Male LUTS – Introduction and Overview

Thenappan Chandrasekar, MD
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Male LUTS - Introduction and Overview

Thenappan Chandrasekar, MD
Urologic Oncology & Urology
TJU Center City & Abington
Outline & Goals

• Background - What are “LUTS”?
• Anatomy
• Pathophysiology
  • Storage - bladder filling symptoms
  • Voiding - urine flow symptoms
  • Post-micturition
• Major etiologies and management
  • BPH / BOO
  • OAB
  • Nocturia
• Related to Prostate Cancer?
What are “LUTS”

• Non-specific!

• Any combination of urinary symptoms or
• Symptoms primarily associated with overactive bladder (frequency, urgency, and nocturia)

• International Consensus Conference (2005) defined LUTS to include symptoms relating to storage and/or voiding disturbances common among aging men

• So, the more detail you get, the better you can identify the problem!
Epidemiology

Rancho Bernardo study - prospective administration of AUA Symptom Index (0-35 points)

- 60% of the entire cohort had LUTS - but increased significantly with each decade age

Aging Population

- The number of Americans ages 65 and older will more than double over the next 40 years, reaching 80 million in 2040.

- The number of adults ages 85 and older, the group most often needing help with basic personal care, will nearly quadruple between 2000 and 2040.
Aging Population

Total population in the United States by gender from 2010 to 2024 (in millions)

Source
IMF
© Statista 2019

Additional Information:
United States; IMF; 2019 to 2017
Sphincter mechanism
Pathophysiology of LUTS

**Storage**
- Frequency:
  - increased frequency of diurnal urination
- Nocturia:
  - increased frequency of nocturnal urination
- Urgency:
  - relative inability to postpone urination
- Incontinence:
  - involuntary leaking of urine

**Voiding**
- Hesitancy:
  - experiencing a delay before being able to start urination
- Straining:
  - pushing or straining to start urination
- Weak stream:
  - reduced bore or force of urinary stream
- Intermittency:
  - stopping and starting during urination
- Incomplete emptying:
  - feeling that the bladder has not fully emptied after urination

**Postmicturition**
- Postmicturition dribbling:
  - leaking a small amount of urine shortly after urination is thought to have finished
# Pathophysiology of LUTS

## Storage
- **Frequency**: increased frequency of diurnal urination
- **Nocturia**: increased frequency of nocturnal urination
- **Urgency**: relative inability to postpone urination
- **Incontinence**: involuntary leaking of urine

## Voiding
- **Hesitancy**: experiencing a delay before being able to start urination
- **Straining**: pushing or straining to start urination
- **Weak stream**: reduced bore or force of urinary stream
- **Intermittency**: stopping and starting during urination
- **Incomplete emptying**: feeling that the bladder has not fully emptied after urination

## Postmicturition
- **Postmicturition dribbling**: leaking a small amount of urine shortly after urination is thought to have finished
Lower Urinary Tract Symptoms in Men

**Storage Symptoms**
- Urgency
- Frequency
- Incontinence
- Nocturia

**Voiding Symptoms**
- Poor flow
- Intermittency
- Straining
- Hesitancy
- Terminal dribble

**Post-Micturition Symptoms**
- Post-void dribble
- Incomplete emptying

Are there specific considerations for males?

Proportion of types of urinary symptoms in men:
Most men have BOTH voiding and storage symptoms
- N = 14,139 men ≥ 40 years old
- 71% reported LUTS


However, OAB and BPH frequently co-exist
Etiologies of LUTS
BPH & BOO

First, we need to define these terms:

- **Benign Prostatic Hyperplasia (BPH)**
  - Histologic diagnosis
  - Stromoglandular hyperplasia

- **Benign prostatic enlargement (BPE)**
  - Anatomic enlargement of the gland

- **Bladder Outlet Obstruction (BOO)**
  - Actual manifestation of symptoms
  - Pathophysiologic
  - Obstruction of the urethra & compromise of urinary flow
BPH-Mass Effect
**BPH**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-30</td>
<td>10%</td>
</tr>
<tr>
<td>60</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>85</td>
<td>90%</td>
</tr>
</tbody>
</table>

At age 55, 25% of men will have a decrease in the force of stream.
Prevalence of BPH

![Graph showing the prevalence of BPH versus age. The percentage of men with BPH increases as age increases. The graph ranges from 50 to 80 years of age on the x-axis and from 0% to 90% on the y-axis. The trend line indicates a steady increase in prevalence with age.]
BPE & BOO

- Size doesn’t always matter!

The size of the gland does not necessarily predict symptom severity. Some men with minimally enlarged prostate glands experience many symptoms while other men with much larger glands have few symptoms.
What Are the Symptoms of BPH?

**Storage**
- **Frequency**: increased frequency of diurnal urination
- **Nocturia**: increased frequency of nocturnal urination
- **Urgency**: relative inability to postpone urination
- **Incontinence**: involuntary leaking of urine

**Voiding**
- **Hesitancy**: experiencing a delay before being able to start urination
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**Postmicturition**
- **Postmicturition dribbling**: leaking a small amount of urine shortly after urination is thought to have finished
What Are the Symptoms of BPH?

<table>
<thead>
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<th>Storage</th>
</tr>
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<tbody>
<tr>
<td>Frequency</td>
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<table>
<thead>
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</table>

<table>
<thead>
<tr>
<th>Postmicturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmicturition</td>
</tr>
<tr>
<td>dribbling</td>
</tr>
</tbody>
</table>
BPH - Long-term Complications

- “Silent” BPH
- Urinary retention
- UTI
- Bladder stones
- Bladder decompensation
- Renal insufficiency
- Hematuria
Bladder Changes from BPH

- Detrusor instability
- Decreased compliance (frequency and urgency)
- Impaired detrusor contractility
- Trabeculation (increase in detrusor collagen)
- Diverticulum
AUA Symptom Score Index

Seven questions (0-5):
- Incomplete emptying
- Frequency
- Hesitancy
- Urgency
- Weak stream
- Strained voiding
- Nocturia
AUA Symptom Score Index

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

* Moderate to severe symptoms are 3.5X higher in men with >50 ml prostate
BPH - Diagnosis & Evaluation

• Detailed history (hematuria, UTI, Diabetes, Neurologic Disease, h/o urethral strictures, urinary retention, aggravation of symptoms with cold meds)
• Physical Exam: DRE and focused neurologic exam
• AUA Symptom Score Index
• U/A
• ? Serum Creatinine
• PSA
Diagnosis-Additional Tests

- Urinary flow rate
- Post-void residual (Bladder scan)
- Pressure-Flow studies
- Urethrocystoscopy - indicated for planned invasive therapy, hematuria, strict disease, previous surgery
- Radiologic imaging - Transrectal / Transabdominal U/S or IVU
BPH - Treatment

- In 1990 - 335,000 surgical procedures for BPH
  - TURP was the most common procedure
- Medical therapy and minimally invasive techniques have decreased the number of surgical intervention
- 25% of men by age of 80 will undergo treatment
- Cost issue
BPH - Treatment

- Watchful waiting
- Medical Therapy
- Minimally Invasive Techniques - Prostatic Urethral Lifts and Steam Thermotherapy
- Surgical Therapy
BPH - Treatment Trends

Global Benign Prostatic Hyperplasia Prostate Treatment Market

CAGR 4.6% (2018-2028)

By Treatment Type, 2017A (US$ Mn)

Market Value (2017A) **US$ 24,332.7 Mn**

Source: Future Market Insights, 2018

Note: Market shares are not depicted as per the actual scale and are only for illustration purposes.
BPH Treatment - “Watchful Waiting”

**Advantages**
- No surgery
- No drugs
- “No side effects”

**Disadvantages**
- No improvement in symptoms
- Risk that symptoms or obstruction will worsen
BPH - Medical Therapy

- First line of treatment for LUTS secondary to BPH
- Alpha blockers
- Low dose Tadalafil (Cialis)
- Androgen Suppression
- Phytotherapy
Medical Therapy - Alpha Blockers

- Non selective: Phenoxybenzamine, alfuzosin (IR), Indoramin
- Long acting: terazosin, doxasosin, alfuzosin SR, Silodosin
- Subtype selective: tamsulosin
Medical Therapy - Distribution of alpha-receptors
Medical Therapy - Alpha blockers

- Multicenter, randomized, double-blind, placebo controlled studies have demonstrated safety and efficacy
- Rapid and dose dependent
- Durable
Medical Therapy - Androgen Suppression

- GnRH Analogs- Leuprolide, Nafarelin, Cetrorelix
- Progestational Agents-Megestrol, 17 alpha-Hydrocortisone
- Antiandrogens-flutamide, biculatamide, oxandolone, zanoterone

- 5 alpha reductase inhibitors (5ARIs)
  - Finasteride (Proscar)
  - Dutasteride (Avodart)
Medical Therapy - 5ARI’s

- Safety and efficacy has been established
- Durable
- Reduces prostate size by 20%
- ? Preventive for prostate cancer
Treatment Option – Medical Management

**Advantages**

- No surgery
- Potential for full symptom resolution

**Disadvantages**

- Lifelong commitment
- Side effects
- Effectiveness of drugs lessens over time
- Ongoing out-of-pocket costs
BOO 2/2 BPH - Surgical Treatment

Surgical Management of BPH in New York State, 1997-2012

- TURP
- Laser
- Open Prostatectomy
- TUIP
- TUMT
- TUNA

Year:

Percentage of Patients
Office Based - Minimally Invasive Therapies (MIT)

- **Prostatic Urethral Lift - UroLift**

- **Enlarged Prostate**
  An enlarged prostate can narrow or even block the urethra.

- **Step 1**
  The UroLift Delivery Device is placed through the obstructed urethra to access the enlarged prostate.

- **Step 2**
  Small UroLift Implants are permanently placed to lift and hold the enlarged prostate tissue out of the way and increase the opening of the urethra.

- **Step 3**
  The UroLift Delivery Device is removed, leaving an open urethra designed to provide symptom relief.

- **Steam Thermotherapy - Rezum**
Operating Room - Minimally Invasive Treatment Options

• Laser - TULIP, VLAP, contact laser
• Laser - Holmium Laser Prostatectomy (HoLEP)
• TURP
Surgical Therapy

- TURP - Holmium Laser Prostatectomy (as discussed)
- Open Prostatectomy → → →
- Minimally Invasive Techniques (Robotic) →
TURP is still considered “gold” standard

Open/Robotic Prostatectomy is indicated in patients where prostate glands are greater than 75-80 grams

Holmium Laser Prostatectomy is an alternative to TURP
  - No size limit in the AUA guidelines
  - Only MIT that has no size limit
## Treatment Option - Surgery

### Advantages
- Proven approach
- Durable response
- Can allow patients to be off medications

### Disadvantages
- Requires hospitalization
- Requires general anesthesia
- Side effects can be significant
Surgical Indications

- Recurrent UTI’s
- Gross Hematuria
- Bladder calculi
- Renal insufficiency
- Urinary Retention
- Bladder Diverticulum
BOO - Causes other than BPH

- Urethral Strictures
- Primary bladder neck obstruction
- Bladder neck contracture
- Detrusor-sphincter dyssynergia
- Prostate cancer - late stage prostate cancer
- Meatal stenosis (circumcised men)
Overactive Bladder (OAB)

- Definition: “urinary urgency, with or without urgency urinary incontinence (involuntary loss of urine), in the absence of urinary tract infection or other obvious pathology.”

- It is a clinical diagnosis

- Characterized by STORAGE symptoms - and ideally absence of VOIDING/obstruction symptom
OAB - Epidemiology

Women > Men

But...

Still a problem in men!
Overactive Bladder (OAB) - Presentation

<table>
<thead>
<tr>
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<th>Voiding</th>
<th>Postmicturition</th>
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</tr>
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<td>experiencing a delay before being able to start urination</td>
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<tr>
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<td>feeling that the bladder has not fully emptied after urination</td>
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<tr>
<td></td>
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</tr>
</tbody>
</table>

Jefferson

Philadelphia University +
Thomas Jefferson University

HOME OF SIDNEY KIMMEL MEDICAL COLLEGE
Overactive Bladder (OAB) - Evaluation

- History (detailed)
  - Neurogenic bladder
  - Pelvic floor dysfxn
  - UTI’s recurrent
  - BOO
  - Bladder Ca (hematuria)

- Physical exam

- Urinalysis/Ucx (if indicated)

- Postvoid residual (PVR)

- Symptom questionnaire / bladder diary
Overactive Bladder (OAB) - Secondary to BOO

LUTS categories:
- Storage
- Voiding
- Postvoiding

OAB:
- Urgency
- Frequency
- Nocturia
- Urgency urinary incontinence

BOO due to BPH

↑ sensitivity of cholinergic receptors/
structural changes due to ischaemia
Overactive Bladder (OAB) - Treatment Paradigm

1. FIRST LINE THERAPY
   - INITIATE PATIENT CONTACT
     - Needs Assessment
     - Credentialing of the Provider
     - Initial Patient Education
     - Initial Patient Triage
     - Check Insurance Coverage
   - EVALUATION
     - Frequency, Urgency, Nocturia, Urge Incontinence
   - INITIAL HISTORY, PHYSICAL, URINALYSIS
     - Consider: Post Void Residual, C&S, Voiding Diary
   - CONSERVATIVE TREATMENT / BEHAVIORAL MODIFICATION
     - Pelvic Floor Muscle Training and Exercises,
       Fluid Management, Dietary Changes,
       Timed Voiding, Bladder Training and Control Strategies

2. SECOND LINE THERAPY
   - RN NAVIGATOR TO FOLLOW UP ON MEDICATION
   - MEDICATION #1
     - (4-6 weeks)
     - Anticholinergic
     - Beta3-agonist (Mirabegron)
     - Tricyclic
   - EVALUATION PATIENT DELIVERABLES:
     - Complete OAB Questionnaire
     - Review OAB Guidelines
     - Review Treatment Timeline
     - Deliver OAB Patient Packet
     - Review OAB Video
     - Discuss Treatment Plan
     - Discuss Internal Referral Process
   - FURTHER EVALUATION
   - ADDITIONAL TESTING
     - Consider: Voiding Diary, Urodynamics,
       Cystoscopy, Cytology, C&S, US
   - SPECIALIZED CARE / CONTINENCE SPECIALIST
   - RN Navigator/Urologist explains internal referral process
   - Consultation with Contiinece Specialist
   - Patient is referred from Urologist to Contiinece Specialist
   - Voiding Diary Deliverable
   - COMPPLICATED INCONTINENCE
     - Mixed Incontinence
     - Previous Incontinence Surgery
     - Continuous Incontinence (Fistula)
     - Pelvic Radiation
     - Urinary and Fecal Incontinence
     - Recurrent Incontinence
     - Neurogenic Bladder
     - Radical Pelvic Surgery
     - Pelvic Pain
Overactive Bladder (OAB) - Treatment Paradigm

- **Third Line Therapy**

**Advanced Treatments**

- **Onabotulinum Toxin A Injections (Botox)**
  - (Effective 6-9 months, repeat if desired, as needed)

- **Neuromodulation Evaluation**
  - Interstim®
  - Basic (up to 7 days) or Advanced Evaluation (up to 2 weeks)

- **Percutaneous Tibial Nerve Stimulation (PTNS)**
  - URGENT® PC TIAL
  - (12 week initial therapy)

**Repeat Botox® Treatments**
- (Every 6-9 months)

**Interstim® Implant**
- (Replace battery 4-8 years)

**PTNS Maintenance**
- (Every 3-4 weeks to maintain benefit)
OAB Treatment - Pathophysiology

Anticholinergics
- Block parasympathetic innervation of detrusor muscle

Beta-3 Agonist
- Activates relaxation of detrusor smooth muscle
Overactive Bladder (OAB) - Medical Management

Antimuscarinics

- Ditropan® (oxybutynin) – 1975
- Oxybutynin (generic) – 1989
  - Ditropan® XL (oxybutynin ER) - 1998
  - Detrol® (tolterodine) – 1998
  - Detrol® LA (tolterodine ER) – 2000
  - Oxytrol® (oxybutynin-TDS) - 2003
    - Sanctura® (trospium) – 2004
    - Vesicare® (solifenacin) – 2004
    - Enablex® (darifenacin) – 2004
  - Oxybutynin ER (generic) – 2006
    - Sanctura® XR (trospium ER) – 2007
    - Toviaz® (fesoterodine) – 2008
  - Gelnique® (oxybutynin gel) – 2009
  - Anturol® (oxybutynin gel) - 2011
- Beta-3 Agonists
  - Myrbetriq® (mirabegron) – 2012
**Overactive Bladder (OAB) - Anticholinergics**

<table>
<thead>
<tr>
<th></th>
<th>Oxybutynin</th>
<th>Tolterodine</th>
<th>Solifenacin</th>
<th>Darifenacin</th>
<th>Trospium chloride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical structure</td>
<td>Tertiary amine</td>
<td>Tertiary amine</td>
<td>Tertiary amine</td>
<td>Tertiary amine</td>
<td>Quaternary amine</td>
</tr>
<tr>
<td>Receptor selectivity</td>
<td>Non selective</td>
<td>Non selective</td>
<td>M3 selective</td>
<td>M3 selective</td>
<td>Non selective</td>
</tr>
<tr>
<td>Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral bioavailability only 10%</td>
</tr>
<tr>
<td>Dosing</td>
<td>5 mg 3 times Day</td>
<td>1-2 mg Twice Day</td>
<td>5-10 mg/Day</td>
<td>7.5-15 mg/Day</td>
<td>20-60 mg/Day</td>
</tr>
<tr>
<td>Half life</td>
<td>2hours patch 8hrs ER 12hrs</td>
<td>2hours ER 9hrs</td>
<td>45 -86 hours</td>
<td>13 -19hours</td>
<td>12 -20hours</td>
</tr>
<tr>
<td>Metabolism</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>60% Excreted unchanged in urine</td>
</tr>
<tr>
<td>Side effects</td>
<td>Transdermal has less side effect</td>
<td>• Dry mouth</td>
<td>Dry mouth</td>
<td>Dry mouth</td>
<td>Lower risk of CNS side effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Constipation</td>
<td>Constipation</td>
<td>Constipation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Blurred vision</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDA Approval</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>
Overactive Bladder (OAB) - Beta-3 agonist

Based on individual patient efficacy and tolerability, the dose may be increased.

Myrbetriq™ - mirabegron

Adverse Effects

• Common Adverse Effects

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Mirabegron 25mg (%)</th>
<th>Mirabegron 50mg (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>11.3</td>
<td>7.5</td>
<td>7.6</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>4.2</td>
<td>2.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3.5</td>
<td>3.9</td>
<td>2.5</td>
</tr>
<tr>
<td>Headache</td>
<td>2.1</td>
<td>3.2</td>
<td>3.0</td>
</tr>
</tbody>
</table>
OAB Medication Summary

- Clinicians should offer oral antimuscarinics or oral β3-adrenoceptor ER preferred over IR
- If one anti-muscarinic ineffective, then dose modification, different anti-muscarinic or a β3-agonist
- Can combine modalities for pts refractory to monotherapy

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>FORMULATIONS</th>
<th>COMMON INITIAL DOSES</th>
<th>DOSE ADJUSTMENTS</th>
<th>FREQUENT ADVERSE EVENTS</th>
<th>CLINICAL PEARLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darifenacin (Enablex)</td>
<td>ER tablet: 7.5, 15 mg</td>
<td>ER: 7.5 mg daily</td>
<td>Child-Pugh class B: maximum dose of 7.5 mg daily Child-Pugh class C: use not recommended Renal adjustments not necessary</td>
<td>Dry mouth Constipation</td>
<td>Generic available.</td>
</tr>
<tr>
<td>Fesoterodine (Tovaz)</td>
<td>ER tablet: 4 mg, 8 mg</td>
<td>ER: 4 mg daily</td>
<td>CrCl &lt; 30 ml/min: maximum dose of 4 mg daily Child-Pugh class C: use not recommended as has not been studied</td>
<td>Dry mouth</td>
<td>Available as brand only. Pro-drug which is metabolized to 5-hydroxymethyl tolterodine.</td>
</tr>
<tr>
<td>Oxybutynin (Ditropan, Oxytrol)</td>
<td>Transdermal gel: 3%, 10% Transdermal patch: 3.9 mg/24 hours</td>
<td>IR tablet: 5 mg ER tablet 5, 10, 15 mg</td>
<td>IR: 5 mg 2-3x/day ER: 5-10 mg daily Gel (3%): Apply 3 pumps once daily Transdermal patch: apply 1 patch (3.9 mg/24 hours) twice weekly</td>
<td>Older adults IR: 2.5 mg 2-3x/day No hepatic or renal adjustment necessary</td>
<td>Dizziness Drowsiness Dry mouth Constipation</td>
</tr>
<tr>
<td>Solifenacin (Vescicare)</td>
<td>IR tablet: 5 mg, 10 mg</td>
<td>IR: 5 mg daily</td>
<td>Concomitant CYP3A4 inhibitors, CrCl &lt; 30 ml/min, or Child-Pugh class B: maximum dose of 5 mg daily Child-Pugh class C: use not recommended</td>
<td>Dry mouth Constipation</td>
<td>Available as brand only. One of the lowest risks for systemic anticholinergic side effects in class (also trospium) Solifenacin may increase the QTc interval; this risk is dose related and should be monitored if patients are taking other QTc-prolonging agents</td>
</tr>
<tr>
<td>Tolterodine (Detrol)</td>
<td>IR tablet: 20 mg ER capsule: 60 mg</td>
<td>IR: 20 mg 2x/day ER: 60 mg daily</td>
<td>Patients &lt; 75 years and old: IR 20 mg daily CrCl &lt; 30 ml/min: IR: 20 mg daily, ER: use not recommended</td>
<td>Dry mouth Constipation</td>
<td>One of the lowest risks for systemic anticholinergic side effects in class; recommend for use in older adult population if requiring antimuscarinic therapy</td>
</tr>
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<table>
<thead>
<tr>
<th>Beta-3 Adrenergic Agents</th>
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<td>Mirabegron (Myrbetriq)</td>
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</tbody>
</table>

* Table adapted from information published in Lexi-Comp Online.
Overactive Bladder (OAB) - Surgical Treatments

- **3rd Line Therapy**
  - **Advanced Treatments**
    - Onabotulinum toxin A injections Botox® (Effective 6-9 months, repeat if desired, as needed)
    - Neuromodulation evaluation Interstim®
      - Basic (up to 7 days) or Advanced Evaluation (up to 2 weeks)
    - Percutaneous Tibial Nerve Stimulation (PTNS)
      - Urgent® PC trial
      - (12 week initial therapy)
    - Repeat Botox® treatments
      - (Every 6-9 months)
    - Interstim® implant
      - (Replace battery 4-8 years)
    - PTNS maintenance
      - (Every 3-4 weeks to maintain benefit)

- Nurse Navigator Contact
Nocturia

• Definition: defined as the need to awaken $\geq 1$ times per night to void

• Why talk about this separately?
  • Long been considered one of a range of symptoms associated with LUTS - including BOO and OAB.
  • Although nocturia is urinary frequency that occurs during nighttime sleep, it is not necessarily driven by a lower urinary tract dysfunction
  • It may be driven instead by nighttime urine overproduction, or nocturnal polyuria (NP), resulting from renal, cardiovascular, or pulmonary factors
### Nocturia - Non-Urologic Causes

<table>
<thead>
<tr>
<th>Urologic Conditions</th>
<th>Nonurologic Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• LUTS (OAB, BPH)</td>
<td>• Chronic heart failure</td>
</tr>
<tr>
<td>• Neurogenic voiding dysfunction</td>
<td>• Diabetes mellitus (uncontrolled)</td>
</tr>
<tr>
<td>• Idiopathic nocturnal detrusor overactivity</td>
<td>• Diabetes insipidus</td>
</tr>
<tr>
<td>• Bladder cancer</td>
<td>• Hypoalbuminemia</td>
</tr>
<tr>
<td>• Nocturnal polyuria</td>
<td>• Sleep apnea</td>
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<td>• Multiple sclerosis</td>
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<td></td>
<td>• Depression</td>
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<td></td>
<td>• Chronic pain</td>
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<tr>
<td></td>
<td>• Inadequate fluid intake</td>
</tr>
</tbody>
</table>

BPH, benign prostate hyperplasia; LUTS, lower urinary tract symptoms; OAB, overactive bladder.
Nocturia - Obstructive Sleep Apnea

Sleep disturbance
- Sleep apnea syndrome → Decrease of melatonin
  - Increase of venous return during inspiration
  - Increase of HANP & BNP
    - Nocturnal polyuria
      - Diminished bladder capacity
      - Nocturia
Nocturia - Conservative Treatment Rec’s

Elevate your feet 3-4 hours before bedtime for at least 30 minutes

and then

Stretch and bend your ankles for about 20 times

Lifestyle interventions in nocturia

- Limit drinking, calories, salt, protein restriction
- Bladder and pelvic floor training, weight loss
- Physical activity, salt restriction, weight loss, postural drainage, stockings
- Salt and protein restriction, weight loss; prevention: diabetes, obesity
- Sleep hygiene, losing weight, physical activity
- Sleep hygiene, limit drinking, bladder and pelvic floor training, weight loss in DM
Nocturia - Medical Management

FIRST LINE THERAPY - Anticholinergic medication

If this first line drug therapy is considered ineffective, one or more of the following may be prescribed:

1) Desmopressin - By mimicking ADH or vasopressin, the kidney produces less urine.
2) Imipramine - This medication boasts a 40% success rate but also has a fine line between an effective dose and toxic dose.
3) Furosemide - This loop diuretic helps regulate urine production in the daytime in order to decrease urine production during sleep. Furosemide blocks ion flow in the kidneys, allowing urine production to be more controlled.
4) Bumetanide - This loop diuretic assists in regulating urine production prior to sleep so waking during the nighttime does not occur. Bumetanide must be taken with caution and consultation with a healthcare professional prior to taking this medication is highly recommended.
Nocturia - Medical Management

Fig. 4: Treatment algorithm for nocturia
How does this relate to Prostate Cancer?
Prostate Anatomy

- Prostate Cancer and BPH occur in different regions of the prostate.
- PCa rarely causes urinary symptoms... unless it is quite advanced.
PSA

What Can Cause an Elevated PSA

1. Enlarged prostate
2. Prostatitis
3. Prostate cancer
4. Recent ejaculation
5. Digital rectal exam
6. Bicycle riding