Prolapse Surgery after Transvaginal Mesh: The Evolving Landscape

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Disclosures

- No Relevant Disclosures

Objectives

- Participant will be able to describe:
  - The 2011 FDA Update on the Safety and Effectiveness of Transvaginal Placement of Pelvic Organ Prolapse (POP)
  - ACOG/AUGS, SGS, and SUFU Position Statements regarding the FDA Safety Communication
  - The current evidence regarding the use of Polypropylene Mesh for the Treatment of POP
  - The 2016 FDA Up Classification of Mesh and the impact on patient counseling
  - The current and future directions of multi-centered trials involving transvaginal mesh
  - Physician and Patient Resources related to transvaginal mesh
(Simplified) Objectives
“The Transvaginal Mesh Issue”

- Participant will be able to describe:
  - What happened?
  - What was the response?
  - What do we know? (or...What we do not know?)
  - The most recent news?
  - Where do we go from here, future directions, what’s next?
  - What can we do right now?

A quick word about language

- Mesh
- Recalled Mesh
- "Bad" Mesh
- "Good" Mesh
- Sling Mesh
- Abdominal Mesh
- Vaginal Mesh
- Grafts
- Synthetic Grafts
- Transvaginal Mesh

What Happened?
(A Brief Review)

- Pelvic Organ Prolapse (POP) remains an important health issue affecting women’s quality of life
- Almost 12.6% of women will undergo POP surgery by the age of 80 years
- An estimated 300,000 surgical procedures performed annually
- Efforts to combat high failure rates and improve perceived poor long-term outcomes has led to the development and introduction of materials including synthetic mesh to augment reconstructive repairs
Timeline of Surgical Treatment for POP

- **1950's**
  - Composite repairs attempted to restore normal pelvic anatomy

- **1970's**
  - Gynecologists began using surgical mesh products for sacrocolpopexy

- **1990's**
  - Gynecologists began using surgical mesh for surgical treatment of stress UI and transvaginal repair of POP

- **Beginning of use of surgical mesh for abdominal hernia repair**

FDA 510-K Process for Medical or Surgical Devices

- Decision that a new device (in this case transvaginal mesh) is "substantially equivalent" to a predicate device (a similar device) already on the market
- It typically addresses labeling and performance data including material safety, mechanical performance and animal testing
  - may, for some devices, include clinical studies
  - 1st FDA 510-K review 2001
    - Relative widespread use of transvaginal mesh by 2004
    - 75,000 Transvaginal Procedures for POP Using Mesh Were Performed in the US in 2010

Timeline of Surgical Treatment for POP

- **2001**
  - Approval 510(k) : TV mesh indicated for POP repair, no clinical data/equiv to existing product (class II)
- **2004**
  - Widespread use of TV mesh kits
- **2008**
  - FDA/Public Health Notification
- **2011**
  - FDA safety communication 522 orders given for post-market studies
FDA Safety Communication 2011 reflected POP Adverse Events (MAUDE database), 2005-2010 - Mesh Associated Complications Not Rare

<table>
<thead>
<tr>
<th>Rank</th>
<th>Type of Event</th>
<th>Medical Device Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Erosion</td>
<td>528</td>
</tr>
<tr>
<td>2</td>
<td>Pain</td>
<td>472</td>
</tr>
<tr>
<td>3</td>
<td>Infection</td>
<td>253</td>
</tr>
<tr>
<td>4</td>
<td>Bleeding</td>
<td>124</td>
</tr>
<tr>
<td>5</td>
<td>Dyspareunia</td>
<td>108</td>
</tr>
<tr>
<td>6</td>
<td>Organ Perforation</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>Urinary Problems</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>Vaginal Scarring/Shrinkage</td>
<td>43</td>
</tr>
<tr>
<td>9</td>
<td>Neuromuscular Problems</td>
<td>38</td>
</tr>
<tr>
<td>10</td>
<td>Recurrent Prolapse</td>
<td>32</td>
</tr>
</tbody>
</table>

- Highlighted that discriminant use of synthetic transvaginal mesh to augment vaginal defects should be performed by trained surgeons with experience in complex reconstructive surgery
- Performed only on patients with perceived unacceptable risk of clinical failure using other non-mesh approaches
- Call for long-term clinical trials evaluating benefits and safety of vaginal mesh placement

American Urogynecologic Society (AUGS)/ACOG Committee Opinion

- In summary:
  - FDA recommendations should not apply to the use of synthetic mesh for the treatment of stress urinary incontinence or an abdominal approach to the repair of POP.
  - AUGS focused on the FDA's recommendations for thorough patient informed consent as well as the imperative that surgeons performing vaginal mesh procedures undergo training specific to each procedure
Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU)

- It was recommended that consideration of mesh placement be conducted on a case by case basis with informed discussion.
- As with ACOG and AUGS, SUFU also supported a review of the FDA 510k approval process.

What was the response? (…Not Good)

- 2012 – FDA issued 522 orders postmarket surveillance study orders to all manufacturers of urogynecologic surgical mesh products.
- 2012 – Consolidated multidistrict litigations (MDLs) American Medical Systems, Boston Scientific, C.R. Bard, Johnson & Johnson’s Ethicon, Coloplast Corp. and Cook Medical.
- More than 22,000 lawsuits are included in the six MDLs, and thousands more were being filed in state courts.
Increased CC: “Mesh Issues”

- At UAB 2008-2015: 283 transvaginal mesh excision/revision surgeries

Let’s go back to the data! (What we know and what we don’t know)

- The Basics (Apical, Transvaginal, Traditional)
  - Limited High Quality Data
  - Outcomes depend on criteria – objective vs. subjective
    - Anatomic: POP-Q
    - Patient satisfaction & symptom resolution
  - Objective cure rate traditional repairs 70%
    - Recurrence/reoperation rates 30-50%
  - Patient satisfaction varies

Transvaginal Mesh Procedure Outcomes

- Most outcomes are from prospective cohort or observation studies
- Few randomized trials
- Majority of follow up - one year or less
The Data

- 2008 Systematic Review Group (SSG) showed weak evidence for improved anterior anatomy with transvaginal mesh use compared to native tissue; insufficient data to recommend its use for apical and posterior compartment defects.
- Other reviews reflect increased rates of reoperation for mesh-related complications.
- Transvaginal mesh erosion rates varying from 0 to 25 percent.
- 2010 Cochrane Review evaluated 3,773 subjects in 40 trials of procedures for POP concluded that mesh grafts improved anterior anatomy compared to native tissue repairs, but abdominal approaches were best.

Maher, et al. Cochrane Database 2010

The Data Continued

- RCT of 389 women showed superiority in anterior mesh repairs (60.8%) compared to native tissue repairs (34.5%) at 1 year, aOR 3.6, 95% CI 2.2, 5.9.
- Longer surgical times and increased blood loss in the mesh arm (p<0.001).
- No significant differences in bladder perforations (p=0.07); rates of new SUI 12.3% mesh group vs 6.3% (p=0.05).
- Surgical re-intervention for mesh exposure - 3.2%.


The Data Continued

- Cochrane Review, Maher et al, 2013, 56 RCTs evaluating 5,954 women:
  - Apical: ASC, lower rate of recurrence, less dyspareunia vs SSS (benefits vs risks must be weighed). ASC higher anatomic/less reop than high USS and TV mesh.
  - These benefits must be balanced against:
    - Longer operating time
    - Longer time to return to activities of daily living
    - Increased cost of the abdominal approach.

Maher, et al. Cochrane Database 2013
The Data Continued

- **Cochrane Review, Maher et al, 2013, 56 RCTs evaluating 5,954 women:**
  - **Anterior:** increased recurrent prolapse with native tissue vs polypropylene mesh (RR 3.15, 95% CI 2.50, 3.96)
  - **Mesh Erosions:** 11.4%
  - **Similar reop rates, 3% vs 1.3% (RR 2.18, 95% CI 0.93, 5.10)**
  - **Posterior:** evidence is not supportive of any graft benefit in posterior compartment

- **CARE Study**
  - Colpopexy and Urinary Reduction Efforts
  - ASC for symptomatic POP with or without Burch urethropexy
  - **Long-term (e-CARE) Outcomes**
  - Description of anatomic and symptoms outcomes up to 7-years after ASC
  - 215 subjects (104+Burch/111-Burch)
  - Probability of mesh erosion at 7 years = 10.5%
  - "Abdominal sacrocolpopexy effectiveness should be balanced with long term risks of mesh or suture erosion"

- **SGS Systematic Review Group, 2015:**
  - Outcomes after mesh sacrocolpopexy compared to native tissue vaginal repairs in women with apical prolapse
  - Included 13 comparative studies
  - Moderate-quality evidence supports improved anatomic outcomes after mesh sacrocolpopexy
  - Very-low quality evidence shows no difference in reoperation rates
  - When anatomic durability is a priority…
    - Mesh sacrocolpopexy may be the preferred surgical option
  - When minimizing adverse events…
    - No strong evidence of one approach over the other
The most recent news

- FDA Up Classification of Mesh (January 4th, 2016)
  - The FDA reclassified these medical devices from class II, which generally includes moderate-risk devices, to class III, which generally includes high-risk devices.
  - The FDA required manufacturers to submit a premarket approval (PMA) application to support the safety and effectiveness of surgical mesh for the transvaginal repair of POP.
  - These changes do not pertain to full-length midurethral slings and sacral colpopexy meshes.

Where do we go from here?

- Outcome measures: anatomic & symptom based, complications & reoperation rates
- More data with traditional repairs especially addressing apical suspension
- Research for design of better mesh with robust objective and subjective outcome data, including reports of AE’s

Where do we go from here?

- Data to guide patient selection – who will have better outcomes with mesh vs. native tissue repair
- Research in other directions beyond mesh with which to augment native tissue repairs, or aid pelvic floor support
**What’s next?**

- PFDN to start the “Apical Suspension Repair for Vault Prolapse in a Three-Arm Randomized Trial Design” – ASPIRe
- Compares three surgical procedures
  - Sacral Colpopexy
  - Vaginal Mesh Repair
  - Transvaginal Native Tissue Repair
- > 350 women anticipated to enroll
- 3 year to 5 year followup

**What can we do now?**

**Patient Selection**

- Vaginal mesh reserved where benefit outweighs risk
- Device specific training and experience with reconstructive procedures
- Patient Counseling
- Outcome Reporting
- Pelvic Floor Disorder Registry (PFDR)
  - PFDR-Quality and Research (QR)
  - PFDR-Industry Sponsored (IS)
- New products not assumed to have equal safety and efficacy w/o clinical long-term data

**Co-morbid Conditions to Consider with Transvaginal Mesh Implantation**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Issues</th>
</tr>
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<tbody>
<tr>
<td>BMI</td>
<td>BMI &gt; 30, associated with inc. mesh exposure</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Poor wound healing</td>
</tr>
<tr>
<td>Genital Atrophy</td>
<td>Poor wound healing</td>
</tr>
<tr>
<td>Chronic Steroid Use</td>
<td>Poor wound healing</td>
</tr>
<tr>
<td>Smoking/Tobacco Abuse</td>
<td>Poor wound healing</td>
</tr>
</tbody>
</table>
Patient Counseling

- Background Materials
- Prepared Responses to FDA Suggested Questions
- Informed Consent Supplement Checklist
- Collection of Manufacturers’ Literature
- Patient Education Tools
- Voices of PFD
  - http://www.voicesforpfd.org/p/cm/ld/fid=1

AUGS Resources:
- FDA Surgical Urogynecologic Mesh Implants Fact Sheet
- FDA Recommendations for Patient Undergoing Treatment for Prolapse

ACOG Resources:
- Media Statement on the FDA Orders
- Patient Education FAQ, Surgery for Pelvic Organ Prolapse
  - http://www.acog.org/Patients/FAQs/Surgery-for-Pelvic-Organ-Prolapse
- ACOG video, Pelvic Organ Prolapse
  - http://www.acog.org/Patients/Patient-Education-Videos/Pelvic-Organ-Prolapse
- FDA recommendations for patients

Closing Remarks

- The transvaginal mesh issue is complex
- It will continue to evolve (this will take time)
- Patient selection and counseling are key
- Stay informed (high quality data is coming)