Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms: Individualized Management in Primary Care

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Boston, Massachusetts

Education Partner:
Integritas Communications
Session 5: Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms: Individualized Management in Primary Care

Learning Objectives

1. Describe pathophysiologic mechanisms in benign prostatic hyperplasia and lower urinary tract symptoms (BPH-LUTS) and relationships to comorbid conditions and therapeutic approaches.
2. Conduct comprehensive assessments of patients with suspected BPH and associated LUTS.
3. Evaluate the mechanisms of action and clinical profiles of α-blockers, 5-α reductase inhibitors (5-ARIs), and phosphodiesterase type 5 (PDE-5) inhibitors in the treatment of BPH-LUTS with and without ED.
4. Combine pharmacologic and nonpharmacologic interventions for BPH-LUTS based on symptom severity, common comorbidities, risk of disease progression, and patient goals.
5. Monitor treatment efficacy and adherence in patients with BPH-LUTS to guide therapeutic restructuring and optimize patient outcomes.

Faculty

Matt T. Rosenberg, MD
Medical Director
Mid-Michigan Health Centers
Chief, Department of Family Medicine
Foote Health System
Jackson, Michigan

Dr Matt T. Rosenberg earned his medical degree at the University of California, Irvine, School of Medicine, where he trained in general surgery. He also trained in urologic surgery at Brigham and Women’s Hospital in Boston, Massachusetts, before changing fields to general practice.

Dr Rosenberg has a special interest in the medical management of urologic diseases and has authored or coauthored articles published in *Urology, Journal of Urology, BJU International, International Journal of Clinical Practice*, and other peer-reviewed journals.

He practices in Jackson, Michigan, as medical director of Mid-Michigan Health Centers and on staff at Allegiance Health, where he served as chief of the department of family medicine from 2003 to 2006. Dr Rosenberg is section editor of urology for the *International Journal of Clinical Practice* and is founder and chairman of the Urologic Health Foundation, a nonprofit group dedicated to the education of primary care physicians in the field of genitourinary disease. In 2011, he was appointed by the American Urological Association’s office of education to be the coordinator of primary care education.

David R. Staskin, MD
Associate Professor of Urology
Tufts University School of Medicine
Director, Center for Male and Female Pelvic Health
Steward-St. Elizabeth’s Medical Center
Boston, Massachusetts

Dr David R. Staskin graduated from Hahnemann Medical College in Philadelphia, Pennsylvania, in 1979. He interned at the University of California, San Diego, and then served as a fellow at the National Kidney Foundation, University of Pennsylvania, and the University of California, Los Angeles. He joined the faculty of Boston University Medical Center in 1985, then the faculty of Harvard University-Beth Israel Medical Center in 1989. From 2002 to 2008, Dr Staskin was a member of the faculty of Weill Cornell Medical College at New York Presbyterian Hospital. He recently joined the department of urology at Tufts Medical Center in Boston, Massachusetts, as an associate professor.

Dr Staskin belongs to many leading urological associations and committees, including the Health and Human Services Incontinence Guidelines (member); the World Health Organization’s International Consultation on Incontinence Guidelines for Incontinence (chairperson); the American Urological Association committee “Surgical Management of Female Stress Urinary
Incontinence”; the Society of Urodynamics and Female Urology (board of directors); the American Urogynecological Society (former board of directors); and the American Association of Clinical Urologists (board of directors).

He also serves on the following journals as a reviewer: International Urogynecology Journal (editorial board); Current Urology (editorial board); Journal of Urology; Urology; Neurology and Urodynamics; British Journal of Urology International; and The New England Journal of Medicine.

Dr Staskin has published extensively in the areas of female urology, neuourology, and urodynamics. He is the co-editor of the Textbook of Female Urology and Urogynecology (Cardozo and Staskin, eds.), which was awarded the British Medical Society's first prize for the best second edition medical textbook of 2006.

Dr Staskin is the inventor of SPARC Sling System (American Medical Systems) and has contributed significantly to the development of the Monarc and BioArc slings and Apogee and Perigee for pelvic prolapse repair systems.

Steven A. Kaplan, MD—Virtual Presenter
E. Darracott Vaughan Jr. Professor of Urology
Chief, Institute for Bladder and Prostate Health
Weill Cornell Medical College
Director, Iris Cantor Men’s Health Center
New York Presbyterian Hospital
Weill Cornell Medical Center
New York, New York

Dr Steven A. Kaplan received a BS in biochemistry from The City University of New York—Brooklyn College in 1978, graduated from Mount Sinai School of Medicine in 1982, and was elected to the Alpha Omega Alpha Medical Honor Society. Dr Kaplan’s postgraduate training included an internship and residency in the department of surgery at Mount Sinai Hospital as well as a residency in urology at the Squier Urological Clinic, Columbia University. From 1988 to 1990 he was an American Urological Association (AUA) Scholar focused on identifying molecular markers and urodynamic parameters that herald bladder and prostate dysfunction.

Dr Kaplan was the Given Foundation Professor of Urology and administrator, as well as vice chairman of the department of urology, at Columbia University from 1998 to 2005. Fellowship director for female urology and voiding dysfunction from 1995 to 2005 at Columbia and at Weill Cornell Medical College since 2005, Dr Kaplan is also the E. Darracott Vaughan Jr. Professor of Urology and chief, Institute for Bladder and Prostate Health at Weill Cornell Medical College, and director, Iris Cantor Men’s Health Center at New York Presbyterian Hospital. He is a serial entrepreneur and founder of Medidata Solutions Inc., a publicly held corporation and one of the premier electronic data capture companies in the world; Medivizor, Inc., a medical informatics platform; and Blabbelon, a novel voice over Internet protocol platform.

Dr Kaplan is a diplomate of the American Board of Urology and a fellow of the American College of Surgeons. He is a recognized authority on the study of benign diseases of the prostate and on the association of metabolic factors and voiding dysfunction and female urology. He has published more than 780 articles and 170 abstracts, and has made over 335 presentations in more than 35 countries. The coauthor of 5 books, he is on the editorial boards of Urology, Journal of Urology, and Urology Times.

Dr Kaplan is a member of more than 30 professional organizations, has been awarded 5 National Institutes of Health grants, and has received over 13 million dollars in research funding. He was awarded the John K. Lattimer Award for Lifetime Achievement in Urology by the National Kidney Foundation. Most recently, he chaired the National Institute of Diabetes and Digestive and Kidney Diseases’ Prostate Strategic Planning Committee and the BPH/Prostatitis section of the AUA Core Curriculum.

Faculty Financial Disclosure Statements
The presenting faculty reports the following:

David R. Staskin, MD, is a consultant for Allergan, Inc., AltheRx Pharmaceuticals, Endo Pharmaceuticals Inc./American Systems, Takeda Pharmaceuticals U.S.A., Inc., and Theravida, Inc.; he is also a member of the speakers bureau for Allergan, Inc., and Endo Pharmaceuticals Inc./American Medical Systems.

Steven A. Kaplan, MD, has no financial relationships to disclose.

**Education Partner Financial Disclosure Statement**
The content collaborators at Integritas Communications have reported the following:

Jim Kappler, PhD, has no financial relationships to disclose.

**Suggested Reading List**


BENIGN PROSTATIC HYPERPLASIA AND LOWER URINARY TRACT SYMPTOMS: Individualized Management in Primary Care

SPEAKERS
Steven A. Kaplan, MD (Virtual Presenter)
Matt T. Rosenberg, MD
David R. Staskin, MD

SESSION 5
2:30–4pm

Scientific Primer in BPH-LUTS

Key Points

- BPH-related bladder outlet obstruction is mediated by compression of the urethra by an enlarged prostate and increased smooth muscle tone around the prostatic urethra
- Medications used to treat BPH-LUTS target these factors
  - o-blockers: block norepinephrine binding to α-1-adrenergic receptors, promoting smooth muscle relaxation
  - 5-ARIs: disrupt DHT production, decreasing prostate cell proliferation, increasing apoptosis, and reducing prostate volume
  - PDE-5 inhibitors: increase NO/cGMP activity and inhibit Rho kinase activity to reduce smooth muscle tone
  - Also may reduce ANS overactivity, local inflammation/ischemia, and prostatic and smooth muscle cell proliferation
- BPH-LUTS is associated with metabolic syndrome
  - Central obesity, insulin resistance, dyslipidemia, and hypertension

Scientific and Clinical Insights Into Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms

Steven A. Kaplan, MD
E. Darracott Vaughan Jr. Professor of Urology
Chief, Institute for Bladder and Prostate Health
Weill Cornell Medical College
Director, Iris Cantor Men’s Health Center
New York Presbyterian Hospital
New York, New York

Bladder Function
Filling, Storage, and Voiding

- Normal function
  - Storage capacity (300-500 mL)
    - Adequate low pressure urinary storage (bladder)
  - Adequate outlet resistance (sphincter)
  - Empty to completion (minimal residual)
  - Adequate bladder contraction
  - No outlet obstruction
- Abnormal function
  - Failure to store or empty
  - Voiding frequently in small amounts
  - Uncontrollable urge (urgency) to empty with frequency
  - Incomplete emptying
  - Hesitancy, poor stream, feeling of incomplete emptying

Prostate Function

- Normal function
  - Contributes to continence
  - Produces fluid for seminal emission
  - Does not obstruct urinary flow through the urethra

- Abnormal function
  - Obstruction of urinary flow
  - Sphincteric damage/usually surgical ("stress incontinence")


Overlapping Clinical Constructs

**Definitions**

- **BOO, bladder outlet obstruction**
- **BPE, benign prostatic enlargement**
- **BPO, benign prostatic obstruction**
- **BPH, histologic stromaglandular hyperplasia**
- **LUTS, potential clinical manifestation of these conditions**


**BPH:** Histologic stromaglandular hyperplasia

**BPE:** Anatomic increase in prostate gland size

**BOO:** All pathophysiologic compressions of urethra and bladder outlet that compromise urinary flow

**BPO:** Obstruction confirmed by pressure flow studies or highly suspected based on flow rates and prostate size

**LUTS:** Potential clinical manifestation of these conditions

Case Study

**Roberta**

- 65-year-old African American man
  - Retired mechanic
  - Married with 4 children, several grandchildren
  - Visits PCP for follow-up about hypertension
  - Controlled with lisinopril 20 mg daily

- Mentions need to urinate more frequently, although it is often difficult to start and his urine flow has decreased
  - States that he expects to have problems with urination as he ages

Are bothersome urinary issues a normal part of aging?


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LUTS Evaluations in Men

**An Overview**

**Clinical Interview**
- Symptom profile
  - Categorization
  - Severity
  - Bother, functional effects
- Sexual function

**Patient History**
- Comorbidities
- Medications
- Temporal relationship
- Other risk factors (e.g., smoking, excessive alcohol intake)

**Physical Exam**
- DRE
- General urinary exam
- Abdominal exam
- Neurologic exam

**Lab Tests**
- PSA level
- Urinalysis
- Blood sugar

**Progression Risks**
- Factors that suggest symptoms will worsen or patients may develop serious medical complications (e.g., AUR)

GIR: Digital rectal exam; PSA, prostate-specific antigen; AUR, acute urinary retention
Clinical Interview for Male LUTS
Symptom Categorization

<table>
<thead>
<tr>
<th>Storage</th>
<th>Voids</th>
<th>Postmicturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Hesitancy</td>
<td>Dribbling</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Poor flow</td>
<td>Incomplete emptying</td>
</tr>
<tr>
<td>Urgency</td>
<td>Intermittency</td>
<td></td>
</tr>
<tr>
<td>Urge</td>
<td>Incontinence</td>
<td>Straining to Start/Continue</td>
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</tbody>
</table>


Storage Voiding Postmicturition
Frequency Hesitancy Dribbling
Nocturia Poor flow Incomplete emptying
Urgency Intermittency
Urge Incontinence Straining to Start/Continue

Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?

Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?

Over the past month, how often have you found you stopped and started again several times while urinating?

Over the past month, how often have you found it difficult to postpone urination?

Over the past month, how often have you had a weak urinary stream?

Over the past month, how often have you had to push or strain to begin urination?

Over the past month, how many times did you typically get up to urinate from the time you went to bed until the time you got up in the morning?

Total for Urinary Symptoms:

AUA-SI, AUA Symptom Index; IPSS, International Prostate Symptom Score; QoL, quality of life.


Consider Co-occurring Issues
Common Comorbidities in BPH-LUTS

BPH-LUTS, Erectile Dysfunction, and Metabolic Abnormalities


Erectile Function and LUTS Severity
Examine Sexual Function

IIEF, International Index of Erectile Function.

Medication Effects in BPH-LUTS

<table>
<thead>
<tr>
<th>Medication</th>
<th>LUTS-Related Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedatives</td>
<td>Confusion, secondary incontinence</td>
</tr>
<tr>
<td>Alcohol, caffeine, diuretics</td>
<td>Diuresis</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Impaired contractility, voiding difficulty, overflow incontinence</td>
</tr>
<tr>
<td>α-Blockers</td>
<td>Increased outlet resistance, voiding difficulty</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>Decreased urethral closure, stress incontinence</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>Reduce bladder smooth muscle contractility</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>Induce cough, stress urinary incontinence</td>
</tr>
<tr>
<td>First-generation antihistamines</td>
<td>Increase outlet resistance</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Precipitate urge incontinence</td>
</tr>
</tbody>
</table>


PSA and Prostate Size

- DRE tends to underestimate size of larger prostates
  - Full length and anterior portion of the gland often not examined
- PSA is more accurate than DRE
  - PSA ≥1.5 ng/mL suggests a prostate volume >30 mL

Other risk factors: older age, higher baseline IPSS, and history of AUR, metabolic syndrome, chronic prostatitis, depressive symptoms, or excessive alcohol use.

Robert Clinical Workup

- Physical exam
  - BMI, 29.8 kg/m²
  - BP, 125/88 mm Hg
- Medical history
  - Hypertension
  - Lisinopril 20 mg daily
- Family history
  - Brother died of prostate cancer
  - Worry about his symptoms suggest prostate cancer

What should the PCP tell Robert about the relationship between BPH-LUTS and prostate cancer?

Men With LUTS

Risks of Prostate Biopsy or Cancer Diagnosis
Physical Activity and the Risk of BPH or LUTS

<table>
<thead>
<tr>
<th>Source</th>
<th>Moderate*</th>
<th>Vigorous*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gann et al, 1995</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platz et al, 1996</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bresolin et al, 2001</td>
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<tr>
<td>Lacey et al, 2001</td>
<td></td>
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<tr>
<td>Del Campo et al, 2006</td>
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<tr>
<td>Rohrmann et al, 2005</td>
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<tr>
<td>Hong et al, 2005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rohrmann et al, 2006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>P&lt;0.005</td>
<td>P&lt;0.006</td>
</tr>
</tbody>
</table>

Odds Ratios: 0.19, 0.74, 0.19, 0.74, 0.74.

*After stratifying physical activity into low, moderate, and vigorous levels, groups were compared to a sedentary reference group.

N=35,675 men with BPH-LUTS from 8 studies.

Rohrmann et al, 2006
Hong et al, 2006
Rohrmann et al, 2005
Lacey et al, 2001
Meigs et al, 2001
Platz et al, 1998
Gann et al, 1995
Sarma AV, et al.

Robert
Treatment and Follow-up

- Advised on fluid intake, increased physical activity, and bladder training
- Alfuzosin 10 mg daily
- 1-month follow-up
  - IPSS, 15 (moderate)
  - Previous score, 18 (moderate)
  - Reports little change in fluid intake and occasionally forgetting to take his medication

What can be done to improve Robert’s adherence to the PCP’s treatment recommendations?

Robert
Treatment Tailoring

- Physical exam
  - BMI, 29.8 kg/m²
  - BP, 125/88 mm Hg
- Medical history
  - Hypertension
- Family history
  - Brother died of prostate cancer
- LUTS workup
  - IPSS, 15 (moderate)
  - Frequency
  - Poor flow and intermittency
  - Strains to urinate
  - PSA level, 1.7 ng/mL
  - DRE, firm and symmetrically enlarged with no nodules
  - Urinalysis, no abnormalities
  - Sexual function
  - Some trouble over last year attaining an erection

Is Robert a candidate for combination therapy? Which combinations?

Improving Patient Adherence

- Patient adherence and satisfaction reflect perceived treatment efficacy and side effects
  - Choose agents with fewer side effects
- Consider online patient education about BPH symptoms, treatments, and complications
- Optimize the provider-patient relationship
  - Understand effects of social and demographic parameters
  - For watchful waiting, discuss monitoring parameters and behavioral changes in detail
  - For pharmacotherapy, discuss side effect profiles
  - For more invasive therapy, discuss recovery times, risks, and complications


BPH-LUTS Management
Pharmacologic Therapy

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Minimum Duration for Clinical Effect</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>a-Blockers</td>
<td>2-4 weeks</td>
<td>Erectile dysfunction, abnormal ejaculation, dry eyes, headaches, hypertension</td>
</tr>
<tr>
<td>5-ARIs</td>
<td>2-4 months</td>
<td>Erectile dysfunction, abnormal ejaculation, gynecomastia, decreased PSA level</td>
</tr>
<tr>
<td>T3-Extrabodies</td>
<td>4 weeks</td>
<td>Headache, indigestion, back pain, flushing, nasal congestion</td>
</tr>
</tbody>
</table>

Antimuscarinics: Selective (eg, tamsulosin, silodosin)
Antimuscarinics: Nonselective (eg, tamsulosin, silodosin)
Antimuscarinics: Dual-drug products (eg, tadalafil) 4 weeks Headache, indigestion, back pain, flushing, nasal congestion
Erectile dysfunction, abnormal ejaculation, decreased PSA level, headache, decreased PSA level


Detailed Management
Persistent, Bothersome BPH-LUTS

- OAB (Storage Symptoms)
- No Evidence of BOO
- LUTS workup
- Frequency
- Poor flow and intermittency
- Strains to urinate
- PSA level, 1.7 ng/mL
- DRE, firm and symmetrically enlarged with no nodules
- Urinalysis, no abnormalities
- Sexual function
- Some trouble over last year attaining an erection

Recommended Tests
- Validated Questionnaires
- Frequency/Volume Chart

Evidence of BOO
- Discuss Treatment Options
- Shared Decision

MIST or Surgery Options
- Select Monotherapy or Combination Therapy
  - Symptom profile
  - Predominant BOO vs Mixed OAB/BOO
  - Prostate size
  - PSA level
  - Comorbidities

Available at www.bph-luts.net

*PSA <1.5 ng/mL suggests small gland; PSA >4 ng/mL suggests large gland.

The PCP considers adding a 5-ARI or PDE-5 inhibitor to LUTS workup. Progression defined as an increase of 
N=3047 men recurrent UTI.

McConnell JD, et al.

Delayed combination therapy, initiation of a 5-ARI >30 days and <180 days after initial 
clinical progression, de

OR, odds ratio.

Morlock R, et al.

Compared with placebo, doxazosin (α-blocker) reduced the risk of clinical progression by 66%. 
Compared with doxazosin (α-blocker) and an

Combination therapy reduced the relative risk of AUR or BPH-related surgery 19.6% compared with duloxetine (5-ARI) monotherapy.

“Progression” defined as the occurrence of AUR or prostate surgery during the 12 months after first prescription.

Better outcomes with delayed combination therapy.

Better Outcomes With Delayed Combination Therapy

Combination Therapy

Early vs Delayed Combinations

Early vs Delayed Combinations

5-ARI and α-Blocker

Source

IPSS

Mean Differences

IEF Score

Mean Differences

Qmax

Mean Differences

Kaplan et al, 2007
-4
-2
-1
2
2
4
6
0
P<0.001

Bechara et al, 2008
-4
-2
-1
2
2
4
6
0
P<0.0001

Liguori et al, 2009
-4
-2
-1
2
2
4
6
0
P<0.0001

Tuncel et al, 2009
-4
-2
-1
2
2
4
6
0
P<0.0001

Gacci et al, 2012
-4
-2
-1
2
2
4
6
0
P<0.0001

Overall
-4
-2
-1
2
2
4
6
0
P<0.0001

PDE-5 Inhibitors and α-Blockers

Effects on BPH-LUTS, Erectile Dysfunction, and Flow Rate

Compared with α-blockers alone, the combination regimen significantly improved IPSS (P=0.005), IIEF scores (P<0.0001), and Qmax (P=0.001).

PDE-5 Inhibitors Pharmacokinetics

If a PDE-5 inhibitor is prescribed, how should it be dosed?
Tadalafil in BPH-LUTS
Once-Daily Dosing

N=427 men who completed a 12-week, placebo-controlled, dose-finding study assessing once-daily tadalafil for BPH-LUTS.


Total IPSS Change From Baseline
IPSS-HRQoL Change From Baseline

Adverse Events With Tadalafil Once-Daily vs On-Demand Dosing

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>5 mg Once Daily(a)</th>
<th>5/10/20 mg On Demand(b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>2.1%</td>
<td>15.8%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>3.8%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>5.9%</td>
<td>11.4%</td>
</tr>
<tr>
<td>Back pain</td>
<td>5.0%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>2.5%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Discontinuation due to adverse events possibly related to the study drug</td>
<td>0.8%</td>
<td>3.1%</td>
</tr>
</tbody>
</table>

\(a\)24-month extension trial of tadalafil 5 mg once daily for erectile dysfunction.

\(b\)Pooled 24-month extension trial data from five 8- or 12-week studies examining on-demand tadalafil for erectile dysfunction.


Robert
Treatment Tailoring

- LUTS workup
  - IPSS, 15 (moderate)
  - Poor flow, intermittency, strains to urinate
  - PSA level, 1.7 ng/mL
  - DRE, firm and symmetrically enlarged with no nodules
  - Alfuzosin 10 mg daily
  - Self-report of some erectile dysfunction
- The PCP decides to adjust the treatment regimen

What would be your recommended approach to tailoring treatment?

Robert
Alternative Presentations

- Physical exam
  - BMI, 29.8 kg/m²
  - BP, 125/88 mm Hg
- Medical history
  - Hypertension
    - Lisinopril 20 mg daily
- Family history
  - Brother died of prostate cancer

How should management change if the DRE revealed a prostate volume of 50 mL with a PSA level of 4.6 ng/mL? What would you do if Robert’s symptoms were refractory to treatment with an \(\alpha\)-blocker together with a 5-ARI?

Red Flags: Consider Urologist Referral

- Presence of LUTS associated with results of DRE suggesting prostate cancer
- Hematuria
- Abnormal PSA levels
- Recurrent UTI
- Palpable bladder
- History/risk of urethral stricture
- Neurologic disease raising likelihood of primary bladder disorder

Conclusions

- BPH-LUTS is a progressive condition characterized by storage, voiding, and postmicturition symptoms
- Common comorbidities of BPH-LUTS include hypertension, metabolic syndrome, and erectile dysfunction
- These conditions are pathogenically linked
- Effective medical management of BPH-LUTS often requires behavioral modifications and pharmacotherapy
- In select patients, multidrug therapy can more effectively reduce BPH-LUTS and risks of disease progression compared with monotherapy
Build-a-Case

Joseph: Patient Background

- 65-year-old Caucasian man
  - Retired 10 years ago
  - Lives with wife of 40 years
- Presents to his PCP
- Reports feeling somewhat tired during the day

Build-a-Case

Joseph: Medical History

- Dyslipidemia
  - Simvastatin 40 mg daily
  - Takes longer to urinate

Build-a-Case

Additional Considerations in BPH-LUTS

Alcohol Use, Hepatic Impairment

- Prescribing considerations for patients with mild, moderate, or severe hepatic impairment
  - α-Blockers are not recommended in patients with severe hepatic impairment
    - No dose adjustment required for silodosin or tamsulosin in patients with mild or moderate hepatic impairment
    - Effects of hepatic impairment on finasteride and dutasteride have not been studied
    - These agents are metabolized extensively in the liver, and caution is required for individuals with abnormal liver function

References:
1. See Drugs@FDA (http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019668s021lbl.pdf)
2. See Drugs@FDA (http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020579s027lbl.pdf)
3. See Drugs@FDA (http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022206s006lbl.pdf)
4. See Drugs@FDA (http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021287s011lbl.pdf)
5. See Drugs@FDA (http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021319s023s025lbl.pdf)
6. See Drugs@FDA (http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/020180s037lbl.pdf)
How does the fact that Joseph complains of disturbed sleep and daytime fatigue affect your approach to patient assessment or treatment?

Additional Considerations in BPH-LUTS

**Disturbed Sleep, Daytime Fatigue**

- Nocturia increases risk of falls and hip fractures in older individuals¹
- CAMUS trial²
  - Men with LUTS and smaller prostates and/or lower PVR volumes were at greatest risk for sleep problems
  - Data suggest that systemic and/or nonprostatic factors contribute to poor sleep in these patients
- Lack of studies evaluating effects of BPH-LUTS medications on sleep parameters³

CAMUS, Complementary and Alternative Medicine for Urological Symptoms.


How does the fact that Joseph has a large waist circumference affect your approach to patient assessment and treatment?

**Additional Considerations in BPH-LUTS**

**Large Waist Circumference**

- Increased waist circumference is associated with worsened voiding¹
- Mechanistic relationships between obesity, erectile dysfunction, and BPH-LUTS
  - Obese men have relatively low testosterone/high estrogen hormonal profiles²,³
  - May increase risks of BPH-LUTS and erectile dysfunction
  - Hyperinsulinemia may induce prostate growth²,³
- Lifestyle modifications for obesity
  - How long until erectile function improves?
  - How long until BPH-LUTS improve?


Build-a-Case

**Joseph: Patient Workup**

- **Urinary symptoms**
  - Terminal dribbling
  - Weak urine stream
  - Urinates 2 or 3 times each night
- **Physical exam**
  - Abdomen is soft
  - No signs of malignancy

- **BMI, 29.9 kg/m²**
- **BP, 135/85 mm Hg**
- Does not smoke or drink alcohol
- Urinalysis negative
- Some trouble achieving an erection

BMI: body mass index; BP: blood pressure.
**Joseph**

**Potential Evaluation Techniques**

- **DRE**
  - Rule out induration, mass, or nodularity indicative of neoplasm or inflammatory process
  - Anal sphincter tone assessed to rule out neurologic causes
- **PSA testing**
  - Compared with DRE, PSA better estimates prostate volume
  - High PSA levels suggest higher risk of disease progression
  - PSA levels can guide treatment selection and follow-up frequency
- **Serum creatinine measurement**
  - Screening test for obstructive uropathy
  - Serum creatinine test can be useful in patients with high PVR volumes
  - Guidelines no longer recommend routine creatinine measurement


**Build-a-Case**

**Joseph: Additional Workup**

- **DRE**
  - Nontender, enlarged, normally shaped prostate
  - No nodules
- **PSA level, 1.7 ng/mL**
- **Other lab tests normal**
- **Diagnosis of LUTS secondary to BPH**

**How does the presence of comorbid type 2 diabetes affect your treatment choices for Joseph?**

**Additional Considerations for BPH-LUTS**

**Diabetes**

- Intensive glycemic control did not reduce the risk or severity of LUTS in men with type 1 diabetes
- Precise mechanisms underlying associations between diabetes and nocturia are unclear


**How does the presence of controlled hypertension affect your treatment choices for Joseph?**

**Additional Considerations in BPH-LUTS**

**Hypertension**

- Risk of hypertension increases by 5.3% and 5.0% with each year of age and IPSS point, respectively
- **ALLHAT**
  - Compared chlorthalidone (thiazide diuretic) and doxazosin (α-blocker) to prevent new onset of heart failure
  - Doxazosin was associated with a 2-fold higher risk of congestive heart failure among high-risk hypertensive patients

How does the presence of chronic pelvic pain syndrome affect your treatment choices for Joseph?

Additional Considerations in BPH-LUTS

Chronic Pelvic Pain Syndrome

- Chronic pelvic pain syndrome often precedes BPH-LUTS
  - Chronic pelvic pain syndrome commonly develops in patients between 35 and 50 years of age
  - BPH-LUTS commonly affects men aged ≥60 years
- MTOPS and REDUCE trials revealed associations between histologic prostate inflammation and:
  - Prostate enlargement
  - LUTS severity


Build-a-Case

Joseph: Initial Treatment

- Silodosin 8 mg daily
- Increased physical activity
- Modified fluid intake

Joseph: Follow-up

- More physical activity
- Adherent to silodosin
- Little symptomatic improvement
  - Nocturia
  - Weak urinary stream
  - Voiding up to 10 times daily
- Sexual symptoms worsened

Joseph

Concluding Comments

- α-Blockers and 5-ARIs, alone or in combination, may precipitate a number of adverse effects
  - Dizziness, hypotension, sexual dysfunction
- Compared with more uroselective medications, nonuroselective α-blockers produce fewer effects on ejaculation
- PDE-5 inhibitors are safe and effective in combination with or instead of α-blockers for patients with BPH-LUTS ± erectile dysfunction
- Data supporting antimuscarinic monotherapy are lacking
  - Combination regimens with α-blockers can reduce storage symptoms
  - Baseline PVR should be checked before initiating therapy

ASK THE EXPERTS: QUESTION & ANSWER SESSION