Indications, Contraindications, and Complications of Synthetic Mesh Use in the Surgical Treatment of Pelvic Organ Prolapse

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Objectives

- To provide the rationale for the use of transvaginal synthetic mesh for pelvic organ prolapse repair
- To understand consensus indications and contraindications for the use of transvaginal synthetic mesh for POP
- To review the efficacy and safety of transvaginal mesh use for pelvic organ prolapse
Introduction

- National population-based estimate using validated measures reported an overall 2.9% prevalence of symptomatic prolapse; other estimates as high as 8%
- An estimated 300,000 surgical procedures performed annually
- Lifetime risk for intervention, 11-19% with reoperation rates of 30-50%
- 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

Pelvic Floor Support

- Levels of support
  - Level 1: Uterosacral/cardinal ligament (most cephalad)
  - Level 2: Paravaginal, arcus tendineus fascia
  - Level 3: Perineum (distal support)
- *All levels connected through endopelvic fascia

Classification of Loss of Support

- Level I – Apical defects
  - Loss of support of the upper vagina/cervix
  - Uterine prolapse, vaginal vault prolapse, or enterocoele
Classification of Loss of Support

- Level II – Midvaginal defects
  - Anterior – Cystocele, Hypermobile urethra
  - Posterior – Rectoceles
- Level III – Lower vaginal/Perineal defects
  - Urethral hypermobility
  - Perineal defects
  - Rectoceles

Mechanisms that protect against prolapse:

- Uterus and vagina are attached to the pelvic walls by endopelvic CT and suspensory ligaments
- Levator ani muscles constrict the lumen of these organs until they are closed. The pelvic organs rest on the levator ani muscles.
- A suspended vagina rests against the levator ani with increases in pressure force

Pathophysiology of Pelvic Organ Prolapse (POP)

- Levator ani muscles lose or decrease tone
- Pelvic support is more reliant upon level I and II support that may be damaged
- Increases in intra-abdominal pressure results in stretching/tearing/breaking of level I and II support
- POP and/or failure of continence (urine/fecal)
Pelvic Organ Prolapse Quantification System

Stage 0: No prolapse
(Aa, Ap, Ba, Bp = -3)
Stage 1: Most distal prolapse is >1cm above hymen (<-1)
Stage 2: ≥ -1 but ≤ +1
Stage 3: >+1 but < TVL – 2cm
Stage 4: complete eversion (TVL – 2)

Timeline of Surgical Treatment for POP

1800-1900
Surgery addressed what was coming out

1950's
Composite repairs attempted to restore normal pelvic anatomy

Beginning of use of surgical mesh for abdominal herna repair

1970's
Gynecologist began using surgical mesh products for abdominal repair of POP (Bacoclopexy)

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

2002
FDA cleared the first surgical mesh product specifically for use in POP

2004-current
Increased production and use of transvaginal mesh for POP
Clinical Case

- 56 yo P3003 presents with a 4 year h/o increasing vaginal protrusion and pressure
- She now sees protrusion through the vaginal introitus
- She does not wish to use a pessary, “She just wants it fixed”
- She is healthy, on no medications, is sexually active and runs an IT company
- She exercises regularly (BMI=26)

Stage 3 Uterovaginal Prolapse

Questions

- How would you fix this?
- What is the role of mesh use with these clinical findings?
- How will you counsel her regarding her options?
- What if she wants to keep her uterus?
Traditional Surgical Management

- Anterior & Posterior Colporrhaphy
- Apical suspension (uterosacral, sacrospinous)
- Sacrocolpopexy (abdominal, laparoscopic/robotic)
- Hysterectomy (TVH)
- Hysteropexy

Outcomes of Traditional Repairs

- Depends 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

Why MESH?

- POP due to weakness in tissue: inherent, trauma (OB), chronic strain
- Purpose of a graft: to provide a scaffold for tissue ingrowth, provide support, restore normal pelvic anatomy & function
- Indications may include:
  1. Failed prior repair
  2. Tissue factors: inherent weakness/laxity, poor quality fascia
  3. Unavoidable stress on repair (COPD, etc.)
  4. Need to bridge a space
  5. Concern about vaginal length with traditional repair
  6. Use with uterine conservation
What is it?

The Ideal Graft
- Strong, pliable, non-immunogenic, non-carcinogenic, not modifiable by host, available, affordable, infection resistant, shrinkage resistant

Synthetic Graft Properties: strength, pore size, filament weave/type, density, elasticity
- Type I: macroporous, monofilament: polypropylene, Marlex
- Type II: microporous, monofilament: gortex
- Type III: macroporous, multifilament: mersilene, teflon
- Type IV: submicronic: silastic

*Pore size important for infection prevention
*Type I: low density, large pore, monofilament polypropylene meshes have ideal profile

How did it come to be?

2001 – Approval 510(k) TV mesh indicated for POP repair, no clinical data because equivalent to existing product (class II)

2004 – Widespread use of TV mesh kits

2011 – FDA safety communication issued, 522 orders given, post-market studies

2012 – Consolidated multi-district lawsuit

~75,000 Transvaginal Procedures for POP Using Mesh Were Performed in the US in 2010


Indications for Transvaginal Mesh Use for Repair of POP

- Historically, indications for treatment of POP focused on patient symptomatology including vaginal protrusion, pressure other discomfort and impact on urinary, bowel, sexual function
- Limited Level 1 data exist to guide us regarding decision making and indications for mesh use
- Consensus of the 2nd International Urogynecological Association (IUGA) Graft Roundtable-“indications” was “too strong” a term regarding mesh use
- Elected to use terminology which stratified for degree of impact on surgical outcomes

Factors for the Consideration of Use of Vaginal Mesh in POP Surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Likely Benefit</th>
<th>Possible Benefit</th>
<th>Unlikely Benefit</th>
<th>Not Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
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<td></td>
<td>*</td>
</tr>
<tr>
<td>&lt; 50 years</td>
<td>*</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>≥ 50 years</td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Recurrent (same site)</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystocele/Anterior Compartment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ Stage 2</td>
<td>*</td>
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<td></td>
<td>*</td>
</tr>
<tr>
<td>≤ Stage 2</td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Apex (vault, cuff, cervix)</td>
<td>*</td>
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<td></td>
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<tr>
<td>Deficient Fascia</td>
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</tbody>
</table>

Factors for the Consideration of Use of Vaginal Mesh in POP Surgery

- Chronic increase intra-abdominal pressure
- Pain Syndromes (local/systemic)
- Possibility of Pregnancy
- Combination of Factors
  - Recurrent + Cystocele > Stage 2
  - Recurrent + Posterior Compartment
  - Recurrent + Apex/Cuff/Cervix
  - Recurrent + Increased Abdominal Pressure
  - Recurrent + Deficient Fascia
  - Cystocele > Stage 2 + Increased Intra-abdominal pressure
  - Cystocele > Stage 2 + Deficient Fascia

Co-morbid Conditions to Consider with Vaginal Mesh Implantation (?Contraindications)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>BMI &gt; 30, associated with increased mesh erosion</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>

Age also noted to be associated with increased risk of mesh erosion (2 X risk, >60 years)

Although not a contraindication, but quite often a concomitant procedure, hysterectomy at the time of anterior mesh augmentation associated with increased risk for mesh exposure
Most outcomes are from prospective cohort or observation studies
Few randomized trials
Majority of follow up - one year or less
Systematic Reviews

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 in 3.2% of 186 patients

Several systematic reviews (SGS, WHO/ICI) showed weak evidence for improved anterior anatomy with 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 compared to native tissue.

Cochrane Review 2010 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.

SOGC review reflecting 18 studies (only 1 RCT) where cure defined as <Stage 2, 79-100% and recommended that this approach be considered novel requiring specialized training and significant patient counseling.

Summary: weak evidence for anterior compartment benefit; no robust longer-term outcomes. No posterior compartment benefit.

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>
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</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>255</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>

Mesh Complications

Numerous known complications of all vaginal prolapse surgery: bleeding, infection, injury to surrounding organs, vaginal shortening, dyspareunia and recurrence.

Compared to native tissue repair, synthetic mesh exposure/erosion/extrusion is unique.

Terms often used interchangeably.

IUGA classification system:
- exposure defined as vaginal mesh visualized through separated epithelium
- extrusion defined as a gradual passage of mesh out of a body structure or tissue.

Haylen et al. Intl Urogynecol J, 2011
Mesh Complications

- Overall complication rates from mesh range from 1 – 15%
- Exposure vs. Extrusion (IUGA)

Complications, cont

- Overall mesh complications in repair of POP: 1-15%
- Small but significant group experience QOL sequelae, even death
- SGS Systematic Review update revealed overall mesh erosion rate of 10.3%
- Rardin and colleagues reported erosion rates of 0-25%
- Exposure rates for Level 1 studies range from 5 to 19%

Other Complications:
- Vaginal contracture
- Dyspareunia
- Vaginal pain
- Fistula

Management Options

- Symptomatic erosion/exposure: generally remove exposed portion, or bunched/rolled portion
- Asymptomatic exposure: expectant + estrogen cream (symptomatic partner?)
- Tension on arm: cut arm or remove segment
- Pain across arm: remove arm
- Infection: remove, antibiotics
Where do we go from here?

- FDA: Discussed change to Category III, 522 post-market studies (requiring pre-market Level 1 data)
- ACOG/AUGS:
  - Outcome reporting: Success defined objectively and subjectively, complications & reoperation rates should be reported
  - Vaginal mesh reserved where benefit outweighs risk
  - Surgeons require device specific training, experience with reconstructive procedures
  - New products not assumed to have equal safety/efficacy w/o clinical long-term data
  - Continued audit and review of outcomes (IUGA criteria), development of registry for surveillance
  - Informed consent is key: www.augs.org/informedconsent

ACOG/AUGS Committee Opinion 2011

Summary of Considerations for Synthetic Mesh in POP

- Patient selection
- Surgeon training/selection
- Outcome measures: anatomic & symptom based, complications & reoperation rates
- Need:
  - 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
  - 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

Case

- Most evidenced-based approach: TVH, USVVS/SSS, other vaginal repairs as indicated
- If she wishes uterine conservation, consider Uphold mesh suspension*

*Vu et al, 2012; Intl Urogyn J. 23:1753