
BPH update: medical versus interventional management

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Benign prostatic hyperplasia (BPH) is a common condition that afflicts a large proportion of aging men. The primary care physician has an important role with the identification and early treatment of bothersome urinary symptoms caused by BPH. This includes a detailed history and physical exam, as well as initiation of a number of

medications such as alpha-blockers, 5-alpha reductase inhibitors and phosphodiesterase-5 inhibitors. It is also very important for the primary care giver to determine when additional evaluation and referral to a urologist needs to occur, specifically when surgical intervention is needed. This review will summarize the management of this common disorder and is designed to aid the generalist with the pertinent information needed to provide excellent care.

Key Words: BPH, benign prostatic hyperplasia

Background

Benign prostatic hyperplasia (BPH) is a common disease in men with incidence that increases with age. It is estimated that 50% of men age 60 or older, and 80% of men aged 80 or older, suffer from some form of the disease.¹ BPH involves the growth of the prostate to a point where the flow of urine is obstructed, causing bladder outlet obstruction (BOO) and resulting in lower urinary tract symptoms (LUTS). BPH can physically obstruct the urethra in addition to causing increased smooth muscle tone, both of which result in BOO.² The combination of benign prostatic hyperplasia and resulting lower urinary tract symptoms is commonly

referred to as BPH-LUTS. Common LUTS can be subdivided into storage and voiding symptoms. Storage LUTS includes frequency, urgency and nocturia. Voiding LUTS includes weak stream, hesitancy, intermittent stream, straining and incomplete emptying. Progression of BPH can lead to a significant reduction in quality of life (QoL), and is associated with depression and anxiety amongst elderly men.³ Furthermore, if left untreated, there may be eventual development of urinary retention, recurrent urinary tract infections (UTIs), and hydronephrosis. Thus, as common as this condition is, it is in fact an important issue to recognize, monitor and treat appropriately. Moreover, as the population ages, primary care physicians will be encountering men with this problem with increasing frequency.⁴ As such, the purpose of this article is to familiarize the general practitioner with the work up and current recognized treatment options available for BPH.

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Diagnosis and work up

A detailed clinical history is the initial and most important tool that the primary care physician must utilize in order to make a diagnosis of BPH-LUTS. Along with determining the symptomology of the aforementioned LUTS, the purpose of the clinical history is to attempt to delineate the potential causes and comorbidities that may aid in diagnosis. It is crucial to note the patients' previous medical history (diabetes, metabolic syndrome), medication use, social habits (including fluid intake, caffeine and alcohol intake) and family history of BPH – as these may all be important factors that can contribute to the development and progression of the disease. In addition, a recommended tool developed by the American Urological Association (AUA) is the International Prostate Symptom Score

(IPSS), a questionnaire comprised of 8 items assessing symptoms with a total score between 0 and 35.⁵ The questionnaire denotes mild symptoms as < 8, moderate symptoms as 8-19, and severe symptoms as ≥ 20, Figure 1. QoL is independently evaluated with a score ranging from 0 to 6, with higher scores indicating a greater level of symptom bother and poorer QoL.

The spectrum of BPH and associated symptoms is quite broad, with some patients experiencing severe symptoms that interrupt sleep, inhibit activities and significantly affect QoL. Others are simply less affected by their symptoms. Understandably, the degree of bother will affect patient motivation to seek treatment, regulate acceptance of possible side effects and should play a role in proposed treatment or lack thereof.

The second crucial step in correctly diagnosing BPH is the physical exam. Digital rectal examination

In the past month?	Not at all	Less than 1 in 5 times	Less than half the time	About half the time	More than half the time	Almost always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
In the past month?	None	1 time	2 times	3 times	4 times	5 times	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total Score							

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

Figure 1. International Prostate Symptom Score (IPSS).

(DRE) is used to estimate the size of the prostate. Prostate volume (cc) is essential in the guidance of treatment as different treatment modalities may work better for varying prostate sizes. Additionally, DRE can also aid in the assessment of prostate cancer risk, as any questionable nodule or prostate asymmetry may indicate a potential malignancy. The Canadian Urological Association (CUA) recommends testing for prostate-specific antigen (PSA) when considering a diagnosis of BPH-LUTS for all men considering medical or interventional therapy who have a life expectancy beyond 10 years.⁶ It can also serve as a surrogate for prostate volume when prostate cancer is not present, with a PSA of 1.5 ng/mL being associated with a prostate volume of 30 cc or more, and can be further used to assess prostate cancer risk.⁷ The CUA also recommends urinalysis (R+M and C+S) as part of the work up, to rule out UTIs and other causes of LUTS.⁶

It is within the physicians judgment to further investigate the problem with optional tests such as serum creatinine, urine cytology, a voiding diary, and assessment of the patients post void residual with a bladder scanner.

Treatment

Treatment for BPH has evolved throughout the years and there are new and exciting modalities that may aid the primary care physician as well as the practicing urologist. The main goals of treatment are to improve patient symptoms and QoL and to prevent disease progression and potential sequelae of urinary retention.

Conservative management

Patients with mild symptoms, according to the IPSS score, should be counseled to undertake lifestyle modifications in accordance with their motivation and degree of bother. This may include a decrease in the total daily fluid intake, as well as a reduction in diuretic beverages such as coffee, alcohol and soft drinks. Additionally, the patient may be advised to exercise timed voiding, pelvic floor routines and to maintain a regular bowel regimen to avoid constipation.⁸

It is important to note that even with foregoing therapy, a subset of men will experience spontaneous improvement in symptoms over time.⁹ If choosing to undertake this form of surveillance, it is indeed important to monitor and follow these men over time in order to avoid missing a worsening of symptoms.

Pharmacotherapy

The decision to treat BPH with pharmacotherapy must evaluate the benefits of symptom relief versus the potential side effects that the medications may incur.

Alpha-blockers

Alpha-blockers are a class of drugs that work by blocking alpha-1a receptors, thereby relaxing smooth muscle both within the bladder neck and the prostate itself. This causes an opening of the previously tightened urinary channel and reduces the impediment to urinary flow.¹⁰ Studies have shown that alpha-blockers reduce bother symptoms by 30%-40%, but this class of medications work most optimally in patients with smaller prostates (< 30 mL).¹¹ There are five main alpha-blockers: two second-generation drugs— terazosin (Hytrin) and doxazosin (Cardura)—and three third-generation drugs—tamsulosin (Flomax), alfuzosin (Xatral), and silodosin (Rapaflo). Both terazosin and doxazosin require dose titration because of their anti-hypertensive properties. Tamsulosin, alfuzosin, and silodosin usually do not require dose titration and generally are associated with fewer side effects.

Alpha-blockers begin to work within a matter of hours to days, however, they reach their maximal level of efficacy within a few weeks.¹² While alpha-blockers are considered to be relatively safe, there are side effects that patients and caregivers should be aware of. Light-headedness, dizziness, headache, nasal congestion, and retrograde ejaculation are the most common side effects.¹³ Such side effects used to be more common in the first generation versions of these drugs, however, the second and third generations have become significantly more uro-selective, and are associated with a lower occurrence of side effects. On a side note, there have been some occurrences of alpha-blockers causing 'floppy iris syndrome' during cataract surgery in patients who were taking concurrent alpha-blockers. Thus, alpha-blocker treatment may need to be discontinued prior to cataract surgery, and the ophthalmologist should be informed.¹⁴

5-alpha reductase inhibitors

The conversion of testosterone to dihydrotestosterone (DHT) via the enzyme 5-alpha reductase allows for the prostate to grow in size. Consequently, 5-alpha reductase inhibitors (5-ARI) inhibit this conversion of testosterone to DHT, and by doing so are able to preclude prostatic tissue growth and in fact cause prostatic cell apoptosis.^{15,16} This causes prostate size reduction and improvement in BPH-related symptoms. Finasteride (Proscar) and dutasteride (Avodart)

are currently the two most utilized medications, with subtle differences between them. The onset of symptom reduction takes approximately 6 months to alleviate symptoms, and as such requires adherence and patience from both the caregiver and receiver. Side effects primarily involve symptoms related to testosterone deficiency such as erectile dysfunction, ejaculatory dysfunction and decreased libido.¹⁷ Once started on this type of medication, the caregiver should be aware of the fact that PSA levels will decrease to half of the original amount. It is thus crucial to get a baseline measurement of the PSA level, as any rise in the PSA level while the patient is on the medication should be thoroughly investigated for the detection of cancer.¹³

Combination therapy

Patients with severe symptoms, exceptionally large prostates and/or those who failed monotherapy with an alpha-blocker may benefit from combination treatment with an alpha-blocker and a 5-ARI. The synergistic mechanism of the 5-ARI (which shrinks the prostate) along with the alpha-blocker (which relaxes the smooth muscle of the prostate) has consistently been shown to benefit patients.

Two seminal trials, the MTOPS trial¹⁸ and CombAT trial,¹³ have shown superior effects to combination therapy versus monotherapy and placebo. The MTOPS study compared 3047 men who were randomized into four main groups of either placebo alone, finasteride alone, doxazosin alone or combination therapy with finasteride and doxazosin.¹⁸ The study followed the patients over a number of years, and the results demonstrated that combination therapy showed the best profile for symptom improvement and reduction of disease progression. The CombAT trial enrolled over 4000 men and randomized them into receiving tamsulosin alone, dutasteride alone or combination therapy.¹³ Similarly, combination therapy was demonstrated to be superior to either modality alone.

PDE5 inhibitors

While initially approved for the treatment of erectile dysfunction (ED), recent studies have shown that PDE5 inhibitors (PDE5i) are another option for the treatment of BPH-LUTS. PDE5i's increase the intracellular cyclic guanosine monophosphate, which in turn causes a nitric oxide mediated reduction in smooth muscle tone of prostate, as well as the detrusor muscle and urethra. Although the use of these medications will not reduce prostate size (much like alpha-blockers), they have a beneficial effect on LUTS. Tadalafil (Cialis) has been the most popular choice of drug and is currently the

only medication approved by urological guidelines in Canada, the United States and Europe. One study has shown that the use of tadalafil was at least as effective as an alpha-blocker, and also conferred the added benefit of decreasing ED, thus perhaps creating a parsimonious solution for men suffering simultaneously from BPH and ED.¹⁹ Additionally, there is evidence for combination therapy of PDE5i and 5-ARI treatment. One study found the combined treatment of tadalafil and finasteride to be associated with improvement of BPH-LUTS, regardless of pre-existing ED symptoms.²⁰ Side effects of tadalafil can include headache, back pain, facial flushing and dyspepsia. These medications are contraindicated in patients who use nitrates, as hypotension may occur.

Indications for referral

In cases of previous genitourinary trauma or surgery, underlying meatal stenosis, and an uncertain diagnosis, a referral to a urologist should be prompted sooner rather than later. A primary care physician using conservative measures and pharmacotherapy, as outlined above, however, may manage the BPH patient without complications. Referral to a urologist should be considered when the patient presents with certain signs and symptoms that indicate a worsening or evolution of their condition. Primarily, if there is a suspicion of urinary retention, recurrent UTIs, newly identified prostate nodules or rising PSA.

Interventional therapy

Absolute indication for more invasive intervention in the form of surgery usually includes patients with refractory urinary retention and evidence of renal insufficiency. Additionally, patients may elect to undergo surgery if they continue to experience bothersome urinary symptoms despite medical therapy, experience recurrent infections, show signs of bladder stones/kidney infections or have continuous hematuria. Options for surgery have increased considerably within the past few decades. The primary care physician should initiate an informed discussion about the different types of surgery that are available so that the patient arrives to the urologists' office well informed and prepared.

Transurethral resection of prostate (TURP) and laser therapies

TURP has been considered the gold standard in treating BPH for years. The procedure is conducted under direct vision and is done by resecting parts of the prostate

tissue until there is an acceptable channel of urine to flow through the newly acquired prostatic fossa. The procedure usually takes about 60 minutes, and patients generally stay in the hospital for 24 hours for observation and monitoring. Varying types of energy are used for the procedure, ranging from the traditional monopolar TURP, to the more popular bipolar electro-cautery. Newer laser therapies such as GreenLight photovaporization (PVP) and holmium laser enucleation (HoLEP) have improved upon traditional TURP in several ways, including outpatient surgery, faster return to work, and no requirement to stop anti-coagulation.²¹

Risks from this surgery depend on the modality used; the more traditional TURPs were known to have higher risks of bleeding (with a risk of blood transfusion), permanent sexual side effects (such as retrograde ejaculation and less commonly, ED), UTIs and urinary incontinence, although rarely. The newer methods, such as PVP, are associated with little to no blood loss and shorter length of stay within the hospital, thus demonstrating it to be a safe and effective surgical procedure.²²

Numerous studies have shown that patients who had undergone a TURP procedure had decreased bother scores, episodes of urinary retention and risk of kidney damage.²³

UroLift

A much newer technique gaining significant popularity is known as Prostatic Urethral Lift (PUL), which is a minimally invasive approach that works by pulling the lateral lobes of the prostate apart using anchored sutures.²⁴ The main advantage of this technique is that it has been shown to provide acceptable LUTS improvements while preserving erectile function and lowering the risks of operative and postoperative complications. While the evidence is still sparse, some studies have shown promise. A recent study by Roehrborn et al followed over 200 patients in multiple sites across the world for 3 years.²⁵ Compared to a sham procedure (which included cystoscopy and initiation of sounds meant to imitate the procedure), the PUL was found to have significant benefits in symptom scores and QoL, with a relatively low percentage of re-treatment.

Conclusion

This review is aimed at introducing the intricacies of BPH and its treatment options to the primary care physician. The primary caregiver has a significant role to play in diagnosing and initially treating the patient presenting with BPH-LUTS.

Disclosure

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