially more expensive.

However, the recent Medical Therapy of Prostatic Symptoms (MTOPS) study<sup>25</sup> found that long-term combination therapy not only improved symptoms but also slowed clinical progression. More than 3,000 men were randomized to receive placebo, doxazosin, finasteride, or both doxazosin and finasteride. The principal outcome measured was clinical progression, defined as an increase of at least 4 points in the AUA symptom score, urinary retention, incontinence, renal insufficiency, or recurrent urinary tract infection. Other dependent variables included maximal urinary flow rate, serum PSA level, and incidence of invasive therapy.

After a median 4.5 years of follow-up, the AUA symptom score had declined by a median of 4 points in the placebo group, vs 6 points with doxazosin, 5 points with finasteride, and 7 points with combination therapy (all differences were statistically significant).

Clinical progression occurred in 4.5 per 100 patients per year in the placebo group. With combination therapy, the risk of progression was 66% less, vs 39% less with doxazosin monotherapy and 34% less with finasteride monotherapy. The differences between the three active therapies and placebo were all statistically significant, as were the differences between the two monotherapies and combination therapy.

Most of the cases of clinical progression consisted of an increase in the AUA symptom score. Compared with placebo, the risk of

**Finasteride or dutasteride must be taken for months before symptoms improve**

acute urinary retention was 79% less with combination therapy, 31% less with doxazosin alone, and 67% less with finasteride alone. The risk of invasive procedures was 67% less with combination therapy and 64% less with finasteride, but no significant difference was found between doxazosin and placebo.

Secondary analysis showed that prostate volume greater than 40 cm<sup>3</sup> and serum PSA more than 4.0 ng/mL predicted a better response to combination therapy.

Much can be learned from the MTOPS data:

- Combination therapy is superior to monotherapy over the long term for treating symptoms and for slowing disease progression.
- An alpha-blocker alone can reduce clinical progression, as defined by symptom deterioration. However, while doxazosin delayed the time to acute urinary retention, it did not significantly decrease its incidence, nor did it have any effect on the incidence of surgical procedures.
- We can counsel patients with lower urinary tract symptoms that their risk of BPH progression is approximately 20% over 5 years without treatment, based on a clinical progression rate of 4.5 per 100 patients per year in the placebo group.

Although doxazosin and finasteride are the best-tested agents in combination therapy, and despite a lack of head-to-head trials comparing different agents used in combination, the AUA Practice Guidelines Committee feels that all alpha-blockers and 5-alpha-reductase inhibitors should be equally effective in combination.<sup>12</sup>

**In summary,** a better understanding of risk factors and rates of clinical progression of BPH allow tailoring of medical therapy to each patient:

- Men with smaller prostates and serum PSA less than 2.0 ng/mL can be started on an alpha-blocker.
- Those with an increased risk of clinical progression (ie, with a prostate weighing > 50 g and serum PSA > 4.0 ng/mL) and with no suspicion of prostate cancer can start with a 5-alpha-reductase inhibitor or with combination therapy.

### Other therapies

Phytotherapeutic agents (plant extracts) are

widely used throughout the world for treating lower urinary tract symptoms. The Complementary and Alternative Medicines for Urological Symptoms (CAMUS) trial, a longitudinal evaluation sponsored by the National Institutes of Health, is under way to compare phytotherapeutic agents with conventional treatments.

**Saw palmetto**, an extract of the dried ripe fruit of the American dwarf palm tree *Serenoa repens*, is one of the most popular.<sup>26,27</sup> Its effectiveness has been difficult to properly analyze, because the active agent has not been identified and commercial products differ widely in extraction procedures and preparations.

**Botulinum toxin** is injected directly into the prostate, where it is thought to induce selective denervation and atrophy of the gland. In a randomized controlled trial in 30 patients, botulinum toxin reduced prostate volume and serum PSA and improved AUA symptom scores.<sup>28</sup> Larger trials are needed to evaluate its safety and efficacy.

## ■ SURGICAL TREATMENTS

Surgery is recommended if symptoms are refractory to medical therapy or if the patient prefers it. Immediate surgical treatment has traditionally been recommended for urinary retention, recurrent urinary tract infection, persistent gross hematuria, renal insufficiency due to BPH, and bladder stones. However, for patients with an indwelling catheter after a first episode of urinary retention, it is reasonable to start alpha-blocker treatment and remove the catheter for a voiding trial before proceeding to surgical management.<sup>12</sup>

### Open prostatectomy

Surgical resection (open prostatectomy) used to be the primary treatment for BPH. It is still performed for large prostate glands, although “large” is not strictly defined.

### Transurethral resection of the prostate

Endoscopic prostate resection was developed in the 1920s, and electrosurgical TURP became—and remains—the gold standard for treatment of lower urinary tract symptoms due to BPH. TURP improves symptoms and flow rates better than other available treatments.

**The TUR syndrome (dilutional hyponatremia) results from absorption of irrigation fluid**





(Although some of the numbers in **TABLE 2** appear better for the minimally invasive procedures than for TURP, these data should not be directly compared, owing to lack of head-to-head trials; moreover, there has been much more clinical experience with TURP.)

The TURP procedure takes about an hour to perform. In the operating room with the patient under general or spinal anesthesia, a rigid scope is inserted through the urethra into the bladder. Under direct fiber-optic vision, a unipolar wire loop electrocautery device resects prostate tissue in multiple swipes from the bladder neck to the verumontanum (the area where the seminal ducts enter the urethra). Sterile glycine irrigation fluid is used to distend the bladder and urethra during the procedure.

After surgery, a catheter is placed, and the bladder is irrigated continuously overnight with normal saline. Often the catheter can be removed the morning after surgery, and the patient is discharged home after a successful voiding trial.

Immediate postoperative complications include bleeding, urinary tract infection, and “TUR syndrome,” a dilutional hyponatremia resulting from absorbing the hypotonic irrigation solution during the procedure.

The most common long-term complication is recurrent gross hematuria. Others include bladder-neck contracture, erectile dysfunction, incontinence, and retrograde ejaculation.

In a Veterans Administration cooperative study of TURP vs watchful waiting, rates of sexual dysfunction (5%) and incontinence (1%) were similar in both groups.<sup>16</sup>

In the last decade, technological advances have led to refinements and modifications of TURP in an attempt to reduce perioperative and long-term complications. Variations of TURP procedures resect tissue to create a larger channel through which urine can flow.

### **Transurethral vaporization of the prostate**

Transurethral vaporization of the prostate uses a modified TURP electrode with more surface area to deliver uninterrupted high electrical energy to vaporize prostate tissue.<sup>2</sup> Theoretical advantages include less bleeding, less risk of TUR syndrome, a shorter hospital stay, and

lower equipment costs compared with other new technologies.<sup>29</sup>

In a prospective randomized study, Kaplan et al<sup>30</sup> treated 32 men with transurethral vaporization and 32 with TURP and found similar improvements in AUA symptom score and maximal flow rate after 1 year. One transfusion and one episode of TUR syndrome occurred in the TURP group. No perioperative complications occurred in the transurethral vaporization group, although mean operating time was longer (48 vs 35 minutes). Catheterization time, hospitalization time, and days lost from work were significantly lower in the vaporization group. Among patients with normal sexual function preoperatively, one patient in the transurethral vaporization group was impotent postoperatively. Retrograde ejaculation developed in approximately 80% of patients in both groups.

### **MINIMALLY INVASIVE THERAPIES**

New minimally invasive surgical therapies use radiofrequency, microwave, laser, or ultrasound energy to heat prostate tissue and induce coagulation necrosis. Prostate volume is decreased as necrotic tissue is reabsorbed. These procedures can be performed on an outpatient basis in the office with local anesthesia.

In general, these procedures improve symptom scores and flow rates more than medical therapy does but less than TURP. They tend to be safe, with fewer adverse effects than TURP, although they do have side effects. Retreatment rates after minimally invasive surgery are universally higher than after TURP, and the efficacy, cost, and long-term durability of these therapies are still uncertain.

#### **Transurethral needle ablation**

Transurethral needle ablation causes rapid tissue necrosis by delivering radiofrequency energy through needles that are endoscopically positioned in the prostate.<sup>31</sup> The clinical effect is thought to be due to tissue loss and also possibly to thermal damage to intraprostatic nerve fibers. The denervation of sensory receptors causing smooth muscle relaxation may account for some clinical effect.<sup>32</sup>

**Nearly all patients try medical therapy before undergoing TURP**



The procedure can be performed in the office with local anesthesia and anxiolytics.

Ideal candidates are patients with prostates heavier than 60 g and predominant lateral lobe enlargement, those who are poor surgical candidates, and those with chronic urinary retention.<sup>12,29</sup>

In one study, mean symptom scores decreased from 20.8 to 6.8 at 6-month follow-up and to 6.2 after 1 year. The authors concluded that the procedure is safe and effective as an outpatient procedure.<sup>33</sup> Another study reported only 23% of patients required additional treatments (medical or surgical) by 5-year follow-up after an initial procedure.<sup>34</sup>

### **Transurethral microwave thermotherapy**

Transurethral microwave thermotherapy uses a special transurethral catheter equipped with a microwave antenna to transmit heat into the prostate. The absorbed heat causes tissue loss from coagulation necrosis, and may also denervate alpha receptors in the prostate gland and decrease smooth muscle tone of the prostatic urethra.<sup>35</sup> The catheter is also equipped with a cooling device that limits heat damage to the urethral mucosa. This decreases analgesia requirements and reduces postoperative sloughing of necrotic urethral tissue, which tends to cause irritative voiding symptoms.

The procedure is performed in the office with oral anxiolytics and analgesics, and sometimes with a local prostatic block.<sup>36</sup>

Immediate complications include prolonged catheterization (catheters usually remain for 3 to 7 days if patients do not have urinary retention preoperatively), hematuria, urinary tract infection, and dysuria (in about 50% of patients).<sup>37,38</sup> Long-term complications such as impotence and retrograde ejaculation are uncommon.<sup>29</sup>

In a head-to-head trial of transurethral microwave thermotherapy vs TURP, both therapies conferred significant improvement at 1 year in symptom score, voiding parameters, and transrectal ultrasound and cystometry findings, including pressure-flow analyses, although those receiving thermotherapy improved less.<sup>39</sup> Unfortunately, few long-term data are available.

### **Visual laser ablation of the prostate**

Visual laser ablation of the prostate uses an Nd:YAG laser fiber inserted through a cystoscope with a distal reflector, which deflects laser energy at right angles into the prostatic parenchyma.<sup>40</sup> The procedure potentially causes less bleeding, incontinence, and impotence compared with TURP, owing to relatively bloodless tissue ablation.<sup>29</sup>

Visual laser ablation is similar to TURP in its effects on AUA symptom scores, peak flow, and post-voiding residual volumes, but it is associated with significantly fewer transfusions and cases of TUR syndrome.<sup>41</sup> There is, however, a high incidence of prolonged catheterization and postoperative irritative voiding symptoms, which are likely caused by tissue sloughing due to coagulation necrosis in the prostatic urethra.<sup>12,29</sup>

### **Interstitial laser coagulation**

In interstitial laser coagulation, a solid-state diode 830-nm laser fiber is punctured directly into the prostatic tissue under cystoscopic guidance. Heat from the laser energy induces coagulation necrosis, and as the necrotic tissue is reabsorbed without urethral sloughing, symptoms improve without the irritative voiding symptoms seen with the visual laser ablation technique.

Interstitial laser coagulation is normally performed under spinal or general anesthesia as an outpatient procedure. Two randomized trials of the procedure vs TURP revealed similar symptom score improvement at follow-up at 2 and 4 years, but patients who had TURP had slightly better increases in flow rate. Retreatment rates ranged from 11% to 16% for interstitial laser coagulation compared with 0% to 2.2% for TURP. Sexual function was superior in the interstitial laser coagulation groups, but reports of adverse events after this technique vary widely among studies.<sup>42-44</sup>

### **High-power laser vaporization**

A high-power (60-watt) potassium titanyl phosphate (KTP) laser was first used to treat BPH in 1997.<sup>45,46</sup> It offers the advantages of rapid tissue vaporization, low depth of penetration (resulting in less underlying tissue damage), and excellent hemostasis. Recent reports have shown that 60-watt laser prosta-

**It is uncertain which minimally invasive BPH procedure is best**

tectomy is safe and effective in patients with a prostate weight of less than 90 g.<sup>47</sup> Initial multicenter experience has also shown an 80-watt laser to be simple, safe, and efficacious.<sup>48</sup>

Which minimally invasive procedure is

best is uncertain. An ongoing trial by the National Institutes of Health is comparing transurethral needle ablation, transurethral microwave thermotherapy, and medical therapy with alfuzosin plus finasteride, and may provide some answers.<sup>36</sup>

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