Benign Prostate Disease

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Benign Prostate Disease - Definitions

Of men with histologic *hyperplasia* (BPH)

Half have *hypertrophy* (BPE)
Benign Prostate Disease - Definitions

60% have obstruction (BOO)

- 60% Obstruction
- 40% no obstruction
Benign Prostate Disease - Definitions

- Obstructed
- No obstruction
- BPH no LUTS
- No BPH

Lower urinary tract symptoms (LUTS)
Lower Urinary Tract Causes of Male LUTS

- Uninhibited bladder contractions
- Outlet obstruction
- Impaired detrusor contractility
- Bladder or prostate inflammation
# Frequency and Nocturia – Not Just the Lower Urinary Tract

| Frequency | High fluid intake  
|           | High urine output  
|           | Urge UI           
|           | Incomplete emptying (↑PVR) |
| Nocturia  | Nocturnal polyuria  
|           | Sleep disturbance  
|           | Sleep apnea        
|           | Urge UI, obstruction |
Risk Factors and Natural History

- Risk factors for LUTS in men
  - Age
  - African American
  - Large prostate (>30 cc), PSA > 1.5 ng/ml
  - Obesity, diabetes
- Risk factors for urinary retention and need for treatment
  - Large prostate, high PSA, severe sx, PVR > 100 ml
- Natural history of LUTS and need for treatment over 4-5 years

<table>
<thead>
<tr>
<th>Base Sx level</th>
<th>No Rx</th>
<th>Med Rx</th>
<th>TURP</th>
<th>Sx level without Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>45%</td>
<td>19%</td>
<td>7%</td>
<td>Mild 32% Mod 58% Severe 10%</td>
</tr>
<tr>
<td>Mod</td>
<td>34%</td>
<td>23%</td>
<td>18%</td>
<td>Mild 32% Mod 58% Severe 10%</td>
</tr>
<tr>
<td>Sev</td>
<td>25%</td>
<td>20%</td>
<td>29%</td>
<td>Mild 4% Mod 14% Severe 82%</td>
</tr>
</tbody>
</table>

**Morbidity**
- Acute retention - <8%
- Renal insufficiency – 2%
- High postvoid residual – 9%

Evaluation

- LUTS, Comorbidity
- PE, DRE
- U/A
- Consider PSA
- Bladder diary
- AUASI
- PVR (Optional)
- Patient preferences
- Urologist

- Renal insufficiency
- Retention
- Hematuria
- Recurrent UTIs
- Nocturnal polyuria

References:
- Abrams P et al, J Urol 2013
- AUA 2014
AUA Symptom Index (AUASI or IPSS)

1. Incomplete emptying
2. Frequency
3. Intermittency
4. Urgency
5. Weak Stream
6. Straining
7. Sleeping/Nocturia

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Scoring
- Mild \(\leq 7\)
- Moderate \(8–19\)
- Severe \(> 20\)

## Use of bladder diary in evaluating nocturia

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Measured Amount of Urine (mL)</th>
<th>Are You Wet or Dry?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>3:50 pm</td>
<td>90</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>6:05 pm</td>
<td>90</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>8:15 pm</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>10:20 pm</td>
<td>150</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>12:00 am</td>
<td>30</td>
<td>Dry</td>
</tr>
<tr>
<td>Day 2</td>
<td>2:15 am</td>
<td>150</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>3:40 am</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>5:00 am</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>6:05 am</td>
<td>240</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>8:40 am</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>12:50 pm</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>6:00 pm</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>9:20 pm</td>
<td>210</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>11:40 pm</td>
<td>120</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>2:00 am</td>
<td>150</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>4:50 am</td>
<td>180</td>
<td>Dry</td>
</tr>
<tr>
<td></td>
<td>6:20 am</td>
<td>180</td>
<td>Dry</td>
</tr>
</tbody>
</table>

### Nocturnal polyuria = nocturnal output > 33% total 24 hr output

**Daytime output 570 ml**

**Nocturnal output 650 ml**
Who needs to see a urologist?

<table>
<thead>
<tr>
<th>Complicated lower urinary tract symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of prostate cancer</td>
</tr>
<tr>
<td>Elevated PSA level</td>
</tr>
<tr>
<td>Hematuria</td>
</tr>
<tr>
<td>Bladder stones</td>
</tr>
<tr>
<td>Bladder cancer</td>
</tr>
<tr>
<td>Urethral stricture</td>
</tr>
<tr>
<td>Spinal cord injury</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Prostatitis</td>
</tr>
<tr>
<td>Urinary retention</td>
</tr>
<tr>
<td>Recurrent or persistent urinary tract infections</td>
</tr>
<tr>
<td>Failure of medical therapy</td>
</tr>
<tr>
<td>Patient’s preference for nonpharmacologic treatment</td>
</tr>
</tbody>
</table>

**Absolute indications for intervention**

- Renal compromise due to urinary retention
- Bladder stones
- Persistent or recurrent urinary retention
- Chronic urinary tract infections

Treatment: Watchful waiting

- Symptoms do improve
  - 38% ↓ AUASI at 3 yr (vs 68% with TURP)
  - 36% cross over to TURP, but other Rx failures rare
- Self management with life-style and behavior changes may improve outcomes
  - Self-management resulted 30-50% less need for drugs or surgery than standard care; also improved quality of life
- Appropriate for mild-moderate symptoms

van der Meulen et al, BMJ 2007

Alpha blockers

- Mechanism: relax prostate/urethral smooth muscle
- Less specific: doxazosin, terazosin
- More specific: tamsulosin, silodosin, alfluzosin

**Efficacy**
- 40% ↓ sx (mean difference from placebo 12-21%)
- Onset of symptom relief 2 - 4 wks

**Side effects:**
- Dizziness, asthenia, nasal congestion, retrograde ejaculation
- Orthostatic hypotension, esp with HTN, HTN meds, diastolic dysfunction, concomitant ED meds
- Increased risk of CHF (doxazosin)
- ED: tamsulosin 10%, others 1%
- Floppy iris syndrome during cataract surgery
5-alpha reductase inhibitors (5ARI)

- Finasteride and dutasteride: block conversion of testosterone to DHT, the androgen that stimulates prostate growth
- Efficacy:
  - PLESS trial: decreased risk of urinary retention and TURP by ~56% (NNT to prevent retention 26-49, for TURP 18-31)
  - Better response with PSA > 1.4
- Side effect: sexual dysfunction, gynecomastia
- Need life time treatment

Boyle et al. Urology 1996;48:398
McConnell et al. NEJM 1998;338: 557
**5ARI effects on PSA and PCa**

- Decreases PSA ~ 50% by 6 months
- Biopsy indicated if PSA rises during 5ARI therapy, even if still “within normal limits”
- Although *overall* prostate cancer incidence decreased with 5ARIs in the Prostate Cancer Prevention and REDUCE trials, incidence of *high grade tumors* significantly increased
- FDA added warning in 2011 about risk of high grade prostate cancer

Thompson et al. NEJM 2003;349:215
Andriole GL et al. NEJM 2010362:1192
http://www.fda.gov/Drugs/DrugSafety/ucm258314.htm
Phosphodiesterase Type 5 Inhibitors (PDE5)

- Randomized trials demonstrate significant but modest decreases in symptom score:
  - Tadalafil 5 mg daily
  - Vardenafil 10 mg daily (no men > 65)
  - Sildenafil 25mg daily
- ED an inclusion criteria; variable number of older men
- Adverse effect – flushing, dyspepsia, GERD, headache
- Efficacy and safety of combining with alpha-blocker
  - Combination better than either agent alone for decreasing symptoms
  - One safety study excluded men with HTN treated with anything but doxazosin; mean 6 mg decrease in SBP

Combination Therapy and Antimuscarinics

- Alpha blocker +/- finasteride vs. placebo (MTOPS)
  - 1 year outcome: ↓symptoms all due to alpha blocker
  - 5 year: finasteride more effective than doxazosin, and combination more effective than either alone
  - Caveats: used “clinical progression” not sx as primary outcome; high withdrawal rates; ↑side effects with combo

- Alpha Blocker +/- tolterodine vs. placebo
  - 12 wk RCT 80% improvement in subjective LUTS with combination, vs 62% with placebo, 65% with Detrol LA alone, 71% with Tamsulosin alone
  - 4 cases of urinary retention (2 in placebo group)

- Solifenacin vs placebo
  - Pooled secondary analysis showed greater reduction in urgency, frequency and incontinence – unpublished, guidelines recommend against monotherapy

McConnell et al. NEJM 2003;349:238
Kaplan et al. JAMA. 2006;296:2319-2328
Phytotherapy

• Saw palmetto (*Serenoa repens*)
  • Cochrane review update (2009) and newer RCT – no significant from placebo
• Beta sitosterol - ?
• SAM-E - estrogenic
TURP – surgical and laser

- Efficacy: 10 pt ↓ AUASI, 90% ↓ sx
  - Sx effect decreases to 75% at 7 yr, <80% in elderly
- Treatment failure (↑ sx, retention, UI, CRI, stones, death)
  - 10% at 5 yr, vs 21% with no Rx (NNT 9)
  - Re-operation rate 1-2% per year
- Adverse effects
  - Retrograde ejaculation 67-74%
  - Impotence 5-30% (mean ~14%, ↑ with age)
  - Urinary incontinence 5%
  - Early morbidity 26-40%, serious morbidity 18-30%; increases with age
  - Mortality <0.5%; up to 2-3% over age 80
UroLift® device

Efficacy in reducing IPSS > drugs and < surgery

Adverse events in 140 pts
- 1/3 required post-op catheter
- 15 required repeat surgery
- 10 required removal

Treatment Approach

- LUTS, Comorbidity
  - PE, DRE
  - U/A
  - Consider PSA

- Prostate size, PSA
  - Small/low: Alpha Blocker
  - Large/high: 5ARI

- Watchful Waiting
  - AUASI < 7
  - AUASI ≥ 7

- Watchful Waiting
  - PVR (Optional)

- Medications
  - Patient Preferences

- Surgery

- Swing-in symptoms
  - Retention
  - Hematuria
  - Recurrent UTIs

- Nocturnal polyuria
  - Fluid/diuretic/med adjustment
  - Consider OSA
  - Avoid desmopressin

References:
- Abrams P et al, J Urol 2013
- AUA 2014
Geriatric Considerations

- Medication review: anticholinergics, calcium blockers, narcotics, alpha-agonists can cause LUTS
- Cognitive and functional status
- Remaining life expectancy (esp regarding 5ARI treatment)
- Goals of care
- Tolerance of potential adverse effects of treatment