Benign Prostatic Hypertrophy: Dx and Rx

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Benign Prostatic Hyperplasia

Uses of the term BPH

– The enlargement of the prostate gland that occurs with aging

– The lower urinary tract symptoms thought to be associated with that enlargement

– Bladder Outlet Obstruction
Normal BPH

Hypertrophied detrusor muscle

Obstructed urinary flow

BLADDER

PROSTATE

URETHRA

## Natural history of BPH: Size of prostate by age

<table>
<thead>
<tr>
<th>Age</th>
<th>Prostate Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>1 gram</td>
</tr>
<tr>
<td>12</td>
<td>4 gm</td>
</tr>
<tr>
<td>25</td>
<td>20 gm (&quot;normal&quot;)</td>
</tr>
<tr>
<td>70</td>
<td>30-60 gm</td>
</tr>
</tbody>
</table>
Determining Prostate Size

- DRE underestimates prostate size, if TRUS volume is greater than 30 mL
  - Roehrborn et al, UROLOGY 49 (4), 1997

- PSA correlates with gland size & can be used as surrogate.

- “Walnut” = 1+, 25 gm, 2+ 35 gm, etc.
BPH: IVP vs. CT scan
Major Risk Factors for BPH

- Increasing Age
- Normal Androgen Levels (Functioning Testes)

Statistics

- 43% risk of BPH in your lifetime
- 9% risk of prostate cancer
- Prostatitis (5% of urologists’ visits)
- Vestige organ: semen on cervix to procreate
Prevalence of BPH Versus Other Common Conditions

- **BPH** (Men Ages 61 to 72)
- **Diabetes** (Adults Over 65)
- **Asthma** (Entire Population)


**CDC. 1998 Forecasted State-Specific Estimates of Self-Reported Asthma Prevalence.** Available at [http://www.cdc.gov/mmwr/preview/mmwrhtml/00055803.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/00055803.htm).
US Men Eligible for BPH Rx*
2000-2020

Number of eligible men 50-79 increases
From 5.6 Mill in 2000 to 11.2 Mill in 2020

*Based on 1994 AHCPR Guidelines and Olmsted County, Minnesota (N=1,317 [study cohort]) IPSS >7 points and Q_max <15 mL/s.
BPH symptoms, size and CAP

- There is not always a correlation between BPH size and symptoms
- There is no correlation between BPH size and prostate cancer
Histology of BPH

Two components BPH

- Glandular hyperplasia
- Stromal hyperplasia
  - more muscle
  - may be more responsive
to relaxation of muscle
Possible sequelae of BPH

- Urinary retention
- Hydronephrosis and renal failure
- Bladder stones
- Urinary tract infections
- Bother to the patient
AUA Symptom Score (0-35)

- Incomplete Emptying (0-5) None-always
- Frequency (0-5)
- Intermittency (0-5)
- Urgency (0-5)
- Weak Stream (0-5)
- Straining (0-5)
- Nocturia (0-5)
Evaluation of BPH

1. History: can use AUA symptom score

2. Physical examination
   - palpate for bladder
   - neurologic exam
   - prostate examination
     Size, nodular rule out CAP
Indications for Intervention

- AUR
- Bladder Calculi
- Recurrent UTI’s
- Hematuria
- Hydronephrosis
- Failure of Med Rx
- Bladder dysfunction
- Symptoms progress
- Patient choice
Bladder: bag of muscles which stores and empties urine
Voiding Physiology (Push-Pull)
Uro dynamics
Normal Uroflow
Obstructive Uroflow
Other causes of poor flow

- Stricture (STD)
- Bladder stone
- Bladder neck contracture (surg?)
- Bladder cancer
- UTI/prostatitis
- CVA/neuro disease
- Diabetes
- Anti-cholinergic meds (retention!)
Urethral stricture/ scar tissue
Excision of scar tissue, grafting
Replacement with mucosal graft
Foreign bodies can obstruct urethra
Goals of Therapy for BPH

BPH Treatment Success measured by:

- ↓ symptoms (IPSS/AUA)
- ↓ bother (bother score) and ↑ QOL
- ↑ prostate size or arrest further growth
- ↑ Increase in peak flow rate / Relieve obstruction
- Prevention of long-term outcomes/complications
- Acceptable adverse events profile

Treatment options for BPH

- Watchful waiting (conservative steps)

- Medical Therapy
  - Alpha blockers
  - 5-alpha reductase inhibitors

- Surgery/Minimally invasive devices
Medical Therapy for BPH: Alpha blockers

**Rationale:** Prostate and bladder neck are rich in alpha receptors

**Choices:**
- alpha 1 selective
  - subtype selective (α1A): Tamsulosin (Flomax)
  - subtype non selective: Doxazosin (Cardura), Terazosin (Hytrin), Alfuzosin (Uroxatral)
### Subtype selectivity of alpha blockers: ?advantage

<table>
<thead>
<tr>
<th>Selective (Flomax)</th>
<th>Non selective (Cardura, Hytrin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no dose escalation</td>
<td>More hypotensive side effects</td>
</tr>
<tr>
<td>less hypotension</td>
<td>Dose escalation</td>
</tr>
<tr>
<td>does not have to be given at night</td>
<td>Given at night</td>
</tr>
<tr>
<td>more retrograde ejaculation</td>
<td>Alfuzosin (Uroxatral)</td>
</tr>
<tr>
<td>no better for sx</td>
<td></td>
</tr>
</tbody>
</table>
Use of Finasteride for BPH

- Blocks conversion of Testosterone to DHT by blocking 5 alpha reductase
- Reduces size of gland over 3-6 months
- Initial use in early 1990’s - not much effect on symptoms in all comers
- Found to have much more effect on large glands (> 40 grams, PSA 1.4)
Rationale for Combination Therapy

5α-Reductase Inhibitors:
Arrest Disease Progression

Alpha-Blockers:
Relieve Symptoms Rapidly

Combination Therapy: Arrest Disease Progression and Rapidly Relieve Symptoms
2115 white men ages 40 to 79 from Olmsted County, Minnesota

Symptoms measured via questionnaire

Incidence of acute urinary retention over 4 years ascertained via review of medical records

8344 person-years of data obtained

The Incidence of Acute Urinary Retention/Surgery Over 4 yrs by PSA Range

PSA Ranges

- 0-1.3: 7.9%
- 1.4-3.2: 12.6%
- 3.3-12: 19.9%

[Bar chart showing the incidence of acute urinary retention/surgery over 4 years by PSA range, with the ranges 0-1.3, 1.4-3.2, and 3.3-12, and the corresponding incidences of 7.9%, 12.6%, and 19.9% respectively. The chart includes a legend indicating "Placebo".]
Reductions in Incidence of Acute Urinary Retention/Surgery Over 4 Yrs

- **0-1.3 PSA Ranges:**
  - Placebo: 44%
  - Proscar: 46%
  - Reduction: 2%

- **1.4-3.2 PSA Ranges:**
  - Placebo: 12.6%
  - Proscar: 6.9%
  - Reduction: 56%

- **3.3-12 PSA Ranges:**
  - Placebo: 19.9%
  - Proscar: 8.3%
  - Reduction: 58%
Use of Finasteride for BPH

Useful in larger glands with PSA of $> 1.4$ ($> 40$ gms)

Some effect on symptoms

Used to reduce risk of urinary retention or need for surgery in at risk patients

Side effects: decreased ejaculate, ED, gynecomastia
Phytotherapeutic Agents

- Some patients like the idea of “natural” treatments
- Few placebo-controlled studies, no long term data on side effects (saw palmetto)
- No standardization in product formulations “box of chocolates”
Natural History of BPH: Risk of Surgery Increases

10-Year Probability of Surgery (% of Patients)

Age (y)

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Without prostatic enlargement and obstructive symptoms</th>
<th>With prostatic enlargement and obstructive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>50–59</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>60–69</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>70–79</td>
<td>13</td>
<td>34</td>
</tr>
</tbody>
</table>

TUR: loop cutting prostate tissue
Surgical Rx, alternatives BOO

- Transurethral resection of the prostate (TURP/TUIP) - the Gold Standard

- Everything else
  - Microwave thermotherapy
  - Transurethral needle ablation (TUNA)
  - Laser procedures
  - High Intensity Focused Ultrasound
  - Prostatic Stents
  - Transurethral Balloon Dilation
  - Transurethral Incision of Prostate (TUIP)
Laser TUR (Green Light), “Button” TUR, etc

- Safer, patient can be on blood thinners
- No TUR syndrome (absorption glycine)
- Experience bladder irritability, spasms
- Has been more standard of care
Open Prostatectomy
**Q_max Improvement in Therapies**

- **Open (+175%)**
- **TUIP (+100%)**
- **TURP (+125%)**
- **α-Blocker* (+25.7%)**

Q_max (mL/s)

*Terazosin at baseline and 52 weeks*

Courtesy of Steven A. Kaplan, MD.


The Future

“Graying of America” will dramatically increase incidence of LUTS/BPH

Patients becoming more involved with treatment selection

Efficacy and durability, REIMBURSEMENTS will determine which modalities endure, efficacy

Thank You

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