

Prevalence and Management of BPH

Michael Naslund, MD, MBA

For a CME/CEU version of this article please go to <http://www.namcp.org/cmeonline.htm>, and then click the activity title.

Summary

Benign prostatic hyperplasia (BPH) is common in the over-50 male population. Treatment options include watchful waiting, medications, minimally invasive procedures, and surgery. Combination medication therapy with an alpha blocker and a 5-alpha reductase inhibitor reduces symptoms and risk of progression.

Key Points

- BPH ranks number four in most common diagnoses and number seven in direct medical costs in men over the age of 50.
- Symptoms of obstruction and irritation occur, but irritation symptoms are what bring men to the doctor.
- Compared with the past, men are treated earlier before complications develop.
- Combination therapy with an alpha blocker and a 5-alpha reductase inhibitor is most effective in preventing progression in patients at risk.
- Although less effective in increasing urinary flow, minimally invasive procedures to reduce prostate tissue result in fewer adverse effects than surgical options.

BENIGN PROSTATIC HYPERPLASIA (BPH) is a common problem. It is the number four diagnosis in men over 50.¹ BPH ranks about seventh in terms of costs when looking at one-year disease-specific medical costs in men over 50.² In one study, at 24 months postdiagnosis, 12.5 percent of patients had experienced an acute urinary retention (AUR) event and 7.2 percent had undergone prostate surgery. The average cost of an AUR event was \$369 and surgery was \$5,699.³

The process of BPH occurs in all men to some degree. As men get older, the prostate gland enlarges and obstructs the outlet for urine. The bladder is a muscle and when a muscle works harder, it gets thicker. When thickened, the bladder muscle does not stretch well. Thus, the functional capacity of the bladder decreases with BPH. With BPH, the bladder becomes hypersensitive and the result is lower urinary tract symptoms (LUTS). As shown in Exhibit 1, there are symptoms of obstruction and irritation.⁴

The irritation symptoms are actually the most common complaints. Frequency and nocturia are the two major complaints men have when they seek medical attention, but these symptoms are not from the obstruction, they are from the bladder's response to the obstruction. Importantly to a BPH

patient's quality of life, the "Multinational Survey of the Aging Male" found that sexual activity declines with increasing severity of lower urinary tract symptoms independent of age.⁵ The survey also found that erectile function also declines in a similar pattern.

The symptoms of BPH can be quantified using the American Urological Association symptoms index (AUA-SI)⁶. It is mainly used for scientific studies on BPH, but it quantifies the extent of symptoms, and it quantifies improvement in symptoms from treatment.

The consequences or complications of BPH are shown in Exhibit 2. As men get older, their chances of having acute urinary retention and needing surgery go up. The reason for that is, statistically, as men get older their prostates get larger and prostate size drives the risk of progression to surgery and retention. Historically, about 40 percent of men required surgery. Nowadays, most men are treated when they have LUTS before they have any long-term complications. The need for surgery and the risk of bladder and kidney complication decrease with early symptomatic treatment.

The progression of BPH varies from patient to patient. The risk factors, which have been identified for progression, include age 50 or older, AUA-SI score of more than 7, enlarged prostate (equal to

Exhibit 1: Lower Urinary Tract Symptoms (LUTS)

Obstructive Symptoms

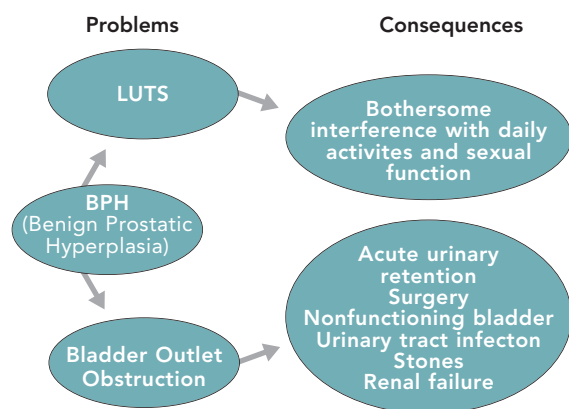
- Hesitancy
- Weak stream
- Straining to pass urine
- Prolonged micturition
- Feeling of incomplete bladder emptying
- Urinary retention

Irritative Symptoms

- Urgency
- Frequency
- Nocturia
- Urge incontinence

Kirby RS et al. *Benign prostatic hyperplasia*. Health Press, 1995.

Exhibit 2:



or more than 30 to 40 ml), and prostate specific antigen (PSA) equal to or more than 1.5.^{7,8} The PSA blood test is a good proxy for prostate size. A PSA of 1.5 or higher suggests an enlarged prostate of at least 35 milliliters.⁹

Once diagnosed with BPH, the majority of men are prescribed watchful waiting. With watchful waiting, the patient is followed annually but receives no active intervention for symptoms.¹⁰ This is an appropriate option for patients with mild symptoms, and for many with moderate to severe symptoms if they are not bothered.¹⁰ Many of these men can go five or 10 years before they need any treatment.

For men that have symptoms that bother them, medications are recommended the majority of the time (Exhibit 3). The medications include alpha blockers, 5-alpha reductase inhibitors, or a combination of these two. Alpha blockers work because there are alpha receptors in the bladder, neck, and prostate. These receptors modulate smooth muscle tone. Normally, when a man urinates his bladder squeezes and his prostate opens so there is flow of urine. As men get older, that muscle does not relax

Exhibit 3: Treatment Options for BPH

- **Watchful waiting**
- **Pharmacological therapy**
 - alpha-adrenergic blockers for BPH symptoms [doxazosin, terazosin, tamsulosin (Flomax®), alfuzosin (Uroxatral®)]
 - 5-ARIs
 - combinations of those above
- **Minimally invasive therapy**
 - TUMT
 - TUNA
 - Interstitial Laser
- **Laser surgery**
 - Greenlight
 - Holmium
- **Major surgery**
 - TURP (gold standard)
 - TUIP
 - Open Prostatectomy

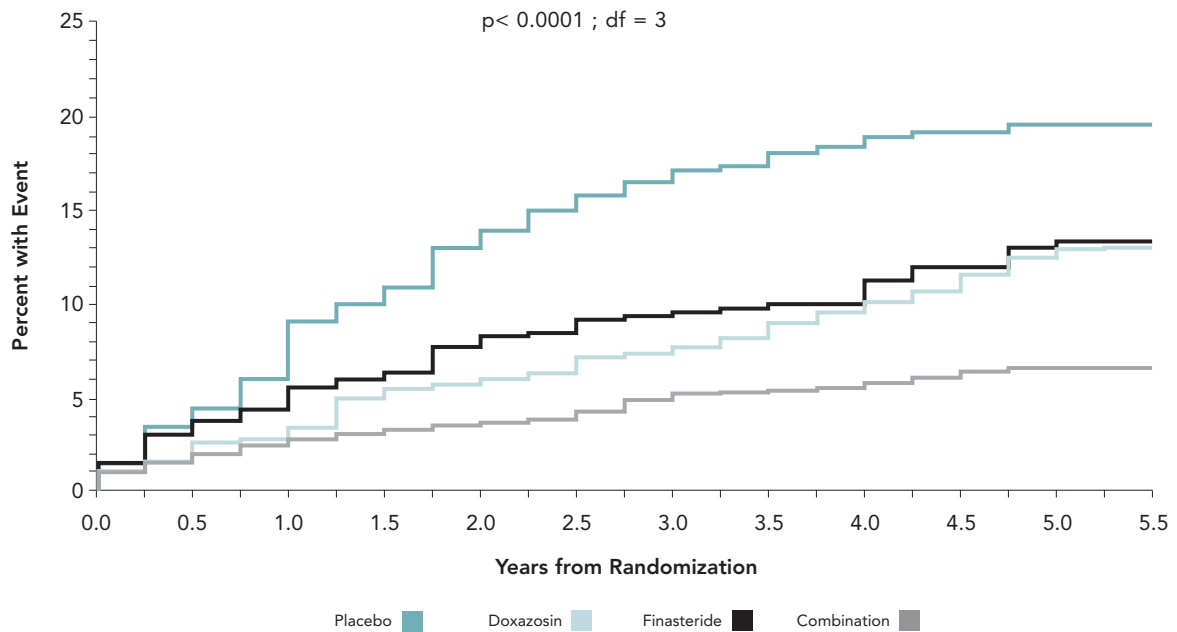
5-ARIs=5-alpha-reductase inhibitors
 ILC=interstitial laser coagulation (also known as LITT)
 TUIP=transurethral incision of prostate
 TUMT=transurethral microwave thermotherapy
 TUNA=transurethral needle ablation
 TURP=transurethral resection of prostate

as well so there is more resistance to flow. Alpha blockers relax the muscles to allow better urine flow. All four alpha blockers have equivalent efficacy for improving symptoms. These medications work within a day or two and are generally well tolerated.

The major difference in the older drugs available generically and newer agents is the antihypertensive effect of the older agents. When doxazosin or terazosin is given at full dose, many men will have low blood pressure and fainting. The older agents have to be titrated over a week or two to avoid severe changes in blood pressure. Because the newer agents lack effects on blood pressure, the dosage does not need to be titrated. Alfuzosin and tamsulosin also have slightly different adverse effect profiles. Dizziness and erectile dysfunction occur less often with alfuzosin.^{11,12}

The 5-alpha-reductase inhibitors work by a different mechanism than the alpha blockers. The reductase inhibitors prevent the conversion of testosterone to dihydrotestosterone (DHT), which is the active form that makes the prostate grow. Over time with reductase inhibitor therapy, the prostate shrinks in size. Dutasteride more completely blocks the production of DHT than finasteride. In addition to prostate reduction, symptomatic improvement occurs to a similar degree as that seen

Exhibit 4: Cumulative Incidence of BPH Progression



with alpha blockers. The difference is, with an alpha blocker, maximum symptomatic improvement occurs in two weeks, whereas it may take three or four years to achieve the same improvement with the 5-alpha-reductase inhibitors. The reductase inhibitors are not good first line drugs for symptoms but are very good first line drugs to lower the progression rate of BPH. Treatment with a reductase inhibitor results in a 50 to 60 percent decrease in the risk of retention and surgery compared with alpha blockers.¹³

Use of a reductase inhibitor lowers PSA values around 50 percent. This must be taken into account when monitoring PSA values in a patient who is receiving a reductase inhibitor. A new PSA baseline should be established once the patient has been on a reductase inhibitor for one year. Subsequent increases in PSA may indicate medication noncompliance, prostate cancer, or other prostate-related conditions that may need evaluation.

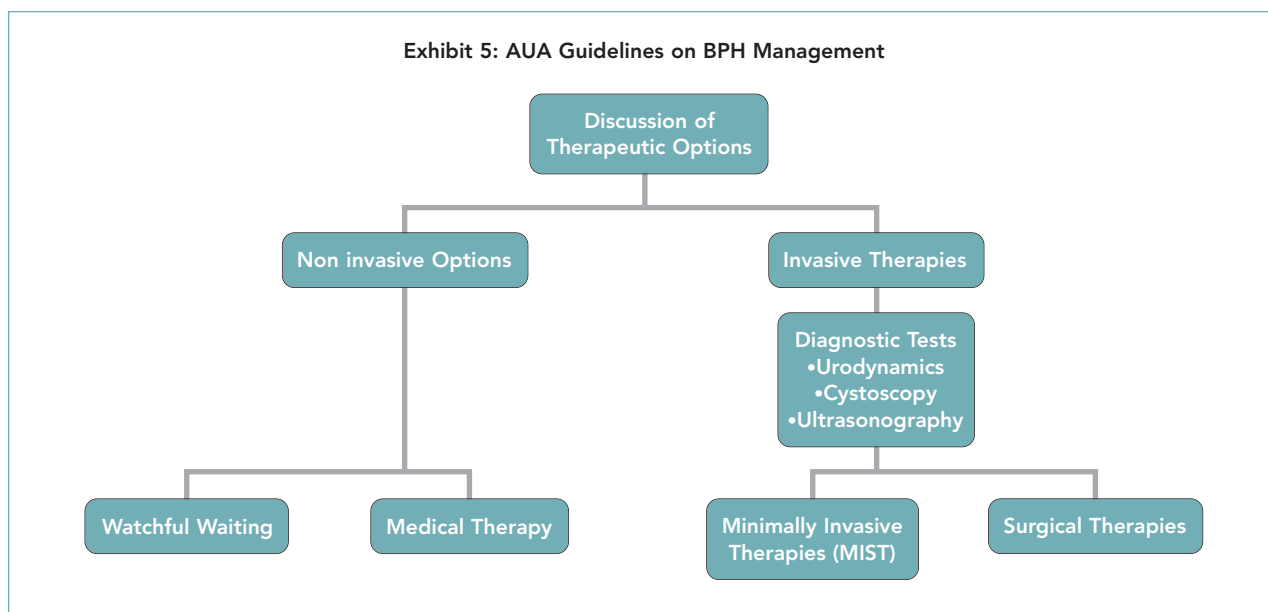
The benefits of combination therapy with an alpha blocker and a reductase inhibitor were established in the Medical Treatment of Prostatic Symptoms (MTOPS) trial.⁷ This trial changed the way urologists treat this disease. Prior to publication of this trial, combination therapy was rarely used. MTOPS showed that in selected patients, combination therapy with an alpha blocker and a reductase inhibitor is most effective in reducing risk of clinical progression, improving AUA symptom score, and improving maximum urinary flow rate.⁷ In this

study, finasteride (the reductase inhibitor used) and combination therapy significantly reduced the risk of AUR and invasive therapy.⁷ Doxazosin (the alpha blocker used) prolonged the time to progression of AUR and invasive therapy, but did not reduce overall risk (Exhibit 4).⁷

When the medications do not work, stop working, cause side effects, or when a patient just doesn't want to take medicine, minimally invasive procedures or prostate surgery are considered. Transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), and interstitial laser coagulation (ILC) all use different methods to achieve the same outcome – destruction of prostatic tissue to relieve the obstruction. The key with these minimally invasive procedures is that general anesthesia is not needed so the procedure can be done in the urologist's office thus resulting in lower costs. These procedures are somewhat less effective than more invasive procedures but cause significantly lower rates of long-term side effects such as impotence, urinary incontinence, and urethral stricture.

Transurethral incision of prostate (TUIP), transurethral resection of prostate (TURP), and open prostatectomy are more invasive surgical procedures which require general anesthesia and hospitalization. At least when comparing TURP with TUNA, the more invasive procedure does result in better urine flow but also more adverse effects. The impotence risk is much less with laser TURP com-

Exhibit 5: AUA Guidelines on BPH Management



pared with electrocautery TURP. With an electrocautery TURP, the heat from the electrocautery goes through the prostate to a nerve bundle right outside the prostate. With the laser, the heat does not get outside the prostate. Laser TURP also does not require an overnight hospital stay like an electrocautery TURP. Exhibit 5 outlines the overall management of BPH.

Conclusion

In the past, a patient's options were a TURP or nothing. Men would have to live with their symptoms for a long time. Nowadays, with the medications, minimally invasive therapies, and surgery, the disease can be treated very effectively. **JMCM**

Michael Naslund, MD, is director of the Maryland Prostate Center. He is a professor of surgery and interim head of the division of urology at the University of Maryland School of Medicine.

References

1. Issa MM, Fenter TC, Black L, et al. An assessment of the diagnosed prevalence of diseases in men 50 years of age or older. *Am J Manag Care.* 2006;12(4 Suppl):S83-S89.
2. Fenter TC, Naslund MJ, Shah MB, et al. The cost of treating the 10 most prevalent diseases in men 50 years of age or older. *Am J Manag Care.* 2006;12(4 Suppl):S90-8.
3. Black L, Naslund MJ, Gilbert TD Jr, et al. An examination of treatment patterns and costs of care among patients with benign prostatic hyperplasia. *Am J Manag Care.* 2006;12(4 Suppl):S99-S110.
4. Kirby RS, McConnell JD. *Fast Facts: Benign prostatic hyperplasia.* 5th ed. Oxford, England: Health Press, 2005.
5. Rosen R. Multinational Survey of the Aging Male (MSAM-7). Presented at

the Annual Meeting of the American Urological Association; May 26, 2002; Orlando, Fla.

6. Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol.* 1992;148:1549-57.
7. McConnell JD, Roehrborn CG, Bautista OM, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med.* 2003;349:2387-2398.
8. Roehrborn CG, McConnell JD, Lieber M, et al. Serum prostate-specific antigen concentration is a powerful predictor of acute urinary retention and need for surgery in men with clinical benign prostatic hyperplasia. PLESS Study Group. *Urology.* 1999;53:473-480.
9. Roehrborn CG, Boyle P, Gould AL, Waldstreicher J. Serum prostate-specific antigen as a predictor of prostate volume in men with benign prostatic hyperplasia. *Urology.* 1999;53:581-589.
10. 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.
11. Brookes ST, Donovan JL, Peters TJ, et al. Sexual dysfunction in men after treatment for lower urinary tract symptoms: evidence from randomized controlled trial. *BMJ.* 2002;34:1059-1061.
12. Lepor H. Phase III multicenter placebo-controlled study of tamsulosin in benign prostatic hyperplasia. Tamsulosin Investigator Group. *Urology.* 1998;51:892-900.
13. Roehrborn CG. Efficacy and safety of once-daily alfuzosin in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a randomized, placebo-controlled trial. *Urology.* 2001;58:953-9.
14. Naslund MJ, Issa MM, Grogg AL, et al. Clinical and economic outcomes in patients treated for enlarged prostate. *Am J Manag Care.* 2006;12(4 Suppl):S111-6.