Disclosures

- Allergan – Scientific trial
- Medtronic – Scientific trial
- Serenity – Investment interest
- Chair AUA Office of Education
Definitions

• Mixed urinary incontinence
  • Complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing*

• UDS findings
  • Combination of urodynamic stress incontinence AND detrusor overactivity incontinence
    • USUI - involuntary leakage of urine during filling cystometry, associated with increased intra-abdominal pressure, in the absence of a detrusor contraction
    • DOI - involuntary leakage of urine associated with an involuntary detrusor contraction

* Haylen BT, et al Neurol Urodyn 2010; 29:4-20
Definitions

- **Insensible urinary incontinence**
  - Complaint of urinary incontinence where the woman has been unaware of how it occurred*

- **UDS findings**
  - In the absence of extra-urethral incontinence this will be caused by either USUI, DOI, incontinence associated with impaired bladder compliance, or overflow incontinence

* Haylen BT, et al Neurol Urodyn 2010; 29:4-20
Spectrum of Mixed Symptoms

Adapted from Wein AJ. J Urol. 2006;175:S6-S10.
Prevalence of Urinary Incontinence in Women


<60 Years Old
- Urgency: 20%
- Stress: 55%
- Mixed: 25%

>60 Years Old
- Urgency: 35%
- Stress: 30%
- Mixed: 35%
Women with MUI Have More Severe Incontinence Than Women with SUI

- Secondary analysis from Phase II Duloxetine clinical trial for SUI – 553 women
  - 31% had MUI
  - 69% SUI

- Women with MUI had more severe incontinence (>mean IEF and PGI-S)

MUI and UDS Findings In Women with Predominant SUI

• For women presenting with predominant SUI (pure or mixed) the major determinant of concurrent urge symptoms is incontinence severity not pathologic condition (UDS)

• More severe SUI, not DO leads to mixed symptoms

• As severity of incontinence improves, mixed symptoms resolve (convert to pure stress)

General Rules for Treating MUI

• Start with least invasive, reversible treatments if practical
• If there is clearly a most bothersome symptom, SUI or UUI, focus treatment on that first
• Basic evaluation is often enough to start treatment
• Utilize advanced testing when necessary
  • UDS
  • Cystoscopy
Basic Evaluation of Women with MUI

• History
• Physical exam
• UA
• PVR
• Additional simple testing when indicated
  • Bladder diary for more severe OAB
  • Uroflow if significant voiding symptoms
MUI – Indications for UDS

- Diagnosis is uncertain
- Not comfortable treating most bothersome/predominant symptom or there is no most bothersome/predominant symptom
- Very severe incontinence, especially in the elderly
- Significant voiding symptoms / abnormal uroflow
- Significantly elevated PVR
- Concern for lower or upper urinary tract decompensation
- Prior SUI surgery
MUI – Indications for Cystoscopy

- Hematuria
- Anatomic abnormality suspected
- Prior SUI surgery especially if MUS
- ? Refractory OAB symptoms
Patients had moderate to severely bothersome SUI and UUI at least one episode of each on a 3-day diary:

1° outcome – change in symptoms at 12 mo on UDI (MCID = 35 points)

2° outcome – change in stress and irritative UDI scores at 12 months MCID’s – 8 pts (stress) and 15 pts (irritative)
Slings did pretty well in treating both SUI and UUI.

Conclusion: Among women with MUI, behavioral and PFMT combined with MUS vs. MUS alone resulted in a small statistically significant difference in urinary continence symptoms at 12 months that did not meet prespecified threshold for clinical importance.

### Table 2. Primary and Secondary Outcomes Through 12 Months

<table>
<thead>
<tr>
<th>Outcome Type</th>
<th>Baseline&lt;sup&gt;b&lt;/sup&gt; (n = 235)</th>
<th>Sling Only (n = 229)</th>
<th>3 Months&lt;sup&gt;b&lt;/sup&gt; (n = 194)</th>
<th>Sling Only (n = 198)</th>
<th>6 Months&lt;sup&gt;b&lt;/sup&gt; (n = 182)</th>
<th>Sling Only (n = 176)</th>
<th>12 Months&lt;sup&gt;b&lt;/sup&gt; (n = 181)</th>
<th>Sling Only (n = 174)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UDI Total Score (Primary)&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
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</tr>
<tr>
<td>Score, unadjusted, mean (SD)</td>
<td>178.0 (42.8)</td>
<td>176.8 (40.5)</td>
<td>35.4 (44.1)</td>
<td>37.2 (44.4)</td>
<td>30.4 (40.1)</td>
<td>36.6 (49.6)</td>
<td>30.7 (42.6)</td>
<td>34.5 (44.7)</td>
</tr>
<tr>
<td>Difference from baseline, adjusted mean (95% CI)</td>
<td>-125.7 (-143.4 to -107.9)</td>
<td>-119.9 (-137.6 to -102.3)</td>
<td>-126.5 (-144.2 to -108.8)</td>
<td>-118.2 (-135.8 to -100.7)</td>
<td>-128.1 (-146.5 to -109.8)</td>
<td>-114.7 (-133.3 to -96.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference-in-difference, adjusted mean (95% CI)</td>
<td>-5.7 (-15.8 to 4.4)</td>
<td>-8.3 (-18.0 to 1.5)</td>
<td>-13.4 (-25.9 to -1.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>P value</td>
<td>.27</td>
<td>.10</td>
<td></td>
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<td></td>
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<td>.04</td>
</tr>
<tr>
<td><strong>UDI-Irritative Score (Secondary)&lt;sup&gt;d&lt;/sup&gt;</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Score, unadjusted mean (SD)</td>
<td>66.0 (19.6)</td>
<td>67.6 (19.7)</td>
<td>15.5 (20.5)</td>
<td>16.9 (21.9)</td>
<td>12.2 (17.7)</td>
<td>16.4 (24.0)</td>
<td>12.2 (18.7)</td>
<td>15.1 (21.2)</td>
</tr>
<tr>
<td>Difference from baseline, adjusted mean (95% CI)</td>
<td>-42.7 (-50.7 to -34.6)</td>
<td>-41.1 (-49.1 to -33.1)</td>
<td>-43.4 (-51.5 to -35.4)</td>
<td>-40.4 (-48.3 to -32.4)</td>
<td>-45.0 (-53.4 to -36.6)</td>
<td>-38.9 (-47.4 to -30.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference in difference, adjusted mean (95% CI)</td>
<td>-1.6 (-6.2 to 3.1)</td>
<td>-3.1 (-7.5 to 1.4)</td>
<td>-6.1 (-12.1 to -0.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>.51</td>
<td>.18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td><strong>UDI-Stress Score (Secondary)&lt;sup&gt;d&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score, unadjusted mean (SD)</td>
<td>86.0 (17.6)</td>
<td>84.9 (18.0)</td>
<td>14.6 (22.7)</td>
<td>14.6 (21.0)</td>
<td>14.1 (21.5)</td>
<td>15.3 (23.9)</td>
<td>13.3 (22.0)</td>
<td>15.3 (23.5)</td>
</tr>
<tr>
<td>Difference from baseline, adjusted mean (95% CI)</td>
<td>-66.4 (-75.2 to -57.7)</td>
<td>-55.1 (-73.8 to -56.4)</td>
<td>-66.6 (-75.3 to -58.0)</td>
<td>-64.0 (-72.6 to -55.3)</td>
<td>-67.1 (-76.1 to -58.1)</td>
<td>-61.6 (-70.7 to -52.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference in difference, adjusted mean (95% CI)</td>
<td>-1.3 (-6.4 to 3.8)</td>
<td>-2.7 (-7.5 to 2.2)</td>
<td>-5.5 (-11.5 to 0.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>.62</td>
<td>.28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.08</td>
<td></td>
</tr>
</tbody>
</table>
MUI based on answers to both questions 2 and 3 on the UDI-6 of:

- “somewhat”
- “moderately”
- “quite a bit”
Concurrent Retropubic Midurethral Sling and OnabotulinumtoxinA for Mixed Urinary Incontinence

A Randomized Controlled Trial

Table 3. Comparison of 3-Month Postoperative Patient Global Impression of Improvement Scores Between Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>OnabotulinumtoxinA</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGI-I score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo postoperatively [n (% total cohort)*]</td>
<td>41 (53)</td>
<td>37 (47)</td>
<td></td>
</tr>
<tr>
<td>Overall incontinence symptoms (percent “improved”††)</td>
<td>34 (83)</td>
<td>31 (84)</td>
<td>1.0</td>
</tr>
<tr>
<td>Stress incontinence symptoms only (percent “improved”‡)</td>
<td>40 (98)</td>
<td>37 (100)</td>
<td>1.0</td>
</tr>
<tr>
<td>Urgency incontinence symptoms only (percent “improved”‡)</td>
<td>30 (73)</td>
<td>24 (65)</td>
<td>.58</td>
</tr>
<tr>
<td>Overall incontinence symptoms (range 1–7)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1.0</td>
</tr>
<tr>
<td>Stress incontinence symptoms only (range 1–7)</td>
<td>1 (1–1)</td>
<td>1 (1–1)</td>
<td>.46</td>
</tr>
<tr>
<td>Urgency incontinence symptoms only (range 1–7)</td>
<td>1 (1–3)</td>
<td>2 (2–4)</td>
<td>.028</td>
</tr>
</tbody>
</table>

PGI-I, Patient Global Impression of Improvement.
Data are n (%) or median (interquartile range) unless otherwise specified.
* PGI-I scale: 1=very much better, 2=much better, 3=a little better, 4=no change, 5=a little worse, 6=much worse, 7=very much worse.
† Primary outcome.
‡ Defined as “very much better” or “much better.”
Concurrent Retropubic Midurethral Sling and OnabotulinumtoxinA for Mixed Urinary Incontinence: A Randomized Controlled Trial

Alix Kumar, MD, Carol E. Bretschneider, MD, Margaret G. Mueller, MD, Christina Lewicky-Gaupp, MD, Sarah Collins, MD, Julia Geynisman-Tan, MD, Meera Taovathia, MPH, and Kimberly Kenton, MD, MS

Table 4. Compared of 3-Month Postoperative Survey Scores and Bladder Diary Scores Between Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>OnabotulinumtoxinA</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-mo survey scores (n (% total cohort)]</td>
<td>41 (53)</td>
<td>37 (47)</td>
<td></td>
</tr>
<tr>
<td>UDI-6 (range 0–100)</td>
<td>4.2 (0.0–6.3)</td>
<td>8.3 (0.0–12.5)</td>
<td>.20</td>
</tr>
<tr>
<td>PFIQ-7 (range 0–300)</td>
<td>0.0 (0.0–14.3)</td>
<td>4.8 (0.0–23.8)</td>
<td>.65</td>
</tr>
<tr>
<td>IQR-7 (range 0–100)</td>
<td>0.0 (0.0–9.5)</td>
<td>4.8 (0.0–23.8)</td>
<td>.24</td>
</tr>
<tr>
<td>PGI-S</td>
<td>Overall incontinence symptoms (range 1–4)*</td>
<td>1 (1–2)</td>
<td>2 (1–2)</td>
</tr>
<tr>
<td></td>
<td>Overall stress incontinence symptoms only (range 1–4)*</td>
<td>1 (1–1)</td>
<td>1 (1–1)</td>
</tr>
<tr>
<td></td>
<td>Overall urgency incontinence symptoms only (range 1–4)*</td>
<td>1 (1–2)</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>3-mo bladder diary leaks [n (% total cohort)]</td>
<td>28 (36)</td>
<td>25 (32)</td>
<td></td>
</tr>
<tr>
<td>No. of leaks due over 3 d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due to overall incontinence</td>
<td>0 (0–2)</td>
<td>0 (0–2)</td>
<td>.37</td>
</tr>
<tr>
<td>Due to stress incontinence</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>.38</td>
</tr>
<tr>
<td>Due to urgency incontinence</td>
<td>0 (0–2)</td>
<td>0 (0–2)</td>
<td>.35</td>
</tr>
</tbody>
</table>

UDI-6, Urinary Distress Inventory; Short Form; PFIQ-7, Pelvic Floor Impact Questionnaire–Short Form; IQR-7, Incontinence Impact Questionnaire, Short Form; PGI-S, Patient Global Impression of Severity; IQR, interquartile range.

Data are medians (interquartile range) unless otherwise specified.

* PGI-S scale: 1 = normal, 2 = mild, 3 = moderate, 4 = severe.

Table 2. Comparison of Adverse Events Between Groups

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>OnabotulinumtoxinA</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (% total cohort)</td>
<td>41 (53)</td>
<td>37 (47)</td>
<td></td>
</tr>
<tr>
<td>Intraoperative edema of left labium majus</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>.47</td>
</tr>
<tr>
<td>Reoperation 1-wk postoperatively for misplaced sling (sling replaced)</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>.47</td>
</tr>
<tr>
<td>Urinary retention or failed VT immediately postoperatively</td>
<td>3 (7)</td>
<td>2 (5)</td>
<td>1.0</td>
</tr>
<tr>
<td>Urinary retention requiring self-catheterization between surgery and 2-wk postoperative visit</td>
<td>5 (12)</td>
<td>2 (5)</td>
<td>.44</td>
</tr>
<tr>
<td>Days of self-catheterization</td>
<td>5 (4–6)</td>
<td>1 (1–2)</td>
<td>.12</td>
</tr>
<tr>
<td>Urinary retention requiring self-catheterization between 2-wk and 3-mo postoperative visits</td>
<td>5 (12)</td>
<td>1 (3)</td>
<td>.20</td>
</tr>
<tr>
<td>Days of self-catheterization</td>
<td>3 (3–3)</td>
<td>3 (3–3)</td>
<td>.19</td>
</tr>
<tr>
<td>Mesh exposure managed expectantly</td>
<td>3 (7)</td>
<td>1 (3)</td>
<td>.21</td>
</tr>
<tr>
<td>UTI</td>
<td>9 (22)</td>
<td>2 (5)</td>
<td>.051</td>
</tr>
</tbody>
</table>

VT, voiding trial; UTI, urinary tract infection.

Data are n (%) or median (interquartile range) unless otherwise specified.
Concurrent onabotulinumtoxinA injection did not improve overall incontinence symptoms at 3 months vs. placebo in women undergoing retropubic MUS.

Women with MUI undergoing sling report significant improvement in overall incontinence symptoms.

Those receiving concurrent onabotulinumtoxinA injections reported less urgency severity and greater improvement in urgency symptoms at 3 months.
50 Year Old Woman with MUI

• Progressive SUI limits physical activity such as exercise
• Usually one episode of UUI per day
• Wearing 2-3 pads/day, bothered and wants treatment
• Did PFME’s and BM – no help
• Physical exam – urethral hypermobility and SUI demonstrated
• PVR = zero
• Further testing?

Probably not
All possible treatments really do not require it
50 Year Old Woman with MUI

- Possible next step treatments
  - PFPT
  - OAB meds (will not help SUI, but may help UUI if that is what patient desires)
  - Urethral bulking
  - SUI surgery
62 Year Old Woman with MUI

- 62 year old woman with mixed incontinence
  - Unhappy and wants treatment
  - 3 diapers/day
  - Unable to tell if stress or urge is worse or which is more bothersome
- Significant insensible incontinence
- Physical exam shows urethral hypermobility and significant SUI
- Normal emptying (PVR = 0), UA negative
- Failed PFME’s and 3 different OAB meds
- Further testing?

Why UDS?
To determine SUI treatment vs. 3rd line OAB treatment
62 Year Old Woman With MUI

Low ALPP – poor urethral resistance
Low pressure DO
65 Year Old Woman With MUI

- Severe Incontinence 2-3 pads / day
- Has both SUI and UUI
- Failed behavioral modification and PFME
- On multiple medications, reluctant to take another
- PE - mild urethral hypermobility no SUI with 200 ml in bladder even standing
- PVR = 20 ml, UA negative
- Further testing?

Why UDS? SUI not demonstrated and patient reluctant to take OAB meds
65 Year Old Woman with SUI

Stress induced DO
No urodynamic SUI
38 Year Old Woman with MUI

- High grade incontinence – insensible + urgency incontinence for years
- Many large pads/day
- PE: High grade SUI with no urethral mobility
- PVR = 0
- No treatment for incontinence yet
38 Year Old Woman with MUI

- 6 years s/p nephrectomy for right staghorn calculus
- Recent sepsis and left hydronephrosis (creatinine from 1.0 to 3.4)
  - Foley placed, sepsis treated, creatinine normalized and hydronephrosis resolved
  - Follow-up imaging showed recurrent left hydronephrosis with no point of obstruction identified
- Further testing?

Why UDS?
Upper tract decompensation suggests dangerous storage problem
38 Year Old Woman with MUI
Leakage starts and persists.