Primary Care Evaluation and Treatment of Men With Lower Urinary Tract Symptoms

Nathan Hale, DO
Kellen Choi, DO
Joshua Lohri, DO

From the Department of Urology at the Charleston Area Medical Center in West Virginia.

Financial Disclosures: None reported.

Support: None reported.

Address correspondence to Nathan Hale, DO, Charleston Area Medical Center–Urology, 3110 MacCorkle Ave SE, Room 58, Charleston, WV 25304-1210.

E-mail: nhale@camc.org

Submitted August 5, 2013; revision received October 25, 2013; accepted November 6, 2013.

Lower urinary tract symptoms (LUTS) affect 50% to 90% of men aged 50 years or older. Primary care physicians should be knowledgeable about the diagnosis and management of this condition. The authors performed detailed PubMed searches using the terms *lower urinary tract symptoms*, *benign prostatic hyperplasia*, *benign prostatic enlargement*, and *overactive bladder*. The authors then reviewed the relevant literature on the evaluation and treatment of men with LUTS. According to the literature, accurate recognition of LUTS is predicated on a focused history and physical examination, as well as serum prostate-specific antigen measurement and urinalysis. For patients with mild symptoms, watchful waiting with ongoing monitoring and lifestyle modifications may be appropriate. For patients with moderate to severe symptoms, pharmacologic therapy is effective. When substantial LUTS persist despite appropriate pharmacologic therapy, specialty urologic evaluation and treatment is warranted.

J Am Osteopath Assoc. 2014;114(7):566-571
doi:10.7556/jaoa.2014.110

Lower urinary tract symptoms (LUTS) are common, affecting nearly 50% to 90% of men aged 50 years or older.[1,2] Although benign prostatic enlargement (BPE) is a common cause, LUTS are often associated with a variety of other conditions, which can be difficult to identify. Patients often have a difficult time clearly describing their symptoms, making interpretation even more problematic for treating physicians. However, accurate diagnosis and appropriate management of LUTS can dramatically improve the patient's quality of life and slow the progression of disease.[3]

Lower urinary tract symptoms include a variety of voiding dysfunctions and may be due to structural or functional abnormalities in multiple areas of the lower urinary tract, which comprises the bladder, bladder neck, prostate, sphincter, and urethra. Abnormalities of the peripheral or central nervous system can also lead to LUTS. The symptoms are commonly divided into 3 categories: storage, voiding, and postmicturition symptoms.[4-6] Symptoms associated with storage include frequency and urgency of urination, nocturia, and incontinence. Voiding symptoms include hesitancy, intermittent stream, slow stream, straining, and terminal dribble, and postmicturition symptoms include incomplete emptying and postmicturition dribble. Subclassifying LUTS can help physicians identify the cause of the symptoms and determine an appropriate treatment plan for the patient.

A common cause of LUTS in men is BPE.[7] The term *benign prostatic hyperplasia* (BPH) is reserved for the histologic pattern found on a pathologic specimen. Benign prostatic enlargement is diagnosed when enlargement of the prostate is noted in examination or

imaging findings. Benign prostatic obstruction is diagnosed when obstruction is noted in pressure flow study or uroflowmetry findings, with prostatic enlargement previously noted. Overactive bladder (OAB) syndrome is another common cause of LUTS, which can occur alone or in conjunction with prostatic enlargement; this syndrome is defined as urgency with or without incontinence and is usually associated with frequent urination and nocturia.[8] Detrusor overactivity is a urodynamic observation characterized by spontaneous or provoked involuntary detrusor contractions during the filling phase.[9] Other causes of LUTS include genitourinary cancer, urethral strictures, prostatitis, comorbid conditions, medications, and pelvic trauma or surgery.[10,11] For these reasons, management of LUTS requires a physician who is knowledgeable about the lower urinary tract.

For the present review article, we conducted a PubMed search using the terms *lower urinary tract symptoms*, *benign prostatic hyperplasia*, *benign prostatic enlargement*, and *overactive bladder*. Using the search results, we reviewed the evaluation and treatment options for men with LUTS seen in the primary care setting.

Diagnostic Evaluation

The initial evaluation of a man with LUTS begins with a detailed medical history and physical examination focused on the genitourinary system. The history must focus on the nature and duration of the patient's symptoms, previous genitourinary surgical procedures, medications, and overall health. The number and severity of symptoms can easily be assessed semiquantitatively using the International Prostate Symptom Score.[12,13] A voiding diary, which includes frequency, volume voided, and fluid consumption during several 24-hour periods, is particularly useful in identifying nocturnal polyuria or excessive fluid intake.[14] Nocturnal polyuria is defined as voiding more than 33% of the 24-hour urine production at night, and its presence suggests a pathophysiologic cause outside the lower urinary tract.[15]

Physical examination should include an assessment of the patient's suprapubic area after urination to rule out bladder distention, as well as an assessment of the sensory and motor function of the lower extremities and perineum to assess for any neurologic dysfunction.[16] Digital rectal examination should be performed to assess anal sphincter tone in addition to prostate gland size, shape, and consistency. Urinalysis should be performed to identify hematuria, proteinuria, pyuria, or other abnormalities.[16] If pathologic findings are identified, urinary sediment analysis and culture may be indicated. The results of the urinalysis may guide additional testing beyond the LUTS evaluation, including prostate-specific antigen (PSA) testing.[17] The risks and benefits of PSA testing should be discussed with the patient. Despite the controversy over routine PSA screening,[18] PSA testing is warranted in a man with LUTS and is not considered screening. The PSA level is a reasonable predictor of prostate volume and can aid physicians in making clinical decisions for these patients.[19]

Any abnormalities noted in the patient's history, physical examination findings, or laboratory evaluation should be addressed by the physician or referred to the appropriate specialist.[20,21] Male patients with LUTS should be referred to a urologist if diagnostic evaluation reveals any of the following: abnormal prostate examination findings, elevated PSA level, urinary retention, history of genitourinary trauma or recurrent urinary tract infections, meatal stenosis, hematuria, or previous genitourinary surgery.[16]

Treatment

The goals of treating men with LUTS are to improve quality of life with minimal adverse effects and to reduce risk of disease progression.[22-24] If assessment reveals that symptoms are minimally bothersome to the patient, watchful waiting may be appropriate. Continued education, reassurance, ongoing monitoring, and lifestyle modifications should be part of the treatment plan in pa-

tients who select watchful waiting. Lifestyle modifications include eating a healthy diet high in fiber, exercising regularly, decreasing fluid intake several hours before going to bed, and decreasing caffeine and alcohol consumption. Primary care physicians can counsel patients on the timing of diuretics, the avoidance of decongestants, and the maintenance of regular bowel function. Many patients are unaware of the anticholinergic effects of most decongestants until after an episode of acute urinary retention; patient education may prevent such an event.

When LUTS are found to be moderate to severe and bothersome, pharmacotherapy should be initiated.[22,25] The first-line treatment for men with predominant voiding symptoms is generally α-adrenergic receptor antagonists (α-blockers), which work by relaxing the smooth muscle tone and increasing the size of the prostatic lumen during urination.[26] Tamsulosin and silodosin are α_{1A} selective, whereas terazosin, doxazosin, and alfuzosin are nonselective α_1-adrenergic receptor blockers. Treatment response is rapid and should be detectible in 7 to 10 days. The most common adverse effects are dizziness, orthostatic hypotension, and retrograde ejaculation. The frequency of α-adrenergic receptor antagonists side effects vary depending on the specific drug.[27]

If the symptoms are related to a problem with urinary storage, then a trial of anticholinergics may be indicated. However, physicians should use caution when prescribing an anticholinergic medication in men with a history of acute urinary retention or elevated postvoid residual volume greater than 250 mL.[22] Oxybutynin, tolterodine, fesoterodine, darifenacin, solifenacin, and trospium are the anticholinergics currently available for the management of OAB.[28,29] Anticholinergics may exert an effect within 1 week but usually achieve their maximal effect after 3 months.[30] The most common adverse effects are dry mouth, dry eyes, and constipation. A major concern regarding the use of anticholinergics in male patients is the risk of urinary retention. However, in the absence of increased postvoid residual volumes, appropriately dosed anticholinergic therapy has shown no greater risk of retention than placebo in randomized controlled trials.[30]

The 5α-reductase inhibitors (ARIs) are considered first-line therapy in men with a clinically enlarged prostate and bothersome LUTS. Finasteride and dutasteride are the 2 drugs in this class, and both work by inhibiting the conversion of testosterone to dihydrotestosterone, thereby reducing the size of the prostate by 25%.[31] The most common adverse effects are impotence, decreased libido, decreased volume of ejaculate, and gynecomastia.[32]

Available data show that ARIs help prevent the progression of BPE and their ability to reduce the risk for acute urinary retention and the need for surgical intervention is statistically significant.[33] They also usually decrease serum PSA levels by 50% within 6 to 12 months; these levels must therefore be multiplied by 2 when they are monitored for the detection of prostate cancer.[34]

In 2013, the US Food and Drug Administration expanded the indications of tadalafil to include LUTS related to BPH.[35] Tadalafil is a type 5 phosphodiesterase (PDE5) inhibitor that has conventionally been used for erectile dysfunction. The PDE5 enzyme is expressed in the bladder, prostate, and urethra. Its inhibition increases smooth muscle relaxation and improves LUTS. Findings of a recent meta-analysis[36] suggested that tadalafil can statistically significantly improve LUTS in men with BPH and can be considered as an alternative treatment option with or without the presence of erectile dysfunction.

In 2012, mirabegron was the first of a new class of β_3-adrenergic agonists approved by the US Food and Drug Administration for the management of OAB.[37] It works by relaxing the detrusor smooth muscle, decreasing afferent signaling from the bladder, improving bladder compliance during filling, and increasing overall bladder capacity. Its most common adverse effects are headache and a mild increase in blood pressure, and it

therefore should not be used in patients with uncontrolled hypertension. Mirabegron reduces the number of micturitions and incontinence episodes in a 24-hour period, compared with placebo.[38,39] It also improves OAB symptoms related to BPH without a substantial difference in postvoid residual volumes.[40] Because this drug has been approved for a short period, many questions about how to best implement its use remain unanswered.

Although monotherapy is sufficient for some men, a combination of treatments may be necessary to achieve maximal therapeutic response. Combination therapy with an α-blocker to rapidly reduce LUTS and an ARI to shrink the prostate can be used.[41] The Medical Therapy of Prostate Symptoms and the Combination Avodart and Tamsulosin trials showed that the combination of an α-blocker and an ARI inhibitor prevents progression of BPH better than either agent alone.[41-43] If monotherapy or combination therapy with an α-blocker and an ARI fails to control symptoms to the patient's satisfaction, specialty evaluation is indicated before further treatment.[44] The medical literature supports the use of other combinations of medications for the management of LUTS in specific clinical scenarios. For example, the combination of a PDE5 inhibitor with an α-blocker is significantly more effective than an α-blocker alone in men with LUTS related to BPH.[45] In addition, in men with BPH, a combination of an α-blocker and an anticholinergic can improve quality of life, voiding symptom scores, urinary urgency and frequency, and nocturia better than either agent alone.[46,47] If combination therapy is unsuccessful, surgical intervention may be necessary.

Conclusion

Lower urinary tract symptoms are a common complaint among male patients in the primary care setting and may have adverse outcomes if left untreated. Benign prostatic enlargement is one of the many causes of LUTS in men. Accurate recognition of LUTS is predicated on a focused history and physical examination, as well as PSA measurement and urinalysis. An experienced physician's assessment can help guide treatment decisions with minimal laboratory tests. Watchful waiting is a reasonable option in men whose symptoms are minimally bothersome. In men with moderately to severely bothersome symptoms, pharmacologic therapy is effective, and a variety of approaches are available to primary care physicians. When substantial LUTS persist after pharmacologic therapy, specialty urologic evaluation and treatment are warranted.

References

1. Parsons JK, Bergstrom J, Silberstein, Barrett-Connor E. Prevalence and characteristics of lower urinary tract symptoms in men aged ⩾80 years. *Urology.* 2008;72(2):318-321.
2. McVary K. BPH: epidemiology and comorbidities. *Am J Manag Care.* 2006;12(5 suppl):S122-S128.
3. Martin S, Lange K, Haren MT, Taylor AW, Wittert G; Members of the Florey Adelaide Male Ageing Study. Risk factors for progression or improvement of lower urinary tract symptoms in a prospective cohort of men. *J Urol.* 2014;191(1):130-137.
4. Abrams P, Cardozo L, Fall M, et al; Standardisation Sub-committee of the International Continence Society. The standardization of terminology of the lower urinary tract function: report from the Standardization Sub-committee of the International Continence Society. *Neurourol Urodyn.* 2002;21(2):167-178.
5. Abrams P, Artibani W, Cardozo L, Dmochowski R, van Kerrebroeck P, Sand P; International Continence Society. Reviewing the ICS 2002 terminology report: the ongoing debate. *Neurourol Urodyn.* 2009;28(4):287.
6. Andersen JT, Blaivas JG, Cardozo L, Thüroff J. Lower urinary tract rehabilitation techniques: seventh report on the standardization of terminology of lower urinary tract function. *Neurourol Urodyn.* 1992;11(6):593-603.
7. Roehrborn C. Male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). *Med Clin North Am.* 2011;95(1):87-100.
8. Suarez O, Osborn D, Kaufman M, Reynolds WS, Dmochowski R. Mirabegron for male lower urinary tract symptoms. *Curr Urol Rep.* 2013;14(6):580-584.
9. Sener NC, Ozturk U, Goktug HN, et al. Efficacy and safety of propiverine and terazosine combination for one year in male patients with LUTS and detrusor overactivity. *Int Braz J Urol.* 2013;39(4):513-518.
10. Wang GC, Zheng JH, Yang B, et al. Impacts of histological prostatitis on sexual function and lower urinary tract symptoms in patients with benign prostatic hyperplasia. *Urology.* 2013;82(5):1094-1097.

11. Rom M, Waldert M, Schatzl G, Swietek N, Shariat SF, Klatte T. Bladder outlet obstruction (BOO) in men with castration-resistant prostate cancer [published online September 5, 2013]. *BJU Int.* doi:10.1111/bju.12438.

12. Barry MJ, Fowler FJ Jr, O'Leary MP, et al; The Measurement Committee of the American Urological Association. The American Urological Association symptom index for benign prostatic hyperplasia. *J Urol.* 1992;148(5):1549-1557.

13. Lee JY, Lee DH, Lee H, Bang WJ, Hah YS, Cho KS. Clinical implications of a feeling of incomplete emptying with little post-void residue in men with lower urinary tract symptoms [published online August 14, 2013]. *Neurourol Urodyn.* doi:10.1002/nau.22473.

14. Doo SW, Lee HJ, Ahn J, et al. Strong impact of nocturia on sleep quality in patients with lower urinary tract symptoms. *World J Mens Health.* 2012;30(2):123-130.

15. Sağlam HS, Gökkaya CS, Salar R, Memiş A, Adsan O. The effects of age, metabolic syndrome, nocturnal polyuria and sleep disorders on nocturia. *Adv Clin Exp Med.* 2013;22(4):489-494.

16. McConnell J, Abrams P, Denis L, Khoury S, Roehrborn C, eds. *Male Lower Urinary Tract Dysfunction: Evaluation and Management.* Paris, France: Health Publications; 2006.

17. Oelke M, Bachmann A, Descazeaud A, et al; European Association of Urology. EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol.* 2013;64(1):118-140.

18. Carroll PR. Vickers AJ. Point/counterpoint: early detection of prostate cancer: do the benefits outweigh the consequences? *J Natl Compr Canc Netw.* 2014;12(5 suppl):768-771.

19. Kayikci A, Cam K, Kacagan C, Tekin A, Ankarali H. Free prostate-specific antigen is a better tool than total prostate-specific antigen at predicting prostate volume in patients with lower urinary tract symptoms. *Urology.* 2012;80(5):1088-1092.

20. Rosenberg MT, Miner MM, Riley PA, et al. STEP: simplified treatment of the enlarged prostate. *Int J Clin Pract.* 2010;64(4):488-496.

21. Rosenberg MT, Staskin DR, Kaplan SA, et al. A practical guide to the evaluation and treatment of male lower urinary tract symptoms in the primary care setting. *Int J Clin Pract.* 2007;61(9):1535-1546.

22. McVary KT, Roehrborn CG, Avins AL, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol.* 2011;185(5):1793-1803.

23. Elterman Ds, Barkin J, Kaplan SA. Optimizing the management of benign prostatic hyperplasia. *Ther Adv Urol.* 2012;4(2):77-83.

24. Roehrborn CG. Currently available treatment guidelines for men with lower urinary tract symptoms. *BJU Int.* 2008;102(suppl 2):18-23.

25. Nordling J, Abrams P, Ameda K, et al. Outcome measures for research in the treatment of adult males with symptoms of lower urinary tract dysfunction. *Neurourol Urodyn.* 1998;17(3):263-271.

26. Schwinn DA, Michelotti GA. α_1-Adrenergic receptors in the lower urinary tract and vascular bed: potential role for the α_{1d} subtype in filling symptoms and effects of ageing on vascular expression. *BJU Int.* 2000;85(suppl 2):6-11.

27. Yuan J, Liu Y, Yang Z, Qin X, Yang K, Mao C. The efficacy and safety of α-1 blockers for benign prostatic hyperplasia: an overview of 15 systematic reviews [published online January 29, 2013]. *Curr Med Res Opin.* 2013;29(3):279-287. doi:10.1185/03007995.2013.766594.

28. Abrams P, Kaplan S, De Koning Gans HJ, Millard R. Safety and tolerability of tolterodine for the treatment of overactive bladder in men with bladder outlet obstruction. *J Urol.* 2006;175(3 pt 1):999-1004.

29. Athanasopoulos A, Gyftopoulos K, Giannitsas K, Fisfis J, Perimenis P, Barbalias G. Combination treatment with an α-blocker plus an anticholinergic for the bladder outlet obstruction: a prospective, randomized, controlled study. *J Urol.* 2003;169(6):2253-2256.

30. Athanasopoulos A, Chapple C, Fowler C, et al. The role of antimuscarinics in the management of men with symptoms of overactive bladder associated with concomitant bladder outlet obstruction: an update. *Eur Urol.* 2011;60(1):94-105.

31. Roehrborn GC. Male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). *Med Clin North Am.* 2011;95(1):87-100.

32. Naslund MJ, Miner M. A review of the clinical efficacy and safety of 5α-reductase inhibitors for the enlarged prostate. *Clin Ther.* 2007;29(1):17-25.

33. Abrams, Chapple C, Khoury S, et al. Evaluation and treatment of lower urinary tract symptoms in older men. *J Urol.* 2013;189(1 suppl):S93-S101. doi:10.1016/j.juro.2012.11.021.

34. Benign prostatic hyperplasia. In: Wieder JA. *Pocket Guide to Urology.* 4th ed. Caldwell, ID: Griffith Publishing; 2010:177.

35. Cantrell MA, Baye J, Vouri SM. Tadalafil: a phosphodiesterase-5 inhibitor for benign prostatic hyperplasia [published online March 25, 2013]. *Pharmacotherapy.* 2013;33(6):639-649. doi:10.1002/phar.1243.

36. Gacci M, Corona G, Salvi M, et al. A systematic review and meta-analysis on the use of phosphodiesterase 5 inhibitors alone or in combination with α-blockers for lower urinary tract symptoms due to benign prostatic hyperplasia [published online February 25, 2012]. *Eur Urol.* 2012;61(5):994-1003. doi:10.1016/j.eururo.2012.02.033.

37. Belavic JM. Drug updates and approvals: 2012 in review. *Nurse Pract.* 2013;38(2):24-42. doi:10.1097/01.NPR.0000425824.44694.e8.

38. Sacco E, Bientinesi R. Mirabegron: a review of recent data and its prospects in the management of overactive bladder. *Ther Adv Urol.* 2012;4(6):315-324.

39. Andersson KE, Martin N, Nitti V. Selective β_3-adrenoceptor agonists in the treatment of the overactive bladder [published online February 28, 2013]. *J Urol.* 2013;190(4):1173-1180. doi:10.1016/j.juro.2013.02.104.

40. Otsuki H, Kosaka T, Nakamura K, Mishima J, Kuwahara Y, Tsukamoto T. β_3-Adrenoceptor agonist mirabegron is effective for overactive bladder that is unresponsive to antimuscarinic treatment or is related to benign prostatic hyperplasia in men. *Int Urol Nephrol*. 2013;45(1):53-60.

41. McConnell JD, Roehrborn CG, Bautista OM, et al; Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med*. 2003;349(25):2387-2398.

42. Roehrborn CG, Siami P, Barkin J, et al; CombAT Study Group. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. *Eur Urol*. 2010;57(1):123-131.

43. Abrams P, Chapple C, Khoury S, Roehrborn C, de la Rosette J; International Scientific Committee. Evaluation and treatment of lower urinary tract symptoms in older men [published online February 23, 2009]. *J Urol*. 2009;181(4):1779-1787. doi:10.1016/j.juro.2008.11.127.

44. Roehrborn CG, Siami P, Barkin J, et al; CombAT Study Group. The effects of dutasteride, tamsulosin and combination therapy on lower urinary tract symptoms in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the CombAT study. *J Urol*. 2008;179(92):616-621.

45. Gacci M, Corona G, Salvi M, et al. A systematic review and meta-analysis on the use of phosphodiesterase 5 inhibitors alone or in combination with α-blockers for lower urinary tract symptoms due to benign prostatic hyperplasia. *Eur Urol*. 2012;61(5):994-1003.

46. Yong Y, Zhao XF, Li HZ, et al. Efficacy and safety of combined therapy in men with terazosin and tolterodine for patients with lower urinary tract symptoms associated with benign prostatic hyperplasia. *Chin Med J*. 2007;120(5):370-374.

47. Kaplan SA, Roehrborn CG, Rovner ES, Carlsson M, Bavendam T, Guan Z. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. *JAMA*. 2006;296(19):2319-2328.