NAVIGATING FEMALE STRESS URINARY INCONTINENCE IN THE ERA OF MESH

Kathleen C. Kobashi, MD, FACS
Virginia Mason Medical Center
Seattle, WA
DISCLOSURES

• Advisory Board and/or Speaker and Investigator
  • Allergan
  • Contura
  • Medtronic

• AUA Guidelines
  • Stress incontinence, Chair, 2015-2017
  • Microhematuria, Member 2018-present
OVERVIEW

- Perspective and impact
- Brief history of slings and mesh
- Current status (in US and abroad)
  - FDA communications
  - Patients, surgeons, industry, attorneys
- What next?
PREVALENCE

• Up to 40% of women have SUI
• Lifetime risk of surgery for POP or SUI
  • 11% on 1995
  • 20% in 2011
• Procedures
  • Increased 27% in US between 2000-2009
    • 2004  28,000
    • 2013  14,490
• In UK:
  • 2000-01  8458
  • 2008-09  13219
  • 2012  11845
## A LITTLE HISTORY

<table>
<thead>
<tr>
<th>Author</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Giordano, 1907</td>
<td>Gracilis muscle</td>
</tr>
<tr>
<td>Goebel, 1910</td>
<td>Pyramidalis</td>
</tr>
<tr>
<td>Fragenheim, 1917</td>
<td>Rectus fascia flap</td>
</tr>
<tr>
<td>Stoeckel, 1917</td>
<td>Plication of muscle around bladder neck</td>
</tr>
<tr>
<td>Price, 1933</td>
<td>Fascia lata fixed to rectus muscle</td>
</tr>
</tbody>
</table>
COMMON BELIEF

Muscle around bladder neck would acquire sphincter-like function
<table>
<thead>
<tr>
<th>Author</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldridge, 1942</td>
<td>2 strips fascia beneath urethra</td>
</tr>
<tr>
<td>Narik, Palmrich, 1962</td>
<td>External oblique aponeurosis attached to pubic tubercle</td>
</tr>
<tr>
<td>Williams, 1962</td>
<td><em>First synthetic sling</em> (<em>mersiline</em>)</td>
</tr>
</tbody>
</table>
SLINGS FELL OUT OF FAVOR

• Efficacy reasonable for the time
• Complications high
  • Fistulas
  • Obstruction
  • Urethral sloughing
  • Abscesses
• Gave way to bladder neck suspensions
SEVERAL THEORIES

- Pressure distribution and differential
- Compressibility of urethra
- Early success reported
- But, eventually....
• McGuire autologous sling
• Blaivas modification

REVIVAL OF THE SLING
## “EARLY” LONG-TERM RESULTS

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Result</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siegel</td>
<td>20</td>
<td>80% no SUI</td>
<td>15.4 years</td>
</tr>
<tr>
<td>Morgan</td>
<td>247</td>
<td>85% of 88 “cured”</td>
<td>4.25 years</td>
</tr>
<tr>
<td>Chaikin</td>
<td>20</td>
<td>95% of 20 “cured”</td>
<td>10 years</td>
</tr>
<tr>
<td>Rodrigues</td>
<td>126</td>
<td>74.4% “cured”</td>
<td>5.86 years</td>
</tr>
</tbody>
</table>

BUT TECHNICALLY CHALLENGING

• Generally limited to a few specialists of the time
• Could it be easier?
• Back to the continence mechanism...
Many continent women have proximal urethral mobility

Many successful anti-incontinence procedures do nothing to proximal urethral mobility
Continence dependent upon:
• Fixation of *midurethra* to pubic bone
• Physiologic backboard
• Support of stretch receptors at proximal urethra

THE HAMMOCK THEORY

- Anterior vaginal wall
- Levator ani
- Pubourethral ligaments

- Suburethral support
  and
- Musculofascial compression

Delancey, 1994
MIDURETHRAL SLING: A POPULAR CHOICE

- Type I polypropylene mesh
- Loosely at midurethra

- Simple
- Efficacious
- Safe
MECHANISM OF ACTION

• Ultrasound
• Rotation of proximal urethra
• Midurethral kinking
• Compression of urethra between sling and symphysis

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>F/U (mos)</th>
<th>Cured % (n)</th>
<th>Improved % (n)</th>
<th>Retention % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulmsten et al., 1998</td>
<td>131</td>
<td>≥12</td>
<td>91 (119)</td>
<td>7 (9)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Wang &amp; Lo, 1998</td>
<td>70</td>
<td>3-18</td>
<td>87 (61)</td>
<td>4 (3)</td>
<td>17 (12)</td>
</tr>
<tr>
<td>Olsson &amp; Kroon, 1999</td>
<td>51</td>
<td>36</td>
<td>90 (46)</td>
<td>6 (3)</td>
<td>Few</td>
</tr>
<tr>
<td>Wang, 2000</td>
<td>39</td>
<td>19</td>
<td>90 (35)*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Nilsson, et al, 2001</td>
<td>90</td>
<td>48-70</td>
<td>84.7 (72)</td>
<td>10.6 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Haab, 2001</td>
<td>46</td>
<td>12-24</td>
<td>86.9 (40)</td>
<td>10.9 (5)</td>
<td>0</td>
</tr>
<tr>
<td>Jeffry et al., 2001</td>
<td>88</td>
<td>25</td>
<td>91 (80)</td>
<td>9 (8)</td>
<td>4 (4)</td>
</tr>
</tbody>
</table>

*Cured/improved reported together*
WARD AND HILTON

- Randomized prospective trial
- n=344 with 2 year follow up

<table>
<thead>
<tr>
<th>Technique</th>
<th>n</th>
<th>Objective cure</th>
<th>Objective cure with intent to treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>TVT™</td>
<td>175</td>
<td>81%</td>
<td>63%</td>
</tr>
<tr>
<td>Colposuspension</td>
<td>169</td>
<td>80%</td>
<td>51%</td>
</tr>
</tbody>
</table>

**TVT™ “EARLY” LONG-TERM RESULTS**

<table>
<thead>
<tr>
<th>Author</th>
<th>F/U</th>
<th>n</th>
<th>“Success” (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chene, 2006</td>
<td>At 5 years</td>
<td>82</td>
<td>79.2</td>
</tr>
<tr>
<td>Ankardal, 2006</td>
<td>At 5 years</td>
<td>707</td>
<td>73</td>
</tr>
<tr>
<td>Doo, 2006</td>
<td>67 (60-76)</td>
<td>134</td>
<td>76.9</td>
</tr>
<tr>
<td>Kuuva, 2006</td>
<td>Mean 6 years</td>
<td>129</td>
<td>74% by stress test</td>
</tr>
<tr>
<td>Tsivian, 2004</td>
<td>55 (48-65)</td>
<td>52</td>
<td>78.9</td>
</tr>
</tbody>
</table>
TVT™ LONG-TERM DATA

- 1- and 5-year follow up
- n=134

<table>
<thead>
<tr>
<th></th>
<th>1-year</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure/improved</td>
<td>97.7%</td>
<td>94.9%</td>
</tr>
<tr>
<td>Cure</td>
<td>90.1%</td>
<td>76.9%</td>
</tr>
</tbody>
</table>

TVT™ : MULTICENTER STUDY

- N=689, 24 month follow up
- 41 hospitals, 54 surgeons

<table>
<thead>
<tr>
<th></th>
<th>2 mos</th>
<th>6 mos</th>
<th>12 mos</th>
<th>24 mos</th>
</tr>
</thead>
<tbody>
<tr>
<td>No leakage</td>
<td>68.30</td>
<td>71.90</td>
<td>71.90</td>
<td>67.70</td>
</tr>
<tr>
<td>Improved</td>
<td>23.00</td>
<td>22.80</td>
<td>24.90</td>
<td>28.30</td>
</tr>
<tr>
<td>No change</td>
<td>7.60</td>
<td>4.20</td>
<td>2.60</td>
<td>3.60</td>
</tr>
<tr>
<td>Worse</td>
<td>1.10</td>
<td>1.10</td>
<td>0.60</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Overall success: 96.00%

OTHER ITERATIONS

• Transobturator
  • Avoid retropubic space
• Single incision slings
  • Avoid passage “anywhere”
FAST FORWARD

Global status
<table>
<thead>
<tr>
<th>YEAR</th>
<th>AUSTRALIA</th>
<th>UNITED KINDGOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>Mesh approved</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>First complication reported</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td>Scotland suspension on mesh</td>
</tr>
<tr>
<td>11/28/17</td>
<td>POP mesh and mini-slings halted</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MUSs remained on registry</td>
<td></td>
</tr>
<tr>
<td>7/10/18</td>
<td></td>
<td>“Pause” on all TV mesh (England, Wales, Ireland)</td>
</tr>
<tr>
<td>9/12/18</td>
<td></td>
<td>Halt on all mesh (Scotland)</td>
</tr>
<tr>
<td>12/1/18</td>
<td>Mesh reclassified IIb→III (med-high→high risk)</td>
<td>Previously approved must reapply by 12/20</td>
</tr>
</tbody>
</table>
UPDATED 2019 NICE GUIDELINES

• NICE
  • Highly regarded
  • Evidence-based by independent committees including professionals, lay members

• Slings remain an option, but not first line

• Patients should be advised
  • Permanent
  • May not be reversible

• Empowers patients to make informed choice
• NHS not compelled to abide by guidelines
• *Pause remains in effect*
• Slings must be done by specialists
• Outcomes be reported to database
• Possible re-look in 2020 once national registry established
• TV mesh continues to evolve
• Complications may occur
• Must be aware of complications
• Surgery may or may not correct condition
• Surgeons need adequate training
• POP may be successfully treated with native tissue repair
• SIS is novel and may have higher risk
CANADIAN POSITION STATEMENT

- Literature supports RMUS and TMUS
- Rare, but serious complications can occur
- May or may not be correctable even with surgery
- Patients must be informed
- Surgeons should be adequately trained
- Must be able to recognize and address

IN THE US...
IN THE BEGINNING…2001

- FDA classified TV mesh for POP as class II
- Similar to abdominal hernia mesh
- Approved without premarket evaluation
- Only 501k process necessary
<table>
<thead>
<tr>
<th>YEAR</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/20/08</td>
<td>FDA notification re: serious complications with TV mesh for POP and SUI</td>
</tr>
<tr>
<td>7/13/11</td>
<td>Update for POP only</td>
</tr>
<tr>
<td>9/8/11</td>
<td>Panel convened to assess POP and SUI mesh</td>
</tr>
<tr>
<td>1/3/12</td>
<td>Post market surveillance (“522”) ordered for POP, mini-sling</td>
</tr>
<tr>
<td>3/27/13</td>
<td>Updated communication regarding slings</td>
</tr>
<tr>
<td>4/29/14</td>
<td>Proposal to reclassify POP mesh, require premarket assessments, 510K for tools</td>
</tr>
<tr>
<td>1/5/16</td>
<td><strong>POP mesh reclassified II→III (high risk)</strong></td>
</tr>
<tr>
<td>1/6/17</td>
<td>(final order requiring 510k for devices)</td>
</tr>
<tr>
<td>7/13/18</td>
<td>Last posterior compartment mesh pulled</td>
</tr>
<tr>
<td>2/12/19</td>
<td>Panel convened to assess specifically POP mesh</td>
</tr>
</tbody>
</table>
FDA PANEL CONCLUSIONS

February 12, 2019

• 36 month safety and outcomes
• Must be superior to native tissue repairs to be supported
APRIL 16, 2019

FDA MANDATE:

Distribution of all transvaginal mesh for prolapse repair halted

EFFECTIVE IMMEDIATELY
SUFU RESPONSE

• Corresponded with FDA
• Partnering with AUA, AUGS, ACOG, SGS
  • ICS, IUGA on international front

• **Must maintain differentiation of TV POP mesh from midurethral slings (and transabdominal POP mesh)**
• Acknowledge risks
• Preserve choices for patients
LEGAL CLIMATE IN US

• After 2008 statement, 100 cases filed\(^1\)
• After 2011, 32,296/year\(^2\)
• By 2015, 74,514\(^3\)
• Distribution:
  • 63% SUI
  • 14% POP
  • 23% POP and SUI

\(^2\)Litigation USJPoM, 2015
\(^3\)Souders et al. Female Pelvic Med Reconstr Surg 2018; 24: 21-25
SO, WHERE NEXT?

Back to more invasive options?
Less effective choices?
Efficacy and safety must be known
SO, WHAT ARE OUR OPTIONS?

<table>
<thead>
<tr>
<th>Non-surgical</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic floor muscle exercises</td>
<td>Urethral bulking injection</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>Sling</td>
</tr>
<tr>
<td>Continence pessary</td>
<td>Burch</td>
</tr>
<tr>
<td>Vaginal inserts</td>
<td>Clinical trials</td>
</tr>
</tbody>
</table>
CURRENT LITERATURE

- Large meta-analysis
- 175 RCTs with 21,598 patients
- 21 treatment comparisons
- Outcomes measures:
  - 105 on “cure”
  - 120 on “improved”
• 8 reviews of RCTs regarding 9 procedures
• Lack of standardization in procedures and assessment
  • → Interpretation difficult
• Primary outcomes: Cure and improvement
• Again, no standardization, so hierarchy applied
  • Cure: PROMS, composite scores, pads, UDS
  • Improved: subjective, satisfaction, pads, UDS
OTHER PROBLEMS

- Small sample sizes
  - (n=15-655, mean 91)
- Short follow up
  - (1-126 months, mean 12 months)
- Only 41 studies had ≥3 years follow up
STILL...TO DATE,

Best studied technique
Most robust assessment
CURRENT LITERATURE

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cure</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pubovaginal sling</td>
<td>89.4</td>
<td>67.7</td>
</tr>
<tr>
<td>Retropubic MUS</td>
<td>89.1</td>
<td>97.0</td>
</tr>
<tr>
<td>Colposuspension</td>
<td>76.7</td>
<td>63.8</td>
</tr>
<tr>
<td>Transobturator MUS</td>
<td>64.1</td>
<td>76.1</td>
</tr>
</tbody>
</table>
## ODDS RATIO VERSUS RMUS

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cured</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>Evidence</td>
</tr>
<tr>
<td>Pubovaginal sling</td>
<td>1.06</td>
<td>Low</td>
</tr>
<tr>
<td>Colposuspension</td>
<td>0.85</td>
<td>Very low</td>
</tr>
<tr>
<td>Transobturator MUS</td>
<td>0.74</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
RETROSPECTIVE STUDIES

**Britain**
- >92K women over 8 years
- 9.8 % periprocedural complications (up to 5 years)
- 5.9% readmitted within 5 years

**Scotland**
- >16K women between April 1997 and March 2016
- Immediate complications, readmission, reoperation low

Keltie K et al.: Sci Rep 2017;7:12015
ADVERSE EVENTS

- De novo urgency
- Vaginal extrusion
- Urinary tract erosion
- LUTS/Retention
- Visceral or neurologic injury
- Hemorrhage
- Pain
MUS COMPARISON

**Transobturator**
- Highest reoperation
- Groin pain

**Retropubic**
- Suprapubic pain
- Vascular complications
- Urinary tract perforation
- LUTS
COUNSELING (statements 7-10)
• Consider bother
• Should include following options
  • Non surgical
  • Surgical
• Should discuss complications
  • Risks, benefits, alternatives
  • Include specific to mesh

TREATMENT (statements 11-16)
• Nonsurgical
  • Continence pessary
  • Vaginal inserts
  • Pelvic floor muscle exercises
• Surgical
  • Urethral bulking
  • Midurethral slings (synthetic)
  • Pubovaginal sling
  • Burch colposuspension
AUA/SUFU SUI GUIDELINES

OUTCOMES ASSESSMENT (23-24)

Communicate early
• Pain
• Voiding problems
• UTI
• Dysparuenia
• Mesh concerns
• If so, bring in

Formal follow up within 6 mos
• Further intervention may be indicated
• Patient subjective outcome
  • Specifics (pain, voiding problems, etc.)
• Physical exam
• PVR
• Questionnaires optional
ALL AGREE...

- Must be performed by specialists
- Surgeons must be properly trained
- Complications must be considered
- Complications and alternatives must be presented to patients
- Must keep data for long term assessment
• Informed consent critical
  • Non-surgical options
  • Non-mesh alternatives
• Must keep long-term data
• Improve outcomes reporting
  • Patient-centered outcomes
  • Optimal measures
  • Randomized trials
  • Registries
CONCLUSION

• Guidelines generally in agreement
• Full range of options for SUI should be offered
• Do not discount potential complications
• Discuss risks, benefits, and alternatives
• Fully informed patients should have a choice