LUTS in the modern era

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Tyntesfield Medical Group
In the past...!

- Man with urinary symptoms = PROSTATISM
- Prostatism = TURP
- TURP unsuccessful = REDO TURP
- Redo TURP unsuccessful = can’t help you!
The present....

• Vast majority managed in primary care
• Medical management dominates:
  – 24% watchful waiting
  – 73% medical management
  – 3% surgery
• Referral to secondary care only for men with treatment failure (poor efficacy / tolerability)
• Organ based diagnosis – ‘BPH’, ‘OAB’ etc
The Future....

“Computers in the future may weigh no more than 1.5 tons”
Popular Mechanics, 1949

“I think there is a world market for maybe 5 computers”
Thomas Watson, Chairman of IBM, 1943

“There is no reason for any individual to have a computer in his home”
Ken Olson, President, Digital Equipment Corporation, 1977
ASSESSMENT OF LUTS
Assessment

- Urinalysis
- Frequency Volume Chart
- Uroflowmetry including Post-void residual
- PSA
Uroflowmetry and voiding diary

- The physician can decide that a patient needs to keep a complete voiding diary for in total 3 days. Voids, liquid intake and leakage episodes need to be registered.

- The uroflowmeter registers volume, time and flow automatically and the patient is prompted in the app to complete questions related to the void such as type and urge.

- A void can be added manually when the patient has no access to the uroflowmeter

- Liquid intake and leakage episodes can be added manually
UROFLOWMETER CONNECTED TO SOFTWARE FOR PATIENTS AND CLINICIANS

**HOMEFLOW**
Clinician platform

**HOSPIFLOW**
Clinician platform

Patient voiding-diary app

Bluetooth connected uroflowmeter

clinician device-management app
Welcome to the QRISK®2-2015 risk calculator: http://qrisk.org

This calculator is only valid if you do not already have a diagnosis.

About you
- Age (25-84): 63
- Sex: Male
- Ethnicity: White or not stated
- UK postcode: leave blank if unknown
- Postcode: BS48 1EZ

Clinical information
- Smoking status: light smoker (less than 1.0)
- Diabetes status: none
- Angina or heart attack in a 1st degree relative < 60?:
- Chronic kidney disease?
- Atrial fibrillation?
- On blood pressure treatment?
- Rheumatoid arthritis?
- Cholesterol/HDL ratio: 5.1
- Systolic blood pressure (mmHg): 165
- Body mass index
  - Height (cm): 180
  - Weight (kg): 90

Calculate risk over 10 years.

Your results
Your risk of having a heart attack or stroke within the next 10 years is: 40%

In other words, in a crowd of 100 people with the same risk factors as you, 40 are likely to have a heart attack or stroke within the next 10 years.

Risk of heart attack or stroke

Your score has been calculated using the data you entered.
Your body mass index was calculated as 27.78 kg/m².

How does your 10-year score compare?

<table>
<thead>
<tr>
<th>Your score</th>
<th>40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your 10-year QRISK®2 score</td>
<td>40%</td>
</tr>
<tr>
<td>The score of a healthy person with the same age, sex, and ethnicity*</td>
<td>11.7%</td>
</tr>
<tr>
<td>Relative risk**</td>
<td>3.4</td>
</tr>
<tr>
<td>Your QRISK® Healthy Heart Age***</td>
<td>83</td>
</tr>
</tbody>
</table>

* This is the score of a healthy person of your age, sex, and ethnic group, i.e. with no adverse clinical indicators and a cholesterol level of 4.0, systolic blood pressure of 125 and BMI of 25.
** Your relative risk is your risk divided by the healthy person's risk.
*** Your QRISK® Healthy Heart Age is the age at which a healthy person of your sex and ethnicity has your 10-year QRISK®2 score.

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Website and risk engine built by ClinRisk Ltd.
Risk based approach to PSA

ERSPC Risk Calculator

www.prostatecancer-riskcalculator.com
DIAGNOSIS
Diagnosis

“The bladder is an unreliable witness...”
Causes of Male LUTS: ‘Urocentric’

Gratzke C et al. EAU Guidelines on the assessment of non-neurogenic LUTS including BPO. Eur Urol 2015
‘It is misleading to attribute individual symptoms to sex differences or to a specific underlying organ. LUTS are a non–sex-specific, non–organ-specific group of symptoms, which are sometimes age-related and progressive’
Causes of Male LUTS: “Holistic”

- BPH
- Renal
- CNS
- BOO
- Cardiac
- Pituitary
- BPE
Example of ‘Urocentric’ approach to LUTS

- 48 year old male referred to Community Urology Service
- LUTS – already taking tamsulosin & finasteride
- Symptoms uncontrolled by medication – “please assess for TURP”
Case Study

- Main complaint – nocturia, urinary frequency
- No voiding symptoms
- Overweight – BMI 35
- Snorer, tired (assumed due to nocturia)
- Drinks 1L coke in evening, tea+ during daytime
- Amlodipine for blood pressure
Case study – management plan

- Stop tamsulosin & finasteride
- Trial off amlodipine
- Sleep assessment by GP, likely referral to sleep clinic for ?OSA
- Weight loss & exercise
- Check HbA1c
- Changes in fluid intake, leg elevation
Symptom based approach

- Voiding symptoms
  - Low severity / bother – reassure
  - Higher severity / bother – trial of alpha blocker
  - Failure of alpha blocker – consider flow test to exclude urethral stricture / urodynamics to exclude detrusor underactivity
Symptom based approach

• Storage symptoms
  – Discuss fluid intake – type, timing, volume
  – Advice re weight loss / exercise
  – Look at medications
  – Bladder training / PFE

  – Consider anti-muscarinic / mirabegron
  – Urodynamics if not responding
Symptom pattern should determine 1\textsuperscript{st} line therapy

AB = Alpha Blocker
AM = Anti-muscarinic

- Voiding
- Storage
- Post-micturition
Symptom based approach

• Nocturia (isolated, in absence of other storage symptoms)
  – Fluid intake
  – Comorbidities – HF, DM, OSA etc
  – Medications – CCB, Diuretics etc
  – Weight, exercise

– THINK NOCTURNAL POLYURIA
TREATMENT OF LUTS
Lifestyle advice

• What is lifestyle advice??
  – Drink less caffeine to reduce frequency / urgency
  – Drink less in the evening to reduce nocturia
  – Wait until your symptoms are bad enough to justify long term medication

• Anything else??
Tip of the iceberg......

Hammarsten J. Nat Rev Urol 2011; 8; 483-494
Lifestyle Intervention – LUTS/BPH

- “In older men, central obesity and higher physical activity associated with increased & decreased risks of incident LUTS, respectively......”¹
- “Prevention of chronic urinary symptoms represents another potential health benefit of exercise in elderly men.....”¹
- “Statin use associated with 6.5 to 7 year delay in the onset of moderate / severe LUTS....”²

2. St Sauver JL et al BJU Int 2010
The Urologist as the advocate of Men’s Health

“The Urologist as a ‘Men’s Health’ doctor has the opportunity, working in conjunction with the family physician, to identify and treat the hypertension, hyperlipidaemia and diabetes that results in the endothelial damage that causes ED.... this is surely not too demanding or inappropriate a task. The Urologist can also provide lifestyle advice about diet and alcohol, both of which commonly exacerbate the early symptoms of BOO arising from BPH....”

Roger Kirby, BJU Comments 2005
Nocturia is a multifactorial medical condition

Nocturnal polyuria
- Impaired circadian rhythm of AVP, diuretics, congestive heart failure, obstructive sleep apnoea, peripheral oedema, excessive nocturnal fluid intake

Global polyuria
- Diabetes mellitus/insipidus, primary polydipsia, medication, excessive fluid intake

Reduced bladder capacity
- BPH, neurogenic bladder, idiopathic nocturnal DO, other urological conditions/disorders, anxiety disorders, medication

Sleep disorders
- Primary or secondary sleep disorders, neurologic conditions, psychiatric disorders, chronic pain, medication, alcohol

AVP: arginine vasopressin; BPH: benign prostatic hyperplasia; DO: detrusor overactivity

Nocturia is primarily caused by nocturnal polyuria

Nocturnal polyuria based on data from 3- or 7-day frequency-volume charts completed by patients as part of screening for inclusion in subsequent trials of nocturia therapy.

Management should be tailored depending on the aetiology of nocturia

<table>
<thead>
<tr>
<th>Nocturnal polyuria</th>
<th>Global polyuria</th>
<th>Reduced bladder capacity</th>
</tr>
</thead>
</table>

### Behavioural modifications

- Reduce fluid intake
- Therapy for specific medical condition
- Desmopressin
- Change time of taking diuretics

- Reduce fluid intake
- Treat diabetes mellitus/insipidus

- Therapy for OAB/BPH
- Therapy for other urological condition

Therapies for OAB and BPH do not treat nocturia due to nocturnal polyuria.

Patients with nocturia due to nocturnal polyuria (N=997)

- No significant differences between treatment groups and placebo

-0.68
-0.72
-0.64

Mean actual change in number of nocturia episodes from baseline

-0.8 -0.6 -0.4 -0.2 0

- Solifenacin 10 mg (N=400)
- Solifenacin 5 mg (N=211)
- Placebo (N=386)

Patients unresponsive to $\alpha_1$-blocker treatment (N=41)

-85%
-10%
-5%

Nocturnal polyuria, Global polyuria, Normal nocturnal output

Mirabegron for OAB?

- **NICE** recommends Mirabegron as:
  - an option for treating symptoms of OAB only for people in whom antimuscarinic drugs are
    - contraindicated
    - clinically ineffective
    - or have unacceptable side effects
Antimuscarinics: Cognitive Function

- Prospective population based cohort study
- 3434 subjects ≥ 65 yrs
- Cumulative anticholinergic exposure measured using Total Standardised Daily Doses (TSDD)
- Outcomes: Dementia and Alzheimer’s Disease
- Commonest classes of drug used
  - Tricyclics
  - Antihistamines
  - Antimuscarinics
- Higher cumulative anticholinergic use associated with an increased risk of dementia

Mode of action: Antimuscarinics & Mirabegron

Adapted from Betmiga Summary of Product Characteristics, December 2012 and Chu et al., 2006.
Betmiga Summary of Product Characteristics, December 2012

Gras J. Drugs of Today 2012;48(1):25-32
**IPSS: Tadalafil vs placebo & Tamsulosin vs placebo**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline Mean (SD)</th>
<th>12-week Endpoint LS Mean Change (ANCOVA, LOCF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>17.4 (6.0)</td>
<td>-4.2</td>
</tr>
<tr>
<td>Tadalafil 5mg</td>
<td>17.2 (4.9)</td>
<td>-6.3***</td>
</tr>
<tr>
<td>Tamsulosin 0.4mg</td>
<td>16.8 (5.3)</td>
<td>-5.7*</td>
</tr>
</tbody>
</table>

*p<.05, **p<.01, ***p<.001 compared to placebo

*Values for week 1 are based on mIPSS

Tamsulosin is an active control. Both treatments are compared to placebo.

Oelke et al. *Eur Urol* 2012;61: 917 - 925
Male LUTS EAU Guidelines 2015
(without indications for surgery)

- Bothersome symptoms?
  - Nocturnal polyuria predominant?
    - Storage symptoms predominant?
      - Prostate volume >40 ml?
        - Edu/Lifestyle with or without Anti cholinergic
          + Long-term treatment?
            - Edu/Lifestyle with or without Vasopressin Analogue
              - Edu/Lifestyle with or without 5-ARI ± α₁-blocker/PDE5-I
                - Edu/Lifestyle with or without α₁-blocker/PDE5-I
                  - Residual storage symptoms
                    - 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 Anti cholinergic
The UroLift® Implant

- Permanent Transprostatic Tissue Retractor
  - Implant sized *in situ* to prostate lobe
  - Nitinol, PET, Stainless Steel

Delivery Device
Prostatic Urethral Lift (UroLift® System)

- Directly open the urethra
- No tissue removal or ablation
- Improved outcomes, lower morbidity
Immediate UroLift® Effect

- Mechanically opens prostatic urethra
- Result is visible under cystoscopy
- Implants are anterolateral, away from NV bundles or dorsal venous complex
Overall impact on symptoms

- Over 950 patient-years, >60 operators
- Rapid response (2 weeks); durable to at least 4 years

Improvement in storage & voiding LUTS

Roehrborn et al. Can J Urol 2015
## Results and evaluation (LEEDS – thanks to Mr Oliver Kayes)

Over 72 patients have been treated with UroLift. In the majority of these patients, local anaesthetic was used and is now routine. The results of a recent audit are shown in the table below.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of procedures (Jan – Sep 2016)</th>
<th>Average length of stay</th>
<th>Theatre time (Patient turnaround) (mins)</th>
<th>Anaesthetic (local / general)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UroLift</td>
<td>72</td>
<td>3-4 hours</td>
<td>25 mins</td>
<td>LA (85%) GA (15%)</td>
</tr>
<tr>
<td>TURP</td>
<td>122</td>
<td>3 days</td>
<td>56</td>
<td>GA (100%)</td>
</tr>
<tr>
<td>HoLEP</td>
<td>115</td>
<td>17 hours</td>
<td>72</td>
<td>GA (100%)</td>
</tr>
</tbody>
</table>
Summary

• LUTS require a holistic approach to diagnosis & management

• New treatments available – how will national / local pathways & guidelines respond to these changes?