

Benign prostatic hyperplasia

Prostate problems are among the number one reasons why men over 50 visit their physicians

■ by Jack Barkin, MD

LOWER URINARY TRACT SYMPTOMS (LUTS) are among the commonest reasons for doctor visits among 50+ year-old males, and benign prostatic hyperplasia (BPH) is frequently the underlying cause. In fact, half of all men over age 50 will require some type of medical/surgical management for BPH/LUTS. Until about 15 years ago, the most common treatment for BPH was a transurethral resection of the prostate (TURP) operation. Today, most men are first offered medical treatment. Before initiating medical therapy, one must rule out other serious causes of LUTS, such as prostate cancer, bladder cancer, stones and other obstructive phenomena.

There are 2 types of prostatic obstruction that can be reversed or at least treated: **DYNAMIC:** affected by smooth muscle tone; treated with alpha blockers; **FIXED:** related to the bulky growth of the prostate.

For men with an enlarged prostate, there's a good chance that therapy with a 5-alpha-reductase inhibitor (5-ARI) can shrink the prostate, thereby preventing disease progression and usually the need for surgery.

There's been a lot of recent work on different combination therapies for the treatment of BPH/LUTS. If a patient's serum prostate-specific antigen (PSA) level is greater than 1.4 ng/mL (which guarantees prostate volume is greater than 30 cc) and he has significant LUTS, then combination medical therapy of an alpha blocker with a 5-ARI is the most effective therapy. After a careful workup and an assessment of the "bothersome/motivational" index it's appropriate for the primary care physician to initiate such therapy.

Why it's important to arrest disease in a man with an enlarged prostate

- If the disease isn't arrested, over time, men with EP may experience
 - increase in prostate volume
 - decrease in peak urinary flow rate (Q_{max})
 - worsening of symptoms
- Progression of EP may lead to long-term complications
 - decreased quality of life
 - recurrent urinary tract infections
 - recurrent hematuria
 - hydronephrosis
 - renal failure
 - acute urinary retention (AUR)
 - surgery

Risk factors

What are the most significant risk factors for BPH progression?

- Age 50 years or older
- Enlarged prostate (≥ 30 mL)
 - PSA ≥ 1.4 ng/mL (a marker for prostate volume ≥ 30 cc)
- Moderate-to-severe urinary symptoms
 - (AUA-SI score > 7)
- Weak urinary flow

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Workup and investigations

HISTORY

- Symptoms (LUTS*)
 - severity
 - bother
 - AUA-SI
- Hematuria
- Pain, dysuria
- Sexual history
- Prior and current illnesses
- Medications

LABS

- Urinalysis
- Creatinine
- PSA

CPE

- Flank — hydronephrosis
- SP area — distended bladder
- Digital rectal examination

A 2009 update to the 2005 Canadian guidelines suggests the following examinations are reasonable but optional

- Serum creatinine
- Uroflow
- Voiding diary
- Post void residual
- Sexual function questionnaire

These examinations are *not* recommended in routine initial examination of BPH-associated LUTS

- Serum creatinine
- Uroflow
- Voiding diary
- Post void residual
- Sexual function questionnaire

Watchful waiting

It has been shown in many studies that a “large” prostate is a minimum of 30 cc volume, which can be guaranteed by having a PSA of at least 1.4 ng/mL.

A “watchful waiting” approach may alleviate symptoms, but won’t treat the prostate:

- Education and reassurance
- Avoid decongestants, other drugs
- Lifestyle changes
 - avoid bladder irritants, caffeinated beverages, spicy foods
 - cut back on evening fluids
 - avoidance/monitoring of some drugs e.g. diuretics, decongestants, antihistamines, antidepressants
 - avoid/treat constipation
 - smoking cessation
- Other
 - bladder retraining
 - pelvic floor exercises

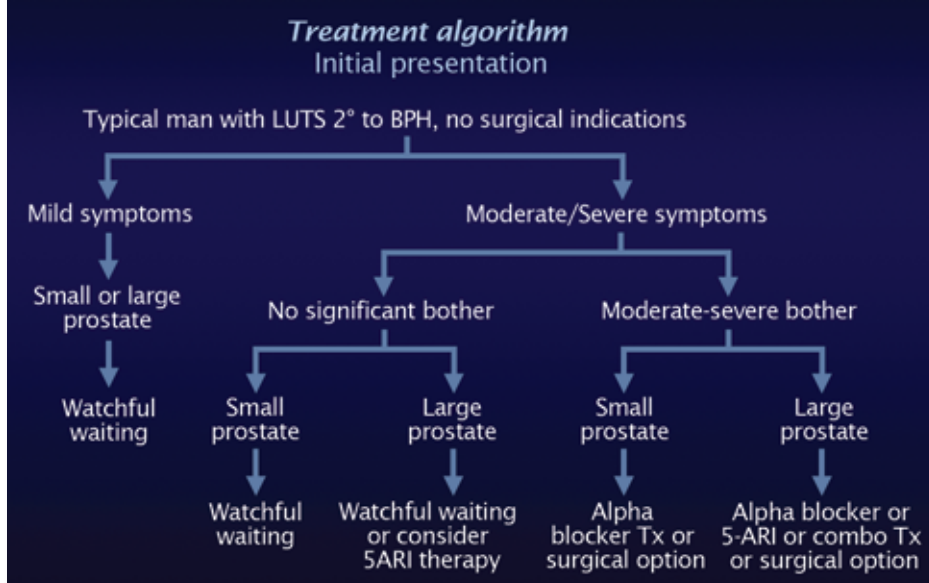
About 20% of patients on watchful waiting will worsen within 5 years¹

Alpha blockers

There are 4 common alpha blockers being used today:

- Terazosin and doxazosin are non-selective alpha blockers
- Alfuzosin and tamsulosin are more uro-selective alpha blockers, which should avoid the cardiovascular side effects of the others
- Naftopidil is a new $\alpha 1D$ blocker being tested for BPH that may have an impact on bladder smooth muscle.² A Cochrane review found it as effective as low-dose tamsulosin, with equally few side effects.³

Canadian guidelines for the management of BPH



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CHECKLIST

5-ARIs

Testosterone is converted to dihydro-testosterone by the 2 iso-enzymes of 5-alpha reductase. DHT is the major stimulus for the growth of the prostate. The inhibition of this enzyme reaction will reduce the level of DHT and thereby shrink the prostate, alleviating some of the symptoms of obstruction. Dual blockade of the iso-enzymes has been shown to decrease the intraprostatic level of DHT by about 92% compared to 70%.⁴

See references on page 64.

Benefits of combination therapy

	5-ARI	Alpha blocker
Reduce prostate size	X	
Maintain reductions in prostate size	X	
Improve symptoms and stream	X	X
Onset of symptom relief in 1-2 weeks		X
Maintain symptom and stream improvements	X	X
Prevent symptomatic progression	X	X
Reduce longer-term risk of AUR and surgery	X	

The integrity of PSA after treatment with a 5-alpha reductase inhibitor

- Mean serum PSA levels reduced ~ 50% (time-dependent with some individual variability)⁶
- Baseline PSA is recommended before treatment
- Establish new baseline PSA after 6 months of treatment
 - failure to drop 50%⁷ or increase in PSA may indicate noncompliance, prostate cancer, or other prostate-related conditions needing evaluation
- To interpret an isolated PSA value in men treated with a 5-ARI for 6 months or more
 - double the PSA value to compare with normal values in untreated men⁸
- Progressively rising PSA on treatment is indication for referral and biopsy⁹

Efficacy of combination therapy proven in trials

Two significant trials looked at the effects of combination therapy in men with BPH.

- **CombAT** (Combination of dutasteride (Avodart) and tamsulosin (Flomax) compared the monotherapies to combination in a “higher risk for progression” population (i.e.: greater volumes, PSAs and symptom scores).
- **MTOPS** (Medical Therapy of Prostate Symptoms) compared the monotherapies of finasteride, doxozasin, a combination of both, and placebo.

In the MTOPS study after 5 years the combination showed a 67% decreased risk of progression, acute urinary retention or need for surgery compared to the placebo arm.

In CombAT, where there was no placebo arm, in the 2-year interim analysis the combination showed a 50% greater improvement in the symptom score compared to either monotherapy arm, and the prostate volume shrunk by almost 30% in the combination or dutasteride arm compared to the alpha-blocker arm.

In a separate review of the CombAT trial there was a statistically significant improvement in the “quality of life “ question on the IPSS scale in the combination arm, that was never before shown.⁵

Summary

- BPH is the most common cause of LUTS after the age of 50
- Most men with symptoms and a large prostate will progress with time
- A large prostate is defined as a volume of > 30 cc or a PSA of at least 1.4 ng/mL
- Combination therapy of an alpha blocker and a 5-alpha reductase inhibitor provides the most rapid symptom response, durability of response and greatest chance of progression prevention
- Once on a 5-ARI for 6 months the patient’s PSA baseline should be reduced by 50% — if not, check compliance and consider other diagnoses.

Just cut on the dotted line and copy for your patients.

If you'd rather calculate the patient's AUA-SI score, simply use the first seven IPSS questions, without the final quality of life question.

But remember: the quality of life score will determine the motivation that the patient will exhibit to accept treatment!

Total score: 0-7 mildly symptomatic; 8-19 moderately symptomatic; 20-35 severely symptomatic.

International prostate symptom score (IPSS)

Name:

Date:

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score
Incomplete emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
Frequency Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
Intermittency Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency Over the past month, how difficult have you found it to postpone urination?	0	1	2	3	4	5	
Weak stream Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining Over the past month, how often have you had to push or strain to begin urinating?	0	1	2	3	4	5	

	None	1 time	2 times	3 times	4 times	5 times or more	Your score
Nocturia Over the past month, how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	

Total IPSS score	
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Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed - about equally satisfied and dissatisfied	Mostly dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6