THE JOURNAL OF FAMILY PRACTICE

What's best for your patient with BPH?

Let symptom scores and patient preferences guide your level of work-up and your treatment approach.

Randall H. Neal, MD
Offutt Air Force Base, Omaha, Neb

Drew Keister, MD
Lehigh Valley Health Network Family Medicine Residency, Allentown, Pa

drew_m.keister@lvh.com

Practice recommendations

- Watchful waiting is recommended for patients with benign prostatic hyperplasia (BPH) whose clinical symptoms do not affect their quality of life (**B**).
- Use a validated patient questionnaire, such as the American Urological Association's Symptom Index, to establish the severity of BPH symptoms and follow their progression (**B**).
- α-Adrenergic blockers (either selective or nonselective) or 5-α reductase inhibitors are appropriate first-line therapies for patients bothered by BPH symptoms (**A**).
- Consider surgery for patients with severe obstructive symptoms who have not benefited from medical therapy or who prefer surgery as first-line treatment (**A**).

Strength of recommendation (SOR)

A Good-quality patient-oriented evidence
B Inconsistent or limited-quality patient-oriented evidence
C Consensus, usual practice, opinion, disease-oriented evidence, case series

By age 60, more than half of men have histopathologic benign prostatic hyperplasia (BPH).[1] And, given the publicity BPH is receiving today, it's quite possible that those who are experiencing symptoms will be less reticent to discuss it than before.

So what does the evidence tell us about how to best manage these patients? Specifically, do you know what the minimal assessment is for those who are experiencing symptoms? When might advanced testing methods be helpful?

Furthermore, among men who are now 50 years old, the expected lifetime incidence for any type of surgical intervention for BPH is approximately 35%.[2] What are the first-line treatments available to these patients? Who might be a candidate for combination drug therapy? Are herbal preparations worth considering? When might surgery be a first choice?

These questions underscore the importance of a proper primary care framework for evaluating and treating BPH, which we can develop based on a consensus guideline released by the American Urological Association (AUA)[1] and on more recent research.

Assessing symptoms: 2 tools can help

Symptoms of BPH can include urinary frequency, nocturia, urgency, hesitancy, weak or intermittent urine stream, straining to void, and a sensation of incomplete voiding.[1] Each patient experiences a unique constellation of these symptoms. Using a urinary symptom scoring system can help define the severity of BPH and be

IN THIS ARTICLE

TABLE 1

Lower urinary tract symptoms are also seen with these disorders[31]

DISORDER	FINDINGS
Bladder calculi	Hematuria, ultrasonography finding
Bladder neck dyssynergia	LUTS in younger patients with normal prostate size, diagnosed by cystoscopy or VCUG
Overactive bladder	Urgency with possible urge incontinence
Prostate cancer	Finding in DRE, elevated serum PSA
Prostatitis	Tender prostate gland
Stricture of the bladder neck	Prior invasive treatment
Urinary bladder cancer	Hematuria, abnormal cytological finding
Urethral stricture	Box-shaped flow curve on urinary flow-rate measurement

DRE, digital rectal examination; LUTS, lower urinary tract symptoms; PSA, prostate-specific antigen; VCUG, voiding cystourethrogram.

useful in monitoring the success of subsequent therapy. Available instruments for this purpose include the AUA's 7-question Symptom Index for BPH (http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=bph) and the International Prostate Symptom Score, which adds an eighth question to the AUA list to gauge the extent to which symptoms bother a patient (http://www.usli.net/uro/Forms/ipss.pdf).[1-5] If the patient is unclear about the pattern of his symptoms, consider asking him to keep a voiding diary.

FAST TRACK

The degree of hypertrophy does not necessarily correlate with severity of obstruction or symptoms.

Ruling out other causes of BPH-like symptoms

TABLE 1 lists the differential diagnoses of obstructive urinary symptoms, otherwise known as lower urinary tract symptoms (LUTS).

Look for clues in the history. Ask the patient whether he uses medications known to cause obstructive urinary symptoms—tricyclic antidepressants, first-generation antihistamines, anticholinergic agents, diuretics, narcotics, and decongestants. Does he have any first-degree relatives with prostate cancer? If the answer is yes, how young was he when the cancer was diagnosed?

Focus your examination. Perform a digital rectal examination (DRE) to check prostate size and to detect palpable nodules, induration, or irregularities associated with malignancy or infection. An enlarged prostate is commonly found on rectal examination; however, the degree of hypertrophy does not necessarily correlate with the degree of obstruction or the severity of symptoms. Any irregularity suggestive of cancer requires that you talk to your patient about his preferences for further investigation.[6]

Conduct a neurologic exam to check mental status, gait, lower extremity strength, and anal sphincter tone to assess for conditions that could cause a neurogenic bladder.

Consider these tests. Urinary tract infection (UTI) or bladder cancer may produce symptoms similar to those of BPH. For any patient who has LUTS, perform a urinalysis to screen for infection or hematuria. If a UTI is found, treat it and re-evaluate the patient. If you detect microscopic hematuria, do a further work-up to rule out bladder cancer. If DRE findings are suggestive of prostate cancer, you'll need an ultrasound-guided biopsy and histological examination to make the diagnosis.

Optional tests in the work-up of LUTS include urinary flow rate measurements, post-void residual urine measurements, and pressure flow studies. These tests may be informative if the diagnosis is unclear based on the history and physical exam or when patients do not respond to initial therapy. Ultrasonography, intravenous pyelography, filling cystometrography, and cystoscopy are not routinely recommended for the evaluation of suspected BPH. However, they may be helpful if a patient has a complex medical history (eg, neurologic disorder or other disease known to affect bladder function, or prior failure of BPH therapy), or if he wants to pursue invasive therapy.[1]

Talk to your patient about the controversial PSA test. Measuring serum prostate-specific antigen (PSA) levels to screen for prostate cancer is controversial, even for patients with LUTS. Although PSA testing can effectively detect prostate cancer in its early pathologic stages, researchers continue to investigate whether early detection significantly improves outcomes. Quite recently, 2 studies demonstrated that the test saves few lives;[7,8] 1410 men would need to be screened and 48 additional cases of prostate cancer would need to be treated to prevent 1 death from prostate cancer.

A subset of detected cancers appears to be clinically significant, but many cancers will not progress during a patient's lifetime.[3,5] The United States Preventive Services Task Force (USPSTF) has concluded that the evidence is insufficient to recommend for or against routine prostate cancer screening due to the uncertainty of the balance of potential benefits (reduction of prostate cancer morbidity and mortality) and risks (false-positive results, unnecessary biopsies, and possible complications) of treatment for early disease.[9-12] Furthermore, in its 2008 update, the USPSTF specifically recommended against screening for prostate cancer in men 75 years of age and older.

The American Cancer Society says that discouraging or not offering testing is inappropriate: Men who ask their physicians to make the decision on their behalf should be tested.[9] A 2006 Cochrane review of this topic found only 2 eligible randomized trials, both of which had high risk of bias. They concluded that insufficient high-quality evidence exists to support or refute the use of any screening for prostate cancer in any patient population, including those with BPH.[13]

Given this conflicting advice, discuss the benefits and limitations of screening with your patient before deciding whether or not to test.

What is the optimal approach to treatment?

Patients who are not bothered by their urinary symptoms—even those with moderate to severe symptom scores—can be managed with watchful waiting. Because of the cost and frequent side effects of medications for BPH, these patients generally will not benefit from drug therapy.[3,5,14,15] However, follow-up monitoring is important, because the severity of BPH can change even without treatment.

Even if patients with moderate or severe AUA symptom scores are not bothered by their symptoms, inform them of appropriate treatment options.[3] When urinary obstruction symptoms from BPH significantly interfere with daily living and sleep activities, treatment is justified.[1]

Medical management, yes, but which option?

Medical therapies are not as effective as surgical intervention,[16] but they often provide adequate symptom relief and cause fewer, less severe, and less permanent adverse effects than surgery. Initiate treatment with medical therapy if (1) the patient is bothered by his symptoms, (2) no significant urinary obstruction exists, and (3) you have followed the patient's

FAST TRACK

Patients not bothered by urinary symptoms—even those with moderate to severe symptom scores—can be managed with watchful waiting.

preference for prostate cancer evaluation. **TABLE 2** lists prescription medications for the treatment of BPH.

Nonselective α-adrenergic blockers, such as doxazosin and terazosin, reduce prostatic smooth muscle tone, thereby improving urinary flow. A Cochrane systematic review and a subsequent large randomized trial found terazosin to be superior to placebo in improving urinary flow and decreasing symptoms in men with BPH.[16,17]

Selective α-adrenergic blockers, such as alfuzosin and tamsulosin, are highly selective α-1_A-adrenergic antagonists. They are believed to be as effective as the nonselective agents, and patients may experience fewer side effects than with nonselective agents.[1,18] However, these drugs are considerably more expensive than their nonselective counterparts.

5-α Reductase inhibitors, such as finasteride and dutasteride, are more effective than placebo for patients with LUTS associated with demonstrable prostate enlargement. In a Cochrane review and subsequent large randomized trial, finasteride proved inferior to terazosin.[16,17] However, finasteride reduces the progression to urinary obstruction and the need for invasive therapy; terazosin does not.[17] Finasteride achieves this effect by reducing prostatic volume by about 20% over 3 to 6 months of treatment.

Finasteride decreases PSA levels by 40% to 50%. If you conduct PSA screening for prostate cancer in a patient taking finasteride, double the PSA level before comparing it with age-related norms. Handled this way, PSA screening will not lose its sensitivity or specificity for the diagnosis of prostate cancer.[19]

Though a 5-mg daily regimen of finasteride reduces the overall risk of prostate cancer from 24.4% to 18.4%, it increases the risk of high-grade disease associated with higher mortality from 5.1% to 6.4%. Warn patients of this risk.[20]

Combining an α-adrenergic blocker and 5-α reductase inhibitor. Combination therapy is appropriate and effective for patients with LUTS associated with demonstrable prostate enlargement for whom monotherapy has failed.[9] Taken together, a 5-α reductase inhibitor and a nonselective α-1_A-adrenergic blocker alleviate symptoms more effectively than either drug can do alone.[21,22] The incidence of most adverse drug reactions with the combination is similar to the baseline risk for each drug. However, ejaculatory abnormalities are reported in 7% of patients in the combination therapy group vs 2% or less in the monotherapy groups. Discontinuation rates for combination therapy are comparable to those in the nonselective α-adrenergic blocker group.[22] The adverse effect profile of combining selective α-adrenergic blockers with 5-α reductase inhibitors has not been reported; however, the combination is often used in practice.

For patients to make an informed decision about treatment, discuss with them the common adverse reactions from these agents (**TABLE 2**) and the need for long-term daily therapy. Also give the patient a reasonable estimate of the risk of his retention symptoms progressing.

FAST TRACK

If you conduct PSA screening for prostate cancer in a patient taking finasteride, double the PSA level before comparing it with age-related norms.

Complementary medicine: Information is still limited

Herbal or complementary medicines are used worldwide to treat BPH. These products are not regulated by the US Food and Drug Administration (FDA), and therefore no standardized formulation or dosing exists. Although a few substances appear to have some positive effects, high-quality clinical trials on clinical outcomes are lacking.

The AUA guideline does not recommend the use of phytotherapy.[1] Despite this, many patients—and any number of physicians—turn to phytotherapy to treat LUTS associated with BPH.

Some patients turn to phytotherapy without their physician's knowledge, so it's important to ask whether they are using any herbal preparations. Agents currently used include saw palmetto, African plum, South African star grass, and Cernilton.

TABLE 2

BPH medications: How they compare

AUA RECOMMENDATION FOR USE WITH LUTS SECONDARY TO BPH[1]	DRUG	DOSE	MOST COMMON SIDE EFFECTS (%)	COSTS
Nonselective α-adrenergic blockers				
Useful as first-line therapy due to efficacy and low cost α-Adrenergic blockers can be used with other therapies as needed	Doxazosin (Cardura, generics)	Start at 1 mg; titrate by doubling dose every 1-2 wk. Goal: 4-8 mg. Maximum dose, 8 mg	Dizziness (16), headache (10), fatigue (8), edema (3), dyspnea (3), orthostatic hypotension (2), abdominal pain (2)*	$4 for 30-day supply for both generic agents†
	Terazosin (Hytrin, generics)	Start at 1 mg at bedtime, increase PRN over 4-6 wk; most patients require 10 mg. If no response at 10 mg, may increase to 20 mg	Dizziness (9), fatigue (7), headache (5), orthostatic hypotension (4), somnolence (4), nasal congestion (2), ED (2)‡	
Selective α-adrenergic blockers				
All believed to be equal in clinical effectiveness	Alfuzosin (Uroxatral or Xatral)	10 mg/d with the same meal	Dizziness (6), headache (3), upper respiratory infection (3), fatigue (3)§	$112 for 30-day supply//
	Tamsulosin (Flomax)	0.4 mg/d (30 min after same meal); may increase after 2-4 wk to 0.8 mg/d if no response	Headache (19), dizziness (15), rhinitis (13), infection (9), fatigue (8), abnormal ejaculation (8)¶	$110 for 30-day supply//
5-α Reductase inhibitors				
All believed to be appropriate and effective treatments for patients with demonstrable prostate enlargement	Finasteride (Proscar)	5 mg/d	ED (8), decreased libido (6), decreased volume of ejaculate (4)#	$70 for 30-day generic supply//
	Dutasteride (Avodart)	0.5 mg/d	ED (5), decreased libido (3), ejaculation disorder (1), gynecomastia (1)**	$20-$30 for 30-day generic supply††

AUA, American Urological Association; BPH, benign prostatic hypertrophy; ED, erectile dysfunction; LUTS, lower urinary tract symptoms.

* http://www.fda.gov/medwatch/SAFETY/2006/Feb_PI/Cardura_PI.pdf.

† Prices listed on Walmart.com as of April 6, 2009.

‡ http://www.fda.gov/medwatch/SAFETY/2006/Feb_PI/Hytrin%20Caps_PI.pdf.

§ http://www.fda.gov/medwatch/safety/2008/Sep_PI/Uroxatral_PI.pdf.

// Prices listed on Drugstore.com as of April 6, 2009.

¶ http://www.fda.gov/medwatch/SAFETY/2008/Apr_PI/Flomax_PI.pdf.

http://www.fda.gov/medwatch/SAFETY/2004/apr_PI/Proscar_PI.pdf.

** http://www.fda.gov/medwatch/SAFETY/2004/sep_PI/Avodart_PI.pdf.

†† Prices listed on Pharmacychecker.com as of April 6, 2009.

FAST TRACK

If monotherapy fails to relieve symptoms, consider combining a 5-α reductase inhibitor and an α-adrenergic blocker.

FAST TRACK

Saw palmetto is a reasonable option for men who prefer a nonprescription product to treat their BPH symptoms.

Saw palmetto (*Serenoa repens*) has been used by more than 2 million men in the United States. In 2006, Bent et al conducted a rigorously designed double-blinded trial in which 225 men older than 49 years with moderate-to-severe symptoms of BPH were treated for 1 year with saw palmetto extract (160 mg twice a day) or placebo.[23] Saw palmetto did not ameliorate the symptoms of BPH. In contrast, a Cochrane systematic review last updated in 2002 asserted that this substance caused mild-to-moderate reductions in urologic symptoms and flow measures when given to men with symptomatic BPH.[24] Long-term efficacy and safety of this product are unknown. Given the efficacy of saw palmetto, it is a reasonable option for men who prefer a nonprescription product to treat symptoms of BPH.

African plum (*Pygeum africanum*) is more effective than placebo in reducing symptoms of BPH and has few side effects, based on poorly designed small studies.[25,26] Comparative data with finasteride or the α-adrenergic blockers are lacking.

South African star grass (*Hypoxis rooperi* and certain species of *Pinus* and *Picea*) contain beta-sitosterols and are sources for phytotherapeutic treatments for BPH. A systematic review analyzed the effects of beta-sitosterols in men and found improved urinary symptom scores and flow measures (n=519; 4 randomized, controlled, double-blind trials; duration, 4-26 weeks).[27] Their long-term effectiveness and safety are not known.

Cernilton, prepared from the rye-grass pollen *Secale cereale*, is marketed for the treatment of BPH. A Cochrane systematic review demonstrated that comparative trials lacked a proven active control. Available evidence suggests that short-term use of cernilton is well tolerated and modestly decreases overall urologic symptoms, including nocturia. Additional randomized placebo and active-controlled trials are needed to evaluate the long-term clinical effectiveness and safety of Cernilton.[28]

Acupuncture was not effective in treating LUTS in men in randomized controlled (single-blinded) trials.[29]

When patients don't respond to medical treatment

Surgery is recommended for patients who have not responded to medical treatment, who have refractory retention with a failed attempt at catheter removal, or who experience recurrent UTIs, persistent hematuria, bladder stones, or renal insufficiency.[3] In addition, surgery can be the initial treatment choice for patients with high AUA symptom scores who opt for this intervention and are good operative candidates.

The specific surgical approach (open or endoscopic; electrocautery or laser) are technical decisions based on the patient's prostate size, the individual surgeon's judgment, and the patient's comorbidities.[1,30] For patients who are not surgical candidates, treatment with intermittent catheterization, an indwelling catheter, or a stent is recommended. ■

Correspondence

Drew M. Keister, MD, Lehigh Valley Health Network, PO Box 7017, Allentown, PA 18105-7017; drew_m.keister@lvh.com

Disclosure

The authors reported no potential conflicts of interest relevant to this article.

Acknowledgements

The authors thank Jen Creer, MA, of Edit Rx, LLC, for her assistance in the preparation of this manuscript. The University of Nebraska Medical Center, with which both authors were previously affiliated, funded this writing assistance.

References

1. American Urological Association. AUA guideline on the management of benign prostatic hyperplasia: diagnosis and treatment recommendations. 2003/updated 2006. Available at: http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=bph. Accessed April 2, 2009.
2. Oesterling JE. Benign prostatic hyperplasia: medical and minimally invasive treatment options. *N Engl J Med.* 1995;332:99-109.
3. McConnell JD. *Clinical practice guideline no. 8: Benign prostatic hyperplasia: diagnosis and treatment.* Benign Prostatic Hyperplasia Guideline Panel. Rockville, Md: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1994. AHCPR publication 94-0582.

4. Austin O, Ricer RE. (1996). Prostate cancer screening: an appraisal of the PSA test. *Fam Pract Recert.* 1996;18:81-91.
5. Barry MJ, Fowler FJ, 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;148:1549-1557.
6. Denis LJ. Diagnosing benign prostatic hyperplasia versus prostate cancer. *Br J Urol.* 1995;76(suppl 1):S17-S23.
7. Andriole GL, Crawford ED, Grubb RL, et al. Mortality results from a randomized prostate-cancer screening trial. *N Engl J Med.* 2009;360:1310-1319.
8. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med.* 2009;360:1320-1328.
9. American Cancer Society Guidelines for the Early Detection of Cancer. Revised March 5, 2008. Available at: http://www.cancer.org/docroot/PED/content/PED_2_3X_ACS_Cancer_Detection_Guidelines_36.asp. Accessed April 6, 2009.
10. US Preventive Services Task Force. *Screening for prostate cancer: recommendation statement.* Available at http://www.ahrq.gov/clinic/uspstf08/prostate/prostaters.htm. Accessed April 3, 2009.
11. American Cancer Society. Cancer Facts & Figures. Atlanta, Ga: 2008. Available at http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf. Accessed on April 3, 2009.
12. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer, *CA Cancer J Clin.* 2006;56:11-25.
13. Ilic D, O'Connor D, Green S, et al. Screening for prostate cancer. *Cochrane Database Syst Rev.* 2006;(3):CD004720.
14. Barry MJ. Evaluation of symptoms and quality of life in men with benign prostatic hyperplasia. *Urology.* 2001;58(suppl 1):S25-S32.
15. Polascik TJ, Oesterling JE, Partin AW. Prostate specific antigen: a decade of discovery—what we have learned and where we are going. *J Urol.* 1999;162:293-306.
16. Wilt T, Howe RW, Rutks I, et al. Terazosin for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2002;(4):CD003851.
17. 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.
18. Wilt T, MacDonald R, Rutks I. Tamsulosin for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2003;(1):CD002081.
19. Guess HA, Gormley GJ, Stoner E, et al. The effect of finasteride on prostate specific antigen: review of available data. *J Urol.* 1996;155:3-9.
20. Thompson IM, Goodman PJ, Tangen CM, et al. The influence of finasteride on the development of prostate cancer. *N Engl J Med.* 2003;349:215-224.
21. Garraway WM, Collins GN, Lee RJ. High prevalence of benign prostatic hypertrophy in the community. *Lancet.* 1991;338:469-471.
22. Lepor HL, Williford WO, Barry MJ, et al. The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. *N Engl J Med.* 1996;335:533-540.
23. Bent S, Kane C, Shinohara K, et al. Saw palmetto for benign prostatic hyperplasia. *N Engl J Med.* 2006;354:557-566.
24. Wilt T, Ishani A, Mac Donald R. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 1999;(1):CD001423.
25. Ishani A, MacDonald R, Nelson D, et al. *Pygeum africanum* for the treatment of patients with benign prostatic hyperplasia: a systematic review and quantitative meta-analysis. *Am J Med.* 2000;109:654-664.
26. Wilt T, Ishani A, MacDonald R, et al. Pygeum africanum for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2002;(1):CD001044.
27. Wilt T, Ishani A, MacDonald R, et al. Beta-sitosterols for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 1999;(4):CD001043.
28. Wilt T, MacDonald R, Ishani A, et al. Cernilton for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2000;(2):CD001042.
29. Johnstone PA, Bloom TL, Niemtzow RC, et al. A prospective, randomized pilot trial of acupuncture of the kidney-bladder distinct meridian for lower urinary tract symptoms. *J Urol.* 2003;169:1037-1039.
30. Keister DM, Neal R. Managing BPH: when to consider surgery. *Am Fam Physician.* 2008;77:1391-1392.
31. Finnish Medical Society Duodecim. Benign prostatic hyperplasia. In: *EBM Guidelines. Evidence-Based Medicine* [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd; 2005.

FAST TRACK

Surgery can be the initial treatment of choice for patients with high AUA symptom scores who opt for this intervention and are good operative candidates.