Complete Summary

GUIDELINE TITLE

The management of benign prostatic hyperplasia

BIBLIOGRAPHIC SOURCE(S)

American Urological Association, Inc. The management of benign prostatic hyperplasia. Baltimore (MD): American Urological Association, Inc.; 2003. Various p. [135 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On November 22, 2005, Boehringer Ingelheim and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revisions to PRECAUTIONS and ADVERSE REACTIONS sections of the prescribing information for Flomax, indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). A surgical condition termed Intraoperative Floppy Iris Syndrome (IFIS) has been observed during phacoemulsification cataract surgery in some patients treated with alpha-1 blockers including Flomax. Most of these reports were in patients taking the alpha-1 blocker when IFIS occurred, but in some cases alpha-1 blocker had been stopped prior to surgery. It is recommended that male patients being considered for cataract surgery, as part of their medical history, be specifically questioned to ascertain whether they have taken Flomax or other alpha-1 blockers. If so, the patient's ophthalmologist should be prepared for possible modifications to their surgical technique that may be warranted should IFIS be observed during the procedure. See the FDA Web site for more information.

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SCOPE

DISEASE/CONDITION(S)

Benign prostatic hyperplasia

GUIDELINE CATEGORY

Diagnosis
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To update the 1994 Agency for Healthcare Policy and Research (AHCPR; now known as the Agency for Healthcare Research and Quality, AHRQ) guideline on benign prostatic hyperplasia
- To provide scientifically based information on treatment outcomes so that physicians can assist their patients in making appropriate treatment decisions

TARGET POPULATION

- Male patients over 50 years of age who present with bothersome lower urinary tract symptoms suggestive of benign prostatic hyperplasia (BPH)
- Male patients over 50 years of age with confirmed symptomatic benign prostatic hyperplasia

INTERVENTIONS AND PRACTICES CONSIDERED

Initial Evaluation/Diagnostic Assessment

1. Medical history

2. Physical examination, including digital rectal exam and focused neurologic examination
3. Urinalysis (urine cytology for high-risk men)
4. Measurement of the serum prostate-specific antigen (PSA)
5. Symptom assessment using a symptom-scoring instrument (e.g., American Urological Association/International Prostate Symptom Score Symptom Index)
6. Urinary flow-rate recording--optional
7. Postvoid residual urine (PVR)--optional

Initial Management and Discussion of Treatment Options

1. Information on the benefits and harms of the BPH treatment options explained to patients considering therapy
2. Watchful waiting for patients with mild, moderate or severe symptoms who are not bothered by their symptoms
3. Optional diagnostic tests (pressure-flow urodynamic studies, urethrocystoscopy and ultrasound [transrectal or transabdominal]) in patients choosing invasive therapies

Treatment

Medical Therapies

1. Alpha-adrenergic blockers
    - Alfuzosin
    - Doxazosin
    - Tamsulosin
    - Terazosin
2. 5 Alpha-reductase inhibitors
    - Dutasteride
    - Finasteride
3. Combination therapy (alpha blocker and 5 alpha-reductase inhibitor)

Minimally Invasive Therapies

1. Transurethral microwave heat treatments
    - CoreTherm™
    - Prostatron® (various versions)
    - Targis®
    - TherMatrx™
2. Transurethral needle ablation
3. UroLume® stent (use only for high risk patients)

Surgical Therapies

1. Transurethral resection of the prostate (TURP)
2. Transurethral electrovaporization
3. Transurethral incision of the prostate
4. Transurethral holmium laser resection/enucleation
5. Transurethral laser vaporization

6. Transurethral laser coagulation (e.g., visual laser ablation)
7. Open prostatectomy

Diagnostic Tests and Therapies Not Recommended

1. Serum creatinine (not recommended routinely)
2. Filling cystometrography (CMG) and imaging of the upper urinary tract by ultrasonography or excretory urography in the absence of hematuria, urinary tract infection, renal insufficiency, or a history of urolithiasis or urinary tract surgery.
3. Balloon dilation
4. Phytotherapeutic agents and other dietary supplements
5. High-intensity focused ultrasound and absolute ethanol injection outside of clinical trials

Therapies that Require Additional Studies before Recommendation as a Treatment Option

1. Interstitial laser coagulation
2. Water-induced thermotherapy
3. PlasmaKinetic™ Tissue Management System

MAJOR OUTCOMES CONSIDERED

Diagnosis

Sensitivity, specificity, and utility of various diagnostic tests

Treatment Outcome

- Symptom severity and frequency (direct measures), using scoring systems, such as the American Urological Association Symptom Index/International Prostate Symptom Score
- Patient quality of life using custom measures
- Measures of physiologic function (indirect outcome measures), such as peak urinary flow rate, average urinary flow rate and postvoid residual urine levels
- Adverse events, such as side effects of drugs and complications associated with minimally invasive and invasive therapies

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original 1994 Guideline

The original Benign Prostatic Hyperplasia (BPH) Guideline Panel (appointed by the Agency for Health Care Policy and Research, now known as the Agency for Healthcare Research and Quality) conducted a literature search in 1994, and extracted data from relevant studies published as early as 1937 through the year 1991 that evaluated the diagnosis and treatment of BPH. From these data, the sensitivity, specificity and utility of various diagnostic tests were explicitly described and used to define diagnostic recommendations and options. In addition, the net value of all treatment modalities was determined using the treatment preferences of individual patients with varying symptoms of BPH as a key factor in the analysis.

2003 Update

The American Urological Association (AUA) Benign Prostatic Hyperplasia Guideline Update Panel, which included many of the original panel members, followed the same basic methodology in developing this updated guideline. For this update, a number of previously extracted randomized, controlled trials (RCTs) that met the Panel´s extraction criteria were carried forward, reextracted, and included in the meta-analysis. The literature published on diagnosis was not revisited. (The rationale for this decision is detailed in Chapter 1 of the original guideline.) Patient preferences were not reassessed because there was no reason to believe that important changes had occurred.

The Panel defined the topics to be addressed, such as the disease entity, which included the syndrome of lower urinary tract symptoms (LUTS), with or without enlargement of the prostate, and the Index Patient, a male greater than 50 years old with classic LUTS but with no other severe or confounding medical morbidities or other known causes of voiding dysfunction.

A comprehensive data extraction form was devised to capture as much pertinent information as possible about each study (see Appendix 2-D-a of the original guideline). The Panel chairpersons and staff developed suitable search terms and criteria. Reference sources included: the MEDLINE database from 1991 to early 2000 using the search terms "benign prostatic hyperplasia" and "human subjects"; Panel members; and a few selected unpublished industry-generated studies. A total of 3413 references were identified. From a review of study titles and abstracts, the Panel chairpersons identified a total of 365 references that were relevant for retrieval and data extraction. Study results were requested from study authors when additional data were needed to permit meta-analysis or when the Panel members knew that the authors had important data about additional outcomes or follow-up times not previously published. Subsequent to the Panel´s initial review of the data, in order to ensure that the guideline was current, additional literature searches identified new technologies and key studies for Panel scrutiny.

NUMBER OF SOURCE DOCUMENTS

251 articles

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Meta-Analysis of Summarized Patient Data
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction

Data extractors recruited from the residency program at the University of Texas Southwestern Medical Center in Dallas were trained to use the extraction form and then were supervised by a Panel chairperson. While no formal quality measures were used, the extraction process included assessing study flaws. All articles were independently extracted by two extractors who then met and resolved differences. Failing a resolution, the Panel chairpersons or staff made the final decision. For unpublished data, the Panel served as extractors.

After reviewing the completed extraction forms, the Panel rejected 114 articles that contained no relevant data, duplicated data, lacked outcomes data, did not provide information that fit the extraction form or were superceded by a later article from the same investigators (see Appendix 2-D-c of the original guideline). The remaining 251 articles were used as the source of data to update the clinical practice guideline (Appendices 2-D-d and 2-D-e of the original guideline). The studies that were actually used in the meta-analysis are listed by treatment modality in the comprehensive version of the outcomes tables (see Chapter 3 of the guideline). All data were entered into a Microsoft Access® (1997 to 2000) database (Microsoft Corporation, Redmond, Washington).

Figure 2-D-i of the guideline categorizes by year of publication the number of articles reviewed and the number accepted for data extraction. Figure 2-D-ii classifies the articles by source. Approximately 77% of the included articles were published in the *Journal of Urology*, the *British Journal of Urology*, *Urology*, *European Urology*, the *Scandinavian Journal of Urology and Nephrology* or the *Journal of Endourology*.

Evidence Combination

The data resulting from the article-selection and data-extraction process were combined to generate the comparative estimates for alternative interventions displayed in the outcomes tables (see Chapter 3 of the original guideline). A variety of methods can be used to combine outcomes evidence from the literature. The choice of methods is based on the nature and quality of the evidence. In this case, the published evidence from the data-extraction process

was a mixture of results from randomized controlled trials (RCTs) and results from uncontrolled studies. Because data were generated from different study designs, they could not be combined directly. In addition, the RCTs employed different outcome measures and did not compare treatments to a standard control.

The original guideline panel treated all studies as single-arm clinical series. When published RCTs were treated as a clinical series, each arm of the study was considered as an independent study. The present analysis found a greater number of RCTs on literature review, making it possible to analyze them as such. Not all outcomes comparisons were possible using RCT data, however. In some cases, only clinical series data were available, or RCT data were reported in an unusable form. Furthermore, RCTs included different control groups. Creating outcomes tables that present comparable outcomes required development of an appropriate means of comparison. This approach combined a Bayesian meta-analysis of RCTs (pairwise analysis of differences between treatment and control) as such, along with Bayesian meta-analysis of the clinical series and the separate arms of RCTs (single-arm analysis). Where formal meta-analysis was not possible due to lack of data on the variances of study outcomes, single-arm weighted averages (SAWA) of all relevant study arms were used. The basic features of this analytical approach are summarized in Chapter 2 and are detailed in Appendix 2-C of the original guideline.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Balance Sheets
Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The American Urological Association (AUA) Benign Prostatic Hyperplasia Guideline Update Panel, which included many of the original panel members, followed the same basic methodology in developing this updated guideline, including:

- A structured evidence review leading to assessments of the benefits and harms of alternative therapies
- Consideration of patient preferences
- Use of multidisciplinary expert panel and consultants to resolve discrepancies and to create clinically relevant practice policy recommendations to assist patients and physicians in a shared decision-making process.

Generally, recommendations were based strictly on evidence as synthesized in the outcomes tables and tempered by the panel's expert opinion. When evidence was not available, the panel's expert opinion was used exclusively. In the development of the present guideline, the Panel also directly reviewed evidence to support recommendations for the few interventions whose outcomes data became available after the meta-analysis was completed.

Panel members graded their recommendations according to three levels of flexibility as determined by strength of evidence and the expected amount of variation in patient preferences (see "Rating Scheme for Strength of the Recommendations.)

Of note, United States Food and Drug Administration (FDA) approval alone was not sufficient to justify a positive recommendation in this guideline. First, FDA approval may be requested by a manufacturer for a non-benign prostatic hyperplasia (BPH) indication because a specific benign prostatic hyperplasia indication may be more complicated and expensive to attain. Second, FDA approval may precede the publication of key pivotal studies precluding Panel analysis. Third, FDA approval once given does not imply that the intervention is still currently recommended or even available (e.g., balloon dilation). Finally, the FDA may have approved a treatment that the Panel believes is not appropriate given the other available treatment options.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Diagnostic Tests

Panel utilized the terms "**recommended**," "**optional**" and "**not recommended**" to indicate desirability of specific diagnostic interventions. A test was categorized as **optional** for the following reasons: 1) if there was clear evidence of its benefit for certain patients but the data were insufficient to demonstrate the test's value in confirming the diagnosis of BPH and in predicting the results of treatment for routine patients; or 2) if the definitions of normal and abnormal test values were uncertain. The evidence is thus insufficient to mandate use of the test prior to a decision to treat. If a test was **not recommended**, the Panel believed either that there was insufficient evidence to indicate clinical value or that in routine cases the test was associated with potential harms that exceeded its potential benefits.

Treatment Policies

With regard to treatment policies, the three levels of flexibility are defined as follows:

1. **Standard**: A policy is considered a standard if the health and economic outcomes of the alternate interventions are sufficiently well known to permit meaningful decisions and if there is virtual unanimity about which intervention is preferred.
2. **Guideline**: A policy is considered a guideline if the health and economic outcomes of the interventions are sufficiently well known to permit meaningful decisions and if an appreciable but not unanimous majority agrees upon the preferred intervention.
3. **Option**: A policy is considered an option if the following criteria apply: a) the health and economic outcomes of the interventions are not sufficiently well known to permit meaningful decisions; b) preferences among the outcomes are not known; c) patients' preferences are divided among the alternative interventions; or d) patients are indifferent about the alternative interventions.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A draft document written and reviewed by the Panel underwent peer review by 58 urologists and other health care professionals. The resulting comments were assembled in a database, sorted, and distributed to the Panel members, who approved the final revisions. The final document was reviewed by the Panel and was approved by the American Urological Association (AUA) Practice Guidelines Committee and the American Urological Association Board of Directors.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the strength of the recommendations (**recommended, optional** and **not recommended; standard, guideline, option**) are defined at the end of the "Major Recommendations" field.

Diagnostic Evaluation of Benign Prostatic Hyperplasia

Initial Evaluation

Recommended: In the initial evaluation of all patients presenting with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH):

- A medical history should be taken to identify other causes of voiding dysfunction or comorbidities that may complicate treatment.
- A physical examination, including both a digital rectal examination (DRE) and a focused neurologic examination, should be performed.
- A urinalysis should be performed by dipstick testing or microscopic examination of the sediment to screen for hematuria and urinary tract infection (UTI).
- Measurement of the serum prostate-specific antigen (PSA) should be offered to the following patients: 1) those with at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management; or 2) those for whom the PSA measurement may change the management of their voiding symptoms.

Optional: Urine cytology may be considered in men with a predominance of irritative symptoms, especially with a history of smoking or other risk factors, to aid in the diagnosis of bladder carcinoma in situ and bladder cancer.

Not recommended: The routine measurement of serum creatinine levels is not indicated in the initial evaluation of men with LUTS secondary to BPH.

Symptom Assessment

Recommended: The American Urological Association (AUA) Symptom Index (identical to the seven symptom questions of the International Prostate Symptom Score [IPSS]) should be used as the symptom-scoring instrument in the initial assessment of each patient presenting with BPH.

Optional: Other validated assessment instruments addressing the frequency or severity of LUTS in men with BPH, bother due to symptoms, interference with daily activities, urinary continence, sexual functioning and health-related general or disease-specific quality of life may be administered.

Optional Diagnostic Tests

Optional: Following the initial evaluation of the patient, urinary flow-rate recording and measurement of postvoid residual urine (PVR) may be appropriate. These tests usually are not necessary prior to the institution of watchful waiting or medical therapy. However, they may be helpful in patients with a complex medical history (e.g., neurologic or other diseases known to affect bladder function or prior failure of BPH therapy) and in those desiring invasive therapy.

Initial Management and Discussion of Treatment Options With the Patient

Management of Patients With Mild Symptoms or Moderate to Severe Symptoms Without Bother

Standard: Patients with mild symptoms of BPH (AUA Symptom Score $\leq$7) and patients with moderate or severe symptoms (AUA Symptom Score $\geq$8) who are not bothered by their symptoms (i.e., they do not interfere with the daily activities of living) should be managed using a strategy of watchful waiting.

Management of Patients With Bothersome Moderate to Severe Symptoms

Option: Treatment options for patients with bothersome moderate to severe symptoms of BPH (AUA Symptom Score $\geq$8) include watchful waiting and the medical, minimally invasive, or surgical therapies defined in Table 1.1. of the guideline document.

Guideline: Information on the benefits and harms of the BPH treatment options (including watchful waiting) should be explained to patients with moderate to severe symptoms (AUA Symptom Score $\geq$8) who are bothered enough to consider therapy.

Optional Diagnostic Tests for Patients Who Choose Invasive Therapy

Optional: Additional diagnostic tests, such as pressure-flow urodynamic studies, urethrocystoscopy and ultrasound (transrectal or transabdominal), are optional in patients choosing invasive therapies, particularly when the outcome of the pressure-flow study may impact choice of intervention or if prostate size and anatomical configuration are important considerations for a given treatment modality. They are not recommended in the initial evaluation of LUTS or in a setting other than those described above.

Not Recommended: Filling cystometrography (CMG) and imaging of the upper urinary tract by ultrasonography or excretory urography are not recommended in the evaluation of the typical patient with symptoms of BPH unless the patient has hematuria, UTI, renal insufficiency, or a history of urolithiasis or urinary tract surgery.

Treatment Recommendations

Recommended Therapies

Watchful Waiting

Watchful waiting is the preferred management strategy for patients with mild symptoms. It is also an appropriate option for men with moderate to severe symptoms who have not yet developed complications of BPH (e.g., renal insufficiency, urinary retention or recurrent infection).

Watchful waiting is a management strategy in which the patient is monitored by his physician but receives no active intervention for BPH. The level of symptom distress that individual patients are able to tolerate is highly variable so that watchful waiting may be a patient's treatment of choice even if he has a high AUA Symptom Index or IPSS score. Watchful-waiting patients usually are reexamined yearly, repeating the initial evaluation.

As prostate volume assessed by DRE and/or serum PSA predicts the natural history of symptoms, flow rate, and risk for acute urinary retention and surgery, patients may be advised as to their individual risk depending on the outcomes of these assessments. Measures to reduce the risk, such as medical intervention, may be offered depending on the circumstances.

Medical Treatment

<u>Alpha-adrenergic blocker therapy</u>

Option: Alfuzosin, doxazosin, tamsulosin and terazosin are appropriate treatment options for patients with LUTS secondary to BPH. Although there are slight differences in the adverse-event profiles of these agents, the Panel believes that all four agents have equal clinical effectiveness.

Guideline: Data are insufficient to support a recommendation for the use of prazosin or the nonselective alpha blocker phenoxybenzamine as treatment options for LUTS secondary to BPH. (The recommendation concerning phenoxybenzamine is based on Panel expert opinion.)

<u>Alpha-reductase inhibitor therapy</u>

Option: The 5 alpha-reductase inhibitors finasteride and dutasteride are appropriate and effective treatments for patients with LUTS associated with demonstrable prostatic enlargement.

Option: Patients with symptomatic prostatic enlargement but without signs of bother may be offered a 5 alpha-reductase inhibitor to prevent progression of the disease. However, the disadvantages of this therapeutic approach (e.g., side effects such as sexual dysfunction) and the need for long-term daily therapy should be presented to the patient in comparison to a reasonable estimate of his baseline risk of progression (i.e., retention and the risks associated with BPH-related surgery) so that an informed decision can be made.

Guideline: 5 Alpha-reductase inhibitors are not appropriate treatments for men with LUTS who do not have evidence of prostatic enlargement.

Combination therapy

Option: The combination of an alpha-adrenergic receptor blocker and a 5 alpha-reductase inhibitor (combination therapy) is an appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement. (This recommendation is based on Panel consensus.)

Minimally invasive therapies

Transurethral microwave heat treatment

Option: The following transurethral microwave heat treatments are effective in partially relieving symptoms in men with BPH: Prostatron®, Targis®, CoreTherm™, and TherMatrx™. There is no evidence from direct comparator trials to suggest superiority of one specific device over another.

Standard: Because unexpected procedure-related injuries have been associated with the use of transurethral microwave heat treatment devices, the safety recommendations published by the United States Food and Drug Administration (FDA) should be followed when using microwave heat treatment devices. (The following bolded text was taken directly from the FDA notice.)

- **When considering a patient for microwave thermotherapy for BPH, ensure that he meets the device's indications, including the criteria for eligible prostate size indicated for the specific system being used. Additionally, it is important to verify that the patient has not had prior radiation therapy to the pelvic area, as these patients are at increased risk of rectal fistula formation. Furthermore, the labeling of each device lists specific patient populations for which safety and effectiveness of this therapy are unknown (e.g., those with prostate cancer).**
- **When discussing the procedure with the patient, it is important to ensure that he understands the risks and benefits listed in the labeling of the specific device. He also should understand the duration of the procedure, the level of pain or discomfort that should be considered normal, the importance of telling the physician of any unusual pain during treatment, how to operate any emergency stop button, and the need to remain as still as possible during treatment.**
- **Carefully follow the instructions for use provided with these microwave systems. Note that they require the physician to continually supervise the procedure throughout the entire treatment**

period. The physician must (1) verify that the retention balloons of the urethral catheter and rectal temperature sensor probe are free of leaks and (2) confirm the placement of the urethral catheter and rectal temperature sensor using acceptable methods (e.g., direct visualization, ultrasound imaging) both prior to treatment and at other specified times consistent with the manufacturer's recommendations. Either patient movement or component breakage may cause migration of a properly placed urethral catheter or rectal temperature sensor.

- **Be careful not to oversedate the patient. As patient perception of pain is an important safety mechanism to ensure that the heating of the tissue is not excessive. General or spinal anesthesia should not be used.**
- **Closely monitor the patient and the equipment throughout the entire treatment, and manually pause treatment if the patient complains of excessive pain or anything unusual occurs.**

While the Panel agrees in principle with the safety recommendations published by the FDA, it recognizes that these procedures can be safely performed under general or spinal anesthesia provided that all other safety measures are taken such as verifying position of the treatment catheter and retention balloon.

Transurethral needle ablation

Option: Transurethral needle ablation (TUNA) is effective treatment in partially relieving symptoms of BPH.

Stents

Guideline: Because prostatic stents are associated with significant complications, such as encrustation, infection and chronic pain, their placement should be considered only in high-risk patients, especially those with urinary retention.

Surgery

Guideline: The patient may appropriately select surgical treatment as his initial treatment if he has bothersome symptoms. Patients who have developed complications of BPH are best treated surgically.

Option: The choices of surgical approach (open or endoscopic and energy source--electrocautery versus laser) are technical decisions based on the patient's prostate size, the individual surgeon's judgment, and the patient's comorbidities.

<u>Emerging therapies</u>

Guideline: Phytotherapeutic agents and other dietary supplements cannot be recommended for treatment of BPH at this time. (This recommendation is based on both evidence and Panel expert opinion.)

Guideline: The Panel believes that additional data are required before the following therapies can be considered as recommended treatment options:

interstitial laser coagulation, water-induced thermotherapy, and the PlasmaKinetic™ Tissue Management System. All of these interventions are categorized as emerging therapies even though several are FDA approved either for BPH or soft tissue ablation. It is not inappropriate for these options to be offered to the patient, but the uncertainty of outcomes compared to the recommended treatment options should be discussed with the patient.

Guideline: High-intensity focused ultrasound and absolute ethanol injection are investigational at this time and should not be offered outside the framework of clinical trials.

Balloon dilatation

Guideline: Balloon dilation is not recommended as a treatment option for patients with symptoms of BPH.

Therapies for patients with uncommon or serious complications of BPH

Guideline: Surgery is recommended for patients with refractory retention who have failed at least one attempt at catheter removal. In patients who are not surgical candidates, treatment with intermittent catheterization, an indwelling catheter or stent is recommended.

Option: Concomitant administration of an alpha blocker is an option prior to attempted catheter removal in patients with urinary retention. (This recommendation is based on Panel expert opinion.)

Guideline: Surgery is recommended for patients who have renal insufficiency clearly due to BPH and in those patients with recurrent UTIs, recurrent gross hematuria, or bladder stones clearly due to BPH and refractory to other therapies. The presence of a bladder diverticulum is not an absolute indication for surgery unless it is associated with recurrent UTI or progressive bladder dysfunction. (This recommendation is based on Panel expert opinion.)

Definitions:

Diagnostic Tests

Panel utilized the terms "**recommended**," "**optional**" and "**not recommended**" to indicate desirability of specific diagnostic interventions. A test was categorized as **optional** for the following reasons: 1) if there was clear evidence of its benefit for certain patients but the data were insufficient to demonstrate the test's value in confirming the diagnosis of BPH and in predicting the results of treatment for routine patients; or 2) if the definitions of normal and abnormal test values were uncertain. The evidence is thus insufficient to mandate use of the test prior to a decision to treat. If a test was **not recommended**, the Panel believed either that there was insufficient evidence to indicate clinical value or that in routine cases the test was associated with potential harms that exceeded its potential benefits.

Treatment Policies

With regard to treatment policies, the three levels of flexibility are defined as:

1. **Standard:** A policy is considered a standard if the health and economic outcomes of the alternate interventions are sufficiently well known to permit meaningful decisions and if there is virtual unanimity about which intervention is preferred.
2. **Guideline:** A policy is considered a guideline if the health and economic outcomes of the interventions are sufficiently well known to permit meaningful decisions and if an appreciable but not unanimous majority agrees upon the preferred intervention.
3. **Option:** A policy is considered an option if the following criteria apply: a) the health and economic outcomes of the interventions are not sufficiently well known to permit meaningful decisions; b) preferences among the outcomes are not known; c) patients' preferences are divided among the alternative interventions; or d) patients are indifferent about the alternative interventions.

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for diagnosis and treatment of benign prostatic hyperplasia (BPH).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on data extracted from 137 controlled trials, 90 case series/reports, 11 cohort studies, 1 database/surveillance, 3 meta-analyses, and 9 other references.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

American Urological Association (AUA) Symptom Index

Alpha-blockers

Alpha-blockers produce a significant symptom improvement that the average patient will appreciate as a moderate improvement. The minor differences in efficacy noted are not statistically or clinically significant.

5 Alpha reductase inhibitors

Finasteride produces a statistically significant improvement in symptom score that the average patient will appreciate as a mild improvement. The symptom improvement is durable for up to 6 years in patients who are maintained on therapy. Finasteride is less effective than alpha-blocker therapy in alleviating lower urinary tract symptoms (LUTS). Although the net benefit of finasteride (placebo versus active treatment) is superior for men with larger prostates (and

higher prostate specific antigen [PSA] levels), the absolute level of symptom improvement is not significantly different. Preliminary analysis suggests that dutasteride has similar efficacy and safety.

Combination Therapy

While in previous studies of 1-year duration or less, combination therapy proved equal to alpha-blocker therapy but superior to 5 alpha-reductase therapy. The Medical Therapy of Prostatic Symptoms (MTOPS) study demonstrated that in the long term, combination therapy is superior to either alpha-blocker or 5 alpha-reductase therapy in preventing progression and improving symptoms.

Minimally Invasive Therapies

All forms of minimally invasive therapies produce significant symptom score improvement. In general, minimally invasive therapies produce greater symptom score improvements than medical therapies but lesser symptom score improvements than surgical therapies. Transurethral microwave thermotherapies and transurethral needle aspiration (TUNA) appear to be effective in the range of 12 to 24 months, but longer term effectiveness and retreatment rates have not been clearly defined.

Surgery

All surgical therapies produce major improvements in the AUA Symptom Index score, with holmium laser resection/enucleation and laser coagulation producing improvements of the greatest magnitude at 1 year.

Peak Urinary Flow Rate

Medical Therapies

Alpha blockers, 5 alpha-reductase inhibitors, and combination therapy produce improvements in peak urinary flow rate that are sustained over time. In the available studies, doxazosin appears to be more effective than tamsulosin and alfuzosin. Combination therapy of finasteride with doxazosin or terazosin appears to be slightly more effective than monotherapy. The results of MTOPS corroborate this finding, at least in the case of finasteride and doxazosin combination.

Minimally Invasive Therapies

Transurethral microwave thermotherapies and TUNA improve the peak urinary flow rate from baseline compared to a sham intervention. These minimally invasive approaches are more effective than medical therapy but generally less effective than surgery.

Surgery

Outcomes of randomized controlled trials, where available, yielded no statistically significant differences among surgical therapies. All surgical therapies provided similar outcomes over time with regard to peak flow.

Benign Prostatic Hyperplasia (BPH) Impact Index

Medical Therapies

Few studies report the effect of medical therapy on the BPH Impact Index. The single-armed weighted averages (SAWA) of placebo arms demonstrated a decrease of approximately 1 point in the BPH Impact Index overall score, which ranges from 0 to 13. Doxazosin, terazosin, finasteride and combination therapy studies report roughly equivalent benefits in the BPH Impact Index, although the trend was for finasteride to be slightly less beneficial than alpha blockers. The effect of dutasteride appears to be similar to that seen with finasteride.

Minimally Invasive Therapies

The BPH Impact Index was not used in any controlled trials of minimally invasive therapies. It was included in a few case series only. The only data available show roughly a 5-point drop for TUNA that extends to the 12- to 16-month time frame.

Disease Specific Quality of Life (QoL)

Medical Therapies

Medical therapy improves quality of life, with alpha blockers being significantly more effective than 5 alpha-reductase inhibitors. There is no advantage to combination therapy in improving QoL Question score. It is important to note, however, that the QoL Question score does not capture all quality-of-life issues related to BPH (e.g., urinary retention and need for surgery).

Minimally Invasive Therapies

Transurethral microwave thermotherapies and TUNA produce improvements in QoL Question scores that are superior to sham treatment. Quality of Life Question score data were not available for stents in any study.

Surgery

Although data are limited, the QoL Question score improved by at least 3 points postsurgery, regardless of the procedure type. These improvements also were shown in the mid- and long-term time periods where data were available.

POTENTIAL HARMS

Detailed listings of adverse effects reported in the literature are offered in Chapter 3 of the original guideline. The following is a summary of some of the common adverse effects and complications associated with treatment of benign prostatic hyperplasia:

- The primary adverse events reported with alpha-blocker therapy are orthostatic hypotension, dizziness, tiredness (asthenia), ejaculatory problems, and nasal congestion.

- Reported adverse events involving 5 alpha-reductase inhibitors are primarily sexually related and include decreased libido, ejaculatory dysfunction, and erectile dysfunction; these are reversible and uncommon after the first year.
- Unexpected procedure-related injuries have been associated with the use of transurethral microwave heat treatment devices, so that the safety recommendations published by the United States Food and Drug Administration should be followed when using microwave heat treatment devices.
- Prostatic stents are associated with significant complications, such as encrustation, infection and chronic pain.
- Common risks of transurethral needle ablation include urinary symptoms that can persist for weeks and temporary urinary retention.
- Complications from transurethral resection of the prostate (TURP) include dilutional hyponatremia that occurs when irrigant solution is absorbed into the bloodstream. Other complications that have been reported in more than 5% of patients include, in order of frequency: sexual dysfunction (which may not be attributable to the surgery in all cases), irritative voiding symptoms, bladder neck contracture, the need for blood transfusion, urinary tract infections, and hematuria.

QUALIFYING STATEMENTS

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- These diagnostic and treatment guidelines pertain only to men over the age of 50 without significant risk (as ascertained by history) of non-BPH causes of lower urinary tract symptoms (LUTS). Men with polyuria, underlying neurologic disease, or prior lower urinary tract disease and younger men with voiding dysfunction will require more extensive evaluation. These important causes of voiding function are not specifically addressed in this guideline.
- The algorithm for diagnosis and treatment is provided as a framework and not as a rigid pathway that must be followed in all cases. Individual patients will present for whom deviations from these policies are appropriate. In such circumstances, the clinician should exercise clinical judgment and act in the patient's best interest.
- Refer to the original guideline document for a discussion of limitations of the methodology used in data analysis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Urological Association, Inc. The management of benign prostatic hyperplasia. Baltimore (MD): American Urological Association, Inc.; 2003. Various p. [135 references]

ADAPTATION

Not applicable: Guideline was not adapted from another source.

DATE RELEASED

2003

GUIDELINE DEVELOPER(S)

American Urological Association Education and Research, Inc. - Medical Specialty Society

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GUIDELINE COMMITTEE

Benign Prostatic Hyperplasia Guideline Panel 2003

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Urological Association (AUA) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Benign Prostatic Hyperplasia (BPH): A Patient's Guide (2003). Baltimore (MD): American Urological Association; 2003. 9 p.

Electronic copies: Available in Portable Document Format (PDF) from the American Urological Association (AUA) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on June 24, 2003. The information was verified by the guideline developer on August 25, 2003. This summary was updated by ECRI on November 30, 2005 following the U.S. Food and Drug Administration (FDA) advisory on Flomax.

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