The American Urological Association 2003 guideline on management of benign prostatic hyperplasia: a Canadian opinion

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The 2003 American Urological Association (AUA) guideline on management of benign prostatic hyperplasia (BPH) was released at the AUA annual meeting in Chicago, April 2003 and the diagnosis and treatment recommendations were published later in 2003. It is likely that the 2003 AUA guideline on the management of BPH will have a profound effect on clinical urologic practice in the USA, but its influence on Canadian urological practice will be different because of our socialized medical system, manpower issues, availability of expensive technology and our unique Canadian perspective. The authors review the 2003 AUA guideline on the management of BPH and based on a perspective obtained from recent publications, consensus/consultant meetings, focus groups and anecdotal experience, attempt to put the recommendations into Canadian context. We conclude that the 2003 AUA guideline for the management of BPH is an important document that should be studied, evaluated and understood by Canadian urologists. Although our perspective is clearly different than our US colleagues, it is likely that the guideline will influence the management of BPH in Canada.

Key Words: benign prostatic hyperplasia, prostate, guidelines, alpha blockers, 5 alpha reductase inhibitors

Introduction

The 1994 benign prostatic hyperplasia (BPH) clinical practice guideline, produced by the Agency for Health Care Policy and Research (AHCPR) of the United States Department of Health and Human Services,[1] standardized the approach to the diagnosis and the treatment of BPH in the United States for almost the last decade. The 2003 American Urological Association (AUA) guideline on management of benign prostatic hyperplasia was released at the AUA annual meeting in Chicago, April 26 – May 1, 2003. The diagnosis and treatment recommendations were published later in August 2003.[2] No Canadian guidelines for the diagnosis and treatment of BPH were developed in Canada but following the introduction of the first US guidelines, many Canadian physicians eventually adopted or generally incorporated the recommendations from the 1994 AHCPR guidelines into their practice. There have been significant changes in not only the approach to the diagnosis of BPH but also in available treatment options for BPH over the last decade. There is little doubt that the 2003 AUA guideline on the management of BPH will affect clinical urologic practice over the next few years. There are a number of recommendations outlined in the 2003 AUA guideline that may warrant modification for Canadian urologic practice. Differences in social priorities, economics, socialized medicine, manpower issues, medicolegal considerations and Canadian practice trends warrant a Canadian perspective on the issues raised in the AUA 2003 guidelines.

The authors review the 2003 AUA guideline on the

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management of benign prostatic hyperplasia and attempt to put the recommendations into Canadian context. This perspective was derived from a recent publication on practice patterns of Canadian urologists published by the Canadian Prostate Health Council,[3] five urology consensus/consultants meetings (approximately 110 Canadian urologists in total) chaired or co-chaired by the authors, and two small focus groups monitored by at least one of the authors held during the fall of 2003. Participants were invited to BPH meetings sponsored by the pharmaceutical companies Merck Frosst Canada Inc., Glaxo-Smith-Kline, Boehringer-Ingelheim, and Sanofi-Synthelabo. At these industry-sponsored meetings, the 2003 AUA guidelines were presented and thoroughly discussed in relation to Canadian urologic practice. This paper represents the authors' best interpretation of the published data and formal and informal discussions from this selected subgroup of Canadian urologists. This interpretation will, to some degree, reflect the authors' opinions and bias.

Background

The expert panelists assembled by the AUA practice guidelines committee conducted a systematic literature review, which spanned the years from 1991 to early 2000. The panel supplemented literature review with additional references from panel members and additional data obtained from the authors. For diagnostic tests, the panel utilized the terms "recommended", "optional", and "not recommended" to indicate the desirability of specific tests. Treatment recommendations were graded according to "standard" (the least flexible of the three), a "guideline" (more flexible), and an "option" (the most flexible).[4] The explanation for these diagnostic and treatment recommendation terms is outlined in Table 1. The diagnostic and treatment guidelines are only relevant in men over the age of 50 without significant risk (as determined by history) of non-BPH causes of lower urinary tract symptoms. Other important causes of voiding dysfunction were not specifically addressed in the guideline.

Diagnostic evaluation of BPH

The expert panel decided that an evidence-based update of the 1994 AHCPR guideline was not necessary. However, the panel did make a number of significant changes, which were derived from the panel's expert opinion Table 2.

Recommended

- Medical history
- Physical examination
- Urinalysis
- Measurement of serum prostate specific antigen for select patients
- AUA Symptom Index

TABLE 1. **Diagnostic and treatment recommendation**

Diagnostic test recommendations[2]

Recommended – evidence to indicate that the test has value in most patients, and that the benefits out weigh its potential harm.
Optional – if there was clear evidence of its benefit for certain patients, but the data were insufficient to demonstrate the test value in confirming the diagnosis of BPH and predicting the results of treatment for routine patients – the definition of normal and abnormal test values was uncertain. The evidence is thus insufficient to mandate use of the test prior to his decision to treat.
Not recommended – insufficient evidence of indicate that the test did have value or had potential harms that exceeded its potential benefits in routine case.

Treatment recommendations

Standard – if the health and economic outcomes of the alternate interventions are sufficiently well known to permit meaningful decisions and if there is virtually unanimity (about which intervention is preferred).
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.
Option – the health and economic outcomes of the interventions are not sufficiently well known to permit meaningful decisions – preferences among the outcomes are not known – patients' preferences are divided among the alternative interventions and/or patients are indifferent about the alternative interventions.

TABLE 2. **Diagnostic recommendations of the 1994 AHCPR guideline were still valid except for the following five exceptions[2]**

1. Serum prostate specific antigen (PSA) measurement is recommended in selected patients.
2. Urine cytology is recommended as an option in men with predominantly irritative symptoms.
3. Other validated symptom assessment instruments are supplementary to the AUA symptom score.
4. Serum creatinine measurement is no longer recommended on initial evaluation in the standard patient.
5. Discussion of treatment options with the patient is recommended before pressure-flow testing is performed.

Canadian comment

There is a clear consensus that a medical history taken to identify other causes of voiding dysfunction or co-morbidities that may complicate treatments as well as the physical examination which includes both a digital rectal examination and focused neurologic examination should be performed. The majority of urologists have been performing urinalysis by dipstick testing (or rarely microscopic examination of the sediment) to screen for hematuria and urinary tract infection and very few did not agree to this test. Canadian urologists have appeared to be somewhat unsure of the 1994 AHCPR guideline in regard to PSA testing and for the most part, are happy with the new recommendations regarding PSA testing. Generally they are agreeable that PSA should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management as well as those for whom PSA measurement may change the management of their voiding symptoms. Although most Canadian urologists routinely evaluate, the severity and bothersomeness of symptoms, the AUA symptom index[5] has not been widely adopted in standard clinical practice. It does not appear that the new AUA guidelines will change that practice. The Canadian urologists surveyed believe that a personal history taking, addressing all the symptoms addressed in the AUA symptom score better reflects Canadian urologists' interaction with their BPH patients. A number of BPH experts attending the meetings suggested that the 2003 guidelines could represent an opportunity to promote the evidence based use of the AUA or other symptom scores (bother score) in Canadian urologic practice.

Optional

- Urine cytology
- Other validated assessment instruments
- Urinary flow rate and post void residual urine determination

Canadian comment

Many Canadian urologists already make use of urine cytology in evaluating 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. Since many Canadian urologists do not routinely employ the AUA symptom score, it is unlikely (except in clinical trials) that they will employ other validated assessment instruments addressing the frequency or severity of LUTS, bother, interference with daily activities, urinary continence, sexual functioning and health related general or disease specific quality of life indices. Canadians are generally aware of the various questionnaires addressing the above issues but will unlikely be using them in general clinical practice. There is general agreement that urinary flow rate recording and measurement of post void residual urine may be helpful in patients with a complex medical history (for example neurologic or other diseases known to affect bladder function), for those who fail medical BPH therapy and in some patients desiring invasive therapy.

For patients who choose invasive therapy

- Pressure-flow urodynamic studies
- Cystoscopy
- Ultrasound (transrectal or trans-abdominal)

Canadian comment

The Canadian urologists surveyed agree that additional diagnostic tests such as pressure flow urodynamic studies, cystoscopy and ultrasound should be optional in patients choosing invasive therapies. This is particularly important if the outcome of a pressure flow study may impact choice of intervention or if the size and anatomical configuration of the prostate gland are important considerations for any given treatment modality. There was general agreement that these tests should not be recommended in the initial evaluation of lower

urinary tract symptoms thought to be secondary to BPH. Over the years, primarily because of the influence of the AHCPR guidelines, the majority of urologists have come to believe that cystoscopy and invasive urodynamics should not be performed in the initial evaluation of LUTS secondary to BPH.

Not recommended

- Routine measurement of serum creatinine levels
- Filling cystometrography (CMG)
- Imaging of the upper urinary tract by ultrasonography or excretory urography.

Canadian comment

Although most agree that baseline renal insufficiency appears to be uncommon in men with BPH, many of those surveyed described anecdotal cases in which an elevated serum creatinine led to a finding of "silent prostatism". It was pointed out in the focus groups that as many as 2% of patients screened for participation in BPH related trials were ineligible because of renal insufficiency. It is reasonable to assume that in some of these cases, the renal insufficiency was due to obstructive uropathy. Many of the urologists surveyed indicated that they will continue to consider serum creatinine as an important option in the baseline assessment of BPH patients. CMG and imaging studies are usually not performed for the initial assessment of the typical patient with symptoms of BPH. However, it is recognized that upper tract imaging is necessary in patients who present with hematuria, urinary tract infection, renal insufficiency, or a history of urolithiasis or urinary tract surgery.

Treatment recommendations

In regard to treatment recommendations, the expert panel had two principle goals:
1. To determine whether or not there was convincing scientific evidence that the benefits (primarily symptom improvement) of a given treatment option outweighed the risks (adverse events).
2. To explicitly define the primary outcomes of the recommended treatment options to assist patients and physicians in an informed decision-making process.

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 should be managed using a strategy of watchful waiting.

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 and surgical therapies defined in Table 3.

Guideline

Information on the benefits and harms of the BPH treatment options should be explained to the patients with moderate to severe symptoms (AUA symptom score $\geq$ 8) who are bothered enough to consider therapy.

Recommended therapies

The expert panel combined various levels of evidence to make their recommendations. They employed meta-analyses of randomized controlled treatments analyzing differences between treatment and control, meta-analyses of various clinical series as well as separate arms of randomized controlled trials. Primary efficacy outcomes (AUA symptom scores, peak urinary flow rate, BPH impact index scores and quality of life scores) were analyzed as estimated changes from pre-treatment values. All side effects and adverse events (side effects, medical interventions and adverse outcomes of invasive therapies) were analyzed as estimated rates of probabilities of occurrence. In the expert panels' analyses, three standard controls were considered – placebo, sham procedure and transurethral resection of the prostate. This type of analyses allowed the various medical therapy, minimally invasive therapies and surgical therapies Table 3 to be compared in terms of efficacy and safety. The methodology and data analysis are present in part in the recently published guideline[2] while the more detailed data is available at www.auanet.org.

Watchful waiting

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 should be managed using a strategy of watchful waiting.

Canadian comment

Canadian urologists we surveyed advocated watchful waiting as a preferred management strategy for patients with mild symptoms or those men who are

TABLE 3. **Treatment options for patients with moderate to severe symptoms of benign prostatic hyperplasia[2]**

Watchful waiting
Medical therapies
Alpha-adrenergic blockers
alfuzosin
doxazosin
tamsulosin
terazosin
5-alpha reductase inhibitors
dutasteride
finasteride
Combination therapy
(alpha-blocker and 5-alpha reductase inhibitor)
Minimally invasive therapy
Transurethral microwave heat treatments
Core Therm™
Prostatrone®
Targis®
Thermatrx™
Transurethral needle ablation
UroLume®
Stent
Surgical therapies
Transurethral resection of the prostate
Transurethral electrovaporization
Transurethral incision of the prostate
Transurethral holmium laser resection – enucleation
Transurethral laser vaporization
Transurethral laser coagulation (e.g., visual laser ablation)
Open prostatectomy

not bothered by their symptoms and have not developed any complications of BPH. Primarily due to manpower issues, the watchful waiting in Canada is often a "shared care" responsibility with the family physician. In Canada, many family physicians are instructed by the urologist (usually in the consultation letters) how to follow these patients and when to refer back to the urologist.

Medical therapy

Alpha blockers

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 efficacy.

Guideline

Data are insufficient to support a recommendation for the use of prazosin or the non-selective alpha-blocker phenoxybenzamine as treatment options for LUTS secondary to BPH.

Canadian comment

Most surveyed were aware of the extensive literature regarding the safety and efficacy of the various alpha-blockers. Alpha-blockers remain the most commonly prescribed medication for LUTS secondary to BPH in Canada. The use of specific alpha-blockers (primarily the titratable alpha-blockers; doxazosin and terazosin) are mandated in many provinces because of cost consideration. The prescribing of the various alpha-blockers in Canada depends on these cost considerations, the need to titrate or not, adverse clinical effects associated with the various alpha-blockers and urologists' personal anecdotal experiences. Most of the urologists surveyed tended to titrate terazosin to 5 mg, doxazosin to 4 mg and tamsulosin to 0.4 mg (although some do titrate to 10 mg, 8 mg and 0.8 mg respectively). Canadian urologists appear to be generally aware that doxazosin monotherapy was associated with a higher incidence of congestive heart failure than seen with other anti-hypertensive agents and do not generally attempt to manage BPH patients concomitant hypertension with alpha-blockade alone. The relative role of specific versus non-specific alpha blockers in combination with other anti-hypertensives in men with co-existent BPH remains a subject of controversy. Prazosin and phenoxybenzamine are not used routinely for the treatment of LUTS secondary to BPH in Canada.

5-alpha-reductase inhibitor therapy

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.

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

Canadian comment
The 5-alpha-reductase inhibitors are not used by Canadian urologists as frequently as alpha-blockers for LUTS secondary to BPH. Recent data, widely presented at Canadian urology conferences, suggests that 5-alpha-reductase inhibitors are more effective in men with large prostates (and in those with a higher base-line PSA), that they reduce the risk of BPH progression (particularly in terms of AUR and need for BPH related surgery) and have long term efficacy and safety demonstrated in major clinical trials (PLESS and MTOPS trials[6,7]). There is increased enthusiasm for the use of finasteride recently, primarily because of this new data that allows for an evidence-based approach to the treatment of BPH patients, particularly those with large prostate glands. 5-alpha-reductase inhibitors are not appropriate treatments for men with LUTS and small prostate glands. Generally Canadians are unlikely to use a 5-alpha-reductase inhibitor in a patient with symptomatic prostatic enlargement without signs of bother. However, more urologists are becoming aware that these patients need to be followed closely. When symptoms do become bothersome, the advantages and disadvantages of long term 5-alpha-reductase inhibitor therapy and the need for long term daily therapy can be presented to the patient. 5-alpha-reductase inhibitor therapy reduces the risk of BPH progression (primarily acute urinary retention and the need for BPH related surgery) and the benefits in terms of risk progression and symptom amelioration increases with rising prostate volume or serum PSA.

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.

Canadian comment
Those surveyed have been aware for sometime that short term combination therapeutic trials with a 5-alpha-reductase inhibitor and alpha-blocker do not demonstrate increased benefits. Combination therapy was very infrequently used in Canada. However, many Canadian urologists are aware of the data from the recent MTOPS trial [7] that clearly demonstrated that combination therapy was more effective in relieving and preventing the progression of symptoms than alpha-blocker monotherapy. Furthermore the addition of a 5-alpha-reductase inhibitor to an alpha-blocker significantly reduced the long- term risk of acute urinary retention and the need for BPH related surgery. These benefits will be weighed against the very real cost of long term combination therapy, both financial, and health related. Many are aware that the men most likely to benefit from combination therapy are those in whom the baseline risk of progression is higher, namely symptomatic patients with larger prostate glands and higher PSA values.

Urologists surveyed described two goals in BPH management: alpha blockers for the goal of short term symptom amelioration and either a 5-alpha-reductase inhibitor or combination therapy for the goal of long term risk reduction particularly in those patients with the greatest risk of symptom and disease progression (large prostates and higher PSA levels). A common practice was to stratify patients according to risk of progression, but most were unwilling to determine a "strict" cut-off point for the value of 5-alpha-reductase inhibitor or combination therapy. Consensus cut-off levels for size were generally agreed to be between 30 cc and 40 cc and cut-off PSA levels ranged from 1.5 ng/ml to 3.0 ng/ml.

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 comparative trials to suggest superiority of one device over another.

Standard
Because unexpected procedure-related injuries have been associated with the use of transurethral microwave heat treatment devices, a number of safety recommendations have been published by the United States Food and Drug Administration (FDA) that should be followed when using microwave heat treatment devices.[8]

Canadian comment
Relatively few Canadian urologic centers offer

transurethral microwave thermotherapy. This is primarily a cost issue since most provincial health care plans do not reimburse this procedure at the level required to be commercially viable. Many Canadian urologists are unaware of the unexpected procedure related injuries that have occurred with the use of transurethral microwave heat treatment devices. Naturally, any Canadian urologist who is performing or planning to perform these treatments, must be fully knowledgeable about the FDA's safety recommendations.

Transurethral needle ablation

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

Canadian comment
A number of Canadian urologists have experience with TUNA, but it is considerably less popular than in the U.S. This clearly reflects reimbursement issues.

Stents

Guideline
Because prostatic stents are associated with significant complications, their placement should be considered only in high risk patients, especially those with urinary retention.

Canadian comment
Most, are aware of problems such as encrustation, infection, chronic pain and difficult removal. Stents are not a popular option in Canada for the treatment of LUTS related to BPH except for the rare high risk patient in 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 co-morbidities.

Canadian comment
Urologists taking part in these Canadian consensus conferences view TURP as the benchmark of surgical therapies for BPH. Most believe that the new surgical technologies have not demonstrated better outcomes than TURP, however certain procedures such as transurethral electrovaporization, transurethral incision of the prostate and/or open prostatectomy may be indicated in individual patients (because of bleeding propensity, size of prostate gland, etc). Laser therapy has been popularized by some Canadian centers. Initial Canadian enthusiasm for transurethral laser coagulation (visual laser ablation of prostate or VLAP) appears to have diminished, probably because of the higher incidence of prolonged postoperative urinary catheterization and post procedure irritative voiding symptoms. The few Canadian centers employing transurethral holmium laser resection/enucleation have impressed many urologists at the BPH meetings that results obtained with this technique were comparable to that of TURP with a reduced risk of bleeding and need for blood transfusion.

Emerging therapies

Guideline
Phytotherapeutic agents and other dietary supplements cannot be recommended for treatment of BPH at this time.

Guideline
Additional data are required before the following therapies can be considered as recommended treatment options: interstitial laser coagulation, water induced thermal therapy, and the plasma kinetic™ tissue management system.

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.

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

Canadian comment
Phytotherapeutic agents (plant extracts) are used extensively by Canadian patients for treatment of LUTS. As in most of the world, the most popular herbal treatment supplement appears to be serenoa repens (saw palmetto) used either as a monotherapy

or in multi-agent regimes. It is generally believed that although these agents probably do not have significant efficacy, they are generally safe. A number of Canadian centers have experience in small numbers of patients with transurethral injection of absolute ethanol, high intensity focused ultrasound and interstitial laser coagulation, however these technologies have not become popular. There is no significant Canadian experience with water induced thermal therapy or plasma energy tissue vaporization. Canadians had extensive experience with balloon dilation (when it was a popular treatment modality). However enthusiasm has died as it has in the US for this particular treatment modality, based on the perception of poor long-term results.

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 of 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.

Guideline

Surgery is recommended for patients who have renal insufficiency clearly due to BPH and in those patients with recurrent UTI's, recurrent gross hematuria, or bladder stones clearly related 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.

Canadian comment

Among Canadian urologists, surgery (usually TURP or open prostatectomy) remains the treatment of choice for a patient with refractory urinary retention. Based on early clinical evidence, many Canadian urologists are administering an alpha-blocker prior to attempted catheter removal in patients with first episode urinary retention. In Canada the standard of practice clearly conforms to the 2003 AUA guidelines regarding absolute indications for surgery.

Summary: a Canadian perspective

The 2003 AUA guideline for the management of BPH is an important document that should be studied, evaluated and understood by urologists, not only in the USA, but also Canada. It will guide the management of BPH for the next decade in the USA and will have a definite effect on the management of BPH by Canadian urologists. US urologists who treat BPH and payers who pay for BPH treatment will employ these guidelines, both to improve patient care and to guide medical-legal and financial considerations. The Canadian perspective varies in a number of respects. This first effort at examining a Canadian perspective on the 2003 AUA guideline for the management of BPH will of necessity evolve over time as urologists refine their own personal diagnostic and therapeutic algorithms. The advent of high quality evidence from large prospective trials in BPH must of necessity drive Canadian urologists to incorporate evidence based medicine into clinical practice within the Canadian context. □

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