TREATMENT TRENDS FOR BPH

George Boline, M.D.
Urology of Central PA
April 23, 2016
Objectives

- Review the current understanding of the pathophysiologic underpinnings of BPH/LUTS
- Discuss current practice patterns and best practices
- Review medical and surgical therapy, including complications thereof
- Highlight new directions in management of BPH
Introduction

• BPH contributes significantly to decreased quality of life
• Chronic obstruction, especially under-recognized and untreated, can result in severe end-organ damage
  • Detrusor failure
  • Renal failure
  • But rarely!
Epidemiology

- No men <30 years old had evidence of BPH
- Prevalence rose with advancing age
- 88% in men in their 80’s
- Findings have been found to be consistent across geographic regions and ethnicities
BPH

Symptomatic BPH

Age In Years

Percent

0-20 21-30 31-40 41-50 51-60 61-70 71-80 81-90+

(Prostate 17: 1990)
Normal Prostate

- Prostate has both stromal and glandular elements.
- Stroma and capsule contain smooth muscle elements.
- Glands surround, and empty secretions into, the urethra.
BPH Prostate

- With BPH there is both stromal and glandular proliferation.
- Also, there is heightened prostatic smooth muscle tone.
- Both processes can restrict urine flow and contribute to clinical manifestations of BPH.
BPH

- Clinical manifestations of BPH are due to both static and dynamic factors.
- Static component is due to obstructed flow caused by the enlarging adenoma.
- Dynamic component is due to heightened smooth muscle tone of stroma and capsule.
OHM’s LAW and Micturition

\[
\text{PRESSURE} = \frac{\text{FLOW}}{\text{RESISTANCE}}
\]
Normal Prostate

- Glandular component is rich with DHT-receptors.
- 5-ARI's target glandular component of BPH.
- Smooth muscle cells have alpha-1a receptors.
- Alpha-blocker therapy targets smooth muscle component of BPH.
BPH

• Medical therapy for BPH is directed at both static and dynamic components.

• 5 alpha-reductase inhibitors address glandular (static) component.

• Alpha-adrenergic blockers address dynamic (smooth muscle) component.

• Can be used separately or in combination.
Clinical manifestations of BPH include:

- Lower urinary tract symptoms (LUTS)
- Incomplete bladder emptying
- Urinary retention
- Renal insufficiency
- Urinary tract infection
- Hematuria
- Bladder calculi
Where Are We Now

- Algorithm-driven guidelines/best practices provide powerful tool for guiding workup and therapy
- Multiple classes of drugs available with well supported benefits and favorable side effect profiles
- TURP is mature but still improving incrementally
- Alternative minimally invasive therapies continue to gain traction
Work-up

• Guiding principles
  • Recognize that lower urinary tract symptoms are not exclusively a product of obstruction
    • Neurologic disease
    • Diabetes
    • Bladder cancer
  • Obstruction is not necessarily at the level of the prostate
    • Urethral stricture
    • Meatal stenosis
    • Dyssynergic voiding
  • Tailor workup based on patient characteristics, i.e., “Only ask the question if you want to know the answer!”
Work-up

• Complete medical history should be taken to identify other causes of voiding dysfunction or comorbidities that may complicate treatment
  • Bladder diary is useful in many patients
• The International Prostate Symptom Score (IPSS) should be utilized in the initial assessment of each patient presenting with LUTS thought to be secondary to BPH
BPH

- Most common indication for treatment of BPH is bothersome LUTS.

- Obstructive symptoms:
  - Hesitancy
  - Weak Stream
  - Incomplete Emptying
  - Intermittency

- Irritative symptoms:
  - Frequency
  - Urgency
  - Nocturia
Work-up

- A physical examination, including both a digital rectal examination (DRE) and a focused neurologic examination, should be performed
  - DRE
    - Correlation between observed and true prostate size poor
    - Screens for locally advanced prostate cancer
  - Neuro
    - general mental status
    - ambulatory status
    - lower extremity neuromuscular function
    - anal sphincter tone
Work-up

• A urinalysis should be performed by dipstick testing or microscopic examination of the sediment to screen for hematuria and urinary tract infection

• Measurement of the serum prostate-specific antigen (PSA) should be offered to the following patients
  • Meets current criteria for prostate cancer screening
  • PSA measurement may change the management of their voiding symptoms
Work-up

Cystoscopy reserved for patients who have:

• Failed medical therapy (under consideration for surgical intervention)
• Atypical features at presentation
  • Hematuria
  • Predominance of irritative over obstructive symptoms
• Suspicion for stricture
Principles of Therapy

Patients with mild symptoms of LUTS secondary to BP (AUA-SI score <8) and patients with moderate or severe symptoms (AUA-SI score ≥8) who are not bothered by their LUTS should be managed using a strategy of watchful waiting.
Principles of Therapy

Treatment options for patients with bothersome moderate to severe symptoms of BPH (IPSS > 8) include watchful waiting and the medical, minimally invasive, or surgical therapies.
Therapeutic Options

- Watching waiting
- Medical therapy
- Invasive therapy
Medical Therapy

“Although medical therapies do not achieve the same level of efficacy as surgery, the attractive features of medical therapy relative to surgery are that clinically significant outcomes are obtained with fewer, less serious, and reversible side effect.”
Alpha-Adrenergic Blockers

• Heightened smooth muscle tone in prostate with BPH.

• Alpha-blocker therapy reduces prostatic smooth muscle tone, alleviating obstruction to flow.

• Addresses the dynamic component of BPH.

• Adverse role of decongestants.
Alpha Blockers

“Alfuzosin, doxazosin, tamsulosin and terazosin are appropriate and effective treatment alternatives for patients with bothersome, moderate to severe LUTS secondary to BPH (AUA-SI score ≥8). Although there are slight differences in the adverse events profiles of these agents, all four appear to have equal clinical effectiveness.

...The effectiveness and efficacy of the four alpha blockers under consideration appear to be similar.”
Alpha Blockers

Side effects

- Orthostatic hypotension
- Dizziness reported in 2-14%
- Retrograde ejaculation
- Rhinitis
- Floppy iris syndrome
5a-Reductase Inhibitors

• Rationale for treatment: development of prostate is dependent on DHT
• Castration noted to be effective therapy for BPH in 19th century
• Finasteride was first 5a-reductase inhibitor developed
• Maximum reduction in prostate volume at 6 months
5a-Reductase Inhibitors

- Finasteride inhibits 5a-reductase type II isoenzyme only
- Dutasteride inhibits type I and type II
- Type I predominates in BPH
- Dutasteride has significantly longer half-life (weeks vs. hours)
- Head-to-head trial demonstrated no advantage of dutasteride over finasteride
5a-Reductase Inhibitors

PLESS trial

- 3040 men with moderate to severe urinary symptoms
- Randomized to finasteride vs. placebo for 4 years
- Baseline prostate volume 55cc
- Treatment-related effects of finasteride on symptom score, flow rate and prostate volume were 2.0 symptom units, 1.7 mL/s, and 32% size reduction
- Demonstrated the durability of symptom and flow improvements by finasteride
- Decreased rate of need for surgical intervention in treatment arm
5a-Reductase Inhibitors

- Sexual side effects can occur
  - Decreased ejaculatory volume
  - ED
- Also useful for treating hematuria secondary to BPH
- Symptom improvement better in patients with larger baseline prostate volume
- Artifactual PSA depression
Combination Therapy

- Use of alpha blockers and 5a-reductase inhibitors together
- MTOPS
  - 3047 patients
  - Randomized to doxazosin, finasteride, combination, or placebo
  - No prostate size exclusion
  - BPH progression risk reduction rates compared with placebo
    - Doxazosin 39%
    - Finasteride 34%
    - Combination therapy 67%
Indications for INVASIVE THERAPY

- URINARY RETENTION due to BPH
- Renal Insufficiency due to BPH/BOO
- Recurrent UTI’s
- Bladder Stones
- Gross Hematuria due to BPH
- LUTS Refractory to medical management
- LUTS if patient preference is a procedure
Invasive Therapy

- Simple open prostatectomy
- Transurethral resection of prostate (TURP)
- Vaporization of Prostate
- Thermal approaches, e.g. Transurethral Needle Ablation (TUNA), Microwave Thermo Therapy (TUMT)
- Prostatic lift procedure (UROLIFT)
Simple Prostatectomy

- Suitable for very large glands (>80-100 cc)
- Outstanding objective response in urinary flow rates and other measures of obstruction
- Higher blood loss and longer hospital stay than endoscopic procedures
TURP

- Has been the gold standard minimally invasive therapy of BPH
- Large body of literature supporting efficacy
- Rates of incontinence and ED low
- Require at least overnight hospitalization and catheterization
Prostate Vaporization

- Laser vaporization of the prostate (PVP)
  - BPH tissue vaporized using high-power KTP 532 nm laser or other systems
  - Generally outpatient
  - Short catheterization times
  - Results appear similar to TURP
  - No risk of hyponatremia but fluid overload possible
- Bipolar Plasma Button
Thermo Therapy

• TUNA of the prostate is an appropriate and effective alternative for moderate to severe LUTS due to BPH
• TUMT is effective in partially relieving LUTS due to BPH
• Can be done in office
• Improved SK, QOL, and flow rates
• Low risk of complications
• ? Durability – no quality long term studies
UROLIFT

• Minimally invasive, can be in office
• Implants compresses prostate tissue opening the urethra
• Best for small to medium size prostate glands
• FDA approved
• Symptom reduction · IPSS 11.1 vs 5.9 (placebo)
• Immediate results, no retrograde ejaculation
• No long term data
BPH TAKE HOME POINTS

• Not all male voiding issues are due to BPH
• Work up includes score (IPSS), DRE, U/A and in most cases a PSA
• In the absence of BPH related complications, treatment is based on
  • degree of bother (QOL)
  • Patient preference
• Meds (single agent or combo Rx) are effective in reducing BPH progression and need for surgery
• A spectrum of effective BPH procedures are available that can be tailored to each patient’s needs and preference
THANK YOU

QUESTIONS?