Update on Benign Prostatic Hyperplasia

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Nobel Prize Winners in Urology

Werner Forssmann - 1956

Charles B. Huggins - 1966
Introduction

• Epidemiology
• Changes in Terminology
• Evaluation
• Medical Therapy
• Surgical Therapy
• BPH and Sex!
A Modern View of BPH
Clinical, Anatomic, and Pathophysiologic Changes

- **BPH = Benign Prostatic Hyperplasia**
  - Histologic: stromoglandular hyperplasia¹

- May be associated with
  - Clinical: presence of bothersome LUTS²
  - Anatomic: enlargement of the gland (BPE = Benign Prostatic Enlargement)²
  - Pathophysiologic: compression of urethra and compromise of urinary flow (BOO = Bladder Outlet Obstruction)²

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Prevalence of BPH Versus Other Common Conditions

Prevalence of Histologic BPH

Prevalence (%) vs. Age

- Pradhan 1975
- Swyer 1944
- Franks 1954
- Moore 1943
- Harbitz 1972
- Holund 1980
- Baron 1941
- Fang-Liu 1991
- Karube 1961
Natural History of BPH: Prostate Volume Increases

- 631 white men ages 40 to 79 from Olmsted County, Minnesota
- Prostate volume measured up to 4 times by transrectal ultrasound during a 7-year follow-up period
- Estimated prostate growth rates increased by 1.6% per year across all ages
- Higher baseline prostate volume associated with higher rates of prostate growth

Prevalence of Symptomatic BPH

Natural History of BPH: $Q_{\text{max}}$ and Voided Volume

Natural History of BPH: Risk of Acute Urinary Retention Increases

- 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

Natural History of BPH: Risk of Surgery Increases

10-Year Probability of Surgery (% of Patients)

Age (y)

40–49: 2, 3
50–59: 2, 7
60–69: 9, 16
70–79: 13, 34

- Red: Without prostatic enlargement and obstructive symptoms
- Blue: With prostatic enlargement and obstructive symptoms

PSA... It’s not just for cancer

- Serine protease produced by epithelial cells
- Dissolves semen coagulum
- Most bound to antiproteases ACT
- Increased with-
  - Malignancy
  - Hyperplasia
  - Infection/Inflammation
Serum PSA and Prostate Volume Increases Correlate with Age

PSA as a Predictor of Future Prostate Growth

% Change in PV at 48 Months

- Low PSA tertile (0.2 to 1.3 ng/mL): 0.7 mL/year
- Middle PSA tertile (1.4 to 3.2 ng/mL): 2.1 mL/year
- High PSA tertile (3.3 to 9.9 ng/mL): 3.3 mL/year

Annualized Growth Rates

- Low PSA tertile: 0.7 mL/year
- Middle PSA tertile: 2.1 mL/year
- High PSA tertile: 3.3 mL/year

Incidence of AUR and/or Surgery Over 4 Years by PSA Tertiles

Left untreated 1 in 6 patients with a PSA of >1.4 ng/mL will experience AUR or BPH-related surgery over a 4-year time period.

What is “BPH”? 

• “Prostatism” and “BPH” 
• Benign Prostatic Hyperplasia is a histological diagnosis 
• New Urological Lexicon
**Terminology**

- **BPH**
  Histologic diagnosis

- **BPE**
  Enlargement due to benign growth (can be without obstruction)

- **BPO**
  Urodynamically proven BOO (static/dynamic components)

BPH = benign prostatic hyperplasia; BPE = benign prostatic enlargement; BPO = benign prostatic obstruction; BOO = bladder outlet obstruction
LUTS

• Symptoms attributable to lower urinary tract dysfunction
  – storage (irritative) symptoms
  – emptying (obstructive) symptoms
  – may be associated with BPH, BPE, and BPO, but not exclusive to these

OAB: US Prevalence by Age

OAB = overactive bladder.

Differential Diagnosis

- Urethral stricture
- Bladder neck contracture
- Bladder stones
- Urinary tract infection
- Interstitial cystitis
- Neurogenic bladder
- Inflammatory prostatitis
- Medications
- Carcinoma of the prostate
- Carcinoma in situ of the bladder
Old Paradigm

Small prostate, thin bladder wall

Enlarged prostate, thick bladder wall
Subsequent Paradigm

- Normal prostate
- Enlarged prostate
- Small prostate with $\alpha$-receptors
Current Paradigm

Normal

Enlarged

α-receptors

Brain/Spinal column/Prostate
BPH/LUTS Pathophysiology

- Prostate Hyperplasia
  - Bladder Outlet Obstruction
    - Non-BPH Causes of Obstruction
      - Detrusor Aging Effects
      - Neurogenic Disease
      - Primary Bladder Disease
  - Detrusor Response
    - Lower Urinary Tract Symptoms
      - Polyuria

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Initial Evaluation

- Detailed medical history
- Physical exam
  - including DRE and neurologic exam
- Urinalysis
- Serum creatinine no longer mandatory
- PSA*
- Symptom assessment (AUA-SS)

PSA = prostate-specific antigen
*Per physician’s clinical judgment

AUA BPH Guidelines 2003
Evaluation (Part 1)

Initial evaluation:
- History
- DRE & focused exam
- Urinalysis
- PSA\(^1\)

Objective Symptom Assessment

Mild IPSS ≤ 7
- Watchful waiting

Moderate to severe IPSS ≥ 8
- Offer treatment alternatives
  - Minimally invasive therapies
  - Surgery
  - Cystoscopy, if important in planning operative approach

\(^1\)Optional in AHCPR Guidelines; Recommended by International Consensus Committee Clinical Practice Guideline, Number 8. AHCPR Publication No. 94-0582.
Evaluation (Part 2)

Initial evaluation
• History
• DRE & focused exam
• Urinalysis
• PSA

Objective Symptom Assessment
Moderate to severe IPSS ≥ 8

Additional diagnostic tests
• Flow rate test
• Residual urine
• Pressure-flow

Compatible with obstruction
Not compatible with obstruction
Non-BPH problems identified and treated

Presence of:
• Refractory retention
• Any of the following clearly 2° BPH:
  • Recurrent or persistent gross hematuria
  • Bladder stones
  • Renal insufficiency

Surgery

1 Optional in AHCPR Guidelines; Recommended by International Consensus Committee
2 Optional in both AHCPR and International Consensus recommendations
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

Medical Treatments for BPH, LUTS, BOO

- α-adrenergic blockers
  - Dynamic component
- 5 α-reductase inhibitors
  - Anatomic component
- Anticholinergic Therapy
  - Storage Sx’s
Role of $\alpha_1$-Adrenoreceptors

$\alpha_1$-ARs and Human LUTS

Prostate
Smooth muscle contraction
$\alpha_{1A}$

Spinal cord
Lumbosacral
$\alpha_{1D}$

Detrusor
Instability
Irritative symptoms
$\alpha_{1D} > \alpha_{1A}$

Vessels
Resistance vessels
$\alpha_{1A}$
Aging effects
$\alpha_{1B} > \alpha_{1A}$

# Comparison of α-Adrenergic Blockers

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosing</th>
<th>Titration</th>
<th>Uroselective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terazosin (Hytrin®)</td>
<td>1 mg, 2 mg, 5 mg, 10 mg, 20 mg</td>
<td>+</td>
<td>NO</td>
</tr>
<tr>
<td>Doxazosin (Cardura®)</td>
<td>1 mg, 2 mg, 4 mg, 8 mg, 16 mg</td>
<td>+</td>
<td>NO</td>
</tr>
<tr>
<td>Tamsulosin (Flomax®)</td>
<td>0.4 mg, 0.8 mg (for improved efficacy)</td>
<td>+/-</td>
<td>YES (Relative affinity for $\alpha_{1A}$ receptors over $\alpha_{1B}$)</td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>10 mg</td>
<td>-</td>
<td>YES (Highly diffused in prostatic tissue vs serum)</td>
</tr>
</tbody>
</table>

2. Cardura® (doxazosin mesylate tablets) Prescribing Information, Pfizer Inc.
3. Flomax® (tamsulosin hydrochloride) Prescribing Information, Boehringer Ingelheim Pharmaceuticals Inc.
4. Uroxatral® (alfuzosin HCl extended release tablets) Prescribing Information, Sanofi-Synthelabo Inc.
Tamsulosin: Clinical Efficacy

Mean Change in Q\textsubscript{max} (mL/s)

- Study 1 (13 wk; 0.8 mg, 0.4 mg)
  - Tamsulosin: 1.78
  - Placebo: 0.52

- Study 2 (13 wk; 0.8 mg, 0.4 mg)
  - Tamsulosin: 1.79
  - Placebo: 0.93

Mean Change in Symptom Score

- Study 1 (13 wk; 0.8 mg, 0.4 mg)
  - Tamsulosin: -9.6
  - Placebo: -5.5

- Study 2 (13 wk; 0.8 mg, 0.4 mg)
  - Tamsulosin: -8.3
  - Placebo: -5.8

*\(P \leq 0.05\) statistically significant difference from placebo.

*Tamsulosin Prescribing Information.*
Dihydrotestosterone (DHT) Action

- Testosterone is converted to DHT by two 5α-reductase isoenzymes
- The target for DHT is the androgen receptor
- DHT has approximately 5 times greater affinity for the androgen receptor than testosterone
- The greater affinity makes DHT a more potent androgenic steroid at physiologic concentrations
- The DHT/androgen receptor complex alters gene expression
Clinical Efficacy of 5-ARIs

<table>
<thead>
<tr>
<th></th>
<th>Finasteride(^1) 48-Mo Controlled Trial in 3040 Men</th>
<th>Dutasteride(^2) 24-Mo Controlled Trial in 4325 Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Finasteride</td>
<td>Placebo</td>
</tr>
<tr>
<td>Volume changes</td>
<td>-18%</td>
<td>+14%</td>
</tr>
<tr>
<td>IPSS reduction</td>
<td>-3.3</td>
<td>-1.3</td>
</tr>
<tr>
<td>Q(_{\text{max}}) improvement</td>
<td>+1.9</td>
<td>+0.2</td>
</tr>
<tr>
<td>AUR risk reduction</td>
<td>57%</td>
<td></td>
</tr>
<tr>
<td>Surgery risk reduction</td>
<td>55%</td>
<td></td>
</tr>
</tbody>
</table>

*Not from a comparative trial.

### Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Finasteride¹</th>
<th>Placebo</th>
<th>Dutasteride²</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Finasteride</td>
<td>Placebo</td>
<td>Dutasteride</td>
<td>Placebo</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>8</td>
<td>4</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Altered libido</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Ejaculatory disorder</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Gynecomastia and breast tenderness</td>
<td>1</td>
<td>0.2</td>
<td>2</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

The new 5 alpha-reductase inhibitor Dutasteride has been shown to be of similar efficacy as Finasteride in terms of symptom score and flow-rate improvement, as well as in the prevention of disease progression, while having a comparable safety profile.³

*Not from a comparative trial.

Rationale for Combination Therapy

5α-Reductase Inhibitors:
- Arrest Disease Progression

Alpha-Blockers:
- Relieve Symptoms Rapidly

Combination Therapy: Arrest Disease Progression and Rapidly Relieve Symptoms
MTOPS

(Medical Treatment of Prostatic Symptoms)

&

Combination Therapy
MTOPS
Doxazosin/Finasteride/Combination

- Double-masked, randomized, placebo-controlled, multicenter study
- 3047 men aged ≥50 years with BPH
- Average follow-up: 4.5 years
- Primary outcome: time to clinical progression
  - AUR
  - Renal insufficiency due to BPH
  - Recurrent UTI or urosepsis
  - Incontinence
  - ≥4-point rise in baseline AUA symptom score confirmed within 2-4 weeks

- Secondary outcomes
  - Changes in symptom and flow rate over time
  - Rate of invasive therapies for LUTS/BPH

MTOPS = Medical Therapy Of Prostatic Symptoms.
Cumulative Incidence of BPH Progression

- Placebo: Risk Reduction = 0%
- Finasteride: Risk Reduction = 34%
- Doxazosin: Risk Reduction = 39%
- Combination: Risk Reduction = 67%

$P < 0.0001; \text{ df}=3$

Cumulative Incidence of AUR

- Placebo
- Doxazosin: Risk Reduction = 67%
- Finasteride: Risk Reduction = 67%
- Combination: Risk Reduction = 79%

P < .0034; df = 3

Cumulative Incidence of BPH-Related Surgery

- Placebo
- Finasteride: Risk Reduction = 64%
- Doxazosin: Risk Reduction = 0%
- Combination: Risk Reduction = 67%

$P<.0001; \text{df}=3$

MTOPS Conclusions

• In selected patients, combination therapy is most effective in
  – Reducing risk of clinical progression
  – Improving AUA symptom score
  – Improving maximum urinary flow rate

• Monotherapy significantly reduces risk of clinical progression of BPH

• Finasteride (5ARI) and combination therapy significantly reduce the risk of AUR and invasive therapy

• Doxazosin (α-adrenergic blocker) prolongs time to progression of AUR and invasive therapy, but does not reduce overall risk

• Both long-term monotherapy and combination therapy are safe and effective

Combination Treatment with An α-Blocker Plus An Anticholinergic for Bladder Outlet Obstruction: A Prospective, Randomized, Controlled Study


J Urol. 2003;169:2253-2256
Detrol® and Tamsulosin Combination Therapy in Men With BOO and OAB

• Randomized, controlled trial (independent research)
  – 50 men
  – 52 to 80 years of age (average, 69 years)
  – Mild/moderate BOO on PFS
  – Concomitant IDO

• Study design
  – Complete QoL 9 UROLIFE questionnaire prior to study onset
  – 1-week tamsulosin 0.4 mg qd, then randomized to receive concomitant Detrol® 2 mg bid or continue tamsulosin monotherapy
  – Repeat QoL 9 and PFS at 12 weeks

## Detrol® and Tamsulosin Combination Therapy in Men with BOO and OAB: Effects on Urodynamic Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tamsulosin (n = 25)</th>
<th>P Value</th>
<th>Tamsulosin+Tolterodine (n = 25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum detrusor pressure (cm H₂O)</td>
<td>-5.2</td>
<td>0.0827</td>
<td>-8.24</td>
<td>0.0082</td>
</tr>
<tr>
<td>Maximum flow rate (mL/second)</td>
<td>+1.16</td>
<td>0.0001</td>
<td>+1.32</td>
<td>0.0020</td>
</tr>
<tr>
<td>Pressure at maximum unstable contraction (cm H₂O)</td>
<td>-2.16</td>
<td>0.05690</td>
<td>-11.16</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Volume at first unstable contraction (mL)</td>
<td>+30.40</td>
<td>0.0190</td>
<td>+100.40</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Detrol® and Tamsulosin Therapy in Men With BOO and OAB: *Effects on QoL*

<table>
<thead>
<tr>
<th>Mean score (QoL 9 UROLIFE)</th>
<th>Baseline (n=25)</th>
<th>12 Weeks (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamsulosin</td>
<td>542.2</td>
<td>548.2</td>
</tr>
<tr>
<td>P=NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamsulosin + Detrol®</td>
<td>525</td>
<td>628.4</td>
</tr>
<tr>
<td>P=0.0003</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Detrol® and Tamsulosin Therapy in Men With BOO and OAB: Conclusions

- **Efficacy**
  - Improved QoL
  - Increased bladder capacity
- **Safety**
  - No acute urinary retention was observed
  - Did not affect quality of urinary flow
  - Did not affect postvoid residual urine volume
- “The proposed combination of Detrol® and tamsulosin appears to be an effective and relatively safe treatment option in patients with bladder outlet obstruction and detrusor overactivity”

## Table 2. Patients Reporting Treatment Benefit at Week 12

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 215)</th>
<th>Tolterodine ER (n = 210)</th>
<th>Tamsulosin (n = 209)</th>
<th>Tolterodine ER + Tamsulosin (n = 217)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol-Specified Intention-to-Treat Analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing, No.</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Patient report, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benefit</td>
<td>132 (61.7)</td>
<td>136 (65.1)</td>
<td>146 (70.5)</td>
<td>172 (80.0)</td>
</tr>
<tr>
<td>No benefit</td>
<td>82 (38.3)</td>
<td>73 (34.9)</td>
<td>61 (29.5)</td>
<td>43 (20.0)</td>
</tr>
<tr>
<td><strong>Pairwise comparison, P value (95% CI for difference), %†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>.48 (−6 to 13)</td>
<td>.06 (−1 to 19)</td>
<td>&lt;.001 (9 to 28)</td>
<td></td>
</tr>
<tr>
<td>Tolterodine ER</td>
<td></td>
<td>.25 (−4 to 15)</td>
<td>.001 (6 to 25)</td>
<td></td>
</tr>
<tr>
<td>Tamsulosin</td>
<td></td>
<td></td>
<td>.03 (1 to 19)</td>
<td></td>
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<tr>
<td><strong>Post Hoc Intention-to-Treat Analysis‡</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Patient report, No. (%)</td>
<td></td>
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<td></td>
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<td>Benefit</td>
<td>132 (59.5)</td>
<td>136 (62.7)</td>
<td>146 (67.9)</td>
<td>172 (76.4)</td>
</tr>
<tr>
<td>No benefit</td>
<td>90 (40.5)</td>
<td>81 (37.3)</td>
<td>69 (32.1)</td>
<td>53 (23.6)</td>
</tr>
<tr>
<td><strong>Pairwise comparison, P value (95% CI for difference), %†</strong></td>
<td></td>
<td></td>
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<td>&lt;.001 (8 to 26)</td>
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<td>.002 (5 to 23)</td>
<td></td>
</tr>
<tr>
<td>Tamsulosin</td>
<td></td>
<td></td>
<td>.06 (0 to 18)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, 95% 2-sided exact confidence interval; ER, extended release.
*Values reflect intention-to-treat analysis in which missing data for patient perception of treatment benefit were handled by imputation using the last observation carried forward.
†Between-group analyses compared percentages of patients who answered “yes” to the question: “Have you had any benefit from your treatment?”
‡Values reflect intention-to-treat analysis in which missing data for patient perception of treatment benefit were handled by imputation assuming no change from baseline values.
Surgical Therapy
Indications for Surgery

Absolute

• None

Relative

• Symptoms
• Pt. Choice
• AUR
• Bleeding
• Bladder Calculus
• UTI
• Renal Insufficiency
# Alphabet Soup

<table>
<thead>
<tr>
<th>Electrosurgical</th>
<th>Laser</th>
<th>Minimally-Invasive</th>
</tr>
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<tbody>
<tr>
<td>TURP</td>
<td></td>
<td>TUMT</td>
</tr>
<tr>
<td>TUVP</td>
<td>PVP</td>
<td>TUNA</td>
</tr>
<tr>
<td>Gyrus</td>
<td>HoLAP</td>
<td>WIT</td>
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<td>CLAP</td>
<td>ILC</td>
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<tr>
<td>Retropubic</td>
<td>VLAP</td>
<td></td>
</tr>
<tr>
<td>Perineal</td>
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</tbody>
</table>
Transurethral Resection of the Prostate (TURP): Overview

Advantages
- Availability of long-term outcomes data
- Good clinical results
- Treats prostates <150 g
- Low retreatment rate
- Low mortality

Disadvantages
- Retrograde ejaculation
- Bleeding
- TUR Syndrome
- Catheter time
- Hospital Stay

TURP: Efficacy

- Symptom improvement in 88% of patients
- 82% decrease in AUA Symptom Score
- 125% improvement in peak flow rate ($Q_{max}$)
- Re-op rate approx. 1.5%/yr

TURP: Complications

- Clot Retention: 16%
- Urethral Stricture: 8.4%
- Transfusions: 7.0%
- TUR Syndrome: 0.9%
- Incontinence: 1.3%

BPH, LUTS & SEX

• LUTS and ED are common in middle age and older men

• Sexual function is an important aspect of quality of life
  - sexual activity decreases with age
  - sexual problems increase with age
BPH, LUTS & SEX

• Erectile dysfunction is often associated with chronic diseases (i.e. diabetes, hypertension, … )
• 25% of men over 60 years have BPH and HTN (4)
• Recent community-based studies have shown a possible relationship between LUTS and sexual dysfunction (1,2,3)

(3) Braun et al. - International Journal of Impotence Research 2000; 12:305-311
(4) Flack.Int. J. Clinical Practice 2002; 56(7): 527-530
Are they related?

- Affects similarly aged populations
- All have significant negative impact upon quality of life
- Association versus Pathophysiologic link?
- Proof of link requires robust epidemiologic data analyzing a large cohort of a representative population in a cross-sectional fashion
BPH and Sexual Dysfunction

- Chances of developing BPH and/or sexual dysfunction increase with age
  - sympathetic overreactivity
- Treatments may cause sexual dysfunction
  - erectile dysfunction (ED)
  - altered ejaculation
- Treatments should be tailored according to QOL and sexual function issues

QOL = quality of life

Objectives:

- To evaluate in a population of men aged 50 to 80 years
  - The incidence of LUTS
  - The sexuality and the incidence of sexual disorders
  - The possible relationship between LUTS, sexual dysfunction, and co-morbid medical conditions
Methodology:

• Patients

  - 14,000 men aged 50 to 80 in 7 countries (US, UK, F, D, I, Sp, NL)

  - In each country, the sample was representative of the target population
Methodology:

- Postal questionnaire
- Demographic characteristics
- I-PSS and Quality of Life index
- Dan-PSS sex (6 questions)
- IIEF (15 questions)
- Co-morbidity factors

12,815 questionnaire were exploitable (89.9%)
Average Number of Sexual Intercourse or Activity per Month

Base: Total sample
Average Number of Sexual Intercourse or Activity per Month

Base: Total sample

- **50 - 59 years**
  - 0 Mild: 8.6
  - 0 Moderate: 7.6
  - 0 Severe: 6.6

- **60 - 69 years**
  - 0 Mild: 5.7
  - 0 Moderate: 4.6
  - 0 Severe: 3.7

- **70 - 79 years**
  - 0 Mild: 4.0
  - 0 Moderate: 3.5
  - 0 Severe: 2.6

LUTS
MSAM-7: Sex Declined With Increasing Severity of LUTS

N=12,815 (total sample)
*Among total sample.
MSAM-7

ED Increased With Increasing Severity of LUTS

Average score on a scale from 1 to 30 (6 questions) measured by IIEF
Per question: 1 = Negative to 5 = Positive

Average Erectile Function Score

Age Effect

LUTS Effect

Base: Men sexually active/sexual intercourse during past 4 weeks (n=9099)

*as measured by IIEF.

Mechanisms for Co-existence of ED and BPH

- Diminished quality of life theory
- Increased sympathetic tone theory
- Ischemia/Endothelial Dysfunction
- NO alteration theory
Sildenafil Citrate Improves LUTS
Mulhall et al, 2002

- Men (n=30) presenting with ED and LUTS (IPSS ≥ 10)
- No prior or current alpha-blocker therapy
- Treated with Viagra (standard fashion)
- Sequential assessment of IIEF and IPSS
- Statistically significant improvement in IPSS on Viagra
Tadalafil for BPH/LUTS

A

Baseline
Week 4
Week 8
Week 12

Mean Change in IPSS
from Baseline to Endpoint

B

Baseline
Week 4
Week 8
Week 12

Placebo
Tad 2.5
Tad 5.0
Tad 10.0
Tad 20

Penn Urology
Take-Home Messages

- Aging Population = More BPH
- Not all Male LUTS = BPH
- Not all BPH = LUTS
- Consider Combination Therapy
- Quality of life issues