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

July 24, 2013

Jacob K. Javits Convention Center
New York, New York

Education Partner:
Integritas Communications
Session 1: Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms: Individualized Management in Primary Care

Educational 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

David M. Albala, MD
Medical Director
Associate Medical Professor
Chief of Urology
Crouse Hospital
Syracuse, New York

Dr David M. Albala graduated with a geology degree from Lafayette College in Easton, Pennsylvania. He completed medical school at Michigan State University and surgical residency at the Dartmouth-Hitchcock Medical Center. Following this, he was an endourology fellow at Washington University Medical Center under the direction of Ralph V. Clayman, practiced at Loyola University Medical Center in Chicago, and rose from the ranks of instructor to full professor in urology and radiology in 8 years. After 10 years, he became a tenured professor at Duke University Medical Center in North Carolina. At Duke, he was co-director of the endourology fellowship and director for the Center of Minimally Invasive and Robotic Urological Surgery.

Dr Albala is chief of urology at Crouse Hospital in Syracuse, New York, and medical director for Associated Medical Professionals (a group of 24 urologists). Considered a national and international authority in laparoscopic and robotic urological surgery, he has been an active teacher in this area for more than 20 years. His research and clinical interests have focused on robotic urological surgery. Further clinical interests include minimally invasive treatment of benign prostatic hypertrophy (BPH) and the use of fibrin sealants in surgery. He has been a visiting professor at numerous institutions across the United States and overseas in countries such as India, China, Iceland, Germany, France, Japan, Brazil, Australia, and Singapore. He has performed operative demonstrations in over 32 countries and 23 states and has trained 16 fellows in endourology and advanced robotic surgery.

He has over 180 publications in peer-reviewed journals and has authored 3 textbooks in endourology and 1 in general urology. On the editorial boards of the Journal of Robotic Surgery, Journal of Endourology, Current Opinions in Urology, and Urology Index and Reviews, he also serves as a reviewer for 8 surgical journals. In addition, Dr Albala is a past White House Fellow who acted as a special assistant to Federico Pena, secretary of transportation, on classified and unclassified public health-related issues.

Matt T. Rosenberg, MD
Medical Director
Mid-Michigan Health Centers
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.

**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 article 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 M. Albala, MD, has no financial relationships to disclose.


Steven A. Kaplan, MD, has no financial relationships to disclose.
**Education Partner Financial Disclosure Statement**

The content collaborators at Integritas Communications report the following:

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

**Suggested Reading List**


SESSION 1
7:45 AM – 9:15 AM

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

SPEAKERS
David M. Albala, MD
Steven A. Kaplan, MD (Virtual Presenter)
Matt T. Rosenberg, MD

Presenter Disclosure Information

The following relationships exist related to this presentation:

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Medications Discussed in Program

• Specific medications
  – Silodosin
  – Tamsulosin
  – Alfuzosin
  – Terazosin
  – Dutasteride
  – Fosfinetron
  – Dutasteride
  – Tadalafil
  – Sildenafil
  – Vardenafil
  – Avanafil
  – Lodenafil
  – Udenafil
  – Darifenacin
  – Solifenacin
  – Tolterodine
  – Terazosin
  – Oxybutynin
  – Fesoterodine
  – Lisinopril
  – Chlorthalidone

Outcomes Question

1. Patients with lower urinary tract symptoms related to benign prostatic hyperplasia will see benefits from 5α-reductase inhibitors within 1 week of treatment initiation.

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly agree
2. Independent of age, erectile function declines with the severity of lower urinary tract symptoms.

1. Strongly disagree  
2. Disagree  
3. Neutral  
4. Agree  
5. Strongly agree

3. Monotherapy with alfuzosin or tamsulosin reduces lower urinary tract symptoms related to benign prostatic hyperplasia by decreasing the size of the prostate over time.

1. Strongly disagree  
2. Disagree  
3. Neutral  
4. Agree  
5. Strongly agree

4. How often do you CURRENTLY specifically assess patients with lower urinary tract symptoms related to benign prostatic hyperplasia for erectile dysfunction?

1. Never  
2. 25% of the time  
3. 50% of the time  
4. 75% of the time  
5. 100% of the time

5. How often do you CURRENTLY recommend self-management approaches to your patients with lower urinary tract symptoms related to benign prostatic hyperplasia?

1. Never  
2. 25% of the time  
3. 50% of the time  
4. 75% of the time  
5. 100% of the time

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

BPH-LUTS and Metabolic Syndrome  
Epidemiologic Relationships

BPH-LUTS is more common in patients with:
- Central obesity
- Insulin resistance
- Dyslipidemia
- Hypertension
**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:
  - α-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

---

**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**

- BPH: Histologic stromal glandular 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

---

**Prostate Volume**

*Progressive Hyperplasia*

A 55-year-old man with a prostate volume of 30 mL and BPH-LUTS can expect a doubling of prostate size in the next 15 years.

---

**Note:**


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**Scientific Primer in BPH-LUTS**

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**Note:**

Urinary Flow Rate Decreases With Age

N=2113 randomly selected men 40–79 years of age with no history of prostate surgery, prostate cancer, or other diseases known to interfere with normal voiding.


Case Study
Robert

- 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?

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
- 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)

Clinical Interview for Male LUTS
Symptom Categorization

Storage
- Frequency
- Urgency

Voiding
- Hesitancy
- Intermittency

Postmicturition
- Dribbling
- Incontinence

- Straining to Start/Continue

IPSS Urinary Symptoms

<table>
<thead>
<tr>
<th>Category</th>
<th>Not at all</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2. Have you had to urinate again less than 2 hours after your last urination?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3. Have you found you stopped and started several times while urinating?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4. Have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5. Have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>6. Have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7. 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?</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Total for Urinary Symptoms: 0-35

Voiding Diary
Evaluation of Frequency and Volume

- Differentiate among LUTS pathologies
- Alert patients to modifiable habits and opportunities for change
- Monitor treatment progress and efficacy
- Typically record for 3-7 days
  - Voids frequency and timing
  - Number and characteristics of incontinence episodes
  - Fluid intake
  - Other urinary symptoms

Erectile Function and LUTS Severity
Examine Sexual Function

N=10,636 men who had been sexually active within the last 4 weeks.
IIEF, International Index of Erectile Function.


ROCK, Rho-associated protein kinase.

Common Pathogenetic Mechanisms: BPH-LUTS and Erectile Dysfunction

- Reduced NO–cGMP Signaling
- Increased RhoA–ROCK Signaling
- Autonomic Hyperactivity
- Pelvic Atherosclerosis

BPH-LUTS, Erectile Dysfunction, and Metabolic Abnormalities

Medication Effects in BPH-LUTS

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<thead>
<tr>
<th>Medication</th>
<th>LUTS-Related Effect</th>
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<td>Confusion, secondary incontinence</td>
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<td>Alcohol, caffeine, diuretics</td>
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<td>α-Agonists</td>
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LUTS Evaluation
Focused Physical Exam

Evaluation Targets
- Abdominal palpation: Tenderness, masses, bladder distension
- Genitalia exam: Meatus, testes, foreskin
- Neurologic exam: General mental status, ambulatory status, motor function
- DRE: Rectal tone, nodules, pain, prostate size, shape, consistency


Consider Co-occurring Issues
Common Comorbidities in BPH-LUTS

Registry Patients, %

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Evaluate Risks for BPH Progression

Risk of Prostate Biopsy or Cancer Diagnosis

Men With LUTS

Management Recommendations

LUTS in Men

Robert
Clinical Workup

Recommended Tests

LUTS Cause Little or No Bother

Informed Surveillance

Robert
Clinical Workup

Recommended Tests

LUTS Cause Little or No Bother

Informed Surveillance

Management Recommendations

LUTS With Little or No Bother

LUTS workup
  • IPSS, 19 (moderate)
  • Frequency
  • Poor flow and intermittency
  • Strains to urinate
  • PSA level, 1.7 ng/mL
  • DRE, firm and asymmetrically enlarged with no nodules
  • Urinalysis, no abnormalities
  • Sexual function
  • Some trouble over last year attaining an erection

How would you initiate treatment for Robert?

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

BMI, body mass index; BP, blood pressure.
### Management Recommendations

#### Bothersome LUTS in Men

**Predominant Significant Nocturia**

- Frequency/Volume Chart
- Polyuria
- No Polyuria
- Polyuria, 24-hour output 25 L/s
- Nocturnal polyuria, 25% output at night
- Fluid intake reduced, consider other causes

**Recommended Tests**

- Bohrson's LUTS
- Standard Treatment
- Drug treatment

**Relief From Bothersome LUTS**

- Continue Treatment
- Failure

**Detailed Management**

- Lifestyle and fluid intake reduced
- Nocturnal polyuria
- 23% output at night

### 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>Moderate</td>
<td>Vigorous</td>
</tr>
<tr>
<td>Meigs et al, 2001</td>
<td>Moderate</td>
<td>Vigorous</td>
</tr>
<tr>
<td>Lacey et al, 2005</td>
<td>Moderate</td>
<td>Vigorous</td>
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<tr>
<td>Del Meco et al, 2006</td>
<td>Moderate</td>
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<tr>
<td>Rohmann et al, 2005</td>
<td>Moderate</td>
<td>Vigorous</td>
</tr>
<tr>
<td>Hong et al, 2006</td>
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<tr>
<td>Combined</td>
<td>Moderate</td>
<td>Vigorous</td>
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**Odds Ratios**

- Moderate: 0.19, 95% CI: 0.60-0.92
- Vigorous: 0.74, 95% CI: 0.59-0.92

### BPH-LUTS Management

#### Pharmacologic Therapy

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Common Side Effects</th>
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<tbody>
<tr>
<td>α-Blockers</td>
<td>Erectile dysfunction, abdominal distention, dysuria, nocturia, hematuria, hemoglobinuria, fatigue, nasal congestion, headache, dry mouth, dry eyes</td>
</tr>
<tr>
<td>5-ΑRIs</td>
<td>Erectile dysfunction, abdominal distention, dysuria, nocturia, decreased PSA level</td>
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<tr>
<td>PDE-5 Inhibitors</td>
<td>Headache, impotence, back pain, flushing, nasal congestion</td>
</tr>
<tr>
<td>Antimuscarinic agents</td>
<td>Constipation, dry mouth, dry eyes, headache</td>
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<td>Dual drug products</td>
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**Recommended Tests**

- Informed Surveillance for BPH-LUTS
- Standard Treatment
- Drug treatment

**Relief From Bothersome LUTS**

- Continue Treatment

**Detailed Management**

- Lifestyle and fluid intake reduced
- Nocturnal polyuria
- 23% output at night

### 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?**
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

Roehrborn CG.

RRR, reduction in relative risk.

N=4844 men

aPSA <1.5 ng/mL suggests small gland; PSA

Abrams P, et al.

MIST, minimally invasive surgical treatment; OAB, overactive bladder.

Antimuscarinics

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Behavioral Therapy

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Combination therapy reduced the relative risk of AUR or BPH-related surgery 68.8%, compared with tamsulosin (α-blocker) monotherapy

19.8% compared with tamsulosin (5-ARI) monotherapy

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19.8% compared with tamsulosin (5-ARI) monotherapy

Early vs Delayed Combinations

5-ARI and α-Blocker

AUR: 49.7% vs 31.8%

Surgery: 28.2% vs 19.2%

Total Costs: $15,000 vs $12,000

Better Outcomes With Delayed Combination Therapy

Early combination therapy, initiation of an α-blocker and a 5-ARI on the same day or a 5-ARI within 30 days of initial α-blocker treatment, was associated with a significant reduction in AUR, surgery, and total costs.

Is Robert a candidate for combination therapy?

Which combinations?

Combination Therapy

MTOPS Study

RRR=31.1%

RRR=67.6%

RRR=70.6%

RRR=65.8%

RRR=18.3%

RRR=31.2%

RRR=65.8%

RRR=44.1%

RRR=19.6%

RRR=34.7%

RRR=44.6%

RRR=31.6%

RRR=53.6%

RRR=18.0%

RRR=41.7%

RRR=18.0%

RRR=27.0%

RRR=47.4%

RRR=54.7%

RRR=74.1%

RRR=17.7%

RRR=24.5%

RRR=17.7%

RRR=42.5%

RRR=32.0%

RRR=13.9%

RRR=47.4%

RRR=17.7%

RRR=24.5%

RRR=17.7%

RRR=42.5%

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RRR=42.5%

RRR=32.0%
These studies examined the PDE-5 inhibitors tadalafil, sildenafil, and vardenafil, and the \(\alpha\)-blockers alfuzosin and tamsulosin.


Kaplan et al, 2007

Bechara et al, 2008

Liguori et al, 2009

Gacci et al, 2012

Overall

<table>
<thead>
<tr>
<th>Source</th>
<th>IPSS Mean Differences</th>
<th>IIEF Score Mean Differences</th>
<th>Qmax Mean Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaplan et al, 2007</td>
<td>-6</td>
<td>-4</td>
<td>-2</td>
</tr>
<tr>
<td>Bechara et al, 2008</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Liguori et al, 2009</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Gacci et al, 2012</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Tuncel et al, 2009

\(\alpha\)-blocker + PDE-5 inhibitor

\(\alpha\)-blocker alone

\(\alpha\)-blocker + PDE-5 inhibitor

Compared with \(\alpha\)-blockers alone, the combination regimens significantly improved IPSS \((P=0.05)\), IIEF scores \((P<0.0001)\), and Qmax \((P<0.0001)\).

\(\alpha\)-blocker + PDE-5 inhibitor

\(\alpha\)-blocker alone

\(\alpha\)-blocker + PDE-5 inhibitor

\(\alpha\)-blocker + PDE-5 inhibitor

\(\alpha\)-blocker alone

\(\alpha\)-blocker + PDE-5 inhibitor

Robert

Treatment Tailoring

• 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
  - Alphuzosin 10 mg daily
  - Self-report of some erectile dysfunction

• The PCP considers adding a 5-ARI or PDE-5 inhibitor to the treatment regimen

If a PDE-5 inhibitor is prescribed, how should it be dosed?

Robert

Treatment Tailoring

• 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
  - Alphuzosin 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 α-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

Question #1
Which of the following patient characteristics should be included in the case study?
1. Mild hepatic impairment due to a history of excessive alcohol intake
2. Disturbed sleep and daytime fatigue
3. A large waist circumference

Question #2
Which of the following comorbid conditions should be included in the case study?
1. Type 2 diabetes
2. Controlled hypertension
3. Chronic pelvic pain syndrome
How does the fact that Joseph has mild hepatic impairment due to a history of excessive alcohol intake affect your approach to patient assessment or treatment?

**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\(^1\)-\(^4\)
    - 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\(^5\),\(^6\)
    - These agents are metabolized extensively in the liver, and caution is required for individuals with abnormal liver function

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 individuals\(^1\)
- CAMUS trial\(^2\)
  - 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 parameters\(^3\)

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 voiding\(^1\)
- Mechanistic relationships between obesity, erectile dysfunction, and BPH-LUTS
  - Obese men have relatively low testosterone/high estrogen hormonal profiles\(^2\),\(^3\)
    - May increase risks of BPH-LUTS and erectile dysfunction
  - Hyperinsulinemia may induce prostate growth\(^2\),\(^3\)
- 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

---

**Build-a-Case**

**Question #3**

Which of the following methods would you find most helpful to evaluate this patient with LUTS?

1. DRE
2. PSA test
3. Serum creatinine measurement
4. 1 and 2
5. All of the above

---

**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

---

**Additional Considerations for BPH-LUTS**

**Diabetes**

- Diabetes-Related Insulin Resistance, Hyperinsulinenia and/or Hyperglycemia

---

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

---

**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


**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**

**Question #4**

How would you restructure Joseph’s treatment regimen?

1. Discontinue silodosin and initiate terazosin
2. Discontinue silodosin and initiate dutasteride
3. Discontinue silodosin and initiate tadalafl
4. Continue silodosin and initiate finasteride
5. Continue silodosin and initiate tadalafl

**Current treatment**

Silodosin 8 mg daily

**Joseph**

**Tailoring Treatment**

- 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


**Demographic Question**

How many patients with lower urinary tract symptoms related to benign prostatic hyperplasia do you see each week?

1. None
2. 1-10
3. 11-20
4. 21-30
5. More than 30
Outcomes Question

1. Patients with lower urinary tract symptoms related to benign prostatic hyperplasia will see benefits from 5α-reductase inhibitors within 1 week of treatment initiation.
   1. Strongly disagree
   2. Disagree
   3. Neutral
   4. Agree
   5. Strongly agree

Outcomes Question

2. Independent of age, erectile function declines with the severity of lower urinary tract symptoms.
   1. Strongly disagree
   2. Disagree
   3. Neutral
   4. Agree
   5. Strongly agree

Outcomes Question

3. Monotherapy with alfuzosin or tamsulosin reduces lower urinary tract symptoms related to benign prostatic hyperplasia by decreasing the size of the prostate over time.
   1. Strongly disagree
   2. Disagree
   3. Neutral
   4. Agree
   5. Strongly agree

Outcomes Question

4. After attending this educational activity, how often do you NOW PLAN TO specifically assess patients with lower urinary tract symptoms related to benign prostatic hyperplasia for erectile dysfunction?
   1. Never
   2. 25% of the time
   3. 50% of the time
   4. 75% of the time
   5. 100% of the time

Outcomes Question

5. After attending this educational activity, how often do you NOW PLAN TO recommend self-management approaches to your patients with lower urinary tract symptoms related to benign prostatic hyperplasia?
   1. Never
   2. 25% of the time
   3. 50% of the time
   4. 75% of the time
   5. 100% of the time

Question & Answer