Case studies LUTS

Professor Mike Kirby FRCP
Editor Trends in Urology & Men’s Health
Disclosures

- Michael Kirby has received funding for research, advice, conference attendance and lecturing from the pharmaceutical industry including:
  - Astellas Pharma
  - Pfizer
  - Takeda
  - Astra Zeneca
  - GSK
  - MSD
  - Sanofi
  - Menarini Group

- He is an advisor to the NHS prostate cancer advisory group and the prostate cancer risk management programme
Max Z., 66 y/o, Fireman

Main complaints: Urgency, frequency & nocturia X 2
?Weak Stream

Bother: Worse over last 3 years

LUTS medication: Herbal treatment

What to do?
Max Z., 66 y/o, Fireman

Prostate Volume 40 G approx
PSA 2.1 ng/ml
DRE soft enlarged gland, no hard nodules
IPSS 20, driven by urgency, frequency & nocturia

Comorbidities CAD, Hypertension
Meds Aspirin, Beta-Blocker, statin
Max Z., 66 y/o, Fireman

Recommendations: ?????
Max Z., 66 y/o, Fireman

Prostate Volume 40 mls
PSA 2.1 ng/ml
DRE not suspicious for PC
Qmax 11.5 ml/sec
PVR 80 ml
IPSS 20, driven by urgency, frequency & nocturia

Comorbidities CAD, Hypertension
Meds Aspirin, Beta-Blocker, statin
8 weeks later:

Prostate Volume    40 mls
PSA                1.9 ng/ml
Qmax               14 ml/sec
PVR                80 ml
IPSS               12

Frequency Volume Chart: Less than 30% at night 2,010 mls
What are lower urinary tract symptoms (LUTS)?

LUTS can be categorised into storage, voiding and post micturition symptoms:\(^1,^2\)

<table>
<thead>
<tr>
<th>Storage symptoms</th>
<th>Voiding symptoms</th>
<th>Post micturition symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Altered bladder sensations</td>
<td>• Hesitancy</td>
<td>• Feeling of incomplete bladder emptying</td>
</tr>
<tr>
<td>• Increased daytime frequency</td>
<td>• Intermittency</td>
<td>• Post micturition dribble</td>
</tr>
<tr>
<td>• Nocturia</td>
<td>• Slow stream</td>
<td></td>
</tr>
<tr>
<td>• Urgency</td>
<td>• Splitting/spraying</td>
<td></td>
</tr>
<tr>
<td>• Urgency incontinence</td>
<td>• Straining</td>
<td></td>
</tr>
<tr>
<td>• Terminal dribble</td>
<td>• Terminal dribble</td>
<td></td>
</tr>
</tbody>
</table>

Storage symptoms are associated with bladder dysfunction, e.g. overactive bladder (OAB) symptoms or urodynamic detrusor overactivity (DO)\(^3\)

Storage symptoms may be secondary to bladder outlet obstruction, though relationship is uncertain

Voiding symptoms are typically attributed to prostatic factors, e.g. prostate enlargement or benign prostatic hyperplasia (BPH)\(^3\)

Male LUTS have multifactorial aetiology

Prostate
- Benign prostatic hyperplasia
- Benign prostatic enlargement
- Benign prostatic obstruction

Bladder
- Overactive bladder symptoms
- Cardiac disease
  - Metabolic syndrome
  - Low testosterone
- Detrusor overactivity

Endocrine system
- Low testosterone

Cardiac disease
- Metabolic syndrome

Neurological disease
- Neurogenic detrusor overactivity
  - Parkinson's disease
  - Cerebral ischaemia

Others
- Urinary tract infection
- Stone disease
- Urethral stricture
- Inflammation
- Medication

LUTS = lower urinary tract symptoms
Male LUTS (without indications for surgery)

- Bothesome symptoms?
  - Nocturnal polyuria predominant?
    - Storage symptoms predominant?
      - Prostate volume >40 ml?
        - Long-term treatment?
          - Residual storage symptoms
            - Watchful waiting with or without Edu/Lifestyle
          - Edu/Lifestyle with or without α₁-blocker/PDE5-I
            - Add muscarinic receptor antagonist + continue with Edu/Lifestyle
        - Edu/Lifestyle with or without 5-ARI ± α₁-blocker/PDE5-I
          - Edu/Lifestyle with or without Muscarinic receptor antagonist
        - Edu/Lifestyle with or without Vasopressin Analogue
      - Nocturnal polyuria predominant
    - Storage symptoms predominant?
      - Prostate volume >40 ml?
    - Nocturnal polyuria predominant?
  - Edu/Lifestyle with or without Muscarinic receptor antagonist

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Current management of men with bothersome LUTS

Bothesome symptoms? 

- Watchful waiting +/- Edu/lifestyle

Further evaluation

Bothesome symptoms:

- Hesitancy
- Intermittency
- Slow stream
- Splitting/spraying
- Straining
- Terminal dribble
- Feeling of incomplete bladder emptying
- Post micturition dribble
- Altered bladder sensations
- Increased daytime frequency
- Nocturia
- Urgency
- Urgency incontinence

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Current management of men with bothersome LUTS

Bothersome symptoms?

- Nocturia predominant?
  - FVC 30%?
    - Further evaluation

Watchful waiting
  +/- Edu/lifestyle

Edu/lifestyle
  +/- Vasopressine analogue

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Current management of men with bothersome LUTS


- Bothersome symptoms?
  - Nocturia predominant?
    - Storage symptoms predominant?
      - Nocturia predominant?
        + Further evaluation
        - Altered bladder sensations
          - Increased daytime frequency
          - Nocturia
          - Urgency
          - Urgency incontinence

- Watchful waiting
  +/− Edu/lifestyle

- Edu/lifestyle
  +/− Anti-Muscarinic or mirabegron

- Edu/lifestyle
  +/− Desmopressin

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Current management of men with bothersome LUTS

- Bothersome symptoms?
  - Nocturia predominant?
    - Storage symptoms predominant?
      + Prostate >40 ml? PSA >1.4 ED?
        - Edu/lifestyle +/- α₁-AR antagonist or PDE5-I
        + Watchful waiting +/- Edu/lifestyle

- Nocturia predominant?
  + Storage symptoms predominant?
    - Prostate >40 ml? PSA >1.4 ED?
      - Long-term treatment?
        - Edu/lifestyle +/- 5-ARI +/- α₁-AR antagonist or PDE5-I
        + Edu/lifestyle +/- Muscarinic receptor antagonist
        + Edu/lifestyle +/- Desmopressin

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Some common comparisons to help assess prostate size

Walnut: 3.2cm diameter, approx. 20cc
Ping Pong Ball: 4cm diameter, approx. 33cc
Golf Ball: 4.3cm diameter, approx. 40cc
Clementine: 5cm diameter, approx. 65cc
Tennis Ball: 6.3cm diameter, approx. 130cc

• A 30 cc prostate is approximately the size of a ping pong ball
Current management of men with bothersome LUTS
Adapted from Oelke M et al. Eur Urol 2013;64:118-40

- Bothersome symptoms?
  - Nocturia predominant?
    - Storage symptoms predominant?
      - Prostate volume >40 ml?
      - Residual storage symptoms
        - Edu/lifestyle +/- α₁-AR antagonist or PDE5-I
        - Watchful waiting +/- Edu/lifestyle
  - Long-term treatment?
    - Edu/lifestyle +/- 5-ARI +/- α₁-AR antagonist or PDE5-I
    - Edu/lifestyle +/- Muscarinic receptor antagonist
    - Edu/lifestyle +/- Vasopressine analogue

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Current management of men with bothersome LUTS

- Bothersome symptoms?
  - Nocturia predominant?
    - Storage symptoms predominant?
      - Prostate volume >40 ml?
        - Long-term treatment?
          - +
            - Edu/lifestyle +/− α1-AR antagonist or PDE5-I
              - Residual storage symptoms
                - Anti-Muscarinic or mirabegron
                  + continue with Edu/Lifestyle

- Watchful waiting +/− Edu/lifestyle

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
α-blocker monotherapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>α₁-blockers should be offered to men with moderate-to-severe lower urinary tract symptoms</td>
<td>1a</td>
<td>A</td>
</tr>
</tbody>
</table>

- α₁-blockers are considered as the first-line drug treatment of moderate-to-severe LUTS
- All α₁-blockers are equally effective
- Because of their rapid onset of action, α₁-blockers can be considered for intermittent use in patients with symptoms of fluctuating intensity

Oelke M et al. EAU Guideline on Male LUTS. Update February 2012
5-ARIs should be considered in men with bothersome LUTS and an enlarged prostate

<table>
<thead>
<tr>
<th></th>
<th>5-ARI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total IPSS</td>
<td>↓~15-30%</td>
</tr>
<tr>
<td>$Q_{\text{max}}$</td>
<td>↑~1.5-2.0 ml/s</td>
</tr>
<tr>
<td>Onset of action</td>
<td>Very slow (6-12 mo)</td>
</tr>
<tr>
<td>Prostate volume</td>
<td>↓~18-28%</td>
</tr>
<tr>
<td>Duration of efficacy</td>
<td>Long-term (years)</td>
</tr>
<tr>
<td>Long-term risk of AUR or BPH-related surgery</td>
<td>+</td>
</tr>
</tbody>
</table>

AUR: acute urinary retention; BPH: benign prostatic hyperplasia; IPSS: International Prostate Symptom Score; $Q_{\text{max}}$: maximum urinary flow rate

Oelke M et al. EAU Guideline on Male LUTS. Update February 2012
# EAU recommendations

## 5-ARI monotherapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-ARIs should be offered to men with moderate-to-severe LUTS and enlarged prostates (&gt;40 ml) or elevated PSA-concentrations (&gt;1.4 - 1.6 µg/l). 5-ARIs can prevent disease progression with regard to acute urinary retention and need-for-surgery</td>
<td>1b</td>
<td>A</td>
</tr>
</tbody>
</table>

## 5ARI combination therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination treatment with $\alpha_1$–blocker together with 5-ARI should be offered to men with moderate-to-severe LUTS, enlarged prostates (&gt;40 ml) and reduced $Q_{max}$ (men likely to develop disease progression). Combination treatment is not recommended for short-term treatment (&lt;1 year)</td>
<td>1b</td>
<td>A</td>
</tr>
</tbody>
</table>

Oelke M et al. EAU Guideline on Male LUTS
Antimuscarinic monotherapy for men with predominant storage symptoms

12-wk placebo-controlled studies in men with predominant storage LUTS

<table>
<thead>
<tr>
<th>Study</th>
<th>Group 1 (N)</th>
<th>Group 2 (N)</th>
<th>Mean % change in voiding frequency vs. baseline at wk 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roehrborn 2006</td>
<td>(N=163)</td>
<td>Antimuscarinic agent: -12</td>
<td></td>
</tr>
<tr>
<td>Kaplan 2006 a</td>
<td>(N=745)</td>
<td>Placebo: -4</td>
<td></td>
</tr>
<tr>
<td>Kaplan 2006 b</td>
<td>(N=425)</td>
<td>Antimuscarinic agent: -10.8</td>
<td></td>
</tr>
<tr>
<td>Dmochowski 2007</td>
<td>(N=745)</td>
<td>Placebo: -7.9</td>
<td></td>
</tr>
<tr>
<td>Herschorn 2010</td>
<td>(N=235)</td>
<td>Antimuscarinic agent: -13.2</td>
<td></td>
</tr>
</tbody>
</table>

* Sign. vs placebo (P<0.05)

Oelke M et al. EAU Guideline on Male LUTS. Update February 2012
Addition of an antimuscarinic to an $\alpha_1$—blocker improves persistent storage symptoms

12-wk double-blind, placebo-controlled add-on studies in pts with OAB symptoms after 4 weeks of $\alpha_1$-AR antagonist treatment

Mean change in storage IPSS from baseline

MacDiarmid 2008
-2.4
-3.7
P < 0.001

Chapple 2009
-2.1
-2.6
P = 0.037

Kaplan 2009
-2.4
-3.15
P < 0.006

Yamaguchi 2011
-1.8
-2.4
P = 0.011

Kaplan 2012
-2.1
-2.4
P > 0.05

P values vs placebo

**Antimuscarinic monotherapy**

<table>
<thead>
<tr>
<th>Recommendations</th>
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<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscarinic receptor antagonists might be considered in men with moderate-to-severe LUTS who have predominantly bladder storage symptoms</td>
<td>1b</td>
<td>B</td>
</tr>
<tr>
<td>Caution is advised in men with bladder outlet obstruction</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

**Antimuscarinic + α₁-blocker combination therapy**

<table>
<thead>
<tr>
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<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination treatment with a muscarinic receptor antagonist and an α₁-blocker and might be considered in patients with moderate-to-severe LUTS if symptom relief has been insufficient with monotherapy with either drug</td>
<td>1b</td>
<td>B</td>
</tr>
<tr>
<td>Combination treatment should be used cautiously in men suspected of having bladder outlet obstruction</td>
<td>2b</td>
<td>B</td>
</tr>
</tbody>
</table>

Oelke M et al. EAU Guideline on Male LUTS. Update February 2012
What is the PVR above which you would avoid using an antimuscarinic agent (alone or in combination)?

1. 50 ml
2. 100 ml
3. 200 ml
4. 300 ml
5. 50% of bladder volume
6. Any volume is potentially significant
7. Doesn’t matter
**PDE5-inhibitors: an option for men with ED?**

- **Meta-analysis:**

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Group difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7 RCTs (N=3,214): PDE-5 inhibitor vs placebo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIEF</td>
<td>+5.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IPSS</td>
<td>-2.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Q&lt;sub&gt;max&lt;/sub&gt;</td>
<td>-0 ml/s</td>
<td>NS</td>
</tr>
<tr>
<td><strong>5 RCTs (N=216): α&lt;sub&gt;1&lt;/sub&gt;-AR antagonist + PDE-5 inhibitor vs α&lt;sub&gt;1&lt;/sub&gt;-AR antagonist monotherapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIEF</td>
<td>+3.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IPSS</td>
<td>-1.8</td>
<td>0.05</td>
</tr>
<tr>
<td>Q&lt;sub&gt;max&lt;/sub&gt;</td>
<td>+1.5 ml/s</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

IIEF: International Index of Erectile Function score; higher score = better function; NS: not significant

PDE5-inhibitors: tolerability

• Typical adverse events: headache, flushing, dizziness, dyspepsia, nasal congestion, myalgia, hypotension, syncope, tinnitus, conjunctivitis and altered vision (blurred, discoloration)

• Contraindicated in men with K+ channel opener or nicorandil due to the risk of hypotension and consecutive myocardial ischaemia

• Should not be used with the α–blockers doxazosin or terazosin
Tadalafil

✓ RCT 12 week
✓ Men ≥45, IPSS ≥13 and Qmax ≥4–15 mL/s
✓ Tadalafil 5 mg vs. Tamsulosin 0.4 mg vs. Placebo.

Table 4 – Uroflowmetry and postvoid residual volume

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 172)</th>
<th>Tadalafil 5 mg (n = 171)</th>
<th>Tamsulosin 0.4 mg (n = 168)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qmax, ml/s:</td>
<td>n = 147</td>
<td>n = 156</td>
<td>n = 144</td>
</tr>
<tr>
<td>Baseline</td>
<td>10.5 ± 4.1</td>
<td>9.9 ± 3.6</td>
<td>9.4 ± 3.3</td>
</tr>
<tr>
<td>Mean change</td>
<td>1.2 ± 4.8</td>
<td>2.4 ± 5.5</td>
<td>2.2 ± 4.1</td>
</tr>
<tr>
<td>Median change</td>
<td>0.3</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>p value vs placebo</td>
<td>–</td>
<td>0.009</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Tadalafil 5 mg and Tamsulosin 0.4 mg improve IPSS and Q\text{max}
EAU recommendations:

PDE-5 inhibitor

<table>
<thead>
<tr>
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<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDE-5 inhibitors reduce moderate to severe male LUTS in men with or without erectile dysfunction</td>
<td>1b</td>
<td>A</td>
</tr>
</tbody>
</table>

Male LUTS (without indications for surgery)

Bothesome symptoms?

Nocturnal polyuria predominant?

Storage symptoms predominant?

Prostate volume >40 ml?

Long-term treatment?

Watchful waiting with or without Edu/Lifestyle

Add muscarinic receptor antagonist + continue with Edu/Lifestyle

Edu/Lifestyle with or without 5-ARI ± α₁-blocker/PDE5-I

Edu/Lifestyle with or without Muscarinic receptor antagonist

Edu/Lifestyle with or without Vasopressin Analogue

Adapted from Oelke M et al. Eur Urol 2013;64:118-40
Mr. TM:

- A 56 year-old married father of 4, managerial position, very inactive
- Symptoms of reduced urinary flow, frequency + some urgency, and the need to get out of bed 4-5 times/night
- IPSS score: 26, IPSS QoL score: 5
- PSA: 1.2 ng/ml
- Erectile function poor
- Previous history of umbilical hernia
- Suffered some stress over the previous 2 years due to family problems
- Non-smoker and light drinker, consuming a glass of wine or 3-4 bottles of beer per week
Mr. TM: on examination

- Blood pressure (BP): 156/88 mmHg
  Pulse: 71 bpm
  Weight: 95 kg
  Waist: 106 cm
  BMI: 31 kg/m²
- The prostate felt firm and slightly enlarged
  ? 30G
- Urine NAD
Activity, weight and LUTS

• Prospective cohort study: Osteoporotic Fractures in Men Study (MrOS); N=1,695 men ≥65 yrs; mean follow-up 4.6 yrs

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio for developing LUTS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 25-29.9 vs. &lt; 25</td>
<td>1.29</td>
<td>0.05</td>
</tr>
<tr>
<td>• &gt; 30 vs. &lt; 25</td>
<td>1.41</td>
<td>0.03</td>
</tr>
<tr>
<td>High physical activity vs. low physical activity</td>
<td>0.71</td>
<td>0.03</td>
</tr>
<tr>
<td>Daily walking vs. no daily walking</td>
<td>0.80</td>
<td>0.03</td>
</tr>
</tbody>
</table>

• Overweight and obese men have higher risk of developing LUTS
• Physical activity reduces risk of developing LUTS

LUTS & ED, how often do they co-exist??
A systematic review

MSAM-7: Erectile Function Declines With Increasing Severity of LUTS Independent of Age

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

IIEF, International Index of Erectile Function;
MSAM-7, Multinational Survey of the Aging Male

Erectile dysfunction and lower urinary tract symptoms: A consensus on the importance of co-diagnosis

M. Kirby¹, C. Chapple², G. Jackson³, I. Eardley⁴, D. Edwards⁵, G. Hackett⁶, D. Ralph⁷, J. Rees⁸, M. Speakman⁹, J. Spinks¹⁰, K. Wylie¹¹

1. Faculty of Health & Human Sciences, University of Hertfordshire, Hatfield AL10 9AB, UK, and The Prostate Centre, 32 Wimpole Street, London, W1G 8GT, UK.
2. Department of Urology, Sheffield Teaching Hospitals NHS Foundation Trust; Sheffield Hallam University, Sheffield, S10 2JF, UK.
3. Department of Cardiology, Guys and St Thomas Hospitals London, London, UK.
4. St James University Hospital, Leeds, LS97TF, UK.
5. White House Surgery, Chipping Norton, Oxon, OX75AL, UK.
6. Good Hope Hospital, Birmingham, B75 7RR, UK.
8. Backwell and Nailsea Medical Group, North Somerset, BS48 3HA, UK.
9. Department of Urology, Taunton and Somerset NHS Foundation Trust, Taunton, Somerset, TA1 5DA, UK.
10. Court View Surgery, 2a Darnley Road, Strood, Kent, ME2 2HA, UK.
11. Department of Urology, Royal Hallamshire Hospital, Sheffield, S10 2JF, UK.

<<IJC DOI to be included>>
Potential pathophysiological pathways leading to LUTS in men: Preclinical evidence

Adapted from Gacci 2011 and Andersson 2011
Evolution in the Understanding of CVD

ED is part of the global risk perspective $\times 1.4$

Multiple Independent Risk Factors

Vascular Disease is an Interplay of Risk Factors

Traditional CVD Perspective

Global CV Risk Perspective

The temporal relationship between ED and CVD & why don’t men talk about it?

- 207 CVD men attending cardiac rehab
- 165 age matched controls
- ED in 66% with CVD – discussed in 53%
- ED in 37% controls – discussed in 43%
- ED on average 5 years before CVD

In half the men there were missed opportunities to assess CVD risk and treat to goal

“Men with ED should be specifically targeted for CVD preventative strategies in terms of lifestyle changes and pharmacological treatments”

# ED Predicts coronary events

1400 men 40-75, with no known CAD 10yr follow up

*Inman et al Mayo Clin Pr 2009;84:108-113*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>ED at baseline</th>
<th>No baseline ED</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td><strong>48.52 (1.23-269.26)</strong></td>
<td><strong>0.94 (0.02-5.21)</strong></td>
</tr>
<tr>
<td>50-59</td>
<td>27.15 (7.40-69.56)</td>
<td>5.09 (3.38-7.38)</td>
</tr>
<tr>
<td>60-69</td>
<td>23.97 (11.49-44.10)</td>
<td>10.72 (7.62-14.66)</td>
</tr>
<tr>
<td>70+</td>
<td>29.63 (19.37-43.75)</td>
<td>23.30 (17.18-30.89)</td>
</tr>
</tbody>
</table>

**CAD events per 1000 pt years with CI interval**
DEGREE of ED & EXTENT of CAD

If you can’t get an erection, your heart is headed in the wrong direction

**BUT**

**SO IS THE BLADDER!**

**SO PDE5is for both??**

Mark Pritzker 2002
What are some recent data on PDE5 inhibitors?

2016: PDE5 inhibitor use in patients with T2DM is associated with a reduction in all-cause mortality (N=5956)\(^1\)

Controlled for: age; eGFR; smoking status; prior cerebrovascular accident; hypertension; prior MI; systolic blood pressure; use of statins, metformin, aspirin, and beta-blockers

2017: ED treatment with PDE5 inhibitor after a first MI had a reduced risk of mortality (N=43,145)\(^2\)

Less risk of heart failure, MACE, non-CVD death, and CVD death

31% less risk of all-cause mortality over 7.5 years

38% less risk of all-cause mortality over mean 3.3 years

MACE = major adverse cardiac events.
The Interpersonal Dilemma

If there's a problem, I hope he brings it up...

I hope he asks me!!
Question to the audience
Do you perform a metabolic screen on men with LUTS?

1. Yes
2. No
Metabolic, Cardiovascular and Endocrine Factors Contribute to Male Pelvic Health.....

• Increasing evidence pointing towards relationship between LUTS and presence of metabolic syndrome
  – Recent epidemiological findings
  – Pathophysiological links have been proposed
• Bear this in mind when developing treatment strategies
  – Consideration of MSx and CVD and relevant links to LUTS and ED

Kaplan SA EU Urol 2007; 52: 316-1317
Metabolic syndrome:  
International Diabetes Federation definition

Focus on waist circumference (WC)

• Abdominal obesity:  
  Europids: ♂ WC >94 cm, ♀ WC >80 cm

• Plus any 2 of (or treatment for) the following:
  • Elevated triglycerides: ≥1.7 mmol/l
  • Reduced HDL-cholesterol: <1.03 mmol/l (♂)
    <1.29 mmol/l (♀)
  • Raised BP: ≥130/85 mmHg
  • Raised fasting plasma glucose: ≥5.6 mmol/l

Visceral fat is an active endocrine organ, promotes insulin resistance and increased CV risk

- ↑ IL-6
- ↓ Adiponectin
- ↑ Leptin
- ↑ TNFα
- ↑ Adipsin (Complement D)
- ↓ Adiponectin
- ↑ Plasminogen activator inhibitor-1 (PAI-1)
- ↑ FFA
- ↑ Insulin
- ↑ IGF
- ↑ Angiotensinogen
- ↑ Lipoprotein lipase
- ↑ Resistin
- ↑ Lactate

Inflammation

Hypertension

Atherogenic dyslipidaemia

Type 2 diabetes

Atherosclerosis

Thrombosis

Mr. TM: metabolic screen

- Total cholesterol 6.5 mmol/l
  LDL: 4.3 mmol/l
  HDL: 1 mmol/l
  triglycerides: 2.7 mmol/l
  haemoglobin A1c (HbA1c): 44 mmol/mol (6.2%)
- BP: 156/86 mmHg
- 10-yr CVD risk calculated at 16%
- Referred for lifestyle advice as first measure
- Urine cultures were negative
- Need to check testosterone
Mr. TM: further follow-up

• Diastolic BP increased 10 mmHg
  Total cholesterol increased to 7.3 mmol/l
  LDL cholesterol increased to 5.5 mmol/l

• Mr. TM was therefore
  • re-advised on diet and exercise
  • prescribed atorvastatin 40 mg, ACE inhibitor and aspirin 75 mg

• Statin therapy:
  • Target:
    • Total cholesterol < 4 mmol/l
    • Non HDL cholesterol < 2.5
Questions to the audience
Mr. TM reminder

- A 56 year-old married father of 4, managerial position, very inactive
- Symptoms of reduced urinary flow, frequency + some urgency, and the need to get out of bed 4-5 times/night
- IPSS score: 26, IPSS QoL score: 5
- PSA: 1.2 ng/ml
- Erectile function poor
- Previous history of umbilical hernia
- Suffered some stress over the previous 2 years due to family problems
- Non-smoker and light drinker, consuming a glass of wine or 3-4 bottles of beer per week
Which treatment would you recommend for this patient’s LUTS?

1. Watch and wait
2. $\alpha_1$-AR antagonist
3. 5α-reductase inhibitor
4. Antimuscarinic agent
5. PDE5-inhibitor
6. Mirabegron
7. Don’t forget FVC!
Mr. TM

- Started on $\alpha_1$-AR antagonist tamsulosin 0.4 mg for his LUTS
- + on demand sildenafil
- Was asked to follow a twice-daily exercise programme + Mediterranean diet to help him lose some weight
- Testosterone was below lower limit of normal
  - (10nmol/l)
- Booked for a follow-up consultation few weeks later
Components of the Metabolic Syndrome and Testosterone Levels

In a cohort of 803 male outpatients

Number of components of metabolic syndrome

Relative risk of hypogonadism (TT<8.0nmol/L)

Mediterranean diet

http://oldwayspt.org/resources/heritage-pyramids/Mediterranean-pyramid/overview; March 2014
In patients with a high CV risk, a Mediterranean diet reduces the incidence of major cardiovascular events.

Mr. TM: further follow-up

- Continues on atorvastatin 40 mg, ezetimibe 10 mg, ramipril 5 mg, aspirin 75 mg, tamsulosin 0.4 mg
- 1 month later: 4 kg weight loss and symptom improvement
- 3 months later:
  - Still unhappy about sexual function
Question to the audience
Mr. TM: what’s next?

1. No change
2. 5α-reductase inhibitor
3. Antimuscarinic agent
4. Combined antimuscarinic agent and α₁-AR antagonist
5. Mirabegron
6. DailyPDE5-inhibitor
7. Check testosterone again
8. TURP