



Benign prostate hyperplasia: a clinical review

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Benign prostatic hyperplasia (BPH) has a profound impact on the quality of life of the aging male, with as many as 80% to 90% of men showing histological changes by age 80. Medical history and physical examination are essential for diagnosing and grading BPH. Symptoms often encountered include weak urinary stream, straining, urinary hesitancy, urgency, and frequency. It is important for the primary care physician to be aware of these symptoms and the appropriate treatment to not only enhance the quality of life but to be able to screen for other diseases such as prostate cancer. This article reviews the diagnostic workup and treatment modalities for BPH.

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Introduction

Benign prostatic hyperplasia (BPH) is a disorder commonly encountered in primary care and will become more common as the population of the United States ages.

BPH is, by nature, a disease of men and more specifically of older men. The prevalence of BPH increases dramatically as age increases, with 10% to 20% of men showing histological changes at age 30 and 80% to 90% showing changes at age 80.¹⁻⁵ Prostate volume also correlates with age. An average prostate at age 50 is about 20 mL, increasing to a mean volume of 34 mL at age 80.¹⁻⁵ No strong evidence of a relationship between race, socioeconomic status, or religion and BPH has been found.² There may, however, be an increased risk of BPH in obese men.¹ An understanding by the family physician of the presentation, diagnosis, and treatment of BPH can aid many men in leading a life with fewer urinary symptoms.

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Pathophysiology

Histologically, BPH is characterized by a nonmalignant increase in the number of both epithelial and stromal cells in the periurethral area of the prostate.^{2,5} Initially, these are discrete nodules of hyperplasia, but it has also been shown that the entire transitional zone of the prostate enlarges with age.² The exact etiology of this process is still unclear. It is known that androgens from the testes must be present for the development of BPH because androgens are required for normal cell proliferation in the prostate.² They do not appear to be the only causative agent, however. Hyperplasia develops when the proliferation of cells is faster than the destruction of cells. Many factors including androgens, estrogens, growth factors, and neurotransmitters may either alone or in concert, cause this disequilibrium (Table 1).²

BPH is of clinical significance when it causes lower urinary tract symptoms (LUTS). Because hyperplasia is centered around the urethra, local pressure exerted by the prostate was originally thought to be the sole cause of LUTS^{1,2} and treatment was aimed at shrinking the size of the prostate. However, a relationship between prostate size and severity of symptoms is not linear.^{1,2,4,5} This indicates that factors other than prostate volume may play a role in the development of LUTS. A capsule that may restrict

Table 1 Causative factors in BPH

Androgens
Estrogens
Growth factors
Neurotransmitters

growth and cause transmitted pressure to the urethra surrounds the human prostate gland. In addition, increased prostatic smooth muscle tone may lead to obstructive symptoms.³ In addition, the detrusor muscle often undergoes reactive changes because it has to overcome prostatic resistance, and this alone can cause LUTS.² Different treatment options are targeted at these various aspects of the disease (Table 2).

History and physical examination

The diagnosis of BPH is made based on patient symptoms, physical examination, and laboratory studies, which are mainly used to exclude other disorders. The history is essential for diagnosing and grading BPH. Typical LUTS can be divided into obstructive and irritative symptoms. Obstructive symptoms include weak stream, straining, hesitancy, feeling of incomplete voiding, and intermittency. Irritative symptoms include urgency, frequency, and nocturia. In a patient under 40 years, BPH should be considered, whereas in men older than 50, BPH will be the most common cause of these symptoms (Table 3).⁵

In addition to symptoms, obtaining a medical history to rule out other conditions and contraindication to medical therapy is important.⁶ Conditions that can cause LUTS include bladder cancer, congestive heart failure, diabetes mellitus, Parkinson’s disease, spinal cord injury, and prostate cancer. Medications can also contribute to or cause LUTS. Classes of medications that have been implicated include antihistamines, decongestants, diuretics, opiates, and tricyclic antidepressants.⁷ The American Urological Association Symptom Index (AUASI) can be used to objectively evaluate patients’ symptoms. It is most useful in assessing symptom severity and response to treatment but should not be used alone to diagnose BPH.⁸ The AUASI is a validated tool and strongly correlates with global symptom severity (Tables 4 and 5).⁹

An initial physical examination should evaluate the neurologic and urologic systems. A neurologic examination

Table 2 Causative factors in LUTS

Local pressure
Transmitted pressure caused by growth restriction by capsule
Increased prostatic smooth muscle tone
Detrusor muscle instability

Table 3 LUTS symptoms

Obstructive	Irritative
Weak stream	Urgency
Straining	Frequency
Hesitancy	Nocturia
Incomplete voiding	
Intermittency	

should consist of checking a patient’s mental status, ambulatory function, rectal sphincter tone, and lower extremity neuromuscular function. The urologic examination should include a genital examination and digital rectal examination. The prostate should be assessed for size, symmetry, and the presence of any nodules.⁶

Diagnostic testing

The American Urological Association (AUA) recommends urinalysis for all men complaining of LUTS to help rule out urethral strictures, urinary tract infections, bladder cancer, and bladder stones. Urine cytology should be considered in persons with predominant irritative symptoms and risk factors for bladder cancer such as smoking.⁸

The AUA only recommends prostate-specific antigen (PSA) testing in men with at least a 10-year life expectancy and who would consider other treatments in the management of prostate cancer or if PSA measurement would change treatment of their LUTS.⁸ PSA measurement has been shown to help predict clinical progression of BPH.^{10,11} PSA levels have also been shown to be helpful in choosing which medication to use. Men with elevated PSAs have been shown to respond better to finasteride (Table 6).¹²

Cystoscopy, urinary flow-rate recording, measurement of postvoid residual, and ultrasound are not recommended in the initial evaluation of LUTS or before initiation of therapy. These tests may be helpful if other coexisting conditions are suspected or before invasive treatments.⁹

Treatment

Treatment of BPH, which includes watchful waiting, pharmacotherapy, and surgery, is generally based on the severity

Table 4 Differential diagnosis for LUTS

Bladder cancer
Congestive heart failure
Diabetes mellitus
Parkinson’s disease
Prostate cancer
Spinal cord injury
Medications: Antihistamines, decongestants, diuretics, opiates, tricyclic antidepressants

Table 5 American Urologic Association Symptom Index²⁴

Use the following point scale to answer the questions.

- 0 points means you answered “never” to the question.
- 1 point means you answered “less than 1 out of 5 times” to the question.
- 2 points means you answered “less than half of the time” to the question.
- 3 points means you answered “about half of the time” to the question.
- 4 points means you answered “more than half of the time” to the question.
- 5 points means you answered “almost always” to the question.

Prostate Symptom Score Questions

1. Over the past month, how often have you had the feeling of not completely emptying your bladder after you finished urinating?
2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?
3. Over the past month, how often have you found that you stopped and started again several times when you urinated?
4. Over the past month, how often have you found it hard to hold your urine?
5. Over the past month, how often have you had a weak urine stream?
6. Over the past month, how often have you had to push or strain to begin urination?
7. Over the past month, have you had to get up to urinate during the night? Give a score to the number of times.
8. Over the past month, how often have you had the feeling of not completely emptying your bladder after you finished urinating?
9. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?
10. Over the past month, how often have you found that you stopped and started again several times when you urinated?
11. Over the past month, how often have you found it hard to hold your urine?
12. Over the past month, how often have you had a weak urine stream?
13. Over the past month, how often have you had to push or strain to begin urination?
14. Over the past month, have you had to get up to urinate during the night? Give a score to the number of times.
 - 0 means you did not get up at all.
 - 1 means you got up 1 time.
 - 2 means you got up 2 times.
 - 3 means you got up 3 times.
 - 4 means you got up 4 times.
 - 5 means you got up 5 times or more.

Score and severity of Problem

Score	Severity
0–7	Mild
8–19	Moderate
20–35	Severe

of LUTS and the presence or absence of complications. In the Medical Treatment of Prostatic Symptoms (MTOPS) Trial, the AUA BPH Symptom Score worsened by an average of four points over 4.5 years and there were no cases of renal failure.¹³ Therefore, it would be reasonable for men with mild symptoms (defined as BPH Symptoms Score of <7 points) to opt for watchful waiting. Recommended non-pharmacological interventions to decrease LUTS include

moderation of alcohol and caffeine intake, limitations in salt and total fluid intake, and using a time voiding schedule (Table 7).¹⁴

Medical therapy includes the α -adrenergic blockers and the 5 α -reductase inhibitors. The α -adrenergic blockers relax prostate smooth muscle in the prostate stroma, bladder neck, and urethra and may also influence the sympathetic and parasympathetic outflow to the bladder. Nonselective α -adrenergic blockers (e.g., phenoxybenzamine) have a higher incidence of side effects, including nasal congestion, orthostatic hypotension, and dizziness, than do selective agents

Table 6 Diagnostic testing recommendations for BPH

Urinalysis	All men complaining of LUTS
Urine cytology	Irritative symptoms and risk factors for prostate cancer: Smoking
PSA	At least a 10-year life expectancy; patient’s willingness to pursue further treatment

Table 7 Nonpharmacologic treatments to decrease LUTS

- Moderation of alcohol intake
- Limit salt and total fluid intake
- Use of timed voiding schedule

Table 8 Medical therapy for BPH

Class	Mechanism of action	Drug	Dosing	Side effects
α -adrenergic blocker	Relax prostate smooth muscle, bladder neck, and urethra	Terazosin (Hytrin)	5–10 mg once daily at bedtime	Nasal congestion
		Doxazosin (Cardura)	4–8 mg once daily at bedtime	Orthostatic hypotension
		Alfuzosin (Uroxatral)	10 mg once daily	Dizziness
5 α -reductase inhibitors	Prevent conversion of testosterone to DHT (major prostate growth stimulator)	Finasteride (Proscar)	5 mg once daily	Decreased libido
		Dutasteride (Avodart)	0.5 mg once daily	Erectile dysfunction Ejaculatory dysfunction

(e.g., prazosin). Long-acting α -adrenergic blockers (e.g., terazosin, doxazosin, alfuzosin) can be taken daily. Tamsulosin specifically targets the α 1A-adrenergic receptor, which constitutes more than 70% of all α -receptors in the prostate. Most α -adrenergic blockers begin working within 48 hours, although the full effect may not be seen for up to four weeks.¹⁵

Five- α -reductase inhibitors prevent the conversion of testosterone into dihydrotestosterone (DHT), which provides the major growth stimulus to prostatic tissue and has a much greater affinity for prostate tissue than testosterone.¹⁶ The 5 α -reductase inhibitors finasteride and dutasteride reduce prostate volume by 20% to 30%, but this takes three to six months.¹⁵ Side effects of these medications include decreased libido, erectile dysfunction, and ejaculatory dysfunction. Finasteride also decreases PSA levels by up to 50% therefore, men taking it should have their PSA level doubled before it is compared with age-specific norms.¹⁷ There has been some interest in evaluating the chemoprophylactic role of 5 α -reductase inhibitors. The Prostate Cancer Prevention Trial compared finasteride with placebo in more than 18,000 healthy men and showed a 25% reduction in the incidence of prostate cancer in the treatment group. However, the incidence of high-grade prostate cancer was also higher in the treatment group.¹⁸ Finasteride is not currently recommended for the prevention of prostate cancer.

Both classes of medications are effective for treating LUTS associated with BPH, although men with normal prostate volumes may benefit more from α -adrenergic blockers. Results from the MTOPS trial and the more recent CombAT study both show that the combination of an α -adrenergic blocker and a 5 α -reductase inhibitor produce somewhat better improvements in LUTS than either agent alone (Table 8).^{13,19}

There are many over-the-counter herbal remedies targeted at BPH and prostate health. The most popular, saw palmetto, was evaluated in a randomized controlled trial in men with moderate to severe BPH and no other therapy. After one year of therapy, there were no differences noted between the treatment and control groups.²⁰ Thus, saw palmetto is not recommended for the treatment of BPH.

Men with BPH may require surgical therapy if they have refractory urinary retention, recurrent urinary tract infec-

tion, persistent hematuria, or they develop renal insufficiency if medical therapy fails.¹⁵ The most common surgical procedure for BPH is transurethral resection of the prostate (TURP), which is effective in almost 90% of men. As much as 10% of men undergoing TURP will need another procedure within five years to treat recurrent LUTS.²¹ A Cochrane review comparing TURP with laser prostatectomy concluded that laser procedures had shorter recovery times and fewer side effects but a higher incidence of reoperation because of persistent LUTS.²²

Conclusion

The incidence of BPH/LUTS has been found to be in the range of 2.7% among males 45–49 years of age and increases with age to a maximum of 24% at the age of 80 years.²³ This increase in symptoms requires the physician who treats elderly males to be familiar with the presentation, diagnostic work up and treatment options for this disease. Clearly, history offers the most insight in to the diagnosis with the use of the AUASI being a vital tool to objectively grade symptom severity and guide treatment options. Most symptoms can be controlled with pharmacological therapy. The major pathophysiologic processes include spasm of the prostate smooth muscle where α -adrenergic blockers have their effect and growth stimulators to prostatic tissue which can be mediated by the use of 5 α -reductase inhibitors by preventing the conversion of testosterone into dihydrotestosterone. These two classes can be used in conjunction to help reduce the over all lower urinary tract symptoms.

There are many over-the-counter herbal remedies targeted at BPH and prostate health. The most popular of these is saw palmetto. It should be noted that in a randomized controlled trial in men with moderate to severe BPH who received saw palmetto and no other therapy there was no differences noted between the treatment and control group.

Surgery is often the final option for male patients who fail medical therapy and have refractory urinary tract symptoms. The most common surgical procedure is the TURP which while highly successful initially there is an increased risk of impotence. Up to a 10 percent of patients will need another procedure in 5 years to treat LUTS.

When diagnosing and treating BPH it is important for the clinician to understand the progression of symptoms and identify red flag symptoms which require more immediate intervention such as urinary retention and renal insufficiency. Treatments options must be reviewed with the patient for their risk benefit analysis and should progress in a stepwise fashion from watchful waiting to medical therapy and finally surgical intervention for refractory cases.

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