Benign Prostatic Hyperplasia: Optimizing Management in the Primary Care Setting

Educational Partner: Asante Communications, LLC

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Session 2: Benign Prostatic Hyperplasia: Optimizing Management in the Primary Care Setting

Learning Objectives
1. Conduct an initial and ongoing assessment of patients with benign prostatic hyperplasia (BPH), addressing lower urinary tract symptoms (LUTS), coexisting disorders, and patient quality of life and function.
2. Evaluate the risk of BPH disease progression and complications.
3. Teach patients with BPH-LUTS practical self-management approaches and behavioral modifications to slow disease progression.
4. Evaluate the clinical profiles and utility of 5-α reductase inhibitors (5-ARIs), α-1 adrenergic receptor blockers, and phosphodiesterase-5 (PDE-5) inhibitors for patients with BPH-LUTS with and without erectile dysfunction (ED).
5. Tailor monotherapy and multidrug regimens for patients with BPH-LUTS based in part on signs and symptoms, prior medication history, ED and other common comorbidities, risk of disease progression, and patient goals.

Faculty
Martin M. Miner, MD, FAAFP
Clinical Associate Professor of Family Medicine and Urology
The Warren Alpert Medical School of Brown University
Co-Director, Men’s Health Center
Chief of Family and Community Medicine
Miriam Hospital
Providence, Rhode Island

Dr Miner is clinical associate professor of family medicine and urology at the Warren Alpert Medical School of Brown University in Providence, Rhode Island. Within the Lifespan/Brown University system, he is developing a multidisciplinary men’s health center. He is also chief of family and community medicine and co-director of the Men’s Health Center at The Miriam Hospital in Providence.

Dr Miner received his medical degree from the University of Cincinnati College of Medicine in Ohio, and completed his residency at Brown University. He is a member of the American Academy of Family Physicians, Massachusetts Academy of Family Physicians, and American Urological Association. In addition, Dr Miner is a fellow of the Sexual Medicine Society of North America (SMSNA), Inc., and a member of the SMSNA board of directors. He is also a member of the International Society for the Study of Women’s Sexual Health and the steering committee for the International Society of Men’s Health.

Dr Miner is active in several research studies on men’s health. He has published extensively in the areas of erectile dysfunction and cardiovascular disease, benign prostatic hyperplasia and lower urinary tract symptoms, and male sexuality and hormone replacement therapy. He is the author/coauthor of numerous articles in such journals as Cleveland Clinic Journal of Medicine, The Journal of Sexual Medicine, Mayo Clinic Proceedings, and American Journal of Medicine. He also serves on several editorial boards.

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

Matt T. Rosenberg, MD, earned his medical degree at the University of California, Irvine. He trained in general surgery at the University of California, Irvine, and in urologic surgery at the Brigham and Women’s Hospital in Boston before changing fields to general practice. Dr Rosenberg now practices in Jackson, Michigan, and serves as medical director of Mid-Michigan Health Centers. He is also actively on the staff of the Foote Health System, where he served as chief of the department of family medicine from 2002 to 2006.

Dr Rosenberg has a special interest in the medical management of urologic diseases and has authored and coauthored articles appearing in Urology, the Journal of Urology, BJU International, and other peer-reviewed journals. He has presented his original research at many national meetings, including those of the National Institutes of Health, the American Urological
Association, the Sexual Medicine Society of North America, and the European Society for Sexual Medicine. He is a reviewer for several national and international journals and was recently selected to be the section editor of urology for the *International Journal of Clinical Practice*.

Dr Rosenberg was honored as the most recent recipient of the Continence Care Champion award by the National Association For Continence (NAFC). This nationwide award is bestowed by the NAFC board of directors to a healthcare provider who has distinguished himself in research, clinical practice, and education with accomplishments meaningful to continence care.

In the summer of 2006, Dr Rosenberg was featured in a PBS documentary on interstitial cystitis as part of the *Healthy Body, Healthy Mind* series, which focused on some of his research findings in this clinical area.

**Faculty Financial Disclosure Statements**

The presenting faculty reports the following:

Martin M. Miner, MD, serves as a consultant for Abbott Laboratories and receives research grants from Auxilium Pharmaceuticals, Inc.

Matt T. Rosenberg, MD, serves as a consultant for Astellas Pharma US, Inc.; Eli Lilly and Company; Ferring Pharmaceuticals Inc.; Horizon Pharma; and Pfizer Inc. He is on the speakers bureau for Astellas Pharma US, Inc.; Forest Laboratories, Inc.; Horizon Pharma; Ortho-McNeil-Janssen Pharmaceuticals, Inc; and Pfizer Inc.

**Education Partner Financial Disclosure Statement**

The content collaborators at Asante Communications, LLC, have reported the following: Christopher S. Ontiveros, PhD, Group Scientific Supervisor, has no financial relationships to disclose.

**Suggested Reading List**


Pharmacotherapeutic Agents in this Program

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfuzosin</td>
<td>Uroxatral®</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>Cardura®, Cardura XL®</td>
</tr>
<tr>
<td>Dutasteride</td>
<td>Avodart®</td>
</tr>
<tr>
<td>Finasteride</td>
<td>Propecia®, Proscar®</td>
</tr>
<tr>
<td>Metformin</td>
<td>Fortamet®, Glucophage®, Glucophage XR®, Glumetza®, Riomet®</td>
</tr>
<tr>
<td>Pioglitazone hydrochloride</td>
<td>Actos®</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Revatio®, Viagra®</td>
</tr>
<tr>
<td>Silodosin</td>
<td>Rapaflo®</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>Adcirca®, Cialis®</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>Flomax®</td>
</tr>
<tr>
<td>Terazosin</td>
<td>Hytrin®</td>
</tr>
<tr>
<td>Vardenafil</td>
<td>Levitra®, Staxyn®</td>
</tr>
</tbody>
</table>

XL, extended release; XR, extended release.

Benign Prostatic Hyperplasia

Optimizing Management in the Primary Care Setting

Faculty

Matt T. Rosenberg, MD
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Chief, Department of Family Medicine
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Martin M. Miner, MD
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Co-Director, Men’s Health Center
Maimonides Hospital
Providence, Rhode Island

Educational Objectives

Upon completion of this CME initiative, participants should be better prepared to:
1. Conduct an initial and ongoing assessment of patients with benign prostatic hyperplasia (BPH), addressing lower urinary tract symptoms (LUTS), coexisting disorders, and patient quality of life and function
2. Evaluate the risk of BPH disease progression and complications
3. Teach patients with BPH-LUTS practical self-management approaches and behavioral modifications to slow disease progression
4. Evaluate the clinical profiles and utility of 5-α reductase inhibitors (5-ARIs), α-1 adrenergic receptor blockers, and phosphodiesterase-5 (PDE-5) inhibitors for patients with BPH-LUTS with and without erectile dysfunction (ED)
5. Tailor monotherapy and multidrug regimens for patients with BPH-LUTS based in part on signs and symptoms, prior medication history, ED and other common comorbidities, risk of disease progression, and patient goals

Pre-Activity Evaluation

- In men with LUTS, frequency and nocturia are usually associated with bladder problems whereas hesitancy and poor flow are usually associated with prostate problems.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Pre-Activity Evaluation

- Alfuzosin and tamsulosin monotherapy reduce the risk of BPH-LUTS disease progression.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree
Pre-Activity Evaluation

• Physical activity reduces the risk of BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Pre-Activity Evaluation

• Compared to either drug alone, combination therapy with tamsulosin and dutasteride is significantly more effective at reducing clinical progression of BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Pre-Activity Evaluation

• Phosphodiesterase-5 inhibitor monotherapy reduces BPH-LUTS and ED.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Pre-Activity Evaluation

• Tamsulosin monotherapy reduces BPH-LUTS and ED in patients with both conditions.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Pre-Activity Evaluation

• I currently obtain serum PSA measurements in patients with LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Pre-Activity Evaluation

• I currently recommend self-management approaches to my patients who have BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree
Pre-Activity Evaluation

- I currently consider combination pharmacotherapy for my patients with BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Establishing BPH-LUTS as a Clinical Construct
Assessment and Diagnosis in Primary Care

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

Prostate Function

- Normal Function
  - Does not grow (enlarge) into the urethra allowing unobstructed urinary flow
  - Contributes to continence mechanism
  - Produces fluid for seminal emission

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

BPH Is a Histologic Construct

- Progressive disease associated with stromal-glandular hyperplasia within the prostate

Bladder Function

Filling, Storage, and Voiding

- Normal function
  - Storage capacity (300 – 400 mL)
    - Adequate low pressure urinary storage (bladder)
    - Adequate outlet resistance (sphincter)
  - Empty to completion (minimal residual)
    - Adequate bladder contraction
    - Absence of outlet obstruction

- Abnormal function
  - Voiding frequently small amounts
    - Uncontrollable urge (urgency) to empty with frequency
  - Incomplete emptying
    - Hesitancy, poor stream, feeling of incomplete emptying

Overactive Bladder

- Syndrome that includes urinary urgency (intense, sudden desire to void) with or without incontinence, urinary frequency, and nocturia
- Present without any pathologic or metabolic disorders that might otherwise result in symptoms
- Etiology is heterogeneous and may result from abnormal signaling, a sensory amplification (afferent), or increased motor output (efferent)
Male Lower Urinary Tract Symptoms

**BPH-LUTS vs OAB**

<table>
<thead>
<tr>
<th>Storage (bladder/OAB)</th>
<th>Voiding (prostate/BPH-LUTS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgency</td>
<td>Hesitancy</td>
</tr>
<tr>
<td>Frequency</td>
<td>Poor flow/weak stream</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Intermittency</td>
</tr>
<tr>
<td>Urge incontinence</td>
<td>Straining to void</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>Terminal dribble</td>
</tr>
<tr>
<td>Mixed incontinence</td>
<td>Prolonged urination</td>
</tr>
<tr>
<td>Overflow incontinence</td>
<td>Urinary retention</td>
</tr>
</tbody>
</table>

Many patients exhibit both OAB and BPH-LUTS

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**Prevalence and bother of urinary symptoms in BPH-LUTS**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>BPH-LUTS Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder Pain</td>
<td>40</td>
</tr>
<tr>
<td>Urgency</td>
<td>35</td>
</tr>
<tr>
<td>Pooling, Draining</td>
<td>25</td>
</tr>
<tr>
<td>Frequency</td>
<td>20</td>
</tr>
<tr>
<td>Nocturia</td>
<td>15</td>
</tr>
<tr>
<td>Urge</td>
<td>10</td>
</tr>
<tr>
<td>Incomplete Emptying</td>
<td>8</td>
</tr>
<tr>
<td>Intermitiency</td>
<td>5</td>
</tr>
<tr>
<td>Incontinence</td>
<td>5</td>
</tr>
<tr>
<td>Terminal dribble</td>
<td>3</td>
</tr>
</tbody>
</table>

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**BPH-LUTS common comorbidities**

<table>
<thead>
<tr>
<th>Condition</th>
<th>BPH-LUTS Registry Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erectile dysfunction</td>
<td>45</td>
</tr>
<tr>
<td>Hypertension</td>
<td>40</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>35</td>
</tr>
<tr>
<td>Heart disease/heart fail</td>
<td>30</td>
</tr>
<tr>
<td>General pain/inflammation</td>
<td>25</td>
</tr>
<tr>
<td>Digestive tract disorder</td>
<td>20</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15</td>
</tr>
<tr>
<td>Arthritis</td>
<td>10</td>
</tr>
<tr>
<td>Allergies/Cold/Flu/Concentration</td>
<td>5</td>
</tr>
</tbody>
</table>

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**BPH-LUTS and ED common pathophysiologic mechanisms**

- Reduced NO–cGMP signaling
- Increased RhoA–ROCK signaling
- Autonomic hyperactivity
- Pelvic atherosclerosis

**Functional consequences at tissue level**

- Reduced function of nerves and endothelium
- Altered smooth muscle relaxation or contractility
- Arterial insufficiency, reduced blood flow, and hypoxia-related tissue damage

**Comorbidities**

- Hypertension
- Metabolic Syndrome
- Diabetes, etc.
- Chronic inflammation
- Steroid hormone unbalance

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**Erectile function declines with LUTS severity**

<table>
<thead>
<tr>
<th>Severity</th>
<th>LUTS Effect</th>
<th>Age Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal ED</td>
<td>22.2</td>
<td>19.3</td>
</tr>
<tr>
<td>50-59</td>
<td>21.1</td>
<td>18.9</td>
</tr>
<tr>
<td>60-69</td>
<td>19.3</td>
<td>18.9</td>
</tr>
<tr>
<td>70-79</td>
<td>15.8</td>
<td>13.2</td>
</tr>
<tr>
<td>80-89</td>
<td>12.4</td>
<td>10.3</td>
</tr>
<tr>
<td>90+</td>
<td>9.3</td>
<td>7.5</td>
</tr>
</tbody>
</table>

---

**BPH-LUTS and ED complex interrelationship**

<table>
<thead>
<tr>
<th>All Men &gt;40 y</th>
<th>Histologic BPH</th>
<th>EP</th>
<th>BNO</th>
<th>LUTS</th>
</tr>
</thead>
</table>

---

**BPH-LUTS and ED complex interrelationship**

- BOO, bladder outlet obstruction; EP, enlarged prostate; LUTS, lower urinary tract symptoms.

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**BPH-LUTS and ED complex interrelationship**

- BOO, bladder outlet obstruction; EP, enlarged prostate; LUTS, lower urinary tract symptoms.
Dennis
Presentation to PCP

“I'm going to the bathroom more frequently and afraid that my diabetes is getting worse.”

PCP, primary care physician.

LUTS Evaluation
Focused Physical Exam

- Abdominal palpation for tenderness, masses, or bladder distension
- Neurologic evaluation to assess general mental status, ambulatory status, and motor function
- Genitalia exam including the meatus and testes
- Digital rectal exam (DRE) to evaluate rectal tone, prostate size, consistency, nodules, or pain


Voiding Diary
Evaluation of Frequency and Volumes

- Differentiates between behavioral and LUTS pathology
- Alerts the patients to modifiable habits/opportunities
- Monitors treatment progress and efficacy


Medications Can Cause or Exacerbate BPH-LUTS

<table>
<thead>
<tr>
<th>Medication</th>
<th>LUTS-Related Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedatives</td>
<td>Confusion, secondary incontinences</td>
</tr>
<tr>
<td>Alcohol, caffeine, diuretics</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Impaired contractility, voiding difficulty</td>
</tr>
<tr>
<td>α-Agonists</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</td>
<td>Induce cough, stress urinary incontinence</td>
</tr>
<tr>
<td>First-generation anticholinesterases</td>
<td>Increase outlet resistance</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Precipitate urge incontinence</td>
</tr>
</tbody>
</table>

Opioids
Constipation


Relationship Between PSA and Prostate Size

- DRE tends to underestimate prostate size in larger prostates
- PSA is more accurate than a DRE when estimating prostate size
- PSA ≥1.5 ng/mL suggests a prostate volume >30 mL

**Differential Diagnosis of LUTSD**

- Bladder cancer
- Prostate cancer
- Prostatitis
- Bladder stones
- Interstitial cystitis
- Radiation cystitis
- Urinary tract infection
- Diabetes mellitus
- Parkinson's disease
- Primary bladder neck hypertrophy
- Congestive heart failure
- Lumbosacral disc disease
- Multiple sclerosis
- Nocturnal polyuria

Symptom onset may provide a clue to the etiology


---

**Dennis**

**Patient Evaluation**

- **Personal history**
  - 62 years old
  - Married 35 years
- **Medical history**
  - Diagnosed 6 years earlier with type 2 diabetes controlled with medication and diet
  - Metformin ER: 1000 mg daily
  - Pioglitazone hydrochloride: 30 mg daily
- **Symptom onset may provide a clue to the etiology**


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**AUA Symptom Index**

<table>
<thead>
<tr>
<th>Urinary Symptoms</th>
<th>Never</th>
<th>Less Than One Time</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Over the past month, how often have you noticed a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Over the past month, how often have you had a difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>10. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**Total for Urinary Symptoms:**

Mild: 0-7; Moderate: 8-19; Severe: 20-35

AUA, American Urological Association.


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**Risk of BPH Progression**

- Worsening of symptoms
- Deterioration of urinary flow rate
- Increase in prostate volume
- Outcomes such as AUR and need for surgery
- Renal insufficiency
- Recurrent urinary tract infection

PV, prostate volume.


---

**Dennis**

**Patient Interview**

- Are patient-administered questionnaires practical during an often time-constrained primary care visit?
- In your practice, how do you determine the severity of the patient’s symptoms?

---

**Natural History of Disease Progression**

<table>
<thead>
<tr>
<th>Age</th>
<th>55 yrs</th>
<th>60 yrs</th>
<th>65 yrs</th>
<th>70 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td>30 mL</td>
<td>&gt;40 mL</td>
<td>&gt;50 mL</td>
<td>&gt;61 mL</td>
</tr>
<tr>
<td>PSA</td>
<td>1.5 ng/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A 55-year-old man with a 30 mL prostate volume, PSA=1.5 ng/mL, and BPH-LUTS can expect a doubling of prostate size over the next 15 years.

PV, prostate volume.


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*Not uniformly recommended as part of laboratory evaluation in patients with possible LUTS; however, this test provides information about the status of renal function.

BP, blood pressure; BMI, body mass index; bpm, beats per minute; HR, heart rate; LUT, urinary tract infection.

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AUR/BPH-Related Surgery Rates Increase With Increasing Baseline PSA
PLESS Placebo 4-Year Data

Risk Evaluation of BPH-LUTS Progression
Baseline Factors as Predictors

Five risk factors
1. Total prostate volume ≥31 mL
2. PSA ≥1.6 ng/mL
3. Age ≥62
Not usually evaluated by the PCP
4. $Q_{\text{max}}$ <10.6 mL/s
5. PVR ≥39 mL

LUTS and Indications for Referral

• Suspicion of neurologic cause of symptoms
• History of recurrent UTI or other infection
• Findings or suspicion of urinary retention
• Abnormal prostate exam (nodules)
• Microscopic or gross hematuria
• History of genitourinary trauma
• Prior genitourinary trauma
• Uncertain diagnosis
• Meatal stenosis
• Elevated PSA
• Pelvic pain

Conclusions

• BPH is a histologic construct; BPH-LUTS is a clinical construct
• BPH-LUTS is often comorbid with other disorders (eg, ED)
• BPH-LUTS is a progressive disease
• Assessment of BPH-LUTS is based primarily on a focused physical exam and history, laboratory tests, and evaluation of symptom bother

Formulating an Approach to Initial and Ongoing Management of BPH-LUTS in Primary Care

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The Warren Alpert Medical School of Brown University
Co-Director, Men’s Health Center
Chief of Family and Community Medicine
Miriam Hospital
Providence, Rhode Island

Treatment Now Can Be Empiric

• No identifiable etiology
• No reversible causes
• Bother?
  —No, watchful waiting
  —Yes, treatment
    • Weak flow – think prostate
    • Poor voiding volumes – think bladder

**Worse IPSS**

**SM**

**3.1**

**Same IPSS**

**SM**

**Better IPSS**

**2.0**

SM, self-management.

BII, BPH Impact Index; IPSS, international prostate symptom score; QoL, quality of life; SC, standard care; ED, medical treatment and surgery was left to the discretion of the clinician and patient. The SM group included SC as well as 3 small group sessions comprising education, lifestyle advice, and training in problem solving and goal setting.

Brown CT, et al.

**— Diagnosed with BPH-LUTS**

**— What nonpharmacologic treatment recommendations could you provide if the patient prefers not to take medication?**

**— Does his AUA Symptom Index score of 18 (moderate severity) influence your recommended treatment approach?**

— Would your treatment recommendation change if his score indicated mild symptoms or severe symptoms?

**Medical Management of BPH-LUTS±ED**

<table>
<thead>
<tr>
<th>Predominant Bladder Outlet Obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Gland and/or Low PSA*</td>
</tr>
<tr>
<td>*α-Blocker</td>
</tr>
<tr>
<td>Larger Gland and/or Higher PSA†</td>
</tr>
<tr>
<td>*5α-Reductase Inhibitor</td>
</tr>
<tr>
<td>PDMS Inhibitor</td>
</tr>
</tbody>
</table>

PSA*: <1.5 ng/mL, *PSA: >1.5 ng/mL.

BDO, bladder outlet obstruction; PDMS, phosphodiesterase 5. American Urological Association (AUA) defines BDO as the generic term for all forms of obstruction to the bladder outlet, eg, anatomical, structural, or functional etiology. Lower urinary tract symptoms (LUTS) associated with BDO are classified into 4 types: (1) obstruction, (2) irritative voiding, (3) obstructive/irritative, and (4) neurogenic bladder.

**α-Adrenergic Receptor Antagonists**

- Relieve BDO by inhibiting α1-adrenergic-mediated contraction and relaxing smooth muscle contraction of the urethra and bladder.
- Symptomatic relief usually occurs within the first week of treatment.
- Potential side effects are decreased with unselective agents

<table>
<thead>
<tr>
<th>1A</th>
<th>1B</th>
<th>1D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphodiesterase</td>
<td>Alpha 1 blocker</td>
<td>Alpha 2 blocker</td>
</tr>
</tbody>
</table>

**Side Effects**
- DOXAZOSIN: Dizziness, dry mouth, drowsiness, fatigue, somnolence
- TANZOSIN: Dizziness, upper respiratory tract infection
- ALFUSIZON: Dizziness, increased cough, infection
- TAMSULOSIN: Retinal detachment, visual disturbances
- TEREZOSIN: Nausea, vomiting, diarrhea

*Adverse effects present in <1% of treated vs non-treated subjects.*

**Progression was defined by an increase of**
- *PSA <1.5 ng/mL; †PSA >1.5 ng/mL.*

**Relieve BOO by Inhibiting α1-Adrenergic Receptors**

- **Combination Therapy**
  - Allows for immediate symptom relief from the α-blocker while facilitating prostate reduction from the 5α-reductase inhibitor.

**Rationale for Combination Therapy**

- Blocks conversion of testosterone to DHT, shrinking the prostate and preventing further growth
- Improves flow and bothersome symptoms similar to α-blockers but may take 3–6 months

- **Small Gland and/or Low PSA**
  - Predominant Bladder Outlet Obstruction
  -およびα-blocker

- **Larger Gland and/or Higher PSA**
  - Predominant Bladder Outlet Obstruction
  - α-blocker + 5α-reductase inhibitor

**Combination Therapy**

- MTOPS Study
  - **RRR=65.8%**
  - **RRR=19.6%**

- **CombAT Study**
  - **RRR=15.1%**
  - **RRR=6.1%**

**5α-Reductase Inhibitors Regulate Prostate Growth and BPH Development**

- Dutasteride (Type I and II 5α-reductase Inhibitor)
- Finasteride (Type II 5α-reductase Inhibitor)

**Prostate Growth and BPH Development**

- **PSA ~50% reduction**
- **DHT ~98% reduction**
- **Intraprostatic volume ~25% reduction**
- **Half-life 5 weeks <1 day**
- **Reduced incidence of AUR or BPH-related surgery**

*Adverse effects present in <12% of treated vs non-treated subjects.*

**α-Blockers reduce symptoms but not the risk of AUR or BPH-related surgery.**

**CombAT Study**

- **RRR=19.6%**
- **RRR=6.1%**
Management of Patient With ED and BPH-LUTS

Common Clinical Questionnaires

- International Prostate Symptom Score (IPSS) assesses:
  - Incomplete emptying
  - Frequency
  - Intermittency
  - Urgency
  - Weak stream
  - Straining
  - Nocturia
  - Quality of life
- Clinical interpretation of IPSS:
  - Mildly symptomatic: 0-7
  - Moderately symptomatic: 8-19
  - Severely symptomatic: 20-35

- International Index of Erectile Function (IIEF) score assesses:
  - Erectile function
  - Orgasmic function
  - Sexual desire
  - Intercourse satisfaction
  - Overall satisfaction
- Clinical interpretation of IIEF score:
  - Severe dysfunction, 0-4
  - Moderate dysfunction, 5-10
  - Mild to moderate dysfunction, 11-17
  - Mild dysfunction, 18-21
  - No dysfunction, 22-25

Sildenafil at 12 Weeks Reduces Symptoms in BPH-LUTS+ED

Vardenafil at 8 Weeks Reduces Symptoms in BPH-LUTS±ED

Phosphodiesterase 5 Inhibitors

<table>
<thead>
<tr>
<th>PDE5 Inhibitor</th>
<th>Indication</th>
<th>Adverse Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sildenafil</td>
<td>Erectile dysfunction</td>
<td>Abnormal vision, diarrhea, dyspepsia, flushing, headache, nasal congestion</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>Erectile dysfunction and the signs of BPH</td>
<td>Back pain, dyspepsia, flushing, headache, limb pain, myalgia, nasal congestion</td>
</tr>
<tr>
<td>Vardenafil</td>
<td>Erectile dysfunction</td>
<td>Dyspepsia, flushing, headache, rhinitis, sinusitis</td>
</tr>
</tbody>
</table>

*Adverse effects present in ≥2% of treated vs non-treated subjects.
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020895s036lbl.pdf
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021400s013lbl.pdf
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021368s20s21lbl.pdf
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021368s29bl.pdf

Increasing IIEF-EF denotes improvement in erectile function; Decreasing IPSS denotes reduced LUTS.

Vardenafil is not FDA approved for the treatment of BPH-LUTS.

*Adverse effects present in <2% of treated vs non-treated subjects.
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020895s036lbl.pdf
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021400s013lbl.pdf
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021368s20s21lbl.pdf
http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021368s29bl.pdf

Phosphodiesterase 5 Inhibitor Therapy

Potential Overlapping Role in BPH-LUTS and ED

- Alters signaling pathways (eg, NO/cGMP and smooth muscle relaxation)
- Modulates ANS overactivity and afferent nerve activity from bladder and prostate
- Increases pelvic blood perfusion reducing lower urinary tract chronic ischemia
- Reduces inflammation
Tadalafil and Tamsulosin Monotherapy

BPH-LUTS and ED

• Tadalafil or tamsulosin monotherapy similarly reduced BPH-LUTS
• Tadalafil reduced erectile dysfunction

![Graph showing the change in IPSS and IIEF-EF scores with different treatments over time.]

IIEF-EF, International Index of Erectile Function-Erectile Function Domain; LS, least square.


IPSS Score,

<table>
<thead>
<tr>
<th>Duration of Treatment, Weeks</th>
<th>Tadalafil 5 mg</th>
<th>Tamsulosin 0.4 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
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</tr>
</tbody>
</table>

Tadalafil 5 mg Tamsulosin 0.4 mg Placebo

• Tadalafil or tamsulosin monotherapy similarly reduced BPH-LUTS
• Tadalafil reduced erectile dysfunction

PDE5 Inhibitors + α-Blockers

BPH-LUTS, ED, and Flow Rate

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

Compared with monotherapy, α-blocker + PDE5 inhibitor combination therapy results in greater IPSS, IIEF, and Qmax improvement.

PDE5 inhibitors included in the meta-analyses are sildenafil, tadalafil, vardenafil, and UK-369003; α-blockers included in the meta-analyses are alfuzosin and tamsulosin.


Dennis

• What pharmacologic treatment would you recommend for Dennis’ BPH-LUTS?
• How would you restructure therapy if Dennis’ diabetes remains well controlled and his LUTS persist at a 3-month follow-up appointment?
• Would a comorbid diagnosis of ED influence your treatment choice?

Conclusions

• Behavioral modifications and pharmacotherapy comprise potential treatment approaches for BPH-LUTS
• Treatment regimens are based in part on signs and symptoms, medication history, comorbidities, risk of disease progression, and patient preferences
• Combination therapy with an α-blocker and 5α-reductase inhibitor is significantly more effective at reducing clinical progression than either drug alone
• PDE5 inhibitors are a newly available pharmacotherapy to reduce LUTS and ED

Post-Activity Evaluation

• In men with LUTS, frequency and nocturia are usually associated with bladder problems whereas hesitancy and poor flow are usually associated with prostate problems.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Post-Activity Evaluation

• Alfuzosin and tamsulosin monotherapy reduce the risk of BPH-LUTS disease progression.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree
Post-Activity Evaluation
• Physical activity reduces the risk of BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Post-Activity Evaluation
• Compared to either drug alone, combination therapy with tamsulosin and dutasteride is significantly more effective at reducing clinical progression of BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Post-Activity Evaluation
• Phosphodiesterase-5 inhibitor monotherapy reduces BPH-LUTS and ED.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Post-Activity Evaluation
• Tamsulosin monotherapy reduces BPH-LUTS and ED in patients with both conditions.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Post-Activity Evaluation
• I now plan to obtain serum PSA measurements in patients with LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Post-Activity Evaluation
• I now plan to recommend self-management approaches to my patients who have BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree
Post-Activity Evaluation

• I now plan to consider combination pharmacotherapy for my patients with BPH-LUTS.
  1. Strongly Disagree
  2. Disagree
  3. Neutral
  4. Agree
  5. Strongly agree

Audience Question & Answer Session