



Weill Medical College of Cornell University Reports on Men's Urologic Health

Editor: Steven A. Kaplan, MD, Professor of Urology, and Chief, Institute for Bladder and Prostate Health, Weill Medical College of Cornell University, New York, NY

Benign Prostatic Hyperplasia and Enlarged Prostate Guidelines: How They Can Be Useful to Primary Care

By Steven A. Kaplan, MD*

Evidence-based guidelines for the management of enlarged prostate (EP), also referred to as benign prostatic hyperplasia (BPH), are an important feature of clinical practice and serve as an accepted standard of care. In fact, at least 15 guidelines have been published worldwide.¹ In the 1990s, under the aegis of what is now the United States Agency of Healthcare Research and Quality (AHRQ), the Benign Prostatic Hyperplasia Guidelines Panel published recommendations on the diagnosis and treatment of BPH.² A multidisciplinary, 13-member, private-sector panel based the guidelines on a review of available literature (1,200 abstracts and 200 articles) on BPH. The thrust

*Professor of Urology, and Chief, Institute for Bladder and Prostate Health, Weill Medical College, Cornell University, New York, NY

of the guidelines was that patients should consult with physicians and decide on a treatment based on likely treatment outcomes.

Several of these guidelines, including those published in the United States and Europe, have been updated recently to reflect changes in our understanding of the disease and in treatment options. Although most of the guidelines were developed for use by urologists, many of them were also targeted for use by general practitioners.¹ This is particularly the case for the 1994 AHCPR guidelines.^{2,3} The 2003 updated guidelines developed by the American Urological Association (AUA) are targeted mainly for urologists.⁴

The role of primary care physicians in the management of BPH has changed considerably over the past decade.⁵ Today, most men who suffer from troublesome symptoms of EP secondary to BPH present first to their pri-

mary care provider (PCP).⁶ A recent National Institutes of Health survey reported that at least 6.3 million American men 30 years of age and older are affected by EP,⁷ accounting for 6.4 million doctor visits.⁷ However, the lack of guidelines specifically designed for use by PCPs has resulted in uncertainties in the diagnosis and medical management of EP. For example, a survey of PCPs examining the use of guidelines on diagnosis found that almost two thirds of them rarely or never used the AUA Symptom Index (AUA-SI), which provides a reliable and valid way to measure and track over time a patient's symptom severity.⁸ Moreover, this survey reported that PCPs prescribed an α -blocker more frequently than a 5 α -reductase inhibitor (5 α RI) for the management of EP secondary to BPH,⁸ even though the latter class of drugs has been shown to be more effective.

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Weill Medical College of Cornell University

The Cornell Urology physicians work together as part of Weill Cornell Medical Center of New York Presbyterian Hospital in New York City. The mission of the Department of Urology is to provide unequalled urologic care in a compassionate setting. The Department also seeks to make significant contributions to urology through research and training of future urologic specialists.

The Department of Urology offers a wide spectrum of subspecialties including urologic oncology, management of benign prostate problems (BPH, prostatitis), men's health (including male infertility and sexual dysfunction), minimally invasive surgery (including laparoscopy), female urology, as well as pediatric urology. The department is dedicated to being a center of discovery and invests in basic research to accelerate groundbreaking findings into innovative patient care.





Joan and Sanford I. Weill Medical College

STEVEN A. KAPLAN, M.D.
Chief, Institute for Bladder and Prostate Health
Professor of Urology
Attending Urologist

James Buchanan Brady Foundation
Department of Urology

Dear Colleague:

The incidence of benign prostatic hyperplasia (BPH) continues to rise in the United States, along with the increase in longevity and the aging population.

About 80% of the time, irregularities of urination in men—including control problems with urination and increased frequency of urination—are caused by BPH.

The incidence of BPH is at least 50% for all men at the age of 50, and rises to at least 80% of all men in their eighth decade of life. However, only about 25% of men will actually be treated for BPH by the age of 80.

About 50% of men with an enlarged prostate gland have a condition in which there is some degree of obstruction of the bladder outlet.

Researchers are uncovering valuable information about BPH, its prevention and effective treatment.

Consequently, there is a need for medical education that examines this and other urologic disorders in men. To accomplish these objectives, we are pleased to introduce to you this new clinical monograph series, *Weill Medical College of Cornell University Reports on Men's Urologic Health*.

This monograph series will inform clinicians about the latest developments in prostate problems as well as other urologic disorders that challenge men. Each original issue will be written by an expert in the field.

We wish to thank GlaxoSmithKline for supporting this medical education project. We invite suggestions and comments from readers.

Sincerely,

A handwritten signature in black ink, appearing to read "S. Kaplan", with a long, sweeping underline that extends to the right.

Steven A. Kaplan, MD
Professor of Urology
and Chief, Institute for Bladder and Prostate Health
Weill Medical College of Cornell University
New York, New York

Historically, EP and BPH have been viewed as a symptomatic condition, with the relief of voiding symptoms driving therapy. This dovetails with and supports the use of α -blockers as prime agents in medical management. However, during the past 10 years, we have become increasingly aware that EP secondary to BPH is a progressive disorder, often manifested by clinical complications such as acute urinary retention (AUR) and prostate surgery. Two pivotal multicenter, randomized clinical trials clearly demonstrated the effectiveness of 5 α RIs in reducing the complications of EP, including AUR and prostate surgery.^{9,10} Recent understanding of EP as a naturally progressive disorder with a considerable risk of AUR justifies medical intervention with 5 α RIs to prevent progression.^{11,12}

Despite such evidence, there are notable gaps in primary care management of EP.

Practice patterns among PCPs on the minimal use of 5 α RIs have not changed over the years, as exemplified by a recent Internet survey.¹³ The 2003 AUA guidelines recommend the use of 5 α RIs to prevent progression in men with demonstrable prostatic enlargement.⁴ However, these recommendations have not been fully disseminated to PCPs. To manage their patients appropriately, PCPs should be familiar not only with the prevalence and symptoms of EP, but also with the underlying disease process, evidence-based treatment options from landmark studies, outcomes, alarming features, and indications for referral to urologists. Thus, there is an immediate need to develop guidance tools for use in everyday primary care management of men with BPH and EP.

This paper is a compendium of diagnostic and treatment strategies based on input from the AUA BPH Guidelines Committee as well as from PCPs with expertise in EP and BPH. These strategies are meant to be a template to treat the symptoms secondary to BPH and, just as importantly, to address therapeutic algorithms for long-term disease management.

Patient Profiles

Patients seeking treatment for EP are commonly identified by one of three different clinical scenarios: (a) those who approach their PCP with lower urinary tract symptoms (LUTS); (b) those whose prostate glands are palpably enlarged on digital rectal examination (DRE); and (c) those with an enlarged prostate identified in a routine physical examination such as measurement of prostate-specific antigen (PSA) levels.

Enlarged prostate or BPH is very common in aging males, occurring in more than 50% of men 50 to 60 years of age.¹⁴ In addition, half of all men who have a histologic diagnosis have moderate-to-severe LUTS.⁴ The clinical manifestations of EP can range from minimally bothersome symptoms of LUTS to complications such as AUR and renal failure.¹⁵

A comprehensive assessment is essential to confirm a diagnosis of EP. Physicians need to recognize and address or correct other factors that may contribute to LUTS, and refer patients with 'alarm symptoms' to a urologist.

Patients usually have LUTS for years before they seek consultation and do not report symptoms until the condition affects their quality of life.⁶ Indeed, patients are often embarrassed to discuss prostate problems with their family physicians. Some men consider changes in urinary function to be part of the normal 'aging' process, or fail to report symptoms because of the fear of surgery, lack of awareness of effective medical therapies, or previous experience with treatment-related adverse events.⁶ This failure to report symptoms of EP can result in underdiagnosis and underscores the importance of a routine symptom evaluation in men aged >50 years.

Symptoms of LUTS are not specific to EP. Many urologic and nonurologic conditions—such as prostate cancer, prostatitis, bladder cancer, bladder stones, overactive bladder, interstitial cystitis, radiation cystitis, urinary tract infection (UTI), primary bladder neck hypertrophy, diabetes mellitus, Parkinson's disease, congestive heart failure, lumbosacral disc disease, and multiple sclerosis—can also cause LUTS.¹⁶ Medications that increase obstructive urinary symptoms include tricyclic antidepressants, anticholinergic agents, diuretics, narcotics, and first-generation antihistamines and decongestants (common cold medications).¹⁶ In addition, obesity, cigarette smoking, regular alcohol consumption, and elevated blood pressure are risk factors for the development of LUTS.¹⁷ Therefore, it is critical that probable differential diagnoses be considered when evaluating men with LUTS.¹⁶ An appropriate evaluation, as outlined in the AUA 2003 guidelines, includes a comprehensive assessment that begins with a careful, detailed medical history, symptom assessment using AUA-SI score or BPH impact index, combined with a physical examination, urinalysis, and subsequent serum PSA test in appropriate patients to exclude cancer.^{4,18}

A urinalysis should be performed to screen for hematuria and UTI.⁴ Although the

routine assessment of serum creatinine levels is not indicated in the initial evaluation of men with LUTS secondary to BPH,⁴ primary care physicians may measure serum creatinine levels to rule out renal insufficiency secondary to other causes, such as diabetic nephropathy. Presence of EP in men <45 years of age, refractory retention, persistent gross hematuria, bladder stones, recurrent UTIs, abnormally high PSA levels, and renal insufficiency are 'alarm symptoms' that require referral to a urologist.⁴

Assessing Symptoms

The population-based Olmsted County Study suggests that bother, frequency of symptoms, and interference in life caused by symptoms are significant predictors of health-care-seeking behavior.¹⁹ Indeed, the patient's perception of the bothersome nature of symptoms, rather than merely their presence or absence, is an important consideration for management⁴ to improve quality of life.²⁰

Evidence during the last decade clearly demonstrated that EP is a progressive disease that is characterized by a number of factors, including a deterioration in LUTS, decreased urinary flow, continued growth of the prostate, and increased risk of AUR/need for surgery, bladder complications, hematuria and recurrent UTIs, all of which lead to a worsening of the patient's quality of life.²¹

EP influences clinical progression

The largest body of evidence for the progression of BPH comes from the Olmsted County, Minnesota, epidemiologic study. The 6-year longitudinal follow-up reported a decline of 2% per year in the peak urinary flow rate.²² This analysis also showed that men with larger prostates were most at risk for rapid decline in peak urinary flow rate.²² The 7-year longitudinal follow-up of these men demonstrated that prostate volume increased by an average 1.6% per year.²³ Jacobsen et al demonstrated a slow but measurable progression in urinary symptom severity during 42 months of follow-up among men in the study.²⁴ Greater increases in symptom progression were noted among men in their 60s compared with men in their 40s.²⁴ At 18 months, 14% of men with mild symptoms at baseline reported moderate to severe symptoms, and at 42 months 22% of men with mild symptoms at baseline crossed over to moderate to severe symptoms.²⁴ This finding was also confirmed in a study by Djavan et al, in which 31% of men with mild symptoms (IPSS <8) progressed to the moderate symptom group

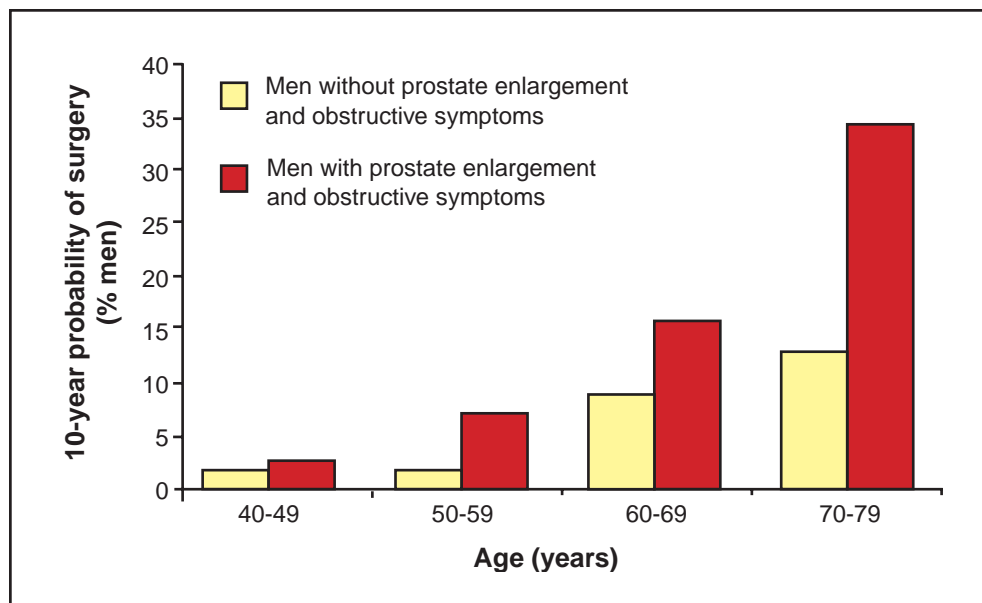


Figure 1: Prostate enlargement contributes to risk of BPH-related surgery.³³

(IPSS of 8 to 18) during a 48-month follow-up. Furthermore, a PSA of more than 1.5 ng/mL and transitional zone volume (TZV) of more than 25 cm³ accurately predicted clinical progression in 82% of these patients.²⁵

Progression is associated with increased risk of AUR and prostate surgery

The Olmsted County study demonstrated that enlarged prostates, older age, LUTS, and depressed peak urinary flow rates are independent predictors of risk of AUR.²⁶ Men 70 to 79 years of age were at eight times the risk of AUR compared to men 40 to 49 years of age. Among men with no symptoms or with mild symptoms (AUA symptom index ≤ 7), the incidence of AUR increased from 2.6/1,000 person-years among men 40 to 49 years of age to 9.3/1,000 person-years among men 70 to 79 years of age. However, men with moderate to severe symptoms (AUA symptom index > 7) were at three times the risk for AUR than men with no or mild symptoms. The relative risk associated with EP was also of similar magnitude (RR = 3.0).²⁶ Based on these incidence rates, a 60-year-old man with moderate to severe symptoms would have a 13.7% chance of developing acute retention in the following 10 years,²⁷ and the presence of EP can further increase this risk. This risk is similar to other conditions commonly associated with aging, such as diabetes, stroke, myocardial infarction (MI), and hip fracture.²⁷ Preventive medicine is widely practiced for diabetes,²⁸ stroke,²⁹ MI,³⁰ and hip fracture.³¹ Because prostatectomy resulting from AUR is associated with increased morbidity and increased risk of death during and after surgery,³² prevention of AUR is desirable.

The Baltimore Longitudinal Study of Aging demonstrated that men with EP and obstructive symptoms were five to eight times more likely to require prostatectomy within 10 years than those of the same age without EP³³ (Figure 1).

Fear of AUR and surgery is a major concern to patients

The AUA Guidelines Committee strongly advocated that the patient should play a central role in determining his need for treatment.⁴ The potential for AUR and/or surgery is a major concern to patients. In a Canadian survey, 57% of all men with EP were concerned about the prospect of AUR, and 67% were significantly concerned about the prospect of surgery. Moreover, patients considered the insertion of a catheter for AUR to be more detrimental to their quality of life than surgery.³⁴ A French survey reported that a reduction in the risk of major urologic complications and the need for surgery were more important to patients when considering intervention than were improving symptoms and quality of life.³⁵ Although such surveys are lacking in the United States, preference to avoid surgery can be considered a universal choice for most patients.

Because all the evidence points toward EP as a risk factor for disease progression resulting in complications, prostate size is an important factor to be considered when deciding if and how to treat. The recent British guidelines for the primary care management of male LUTS include prostate size (large prostate > 30 mL or a PSA > 1.4 ng/mL) as a criterion for both the decision to treat and the treatment choice.³⁶ However, measuring prostate volume

using transrectal ultrasonography (TRUS) is not practical in a primary care setting. A correlation between prostate volume, serum PSA levels, and age has been demonstrated.³⁷ In addition, several studies showed that serum PSA concentration is a powerful predictor of AUR and need for surgery in men with EP.³⁷

Based on these findings, the British guidelines for the primary care management of LUTS recommend measurement of serum PSA level as a proxy for prostate size.³⁶ The 2003 AUA guidelines, however, do not recommend the routine use of PSA as a measure for EP in asymptomatic men.⁴ Because of the overlap between serum PSA values in men with BPH and those with clinically localized prostate cancer, the diagnostic specificity of serum PSA measurement for routine EP evaluation is uncertain and, therefore, optional.⁴ The diagnosis of EP in primary care is thus limited to DRE.

Accurately estimating the size and volume of a prostate using DRE is a common challenge faced by PCPs. Studies have frequently reported an underestimation of prostate volume on DRE; this underestimation is particularly pronounced in men with larger prostates.³⁸ A possible ramification of underestimating prostate volume is inappropriate management, particularly prevention of disease progression. When left untreated, EP can progress to complications of AUR, leading to surgical intervention, bladder decompensation, and upper urinary tract compromise. Therefore, it is important to have a simple way to accurately predict the presence of EP. The prostate is a chestnut-shaped gland with three dimensions: transverse (T, width), longitudinal (L, length), and antero-posterior (AP, height). Prostate volume can be calculated by the prostate ellipsoid formula ($0.52 \times \text{width} \times \text{length} \times \text{height}$).³⁹ The index finger can obtain a close approximation of the T (width) and L (length) dimensions, but not the AP (height), although AP is often similar in dimension. Thus, if the index finger measures of L and T dimensions are approximately 3 cm each, and we assume that AP is also 3, the prostate volume would be approximately 14 mL ($3 \times 3 \times 3 \times 0.52$). On the other hand, when the L and T dimensions as measured by index finger reach 5 cm, the prostate volume is approximately 65 mL ($5 \times 5 \times 5 \times 0.52$), assuming that the AP diameter is also 5 cm. If the AP diameter is only 3 cm, the prostate would still be considered enlarged at approximately 40 cc ($5 \times 5 \times 3 \times 0.52$). The width of most adult index fingers ranges between 1.5

and 2.0 cm. Thus, depending on the size of the examiner's index finger, a greater than two-finger width (or 2.5 for smaller fingers) of T diameter should indicate EP (prostate volume >25 mL). Although this is a crude technique, it can guide the PCP in determining whether the prostate is enlarged.

Disease modification is an essential component of medical management

AUR is not life threatening; however, it is a serious morbid disorder, usually accompanied by great discomfort, hospitalization, and surgery.^{32,40} Prevention is desirable, particularly in men with known risk factors such as moderate to severe LUTS, large prostates, and poor urinary flow rates.³² Historically, treatment with pharmacotherapy has been symptom driven, particularly when associated with bother. Preferred medical treatment is with either an α -blocker, which reduces smooth muscle tone in the prostate and bladder neck, or with a 5 α RI, which reduces prostate volume.^{18,41} The landmark Medical Therapy of Prostatic Symptoms (MTOPS) study investigated whether therapy with an α -blocker (doxazosin) or a 5 α RI (finasteride), alone or in combination, would delay or prevent clinical progression of BPH.¹² One of the largest EP studies, MTOPS enrolled 3,047 men of at least 50 years of age with moderate to severe symptoms (AUA symptom score of 8 to 35), who were followed for 5 years. The rate of overall clinical progression (defined as the first occurrence of an increase over baseline of at least 4 points in the AUA-SI score, AUR, renal insufficiency, recurrent UTI, or urinary incontinence) at 4 years was 17% in the placebo group, 10% each in the doxazosin group ($P < 0.001$ vs placebo) and the finasteride group ($P = 0.002$ vs placebo), and 5% in the combination group ($P < 0.001$ vs placebo). When the events of AUR were analyzed, significant treatment differences were observed with α -blocker vs 5 α RI and combination therapy. The rate of AUR in both the finasteride group (0.2 per 100 person-years; risk reduction, 68%; $P = 0.009$) and the combination group (0.1 per 100 person-years; risk reduction, 81%; $P < 0.001$) was significantly lower compared with the rate of AUR in the placebo group (0.6 per 100 person-years). Although doxazosin delayed the time to AUR, it did not significantly reduce the cumulative incidence, compared with placebo ($P = 0.23$). Likewise, treatment with finasteride and combination therapy significantly reduced the risk of invasive therapy by 64% and 67%, respectively, compared with placebo ($P < 0.001$ vs placebo for both treat-

ment groups). In contrast, doxazosin did not significantly reduce the cumulative incidence of invasive therapy. The findings from the MTOPS study were also observed in real-life clinical practice. Retrospective analyses of data from the General Practice Research Database from the United Kingdom (UK GPRDS) and from the Netherlands PHARMO Record Linkage System reported that patients who received an α -blocker were significantly more likely to experience AUR (hazard ratio 2.35) or have a higher risk of prostate surgery (hazard ratio 1.52-1.78) than patients who were prescribed a 5 α RI.^{42,43} The investigators of the Netherlands study interpreted their findings as one additional case of prostatic surgery occurring for every 14 patients treated with α -blockers for 4 years relative to patients treated with 5 α RI.⁴³ The MTOPS data clearly suggest that 5 α RI can prevent progression of EP and reduce the risk of prostate surgery.⁴⁴ The ability of the 5 α RI to reduce the risk of AUR and the need for invasive therapy may be attributed to a reduction in prostate size.¹²

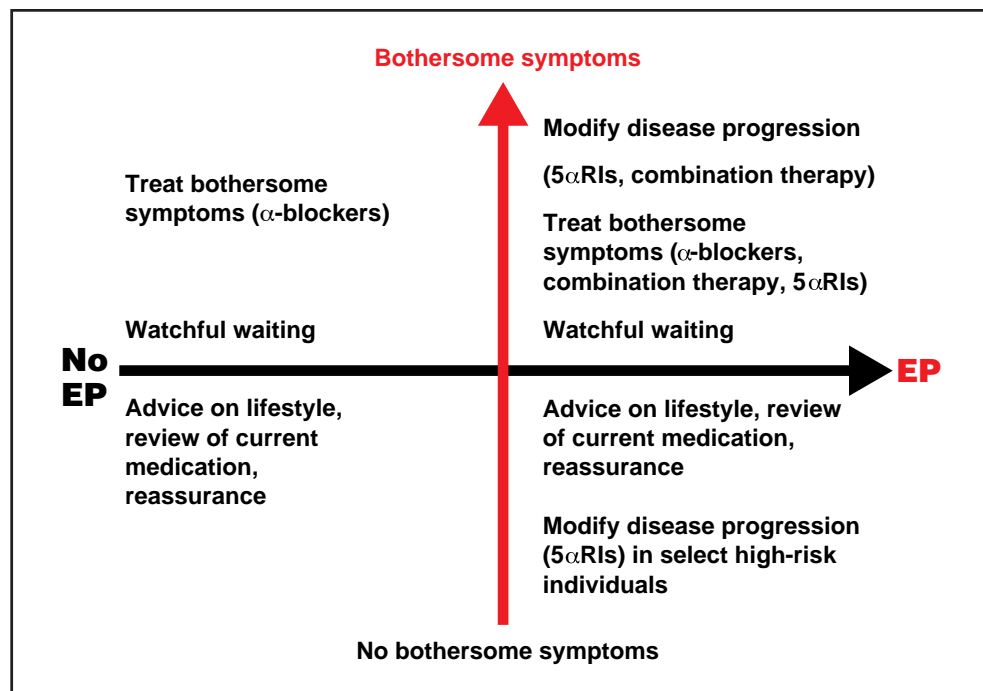


Figure 2: The goals of therapy for patients diagnosed with EP.

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Medical Management of EP in Primary Care

The goals of management should focus on disease modification and treatment of bothersome symptoms. Based on the evidence presented here, EP can be considered a two-dimensional disorder with symptoms (bothersome or not bothersome) and enlargement (presence or absence of large prostate) that in-

fluence management. Treatment options of watchful waiting, symptomatic management of bothersome symptoms, and prevention of disease progression can be used, depending on the bothersome symptoms and size of prostate.

Therapies in the management of EP (Figure 2) include:

- (a) watchful waiting: a management strategy in which the patient is monitored by his physician but receives no active intervention;
- (b) symptomatic treatment: α -blocker or 5 α RI;
- (c) modification of disease progression: 5 α RI;
- (d) combination therapy with a 5 α RI to modify disease progression and an α -blocker for improved symptom control.

The British guidelines for the primary care management of male LUTS are based on patient presentation.³⁶ A similar format is used in this examination of treatment recommendations.

Figure 3 represents a practical algorithm for the treatment of EP in primary care.

1. Men with smaller prostates (estimated < 30 mL) and no bothersome symptoms

As with the recommendations outlined in the British primary care guidelines for management of LUTS,³⁶ the preferred management strategy for these patients is watchful waiting, advice on lifestyle, and a review of current medication along with reassurance. According to the AUA 2003 guidelines, watchful waiting is the preferred management strategy for patients with mild (AUA-SI ≤ 7), moderate, or severe symptoms (AUA-SI ≥ 8) who are not bothered by their symptoms.⁴

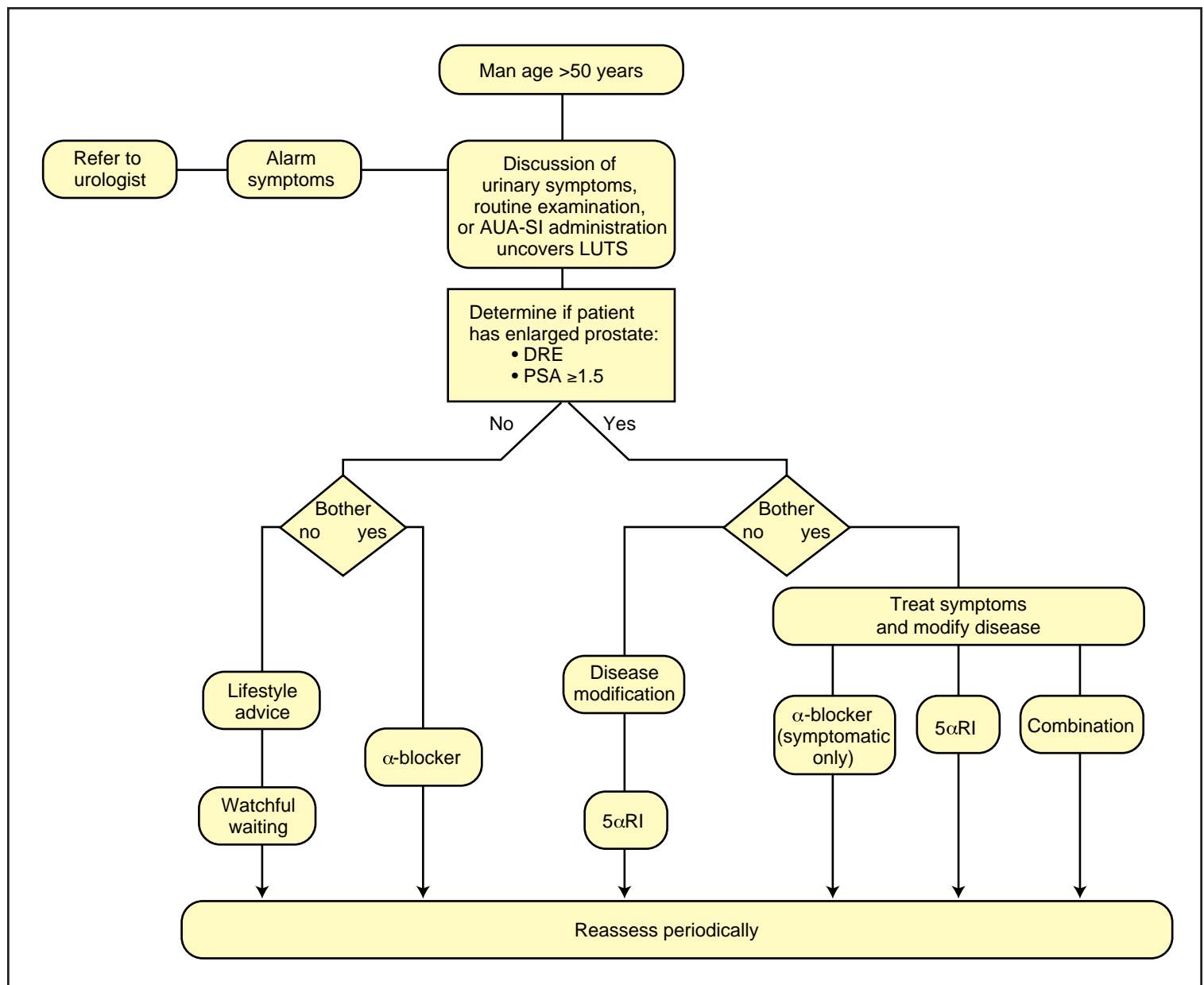


Figure 3: Practical algorithm for the treatment of EP in primary care.

2. Men with smaller prostates (estimated <30 mL) and bothersome symptoms

Men with smaller prostates and bothersome symptoms may benefit from treatment with α -blockers. The British guidelines also recommend this strategy.³⁶ α -Blockers relax the smooth muscle of the prostate gland and bladder neck to relieve bladder outlet obstruction and improve urinary flow. When administered at their recommended therapeutic dose, α -blockers have reduced symptom scores by 30% to 45% and improved urinary flow rates by 15% to 30%.⁴⁵ The main difference among α -blockers relates to their tolerability profiles. The primary adverse events reported with α -blockers are orthostatic hypotension, dizziness, tiredness, ejaculatory problems, and nasal congestion.⁴ Patients are more likely to discontinue α -blocker therapy because of vasodila-

tory adverse events such as dizziness.⁴⁵ Dizziness leading to falls and fractures are of particular concern in the elderly or in those with cardiovascular comorbidity/comedication.⁴⁵ Among the once-daily preparations (alfuzosin extended-release formulation, tamsulosin, doxazosin extended-release, and terazosin), tamsulosin tends to have a lower probability of vasodilatory adverse events.^{4,45}

3. Men with enlarged prostates (≥ 30 mL) and no bothersome symptoms

Some men with enlarged prostates will present with symptoms that may not be bothersome. Traditionally, such patients are managed using a strategy of watchful waiting.⁴ Based on evidence from the landmark MTOPS, the recent AUA guidelines recommend use of 5 α RI to prevent progression of disease as an optional therapy in patients

with symptomatic EP but without signs of bother.⁴ A patient should be presented with a reasonable estimate of his baseline risk of progression along with the benefits and risks of medical therapy and the need for long-term treatment so that an informed decision can be made.⁴

4. Men with enlarged prostates (≥ 30 mL) and bothersome symptoms

A 5 α RI should be used to modify disease progression by shrinking the prostate, reducing urinary symptoms, and reducing the risk of AUR and prostate-related surgery. This class of medications works by inhibiting the production of dihydrotestosterone (DHT), which mediates cell death. Two 5 α RI are available; finasteride was the first and works by blocking type II 5 α -reductase to result in a 70% DHT reduction. Dutasteride is the

newer 5 α RI and it blocks both type I and II for a 93% DHT reduction.

In the long term, a patient who presents with EP and bothersome symptoms can be managed by 5 α RI alone, particularly if he perceives the bother as tolerable, and it has a high risk of clinical progression. Although 5 α RI are effective in relieving symptoms, α -blockers have a rapid onset of action.⁴¹ Thus, for a patient whose symptoms are particularly bothersome and who is unable to wait for the delayed symptomatic benefit of a 5 α RI, an α -blocker can be added to therapy. The use of combination therapy (5 α RI + α -blocker) is most appropriate in men with bothersome symptoms and a high risk of progression (enlarged prostates, age >70 years, and a high symptom score).^{4,36} Monotherapy with α -blockers should be chosen as treatment only in patients with no additional risk factors of clinical progression. In the MTOPS study, the overall risk of progression, mostly due to symptomatic progression, was reduced by 45% for the doxazosin group, 30% for the finasteride group, and 64% for the combination therapy group.¹² The AUA 2003 panel assumed that the combination of any effective α -blocker and 5 α RI produces a comparable benefit.⁴ Preliminary studies examining the effects of discontinuation of an α -blocker after initial combination therapy with a 5 α RI, reported that patients are likely to tolerate discontinuation following 6 to 9 months of combination therapy.^{46,47} Although the findings of these studies suggest a possibility of withdrawing the α -blocker after 6 to 9 months of combination therapy, further studies are needed to make any recommendation.

Monitoring Patients

Patients undergoing treatment for EP should be assessed periodically for disease progression. The AUA 2003 guidelines do not provide any clear-cut recommendations for follow-up.⁴ Likewise, the recent British guidelines for primary care management of male LUTS do not have any recommendations on follow-up.³⁶ The only guidelines recommending follow-up are the European guidelines on BPH.⁴⁸ Follow-up schedules as outlined in the European guidelines depend on the type of management: (a) watchful waiting: patients on watchful waiting should be followed up at 6 months and each year thereafter provided there is no deterioration of symptoms⁴⁸; (b) α -blocker therapy: after 6 weeks of therapy following initiation, patients should be reviewed to determine re-

sponse. Treatment may be continued if the patients gain symptomatic relief without any troublesome side effects. Patients should be followed up at 6 months and each year thereafter provided there is no deterioration of symptoms⁴⁸; (c) 5 α RI: patients should be reviewed after 12 weeks and at 6 months to determine their response. Thereafter, these patients should be followed up annually provided there is no deterioration of symptoms.⁴⁸

With the first sign of deterioration of symptoms with either watchful waiting or medical management, the patient should be referred to a urologist. In addition, any time the clinician is uncertain about the progress of a patient, it is appropriate to consider urologic referral.⁶

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