URINARY INCONTINENCE

For managing stress incontinence, new data on the efficacy of pessaries and behavioral therapy and the safety and success of sling procedures, including single-incision technique

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Urinary incontinence affects as many as 50% of adult women[1]; 16% have bothersome symptoms[2] and as many as 10% undergo surgical correction of their condition.[3] The prevalence of urinary incontinence increases with age; with the aging US population expected to more than double by 2050,[4] more and more women will seek treatment.

This notion of a growing population of women who want treatment is supported by a recent article that evaluated trends in surgery for urinary incontinence between 1998 and 2007: The researchers found that **the number of inpatient urinary incontinence surgeries nearly tripled over 1 decade.**[5]

Therapeutic revolution

Introduction of the retropubic mid-urethral sling in 1996[6] transformed the surgical management of stress incontinence; the procedure has become the gold standard. Subsequent iterations of the sling procedure include a transobturator approach[7] (known as the "TOT" sling) and, more recently, single-incision slings—alternatives intended primarily to improve the safety profile and ease of the procedure while maintaining its efficacy.

The newer sling procedures—many including novel mesh materials, some delivered in kit form—came to market under the US Food and Drug Administration's so-called 510(k) rule, however, allowing manufacturers to launch them with little or no data supporting safety and efficacy. Given those circumstances, the **optimal surgical management of stress urinary incontinence (SUI) remains controversial,** and surgeons must take into account individual patient characteristics and treatment goals when developing a plan for surgical management. Providers must also remember that not all women will opt for, or are good candidates for, surgical intervention. These women need alternatives to operative management.

In this Update, we review and comment on four published papers that **1)** highlight recent developments in the treatment of SUI and **2)** provide concrete guidance to clinicians for providing optimal management:

- A randomized trial of nonsurgical management of stress incontinence using a continence pessary, compared with behavioral therapy and with combined (pessary plus behavioral therapy) treatment (the ATLAS trial)

- A randomized clinical trial that compared the efficacy of retropubic slings and TOT slings, with 1-year follow-up (the TOMUS trial)
- A randomized clinical trial that compared the efficacy of retropubic slings and TOT slings in women who have intrinsic sphincter deficiency
- A meta-analysis of the safety and efficacy of single-incision slings.

Conservative therapy is still an important, effective option for SUI

Richter HE, Burgio KL, Brubaker L, et al; Pelvic Floor Disorders Network. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. Obstet Gynecol. 2010;115(3):609–617.

Conservative treatment options for SUI are limited. They include:

- a pessary
- behavioral/pelvic floor physical therapy
- duloxetine (Cymbalta), a serotonin and norepinephrine reuptake inhibitor antidepressant (as an off-label use).

Level-I evidence exists to support utilization of behavioral pelvic floor therapy, based on a Cochrane review.[8] Yet, little evidence exists by which we can compare the efficacy of various incontinence pessaries and their efficacy when combined with behavioral therapy.

Study design. This multi-center, randomized trial was conducted to fill this gap in the evidence. Four hundred forty-six women who had SUI were randomized to three groups: pessary only (149); behavioral therapy only (146); and pessary plus behavioral therapy (151). Women 18 years and older who had either SUI alone or stress-predominant incontinence were eligible. At baseline, 20.7% of subjects had undergone nonsurgical incontinence treatment; 6.9% had had surgical management. There was no significant difference in regard to prior treatment among the study groups.

Behavioral therapy comprised four visits at 2-week intervals, conducted by a nurse or a physical therapist who had undergone standardized training. Visits focused on engaging pelvic floor muscles; subjects received a "prescription" for home practice.

Women in the pessary groups were fitted at as many as three clinic visits with an incontinence ring or dish.

Measures of primary outcomes included the Patient Global Impression of Improvement (PGI-I) and the stress incontinence subset of the Pelvic Floor Distress Inventory (PFDI) at 3 months (follow-up continued to 12 months).

Findings. At 3 months, 40% of subjects in the pessary-only group, 49% in the behavioral therapy-only group, and 53% in the combined group reported (on the PGI-I) that their symptoms were "much" or "very much" better. Furthermore, 33% in the pessary-only group, 49% in the behavioral therapy-

WHAT THIS EVIDENCE MEANS FOR PRACTICE

The modest success rate of the conservative measures for treating SUI that were studied here, and the decline in their efficacy over time, might be discouraging at first glance. But more than one third of patients experienced benefit in the end—in the face of low risk. Consider a pessary or behavioral therapy to be a workable, low-risk option for your patients who have SUI, therefore. Combining those two measures does not, however, provide superior results.

FAST TRACK

Consider a pessary or behavioral therapy to be a workable, low-risk option

only group, and 44% in the combined group reported (on the PFDI) no bothersome stress incontinence.

Only PFDI measures were significantly different between pessary and behavioral therapy groups. Both PFDI and PGI-I demonstrated a significant difference in combined therapy compared to a pessary, but not in combined therapy compared to behavioral therapy. Because combination therapy was not superior to both single-therapies, the researchers concluded that combination therapy was not superior to single therapy.

By 12 months, efficacy declined in all groups: 32% of all women reported they were "much" or "very much" better, and 36% denied symptoms of stress incontinence. There was no difference in efficacy across the three groups by the end of the follow-up period.

TOT, retropubic slings equally effective for SUI—but complications differ

Richter H, Albo M, Zyczynski H, et al; Urinary Incontinence Treatment Network. Retropubic versus transobturator midurethral slings for stress incontinence. N Engl J Med. 2010;362(22):2066–2076.

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You can anticipate similar success rates with retropubic and TOT approaches to placing a mid-urethral sling

This large, randomized, prospective multicenter study from the well-respected Pelvic Floor Disorders Network demonstrated that the efficacy of retropubic and TOT slings is equivalent. At the same time, the trial highlighted important differences in the complication profiles of these two surgical approaches. Given the high success rate of retropubic slings, the study was designed as an equivalence trial, with the principal aim of demonstrating whether both approaches share a similar success rate.

Study design. Investigators recruited women who had been given a diagnosis of SUI and were planning to undergo surgical correction, randomizing 597 who had predominant stress loss symptoms and a positive stress test (urodynamics were not required); 565 completed the 12-month follow-up.

Findings. Objective and subjective cure rates were similar in both groups at 12 months. ("Objective cure" was defined as a negative stress test, negative pad test, and no re-treatment within the follow-up period; "subjective cure" was defined as no re-treatment, no episodes of leakage on a voiding diary, and no self-report of stress loss.)

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This well-designed trial confirmed the current standard of practice and supports the findings of a recent Cochrane review that reported a success rate of 88% for the retropubic approach and 84% for the TOT approach.[9] The trial also demonstrated that you can anticipate similar success rates with retropubic and TOT approaches to placing a mid-urethral sling.

Note: The design of this study did not call for urodynamic evaluation, but more than 85% of subjects did undergo such testing, including measurement of the Valsalva leak-point pressure (VLPP) and the maximum urethral-closure pressure (MUCP). The investigators' linear regression analysis revealed no change in outcomes between the two approaches when adjusting for VLPP and MUCP. This supportive finding suggests that a TOT sling would be just as beneficial as a retropubic sling in women who have ISD—although other recent studies that specifically addressed this matter came to a different conclusion.

At 12 months, the objective cure rate was 81% for the retropubic sling and 78% for the TOT sling (the difference of three percentage points had a 95% confidence interval [CI] of –3.6–9.6). Despite very close findings, the subjective cure rate was lower in the TOT group (56%) than in the retropubic group (62%) (the difference of just over six percentage points had a 95% CI of –1.6–14.3) and did not meet criteria for equivalence.

There was no difference between the two groups in the incidence of urge incontinence; patient satisfaction; and quality-of-life outcomes.

But divergence was seen in complications. A higher incidence of voiding dysfunction that required re-operation was seen in the retropubic group (2.7%) than in the TOT group (0%) (P = .004). The retropubic sling group also exhibited a higher incidence of mesh exposure and bladder perforation. The TOT group had a higher incidence of neurologic sequelae (numbness, weakness) than the retropubic group (9.4% and 0.04%, respectively) (P = .01).

Intrinsic sphincter deficiency might be a risk factor for failure of a TOT sling

Schierlitz L, Dwyer P, Rosamilla A, et al. Effectiveness of tension-free vaginal tape compared with TOT tape in women with stress urinary incontinence and intrinsic sphincter deficiency: a randomized controlled trial. Obstet Gynecol. 2008;112(6):1253–1261.

In the trial by Richter and colleagues that we reviewed above, the investigators found that ISD—defined as low VLPP or low MUCP—did not have an impact on outcomes after placement of retropubic and TOT slings. Yet, other recent studies have concluded differently: In this trial from Australia, researchers concluded that a retropubic sling was more effective than a TOT sling in women who had ISD.

Study design. This randomized, prospective study of 164 women who had SUI and ISD (defined as MUCP <20 cm H_2O or VLPP <60 cm H_2O) randomized subjects to placement of a retropubic sling or a TOT sling. The primary outcome was the presence or absence of urodynamically documented stress incontinence at 6 months. Secondary outcomes included complications, self-reported SUI, and findings on a quality-of-life questionnaire.

Findings. At 6 months, 138 patients completed an evaluation, including repeat urodynamic study. The success rate in the retropubic group was 79%, compared with only 55% in the TOT group (P = .004). Nine women in the TOT group underwent repeat surgery; none did in the retropubic group. There was no difference between groups in de novo overactive bladder symptoms; overactive bladder symptoms resolved at a nearly equivalent rate: 40% in the TOT group and 36% in the retropubic group. No difference was seen in the rate of intraoperative or postoperative complications, although the rate of bladder perforation was higher in the retropubic group, leaning toward significance (P = .06).

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Women who have ISD are better served by having a retropubic sling, not a TOT sling, placed.

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Women who have ISD are better served by having a retropubic sling, not a TOT sling, placed

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Single-incision slings demonstrate lower efficacy than traditional slings

Adbel-Fattah M, Ford JA, Lim CP, Madhuvrata P. Single-incision mini-slings versus standard midurethral slings in surgical management of female stress urinary incontinence: a meta-analysis of effectiveness and complications. Eur Urol. 2011;60(3):468–480.

FAST TRACK

Data on the success of single-incision slings are limited; an inferior result is possible

The single-incision sling was introduced in 2006 to, ostensibly, simplify surgery and reduce the risk of complications. Yet, essentially, no data on the efficacy or safety of single-incision kits existed when they entered the market!

Study design. This meta-analysis of single-incision slings analyzed the surgical literature from 1996 through early 2011. Investigators found nine studies that met criteria for objective and subjective outcomes in randomized or quasi-randomized clinical trials. They performed the analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

A total of 758 women who participated in nine randomized clinical trials were included for analysis. Seven studies reported on the subjective cure rate; six reported on the objective cure rate.

Findings. The analysis showed that **single-incision slings are associated with lower subjective and objective cure rates** than traditional slings (for single-incision slings, the risk ratio [RR] was 0.83 [95% CI, 0.70–0.99]; for traditional slings, RR was 0.85 [95% CI, 0.74–0.97]). In addition, **re-operation rates were significantly higher in the single-incision sling group** (RR, 6.72 [95% CI, 2.4–18.9]).

The single-incision sling was associated with a shorter operating time and less postoperative pain, but had a higher rate of mesh exposure (RR, 3.86 [95% CI, 1.45–10.3]).

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This is important information about the relative effectiveness of the single-incision sling compared to more traditional retropubic and TOT approaches. If you are going to offer a single-incision sling, you must **1)** select patients carefully and **2)** counsel appropriate candidates on two key points: data on the success of single-incision slings are limited and an inferior (that is, inferior to traditional techniques) result is possible.

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BONUS COVERAGE OF THIS TOPIC

More developments in SUI management
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Stay tuned for more developments in SUI management!

From stem-cell research. This expanding component of a number of medical specialties includes urologic applications. Animal-based studies have been supportive here,[1-3] and two studies have translated the use of stem cells for correcting SUI to humans.[4,5]

Taken together, the human studies treated 20 women with autologous muscle-derived stem cells or muscle progenitor cells that were injected periurethrally or intrasphincterically. Seventeen subjects completed follow-up; improvement was demonstrated in all but two of them.[4,5]

The promise of stem-cell applications for treating SUI is exciting. We need additional investigation into methods and safety, however—making widespread application in humans not yet suitable. Still, the field is rapidly expanding and this remains a hopeful treatment option for the future.

For repairing vaginal prolapse. Unpublished findings from the Outcomes Following Vaginal Prolapse Repair and Mid Urethral Sling (OPUS) trial—the "vaginal counterpart," one could say, to the notable CARE trial of cholesterol level management—were presented at the annual scientific meeting of the American Urogynecologic Society (AUGS) in September. This landmark study demonstrated that a prophylactic midurethral sling placed at the time of vaginal prolapse repair results in superior continence at 3 and 12 months in women who did not have preoperative symptoms of incontinence. Publication of this study—it has been submitted to a leading medical journal—will have a significant impact on the counseling that providers offer to asymptomatic patients who are undergoing vaginal reconstructive surgery about having a prophylactic sling placed.

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