

Update on Surgical Mesh for Stress Urinary Incontinence (SUI)

FDA Meeting of the Obstetric and Gynecologic Devices Panel

September 9, 2011

Introduction

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AdvaMed

Stress Urinary Incontinence (SUI)

- Common and often debilitating condition
- Mid-urethral slings
 - Safe, effective, less invasive procedure
 - Less pain
 - Quick return to regular activity

510(k) Process

- All mid-urethral slings for SUI have been brought to market under 510(k) process
 - Process works
 - Allows for medical advances to occur

Agenda

Unmet Medical Need

Suzette E. Sutherland, MD

Surgeon, Metro Urology
Adjunct Associate Professor
University of Minnesota

Clinical Overview

Piet Hinoul, MD, PhD

Director, Medical Affairs
Ethicon Women's Health and Urology

Regulatory Pathways

Ginger Glaser

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Unmet Medical Need

Suzette E. Sutherland, MD

**Metro Urology
Centers for Continence Care and Female Urology
The Pelvic Floor Center
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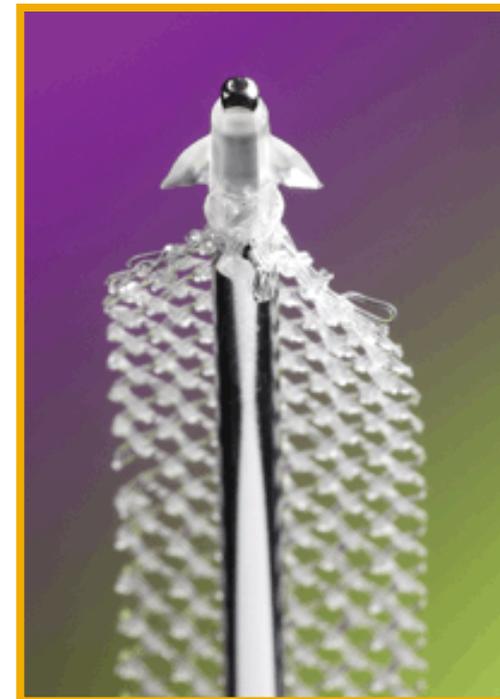
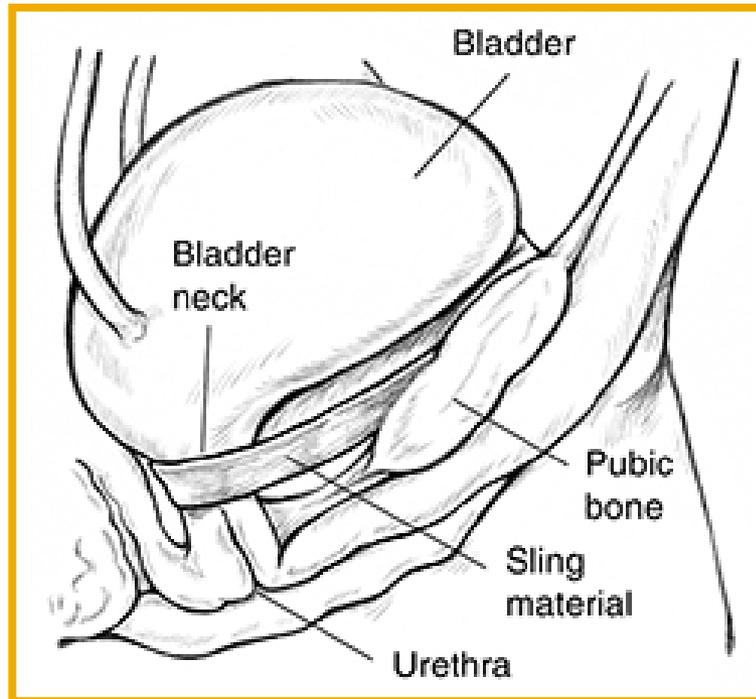
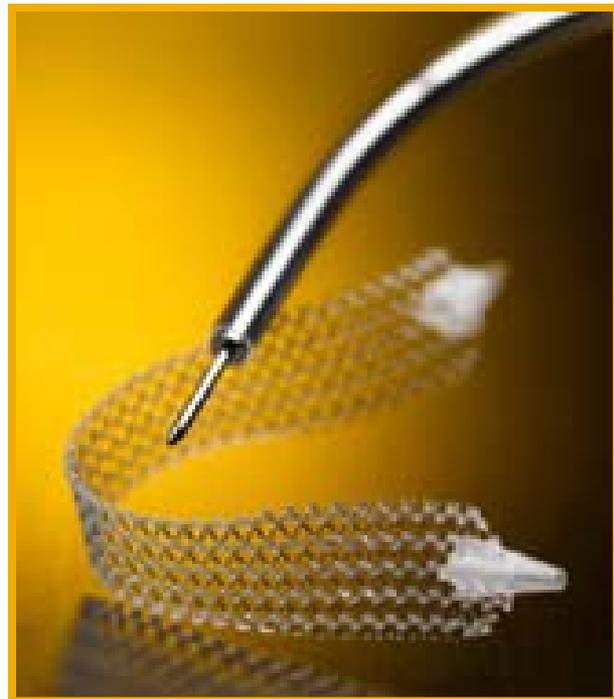
Stress Urinary Incontinence (SUI) Patient Profile

- Typical age range
 - 40-60 years old
- Physically active with young children
- Use of protective pads or diapers
- Avoids seeking treatment

Earlier Treatment Optimal

- Woman healthier with fewer concomitant issues
- Benefits all ages

Standard of Care Mid-Urethral Sling



Clinical Experience Presented at ICS/IUGA Meeting 2010

- 367 consecutive single incision slings
- 91% subjective cure @ 12 mo
- 92% objective cure @ last follow-up
- Statistically significant improvements
 - UDI-6, IIQ-7, QOL , PISQ-12
- 2.7% (10 patients) sling revision due to obstruction
- No mesh-related erosions, extrusions, infections
- No-to-minimal pain reported at 2 weeks
- No dyspareunia related to sling

Comparison of Procedures

TRADITIONAL SURGERY

- More involved procedure
- 1 hour +
- Hospitalized 1 – 2 nights
- Pain along incision
- Post-operative catheter
- Longer recovery period

MID-URETHRAL SLINGS

- Easier procedure
- 15 – 20 minutes
- Outpatient
- IV sedation/local
- Less risk, less pain
- Equally or more effective
- Return to daily routine within 24 hours

Mid-Urethral Sling for SUI

- Very effective
- Long-lasting repair
- Complications are rare

Complications with Mid-Urethral Slings

- Risk of exposure decreases with surgeon experience
- Most complications can be easily treated
 - Topical estrogen application
 - Minor surgical excision
- Dyspareunia usually related to superficial placement

Complications with Traditional Burch/Bladder Neck Suspensions

- Greater interoperative bleeding
- Greater risk of bowel/bladder injuries
- DVT/PE
- Abdominal wound healing complications
- Greater post-op voiding dysfunction
- More post-operative pain

Conclusions

- Great progress in SUI treatment
- Transvaginal mid-urethral sling surgery
 - Is safe and effective
 - Has a long-lasting effect on a patient's life

Safety & Efficacy

Piet Hinoul, MD, PhD

Director, Medical Affairs

Ethicon Women's Health and Urology

Evolution of SUI Devices



1961



Evolution of SUI Devices



1961

1996



Evolution of SUI Devices



1961

1996

2001



Evolution of SUI Devices



1961

1996

2001

2007

Mid-Urethral Slings

- 800+ publications in the past 15 years
- RCTs and observational studies show superiority of mid-urethral slings vs. old gold standard
- > 2,000,000 women successfully treated with slings

Cochrane Database Findings

Mid-urethral Sling vs. Colposuspension

Study	MISO (n/N)	Open Colpo (n/N)	Risk Ratio (M-H, Fixed, 95% CI)
Bai 2005	27/31	29/33	0.99 (0.82 , 1.19)
Drahoradova 2004	75/79	59/60	0.97 (0.91 , 1.03)
El-Barky 2005	18/25	18/25	1.00 (0.71 , 1.41)
Sivaslioglu 2007	42/49	43/51	1.02 (0.86, 1.20)
Wang 2003	45/49	38/41	0.99 (0.88, 1.12)
Ward 2002	103/159	90/127	0.91 (0.78, 1.07)
Total (95% CI)	392	337	0.96 (0.90, 1.03)

- Heterogeneity: $\text{Chi}^2 = 1.17$, $\text{df} = 5$ ($P = 0.95$); $I^2 = 0.0\%$
- Test for overall effect: $Z = 1.08$ ($P = 0.28$)

Landmark RCTs



Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence

Karen Ward and Paul Hilton

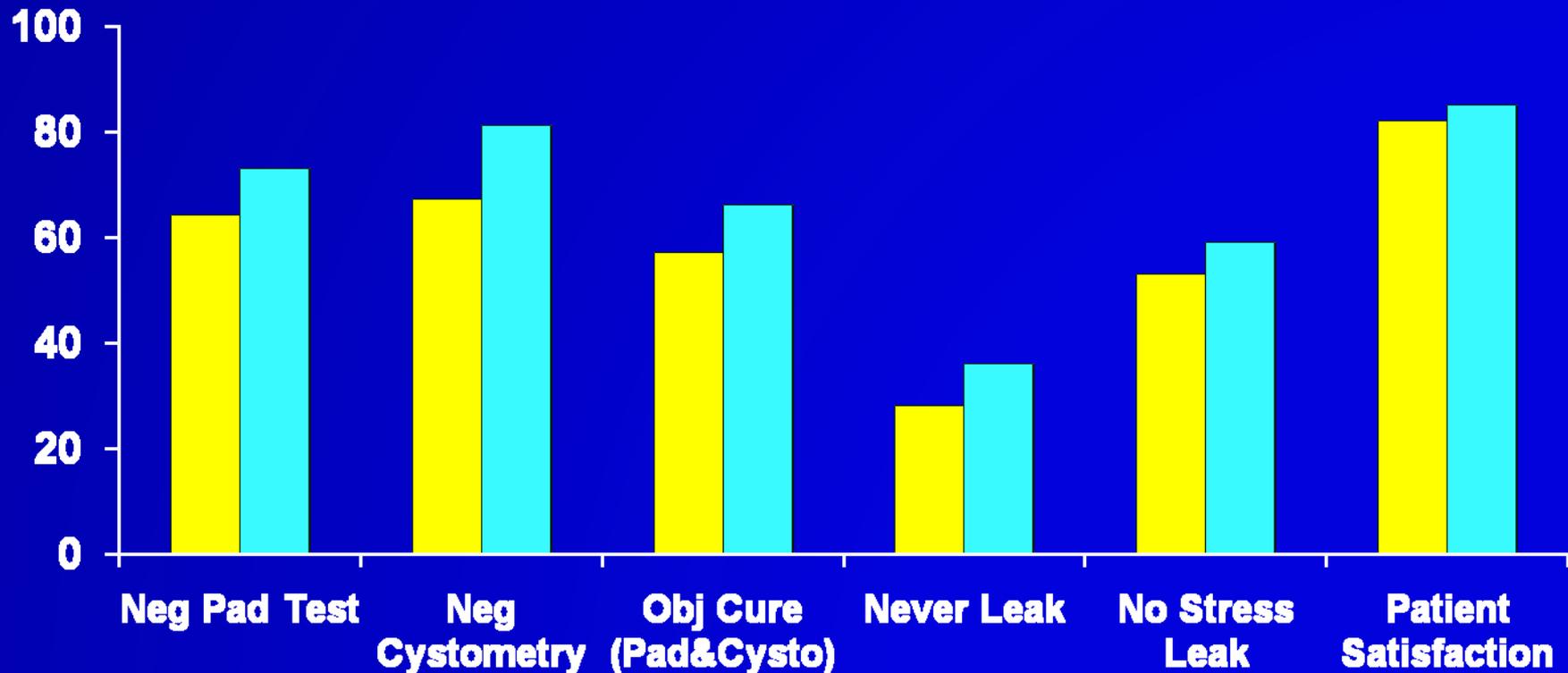
BMJ 2002;325:67-
doi:10.1136/bmj.325.7355.67

- TVT: 175 women
- Burch: 169 women

TVT vs. Colposuspension Study

Percentage "Cured" at 6 months
(by outcome measure)

■ Burch ■ TVT



Landmark RCTs

DOI: 10.1111/j.1471-0528.2007.01548.x
www.blackwellpublishing.com/bjog

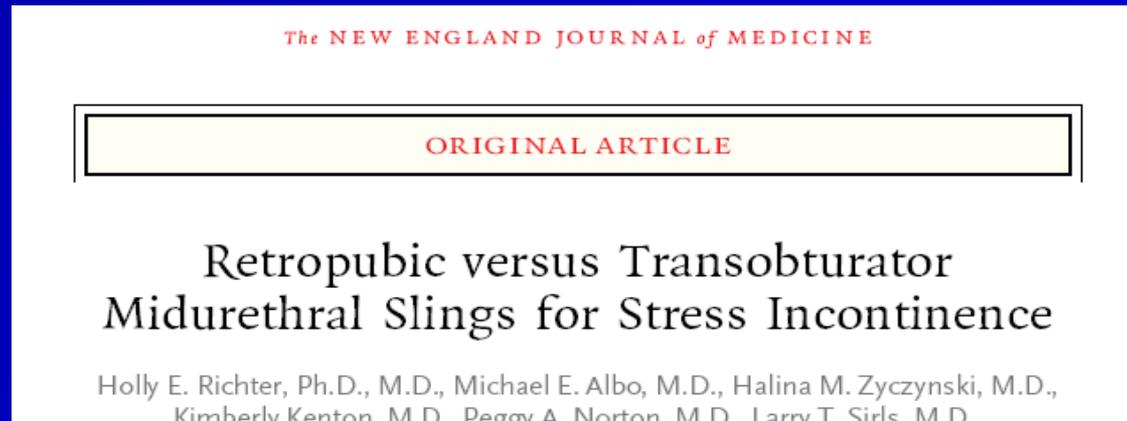
Urogynaecology

Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up

KL Ward, P Hilton on behalf of the UK and Ireland TVT Trial Group*

- Both procedures provide long-term effect on incontinence and improvement in QoL
- Vaginal wall prolapse more frequent after Burch-colposuspension

Landmark RCTs



- 597 women randomized
- Objective success
 - 81% (retropubic) vs. 78% (transobturator)
- Subjective success
 - 62% (retropubic) vs. 56% (transobturator)

RCT Cure Rates for Mini-Slings

Single-Incision Mini-Slings vs. Mid-urethral Slings

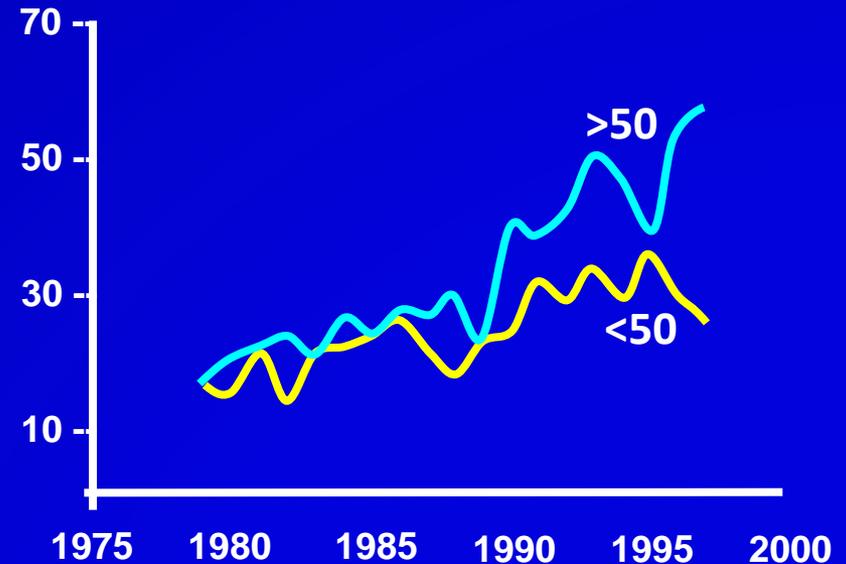
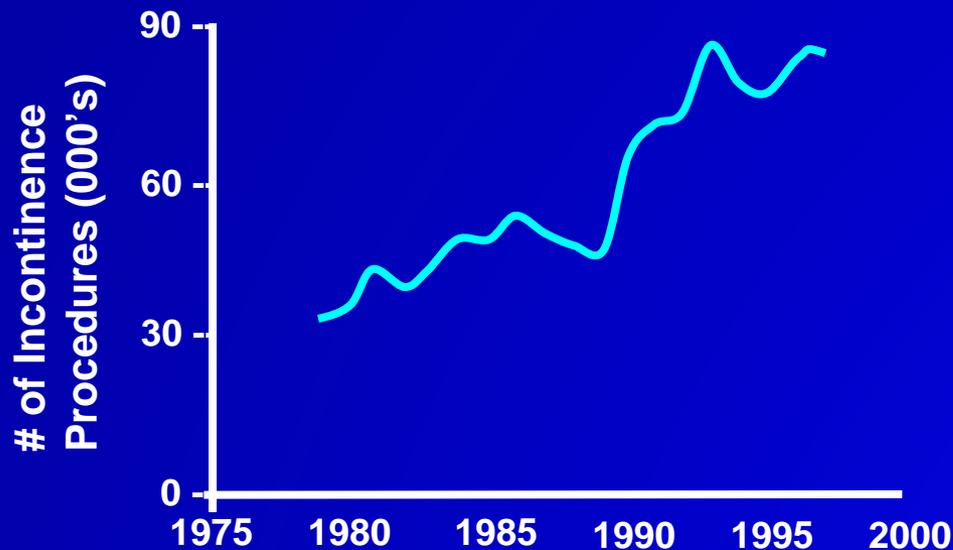
Study	Follow-Up (months)	Single-incision Mini-Slings n/N (%)	Mid-urethral Slings n/N (%)	p-value
Basu 2010	6	22/37 (59.5%)	31/33 (93.9%)	<0.001
Hinoul 2011	12	81/97 (83.5%)	96/98 (98.0%)	<0.001
Tommaselli 2010	12	31/37 (83.8%)	31/38 (81.6%)	0.801
TOTAL		134/171 (78.4%)	158/169 (93.5%)	<0.001*

*Cochran-Mantel-Haenszel procedure

Mini-Sling Outcomes in 2010

Mini-sling	Study	Patients (n)	Objective Cure (%)	Subjective Cure (%)
TVT-Secur	Lim 2010	42 U	58.2	51.3
	Khandwala 2010	128 H; 13 U	-	85
	Gagnon 2010	23 H; 25 U	-	69; 100
	Liapsis	43 H; 39 U	62.8; 71.8	60.5; 69.2
	Kim	62 H; 53 U	87.1; 88.7	82.9; 83.7
	Lee	141 H; 144 U	80.1; 87.5	75.7; 77.1
	Jeong	31 TVT-S; 33 TOT	71.0; 84.8	80.6; 78.8
	Tommaselli	37 TVT-S; 38 TVT-O	83.8; 81.6	10.8; 13.1
MiniArc	Kennelly	157	90.6	87.3
	De Ridder	75 MiniArc; 56 Monarc	85; 89	-
	Pickens	120	-	94
AJUST	Meschia	102	91.4	85.7

Rise in Urogynecologic Services



Expected rise in urogynecologic services of 45% in the next two decades, whilst the population expansion is projected to be only 22% in that time period

Mini-Sling Peri-Operative AEs

	TVT-O	TVT-S	p-value
Mean Blood Loss (mL)	59	74	0.02
Peri-operative Complications			0.09
Bleeding >100cc	19%	29%	
Bleeding >500cc	1%	0	
Cystotomy	0	1%	
Vaginal Perforation	0	1%	
Transfusion	0	0	

Evolution of SUI Devices



Conclusions

- Mid-urethral slings are well-understood
 - Mechanism of action
 - Mesh properties and mesh-specific morbidities
 - Impact of learning curve

Regulatory Pathway

Ginger Glaser

Sr. Director, Global Quality & Regulatory Affairs

American Medical Systems

FDA Questions

- (1.b) Given the incidence and severity of the adverse events, is there reasonable assurance of the safety of suburethral slings for SUI?
 - Yes
- (1.c) Does the clinical benefit outweigh the risk associated with the use of mesh suburethral slings?
 - Yes

Definitions

- Safety
 - Probable benefits outweigh the probable risks
- Effectiveness
 - Significant portion of the target population experiences clinically significant results

Reasonable Assurance of Safety & Effectiveness

- 7000 patients
- As effective as traditional fascial slings
 - Risk ratio 1.03, 95% CI (0.94-1.13)
- As effective as Burch colposuspension
 - Risk ratio 0.96, 95% CI (0.90-1.03)

FDA Question

- (1.d) Should future premarket submissions for mesh products indicated for female SUI be supported by clinical performance data?
 - Per FDA guidance
- Final FDA Clinical Guidance, 2011

**Guidance for Industry and
Food and Drug Administration Staff**

**Clinical Investigations of Devices
Indicated for the Treatment of
Urinary Incontinence**

Document issued on: March 8, 2011
The draft of this document was issued on September 19, 2008.

FDA Note

- (1.d note) If FDA requires premarket clinical study with a control arm of traditional repair without mesh, reclassification may be necessary?
 - Reclassification not necessary

FDA Question

- (1.e) Should manufacturers conduct post-market surveillance studies on currently marketed first generation suburethral slings?
 - No

FDA Question

- (2.a) Is there adequate safety and effectiveness data on suburethral mini-slings?
 - Yes
- Mini-Sling study outcomes
 - Adverse events as low as first generation slings
 - Recent efficacy rates are 85 – 90%

FDA Question

- (2. b) Should future premarket submissions for mini-slings be supported by clinical performance data?
 - Per FDA Guidance
- (2.b note) If FDA requires premarket clinical study with a control arm of traditional repair without mesh, reclassification may be necessary
 - Reclassification not necessary

FDA Question

- (2.c) Should manufacturers conduct post-market surveillance studies on currently marketed mini-slings?
 - No

Conclusion

- SUI mesh is safe and effective
- 522 studies are not needed for existing products
- Clinical requirements can be managed via existing SUI guidance for future products

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