Management of Lower Urinary Tract Symptoms (LUTS) in Older Men

Victoria Sharp, MD, MBA, FAAFP
Clinical Professor of Urology and Family Medicine

Conflict of Interest

Victoria Sharp, MD, MBA, FAAFP
Market Chief Medical Officer
AmeriHealth Caritas Family of Companies
Office phone: (515) 330-3740
Cell phone: (319) 331-3815
Email: vsharp@amerihealthcaritas.com

Learning Objectives
1. Describe the presenting signs and symptoms associated with Lower Urinary Tract Symptoms.
2. Describe the various methods used in the initial evaluation of LUTS.
3. Understand the natural history of LUTS/BPH and complications based on progression.
4. Be aware of the various treatment modalities for LUTS and the appropriate context in which they are used.
**Terminology**
- Lower urinary tract symptoms (LUTS) secondary to BPH (LUTS/BPH)
- Lower urinary tract symptoms independent of BPH
- Overactive bladder syndrome—urgency w or w/o urge incontinence, usually with frequency and nocturia
- Bladder outlet obstruction (BOO)—generic term for all forms of obstruction
- Benign Prostatic Hyperplasia (BPH)—pathological term
- Detrusor overactivity—urodynamic term
- Benign prostatic obstruction (BPO)—pressure flow studies term

**Definition**
- An increase in the numbers of stromal cells in the transition zone of the prostate
- An increase in the number of alpha-1 receptors

**Can Affect Quality of Life (Bother)**
- Interference with activities of daily living
- Interference with psychological well being
- Interference with sleep
Prostate growth is dependent on:
- Time (aging)
- Presence of androgen (primarily Testosterone)
- Dihydrotestosterone (DHT) – concentrated intranuclearly primarily in prostatic stromal cells

Resistance is increased by:
- Prostate volume
- Alpha-1 adrenergic stimulation – concentrated in prostatic smooth muscle at bladder neck

*Degree of bladder outlet obstruction doesn’t always correlate with severity of symptoms
### Suggestive Symptoms

<table>
<thead>
<tr>
<th>Obstructive (Voiding)</th>
<th>Irritative (Storage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weak stream</td>
<td>Frequency</td>
</tr>
<tr>
<td>Prolonged micturition</td>
<td>Nocturia</td>
</tr>
<tr>
<td>Straining</td>
<td>Urgency</td>
</tr>
<tr>
<td>Hesitancy</td>
<td>Incontinence</td>
</tr>
<tr>
<td>Intermittent stream</td>
<td></td>
</tr>
<tr>
<td>Feeling of incomplete bladder emptying</td>
<td></td>
</tr>
</tbody>
</table>

### Complications

- Urinary retention
- Renal impairment
- Urinary tract infection
- Gross hematuria
- Bladder stones
- Bladder damage (trabeculations, cellules, diverticula)
- Urge/overflow incontinence

### Initial Evaluation

- History and AUA symptom score
- Physical examination
- Including DRE and neurological evaluation
- Urinalysis, Urine culture
- Creatinine, BUN (with high PVR – not routinely recommended)
- PSA (as appropriate)
AUA Symptom Index (AUA–SI)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete emptying</td>
<td>0 – Not at all</td>
</tr>
<tr>
<td>Frequency</td>
<td>1 – Less than 1 time in 5</td>
</tr>
<tr>
<td>Intermittency</td>
<td>2 – Less than half the time</td>
</tr>
<tr>
<td>Urgency</td>
<td>3 – About half the time</td>
</tr>
<tr>
<td>Weak stream</td>
<td>4 – More than half the time</td>
</tr>
<tr>
<td>Straining</td>
<td>5 – Almost always</td>
</tr>
<tr>
<td>Nocturia: number of events per night (0–5)</td>
<td></td>
</tr>
</tbody>
</table>

AUA Symptom Index (AUA–SI)

<table>
<thead>
<tr>
<th>Classification</th>
<th>AUA–SI Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>0–7</td>
</tr>
<tr>
<td>Moderate</td>
<td>8–19</td>
</tr>
<tr>
<td>Severe</td>
<td>20–35</td>
</tr>
</tbody>
</table>

PSA Testing

- Increases detection rate for prostate cancer over DRE alone

<table>
<thead>
<tr>
<th>Age range</th>
<th>PSA values (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>0.00–2.50</td>
</tr>
<tr>
<td>50–59</td>
<td>0.00–3.50</td>
</tr>
<tr>
<td>60–69</td>
<td>0.00–4.50</td>
</tr>
<tr>
<td>70–79</td>
<td>0.00–6.50</td>
</tr>
</tbody>
</table>

- Nonspecific for prostate cancer
Evaluation

Objective diagnostic data
- PVR
- Uroflow/BVI (urinary flow/pressure study)
- Cystoscopy
- Urodynamic Studies
- Transrectal ultrasound
- Urine cytology (irritative symptoms)

Uroflow/BVI

Differential Diagnosis of Lower Urinary Tract Symptoms Includes...

- BPH
- Overactive bladder
- Prostate cancer
- Bladder cancer
- Urinary tract infection
- Urethral stricture
- Neurogenic bladder — neurologic conditions
Summary

- Patient history, physical exam and appropriate laboratory tests for initial evaluation
- Differential diagnosis and rule out prostate cancer
- Assess risk of LUTS/BPH-related outcomes
- Discuss treatment options

Questions

- What are the differences in treating men vs women?
- How common are UTIs in older men?
- How do you decide to treat if not symptomatic?
- When and how to use UA/micro/culture?
- What are the common organisms?
- Are there new resistant organisms arising that make treatment more difficult?

Goals of Treatment

- Alleviate bothersome symptoms
- Alteration of disease progression
- Prevent complications (AUR, surgery)
General Recommendations

› Avoid substances that exacerbate symptoms or cause retention
  • α-agonists
  • Decongestants—pseudoephedrine
  • Diet supplement—ephedra
  • Anticholinergics
  • Caffeine, Alcohol, spicy, acidic foods

› Reduce nocturia
  • Decrease evening fluid intake
  • Avoid diuretics in the evening
  • If lower extremity edema, elevate legs one hour before bedtime

Treatment Options

› Watchful waiting
› Phytotherapy
› Medical therapy
› Minimally invasive procedures
› Surgery

Watchful Waiting

› Minimal symptoms
› Decision not to undergo further treatment now
› Monitor clinical course
Phytotherapy

- Saw palmetto (*Serenoa repens*)
- African plum (*Pygeum africanum*)
- Stinging nettle (*Urtica dioica*)

Medical Therapy

- **Alpha-adrenergic receptor blockers**
  - Cardura® (doxazosin mesylate)
  - Hytrin® (terazosin hydrochloride)
  - Uroxatral® (alfuzosin hydrochloride)
  - Flomax® (tamsulosin hydrochloride)*
  - Rapaflo® (silodosin hydrochloride)*

  *Selective

- **Type II 5-α reductase inhibitors**
  - Proscar® (finasteride)
  - Avodart® (dutasteride)

Medical Therapy

- **Combination Therapy**
  - Alpha blocker and 5-alpha-reductase inhibitor
    - Jalyn® (dutasteride/tamsulosin)

  - Alpha blocker and anticholinergics

- **Anticholinergic Agents**
**Alpha–Blockers: Mode of Action and Efficacy**

Relaxes prostate and bladder neck smooth muscle tone

- Significant improvement in symptom scores and flow rate
-Improves symptoms rapidly
- No change in PSA or prostate size
- Not indicated to reduce incidence of AUR or TURP

**Alpha blockers**

Dose dependent improvement in urinary symptoms score and maximum urinary flow rate

- Near max improvement in urinary flow rate
  - Within 8 hours (selective blockers)
  - May take 2–4 weeks (non-selective)

- Near maximum in voiding symptoms
  - May take 1–3 months for all

**Intraoperative Floppy Iris Syndrome**

AUA 2010 Guideline Recommendations

- Men with LUTS/BPH for whom alpha–blocker therapy is offered should be asked about planned cataract surgery. Men with planned cataract surgery should avoid the initiation of alpha–blockers until their cataract surgery is completed

- In men with no planned cataract surgery, there are insufficient data to recommend withholding or discontinuing alpha blockers for bothersome LUTS/BPH

More common with selective alpha blockers
**Alpha-Blockers:**

**Adverse Reactions**

- Asthenia
- Postural hypotension
- Dizziness
- Nasal congestion/rhinitis
- Abnormal ejaculation
- Fatigue
- Somnolence

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**Type II 5-a reductase inhibitors:**

**Mode of Action**

- Specific inhibitor of the Type II 5-a-reductase enzyme
- Significant decrease in serum and prostatic DHT
- Testosterone remains in normal physiologic range
- PSA and Prostate size decreases

**Type II 5-a reductase inhibitors:**

**Efficacy**

- Significantly reduces AUR
- Significantly reduces BPH-related surgery
- Significantly improves symptoms and flow rates yearly (>4 years)
- Achieves and maintains reductions in prostate volumes over 4 years

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Type II 5-a reductase inhibitors:
Adverse Reactions

- Impotence
- Decreased libido
- Decreased ejaculate
- Ejaculation disorder
- Breast enlargement
- Breast tenderness
- Rash and hypersensitivity reaction
- Testicular pain

PSA and Type II 5-a reductase inhibitors

- Approximate 50% decrease in PSA (may vary in individual patients)

Therefore: Double PSA value in patients treated 6 months or more for comparison with normal ranges

- Percent free PSA unaffected

- Any sustained increase in PSA levels for patients on Type II 5-a reductase inhibitors: should be carefully evaluated

Black Box warning

- The effects of finasteride on prevention of prostate cancer were evaluated in a large, randomized, placebo controlled study in men considered at increased risk for prostate cancer, and a statistically significant increase in the incidence of higher grade prostate cancer (Gleason score $\geq 7$) was found in men who received finasteride (Thompson 2003; Thompson 2013).
**MTOPS Study**

**Combination of finasteride and doxazosin**
- Reduced disease progression by 66% compared to placebo (39% doxazosin alone, 34% finasteride alone)
- Greater symptom relief & improvement in urinary flow rate
- Reduced risk of invasive therapy by 67% compared (64% finasteride)
  - Especially effective: Prostate >40 ml or PSA >4 ng/ml

**Anticholinergic Therapy**

Overactive Bladder (OAB) and BPH often coexist
- Generally treat BPH/LUTS first
- Antimuscarinic therapy shown effective in men
  - Tolterodine shown no increased risk of AUR
- Monitor PVR (post void residual) in men at risk for AUR

**Overactive Bladder Treatments**
- **Oxybutynin** ( Ditropan, Ditropan XL, Oxytrol patch, Gelnique gel & generic)
- **Darifenacin** (Enablex)
- **Fesoterodine** (Toviaz)
- **Tolterodine** (Detrol, Detrol LA)
- **Trospium** (Sanctura, Sanctura XR)
- **Solifenacin** (Vesicare)
  - Side effects: dry mouth, constipation, dry eyes, blurred vision, dizziness, urinary hesitancy, urinary retention, confusion, falling, drowsiness
- **Mirabegron** (Myrbetriq) beta-3 adrenergic agonist
- **Botox**
- **Interstim**
Other Non-Surgical Therapy

Clean intermittent catheterization (CIC)
- Lower incidence/risk of urine infection compared to an indwelling urinary catheter
- Prophylactic antibiotics not recommended

Indications for Surgery
- Acute retention of urine
- Chronic retention due to prostatic obstruction
- Recurrent urinary tract infection/hematuria
- Bladder stones secondary to BPH
- Renal insufficiency due to BPH
- Large bladder diverticulum/diverticula
- Patient preference

Minimally Invasive Treatments
- Laser (Nd:YAG, Holmium)
- Transurethral electrovaporization of the prostate (TUEVP)
- Microwave thermotherapy (TUMT)
- Radio frequency applications (TUNA)
- High-Intensity focused ultrasound (HIFU)
- Urethral stents (Urolume)
  - Long-term efficacy unknown in comparison to TURP

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Surgery

- Transurethral Resection of the Prostate (TURP)
  - Common form of surgical intervention
  - Highly efficacious

- Transurethral Incision of the Prostate (TUIP)

- Open Prostatectomy
Summary

- LUTS/BPH is a common disease with potentially serious outcomes
- As the population ages, LUTS/BPH will be an increasing medical concern for physicians
- Evaluation of the prostate/urinary symptoms in older men should be part of routine office practice

Questions?

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